EDITION 4

Essence of ANESTHESIA PRACTICE

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To our patients who deserve the best care given their medical conditions and medications.
To their anesthesiologists, nurse anesthetists, internists, and pediatricians who are looking for the newest information to ensure that best care.
To our loved ones who supported us in supporting you!

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Preface

It has been 6 years since the last edition of *Essence of Anesthesia Practice* was published and 2 decades since the first edition. The goal of this text was, and continues to be, to provide a concise summary that allows you to act for your patient with more complete knowledge of the pathophysiology of both common and rare conditions seen in the perioperative period as well as the medications used to treat these conditions. We have eliminated the summaries for surgical procedures in favor of more rare diseases as well as general drugs that patients take on an outpatient basis.

These summaries are structured in a defined way to enable you to focus on the key facts and issues as well as the anticipated concerns regarding these conditions and medications in order that you, the anesthesiologists, can function as perioperative physicians and provide optimal care of the patient. We have done PubMed and Google searches, selected key references, read the articles and case reports, and boiled the hours of reading into 10 minutes of summary with all the key points highlighted. Treatments, including medications for chronic conditions, continue to evolve, and it is difficult to keep up with the perioperative implications and appropriate preoperative evaluation without this effort. We also felt that in previous editions we did not include as many uncommon conditions as we would like and as you wanted. We therefore enrolled more than 500 authors, some of whom wrote the original chapters and many of whom are new, and have either updated the original chapters or added new topics to address these concerns in the fourth edition of *Essence of Anesthesia Practice*.

This edition continues to improve and update the material that went before and to add the most up-to-date topics and new medications. We continue to include a large section on herbal medications given their popularity and common use by our surgical patients. We believe that the current format lends itself to quick review and orientation of the practitioner to perioperative implications at the point of care.

We wish to thank the authors of the previous edition upon which many of the new authors produced revised chapters. We also thank Dolores Meloni, our Executive Content Strategist at Elsevier, and Rae Robertson, our Senior Content Development Specialist, for ensuring that our book received appropriate editing and development as well as providing the relentless support for this text to be published in a timely manner.

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Abbreviations

SYMBOLS

±	plus or minus
?	questionable
~	approximately
° C	degrees centigrade
° F	degrees Fahrenheit
1°	primary; first degree
2°	secondary; second degree
3°	third degree
ΔΔ	delta gap

A

A-a	alveolar-arterial
AA	arachidonic acid
AAA	abdominal aortic aneurysm
A-aDO_2	alveolar-arterial oxygen delivery
AAT	alpha$_1$-antitrypsin; automatic atrial tachycardia
AAP	American Academy of Pediatrics
abd	abdomen; abdominal
ABG	arterial blood gas
ABI	aorto-bi-iliac bypass
abd	abdominal
abn	abnormal; abnormality
ACE	angiotensin-converting enzyme
ACEI	angiotensin-converting enzyme inhibitor
ACG	angle-closure glaucoma
Ach	acetylcholine
AChE	acetylcholinesterase
ACIP	Advisory Committee on Immunization Practices
ACL	anterior cruciate ligament
ACLS	advanced cardiac life support
ACOG	American Congress of Obstetricians and Gynecologists
ACS	acute confusional state
ACT	activated clotting/coagulation time
ACTH	adrenocorticotropic
ADEM	acute disseminated encephalomyelitis
ADH	antidiuretic hormone
ADHD	attention-deficit hyperactivity disorder
ADI	atlas-dens interval
ADL	activities of daily living
admin	administration; administered
ADP	adenosine diphosphate
AE	alveolar echinococcus
AED	automated external defibrillator
AFE	amniotic fluid embolism
AFIB	atrial fibrillation
AFLT	atrial flutter
AFP	alpha-fetoprotein
AG	anion gap
AH	autonomic hyperreflexia
AHQR	Agency for Healthcare Research and Quality
AI	aortic insufficiency
AICD	automatic implantable cardioverter defibrillator
AIDS	acquired immunodeficiency syndrome
AIH	anesthetic-induced hepatitis
AIM	anesthetic-induced myodystrophy
AIP	acute intermittent porphyria
AKA	above-knee amputation; also known as
AKI	acute kidney injury
AKIN	Acute Kidney Injury Network
ALA	δ-aminolaevulinic acid
alb	albumin
alk phos	alkaline phosphatase
A-line	arterial line
ALL	acute lymphoblastic leukemia
ALS	amyotrophic lateral sclerosis
ALT	alanine aminotransferase
Alv	alveolar
AM	morning
AML	acute myelogenous leukemia
AMP	adenosine monophosphate
ampl	amplitude
ANA	antinuclear antibody
angio	angiogram
ANS	autonomic nervous system
ant	anterior
anticoag	anticoagulation
AOM	acute otitis media
AP	accessory pathway; action potential; anteriorposterior
APC	activated protein C
API	alkaline protease inhibitor
approx	approximate; approximately
APTT	activated partial thromboplastin time
AR	aortic regurgitation
ARB	angiotensin receptor blocker
ARDS	acute respiratory distress syndrome
ARF	acute renal failure
art	arterial
AS	aortic stenosis
ASA	acetylsalicylic acid; Adams-Stokes attack; American Society of Anesthesiologists
ASAP	as soon as possible
ASCVD	atherosclerotic cardiovascular disease
ASD	atrial septal defect
ASRA	American Society of Regional Anesthesia
assoc	associated
AST	aspartate aminotransferase
AT	antithrombin
AT1	angiotensin receptor 1
ATG	anti-thymus globulin
ATN	acute tubular necrosis
ATP	adenosine triphosphate; antitachycardia pacing
Au	gold
AV	atrioventricular
AVB	atrioventricular block
AVM	arteriovenous malformation
AVR	aortic valve replacement

B

β-hCG	beta human chorionic gonadotropin
BAER	brainstem auditory evoked response
BAL	bronchoalveolar lavage
BBB	bundle branch block; blood-brain barrier
BCI	blunt cardiac injury
BCNU	nitrosourea (carmustine)
BD	Behçet disease
BF	bifascicular; blood flow
bid	twice per day
BIG	botulism immune globulin
bilat	bilateral
BIS	bispectral index
BLS	basic life support
BLT	bleomycin sulfate toxicity
BM	bowel movement
BMI	body mass index
BMP	basic metabolic panel
BMR	basal metabolic rate
BMS	bare metal stent
BMT	bone marrow transplantation
BMV	bag mask ventilation
BNP	brain natriuretic
BO	bronchiolitis obliterans
BOOP	bronchiolitis obliterans with cryptogenic organizing pneumonia
BOS	bronchiolitis obliterans syndrome
BP	blood pressure
BPD	bronchopulmonary dysplasia
BPEG	British Pacing and Electrophysiology Group
BPH	benign prostatic hyperplasia/hypertrophy
bpm	beats per minute
BPP	biophysical profile
BRBPR	bright red blood per rectum
BS	breath sounds
BSA	body surface area
BT	bleeding time; Blalock-Taussig (shunt)
BUN	blood urea nitrogen
BWS	Beckwith-Wiedemann syndrome
Bx	biopsy
BZD	benzodiazepine

C

CA	cancer, cold agglutinins
ca.	about (circa)
Ca^{2+}	calcium
CAB	coronary artery bypass
CABG	coronary artery bypass graft
CACT	carnitine-acylcarnitine translocase
CAD	coronary artery disease
cAMP	cyclic adenosine monophosphate
Cao_2	arterial oxygen concentration
cardiopulm	cardiopulmonary
CAS	coronary artery spasm
CASS	Coronary Artery Surgery Study
CATCH 22	cardiac defect, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcemia (syndrome)
cath	catheter; catheterization
CBC	complete blood count
CBF	cerebral blood flow
CBG	capillary blood glucose
CBV	cerebral blood volume
CCAM	congenital cystic adenomatoid malformation
CCB	calcium-channel blocker
CCNU	nitrosourea (lomustine)
CD4	antigenic marker on helper/inducer T cells
$CD4^+$	presence of CD4
CDC	Centers for Disease Control and Prevention
CEA	carotid endarterectomy
cGMP	cyclic guanosine monophosphate
C-GSF	granulocyte colony-stimulating factor
CHARGE	coloboma, congenital heart defects, choanal atresia, retardation of growth and/or other development, genital anomalies, and ear anomalies with deafness
CHB	complete heart block
CHCT	caffeine halothane contracture test
CHD	congenital heart disease; congenital heart defect
ChE	cholinesterase
CHF	congestive heart failure
CHO	carbohydrate
CHTN	congenital hypertension
CI	cardiac index; confidence interval

Abbreviations

CIED	cardiac implantable electronic device
CIN	cervical intraepithelial neoplasia
circ	circulation; circulatory
CJD	Creutzfeldt-Jakob disease
CK	creatine kinase
CKD	chronic kidney disease
CK-MB	isoenzyme of creatine kinase with muscle and brain subunits
CLL	chronic lymphocytic leukemia
cLQTS	congenital long QT syndrome
CLR	chlorambucil
CML	chronic myelogenous leukemia
CMP	comprehensive metabolic panel
$CMRO_2$	cerebral metabolic rate of oxygen
CMS	Centers for Medicare and Medicaid Services
CMT	Charcot-Marie-Tooth disease
CMV	cytomegalovirus
CMZ	carbamazepine
CN	cranial nerve; cyanide
CNH	central neurogenic hyperventilation
CNS	central nervous system
CO	carbon monoxide; cardiac output
CO_2	carbon dioxide
coag	coagulation
COHb	carboxyhemoglobin
COM	chronic otitis media
COMT	catechol-o-methyltransferase
conc	concentration
COPD	chronic obstructive pulmonary disease
COX	cyclooxygenase
COX-2	cyclooxygenase-2
cP	centipoise
CP	cerebellopontine (angle); cerebral palsy; constrictive pericarditis
CPAP	continuous positive airway pressure
CPB	cardiopulmonary bypass
CPD	cephalopelvic disproportion
CPEO	chronic progressive external ophthalmoplegia
CPK	creatine phosphokinase
CPM	central pontine myelinolysis
CPN	central pontine myelinolysis
CPP	cerebral perfusion pressure
CPR	cardiopulmonary resuscitation
CPT	carnitine palmityl transferase
Cr	creatinine
CRAO	central retinal artery occlusion
CrCl	creatinine clearance
CREST	calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia
CRF	cancer-related fatigue
CRI	chronic renal insufficiency
CRP	c-reactive protein
CRPS	complex regional pain syndrome
CRS	congenital rubella syndrome
CRRT	continuous renal replacement therapy
CRT	cardiac resynchronization therapy
cryo	cryoprecipitate
CS	chondroitin sulfate
C-section	cesarean section
CSE	combined spinal epidural
CSF	cerebrospinal fluid
CSH	carotid sinus hypersensitivity
CSM	carotid sinus massage
C-spine	cervical spine
CSS	carotid sinus syndrome
CT	computed tomography; connective tissue
CTX	cyclophosphamide (Cytoxan)
CV	cardiovascular
CVA	cerebrovascular accident
CVC	central venous catheter
CVD	cerebrovascular disease
CVL	central venous line
CVP	central venous pressure
CVS	cardiovascular status
CVHH	continuous veno-venous hemofiltration
CXR	chest x-ray
CYP	cytochrome P450
cysto	cystoscopy

D

2,3-DPG	2,3-diphosphoglyceric acid
2D	two-dimensional
d	day
D&A	drug(s) and alcohol
D and T	diphtheria and tetanus
D/C	discontinue(d)
D_5	dextrose 5% in water
DA	dopamine
DBP	diastolic blood pressure
DC	direct current
DCM	dilated cardiomyopathy
DDAVP	1-deamino(8-d-arginine) vasopressin; desmopressin acetate
DDT	dichlorodiphenyltrichloroethane
DEA	Drug Enforcement Agency
DEB	dystrophic epidermolysis bullosa
dec	decleration(s)
deriv	derivative(s)
derm	dermatology
DEXA	dual-energy x-ray absorptiometry
DFA	direct immunofluorescent assay
DFT	defibrillation threshold
DGL	deglycyrrhized licorice
DGLA	dihomo-γ-linolenic acid
DHA	docosahexaenoic acid
DHEA	dehydroepiandrosterone
DHT	dihydrotestosterone
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
diff	differential
Dig	digoxin
DKA	diabetic ketoacidosis
DKS	Damus–Kaye–Stansel (procedure)
DLB	dementia with Lewy bodies
DLco	carbon monoxide diffusion capacity in the lungs
DLT	double lumen endotracheal tube
DM	diabetes mellitus
DMARD	disease-modifying antirheumatic drug
DMD	Duchenne muscular dystrophy
DMR	depolarizing muscle relaxant
DMSO	dimethylsufoxide
DNA	deoxyribonucleic acid
DNR	do not resuscitate
DOB	dobutamine
DOE	dyspnea on exertion
DPI	dry powder inhaler
DPNB	dorsal penile nerve block
dSSEP	dermatomal somatosensory evoked potentials
DTIC	dimethyltriazenoimidazole carboxamide (dacarbazine)
DTPA	diethylenetriaminepenta-acetic acid
DTR	deep tendon reflex
DTs	delirium tremens
DVT	deep vein thrombosis
Dx	diagnosis; diagnostic
DXA	dual-energy x-ray absorptiometry

E

EACA	epsilon-aminocaproic
EBL	estimated blood loss
EBT	external beam therapy
EBV	Epstein-Barr virus
EC	eclampsia
ECA	ethacrynic acid
ECC	extracorporeal circulation
ECD	endocardial cushion defect
ECF	extracellular fluid
ECFV	extracellular fluid volume
ECG	electrocardiogram
ECHO	echocardiogram
ECMO	extracorporeal membrane oxygenation
ECoG	electrocorticography
ECT	electroconvulsive therapy
ED50	median effective dose
EDAS	encephalodural arteriosynangiosis
EDTA	ethylenediaminetetraacetic acid
EDV	end-diastolic volume
EEC	ectrodactyly-ectodermal dysplasia, cleft (syndrome)
EEG	electroencephalogram
EENT	eyes, ears, nose, throat
EF	ejection fraction
EGD	esophagogastroduodenoscopy
E-L	Eaton-Lambert
ELBW	extremely low birth weight
ELISA	enzyme-linked immunosorbent assay
EMD	electromechanical dissociation
EMG	electromyography
EMI	electromagnetic interference; electromechanical interference
EMLA	eutectic mixture of local anesthetics
endo	endocrine
ENT	ear, nose, and throat
EP	electrophysiologic
EPA	eicosapentaenoic acid
EPI	epinephrine
EPO	evening primrose oil
EPS	electrophysiologic study; extrapyramidal side effects
ER	emergency room
ERCP	endoscopic retrograde cholangiopancreatography
ERV	expiratory reserve volume
ES	Eisenmenger syndrome
es	estimated
ESLD	end-stage liver disease
ESM	ethosuximide
esp	especially
ESR	erythrocyte sedimentation rate
ESRD	end-stage renal disease
ESS	endoscopic sinus surgery
ESU	electrosurgery
ESV	end-systolic volume
ESWL	extracorporeal shock wave lithotripsy
ET	endotracheal
$ETCO_2$	end-tidal carbon dioxide
ETD	eustachian tube dysfunction
ETN_2	end-tidal nitrogen
ETOH	ethanol
ETT	endotracheal tube; exercise tolerance test
eval	evaluation
EVD	external ventricular drain
Ex	exercise
exam	examination
ext	exterior

Abbreviations

F

5-FU	5-fluorouracil
F	female(s)
Fab	fragment, antigen-binding
FAD	flavin adenine dinucleotide
FAO	Food and Agriculture Organization of the United Nations
FB	foreign body
FBC	full blood count
FBS	fasting blood sugar
FDA	Food and Drug Administration
FDP	fibrin-degradation product
Fe	iron
Fe^{2+}	ferrous
Fe^{3+}	ferric
FEES	fiberoptic endoscopic evaluation of swallowing
FEIBA	factor eight inhibitor bypassing activity
FEN	fluids, electrolytes, and nutrition
FENa	excreted fraction of filtered sodium
FES	fat embolism syndrome
FEV	forced expiratory volume
FEV_1	forced expiratory volume in 1 second
FFA	free fatty acid
FFP	fresh frozen plasma
FHR	fetal heart rate
FGF	fibroblast growth factor
FGFR	fibroblast growth factor receptor
FIO_2	fractional inspired oxygen
FIX	factor IX
FLAIR	fluid-attenuated inversion recovery
FMTC	familial medullary thyroid carcinoma
FNA	fine-needle aspiration
FOB	fiberoptic bronchoscopy
FOI	fiber optic intubation
FRC	functional residual capacity
freq	frequent; frequency
FS	Fanconi syndrome
FSBG	fingerstick blood glucose
FSH	follicle-stimulating hormone
FSP	fibrin split products
FT_4E	free thyroxine estimate
FTT	failure to thrive
FVC	forced vital capacity
FVIII	factor VIII
FVL	factor V Leiden

G

G	gauge
G6PD	glucose-6 phosphate dehydrogenase
GA	general anesthesia
GABA	gamma-aminobutyric acid
GAG	glycosaminoglycan
GBE	*Ginkgo biloba* extract
GBL	gamma butyrolactone
GBM	glomerular basement membrane
GCS	Glasgow coma scale
G-CSF	granulocyte colony-stimulating factor
GDM	gestational diabetes mellitus
GE	gastroesophageal
GER	gastroesophageal reflux
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GGT	gamma glutamyltransferase
GH	growth hormone
GHB	gamma hydroxybutyrate
Gi	inhibitory G protein
GI	gastrointestinal
GLA	γ-linolenic acid
glu	glucose
GPi	globus pallidus
GPN	glossopharyngeal neuralgia
GTP	guanosine triphosphate
GTT	glucose tolerance test
GU	genitourinary
GVHD	graft versus host disease
gyn	gynecologic

H

5-HIAA	5-hydroxyindoleacetic acid
5-HT	5-hydroxytryptamine
H&N	head and neck
H&P	history and physical
H_1	histamine receptor type 1
H_2	histamine receptor type 2
H_2O	water
HAART	highly active antiretroviral therapy
HAF-PCM	hypoalbuminemic form of protein-calorie malnutrition
HAV	hepatitis A virus
HB	heart block
Hb	Hemoglobin
HbA_{1c}	glycosylated hemoglobin
HbM	hemoglobin Milwaukee
HbO_2	oxyhemoglobin
HBV	hepatitis B virus
HCG or hCG	human gonadotropic hormone
HCM	hypertrophic cardiomyopathy
HCN	hydrogen cyanide
Hct	hematocrit
HCTZ	hydrochlorothiazide
HCV	hepatitis C virus
HD	heart disease; Hodgkin's disease
HDL	high-density lipoprotein
HDL-C	HDL cholesterol
HDU	high dependency unit
HDV	hepatitis D virus
He	helium
HEENT	head, eyes, ears, nose, throat
HELLP	hemolysis, elevated liver enzymes, and low platelet count (syndrome)
heme	hematology
HEPAT	hepatic
HEV	hepatitis E virus
HF	heart failure
HFM	hemifacial microsomia
HFOV	high-frequency oscillatory ventilation
Hg	mercury
Hgb	hemoglobin
HGPRT	hypoxanthine-guanine-phosphoribosyltransferase
HHS	hyperglycemic hyperosmolar state
HHT	hereditary hemorrhagic telangiectasia
HHV-3-6	human herpes viruses
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HLHS	hypoplastic left heart syndrome
HMG CoA	3-hydroxy-3-methylglutaryl
HMPV	human metapneumovirus
HMSN	hereditary motor and sensory neuropathy
HN_2	nitrogen mustard
HNP	hernia nuclei pulposi
h/o or H/O	history of
hosp	hospitalization
HPA	hypothalamic-pituitary-adrenal
HPS	hepatopulmonary syndrome
HPV	hypoxic pulmonary vasoconstriction
h or hr	hour(s)
HR	heart rate
HRCT	high-resolution computed tomography
HSAN	hereditary and sensory autonomic neuropathy
HSCR	Hirschsprung disease
HSP	Henoch-Schönlein purpura
HSV	herpes simplex virus
HSV-1	HSV type 1
HSV-2	HSV type 2
ht	height
Htn/HTN	hypertension
HUS	hemolytic uremic syndrome
HVPG	hepatic venous pressure gradient
Hx	history

I

I&D	incision and drainage
I/O	intake-output
IABP	intra-aortic balloon pump
IADH	inappropriate antidiuretic hormone
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
IBW	ideal body weight
ICA	internal carotid artery
ICD	implantable cardioverter defibrillator
ICF	intracellular fluid
ICH	intracranial hypertension
ICP	intracranial pressure
ICU	intensive care unit
ID	infectious disease
IDDM	insulin-dependent diabetes mellitus
IDL	intermediate-density lipoprotein
I:E	inspiratory:expiratory ratio
IFN	interferon
Ig	immunoglobulin
IgA	immunoglobulin A
IgE	immunoglobulin E
IgG	immunoglobulin G
IGF	insulin-like growth factor
IGF-I	insulin-like growth factor I
IgM	immunoglobulin M
IHD	intermittent hemodialysis; ischemic heart disease
IL	interleukin
IM	intramuscular
immuno	immunologic
in	inch
incl	including
inf	inferior
info	information
INFOSAN	International Food Safeties Authorities Network
INH	isoniazid
inj	injection
INR	international normalized ratio
insp	inspiratory
intox	intoxication
intraop	intraoperative
IOL	intraocular lens
ION	ischemic optic neuropathy
IOP	intraocular pressure
IP	impedance plethysmography; intraperitoneal; intraperitoneally
IPPB	intermittent positive pressure breathing
IPF	idiopathic pulmonary fibrosis
IPL	intense pulsed light
IPPV	intermittent positive pressure ventilation
iPTH	intact parathyroid hormone
IQ	intelligence quotient
ITP	immune thrombocytopenic purpura
IUGR	intrauterine growth restriction

Abbreviations

IV	intravenous
IVC	inferior vena cava
IVDU	intravenous drug user
IVF	intravascular fluid; intravenous fluid
IVP	intravenous pyelogram
J	
JEB	junctional epidermolysis bullosa
JGA	juxtaglomerular apparatus
JNC	Joint National Committee
JV	jugular vein
JVD	jugular venous distention
JVP	jugular venous pressure
K	
K^+	potassium
KS	Kartagener syndrome
KSS	Kearns-Sayre syndrome
KUB	kidney, ureter, and bladder
L	
L	left
LA	left atrial; left atrium; linoleic acid; local anesthetic
lab	laboratory
LAD	left anterior descending (coronary artery)
LAFB	left anterior fascicular block
LAP	left atrial pressure
lat	lateral
LBBB	left bundle branch block
LBM	lean body mass
LCAT	lecithin-cholesterol acyltransderase
LCH	Langerhans cell histiocytosis
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LDL-C	LDL cholesterol
L-DOPA	levodopa
LE	lower extremity
LES	lower esophageal sphincter
LFT	liver function test
LGL	Lown-Ganong-Levine syndrome
LH	luteinizing hormone
LHON	Leber hereditary optic neuropathy
LMA	laryngeal mask airway
LMW	low molecular weight
LMWH	low molecular weight heparin
LOC	level of consciousness; loss of consciousness
LOS	length of stay
LP	lumbar puncture
L-PAM	melphalan (Alkeran)
LQTS	long QT syndrome
LR	lactated Ringer's (solution)
LRI	lower respiratory tract infection
LSB	lumber sympathetic block
LSD	lysergic acid diethylamide
LTG	lamotrigine
L-to-R	left to right
LUQ	left upper quadrant
LV	left ventricle
LVAD	left ventricular assist device
LVEDP	left ventricular end-diastolic pressure
LVEDV	left ventricular end-diastolic volume
LVEF	left ventricular ejection fraction
LVF	left ventricular failure
LVH	left ventricular hypertrophy
LVOT	left ventricular outflow tract
lytes	electrolytes
M	
M	male(s)
M:F	male to female ratio
M2	muscarinic
MAC	minimum alveolar concentration; monitored anesthesia care
MACE	minor adverse cardiac event
MAHA	microangiopathic hemolytic anemia
MALA	metformin-associated lactic acidosis
MAO	monoamine oxidase
MAOI	monoamine oxidase inhibitor
MAP	mean arterial pressure
MAST	medical antishock trousers
MAT	multiform atrial tachycardia
max	maximum; maximal
MBC	maximal breathing capacity
MC	myotonia congenita
MCV	mean corpuscular volume
MD	muscular dystrophy
MDI	metered-dose inhaler
MEA	multiple endocrine adenomas
mech	mechanical; mechanism
med	medication
MELAS	mitochondrial encephalomyopathy, lactic acidosis, and stroke-like symptoms
MEN	multiple endocrine neoplasia
MEN I	multiple endocrine neoplasia type I
MEN II	multiple endocrine neoplasia type II
MEP	motor/multimodality evoked potential
MERRF	myoclonic epilepsy with ragged red fibers
MET	metabolic equivalent
Metab	metabolism; metabolic
metHb	methemoglobin
metHbemia	methemoglobinemia
mets	metastases
MF-PCM	marasmic form of protein calorie malnutrition
Mg^{2+}	magnesium
$MgSO_4$	magnesium sulfate
MGUS	monoclonal gammopathy of undetermined significance
MH	malignant hyperthermia
MI	myocardial infarction
MILS	maternally inherited Leigh syndrome
min	minimal; minimum; minute
MIsch	myocardial ischemia
MIV	mivacurium
mm Hg	millimeter(s) of mercury
MMEFR	maximal midexpiratory flow rate
MMSE	Mini–Mental State Examination
mo	month
mod	moderate
MODS	multiorgan dysfunction syndrome
MOF	multiple organ failure
MP	mucopolysaccharide
MPAP	mean pulmonary artery pressure
MPS	mucopolysaccharidoses
MR	mitral regurgitation
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MRSA	methicillin-resistant *Staphylococcus aureus*
MS	mental status; mitral stenosis; multiple sclerosis; musculoskeletal
ms	milliseconds
MSK	musculoskeletal
MSSA	methicillin-sensitive *Staphylococcus aureus*
MTTP	microsomal triglyceride transfer protein
MTX	methotrexate
MU	million units
mucocut	mucocutaneous
MUGA	multiple gated acquisition
musc	muscular
MV	mitral valve
MVA	motor vehicle accident
MVD	microvascular decompression
MVP	mitral valve prolapse
MW	molecular weight
MYL	Myleran (busulfan)
N	
N	nitrogen
n.	nerve
N/A	not applicable
N/V	nausea/vomiting
N_2O	dinitrogen monoxide (nitrous oxide)
Na^+	sodium
NAAT	nucleic acid amplification test
NAC	*N*-acetyl-l-cysteine
NADH	nicotinamide adenine dinucleotide reduced form
NADPH	nicotinamide adenine dinucleotide phosphate, reduced form
NAPA	*N*-acetyl procainamide
NASH	non-alcoholic steatohepatitis
naso	nasograstric
NASPE	North American Society of Pacing and Electrophysiology
NB	nota bene (note well)
NCS	nerve conduction studies
NCV	nerve conduction velocity
NDMB	nondepolarizing neuromuscular blocker
NDMR	nondepolarizing muscle relaxant
Nd:YAG	neodymium:yttrium-aluminum-garnet
NE	norepinephrine
NEB	nebulizer
NEC	necrotizing enterocolitis
neg	negative
neuro	neurologic
NF	necrotizing fasciitis; neurofibromatosis; neurologic findings
NF-1	neurofibromatosis
NG	nasogastric
NGF	nerve growth factor
NGT	nasogastric tube
NH_3	ammonia
NHANES	National Health and Nutrition Examination Survey
NHL	non-Hodgkin's lymphoma
NHLBI	National Heart, Lung, and Blood Institute
NIBP	noninvasive blood pressure
NICU	neonatal intensive care unit
NIDDM	non–insulin-dependent diabetes mellitus
NIF	negative inspiratory force
NIH	National Institutes of Health
NIPHS	noninsulinoma pancreatogenous hypoglycemia syndrome
NIRS	near-infrared spectroscopy
NK	natural killer (cell)
NM	neuromuscular
NMB	neuromuscular blockade
NMBA	neuromuscular blocking agent
NMBD	neuromuscular blocking drug

Abbreviations

NMDA	*N*-methyl-D-aspartate
NMJ	neuromuscular junction
nml	normal
NMO	neuromyelitis optica
NMS	neuroleptic malignant syndrome
NO	nitric oxide
no.	number
nondep	nondepolarizing
NP	nasopharyngeal
NP-D	Niemann-Pick disease
NPH	neutral protamine Hagedorn
NPO	nil per os (nothing by mouth)
NPPB	normal perfusion pressure breakthrough (syndrome)
NRI	nutritional risk index
NRT	nictotine replacement therapy
NS	normal saline (solution)
NSAID	nonsteroidal anti-inflammatory drug
NT	nasotracheal
NTG	nitroglycerin
NTP	nucleoside triphosphate
NYHA	New York Heart Association

O

O_2	oxygen
OA	osteoarthritis
OAVRT	orthodromic atrioventricular reciprocating tachycardia
OB	obstetric
OB/GYN	obstetrics/gynecology
OC	oral contraceptive
OCD	obsessive-compulsive disorder
OD	overdose
OFC	occipital frontal circumference
OG	orogastric
OGT	orogastric tube
OGTT	oral glucose tolerance test
OHS	obesity hypoventilation syndrome
OKT3	Ortho Kung T cell (muromonab-CD3)
OLD	obstructive lung disease
OM	otitis media
OMIM	Online Mendelian Inheritance in Man
ONH	optic nerve hypoplasia
OPHTH or ophthal	ophthalmologic
OR	operating room
ORIF	open reduction internal fixation
ORTHO	orthopedic
OSA	obstructive sleep apnea
Osm	osmole; osmolality
OTC	over-the-counter

P

P	phosphorus
$P(A\text{-}a)o_2$	alveolar-arterial oxygen difference
PA	plasma aldosterone; pulmonary artery
PAC	premature atrial contraction
$Paco_2$	partial pressure of carbon dioxide, arterial
PACU	postanesthesia care unit
PAF	platelet activating factor
PAH	pulmonary arterial hypertension
PAIR	puncture-aspiration-injection-respiration
palp	palpation of
Pao_2	partial pressure of oxygen in arterial blood
PAOP	pulmonary artery occlusion pressure
PAP	pulmonary artery pressure
PAPVD	partial anomalous pulmonary venous drainage
PAT	paroxysmal atrial tachycardia
Paw	mean airway pressure
PAWP	pulmonary artery wedge pressure
PBC	primary biliary cirrhosis
PBF	pulmonary blood flow
PBG	porphobilinogen
PBS	peripheral blood smear
PCA	patient-controlled analgesia
PCC	prothrombin complex concentrate
PCD	primary ciliary dyskinesia
PCI	percutaneous coronary intervention
PCM	protein calorie malnutrition
PCO	polycystic ovary
Pco_2	partial pressure of carbon dioxide
PCP	phencyclidine
PCR	polymerase chain reaction
PCW	post conceptual week(s)
PCWP	pulmonary capillary wedge pressure
PD	Parkinson disease; peritoneal dialysis
PDA	patent ductus arteriosus
PDE II	phosphodiesterase III (inhibitors)
PDL	pulsed dye laser
PDPH	post-dural puncture headache
PD/PK	pharmacodynamic/ pharmacokinetic
PE	physical examination; preeclampsia; pressure equalization; pulmonary embolism
PEAC	prolonged expiratory apnea with cyanosis
PEEP	positive end-expiratory pressure
PEF	peak expiratory flow
PEG	percutaneous endoscopic gastrostomy
PEP	positive expiratory pressure
periop	perioperative
PET	positron emission tomography
$PETCO_2$	end-tidal partial pressure of carbon dioxide
PFO	patent foramen ovale
PFT	pulmonary function test
PG	prostaglandin
PGD_2	prostaglandin D_2
PGE_1	alprostadil (prostaglandin E_1)
pharm	pharmaceutical; pharmacy
pheo	pheochromocytoma
pHTN	pulmonary hypertension
physiol	physiologic
PID	pelvic inflammatory disease
PIH	pregnancy-induced hypertension
PIP	peak inspiratory pressure
pit	pituitary
PJP	*Pneumocystis jirovecii* pneumonia
pKa	negative logarithm of the dissociation constant of an acid
PKU	phenylketonuria
plt(s)	platelet(s)
pM	picomolar
PM	evening
PMI	posterior myocardial infarction; point of maximal intensity
PMS	premenstrual syndrome
PNB	peripheral nerve block
PND	paroxysmal nocturnal dyspnea
PNS	peripheral nervous system
PO	per os
Po_2	oxygen partial pressure
PO_4	phosphate
PONV	postoperative nausea and vomiting
pos	positive
poss	possible; possibly
postop	postoperative
PPAR	peroxisome proliferator-activated receptor
PPD	purified protein derivative (tuberculin)
PPH	persistent pulmonary hypertension
PPHN	persistent pulmonary hypertension of newborn
PPI	proton pump inhibitor
Pplat	plateau pressure
ppm	parts per million
PPV	positive predictive value; positive pressure ventilation
PR	per rectum
PRA	plasma renin activity
PRBCs	packed red blood cells
preop	preoperative
prep	preparation
prn	as needed
PRS	Pierre Robin sequence
PS	pulmonary stenosis
PSA	prostate-specific antigen
PSC	primary sclerosing cholangitis
PSG	polysomnography
PSVT	paroxysmal supraventricular tachycardia
psych	psychological
pt	patient
PT	physical therapy; prothrombin time
PTCA	percutaneous transluminal coronary angioplasty
PTH	parathyroid hormone
PTLD	post transplant lymphoproliferative disease
pts	patients
PTSD	posttraumatic stress disorder
PTT	partial thromboplastin time
PTU	propylthiouracil
PUD	peptic ulcer disease
pulm	pulmonary
PUVA	psoralens plus ultraviolet A
PVC	polyvinyl chloride; premature ventricular contraction
PVD	peripheral vascular disease
PVO_2	partial pressure of oxygen, venous
PVR	pulmonary vascular resistance
PVS	primo vascular system

Q

Q	perfusion
q	every
q.a.m.	every morning
q.n.	every night
q.p.m.	every evening
qhs	every hour of sleep
qid	four times per day
Qp:Qs	ratio of pulmonary blood to systemic blood flow
QRS	Q wave, R wave, S wave
QSART	quantitative sudomotor autonomic reflex testing

R

R	right
R/O or r/o	rule out
RA	rheumatoid arthritis; right atrial; right atrium
RAAS	renin-angiotensin-aldosterone system
RAD	reactive airway disease
RAE	right atrial enlargement

Abbreviations

RAH	right atrial hypertrophy
RAI	resting ankle index
RAST	radioallergosorbent test
RBBB	right bundle branch block
RBC	red blood cell
RBF	renal blood flow
RCM	congenital methemoglobinemia of the recessive type
RCRI	Revised Cardiac Risk Index
RCT	randomized controlled trial
RDA	recommended daily allowance
RDS	respiratory distress syndrome
reg	regular
rehab	rehabilitation
REM	rapid eye movement
reprod	reproductive
resp	respiratory
RFT	respiratory function test
RH	releasing hormone
RHC	right heart catheterization
RHD	rheumatic heart disease
RHF	right heart failure
RIA	radioimmunoassay
RIPA	ristocetin-induced platelet agglutination
RLN	recurrent laryngeal nerve
RNA	ribonucleic acid
ROM	range of motion
ROP	retinopathy of prematurity
ROS	review of systems
ROSC	return of spontaneous circulation
RPGN	rapidly progressive glomerulonephritis
RR	respiratory rate
RRP	recurrent respiratory papillomatosis
RSV	respiratory syncytial virus
RT	radiation therapy
RTA	renal tubular acidosis
RTK	receptor tyrosine kinase
R-to-L	right-to-left
RUQ	right upper quadrant
RV	residual volume; right ventricle
RVE	right ventricular enlargement
RVH	right ventricular hypertrophy
RVOT	right ventricle outflow tract
Rx	therapy; treatment; therapeutic

S

S	Svedberg unit
S/P	status post
SA	sinoatrial; beta S/beta A globin gene
SAH	subarachnoid hemorrhage
SAM	systolic anterior motion
SAMe	S-adenosyl-L-methionine
SaO_2	oxygen saturation in arterial blood
SAP	systematic arterial pressure
SAS	sleep apnea syndrome
SAT or sat	saturation
SBDP	syndromic bile duct paucity
SBE	standard base excess; subacute bacterial endocarditis
SBP	systolic blood pressure
SCC	squamous cell carcinoma
SCD	sudden cardiac death
SCH	succinylcholine
SCID	severe combined immunodeficiency
SCLC	small cell lung cancer
SCM	sternocleidomastoid
SCS	spinal cord stimulation
SD	standard deviation(s)
SDH	succinate dehydrogenase
SDS	Shy-Drager syndrome
SEB	simplex epidermolysis
sec	second(s)
SEP	sensory evoked potential
SERM	selective estrogen receptor modulator
SG	specific gravity
SGOT	aspartate aminotransferase; serum glutamic-oxaloacetic transaminase
SGPT	alanine aminotransferase; serum glutamate pyruvate transaminase
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
SICU	surgical ICU
SIDS	sudden infant death syndrome
SIRS	systemic inflammatory response syndrome
SJS	Stevens-Johnson syndrome
SJS-TEN	Stevens-Johnson syndrome–toxic epidermal necrolysis
SL	sublingual
SLE	systemic lupus erythematosus
SMA	superior mesenteric artery
SND	sinus node dysfunction
SNP	single nucleotide polymorphism
SNS	sympathetic nervous system
SOB	shortness of breath
SOBOE	shortness of breath on exertion
soln	solution
SPECT	single-photon emission computed tomography
SpO_2	oxygen saturation as measured by pulse oximetry
spont	spontaneously
SQ	subcutaneous; subcutaneously
SSEP	somatosensory evoked potential
SSP	subclavian steal syndrome
SSRI	selective serotonin reuptake inhibitor
SSS	sick sinus syndrome
ST	spasmodic torticollis
STD	sexually transmitted disease
stim	stimulation
STN	subthalamic nucleus
STSG	split-thickness skin graft
STSS	streptococcal toxic shock syndrome
Stz	streptozocin
sup	superior
surg	surgery; surgical
SV	stroke volume
SVC	superior vena cava
SVO_2	mixed venous continuous oxygen saturation
SVR	systemic vascular resistance
SVT	supraventricular tachycardia
Sx	signs and symptoms

T

T	temperature
T&C	type and crossmatch
$T_{½}$	half-life
T_3	triiodothyronine
T_4	thyroxine
TA	tricuspid atresia
TACO	transfusion-associated circulatory overload
TAH	total abdominal hysterectomy
TAPVD	total anomalous pulmonary venous drainage
TAPVR	total anomalous pulmonary venous return
TAVR	transcatheter aortic valve replacement
TB	tuberculosis
TBI	traumatic brain injury
TBSA	total body surface area
TBW	total body water
TCA	tricyclic antidepressant
TCD	transcranial Doppler
TCS	Treacher Collins syndrome
TCT	thrombin clotting time
TEE	transesophageal echocardiography
TEF	transesophageal fistula
TEG	thromboelastography
temp	temperature
TEN	toxic epidermal necrosis
TENS	transcutaneous electrical nerve stimulation
tet	tetralogy of Fallot
TFA	trifluoroacetic acid
TFT	thyroid function test
TGA	transposition of the great arteries
TGF	transforming growth factor
THAM	tromethamine
THC	delta-9-tetrahydrocannabinol
TIA	transient ischemic attack
TIBC	total iron-binding capacity
tid	three times per day
TIPS	transjugular intrahepatic portosystemic shunt
TIVA	total intravenous anesthesia
TJC	The Joint Commission
TKI	tyrosine kinase inhibitor
TLC	total lung capacity/compliance
TM	temporomandibular
TMEP	telangiectasia macularis eruptive perstans
TMJ	temporomandibular joint
TMO	trimethadione
TMP/SMX	trimethoprim/sulfamethoxazole
TN	trigeminal neuralgia
TNF	tumor necrosis factor
TOF	train-of-4; tetralogy of Fallot
TOLAC	trial of labor after cesarean
TP	total protein
t-PA	tissue plasminogen activator
TPN	total parenteral nutrition
TPR	transient potential receptor
TR	tricuspid regurgitation
TRALI	transfusion-related acute lung injury
TRH	thyrotropin-releasing hormone
TRPA1	transient receptor potential ankyrin-1
TRPV1	transient receptor potential vanilloid-1
TRUP	transurethral resection of the prostate
TSH	thyroid-stimulating hormone
TT	thrombin time
TTE	transthoracic echocardiography
T-TEPA	triethylene-thiophosphoramide (thiotepa)
TTP	thrombotic thrombocytopenic purpura
TURBT	transurethral resection of bladder tumor
TURP	transurethral resection of the prostate
TV	tidal volume
Tx	transplant; transfusion
TXA_2	thromboxane A_2
TXA_3	thromboxane A_3
TXB_2	thromboxane B_2
TZD	thiazolidinedione

U

UA	urinalysis
UE	upper extremity
UGI	upper gastrointestinal

Abbreviations

UK	United Kingdom
UO	urine output
UP	urticaria pigmentosa
URI or URTI	upper respiratory tract infection
urol	urology; urologic
US	ultrasound
USA	United States of America
UT	urinary tract
UTI	urinary tract infection
UV	ultraviolet
UVGI	ultraviolet germicidal irradiation

V

V	ventilation
V/Q	ventilation-perfusion
VACTERL	vertebral, anal, cardiac, tracheal, esophageal, renal, and limb
VAE	venous air embolism
VAP	ventilator-associated pneumonia
VAS	Visual Analogue Scale
vasc	vascular
VATS	video-assisted thoracoscopic surgery
VC	vital capacity; vocal cord
VCO_2	carbon dioxide consumption per unit time
V_d	volume of distribution
VEGF	vascular endothelial growth factor
vent	ventilation
VEP	visual evoked potential
VEPTR	vertical expandable prosthetic titanium rib
VF or VFIB	ventricular fibrillation
VGCC	voltage gated calcium channel
VHLD	Von Hippel-Lindau disease
VIM	ventralis intermedius nucleus
VIPoma	vasoactive intestinal peptide-secreting tumors
vit	vitamin
VKDB	vitamin K deficient bleeding
VLBW	very low birth weight
VLDL	very low density lipoprotein
VMA	vanillylmandelic acid
VO_2	oxygen consumption per unit time
vol	volume
VP-16	etoposide
VPA	valproic acid
VQ	ventilation-perfusion
VR	venous return
VS	vital signs
vs.	versus
VSD	ventricular septal defect
VSS	video swallow study
VT	venous thrombosis; venous thrombus
VTach	ventricular tachycardia
VTE	venous thromboembolism
VVB	venovenous bypass
VVI	ventricular inhibited
vWF	von Willebrand factor

W

w/	with
w/o	without
WBC	white blood cell
WHO	World Health Organization
wk	week(s)
WPW	Wolff-Parkinson-White syndrome
wt	weight

XYZ

Xe	xenon
XR	x-ray
XS	excessive
y	year(s)

Airway
- Avoid nasal manipulation.
- Use extreme caution with friable oral and pharyngeal mucosal surfaces.

Preinduction/Induction
- May exhibit hypotension and excessive fluid requirements to maintain adequate CO.
- Central neuraxial blockade contraindicated in ongoing thrombocytopenia requiring transfusion.
- Peripheral neural blockade may be approached cautiously if coagulation status is judged adequate.

Maintenance
- PEEP assures adequate tissue oxygenation at lower FIO_2 as hyperoxia depresses normal erythropoietin synthesis and marrow function.
- Nitrous oxide depresses BM function even after brief exposure; best to use O_2-air mixture.
- Normothermia promotes coagulation.
- Chronically anemic pts may tolerate lower Hct; adequacy of tissue O_2 must be addressed if CV decompensation ensues.
- Avoid induced hypotension in anemic pts.

Extubation
- Period with greatest O_2 demands

Postoperative Period
- Continued monitoring of coagulation status
- Transfusion requirements >normal
- Increased susceptibility to infection
- Pain management requires balance between pulm toilet versus sedation

Anticipated Problems/Concerns
- Age of RBC in pts with aplastic anemia is older than usual, with lower 2,3-DPG levels inside cells resulting in increased O_2 binding by Hgb (shift to the right) and decreased delivery of oxygen to tissues for same SaO_2.

Anemia, Chronic Disease/Inflammation

Hayden R. Hughes

Risk
- Incidence in USA: 5%; incidence in surgical population: 5% to 75%.
- Historically thought to be due to chronic infectious, inflammatory, or malignant conditions. Now known to occur with severe trauma, DM, aging, and acute immune activation.
- More than 130 million Americans living with chronic diseases.

Perioperative Risks
- Risks related to underlying diseases
- Transfusion related risks (e.g., TRALI, TACO, hemolytic reactions, immunosuppression)
- Risks related to compensatory mechanisms for increasing O_2 delivery (e.g., angina, heart failure, dysrhythmias)

Worry About
- Underlying diseases and their periop complications.
- Impaired tissue O_2 delivery and compensatory mechanisms aimed at correcting it.
- Delayed wound healing and infection.

Overview
- WHO definition of anemia: children 6 mo to 6 y: Hgb <11 g/dL; 6 to 14 y: Hgb <12 g/dL; nonpregnant females: Hgb <12 g/dL; pregnant females: Hgb <11 g/dL; males: Hgb <13 g/dL.
- Usually mild with Hgb 8-11 g/dL.
- Usually normochromic, normocytic with low reticulocyte count.
- Low serum Fe, TIBC, and transferrin levels.
- ACD/I due to disturbances of Fe homeostasis – diversion of Fe from the circulation into storage sites within the reticuloendothelial system and reduced GI absorption of Fe.

Etiology
- Relative Fe deficiency
- Reduction in RBC production and mild decrease in RBC survival time
- Certain treatments for chronic conditions

Usual Treatment
- Treatment of underlying disease
- Fe, folic acid, and cobalamin supplementation
- Erythropoiesis-stimulating agents
- Allogeneic blood transfusion

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hyperdynamic circulation Myocardial ischemia CHF	Palpitation Pounding pulse Angina Sx, dyspnea Exercise intolerance	Tachycardia Wide pulse pressure	ECG Exercise ECG
RESP		Dyspnea		
GI	Chronic blood loss Hypoperfusion	Blood in stool Angina equivalent (pain, nausea, indigestion)		Occult blood in stool See CV
HEME	Hgb below WHO definition level (see Overview)	Decreased exercise tolerance		Hgb
RENAL	Chronic renal failure	Decreased urine output Dialysis	Shunt	Cr K^+
CNS	Decreased cerebral O_2 delivery	Dizziness Headache Transient cerebral ischemia		
MS	Low exercise capacity	Fatigue		

Key References: Gangat N, Wolanskyj AP: Anemia of chronic disease, *Semin Hematol* 50:232, 2013; Shander A: Anemia in the critically ill, *Crit Care Clin* 20(2):159–178, 2004.

Perioperative Implications

Preoperative Preparation
- Standard monitoring.
- Warm the room.
- CVP, Hgb, electrolytes.
- ST-segment analysis in pts with signs of CAD.
- PA cath for large fluid shifts or pts with signs of LV dysfunction or advanced renal failure.
- ABG.

Airway
- None

Preinduction/Induction
- Prehydrate liberally if CV status will tolerate.
- Avoid CO reduction.
- Avoid hypoxemia.
- Choose drugs according to underlying conditions.

Maintenance
- Avoid hypoxemia.
- Maintain CO.
- Avoid hypovolemia.
- Keep pt warm.
- Maintain Hgb above critical level for pts taking comorbidities into account.

Extubation
- Keep pt warm.
- Maintain high PaO_2.
- In pts with CAD, this is the period of greatest risk for ischemia.

Postoperative Period
- Keep pt warm, prevent shivering.
- Maintain high PaO_2.

Adjuvants
- According to underlying disorder

Anticipated Problems/Concerns
- Myocardial ischemia/infarction or CHF in pts with concomitant CAD.
- Deterioration of renal function in pts with CRI.
- Prolonged effects of drugs in pts with impaired renal and/or hepatic function.

Abruptio Placentae

Nathaniel N. Hsu

Risk

- Occurs in 0.4-1% of pregnancies, and the incidence is increasing, particularly among African Americans.
- Associated with the following conditions: preeclampsia, hypertension, chorioamnionitis, cocaine use, alcohol use, trauma, increased age and parity, smoking, premature rupture of membranes, prior abruption, and multiple gestation.

Perioperative Risks

- Maternal: Antepartum and postpartum hemorrhage, DIC, and death.
- Fetal: Hypoxia, prematurity, and fetal demise. Placental separation may lead to reduced gas exchange surface area, and maternal hypotension will worsen uteroplacental blood flow.
- Maternal risk lies in severity of abruption, whereas fetal risk depends on both severity and gestational age at time of abruption.

Worry About

- Concealed hemorrhage in a retroplacental hematoma may not manifest as vaginal bleeding and can lead to considerable underestimation of maternal hypovolemia.
- Postpartum hemorrhage refractory to usual oxytocic agents; some believe old blood can infiltrate into and between uterine muscle fibers and decrease the effectiveness of uterine contractions (Couvelaire uterus). May need peripartum hysterectomy as a last resort.
- Maternal coagulopathy occurs in 10% of cases.
- Fetal distress and demise.

Overview

- Along with placenta previa, a major cause of antepartum hemorrhage, maternal mortality, and perinatal mortality.
- Perinatal mortality is 12%, but it varies depending on severity of abruption and gestational age.
- Classical clinical triad of metrorrhagia, uterine hypertonia, and abdominopelvic pains presents in only 9.7% of cases.
- Placental abruption is the most common condition (37%) associated with DIC in obstetric pts. DIC is probably because of the release of thromboplastin into the central circulation by placental tissues at abruption site.
- Postpartum hemorrhage correlates directly with severity of coagulopathy.
- Blood and blood clots in muscle fibers may inhibit ability of uterus to contract, which leads to more blood loss.

Etiology

- Separation of placenta from uterine wall along decidual plane between membranes and uterus

Usual Treatment

- Meticulous attention to maternal volume status and fetal surveillance.
- Timing and route of delivery depend on degree of maternal and fetal compromise and estimated gestational age.
- If fetus is preterm and both maternal/fetal status are reassuring, careful observation to optimize fetal maturation is appropriate.
- If fetus is at or near term and both maternal/fetal status are reassuring, vaginal delivery is reasonable.
- If maternal or fetal status is nonreassuring, cesarean delivery is necessary. Cesarean delivery rates are as high as 90%, with 51% being performed under general anesthesia.
- If fetus demise occurs and mother is stable, then vaginal delivery may be considered, if imminent.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hemorrhage	Vaginal bleeding and abdominal pain	Vaginal bleeding and firm, tender uterus; hypotension; tachycardia; low CV and wedge pressures; decreased urine output	Hemoglobin, hematocrit
HEME	Hypovolemia; acute anemia	Bleeding diathesis	Hypotension, tachycardia, bleeding from puncture sites, easy bruisability	Hgb; Hct; clotting evaluation that includes platelets, fibrinogen, and fibrin split products
RENAL	Oliguria and/or acute renal failure	Urine output	Signs of hypovolemia	Urinalysis to include specific gravity and sodium excretion, possibly in addition to invasive hemodynamic monitoring values
UTERUS/ VAGINA	Abruption; hemorrhage	Painful vaginal bleeding	Tender, firm uterus; vaginal bleeding may be less prominent than CV signs and symptoms, indicating concealed hemorrhage	Hgb, Hct, and hemodynamic monitoring values
FETUS	Fetal distress and/or demise; fetal growth restriction	Presence or absence of fetal movement	Fetal movement, heart rate	Electronic fetal monitoring

Key References: Scavone BM: Antepartum and postpartum hemorrhage. In Chestnut DH editor: *Obstetric anesthesia,* ed 5, Philadelphia, PA, 2014, Saunders, pp 881-914; Oyelese Y, Ananth CV: Placental abruption, *Obstet Gynecol* 108(4):1005-1016, 2006.

Perioperative Implications—For Labor and Vaginal Delivery

Preinduction/Induction/Maintenance

- Optimize maternal CV status and evaluate coagulation system. Closely monitor for further bleeding and hemodynamic changes.
- Neuraxial analgesia may be offered if intravascular volume status and coagulation profile are adequate. Consider using smallest effective analgesic doses.
- Coagulopathic pts presenting for vaginal deliveries may be offered IV pt-controlled opioid analgesia.
- Electronic fetal monitoring is essential.

Perioperative Implications—For Cesarean Delivery

Preinduction/Induction/Maintenance

- Optimize maternal CV status, usually with intravascular volume replacement.
- Obtain large-bore IV access; draw blood to assess hematocrit, coagulation status, and type and crossmatch.

Monitoring

- Urethral cath to monitor urine output.
- Consider invasive monitoring (arterial cath and/or central venous cath), depending on severity of hemorrhage.

General Anesthesia

- Preferred anesthetic approach for unstable maternal and/or fetal status.
- Aspiration prophylaxis.
- Rapid-sequence induction with cricoid pressure.
- Consider ketamine or etomidate for induction if there is concern for significant hypotension in response to propofol.
- Monitor for persistent hemorrhage after delivery of infant as a result of uterine atony or coagulopathy. Replacement of coagulation factors and red blood cells may be needed. Therapies for uterine atony include
  - Uterotonics, such as oxytocin, methergine, and prostaglandin $F_{2\alpha}$.
  - Intrauterine balloon tamponade.
  - Uterine compression suture (B-lynch suture).
  - Embolization/ligation of uterine or hypogastric arteries.
  - Peripartum hysterectomy.
  - Recombinant factor VIIa.

Neuraxial Anesthesia

- May be considered if intravascular volume status and coagulation profile are adequate.
- Aspiration prophylaxis.
- Epidural preferred over spinal because the level can be raised slowly, but could do with continuous spinal cath.
- Treat hypotension early and vigorously, usually with ephedrine or phenylephrine.
- Monitor for persistent hemorrhage as noted above.

Postoperative Period

- Majority of mothers recover quickly and completely.
- Recovery should be in a multidisciplinary intensive care unit for pts who had massive transfusion or significant hypotension.
- Aggressive monitoring for persistent hemorrhage and/or development of coagulopathy.
- Need early replacement of coagulation factors, especially fibrinogen.

Anticipated Problems/Concerns

- Amount of bleeding may be considerably greater than what is evident per vagina because a significant amount of blood can be concealed behind the abruption.
- Possible need for emergency cesarean delivery for fetal distress and/or maternal hemodynamic instability.
- Definitive therapy is delivery of the infant and placenta via vaginal or cesarean method.
- Hemorrhage may continue postpartum from uterine atony that is refractory to the usual uterotonic agents or from coagulopathy.
- Peripartum hysterectomy may be necessary, which may in itself be accompanied by large amount of blood loss.
- If massive blood transfusion is needed, be aware of possible dilutional thrombocytopenia and need for coagulation factor replacement.

Achondroplasia, Dwarfism

Minh Chau Joe Tran | Carl Ying

Risk

- 1 per 15,000 to 40,000 births worldwide
- Females ≥ males
- No race predilection
- Most common type of dwarfism

Perioperative Risks

- Cervical spine instability
- Spinal cord compression
- Cardiopulmonary disease

Worry About

- Difficult airway and ventilation
- Central and/or obstructive sleep apnea
- Cervicomedullary compression and foramen magnum stenosis
- Spinal cord and nerve root compression
- Restrictive lung disease
- Pulmonary hypertension, cor pulmonale

Overview

- Results from overactive FGFR3, leading to inhibition of cartilage proliferation, leading to characteristic disproportionate dwarfism with relative macrocephaly, frontal bossing, midface hypoplasia, spine deformations, long narrow trunk, short extremities, and trident hands.
- Average adult height is 4 feet 4 in. for males, 4 feet 1 in. for females.
- Average adult weight is 120 lbs (55 kg) for males, 100 lbs (45 kg) for females.
- Atlantoaxial instability, cervicomedullary compression, foramen magnum or spinal stenosis leading to cord compression and cauda equina syndrome may require neurologic intervention.
- Brainstem compression contributes to central apnea while midface structural abnormalities lead to obstructive sleep apnea.
- Kyphoscoliosis and rib cage deformities lead to restrictive lung disease.
- Chronic hypoxia and hypercarbia from restrictive lung disease and sleep apnea lead to pulmonary hypertension and cor pulmonale.
- Increased mortality from resp and neuro complications during childhood.
- Heart-disease-related mortality approaches 10 times the general population in ages 25 to 35.
- Intelligence is usually normal; overall life expectancy is decreased by 10 y.

Etiology

- Caused by mutation of FGFR3 on chromosome 4p.
- >80% of cases are spontaneous gene mutations.
- Autosomal dominant trait with complete penetrance (heterozygous parent has a 50% chance of passing on the altered gene).
- Homozygous fatal in first few wk due to severe resp or neuro impairment.
- Advanced paternal age (age >35 y) is a risk factor in de novo cases.

Usual Treatment

- ENT: tonsillectomy, adenotomy, tympanostomy tubes
- Neurosurgery: craniectomy, VP shunts, laminectomy
- Orthopedics: distraction osteogenesis, malpositioned extremities
- Spinal surgery: spinal canal stenosis, kyphoscoliosis
- Dental, bariatric, tracheostomy, C-section

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Megalocephaly, short cranial base with small foramen magnum, midface hypoplasia, short eustachian tubes, ossicular chain stiffness, narrow nasal passages, macroglossia, prominent mandible Possible tracheomalacia OSA is common, possibly improved with tonsillectomy and adenoidectomy Crowded and misaligned dentition	Recurrent otitis media Congenital or acquired hearing loss from otitis media Apnea with cyanotic spells Speech and language delay	Limited neck ROM Limited ability to visualize glottic opening Hearing loss Delayed speech acquisition	Cervical flexion/extension neck films Hearing test
CV	Pulmonary hypertension leading to cor pulmonale	SOB with routine activities, fatigue, dizziness, syncope, supplemental oxygen use	JVD distention, lower extremity edema, hypoxia, rales, orthopnea, cyanosis, tachycardia, arrhythmia	ECG, ECHO, angiography
PULM	Restrictive lung disease from severe scoliosis and rib cage deformities Expect decreased FRC, hypoxemia, hypercapnia, apnea even in childhood. Thoracic cage constriction improves over time May have bronchomalacia	Apnea with cyanotic spells, SOB Daytime somnolence, loud snoring Recurrent resp infections	Ribcage deformities, tachypnea	CXR, ABG, PFT, sleep study
GI	Obesity very common Gastric hypomotility	GERD, aspiration, dysphagia, globus hystericus	BMI	CXR
CNS	Small and funnel shaped foramen magnum may cause hydrocephalus, elevated ICP Cervical spine instability, stenosis and fusion Progressive narrowing of spinal canal caudally, possible cauda equina Spinal cord or root compression at any level	Headaches, irritability, lethargy, vomiting Cervical myelopathy, ataxia, incontinence Snoring, daytime somnolence Depression	Mental status changes, low back pain, ataxia, radiculopathy, dysesthesia, paresthesia, paraparesis, hyperreflexia, hypertonia, sustained clonus, incontinence	Axial head or spine CT or MRI motor evoked potentials, SSEP Sleep study
MS	Pectus carinatum or excavatum, genu varum, rhizomelic shortening of arms and legs, small thoracic cage	Delayed motor milestones, premature degenerative joint disease	Thoracolumbar kyphoscoliosis, proximal limbs shorter than distal limbs, brachydactyly, trident hand configuration Hyperextensibility of most joints (knees in particular), incomplete elbow extension Bowing of lower extremities	Spine films, x-rays, bone scans

Key References: Baum V: Achondroplasia. In *Anesthesia for genetic, metabolic, and dysmorphic syndromes of childhood,* ed 3, Philadelphia, PA, 2015, Lippincott Williams & Wilkins, pp 47–54; Oppitz F, Speulda E, Goeters C, et al.: Anesthesia recommendations for patients suffering from achondroplasia. <www.orpha.net/data/patho/Pro/en/Achondroplasia_EN.pdf>, 2011.

Perioperative Implications

Preoperative Preparation

- General anesthesia is usually the method of choice.
- Neuraxial anesthesia is possible, but is difficult due to anatomy and carries increased risk.
- Conscious sedation is also possible, a concern for sleep apnea syndrome.
- Assess individual pt based on systems approach and review relevant studies.
- Assume difficult intubation, ventilation and unstable cervical neck. High spinal cord injury and death have been reported with routine neck manipulation.
- Consider prophylaxis for gastroesophageal reflux and hypersalivation.
- Pts generally more anxious but avoid presedation if possible.

Monitoring

- Standard ASA monitors
- A-line recommended for invasive surgeries or any cardiopulmonary compromise.
- Foley; CVP; MEP; SSEP (spinal cord surgeries or abnormal positioning to identify early cord compression).
- Use appropriate BP cuff (two-thirds upper arm length) to avoid falsely elevated BP.

Airway

- Anticipate difficult mask ventilation due to facial anatomy.
- Nasal airway/intubation difficult due to narrow nasopharynx and choanal stenosis.
- Oral airway often necessary to relieve obstruction from macroglossia.
- Avoid hyperextension or hyperflexion, especially in those with atlantoaxial instability or foramen magnum stenosis, thus AFOI is the safest/preferred method.
- Most require intubation due to restrictive lung disease, but have LMA as rescue device.

- ETT sizes correlate better with weight than age; they have a smaller tube ready.

Induction

- No specific drug contraindications; limited data on dosages.
- Low functional residual capacity can lead to rapid desaturation with induction.
- Avoid hypoxia, hypercarbia, and acidosis, which can worsen pulmonary hypertension.

Maintenance

- Mechanical ventilation may require reduced tidal volume and higher rate.
- Pressure-controlled ventilation may be superior; careful attention to PAP.
- Careful positioning of hyperextensible joints.
- Consider OG tube for gastric decompression.
- Use peripheral nerve stimulator to guide NMBD dosage.

Postoperative Period

- Continuous pulse oximetry due to high incidence of sleep apnea.
- Prepare for prolonged resp insufficiency and mechanical ventilation.
- May need to remain intubated and/or monitored in an ICU.
- Pain control critical to postop resp status.

Anticipated Problems/Concerns

- Difficult airway and ventilation
- Neurologic impairment
- Resp insufficiency and postop ventilation
- Pain control

Acidosis, Lactic/Metabolic

Justin D. Ramos | Peter M. Schulman

Risk

- Incidence in USA: Unknown
- Present in a variety of disease states, from mild to severe systemic illness

Perioperative Risks

- Hemodynamic instability (due to arteriolar vasodilation and decreased cardiac output)
- Hyperkalemia
- Insulin resistance and hyperglycemia
- Stimulation of inflammation and suppression of immune response
- Acute resp failure

Worry About

- Decreased responsiveness to vasopressors and inotropes
- Decreased activity of local anesthetic agents
- Arrhythmias

Overview

- Physiologic disturbance resulting from excess acid production, failure of organic acid excretion, or inappropriate bicarbonate loss causing increased serum acidity.
- A marker of an underlying disease process.
- Severe when, in the presence of resp compensation, serum $[HCO_3]$ is ≤10 mmol/L or pH < 7.20.
- Acute metabolic acidosis is associated with increased morbidity and mortality.

Etiology

- Broadly differentiated by calculating the AG: AG = $[Na^+]$ – ($[Cl^-]$ + $[HCO_3^-]$). The AG corresponds to the presence of unmeasured anions in serum. The presence or absence of an elevated AG helps to determine the underlying cause and direct appropriate therapy. Normal AG is 7 ± 4 mEq/L and decreases 2.5 mEq/L for every 1 g/dL decrease in serum albumin. Corrected AG can be calculated:
  - Corrected AG = Calculated AG – {2.5 * (4.0 – [albumin])}.
- High AG metabolic acidosis: Results from an accumulation of excess acid in the serum. Specific causes are due to production of lactate or ketones (diabetic, alcoholic, or starvation ketoacidosis), toxic ingestion (methanol, ethylene glycol, salicylates), uremia, or medication side effects (propofol infusion syndrome, lactic acidosis associated with metformin).
- Normal AG (hyperchloremic) metabolic acidosis: Associated with excess HCO_3^- loss from the kidney or GI tract, failure of the kidney to excrete H^+, or rapid IV infusion of unbuffered solutions (e.g., normal saline).
- Delta gap (ΔΔ): Used to determine the presence of concomitant metabolic derangements and is calculated as ΔAG/Δ $[HCO_3^-]$, where ΔAG = (calculated AG – expected AG) and Δ $[HCO_3^-]$ = (24–$[HCO_3^-]$). ΔΔ < 1 indicates AG metabolic acidosis *and* concurrent non-AG acidosis. ΔΔ > 2 indicates AG metabolic acidosis and concurrent metabolic alkalosis. ΔΔ = 1 to 2 indicates a pure AG metabolic acidosis.

Usual Treatment

- Centered on rapid identification and treatment of the underlying physiologic disturbance (e.g., DKA, sepsis, inadequate resuscitation, CV failure, abdominal ischemia).
- In high AG metabolic acidosis, alkali therapy may be indicated as a temporizing measure for acute, severe acidemia (pH <7.20). In normal AG metabolic acidosis, alkali therapy may be indicated to replace bicarbonate losses.
  - Sodium bicarbonate remains the most widely used buffer; however, its use in correcting acute metabolic acidosis is controversial because it may increase $PaCO_2$ and paradoxically worsen intracellular acidosis. Other untoward effects of bicarbonate include hyperosmolarity and hypernatremia. Bicarbonate administration has not been proven to improve cellular function or reduce mortality in lactic or ketoacidosis.
  - THAM is an alternate buffer designed to limit CO_2 generation, offering theoretical benefits over bicarbonate. It buffers via the ammonia moiety, but elimination of protons is dependent on urinary excretion or removal via dialysis.
  - When alkali therapy is indicated, the bicarbonate deficit can be calculated to guide appropriate dosing. Bicarbonate should be administered as an isotonic infusion, rather than a bolus of hypertonic solution. Bicarbonate deficit (mEq) = 0.4 × body weight (kg) × (24 – $[HCO_3^-]$).
- In some instances (hyperventilation syndromes, high altitude), acidosis may be compensatory and not require treatment.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Altered mental status, seizures	Level of consciousness, delirium, somnolence nausea/vomiting, seizures, toxic ingestion	Obtunded, confused, somnolent	Toxicology screen, osmolal gap, serum lytes
CV	Arteriolar vasodilation, hypotension, decreased response to vasopressors and inotropes, arrhythmias, hypocontractility	Signs of end-organ hypoperfusion	Tachycardia, hypotension, poor peripheral pulses, cold extremities, poor capillary refill	Invasive hemodynamic monitoring, ECHO, ECG
PULM	Hypoxemia, hyperventilation, resp failure	Tachypnea, dyspnea	Rapid and shallow breathing, accessory muscle use, hypoxia, hypercarbia	CXR, ABG, pulse oximetry
RENAL	Oliguria, acute kidney injury, ATN	Urine output, chronic renal disease	Signs of hypovolemia or hypervolemia	UO, Cr, BUN, urine lytes, UA, serum lytes
GI		Nausea, vomiting, diarrhea, melena, abdominal pain	Abdominal pain to palpation	Serum lactate, radiographic imaging, upper/lower endoscopy
ID		Fever, rigors	Hyperthermia or hypothermia, signs of focal infection	WBC with differential, cultures, radiographic imaging
ENDO	Hyperglycemia, insulin resistance	DM, polyuria, polydipsia, hyperphagia	Signs of dehydration	Blood glucose, serum ketones

Key References: Kraut JA, Madias NE: Metabolic acidosis: pathophysiology, diagnosis and management, *Nat Rev Nephrol* 6:274–285, 2010; Kraut JA, Madias NE: Treatment of acute metabolic acidosis: a pathophysiologic approach, *Nat Rev Nephrol* 8:589–601, 2012; Kimmoun A, Novy E, Auchet T, et al.: Hemodynamic consequences of severe lactic acidosis in shock states: from bench to bedside, *Crit Care* 19:175, 2015.

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Perioperative Implications

Preoperative Preparation

- Pts with metabolic acidosis may be hemodynamically unstable and demonstrate decreased responsiveness to inotropes and vasopressors.
- Consider postponing surgery until the underlying cause is corrected, unless treatment requires immediate surgical intervention.
- If surgery is urgent or emergent, consider ways to optimize the pt preop.

Intraoperative

- Invasive monitoring may be indicated, depending on the severity of illness.
- Goal for induction is hemodynamic stability.
- Inotropes and vasopressors should be readily available.
- Consider the need for pt to remain intubated postop.

Postoperative Period

- Pt may require postop ICU care and prolonged mechanical ventilation.

Anticipated Problems/Concerns

- Hemodynamic instability with decreased responsiveness to inotropes and vasopressors.
- Compensation for profound metabolic acidosis may lead to acute resp failure.
- Treatment with bicarbonate may paradoxically increase $PaCO_2$ and worsen intracellular acidosis and resp status.

Acidosis, Renal Tubular

Amit Prabhakar | Alan David Kaye

Risk

- Incidence in USA: Unknown
- Present in a variety of disease states, from mild to severe systemic illness

Perioperative Risks

- Hemodynamic instability (related to arteriolar vasodilation, acidosis, and decreased cardiac output)
- Hyperkalemia
- Insulin resistance and hyperglycemia
- Acute respiratory failure

Worry About

- Decreased responsiveness to vasopressors and inotropes
- Decreased activity of local anesthetic agents
- Arrhythmias

Overview

- RTA is a type of metabolic acidosis that is due to either abnormal bicarbonate loss or acid excretion by the kidneys in presence of a normal or near normal glomerular filtration rate.
- Results in non-anion gap metabolic acidosis.
- Metabolic acidosis not due to gastrointestinal bicarbonate loss or acute/chronic renal insufficiency.
- Related to either proximal tubule dysfunction of bicarbonate reabsorption, failure of distal tubule excretion of acid, or mineralocorticoid deficiency.
- Other findings may include recurrent nephrocalcinosis, growth retardation, and osteomalacia/rickets in children.
- Can be either inherited, transient, or acquired.

Etiology

- Distal RTA (type 1) is due to defective distal tubular H^+ secretion.
  - Clinical features include impairment of growth, polyuria, hypercalciuria, lithiasis, nephrocalcinosis, and K^+ depletion.
  - Acquired forms related to hypergammaglobulinemia, autoimmune disorders such as SLE or Sjögren syndrome, and pts with chronic liver disease.
  - Can be associated with sensorineural hearing loss.
- Proximal RTA (type 2) is due to defective proximal tubule reabsorption of bicarbonate.
  - Manifests as stunted growth in children.
  - Can be associated with Fanconi syndrome, and if so, can manifest with osteomalacia and rickets.
  - Other causes include medications and toxins such as acetazolamide, aminoglycoside antibiotics, expired tetracyclines, lead, cadmium, and mercury.
- Type 3 RTA is a combination of types 1 and 2.
  - Can be transient in pediatric pts with type 1 RTA.
  - Carbonic anhydrase II deficiency is an AutoR syndrome associated with osteoporosis, RTA, cerebral calcification, and mental retardation.
- Hyperkalemic RTA (type 4): Due to either mineralocorticoid deficiency or hormone resistance
  - Most frequently observed in children with hypo- or pseudohypoaldosteronism
  - Also found to be related with diabetic nephropathy, SLE, and AIDS nephropathy
  - Drug induced causes include COX inhibitors, ACE-I's, heparin, K retaining diuretics, trimethoprim, and others

Diagnosis

- Should be suspected anytime metabolic acidosis is accompanied with hyperchloremia and a normal plasma anion gap without evidence of gastrointestinal bicarbonate loss or acid ingestion
- Differential diagnosis (common distal causes of RTA):
  - Hypokalemic or normokalemic: Primary, hypercalcemia, renal transplant rejection, multiple myeloma, SLE, nephrocalcinosis, hepatic cirrhosis, amphotericin B, lithium, and toluene
  - Hyperkalemic: Sickle cell nephropathy, obstructive nephropathy, hypoaldosteronism, and SLE
- Common proximal causes of RTA: Primary, Fanconi syndrome, Wilson disease, metals (mercury, lead, and cadmium), early renal transplant, nephrotic syndrome, and amyloidosis
- Tests used to aid in diagnosis include:
  - CMP to assess plasma electrolytes, baseline kidney function, and plasma anion gap
  - Urine pH and urine anion gap
  - Urine osmol gap and urine PCO_2
  - Urine calcium and citrate excretion
  - Renin: aldosterone ratio
  - Oral administration of acidifying salt (typically with ammonium chloride loading) employed to assess for ammonium secretion; normal individuals achieve a urine pH of less than 5.5, whereas pts with distal RTA are unable to acidify urine
  - Furosemide test: PO or IV dose given to assess distal tubule acidification function
- Metabolic derangements associated with each type
  - Distal: Pt will present with hyperchloremic metabolic acidosis with a positive anion gap or an osmol gap <100 mmol/L. Diagnosis is supported by either normal or decreased plasma K^+ concentration and inability to lower urine pH <5.5 after either acidifying salt (ammonium chloride) loading or furosemide test.
  - Proximal: Pt will present with hyperchloremic metabolic acidosis, negative anion gap, or osmol gap above 100 mmol/L. Definitive diagnosis is made with presence of low urine pH at low plasma bicarb concentration and the presence of normal urine PCO_2 and a high urine bicarb excretion at normal plasma bicarb concentration. GI or renal loss, previous intake of acidifying salt, or excessive use of laxatives must be ruled out.
  - Hyperkalemic RTA: Should be considered if K^+ is increased with urine pH <5.5. Renin and aldosterone levels must be assessed. Hypoaldosteronism is the most common cause of hyperkalemic distal RTA.

Usual Treatment

- Focused on preventing pediatric growth restriction, nephrocalcinosis, and development of chronic renal failure in all ages.
- Treatment based on disease specific alkali replacement using either bicarbonate or citrate.
- Proximal RTA alkali supplementation usually needed until 3 to 5 y of age.
- Distal RTA is more likely to be permanent with treatment needed throughout life.
- Hyperkalemic RTA can be treated with fludrocortisone, furosemide, and alkali supplements if needed.

Perioperative Implications

Preoperative Preparation

- Pts with metabolic acidosis may be hemodynamically unstable and demonstrate decreased responsiveness to inotropes and vasopressors.
- Consider postponing surgery until the underlying cause is corrected, unless treatment requires immediate surgical intervention.
- If surgery is urgent or emergent, consider ways to optimize the pt preop.

Intraoperative

- Invasive monitoring may be indicated, depending on the severity of illness.
- Goal for induction is hemodynamic stability.
- Inotropes and vasopressors should be readily available.
- Consider the need for pt to remain intubated postop.

Postoperative Period

- Pt may require postop ICU care and prolonged mechanical ventilation.

Anticipated Problems/Concerns

- Hemodynamic instability with decreased responsiveness to inotropes and vasopressors.
- Compensation for profound metabolic acidosis may lead to acute resp failure.
- Treatment with bicarbonate may paradoxically increase $PaCO_2$ and worsen intracellular acidosis and resp status.

Acidosis, Renal Tubular

Amit Prabhakar | Alan David Kaye

Risk

- Incidence in USA: Unknown
- Present in a variety of disease states, from mild to severe systemic illness

Perioperative Risks

- Hemodynamic instability (related to arteriolar vasodilation, acidosis, and decreased cardiac output)
- Hyperkalemia
- Insulin resistance and hyperglycemia
- Acute respiratory failure

Worry About

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- Distal RTA is more likely to be permanent with treatment needed throughout life.
- Hyperkalemic RTA can be treated with fludrocortisone, furosemide, and alkali supplements if needed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Altered mental status and seizures	Level of consciousness, delirium, somnolence nausea/vomiting, seizures, toxic ingestion	Obtunded, confused, somnolent	Toxicology screen, osmol gap, serum lytes
CV	Arteriolar vasodilation, hypotension, decreased response to vasopressors and inotropes, arrhythmias, hypocontractility	Signs of end-organ hypoperfusion	Tachycardia, hypotension, poor peripheral pulses, cold extremities, poor capillary refill	Invasive hemodynamic monitoring, ECHO, ECG
PULM	Hypoxemia, hyperventilation, respiratory failure	Tachypnea, dyspnea	Rapid and shallow breathing, accessory muscle use, hypoxia, and hypercarbia	CXR, ABG, pulse oximetry
RENAL	Oliguria, acute kidney injury, ATN	Urine output, chronic renal disease	Signs of hypo- or hypervolemia	UO, Cr, BUN, urine lytes, UA, serum lytes
GI		Nausea, vomiting, diarrhea, melena, abdominal pain	Abdominal pain to palpation	Serum lactate, radiographic imaging, upper/lower endoscopy
ID		Fever, rigors	Hyperthermia or hypothermia, signs of focal infection	WBC with differential, cultures, radiographic imaging
ENDO	Hyperglycemia, insulin resistance	DM, polyuria, polydipsia, hyperphagia	Signs of dehydration	Blood glucose, serum ketones

Key References: Morris CG, Low J: Metabolic acidosis in the critically ill: Part 1. Classification and pathophysiology and Part 2. Causes and treatment. *Anaesthesia* 63:294–301, 396–411, 2008; Laing CM, Unwin RJ: Renal tubular acidosis. *J Nephrol* 19(Suppl 9):S46–S52, 2006.

Perioperative Implications

Preoperative Preparation

- Carefully assess for electrolyte abnormalities, pH balance, volume, and kidney function via CMP, phosphorus, and calcium levels.
- Consider elective versus emergent surgery. If elective and found to have multiple metabolic derangements, consider postponement for appropriate medical management and if surgery is urgent or emergent, consider ways to optimize the pt preop.
- Remember that some forms of RTA can be associated with genetic or autoimmune syndromes such as Fanconi or Sjögren. Incorporate other syndrome specific clinical considerations for each case.

Monitoring

- Arterial line and/or central venous pressure can assist in assessment of volume status periop.

Intraoperative Preparation

- Pts with advanced renal pathogenesis should have anesthetic medications that avoid the kidney, including cis-atracurium with neuromuscular blockade requirement, and avoidance of morphine, which is conjugated to morphine 6-glucoronide and an active metabolite, and is eliminated through the kidney.
- Pts may be hemodynamically unstable, demonstrating decreased responsiveness to inotropes and vasopressors.
- Many pts with advanced renal pathogenesis have increased potassium levels, and, therefore, succinylcholine should be avoided as it can further increase potassium levels, leading to adverse effects such as cardiac arrest.

Postoperative Period

- Pt may require postop ICU care and prolonged mechanical ventilation.

Anticipated Problems/Concerns

- Hemodynamic instability with decreased responsiveness to inotropes and to vasopressors
- Compensation for profound metabolic acidosis, which may lead to acute respiratory failure
- Treatment with bicarbonate, which may paradoxically increase $PaCO_2$ and worsen intracellular acidosis and respiratory status

Acquired Immunodeficiency Syndrome

Jordan B. Johnson | Jeffrey R. Kirsch

Risk

- USA incidence of HIV: 50,000 per year
- USA prevalence of HIV: 1.2 million
  - Sub-Saharan Africa prevalence: 25.8 million in 2014
- USA prevalence of AIDS (HIV stages 3 and 4): 26,688
  - All but 8 were age 13 or older

Perioperative Risk

- Susceptibility to infection
- Drug interactions
- Occupational exposure/viral transmission

Overview

- AIDS is the clinical syndrome representing the late and more severe stages of infection with HIV.
- Once inside the host, HIV attaches and is internalized to CD4+ T4 helper lymphocytes. Viral RNA is transcribed into the cell's DNA allowing formation of viral progeny within the host. Host's CD4+ T4 helper lymphocytes become defective and unable to help fight opportunistic infections and neoplasms causing progressive immunocompromisation.
- In 2007 WHO published a clinical classification system for HIV/AIDS; stages 1 to 4 are based on clinical symptoms and presence of associated illnesses, and AIDS is defined by the presents of features of stages 3 and 4.

Etiology

- Transmission can occur when there is contact between HIV-infected blood or contaminated body fluids and open wounds, broken skin, or mucus membranes.
- During sexual encounters, delivery of a fetus, breastfeeding, inoculation by contaminated needles, and occupational exposure.

Usual Treatment

- Regimen of HAART.
  - Target different stages in HIV replication cycle.
- Pts may be taking additional drugs, both for treatment and for prophylaxis targeting associated illnesses, such as other antivirals, antifungals, antibiotics, and/or chemotherapy drugs.

Assessment Points

System	Effect	Possible Pathogenesis
RESP	Bronchitis, sinusitis, pneumonia, pneumonitis, airway obstruction	Direct effect of HIV Opportunistic infections Neoplasm (e.g., Kaposi sarcoma)
CV	Cardiomyopathy, coronary artery disease, pericardial effusion, endocarditis, pulm hypertension, vacuities	Direct effect of HIV Medication side effect, namely antiretroviral drugs (reverse transcriptase inhibitors) Autoimmune disease Neoplasm
HEME	Anemia, neutropenia, thrombocytopenia, lymphadenopathy, coagulopathy, hematologic malignancy	Direct effect of HIV Medication side effect
NEURO	Meningitis, encephalitis, encephalopathy, cognitive impairment, HNCI, AIDS dementia, autonomic and peripheral neuropathies, seizures	Direct effect of HIV Opportunistic infections Neoplasm
RENAL	Acute and chronic renal failure, nephropathy	Direct effect of HIV Medication side effect, namely antiretrovirals
GI	Oral lesions, dysphagia, odynophagia, diarrhea, HIV/AIDS enteropathy, pancreatitis, hepatobiliary involvement	Direct effect of HIV Opportunistic infections Medication side effect Neoplasm
ENDO	Lipodystrophy, metabolic syndrome, hypercortisolism, adrenal insufficiency, SIADH, hyperthyroidism, hypothyroidism, lactic acidosis	Direct effect of HIV Opportunistic infections Medication side effect

Key References: Bajwa SJ, Kulshrestha A: The potential anesthetic threats, challenges and intensive care considerations in patients with HIV infection, *J Pharm Bioallied Sci* 5(1):10–16, 2013; Panlilio AL, Cardo DM, Grohskopf LA, et al.: Updated U.S. Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis, *MMWR Recomm Rep* 54:1–17, 2005.

Perioperative Management

Preoperative Preparation

- Meticulous medication review, specifically for HAART drugs.
- Careful physical exam for signs of illnesses associated with an immunocompromised state (e.g., lymphadenopathy, Kaposi sarcoma lesions).
- Should continue antiretroviral medications throughout the periop period.
- Preop lab work (CBC, coagulation panel, renal and liver enzyme panels).
- Additional tests (ECG and CXR).
- CD4+ cell count to evaluate the severity of individual's disease and the likelihood of opportunistic infections and neoplasm.
  - A positive correlation between viral load and rate of transmission has been observed in certain populations.

Monitors

- Standard ASA monitors
- Additional monitors as indicated

Airway Management

- Should have awareness of active resp pathology such as infection, inflammatory processes, or airway obstruction as a consequence of immunocompromised state or neoplasm.
- Concern for hypotension if active systemic infectious process or cardiac dysfunction.
- Careful dosing of medications to minimize drug interactions.

Choice of Anesthetic

- Based on type of procedure and pt's comorbidities.
- Pts with AIDS, given they are significantly immunocompromised and may have CV or infectious AIDS-defining illness, may not tolerate general anesthesia.
- Regional and neuraxial anesthesia have been used successfully in these pts and should be considered, but coagulopathy should be ruled out.
- HIV-infected pts may be given the option of cesarean section to decrease the risk of mother-baby transmission, though certain cesarean-associated complication rates have been found to be higher in HIV-infected pts.
- Drugs metabolized by CYP450 system should be dose adjusted if pt is on HAART regimen, specifically protease inhibitors and non-nucleotide reverse transcriptase inhibitors.

Extubation

- Standard extubation criteria apply.

Postoperative Period

- Susceptibility to infections.
- Significant cardiac events.
  - The antiretroviral drug abacavir has recently been shown to independently increase the risk of CV disease in HIV-infected pts.

Occupational Exposure

- Periop team members at higher risk of occupational transmission.
- Vigilance and meticulous handling of sharps and contaminated materials to decrease work-related exposure.
- Risk of exposure correlated with depth of skin inoculated, hollow-bore needle usage, and volume of HIV-infected body fluid involved.
- Know your hospital's policy regarding occupational exposures.
- Begin postexposure prophylaxis with a combination of antiretroviral medications as soon as possible but certainly within 72 hr of exposure.

Acromegaly

Russell T. Wall III

Risk

- People within USA:
  - Prevalence is 40 cases/million; incidence is 3 to 8 new cases/million/y.
  - Occurs with equal frequency in men and women and most frequently diagnosed in third to fifth decades of life (5 to 20 y lag between onset of symptoms and diagnosis).

Perioperative Risks

- Common conditions increasing periop risk include airway abnormalities, CV dysfunction (Htn), resp impairment (obstructive sleep apnea), endo abnormalities (hyperglycemia).

Worry About

- Difficulty or inability to ventilate and/or intubate
- Extent of CV disease
- Postop airway obstruction

Overview

- Acromegaly is a slowly progressive, debilitating endocrinopathy resulting from excess secretion of growth hormone, usually from a benign macroadenoma of the anterior pituitary gland, and characterized by overgrowth of soft tissues and bone and cartilage of skeleton (nose, jaw, hands, fingers, feet, toes). Excess growth hormone before puberty (epiphyseal closure) leads to gigantism (<5% of acromegalics).

Etiology

- Greater than 99% of cases result from primary pituitary adenoma.

Usual Treatment

- Surgery—primary therapy:
  - Transsphenoidal pituitary microsurgery versus transcranial; transsphenoidal more common

and preferred, with less morbidity. Smaller tumors (<10 mm diameter) yield probable cure. Otolaryngologists often assist neurosurgeons with access using sublabial or endonasal approach.

- Pituitary radiation—reserved for persistent postsurgical disease or when surgery is contraindicated.
- Medical—adjunctive therapy or for nonsurgical candidates, effective if adenoma cells have dopamine and/or somatostatin receptors:
  - Dopamine agonists—bromocriptine and cabergoline.
  - Somatostatin analogue—octreotide and lanreotide, inhibits GH release.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Bone and soft tissue overgrowth of head and neck	TMJ arthritis Hoarseness Deep voice	Enlarged frontal, nasal bones Enlarged sinuses Macroglossia with glossoptosis Prognathism Hypertrophy of larynx Vocal cord thickening and edema Subglottic narrowing Enlarged thyroid gland (25%) with possible tracheal compression/deviation Recurrent laryngeal nerve paralysis	Indirect laryngoscopy Lateral neck x-rays CT of neck
CV	CAD PVD LV dysfunction Cardiomyopathy	Chest pain Htn CHF Dysrhythmias Diastolic dysfunction	Htn CHF Dysrhythmias Cardiomegaly Diastolic dysfunction	CXR ECG ECHO
RESP	Airway soft tissue overgrowth Upper airway and small airway narrowing	Obstructive sleep apnea (60% of pts)	Barrel chest with kyphosis	PFTs (if indicated) Sleep study
RENAL	Increased GI Ca^{2+} absorption Hypercalciuria Increased total body Na^{+}	Urolithiasis	Peripheral edema	
ENDO	Increased BMR	Heat intolerance	Hyperhidrosis	To diagnose acromegaly: ↑ 24 h GH levels Best screening test: ↑ serum IGF I Definitive test: Oral glucose tolerance test (GH levels do not ↓)
	Hyperprolactinemia (some adenomas secrete GH and prolactin) Hyperthyroidism (3–7%) Insulin resistance (80%) Glucose intolerance (30–45%) Overt DM (15–25%) Hypertriglyceridemia (20–45%) Hyperphosphatemia Colon polyps/malignancy	Men: ↓ Libido, impotence Women: Menstrual abnormalities	Enlarged thyroid (25%)	TFTs Glucose Cholesterol, triglycerides Phosphorus Colonoscopy
CNS	Pituitary mass effect	Headache Hypersomnolence Visual disturbances		CT MRI (with gadolinium) to determine tumor size +/– extrasellar expansion
PNS	Carpal tunnel syndrome	Paresthesias	Median nerve compression	EMG, NCV
MS	Bone and soft tissue overgrowth Osteoporosis Myopathy	Arthralgias Osteoarthritis (knees, hips, shoulders, lumbosacral spine) Fatigue, weakness	Enlarged hands and feet Hip, knee, shoulder, low back pain Muscle weakness	X-ray

Key References: McGoldrick KE: Eye, ear, nose, and throat diseases. In Fleisher LA editor: *Anesthesia and uncommon diseases,* ed 6, Philadelphia, PA, 2012, Elsevier, pp 22–23; Melmed S, Jameson JL: Disorders of the anterior pituitary and hypothalamus. In Jameson JL editor: *Harrison's endocrinology,* ed 3, New York, NY, 2013, McGraw-Hill Education, pp 39–42.

Perioperative Implications

Preoperative Preparation

- Optimize hemodynamics—BP control, no CHF.
- Somatostatin analogue (octreotide) may shrink large macroadenoma.

Monitoring

- Pulse oximeter may be difficult to fit (large fingers, toes); recommend A-line, brachial or femoral preferable. Visual evoked potentials have limited usefulness.

Airway

- Large masks, airways, blades, intubating LMA, tracheostomy equipment available.
- Consider awake fiberoptic endotracheal intubation.

Induction

- If GA, anticipate airway obstruction
- If hypopituitarism from mass effect, then may need hydrocortisone
- Possible lumbar drain if suprasellar extension
- Prophylactic antibiotics

Maintenance

- For PIA or TIVA, use short-acting agent(s) for rapid recovery.
- If OSA, use opioids with caution.
- For transsphenoidal approach, surgical use of cocaine or epinephrine. Beware of increased BP and dysrhythmias.
- For transsphenoidal approach >15-degree head up tilt, caution for VAE.
- If preop pneumoencephalography, do not use nitrous oxide.
- Monitor serum glucose and treat hyperglycemia.
- Pack pharynx before surgery to prevent bleeding into laryngeal area and post-extubation laryngospasm.

Extubation

- Extubate awake with intact reflexes.
- Anticipate airway obstruction.
- No nasal CPAP, possible posttranssphenoidal surgery.

Adjuvants

- If myopathy, cautious use of muscle relaxants.
- If sleep apnea, cautious use of narcotics.
- If peripheral neuropathy, document prior to regional.

Postoperative Period

- Transient diabetes insipidus (20%), permanent 1% to 9%
- CSF rhinorrhea <5% of pts
- Anterior pituitary insufficiency (ACTH, TSH, gonadotropins) (20%); hormonal replacement with tapered cortisol therapy if necessary
- Meningitis, sinusitis, hematoma, cranial nerve palsy (III, IV, VI), nasal septal perforation, visual disturbances <1% each

Anticipated Problems/Concerns

- Airway management
- Hemodynamic stability

Acute Intermittent Porphyria

Mohamed Ehab Ramadan | Klinton McGhee | Hamdy Elsayed-Awad

Risk

- Prevalence: <200,000 cases of porphyria in USA, AIP: 5 to 10 in 100,000 worldwide.
- Highest in Northern Europeans.
- More commonly manifests in females, typically third to fourth decades of life.

Perioperative Risks

- Drugs and/or chemicals that induce heme containing hepatic CYP450 enzyme (e.g., barbiturates, estrogens, smoking, alcohol).
- Induction of ALA synthase enzyme by fever or fasting.
- Psychological stress.

Worry About

- Precipitation of acute crisis in periop period.
- Diagnosis of latent AIP requires high index of suspicion in pts with unexplained acute abdominal pain and neuropsychiatric manifestations.
- Potentially life threatening especially with delayed diagnosis.
- Once diagnosed, all first-degree relatives should be screened.

Overview

- One in eight inherited metabolic disorders of heme synthesis pathway is caused by mutations in the genes coding for each prospective enzyme in the pathway.
- Autosomal dominant with incomplete penetrance.
- Motor neuropathy, autonomic dysfunction, and psychiatric abnormalities.
- Pts may be encountered for acute and chronic pain management.

Etiology

- Gene mutation causing deficiency in PBG deaminase enzyme
- Accumulation of neurotoxic porphyrin precursors: ALA and PBG

Usual Treatment

- Avoid triggers of acute attack.
- Symptomatic treatment: paracetamol and opioids for pain, chlorpromazine and prochlorperazine for nausea and vomiting, propranolol for tachycardia and hypertension, and gabapentin for convulsions
- Oral/IV dextrose (carbohydrates)
- IV Hematin or Heme arginate (not FDA-approved)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Autonomic neuropathy	Palpitation	Tachycardia Hypertension	ECG
RESP	Resp muscle weakness	Dyspnea	Difficult weaning after surgery	Peak expiratory flow rate Arterial blood gas (ABG)
GI	Enteric neuropathy	Severe poorly localized abdominal pain Nausea, vomiting, constipation Less commonly, diarrhea	Abdominal tenderness/rebound tenderness (uncommon)	X-ray may show mild ileus
GU	Neuropathic bladder dysfunction Accumulation of porphyrin precursors	Dysuria, hesitancy, urinary retention Dark or reddish brown urine	Bladder distension	Increased urine PBG and ALA –ve urine dipstick
ENDO	SIADH Electrolyte disturbances (hyponatremia, hypomagnesemia)		Seizures	Serum electrolytes Serum and urine osmolality Urinary Na
CNS	Neurotoxicity Psychiatric abnormalities	Anxiety Restlessness Insomnia	Seizures Depression Coma Delayed recovery after anesthesia	MRI brain: Reversible white matter densities resembling posterior reversible encephalopathy syndrome
PNS	Neuropathy (motor > sensory)		Motor: Weakness, begins proximally, UL > LL, quadriplegia, bulbar paralysis Sensory: Pain in ext/back, numbness, paresthesia	EMG Nerve conduction studies
ANS	Autonomic neuropathy		Postural hypotension Fever Sweating	

Key References: Herrick AL, McColl KE: Acute intermittent porphyria, *Best Pract Res Clin Gastroenterol* 19(2):235–249, 2005; Findley H, Philips A, Cole D, et al.: Porphyrias: implications for anaesthesia, critical care, and pain medicine, *Contin Educ Anaesth Crit Care Pain* 12(3):128–133, 2012.

Perioperative Implications

Preoperative Preparation

- Careful neurologic assessment: motor, sensory and autonomic dysfunction
- Care for withdrawal symptoms in pts on opioids for chronic pain
- Avoid triggers of acute attack:
  - Avoid prolonged fasting, administer oral/IV dextrose (300 g/day);
  - Sedation to avoid stress;
  - Identify unsafe drugs/chemicals.

Monitoring

- Standard monitoring
- Hgb/Hct
- Blood glucose
- Urine color, check urine for PBG/ALA
- Temperature

Airway

- Risk of aspiration

Preinduction/Induction

- Sedation: Midazolam, phenothiazines.
- Unsafe induction agents: Barbiturates, etomidate.
- Safe induction agents: Propofol, succinyl choline, all nondepolarizing muscle relaxants and opioids are generally safe.
- Care for BP and HRfluctuations.
- Regional anesthesia is not absolute contraindication; should be preceded by neurological assessment and documentation. Better avoided in acute crisis.
- Lidocaine, bupivacaine, and procaine are considered safe.

Maintenance

- Inhalational anesthetics are considered safe, incl NO
- Avoid anemia and hypoglycemia
- Normothermia

Extubation

- Evaluate consciousness to exclude neurotoxicity.
- Evaluate muscle power for possibility of ventilatory support.

Adjuvants

- Check websites for safe drug lists: http://www.porphyriafoundation.com, http://porphyria.eu/.

Postoperative Period

- Monitor for up to 5 days.
- Avoid metoclopramide as antiemetic, use chlorpromazine or ondansentron.
- Avoid diclofenac.
- Repeated detailed neurological assessment.
- Oral/IV dextrose to prevent hypoglycemia.

Anticipated Problems/Concerns

- Development of acute crisis:
  - Management: Withdraw triggers, pain control, oral/IV dextrose, IV hematin (3 mg/kg for 4 days in a large vein over 30 min or in central line), or IV heme arginate, to replenish heme pool and inhibit ALA synthase.
  - Peak expiratory flow rate for early detection of respiratory failure.
  - Monitor electrolytes and seizure activity.

Acute Respiratory Distress Syndrome

Jason C. Brainard | Maurizio Cereda

Risk

- Recent data estimates the incidence at 190,000 cases per year in USA. True incidence is unknown due to difficulty in defining the disease and making the diagnosis.
- Represents 10.4% of all ICU admissions and 23.4% of pts requiring mechanical ventilation per a recent 2016 publication.
- Mortality rates vary from 25% to 40%. Mortality rate is strongly influenced by associated conditions (e.g., higher when associated with sepsis, liver disease, and advanced age; lower with trauma, transfusion-related lung injury, drug overdose, or other reversible conditions).

Perioperative Risks

- Increased risk of sudden and profound hypoxia secondary to loss of alveolar recruitment
- Worsening resp status due to effects of anesthesia and surgery
- Difficult balance between maintaining adequate intravascular volume and avoiding pulm edema and right heart strain leading to decreased oxygenation and ventilation

Worry About

- Maintaining required PEEP during pt transport with Ambu bag or Mapleson circuit. Transport with ICU ventilator may be necessary.
- Inability of standard OR ventilators to deliver required minute ventilation, high inspiratory pressures, and inverse ratio ventilation.

Overview

- Berlin definition of ARDS (published in 2012) requires each of the following criteria:
  - Timing—onset within 1 week of a known clinical insult or new or worsening resp symptoms.
  - Chest imaging (CXR or CT)—bilateral opacities; not fully explained by effusions, lobar/lung collapse, or nodules.
  - Origin of edema—resp failure not fully explained by cardiac failure or fluid overload, need objective assessment (ECHO) to exclude cardiogenic pulm edema.
  - Oxygenation:
    Mild—PaO_2/FiO_2 200 to 300 mm Hg with PEEP or CPAP ≥ 5 cm H_2O.
    Mod—PaO_2/FiO_2 100 to 200 mm Hg with PEEP ≥ 5 cm H_2O.
    Severe PaO_2/FiO_2 ≤ 100 mm Hg with PEEP ≥ 5 cm H_2O.
- Though classically defined by severe hypoxia, also can be associated with profound hypercarbia due to elevated alveolar dead space.
- Associated with low pulm compliance and lung volumes (due to alveolar edema and atelectasis) and, in certain pts, with abnormally low chest wall compliance.
- Most deaths are from sepsis or multisystem organ failure (more rarely from refractory hypoxemia or hypercarbia).

Etiology

- Direct or indirect lung injury leading to acute inflammatory alveolar damage characterized by increased microvascular permeability with interstitial and alveolar edema and often progressing to fibrosis.
- Precipitants include aspiration, pneumonia, sepsis, massive transfusion, pancreatitis, trauma, ischemia-reperfusion, drugs and alcohol, CNS injury, air embolism, cardiopulmonary bypass, genetic predisposition.
- Mechanical ventilation may worsen lung injury through alveolar overdistention and shear forces from cyclic opening and closing of collapsed alveoli (ventilator-associated lung injury).

Usual Treatment

- ARDS net trial (2000) demonstrated reduced mortality in pts ventilated with lower tidal volumes and decreased airway plateau pressures. Aim for TVs 6 to 8 mL/kg (ideal body weight) and plateau pressure ≤30 cm H_2O. Maintain ventilation with increased resp rate.
- Do not attempt to correct hypercarbia. Instead, direct ventilation toward maintaining acceptable pH (>7.15). There is no evidence that moderate acidemia is harmful in pts who do not have specific contraindications (i.e., intracranial hypertension).
- Apply PEEP to maintain alveolar recruitment and achieve O_2 saturation ≥88%. No consistent evidence shows benefit from high versus moderate levels of PEEP. Higher PEEP is reasonable if pt remains hemodynamically stable. Monitor for auto-PEEP (air trapping).
- Choose the lowest tolerated FiO_2 (actual FiO_2 associated with oxygen toxicity is unknown).
- Consider sedation, analgesia, and fever reduction to improve ventilator synchrony and decrease O_2 consumption.
- ACURASYS trial (2010) demonstrated reduced mortality in pts with severe ARDS (PaO_2/FiO_2 ratio ≤120) paralyzed with cisatracurium for 48 h.
- PROSEVA trial (2013) demonstrated reduced mortality in pts with severe ARDS (PaO_2/FiO_2 ratio ≤150) treated with intermittent (16 h/day) prone positioning. Prone positioning improves ventilation-perfusion matching of dependent (posterior) alveoli.
- OSCILLATE trial (2013) demonstrated possible increased mortality with HFOV.
- Potential role of ECMO and specifically veno-venous ECMO in treatment of most severe cases, but strong evidence and guidelines for use not yet established
- Role of steroids, incl pt selection, timing, and dosing, remains unclear.
- Diagnose and treat precipitating and underlying conditions.
- Prevent and treat fluid overload.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm Htn RV and/or LV dysfunction Septic shock Fluid overload	Hypotension, ↓ renal and hepatic function, metabolic acidosis	Cool extremities, narrow pulse pressure, JVD, RV heave, peripheral edema, enlarged liver, abdominal distension	PA cath, ECHO, mixed venous oxygen saturation
RESP	Ventilator-associated lung injury Pneumothorax	Increased airway pressures, impaired resp mechanics, worsening blood gases	Bilateral rhonchi, crackles decreased or absent breath sounds, tracheal deviation	CXR, CT chest
ID	Ventilator associated pneumonia Line sepsis	Increased WBC/bandemia, new infiltrates, hypotension	Fever, purulent secretions	CXR, CT chest, blood and sputum culture
GI	Hemorrhage	Decreased Hct	Melena, bloody NG output	Esophagogastroduodenoscopy
GU	Acute kidney injury	Oliguria, increased creatinine	Peripheral edema	Serum creatinine
MS	Prolonged weakness Diaphragm atrophy	Pharmacologic paralysis, high-dose steroids, sepsis, prolonged ventilation	Polyneuropathy, myopathy	Electromyography, muscle biopsy

Key References: Bernard GR: Acute respiratory distress syndrome, *Am J Respir Crit Care Med* 172:798–806, 2005; Guldner A, Kiss T, Serpa Neto A, et al: Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers, *Anesthesiology* 123:692–713, 2015.

Perioperative Implications

Preoperative Preparation

- Assess current ventilator mode and settings in ICU and review last blood gas.
- Assess pt preop hemodynamic and intravascular volume status.
- Use PEEP valve for pt transport or consider transportation to OR on ICU ventilator.
- Consider use of ICU ventilator intraop with concurrent total intravenous anesthesia, particularly when very high minute ventilation and airway pressures are required.
- Maintain comparable levels of mean airway pressure and minute ventilation when transitioning between modes or ventilators and when paralyzing the pt.

Airway

- Avoid suctioning and unnecessary ETT disconnection. Even transient loss of PEEP may result in lung derecruitment and severe hypoxemia that is difficult to correct.

Monitoring

- In most severe pts, PA cath or intraop TEE may be helpful in estimating intravascular volume status and ventricular function.
- Closely monitor airway pressures (peak, plateau, mean airway), tidal volumes, minute ventilation.
- Monitor oxygen saturation and obtain frequent blood gases. $ETCO_2$ may not be representative of arterial PCO_2 due to increased dead space.

Preinduction/Induction

- Expect increased shunt with elevated FiO_2 and/or PEEP requirements due to loss of hypoxic pulm vasoconstriction caused by anesthetics.
- Prepare for worsening resp mechanics and decreased ventilation in spontaneously breathing pt given anesthetics, narcotics, or muscle relaxants.
- Prepare for elevated airway pressures with supping positioning and increased risk of aspiration (suction stomach via NG/OG tube before lying supine).

Maintenance

- Attention to fluid management to avoid worsening pulm edema and right heart strain from excessive fluid administration.
- Consider treating worsening hypoxemia with recruitment maneuvers (apply continuous airway pressure of 40 to 50 cm H_2O for 40 s) followed by increased PEEP setting.

Postoperative Period

- Continued careful monitoring of hemodynamic and volume status.
- Reassess ventilator settings and reduce FiO_2 and airway pressures as tolerated.

Anticipated Problems/Concerns

- Sudden and profound hypoxia can occur if lung recruitment is lost during transport, movement, positioning, or surgical retraction.

Addison Disease

Miguel A. Yaport | Lee A. Fleisher

Risk

- Prevalence 1:100,000 persons
- M:F ratio: 1:1.8

Perioperative Risks

- CV instability, labile BP, hypotension, shock
- Hypovolemia, hyperkalemia, cardiac dysrhythmia
- Limited response to vasopressors

Worry About

- N/V and diarrhea leading to dehydration, electrolyte imbalances, and acid/base disorder.
- Acute adrenal insufficiency leading to hypotension and refractory distributive shock.
- Cardiac dysrhythmia caused by hyperkalemia.
- Hypoglycemia and uremia, muscle weakness, decreased level of consciousness.

Overview

- Addison disease is a specific type of adrenal insufficiency due to a primary inadequate production of glucocorticoids, mineralocorticoids, and androgens by the adrenal glands.
- Nonspecific symptoms and insidious disease progression often result in a delay in diagnosis until after the development of addisonian crisis after a significant stressor or illness.
- Pts often present with chronic fatigue as well as GI disturbances; pain, nausea/vomiting, diarrhea, and may develop episodes of mental status changes.
- Diagnosed by cosyntropin stimulation test; administration of cosyntropin will stimulate ACTH secretion by pituitary but will not increase cortisol levels.
- May be associated with other autoimmune conditions
- Drugs that inhibit cortisol biosynthesis will trigger addisonian crisis; etomidate, antifungals.
- See also Adrenal Insufficiency, Acute or Secondary.

Etiology

- 80% of cases are due to immune destruction of the adrenal cortex by autoantibodies.
- Most often an antibody against 21-hydroxylase. Presence of these autoantibodies may predate development of clinical disease by decades.
- Other causes include infection (TB, histoplasma, HIV, CMV), cancer metastases, bilateral adrenalectomy, sepsis especially meningococcal, hemorrhage, and infiltrative diseases.

Usual Treatment

- Lifelong hormone replacement therapy. Glucocorticoid: Prednisone 3 to 5 mg daily and hydrocortisone 5 to 25 mg divided into 2 to 3 times/d. Mineralocorticoid: Fludrocortisone 0.05 to 0.2 mg daily. Men do not need androgen replacement as their androgens are produced in the testes. Women may benefit from DHEA 25 to 50 mg daily.
- Acute adrenal insufficiency treatment: Supportive treatment with rapid isotonic solution, hydrocortisone IV 100 mg q8h, and electrolyte replacement
- See Adrenal Insufficiency, Acute or Secondary for procedure-adjusted stress dose regiments

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hyponatremic hypovolemia, hypotension, CV instability	Postural symptoms, salt cravings, weight loss	Low BP, orthostatic changes, dry mucous membranes, poor cap refill	CBC, chemistry, BUN/Cr, ACTH stimulation test
MS	Muscle weakness, high urea	Fatigue, anorexia, N/V	Decreased level of consciousness, potentiation of neuromuscular blockade	BUN, nerve stimulator
GI	Dehydration, pH disturbances	Abdominal pain, N/V, diarrhea	See CV	Chemistry panel
ENDO	Hyperkalemia, hyponatremia, hypoglycemia	Weakness, cardiac dysrhythmia, depression	Inability to stand from seated position, flat affect	Chemistry panel, ECG
DERM	Excess corticotropin release	Vitiligo, changes in skin color	Hyperpigmentation	ACTH stimulation test

Key References: Jung C, Inder WJ: Management of adrenal insufficiency during the stress of medical illness and surgery, *Med J Aust* 188(7):409–413, 2008; Michels A, Michels N: Addison disease: early detection and treatment principles, *Am Fam Physician* 89(7):563–568, 2014.

Perioperative Implications

Perioperative Preparation

- Glucocorticoid and mineralocorticoid levels should be checked and optimized.
- Stress dose steroid coverage in periop period.
- Measure electrolytes, BUN, creatinine, glucose, and correct abnormalities.
- Ensure normovolemia.

Monitoring

- Standard ASA monitors.
- Arterial line and central line may be necessary in acute adrenal insufficiency.
- Na^+, K^+, pH, glucose.

Airway

- No specific recommendations

Premedication/Induction

- Avoid etomidate; may be associated with increased mortality in this population.

Maintenance

- Anticipate hypotension; dose adjustment may be required for muscle relaxants.

Extubation

- Appropriate muscle relaxant reversal must be achieved.

Adjuvants

- Glucose/dextrose, pressor drips, fluids, hormone replacement.

Postoperative Period

- Monitor pts for acute adrenal insufficiency, high-risk period.
- Stress dose replacement may be required several days postop.
- Assess pts for complications of steroid use; ulcers, infection, poor wound healing, glucose intolerance.

Anticipated Problems/Concerns

- Previously undiagnosed Addison disease presenting as unrecognized acute adrenal insufficiency resulting in a delay of adequate management.
- Vasopressor-resistant hypotension, acute mental status changes; confusion, lethargy, coma, delayed emergence.
- Refractory hypotension should alert clinicians toward adrenal insufficiency.
- Glucocorticoid replacement and supportive care are the mainstays of treatment in periop period.

Adrenal Insufficiency, Acute or Secondary

Charles B. Hantler | Clare H. Ridley

Risk

- Risk of adrenal insufficiency: 1/1000 to 1/10,000 (if steroids used in prior y).
- With steroids >20 mg/d (cortisol equivalent), >7 to 14 d within 1 y (large variability in pt response to dose, route(s), duration and timing of prior steroid use).
- Clinical signs worsen with stress, such as trauma, surgery, or infection.

Perioperative Risks

- Increases CV instability, fever, CHF, lyte abnormalities.
- High cardiac output failure, or low-output state (hypovolemia) with signs of tissue hypoperfusion.
- Often evidence of systemic vasodilation with decreased reactivity to fluid or vasopressors.

Worry About

- GI: N/V, dehydration (adrenal crisis).
- Anemia; neutropenia with androgen deficiency: Rare.
- CV response; decreased SVR, decreased left ventricular stroke work index and decreased vascular responsiveness to maintain perfusion pressure; steroids necessary for blood vessel. responsiveness to catecholamines.
- Hyperkalemia with or without hyponatremia (usually aldosterone deficiency); hypoglycemia, acidosis, hypercalcemia, and anemia; cardiac conduction abnormalities.

Overview

- Adrenal insufficiency results from inadequate production of glucocorticoids (cortisol), mineralocorticoids (aldosterone), and/or androgens.
- Adrenal insufficiency can be acute or chronic, primary or secondary.
- Primary adrenal insufficiency: Associated with >90% destruction of the adrenal glands and deficiency in both cortisol and aldosterone.
- Secondary adrenal insufficiency develops from the HPA axis dysfunction or failure.
- Inadequate mineralocorticoid production can cause hyperkalemia, hyponatremia, and metabolic acidosis, with or without signs of dehydration.
- Inadequate glucocorticoid production may cause signs of hemodynamic instability (hypotension) during stress.
- Acute adrenal (Addisonian) crisis may develop in periop period when another stress is present (infection, hemorrhage, or major or prolonged surgery), leading to hyponatremia, hyperkalemia, dehydration, abdominal symptoms, and shock. (See also Addison Disease.)
- May present without symptoms until stress.
- Adrenals secrete around 5 to 20 mg of cortisol daily at baseline, 150 mg in periop period, and up to 300 mg during the maximal stress.
- Recovery of the adrenal function may take up to 9 to 12 min after withdrawal of exogenous steroids (>20 mg/d of prednisone × 5 d) and the supplementation of daily cortisol production is advised.
- Critical illness may produce a state of relative adrenal dysfunction. Critically ill pts may appear to have sepsis without an obvious source of infection.
- Chronic adrenal insufficiency from use of steroids in prior year may manifest as weakness, fatigue, nausea, emesis, weight loss, and a variety of psychiatric disturbances.

Etiology

- Primary adrenal insufficiency: Autoimmunity, infection (TB, HIV, CMV), hemorrhage (meningococcal sepsis, trauma, HIT, anticoagulants), drugs (etomidate, antifungals), infiltration (sarcoidosis, amyloidosis, histoplasmosis), metastatic disease (breast, lung, melanoma).
- Secondary adrenal insufficiency: Glucocorticoid therapy (systemic, inhaled, topical), drugs (fluticasone, megestrol, medroxyprogesterone, ketorolac tromethamine), brain injury, pituitary or hypothalamic tumors.
- Pts on corticosteroids (even topical) have a reduced basal secretion of cortisol and a reduced response to stress as a result of negative feedback of the HPA axis.
- Workup: Screening test) AM cortisol: Should be greater than 10 mg/dL; if lower, Cortisol stimulation test (ICU setting; suspected perioperative hypocortisolism should be treated empirically): The baseline cortisol level is measured. Synthetic ACTH at a dose of 250 µg IV is administered, and plasma cortisol levels are measured at 30 and 60 min. Usually the plasma cortisol rises at least 9 mg/dL or to a total of at least 18 g/dL at 60 min.

Usual Therapy

- Mild stress (e.g., colonoscopy): 25 mg/m^2 of hydrocortisone IV on day of surgery only
- Moderate stress (e.g., appendectomy, lobectomy): 50 to 75 mg/m^2 or about 2 × normal production on day of surgery, taper quickly to usual dose over 1 to 2 d (usually a loading dose of 50 with induction and then 25 mg/m^2 divided every 4 h IV or every 8 h oral)
- Major stress (major trauma, major surgery): 100 mg/m^2 of hydrocortisone (if IV divided Q4, if oral divided Q8) on day of surgery, taper quickly to usual dose over 1 to 2 d (usually a loading dose of 50 with induction and then 50 mg/m^2 divided every 4 h IV or every 8 h oral)
- Septic shock in pts who remain hypotensive despite adequate administration of fluids and vasopressors: 50 mg/m^2 (for adults 50 mg) IV q 6 h or 100 mg/m^2 (for adults 100 mg) IV q 8 h for at least 7 d, then taper. No mortality benefit shown, but vasopressor requirements decreased with treatment.
- Early ARDS: Controversial benefit of steroids. Potential benefit in early ARDS (<72 hours after onset): 1 mg/kg methylprednisolone for more than 14 days, followed by taper to usual dose. Increased mortality in late ARDS (>14 days after onset).
- Aldosterone deficiency (manifested by abnormalities in Na^+/K^+ or dehydration): Fludrocortisone (Florinef), 50 to 200 µg/d. Consider concomitant furosemide in pts with CHF.
- Only one very small RCT examines the benefit of supplemental steroids in pts undergoing GA for invasive procedures (Glowniak, 1997, PMID 9037222). The 18-participant study showed no clear benefit but was at high risk of bias; was underpowered to identify any possible benefit.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dehydration, hypotension, high-output failure Fluid/Pressor unresponsive shock	Postural symptoms, fatigue; Wt loss, Hx of surgery on adrenals, pituitary	Low BP, postural drop, signs of dehydration	Hct, BUN/Cr, adrenal, AM cortisol, ACTH stimulation CRH stimulation, insulin tolerance, metyrapone test
RESP	CHF (high or low output)	DOE, SOB	S_3, rales	CXR
GI	Dehydration, nausea, emesis	Appetite, Hx of emesis	See CV	Lytes
HEME	Anemia, neutropenia		Hyperpigmentation (excess corticotropin)	Hct, WBC
CNS	Depression, confusion, psychosis			Reverses with replacement
MS	Weakness, potentiation of neuromuscular blockage			Nerve stimulator

Key References: Marik P: Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: consensus statements from an international task force by the ACCCM, *Crit Care Med* 36(6):1937–1949, 2008; Schwartz J: Endocrine function. In Barash PG, editor: *Clinical anesthesia,* ed 6, Philadelphia, PA, 2009, Lippincott Williams and Wilkins, pp 1279–1304.

Perioperative Implications

Preoperative Preparation

- Consider perioperative steroid coverage if benefits outweigh risks if high index of suspicion of adrenal depression (e.g., prednisone >20 mg/d × 5 d).
- Correct lyte abnormalities, hypoglycemia, and dehydration prior to elective surgery.
- Fludrocortisone with resistant aldosterone (K^+ and Na^+) abnormalities; glucose for hypoglycemia

Monitoring

- ECG for signs of abnormal conduction (QRS duration, u waves with hypokalemia)
- Consider CVP, PCWP, or TEE if fluid/lyte and hemodynamic abnormalities
- Sodium, potassium, bicarbonate, and glucose

Airway

- None

Premedication/Induction

- Consider volume status with regard to hydration and choice of agents. Have vasopressors available.

Maintenance

- No hemodynamic instability; follow with lytes and glucose as needed.
- Hemodynamic instability (hypotension):
  - R/O other causes, then consider hydrocortisone hemisuccinate, 25-100 mg IV, then 100 mg q 12-24 h for 2 or 3 d. In septic shock, consider 200-300 mg IV daily in divided (q 4 h) doses.
  - Fluid resuscitation as needed.

Extubation

- Possible potentiation of nondepolarizing muscle relaxants with use of high-dose steroids; ensure adequate muscle relaxant reversal.

Adjuvants

- Glucose, fluids, careful monitoring of temperature to avoid hyperthermia.

Postoperative Period

- Stress-dose steroids possibly required several days postop.
- High steroid doses may be associated with decreased wound healing and immunosuppression with increased infection risk. Unclear risk if used short-term.
- Consider prolonged steroid coverage if severe stress continues (e.g., severe trauma with multiple operations).

- Mineralocorticoid administration as needed; many glucocorticoids have significant mineralocorticoid action (hydrocortisone, prednisone, prednisolone). Methylprednisolone and dexamethasone have no mineralocorticoid activity.

Anticipated Problems/Concerns

- Severe resistant hypotension, hyperthermia, and CNS abnormalities, such as confusion, coma, lethargy, may occur intraop or postop and may be unpredictable.
- Syndrome may occur in severely traumatized pts without history of steroid use, with clinical picture of sepsis and associated abnormalities in adrenal function; Rx is life saving.

Alagille Syndrome

Christopher J. Cullom | Alan David Kaye | Amit Prabhakar

Risk

- Also known as syndromic bile duct paucity
- Affects cardiac, musculoskeletal, ocular, facial, and neurodevelopmental systems
- Most common inherited disorder that causes chronic liver disease in children
- 1:100,000 births with equal gender incidence

Perioperative Risks

- Cardiac congenital anomaly and hemodynamic instability
- Coagulopathy
- Liver dysfunction
- Musculoskeletal injury from positioning

Worry About

- Vertebral abnormalities
- Facial anomalies
- Ocular abnormalities
- Vitamin deficiencies: A, D, E, K
- Neurologic deficits (neuropathy, mental retardation, cerebellar defect)

Overview

- In addition to liver involvement, includes congenital cardiac disease (97%), dysmorphic face (96%), ocular abnormalities (78%), vertebral anomalies (51%), and kidney malformation (40%).
- Disease ranges from mild cholestasis to progressive liver failure.
- Liver involvement results in the loss of intralobar ducts over months to years.
- Elevated serum bile acids, conjugated bilirubin, alkaline phosphatase, and GGT typically seen.
- Malnutrition and growth failure is common, leading to delayed pubertal development.
- Malnutrition may lead to protuberant abdomen, making pts more prone to regurgitation.
- Ineffective absorption of dietary lipids, essential fatty acids, fat-soluble vitamins.
- Vitamin deficiencies: vitamin K (coagulopathy), vitamin D (rickets), vitamin E/A (retinopathy and neuropathy).
- Vitamin K deficiency and liver dysfunction lead to prolonged PT and PTT as well as thrombocytopenia.
- Cardiac abnormalities: Pulm vascular stenosis (most common with up 90% pts), tetralogy of Fallot, truncus arteriosus, patent ductus arteriosus, VSDs.
- Facial characteristics: Prominent forehead, hypertelorism, saddle or straight nose.
- Vertebral anomalies: Butterfly vertebrae (splitting of the bodies sagittally), spina bifida, fusion of adjacent vertebrae.
- Ocular abnormalities: Posterior embryotoxon, microcornea, macular dystrophy.
- Posterior embryotoxon progresses to glaucoma in 50% of pts.
- Neurologic effects: Cerebellar ataxia and peripheral neuropathy usually due to vitamin E and A deficiency. Mental retardation is also associated with the syndrome.
- There is a 12–14% risk of spontaneous intracranial bleed.
- Renal dysplasia found in 40% of pts.
- Halothane should be avoided as it has a myocardial depressant effect, lowering hepatic blood flow.
- Perfusion pressure to liver and kidney should be maintained with periop hydration and blood pressure control.

Etiology

- Characterized by chronic cholestasis, decreased number of interlobar bile ducts, and variety of congenital malformations
- Autosomal dominant mode of transmission involving mutation in *JAG1* gene

Usual Treatment

- Pts typically require procedures to correct various congenital abnormalities, biliary diversion, and ileal exclusion; may also require biopsy or liver transplantation.
- Symptomatic relief of pruritus can be provided with rifampicin or ursodeoxycholic acid.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm arterial stenosis, tetralogy of Fallot, truncus arteriosus, patent ductus arteriosus	Dizziness Palpitations	Murmur	ECG, ECHO
RENAL	Renal dysplasia			Cr, GFR, UA
GI	Cholestasis, liver failure/cirrhosis	Pruritus	Hepatomegaly, splenomegaly	LFTs, abdominal CT
HEME	Coagulopathy			CBC, PT, PTT, INR
MS	Osteodystrophy		X-ray of extremities/DXA	
NEURO	Intracranial hemorrhage, vertebral anomalies		Cervical spine evaluation	X-ray of vertebrae
HEENT	Xerophthalmia, posterior embryotoxon		Ophthalmoscopic exam	
GENERAL	Facial abnormalities		Prominent forehead, hypertelorism	

Key References: Choudhry D, Rehman M, Schwartz R, et al.: The Alagille's syndrome and its anaesthetic considerations, *Paediatr Anaesth* 8(1):7–82, 1998; Subramaniam K, Myers L: Combined general and epidural anesthesia for a child with Alagille syndrome: a case report, *Paediatr Anaesth* 14(9):787–797, 2004.

Perioperative Implications

Preoperative Preparation

- Assessment of airway and neck mobility.
- Standardized bleeding history as well as clotting profile.
- ECHO and ECG to prepare for cardiovascular abnormalities.
- Evaluate neurologic status.
- Avoid succinylcholine if peripheral neuropathy is present.

Monitoring

- Avoid invasive monitoring whenever possible due to bleeding risk.

Airway

- Neck mobility may create difficulties.

Preinduction/Induction

- Potential usage of rapid sequence induction as pts are prone to regurgitation.
- Careful positioning due to osteodystrophy.
- Eye care paramount due to vitamin A deficiency and dry eyes.

Maintenance

- Use of sevoflurane or isoflurane as they have less myocardial depressant effects and preserve hepatic blood flow.
- Blood pressure control and adequate hydration to maintain liver perfusion.
- Use of cisatracurium for muscle relaxation as metabolism is independent of liver and renal function.

Extubation

- Usual criteria

Postoperative Period

- Careful positioning in PACU

Regional Anesthesia

- Used cautiously due to potential risk of bleeding and vertebral anomalies, but not contraindicated

Anticipated Problems/Concerns

- Cardiac pathology/anomalies
- Hemodynamic instability and hypotension
- Airway difficulty due to vertebral anomalies
- Coagulopathy
- Nerve and soft tissue injury due to positioning
- Liver and renal dysfunction
- Ocular abnormalities requiring extra eye protection
- Various neurologic abnormalities to be aware of before anesthesia

Alcohol Abuse

Scott C. Watkins

Risk

- Incidence in USA: 10% of Americans, incl physicians, will abuse alcohol at some point in their lives.
- 1:5 surgical pts has some form of alcohol use disorder.
- Third leading cause of death and disability, incl 30% of traffic fatalities.
- Male gender and family Hx major are risk factors.

Perioperative Risks

- Severe malnutrition as significant as ETOH-induced end-organ injury.
- Risk of Htn, CVA, diabetes, GI disease.
- Liver is the most severely affected organ.
- Dilated cardiomyopathy.
- Withdrawal symptoms can be life threatening.

Worry About

- Concomitant use of other drugs: Amphetamines, cocaine, benzodiazepines.
- Affects of chronic smoking, such as COPD and emphysema.
- Vasopressor effect of ETOH may cause Htn.
- Acute withdrawal and delirium tremens are life-threatening complications. Symptoms caused by sympathetic stimulation can range from mild tremors to electrolyte disturbances, seizures, and death.

Overview

- Disease characterized by addiction (compulsion and craving despite consequences) to alcohol.
- Clinical syndromes related to direct effect of ETOH and secondary adaptive response to excess ETOH exposure.
- ETOH rapidly absorbed and metabolized.
- Hepatic dysfunction usually takes 10 to 15 y to develop.
- Cirrhosis may develop after 1 or more acute episodes.

Etiology

- Unknown: Likely mutifactorial with environmental, genetic, and psychosocial components

Usual Treatment

Recovery involves some or all of the following:

- Detoxification: Inpatient, residential, day treatment, or outpatient.
- Evaluation for comorbid psychiatric disorder.
- Referral to Alcoholics Anonymous or other alcohol programs.
- Pharmacotherapy to help with withdrawal and prevent relapse:
  - Disulfiram (Antabuse): Acetaldehyde dehydrogenase inhibitor.
  - Naltrexone (Revia): Pure opioid receptor antagonist, blunts ETOH's pleasurable effects and reduces craving. Available as monthly IM depot. May interfere with opioids prescribed for periop pain.
  - Acamprosate (Campral): A synthetic derivative of homotaurine, a structural analog of GABA. Decreases excitatory glutamatergic neurotransmission during alcohol withdrawal.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Cardiomyopathy, arrhythmias, hypertension	Orthopnea, nocturnal urination, coughing, and leg swelling	Dyspnea BP lying and standing HR	ECG, ECHO Lytes
GI	Erosive gastritis, decreased lower esophageal sphincter tone, hepatic cirrhosis, acute hepatitis, pancreatitis, fatty liver	Hx of bleeding, easily bruised, anorexia, N/V	Ascites, jaundice Hepatomegaly, "spider" angiomas Abdominal pain Abdominal pain, hepatomegaly	Upper endoscopy, stool guaiac LFTs Serum amylase Mg^{2+}, K^{+}
ENDO	Gynecomastia, testicular atrophy, irregular menses			
HEME	Leukopenia, anemia, thrombocytopenia			CBC with differential
CNS	Wernicke's syndrome Korsakoff's syndrome Peripheral polyneuropathy Cerebellar degeneration	Amnesia, impaired reasoning	Sixth nerve palsy, ataxia Distal numbness and paresthesias Unsteady gait	MRI or CT scan, CNS exam

Key References: Jones K, Neumann T, Spies C: Perioperative management of patients with alcohol, tobacco and drug dependency, *Curr Opin Anaesthesiol* 23(3):384–390, 2010; Moran S, Isa J, Steinemann S: Perioperative management in the patient with substance abuse, *Surg Clin North Am* 95(2):417–428, 2015.

Perioperative Implications

Preoperative Preparation

- All pts should be screened for substance use routinely.
- Gastric prophylaxis.
- Blood ETOH and toxicology screen if indicated.

Monitoring

- Standard ASA monitors.
- Consider invasive monitors for cardiomyopathy, hepatic dysfunction, and/or end-organ compromise.

Airway

- Consider full stomach in acute intoxication.

Preinduction/Induction

- Consider long-acting benzodiazepine, barbiturate, or α_2-adrenergic agonist.
- Anesthetic doses increased in chronic disease.
- Decreased dose in acute intoxication.
- Rapid sequence in acute intoxication.
- Consider Rx of nutritional/metabolic deficiencies.

Maintenance

- Requirements vary by age, general health, nutrition and hydration states, concomitant disease.
- Acute intoxication may decrease MAC requirement and lower BIS monitoring values.

Extubation

- Ensure return of airway reflexes.

Postoperative Period

- Provide adequate analgesia in PACU.
- Anxiety can worsen withdrawal symptoms.
- Withdrawal syndrome may develop within 6 to 8 h; treat based on symptoms—benzodiazepines for agitation and seizures, alpha-2-agonists for autonomic signs and neuroleptics or olanzapine for hallucinations.
- DTs develop in 5% of pts in withdrawal.
- Ten percent mortality secondary to hypotension, electrolyte disturbances, seizures and/or arrhythmias.

Adjuvants

- Long-term consumption of ETOH impairs hepatic metabolism.
- Short-term consumption inhibits drug metabolism.
- Polyneuropathy is a relative contraindication to regional anesthesia.
- Consider periop clonidine patch.

Anticipated Problems/Concerns

- Recognition and treatment of withdrawal important, as significant mortality occurs if inadequately treated.

Allergy

Jerrold H. Levy

Risk

- Incidence in USA: 5% of adults are allergic to one or more drugs.
- During surgery, the risk of anaphylaxis is ~1:2500 to 1:20,000 depending on the agent, with a mortality rate of 4%.
- Females > males (1.6:1).

Perioperative Risks

- Intensity of Sx variable: From an isolated cutaneous eruption to CV collapse and death.
- CV, cutaneous (incl angioedema), resp systems are mostly involved.
- Increased morbidity and hospitalization time if intensive care required.

Worry About

- Pt's Hx: Knowledge of prior allergic event leads to avoiding drugs or other components involved; however pt may not know.
- Hypotension/shock, bronchospasm, and angioedema may become life-threatening events.

Overview

- IgE anaphylaxis (type I immediate hypersensitivity reaction): Adverse response of host; mediated by antibodies, the antigen bridges with two IgE on the surface of basophils and mast cells; can be reproduced if foreign substance is reinjected. However, IgG reactions with complement may manifest similarly.
- Anaphylactoid reactions or histamine release: Describes a clinically indistinguishable syndrome probably involving similar mediators but not mediated by IgE antibody and not necessarily requiring previous exposure to the inciting substance, associated with vancomycin, benzylisoquinolinium-derived muscle relaxants, but term should be avoided.

Etiology

- Clinical history of allergy or perianesthetic allergic reaction considered to put pt at increased risk for a reaction from neuromuscular blocking agents and induction agents

Usual Treatment

- Preventive therapy with corticosteroids and antihistamines is of unproven value.
- Severe allergic therapy: Stop antigen, maintain the airway with 100% O_2 and intubate if necessary; discontinue all anesthetic drugs, volume expansion, epinephrine (5 to 10 µg IV boluses as starting doses and titrate upward), antihistamines, β-sympathomimetic in case of bronchospasm, arginine vasopressin and/or norepinephrine for refractory shock, phosphodiesterase inhibitors for RV dysfunction, airway evaluation prior to extubation, ICU observation.

Assessment Points

System	Effect	PE	Test
CV	Hypotension, tachycardia, dysrhythmias Pulm Htn Cardiac arrest	BP	ECG PA pressure
RESP	Dyspnea, sneezing Coughing, wheezing Laryngeal edema Fulminant pulm edema Acute respiratory failure	Chest exam	CXR PA cath $ETCO_2$ ABGs
DERM	Urticaria, flushing Perioral, periorbital edema	Skin exam	

Key References: Levy JH, Adkinson Jr NF: Anaphylaxis during cardiac surgery: implications for clinicians, *Anesth Analg* 106:392–403, 2008; Sampson HA, Muñoz-Furlong A, Bock SA, et al: Symposium on the definition and management of anaphylaxis: summary report, *J Allergy Clin Immunol* 115(3):584–591, 2005.

Perioperative Implications

Preoperative Preparation

- Prick tests, intradermal testing: Anesthetic drugs (NM blocking agents)
- Most of the allergic reactions are unexpected. In case of established allergy, those drugs or latex should be strictly avoided.

Monitoring

- Routine.
- If major anaphylaxis occurs, consider pulm and radial arterial catheterization to guide therapeutic interventions.

Airway

- None, except specific care for the asthmatic pt

Preinduction/Induction/Maintenance/Extubation

- Slow injection of drugs, use burette for antibiotics. Avoid histamine-releasing drugs in high-risk pts.

Anticipated Problems/Concerns

- For each pt who has a periop allergic reaction, consider evaluation 1 mo after with skin testing, antigen-specific IgE level dosage (ELISA).
- Measure tryptase if there is an anaphylactic reaction within 1 to 2 h of reaction, then 24 h later to support diagnosis.
- Latex allergy should be considered. Healthcare workers are at greater risk, and Hx has to be evoked at the preanesthetic evaluation.

Alpha$_1$-Antitrypsin Deficiency

Paul S. Myles

Risk

- One of the most common inherited disorders (1 in 2500 in case of European ancestry; uncommon in Asians)
- Less than 10% of individuals with AAT deficiency are currently identified.
- AAT deficiency is the most common genetic cause of liver disease in neonates and children.
- About 1% to 5% of pts with COPD have AAT deficiency.
- Approximately 15% of adults with AAT deficiency develop liver cirrhosis.

Perioperative Risks

- Dynamic hyperinflation (air-trapping or auto-PEEP) with positive pressure ventilation, leading to hypotension and CV collapse
- Resp failure
- Hepatic impairment
- Poor wound healing (panniculitis)

Worry About

- Missed or incorrect (e.g., asthma) diagnosis
- Liver cirrhosis
- Glomerulonephritis and nephrotic syndrome
- Gastrointestinal complications incl ascites
- Panniculitis
- Vascular disease

Overview

- AAT is secreted in the liver as the most abundant of the serine protease inhibitors (serpins), with over 100 genetic variants of AAT identified.
- Panacinar pulm emphysema is the most common manifestation, and is the major cause of disability and death.
- Most commonly presents with slowly progressive dyspnea in mid-life, typically 2 to 3 decades earlier than do smokers with emphysema and normal AAT levels.
- Some pts present with otherwise unexplained hepatic dysfunction.
- Cigarette smoking greatly accelerates the progression of emphysema in AAT deficiency.
- AAT deficiency may present early after birth as neonatal jaundice and hepatitis, in infancy as cholestatic jaundice, or in children as liver cirrhosis or failure.
- AAT deficiency is the most common condition requiring liver transplantation in children.

Etiology

- Autosomal recessive disorder; the most common form is associated with allele Z, or homozygous PiZ (ZZ).
- Emphysema results from the unimpeded neutrophil elastase destruction of the lung alveolar basement membranes.
- Liver disease results from the accumulation of unsecreted AAT protein within the hepatocyte.
- Nonsmokers with the homozygous Z phenotype have minimal symptoms and an almost normal life span.
- Serum levels of AAT in the deficiency states are 10% to 15% of normal levels.
- Emphysema develops in most (but not all) individuals with serum levels less than 9 µmol/l; levels greater than 11 µmol/l seem to be protective.

Usual Treatment

- Treatment of emphysema: smoking cessation, preventive vaccinations, bronchodilators, supplemental oxygen when indicated.
- Replacement ("augmentation") therapy with purified AAT or synthetic elastase inhibition to prevent progression of emphysema.
- End-stage lung or liver disease is treated with transplantation.
- Approximately 12% of all lung transplants are performed for emphysema secondary to AAT deficiency.
- Alternative treatments for emphysema include lung volume reduction surgery or endobronchial valves.
- Emerging therapies include recombinant AAT augmentation/leukoprotease inhibitors, retinoic acid receptor agonists, and gene therapies.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
PRENATAL				Amniocentesis Chorionic villus sampling
HEENT	Sinusitis	Sinus congestion		X-ray or CT scan
RESP	Emphysema Recurrent infection		Barrel chest Limited chest excursion Reduced air entry	CXR CT scan Spirometry (especially decreased FEV_1) ABGs Gas transfer
CV	Sinus tachycardia Cor pulmonale			
GI	Chronic hepatitis Liver cirrhosis Inflammatory bowel disease Reflux	Unintended weight loss		LFTs
HEME	Polycythemia			Hb, Hct
METAB	Fatigue			6-min walk test Serum AAT Genotyping Immunoelectrophoresis Radial immunodiffusion Nephelometry Thin-layer isoelectric focusing

Key References: American Thoracic Society, European Respiratory Society: American Thoracic Society/European Respiratory Society Statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency, *Am J Respir Crit Care Med* 168(7):818–900, 2003; Myles P, Weeks AM: Alpha 1-antitrypsin deficiency: circulatory arrest following induction of anaesthesia, *Anaesth Intensive Care* 20(3):358–362, 1992.

Perioperative Implications

Preoperative Preparation

- Thorough pulm evaluation.
- General anesthesia can be tolerated in most pts with an FEV_1 of ≥1.0 L.
- Consider local, regional, or neuraxial anesthesia.

Monitoring

- Routine, but consider arterial line in case of major surgery (to monitor hyperinflation-induced hypotension).
- Lung ultrasound can be used to rule out pneumothorax.

Induction

- Adjust positive pressure ventilation to prolong expiration time, with an I:E ratio ≥3.
- Avoid high PEEP.

Maintenance

- Permissive hypercapnia

Postoperative Period

- Opioid-sparing analgesic regimen.
- Avoid hepatotoxins; use caution with acetaminophen.
- Titrated oxygen therapy to avoid hyperoxic hypoventilation.
- High-dependency or critical care admission.
- Monitor for concomitant liver and kidney dysfunction.
- Consider AAT augmentation therapy.

Amniotic Fluid Embolism

Ryan Palacio | Mohammed M. Minhaj

Risk

- Risk factors include: advanced maternal age (>35 y); cesarean delivery; placenta previa; meconium; intrauterine fetal demise; placental abruption; meconium staining of the amniotic fluid; chorioamnionitis; and macrosomia.
- True incidence is unknown but estimated to occur in 2 to 8 per 100,000 deliveries.

Perioperative Risks

- Amniotic fluid embolism accounts for approx 6% of maternal deaths in USA.
- Mortality was once as high as 61% to 86%, but more recent registries have reported mortality between 11% and 44% of pts.
- Morbidity is also high as it is suggested that up to 60% of pts have persisting neurologic deficits.

Worry About

- Hypoxia.
- Hypotension/cardiopulmonary collapse.
- Heart failure (can have both right and left ventricular failure).
- DIC: Occurs in nearly all survivors of the initial catastrophic event.
- Hemorrhage: 40% of amniotic fluid embolism-associated deaths are due to hemorrhage.
- Altered mental status.
- Seizures.
- ARDS.
- Acute pulm Htn.

Overview

- Amniotic fluid going to central circulation.
- There are three necessary conditions:
  - Amniotomy (breach in the barrier between the intact fetal membranes that isolate amniotic fluid from the maternal circulation).
  - Laceration of endocervical or uterine vessels or site of placental attachment.
  - Traditionally it was thought that a pressure gradient (intrauterine pressure > CVP or uterine venous pressure) was needed, but the presence of an electrochemical gradient can provide the means for mediators of AFE to inflict damage.
- Immunologic factors also likely to be involved, and complement activation may play a role in the pathophysiology of AFE (e.g., SIRS).

Etiology

- Postulated mechanism of action: Powerful contractions force amniotic fluid into the maternal circulation through a defect in the fetal membranes, placenta, or elsewhere.
- Diagnosis based on clinical symptoms and diagnosis of exclusion of other potential etiologies. No uniform diagnostic criteria exist nor are there specific laboratory findings pathognomonic for AFE. Fetal cells in maternal pulm circulation are not a reliable marker.
- AFE can also occur up to 48 h postpartum and in rare cases following intrauterine surgery or blunt abdominal trauma.

Usual Treatment

- Usually supportive to maintain oxygenation, circulatory support, and correct coagulopathy
- Delivery of fetus as soon as is practical; may require operative or cesarean delivery
- Employ left uterine displacement to prevent aortocaval compression
- Cardiopulmonary resuscitation, often requiring intubation with 100% O_2/PEEP. Case reports of successful outcomes with employment of inhaled nitric oxide, CPB and/or ECMO have been reported in the literature.
- Risks/benefits of uterotonic agents should take into account clinical picture of hypotension and/or hemorrhage considerations.
- Pressors and inotropes will often be required.
- Replacement of clotting factors if pt develops DIC. Clotting factors can also be replaced with recombinant factors in addition to traditional blood product transfusion.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia Hypotension			HR BP
RESP	Hypoxia Pulm edema	Dyspnea	Tachypnea Cyanosis Frothy pink sputum	Pulse oximetry Aspirate blood from pulmonary artery or renal artery Stain buffy coat for cells and mucin
GI		Nausea	Vomiting	
HEME	DIC		Excessive bleeding Thrombolysis (bleeding from IV sites)	PT, PTT, plt, fibrinogen, FSP
CNS		Anxiety	Convulsions Shivering Sweating	

Key References: Rath WH, Hofer S, Sinicina I: Amniotic fluid embolism: an interdisciplinary challenge, *Dtsch Arztebl Int* 111(8):126–132, 2014; McDonnell NJ, Percival V, Paech MJ: Amniotic fluid embolism: a leading cause of maternal death yet still a medical conundrum, *Int J Obstet Anesth* 22(4):329–336, 2013.

Perioperative Implications

- Most common presentation is hemodynamic collapse.

Preoperative Preparation

- Maximize maternal oxygen delivery.
- Place several large-bore IVs; consider central access for inotrope administration and fluid resuscitation.
- Notify blood bank of anticipated coagulopathy and cross-match for several units of packed RBCs, FFP, platelets, and cryoprecipitate.
- Consider preparing for CPB/ECMO if an option.

Monitoring

- If amniotic fluid embolism is suspected, consider PA catheter or cardiac ultrasound (TTE/TEE) for hemodynamic management.

Maintenance

- Usually resuscitative with support of breathing and circulation.
- Case reports of use of CPB, ECMO, inhaled nitric oxide, ventricular assist devices.

Extubation

- If the pt survives, keep intubated until hemodynamically stable.

Anticipated Problems/Concerns

- Even with early and aggressive intervention, AFE can result in maternal and fetal mortality. Given that an AFE can occur unpredictably and then has a high risk for morbidity and mortality, it can be devastating for the pt's family and healthcare providers. Psychological counseling for all parties involved should be considered to deal with any posttraumatic stress.

Amyloidosis

Toby N. Weingarten

Risk

- Incidence in USA: 1:100,000
- Race with highest prevalence: Unknown

Perioperative Risks

- Increased risk of periop renal failure, cardiomyopathy (arrhythmias and ventricular dysfunction), bleeding from coagulopathy
- Autonomic neuropathy

Worry About

- Signs of CHF
- Dysrhythmias
- Decreasing urine output

Overview

- Extracellular deposition of amyloid-type proteins.
- Congo-red stain of tissue reveals green birefringence in a polarizing microscope.
- Associated end-stage renal, myocardial, and neuropathic disease.
- Best diagnosed by subcutaneous abdominal fat pad aspirate or rectal biopsy.

Etiology

- Both acquired and hereditary forms exist.
- Acquired forms are categorized as primary (AL), associated with plasma cell disorders (i.e., multiple myeloma), and secondary (AA), associated with inflammatory and infectious diseases (e.g., osteomyelitis, rheumatoid arthritis).
- Hereditary forms very rare.

Usual Treatment

- Acquired: Treatment of primary (AL) amyloidosis is directed at the underlying plasma cell disorder (e.g., chemotherapy, stem cell transplant). Treatment of secondary (AA) amyloidosis is directed at underlying infection/inflammation.
- Hereditary: Colchicine, liver transplantation.
- Treatments to clear amyloid deposits are being developed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Macroglossia Tracheal stenosis	Enlarged tongue Dyspnea	Macroglossia Stridor	CT scan Flow-volume loop
CV	Restrictive myopathy LV and RV dysfunction Conduction abnormalities	Exercise tolerance Dyspnea Syncope	Increased JVP S_3 Bradycardia	ECHO ECG
RESP	CHF Lung nodules	Cough Chest wall pain	Rales	CXR
GI	Autonomic dysfunction Hepatomegaly	Malabsorption Diarrhea Bleeding	Hepatomegaly Ascites	Biopsy LFTs
HEME	Factor X deficiency Capillary fragility	Bruising Purpura	Periorbital bruises ("raccoon eyes")	Factor X assay
RENAL	Decreased renal perfusion Nephrotic syndrome			BUN/Cr urine
CNS	Autonomic neuropathy Cardioembolic strokes	Inability to sweat; hoarseness; early satiety; postural dizziness	Orthostasis	Biopsy

Key References: Noguchi T, Minami K, Iwagaki T, et al: Anesthetic management of a patient with laryngeal amyloidosis, *J Clin Anesth* 11:339–341, 1999; Thompson CA, Kyle R, Gertz M, et al: Systemic AL amyloidosis with acquired factor X deficiency: a study of perioperative bleeding risk and treatment outcomes in 60 patients, *Am J Hematol* 85:171–173, 2010.

Perioperative Implications

Preoperative Preparation
- Optimize treatment of heart failure.
- Avoid dehydration (renal failure).
- Care with positioning and taping (skin fragility).

Monitoring
- Consider of TEE or PA cath for large fluid shift operations or pts with severe LV dysfunction.

Airway
- Macroglossia or tracheal stenosis
- Increased risk of bleeding into airway from capillary fragility and possible coagulopathy

Preinduction/Induction
- May develop reduced CO and hypotension.
- Coagulopathy may contraindicate regional anesthesia.

Maintenance
- No agent or technique shown superior.
- Maintain adequate urine output.

Extubation
- Pt fully awake to minimize risk of reintubation.
- Use caution with nasal airway as it may cause hemorrhage.

Postoperative Period
- Close monitoring of CV and renal status.
- Consider ICU setting for postop care.

Adjuvants
- Avoid digoxin: Not usually helpful in treating amyloid CHF, associated with increased arrhythmias.

Anticipated Problems/Concerns
- Difficult airway
- CHF
- Hypotension
- Renal failure
- Easy bruising; increased risk of bleeding

Amyotrophic Lateral Sclerosis

Alan David Kaye | Charles Fox III | Elyse M. Cornett

Risk
- Estimated incidence of 1-3:100,000.
- Mean age of onset is in the 60s, but ALS can occur as early as the 20s.
- Disease duration is approximately 3 y from the time of diagnosis to death.
- While there is slight male predominance of sporadic spinal ALS, slight female predominance is found in bulbar ALS
- Most cases are sporadic but 5% to 10% are familial.
- Risk of anesthesia increases as the FVC falls below 50%, ALS pts can be stratified as low risk if the FVC >50%, moderate risk if the FVC is 30% to 50%, and high risk if the FVC <30%.

Perioperative Risks
- Aspiration.
- Respiratory depression.
- Inability of pt to communicate secondary to bulbar weakness.

Worry About
- Succinylcholine-induced hyperkalemia.
- Prolonged resp depression with inability to extubate, even without use of muscle relaxants.
- Hypersensitivity to nondepolarizing neuromuscular blockers.
- Disease exacerbation with use of regional anesthesia.

Overview
- Disease of unclear etiology that leads to progressive degeneration of the upper and lower motor neurons causing amyotrophy (muscle wasting) and lateral sclerosis (gliosis of the corticospinal tracts).
- Located in the motor cortex (upper motor neurons) and anterior horn (lower motor neurons) of the spinal cord.
- ALS has a relenting course that leads to weakness of all skeletal muscles in the body.
- Typically, ALS is asymmetric involving the distal extremities first followed by bulbar muscle weakness as the disease progresses.
- After diagnosis in an adult, pts are usually wheelchair bound by 18 mo and die after 3-5 y from resp suppression.
- Juvenile forms of ALS do exist, present early in life, and are rare.
- Upper motor neuron signs include spasticity, hyperactive reflexes, and upgoing plantar response; lower motor neuron signs include muscle atrophy and fasciculations.
- Disease does not affect ocular muscles, bladder, bowel, and sensation.
- ALS variants include:
  - Primary lateral sclerosis: Progressive degeneration of upper motor neurons;
  - Progressive muscular atrophy: Progressive degeneration of lower motor neurons;
  - Progressive bulbar palsy: Progressive motoneuron loss from lower cranial nerve nuclei and cervical spine.

Etiology
- Familial ALS caused by gene mutations: 14 mutations described. Most studied mutation occurs in the gene encoding superoxide dismutase and forms aggregates leading to mitochondria and muscle complex dysfunction.
- Etiology of sporadic ALS remains uncertain; however, autoimmune, viral, and neurotoxic mechanisms likely contribute.
- Interaction between a genetic susceptibility and environmental factors likely leads to the disease.

Usual Treatment
- Care is mainly supportive, consisting of psychological therapy, symptom management, physical therapy, and palliative care.
- Care in a multidisciplinary clinic is associated with prolonged survival and improved quality of life.
- Riluzole, which inhibits glutamate release, is the only drug shown to improve survival. On average, pts live 2 to 3 mo longer on riluzole versus placebo.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dysarthria, dysphagia, sialorrhea	Slurred speech, coughing with eating, drooling	Decreased gag reflex	Swallow study
CV	Reduced sympathetic tone Vagal dysfunction	Syncope Cardiac arrest		Prolonged QTc Tachycardia
PULM	Aspiration; nocturnal apnea; weak cough	Recurrent pneumonia, nighttime arousals, lethargy	Decreased breath sounds; coarse breath sounds	PFTs Nocturnal oximetry CXR ABG
GI	Malnourished	Caloric intake Food journal	BMI	Albumin
CNS	Motor neuron loss in spinal cord and brain	Weakness Pseudobulbar affect	Weakness Fasciculations Atrophy	EMG/NCS

Key References: Mancuso R, Navarro X: Amyotrophic lateral sclerosis: current perspectives from basic research to the clinic, *Prog Neurobiol* 133:1–26, 2015; Turakhia P, Barrick B, Berman J: Patients with neuromuscular disorder, *Med Clin North Am* 97(6):1015–1032, 2013.

Perioperative Implications

Preinduction/Induction/Maintenance
- Succinylcholine is contraindicated as it can cause hyperkalemia.
- Nondepolarizing agents may be used, but anticipate prolonged weakness.
- Short-acting muscle relaxants should be used when necessary.

Preoperative Considerations
- Preop pulmonary function tests may help to predict anesthetic risk and include FVC and nocturnal oximetry.
- Consider aspiration prophylaxis.
- Avoid opioids and benzodiazepines if possible.
- Bulbar dysfunctions occur in up to 25% of pts. Look for weight loss, dysarthria, and difficulty whistling or using a straw.
- Resp failure is the main cause of death in ALS pts.
- Depression and emotional lability are common in ALS pts and are typically treated with TCAs which

can prolong the QT interval. If the decision is made to stop TCAs before surgery, it must be done 2 wk before the surgery to prevent withdrawal symptoms. If TCA treatment will continue through surgery, an ECG must be obtained prior to the start of surgery.

Monitoring
- Routine.
- Anesthesia should be performed in an inpatient setting.

General Anesthesia
- Avoid if possible.
- May cause significant postop resp depression.
- Diaphragmatic pacing stimulation may improve resp compliance and stimulate respirations.
- Extubate when pt is fully awake.

Regional Anesthesia
- May be preferred compared to general anesthesia.
- Case reports have documented successful use of epidural anesthesia.
- Minimize neuraxial extent of blockade to reduce risk of resp depression.

Postoperative Period
- Anticipate prolonged postop ventilation.
- Use nonsedating medications for pain control.

Anticipated Problems/Concerns
- Anticipate hospitalization secondary to prolonged weaning from ventilator.
- Communication with ALS pts may be difficult because pts have weakened oropharyngeal muscles. Prior to anesthesia, determine the best way to communicate with pts (i.e., letter boards) and have family members available to assist.
- Close resp monitoring is essential following anesthesia. Exacerbation of apnea may result from supplemental oxygen.

Anaphylaxis

Karen Hand

Risk
- Lifetime prevalence of anaphylaxis is 0.05% to 2%, most common triggers being food, stings, and iatrogenic causes.
- Occurs in approximately 1 in 10,000 to 1 in 20,000 anesthetic procedures, and 1 in 6500 administrations of neuromuscular blocking agents (NMDAs). Causes 3% of anesthesia-related deaths.
- Females outnumber males 3:1.
- Hx of atrophy, prior anaphylaxis, and prior adverse reaction to anesthesia.

Perioperative Risks
- Significant risks of life-threatening CV collapse, airway compromise, and bronchospasm.
- Most common causes are NMDAs (60%), latex (15%), and antibiotics (15%).
- Increased risk of life-threatening reactions with beta blockers, ACEIs, asthma, and underlying cardiac disease.

Worry About
- Hx of atrophy, prior anaphylaxis, and prior adverse reaction to anesthesia.
- Timing: Most reactions occur around the time of induction or within 10 min of drug administration. May be difficult to distinguish from other drug reactions or mechanical problems.
- Rapid progression: Time to cardiac or resp arrest is within 5 min for anesthetic reactions, compared to 30 min for food and 15 min for stings.
- Diagnostic difficulty: Varied presentations, tachycardia or bradycardia, less than 50% have bronchospasm, cutaneous signs may be absent or occur later in severe reactions.
- Biphasic response: May recur from 4-24 h later

Overview
- Defined as a severe, life-threatening, generalized or systemic hypersensitivity reaction.
- Classified as:
  - Allergic reactions, usually involving IgE.
  - Nonallergic reactions, previously called anaphylactoid.
  - Itching, burning hands, feet, mouth or genitals, abdominal pain, nausea, and a feeling of doom or tunnel vision may be reported by awake pts.
- Most common initial features during anesthesia are pulselessness, desaturation, and difficult ventilation.

Etiology
- Allergic: IgE antibodies crosslink receptors on mast cells and basophils, causing degranulation, releasing many vasoactive substances, incl histamine, in an inflammatory cascade.
- Usually requires prior exposure. However, can occur with NMDAs with first exposure, thought to be due to common quaternary amine in NMBAs and chemicals (e.g., found in cleaners and cosmetics). In Europe, linked with ingredient in cough syrup, pholcodine.
- Can occur with any muscle relaxant, most commonly succinylcholine. Increasing reports with rocuronium; also reported with sugammadex.
- Risk factors for latex allergy include meningomyelocele, as well as allergy to figs, papayas, or avocados. Increased in healthcare workers
- Rarely due to opiates or local anesthetics (more likely intravascular injection or epinephrine)
- Nonallergic: Related to drug dose and speed of injection. Usually less severe than IgE-mediated reactions.

Usual Treatment
- Halt exposure to trigger
- Epinephrine: Standard treatment (e.g., no IV is 0.3 mg IM to outer thigh). Under anesthesia adjust IV dose according to severity of reaction from 10 s mcg to 100 s mcg to multiple 1 mg doses.
- Clinical Severity Scale:
  - Grade 1: Cutaneous or mucous signs.
  - Grade 2: +/– hypotension, tachycardia, dyspnea, GI disturbance.
  - Grade 3: Life-threatening CV or resp collapse.
  - Grade 4: Cardiac arrest.
- IV fluids (large bore IV); may require large volume.
- O_2 and supportive measures.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Head and neck swelling, and potential glottic edema	Will occur suddenly	Swelling	Clinically obvious
CV	Increased or decreased HR, decreased BP and SVR, increased ectopy, acute coronary events		Hypotension, CV collapse	ECG may reveal premature ventricular contractions PVCs or change in P-R interval
RESP	Bronchospasm		Wheezing	Increased peak inspiratory pressure, decreased O_2 saturation
DERM	Urticaria, erythema, hives, edema		Body rash	May be hidden under drapes or absent initially in severe reactions

Key References: Simons FE, Sheikh A: Anaphylaxis: the acute episode and beyond, *BMJ* 346:f602, 2013; Dewachter P, Mouton-Faivre C, Emala CW: Anaphylaxis and anesthesia: controversies and new insights, *Anesthesiology* 111(5):1141–1150, 2009.

Perioperative Implications

Preoperative Preparation
- Prophylactic H1/H2 blockers and steroids may attenuate the severity, although not the incidence of reactions. There is more support for their use in preventing nonallergic reactions.
- Consider administering antibiotics preop rather than at the time of induction.

Monitoring
- Standard ASA monitors are essential to rapidly identify anaphylaxis.
- Always consider anaphylaxis in CV collapse with or without bronchospasm or cutaneous manifestations during induction.
- The airway may swell, making intubation very difficult.

Induction
- Reactions usually occur during induction. Reactions to latex may occur within 30 min.

Maintenance
- Perpetuation of reaction can occur, particularly if due to latex.
- Significant cross-reactivity between NMDAs (approaching 80%).
- Avoid all muscle relaxants in pts with prior reactions.

Extubation
- Ensure stability from a cardiorespiratory viewpoint.
- Assess for airway edema.
- Beware reactions to sugammadex.

Adjuvants
- H1/H2 blockers and steroids may attenuate the biphasic response.
- In case unresponsive to repeated doses of epinephrine, consider norepinephrine, vasopressin, and ECMO.
- Sugammadex has been used in the treatment of anaphylaxis to rocuronium.
- Epinephrine is drug of choice in true anaphylaxis. Delayed administration increases the incidence of the biphasic response and death.

Postoperative Period
- Tryptase levels should be drawn within 30 min to 2 h of a suspected reaction, then compared to baseline levels at 2 wk.
- Skin testing may be done several weeks after initial event to assess etiologic agent.
- Advise patients exactly which drugs they received.
- Obtain immunology consult.

Anticipated Problems/Concerns
- Early aggressive treatment may be critical.

Anemia, Aplastic

Joanne Shay

Risk
- Incidence in USA: 2000 new cases/y.
  - Per million up to age 9.
- Southeast Asia and South Africa have 10-20 times higher incidence.
- Within USA, related to agricultural areas or petrochemical industry and chemical exposures.

Perioperative Risks
- Infection
- Hemorrhage
- LV dysfunction due to high-output state and fluid overload

Worry About
- Sepsis
- Coexisting congenital anomalies, especially renal and cardiac
- Concomitant GI and intracranial hemorrhage
- Difficulty cross-matching blood products after previous multiple transfusions

Overview
- Self-perpetuating disorder resulting in pancytopenia due to a congenital or acquired loss of hemopoietic pluripotent stem cells.
- Fanconi anemia is congenital familial marrow hypoplasia associated with intellectual disability and kidney, spleen, and skeletal hypoplasia.
- Estren-Dameshek anemia is inherited marrow hypoplasia without physical abnormalities.
- Pathophysiology: Reduction or dysfunction of pluripotent stem cells or their microenvironment from toxic or immunologic causes.
- Prognosis for long-term survival has increased to 40% to 75% in those treated with antilymphocyte serum and 60% to 80% in those treated with BMT.
- Two forms of drug-induced aplastic anemia are possible:
  - Hypersensitivity: Not related to dose or duration.
  - "Reversible" reaction: Often resolves with discontinuation; severity proportional to dosage.

Etiology
- Of cases, 50% to 75% are idiopathic.
- Fanconi anemia demonstrates autosomal recessive inheritance with heterozygote frequency of 1 in 300,000-600,000 in USA.
- Drug-induced: Chloramphenicol, NSAIDs, antiepileptics, and gold and sulfa group-containing compounds.
- Environmental toxins include aromatic hydrocarbons (benzene, naphthalene, toluene, and glue), pesticides (DDT and lindane), and radiation.
- Infectious causes include hepatitis C, CMV, EBV, HIV, TB, and toxoplasmosis.
- Sequelae of other processes such as pancreatitis, pregnancy, lupus erythematosus, paroxysmal nocturnal hemoglobinemia, thymoma, and thymic CA.

Usual Treatment
- Pts <55 y are managed with HLA-matched BMT or hematopoietic stem cell transplant.
- Pts >55 y or those unable to find HLA-matched donor receive immunosuppression and immunomodulation Rx, incl ATG, cyclosporine, steroids, androgens, and G-CSF.
- Hematopoietic growth factors such as G-CSF and GM-CSF may improve the short-term hematologic recovery at the risk of long-term clonal evolution to myelodysplastic syndrome and AML.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Epistaxis Oral/mucosal friability	Headache	Stomatitis	CBC, differential, plt PT, PTT, CT scan
RESP	Pulm embolism Pneumonia Interstitial pneumonitis Pulm edema	Dyspnea Hypoxemia	Tachypnea Lung field consolidation Wheezing Crackles	CXR, V/Q scan CT scan ABGs, bronchoscopy, BAL CXR, ABG
CV	LV failure ASD/VSD	Dyspnea Lethargy	Tachycardia, S_3 Displaced posterior MI	ECG ECHO
GI	GI bleeding GI GVHD Hepatic veno-occlusive disease	N/V, diarrhea Melena	Acute abdomen Hypoactive bowel sounds Jaundice	Endoscopy, bleeding scan Selective angiography Albumin, transferrin LFT, liver biopsy
CNS	Microcephaly, meningitis, intracranial hemorrhage	Irritability, lethargy Headache, seizures	Meningismus Papilledema	Lumbar puncture after coagulopathy treated, head CT, MRI
HEME	Pancytopenia Leukemia Paroxysmal nocturnal hemoglobinuria	Bleeding gums, infections Easy bruisability Fatigue, dark urine	Petechiae Retinal hemorrhage Pallor	CBC, differential Reticulocyte count BM biopsy Ham test
METAB	Electrolyte abnormalities Glucose intolerance Hypoproteinemia Hypothyroidism	Long-term hyperalimentation GI GVHD Hypotension, cold intolerance		Electrolytes Ca^{2+}, Mg^{2+}, phosphate, albumin, transferrin TSH, T3, T4

Key References: Miano M, Dufour C: The diagnosis and treatment of aplastic anemia: a review, *Int J Hematol* 101(6):527–535, 2015; Samarasinghe S, Webb DKH: How I manage aplastic aneamia in children, *Br J Haematol* 157:26-40, 2012.

Perioperative Implications

Preoperative Preparation
- Reverse isolation precautions.
- Adequacy of blood products.
- Evaluate for severe neutropenia; coexisting congenital HD may warrant prophylactic antimicrobial therapy.
- Avoid IM and rectal sedation.
- Concomitant steroid therapy and necessity of stress doses.

Monitoring
- Arterial line if indicated.
- Consider CVP or PA cath as indicated.
- Urine output for new-onset hemoglobinuria as first sign of transfusion reaction.

Airway
- Avoid nasal manipulation.
- Use extreme caution with friable oral and pharyngeal mucosal surfaces.

Preinduction/Induction
- May exhibit hypotension and excessive fluid requirements to maintain adequate CO.
- Central neuraxial blockade contraindicated in ongoing thrombocytopenia requiring transfusion.
- Peripheral neural blockade may be approached cautiously if coagulation status is judged adequate.

Maintenance
- PEEP assures adequate tissue oxygenation at lower FIO_2 as hyperoxia depresses normal erythropoietin synthesis and marrow function.
- Nitrous oxide depresses BM function even after brief exposure; best to use O_2-air mixture.
- Normothermia promotes coagulation.
- Chronically anemic pts may tolerate lower Hct; adequacy of tissue O_2 must be addressed if CV decompensation ensues.
- Avoid induced hypotension in anemic pts.

Extubation
- Period with greatest O_2 demands

Postoperative Period
- Continued monitoring of coagulation status
- Transfusion requirements >normal
- Increased susceptibility to infection
- Pain management requires balance between pulm toilet versus sedation

Anticipated Problems/Concerns
- Age of RBC in pts with aplastic anemia is older than usual, with lower 2,3-DPG levels inside cells resulting in increased O_2 binding by Hgb (shift to the right) and decreased delivery of oxygen to tissues for same SaO_2.

Anemia, Chronic Disease/Inflammation

Hayden R. Hughes

Risk
- Incidence in USA: 5%; incidence in surgical population: 5% to 75%.
- Historically thought to be due to chronic infectious, inflammatory, or malignant conditions. Now known to occur with severe trauma, DM, aging, and acute immune activation.
- More than 130 million Americans living with chronic diseases.

Perioperative Risks
- Risks related to underlying diseases
- Transfusion related risks (e.g., TRALI, TACO, hemolytic reactions, immunosuppression)
- Risks related to compensatory mechanisms for increasing O_2 delivery (e.g., angina, heart failure, dysrhythmias)

Worry About
- Underlying diseases and their periop complications.
- Impaired tissue O_2 delivery and compensatory mechanisms aimed at correcting it.
- Delayed wound healing and infection.

Overview
- WHO definition of anemia: children 6 mo to 6 y: Hgb <11 g/dL; 6 to 14 y: Hgb <12 g/dL; nonpregnant females: Hgb <12 g/dL; pregnant females: Hgb <11 g/dL; males: Hgb <13 g/dL.
- Usually mild with Hgb 8-11 g/dL.
- Usually normochromic, normocytic with low reticulocyte count.
- Low serum Fe, TIBC, and transferrin levels.
- ACD/I due to disturbances of Fe homeostasis – diversion of Fe from the circulation into storage sites within the reticuloendothelial system and reduced GI absorption of Fe.

Etiology
- Relative Fe deficiency
- Reduction in RBC production and mild decrease in RBC survival time
- Certain treatments for chronic conditions

Usual Treatment
- Treatment of underlying disease
- Fe, folic acid, and cobalamin supplementation
- Erythropoiesis-stimulating agents
- Allogeneic blood transfusion

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hyperdynamic circulation Myocardial ischemia CHF	Palpitation Pounding pulse Angina Sx, dyspnea Exercise intolerance	Tachycardia Wide pulse pressure	ECG Exercise ECG
RESP		Dyspnea		
GI	Chronic blood loss Hypoperfusion	Blood in stool Angina equivalent (pain, nausea, indigestion)		Occult blood in stool See CV
HEME	Hgb below WHO definition level (see Overview)	Decreased exercise tolerance		Hgb
RENAL	Chronic renal failure	Decreased urine output Dialysis	Shunt	Cr K^+
CNS	Decreased cerebral O_2 delivery	Dizziness Headache Transient cerebral ischemia		
MS	Low exercise capacity	Fatigue		

Key References: Gangat N, Wolanskyj AP: Anemia of chronic disease, *Semin Hematol* 50:232, 2013; Shander A: Anemia in the critically ill, *Crit Care Clin* 20(2):159–178, 2004.

Perioperative Implications

Preoperative Preparation
- Standard monitoring.
- Warm the room.
- CVP, Hgb, electrolytes.
- ST-segment analysis in pts with signs of CAD.
- PA cath for large fluid shifts or pts with signs of LV dysfunction or advanced renal failure.
- ABG.

Airway
- None

Preinduction/Induction
- Prehydrate liberally if CV status will tolerate.
- Avoid CO reduction.
- Avoid hypoxemia.
- Choose drugs according to underlying conditions.

Maintenance
- Avoid hypoxemia.
- Maintain CO.
- Avoid hypovolemia.
- Keep pt warm.
- Maintain Hgb above critical level for pts taking comorbidities into account.

Extubation
- Keep pt warm.
- Maintain high PaO_2.
- In pts with CAD, this is the period of greatest risk for ischemia.

Postoperative Period
- Keep pt warm, prevent shivering.
- Maintain high PaO_2.

Adjuvants
- According to underlying disorder

Anticipated Problems/Concerns
- Myocardial ischemia/infarction or CHF in pts with concomitant CAD.
- Deterioration of renal function in pts with CRI.
- Prolonged effects of drugs in pts with impaired renal and/or hepatic function.

Anemia, Hemolytic

Kirk Lalwani | Sarah C. Fausel

Risk

- Autoimmune disorders (SLE, RA, scleroderma, cold agglutinin disease).
- Lymphoproliferative disorders (CLL, NHL).
- Prosthetic heart valves (ball-and-cage, and bileaflet valves). Usually subclinical, but can be severe in up to 15% of pts.
- Family history of hemoglobinopathies or RBC membrane defects (thalassemia, sickle cell disease, G6PD deficiency, spherocytosis).
- Exposure to drugs (cephalosporins, penicillins, NSAIDs) or other chemicals (naphthalene, fava beans).
- Infection (*Clostridium perfringens*, *Haemophilus influenza* type B, malaria, HIV).
- Wilson disease (due to toxic effect of copper ions in circulation).

Perioperative Risks

- Anemia, hypoxia.
- Underlying CV compromise.
- Splenomegaly in pts with extravascular hemolysis (within the reticuloendothelial system). Splenectomy is a common surgical procedure in pts with sickle cell disease due to hemolysis and sickling.
- Renal failure due to massive hemolysis (e.g., cold agglutinin hemolysis, sickling, drug reaction)
- Varying levels of liver disease depending on type of hemolytic anemia. Synthetic function of liver is usually normal, but in severe cases can be compromised.

Worry About

- Uncompensated anemia in pts with subacute hemolysis
- Periop hemolysis and/or hypoxia
- Need for transfusion and/or fluids

Overview

- Pts with hemolytic anemia may present with any of the following: fatigue, angina, SOB, tachypnea, tachycardia, or jaundice. The hemolysis can lead to changes in blood viscosity, gallstone production, splenomegaly, and renal failure in severe cases. Many pts will be both iron and folate deficient.
- Epidemiology varies by pt population. For example, G6PD is an X-linked condition and its prevalence is near 50% in Kurdish Jews, but around 1:1000 in North American and European populations.
- Other things to consider incl monitoring periodic Hct levels, and administering prophylactic antibiotics/vaccinations to pts who have had a splenectomy.

Etiology

- Multiple causes; see Risk section (e.g., RBC structural abnormalities, autoimmune reaction, enzyme deficiency, hemoglobinopathies, mechanical heart valves, drugs, infection).

Usual Treatment

- Treatment depends on etiology:
  - Autoimmune: Corticosteroids, plasmapheresis, packed RBC transfusion for symptomatic pts, supportive care;
  - Drug induced: Discontinuation of offending medication, corticosteroids, supportive care;
  - Prosthetic valve: Cardiology consult and transfusion if symptoms rapidly worsen;
  - RBC membrane defect: Splenectomy and supportive care;
  - Enzyme deficiency: Avoidance of triggers, splenectomy, supportive care;
  - Infection: Treatment of underlying infection and supportive care;
  - Wilson disease: Rapid removal of copper, early consideration for liver transplant.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dehydration	Fatigue, dizziness	Hypotension, weak pulses, increased capillary refill	CBC, BNP
HEME	Anemia	Fatigue, SOB, dizziness	Jaundice, pallor, splenomegaly	Hgb, Hct, reticulocyte count, indirect bilirubin, LDH
RENAL	Hemoglobinuria, acute renal failure	Dark urine (episodic)	Possible Htn, resp rate changes	Urine analysis, BUN, Cr
GI	Liver disease		Hepatosplenomegaly	Liver function tests (LFTs)

Key Reference: Eckman JR: Disorders of red cells. In Lubin MF, Dodson TF, Winawer NH, editors: *Medical management of the surgical patient: a textbook of perioperative medicine,* ed 5, Cambridge, 2013, Cambridge University Press, p 215.

Perioperative Implications

Preinduction/Induction/Maintenance

- Preop management and treatment of underlying cause of hemolytic anemia.
- The test obtained periop depends on the etiology, severity, and chronicity of the hemolytic anemia.
- Avoidance of hypoxia, hypercarbia, acidosis, low-flow conditions, and hypothermia (particularly in cold agglutinin disease).
- Optimize CV status with adequate hydration; consider IV fluid treatment the day before surgery if hypovolemic.
- RBC transfusion may be considered to improve O_2 carrying capacity depending on etiology (must be warmed for pts with cold agglutinin disease).
- Normothermia should be strictly maintained in any pt requiring transfusion(s).
- Possible plasmapheresis for acute removal of IgM antibodies in pts with uncontrolled cold agglutinin disease.

Monitoring

- Standard monitors and urine output, CV status, O_2 saturation (pulse oximetry), and temp regulation (avoiding hypothermia)

General Anesthesia

- Choice of anesthetic technique can vary, but all approaches should have the goal of avoiding hypoxia, hypercarbia, acidosis, stasis, low-flow conditions, and hypothermia.
- Avoidance of hypoventilation.

Regional Anesthesia

- Goals for regional anesthesia are the same as for general anesthesia. No specific contraindications.

Postoperative Period

- Supplemental O_2 therapy
- Adequate hydration
- Early ambulation
- Continued temperature regulation
- Active pulm toilet
- Aggressive evaluation and treatment of fever or infection

Anticipated Problems/Concerns

- Acute periop hemolysis; may warrant transfusion.
- Periop sickling event due to hypoxia, acidosis, hypothermia, or low flow. Sickling can be decreased by increasing arterial oxygen tension.
- Hypothermia-induced cold agglutinin hemolysis; decreased by maintaining normothermia.
- Hypoxia and end-organ damage.
- Venous thrombosis, pulm embolism.

Anemia, Megaloblastic

Katherine L. Norgaard | Steven M. Frank

Risk

- Prevalence: Estimates ranging from 1.7-3.6%.
- Most common cause is vitamin deficiency: 65% vitamin B12; 12% combined folate/vitamin B12; 6% folate.
- Pernicious anemia is less common: 1 in 7500 people in USA develops pernicious anemia each year.
- Prevalence increases with advanced age and in countries with higher rates of malnutrition.

Perioperative Risks

- Risk of severe anemia and coagulopathy.
- Risk of coronary, cerebral ischemia secondary to severe anemia.
- Increased plasma volume as compensatory mechanism can predispose pts to CHF.

Worry About

- Exaggerated effect of myocardial depression from anesthesia.
- Preoperative treatment should include supplementation of B12 and folate or transfusion in setting of severe anemia and emergent surgery.
- Decreased platelet count and coagulopathy.
- Anemia causing MI, stroke, or resp failure.

Overview

- An anemia caused by a failure of DNA synthesis which results in large, structurally abnormal and immature red blood cells called megaloblasts (MCV >100 fL/cell).
- Often WBC and platelet counts are also decreased.

- Anemia develops insidiously and due to physiologic compensatory mechanisms it may not cause symptoms until it is severe.
- Symptoms: Fatigue, pallor, dyspnea on exertion, headache, dizziness, tachycardia, nausea, diarrhea, glossitis, and jaundice.
- Vitamin B12 deficiency can interfere with myelination and produce peripheral neuropathy which varies from subtle loss of vibratory sensation and proprioception to frank dementia.

Treatment

- The treatment of megaloblastic anemia depends upon the underlying cause of the disorder.
- Diagnose with complete blood counts, red cell indices, and assays of the vitamin B12 and folate.
- Dietary insufficiency of cobalamin and folate can be treated with appropriate changes to the diet and the administration of supplements.
- Vitamin B12 1000-2000 µg orally can be given once per d but if pts have neurologic signs, vitamin B12 1 mg IM is usually given 1 to 4 times/wk for several wk.
- Folate 400-1000 µg orally once per d.
- Vitamin B12 deficiency must be ruled out before treating with folate alone as this would treat anemia but not the neurologic manifestations.

Etiology

- Most common cause is vitamin B12 and/or folate deficiency due to:
  - Decreased absorption due to gastric or intestinal disease (pernicious anemia, Crohn disease);
  - Decreased intake seen in strict vegan diet, elderly, or alcoholics;
  - Increased requirements seen in pregnancy, patients on hemodialysis, and hemolytic anemia.
- Some drugs and toxins impair vitamin absorption, including methotrexate, chemotherapeutic agents, phenytoin, antacids, and nitrous oxide.
- Much rarer causes include enzyme deficiencies, myelodysplastic syndromes, and acute myeloid leukemia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Headaches and dizziness or vertigo, sore tongue	Yellow eyes, large beefy red tongue	
CV	Increased cardiac output Increased plasma volume	Angina, chest pain, palpitations, tachycardia	Hypotension and tachycardia	Decreased Hgb and Hct, red cell count MCV >100 May have decreased WBC and platelet count
RESP/HEME		Poor exercise tolerance Resp distress	Pallor, DOE, SOB	Large oval cells with hypersegmented neutrophils and large platelets in bone marrow diagnostic feature; Howell-Jolly bodies, nuclear fragment, may be seen in RBCs; low reticulocyte count
GI	Splenomegaly	Symptoms of liver disease, nausea, vomiting, diarrhea	Splenomegaly, jaundice	Liver enzymes, increased LDH
ENDO	Low erythropoietin levels			Bone marrow—macrocytosis, low folate, and B12 stores
CNS		Headaches, fatigue, dizziness, confusion	Dementia, neuropsychiatric disease	Low B12
PNS	Peripheral neuropathy		Loss of vibratory and proprioception especially in LE	Low B12
MS		Fatigue	Easy bleeding, bruising	

Key References: Khanduri U, Sharma A: Megaloblastic anaemia: prevalence and causative factors, *Natl Med J India* 20(4):172–175, 2007; Aslinia F, Mazza J, Yale S: Megaloblastic anemia and other causes of macrocytosis, *Clin Med Res* 4(3):236–241, 2006.

Perioperative Implications

Preoperative Preparation

- Preop workup of cause of megaloblastic anemia; treat cause and any vitamin deficiencies.
- Schilling test was used to identify origin of vitamin B12 deficiency but is no longer available in most hospitals and has been replaced with antiparietal cell and anti-intrinsic factor antibody assays.
- Treatment with folate alone with correct hematologic but not neurologic manifestations.
- May benefit from periop hematology/oncology consult.
- Bone marrow megaloblastic changes are reversed within 12 h after treatment with folate and vitamin B12, and bone marrow morphology appears to be normal within 2 to 3 d.
- Watch for hypokalemia and hypophosphatemia after treatment.

Monitoring

- ST segment changes for myocardial ischemia.
- Large-bore access to facilitate transfusion.

Induction/Maintenance

- Both regional and general anesthesia are options.
- Caution with neuraxial anesthetics or regional anesthetics in case of bleeding diathesis or preexisting neuropathy.
- Avoid nitrous oxide as it inactivates vitamin B12, even with short exposure.

Intraoperative Management

- Intraoperative transfusion as clinically indicated.
- Some pts at risk for increased bleeding and transfusion.

Postoperative Period

- Increased risk for anemia and bleeding diathesis.
- If transfusion given, worry about volume overload due to compensatory increased plasma volume.

Anticipated Problems and Concerns

- Vigilance for prevention, diagnosis, and treatment of ischemic events.
- Be prepared to treat bleeding diathesis.
- Treat symptoms (e.g., resp distress, fatigue, angina, heart failure, tachycardia).

Angina, Chronic Stable

Lee A. Fleisher

Risk

- Incidence in USA: 3 million.
- Annual rates per 1000 new episodes of angina for non-African American men are 28.3 for ages 65–74, 36.3 for ages 75–84, and 33.0 for age 85 and older. For non-African American women in the same age groups, the rates are 14.1, 20.0, and 22.9, respectively. For African American men, the rates are 22.4, 33.8, and 39.5, and for African American women, the rates are 15.3, 23.6, and 35.9, respectively.
- African Americans have highest death rates, although overall death rates are decreasing over time.

Perioperative Risks

- Increased risk of periop MI and death varies, depending on study (3–12%).
- Risk of LV dysfunction, myocardial ischemia, hypotension, and MI.

Worry About

- Increasing frequency of symptoms (i.e., unstable angina)
- Signs of LV dysfunction with ischemia
- Silent myocardial ischemia

Overview

- Chronic stable angina identifies pts at risk for developing myocardial ischemia and MI.
- Angina is present in <25% of episodes of myocardial ischemia.
- Symptoms should be stable for previous 60 d for "stable" diagnosis.
- Can result from
  - Inadequacy of myocardial O_2 supply in pts with critical coronary artery stenosis.

- Coronary vasospasm.
- Inadequacy of myocardial O_2 supply secondary to increased demand from ventricular hypertrophy.
- Endothelial cell-mediated vasoconstriction.

- Thrombosis overlying unstable plaque can lead to unstable angina/MI.

Etiology

- Acquired disease with genetic predisposition.
- Pts with diabetes have higher incidence of CAD, which is frequently silent.
- Other risk factors include Htn, hyperlipidemia, advanced age, tobacco use, and homocysteinemia.

Usual Treatment

- Medical therapy: β-adrenergic receptor antagonist, Ca^2-channel antagonists, nitrates, aspirin, P2Y12 inhibitors, folate, lipid-reducing agents, and combination agents
- Percutaneous coronary interventions with stent placement
- CABG

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia LV dysfunction	Angina Sx Angina-equivalent Sx Dyspnea Exercise tolerance	Displaced posterior maximal impulse S_3	ECG Exercise ECG Exercise radionuclide scintigraphy Pharmacologic stress testing ECHO Coronary angiography Coronary CT
RESP	CHF	Dyspnea Nighttime cough Orthopnea Chest tightness	S_3 Rales Wheezing	CXR
GI		Angina-equivalent Sx LUQ pain Nausea, indigestion		See CV
RENAL	Decreased renal perfusion	Increased UO at night		Cr
CNS	Syncope	Syncope with chest pain		Exercise stress test
MS	Angina-equivalent Sx Arm pain/neck pain			See CV

Key References: Fihn SD, Blankenship JC, Alexander KP, et al.: 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons, *J Am Coll Cardiol* 64(18):1929–1949, 2014; Fleisher LA, Fleischmann KE, Auerbach AD, et al.: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 130(24):2215–2245, 2014.

Perioperative Implications

Preoperative Preparation

- Continuation of chronic antianginal medications associated with a lower incidence of myocardial ischemia/infarction, especially beta blockers, statins, and antiplatelet agents.
- No RCT has definitively demonstrated improved outcome acutely starting any medications.

Monitoring

- ST-segment analysis.
- PA cath for large fluid shift operations or pts with signs of LV dysfunction, although RCT unable to document benefits of routine monitoring.
- TEE is most sensitive, but technical issues of real-time interpretation may occur.

Airway

- None

Preinduction/Induction

- May develop reduced CO and hypotension with ischemia.
- Avoid tachycardia, hypotension.

Maintenance

- Myocardial ischemia may manifest as
  - CV instability.
  - Intraop myocardial ischemia.
  - Reduced CO, increased PCWP.
  - Regional wall motion abnormalities.
- No one agent or technique has been shown superior.
- Maintain normothermia and adequate hematocrit (≥28%).

Extubation

- Period at greatest risk for developing ischemia.

Postoperative Period

- Pain management may be critical.
- Consider monitoring troponin if there are any signs/symptoms of myocardial ischemia. Some authors suggest routine monitoring of troponin in this population.

Adjuvants

- β-adrenergic receptor antagonist, nitroglycerin, Ca^{2+}-channel blockers

Anticipated Problems/Concerns

- Pts with angina who develop dyspnea on exertion are at greatest risk for developing periop cardiac complications.
- Exercise tolerance may be the best predictor of periop risk. Pts with a good exercise tolerance may not require further evaluation for less-invasive procedures.
- Pts who develop periop MI are at increased risk of periop death and long-term morbidity/mortality. Elevated troponin also associated with worse long-term outcomes.

Anhidrosis (Congenital Anhidrotic Ectodermal Dysplasia)

Srijaya K. Reddy | Raafat S. Hannallah

Risk

- Rare: 1:125,000,000
- Clusters in Japan and Israel

Perioperative Risks

- Impaired thermoregulation (risk of fatal hyperpyrexia in infants)
- Postop chest infections

Worry About

- Absence of sweat leads to impaired thermoregulation.
- Insensitivity to superficial and deep painful stimuli with intact tactile perception; still require considerable amounts of inhalational or IV anesthetics to maintain hemodynamic stability and obtund stress response to airway manipulation.

Overview

- Innervation of the eccrine sweat glands is lacking; heat loss by evaporation is impaired.
- Absent mucous glands from resp tract and esophagus; frequent resp infections.
- Partial or complete absence of teeth.
- Hypotrichosis (absent hair).
- Self-mutilating behavior and mental retardation.
- Characteristic facies: Prominent supraorbital ridges, depressed bridge and root of nose, large deformed ears, thick lips, underdeveloped maxilla and mandible.

Etiology

- Sex-linked autosomal recessive disorder.
- Human *TRKA* (*NTRK1*) encodes the RTKs for NGF and is the gene responsible.
- Full expression only in males; carrier females may be mildly affected.

Usual Treatment

- Protect from risks of hyperpyrexia due to infection, hot weather, vigorous exercise

Assessment Points

System	Effect	Assessment by Hx	Test
HEENT	Airway anomalies	Snoring Difficult breathing	
RESP	Decreased mucus	Repeated infections	
ANS	Delayed gastric emptying Hemodynamic instability	Vomiting Hypotension/bradycardia	
OPHTHAL	Decreased lacrimation	Dryness, ulceration	
METAB	Hyperpyrexia		Record/monitor temp

Key References: Zlotnik A, Natanel D, Kutz R, et al: Anesthetic management of patients with congenital insensitivity to pain with anhidrosis: a retrospective analysis of 358 procedures performed under general anesthesia, *Anesth Analg* 121(5):1316–1320, 2015; Zlotnik A, Gruenbaum SE, Rozet I, et al: Risk of aspiration during anesthesia in patients with congenital insensitivity to pain with anihidrosis: case reports and review of the literature, *J Anesth* 24(5):778–782, 2010.

Perioperative Implications

Preoperative Preparation
- Avoid anticholinergic premedication; however atropine has been used to treat bradycardia.

Monitoring
- Routine
- Temp

Airway
- Full stomach precautions.
- Awkward mask fit.
- Laryngoscopy and intubation may be difficult.

Maintenance
- Regional anesthesia may be preferable when possible.
- Humidify anesthetic gases.
- Control room temp to avoid hyperthermia.

Extubation
- Vigorous postop chest physical therapy

Adjuvants
- Protect eyes with tape and ophthalmic ointment (higher risk for corneal abrasion).

Anticipated Problems/Concerns
- Difficult airway (mask and/or intubation)
- Hyperthermia
- Postop chest infections
- Regurgitation/vomiting/aspiration
- High incidence of CV events (hypotension and bradycardia) reported

Ankylosing Spondylitis

John E. Tetzlaff

Risk
- 1:2000 incidence in Caucasians; rare in non-Caucasians
- M:F 10:1; more severe in males
- 18-50% incidence in Native Americans

Perioperative Risks
- Difficult airway and atlantoaxial instability
- "Bamboo spine" with potential for fracture during airway manipulation
- Rigid chest with difficult ventilation
- Myocarditis and myocardial conduction defects
- Increased blood loss due to abnormal chest structure or mechanics

Worry About
- Inability to intubate, spine fracture, arrhythmia, inability to ventilate, and massive blood loss
- Airway edema after extubation

Overview
- An arthritic process, seronegative for rheumatoid factor, which attacks ligamentous attachments of the spinal column
- Characterized by low-back pain, sacroiliitis, multiplane rigidity of the spine, chest stiffness, uveitis, and insidious onset at <40 y of age
- Autosomal dominant and strongly prevalent among first-degree relatives

Etiology
- Etiology unknown
- Genetic transmission led to discovery of a genetic marker, HLA-B27. Also involved are the major histocompatibility complex, numerous HLA-B27 subtypes, IL23R (also associated with ulcerative colitis), and ERAP-1.
- Infectious origin speculated; one species of *klebsiella* is reported to be associated with some cases.

Usual Treatment
- Symptomatic, with exercise and NSAIDs; Immunosuppression can be tried in severe cases.
- Wedge osteotomy is a drastic surgical intervention.
- Infliximab: monoclonal antibody specific for TNF.
- Etanercept: Anti-TNF protein.
- Adalimumab: Monoclonal antibody specific for TNF.

Assessment Points

System	Effect	Assessment By Hx	PE	Test
HEENT	Uveitis TMJ arthritis Arytenoid deviation	Visual disturbance Limited mouth opening, jaw pain, voice abnormality	Funduscopic exam Airway exam Indirect laryngoscopy	Fiberoptic nasopharyngoscopy
CV	Cardiomyopathy, conduction defects	SOB, chest pain, palpitation	Distant heart sounds, rales, arrhythmia	ECG, CXR, ECHO
RESP	Pleuritic inflammation, chest rigidity	Chest pain, limited exercise tolerance	Decreased breath sounds, chest excursion	PFTs, CXR
GI	Irritable bowel syndrome Ulcerative colitis	Abdominal pain, bowel dysfunction	Abdominal pain	
GU	Chronic prostatitis	Pain with urination	Rectal exam	
CNS	Atlantoaxial subluxation, occult spinal fracture	Long tract signs, sphincter abnormality; sometimes no symptoms	Basic neurologic exam	Cervical spine x-ray with flexion-extension, MRI
PNS	Radiculopathy	Radiating pain in extremities	ROM of the extremity	EMG (medicolegal use)
MS	Back pain, sacroiliitis, joint ankylosis, kyphosis ("chin on chest"), "bamboo spine," spondylodiscitis	Review of skeletal function	Spine, skeleton	Radiologic studies

Key References: Hu SS, Ananthakrishman D: Ankylosing spondylitis. In Rothman RA, Simeone FA, editors: *The spine,* ed 5, Philadelphia, 2011, Elsevier; Schlew BL, Vaghadia H: Ankylosing spondylitis and neuraxial anesthesia: a 10 year review, *Can J Anesth* 43(1):65–68, 1996.

Perioperative Implications

Preoperative Preparation
- Airway evaluation, pulm function assessment; consider positioning difficulties.
- Antisialagogue for awake intubation.
- Review MRI of the spine.

Monitoring
- ST-segment analysis; pulm artery cath if severe myocardial dysfunction
- Arterial line, central venous access for extensive osteotomy secondary to blood loss

Airway
- Difficult intubation possible, owing to cervical spine fusion or distortion; fiberoptic intubation may be necessary; cervical spine instability possible; spinal fracture possible with airway manipulation; occult spinal fracture may already be present.
- Increasing role for videolaryngoscopy.

Induction
- If general anesthesia, any approach is acceptable. If limited cardiac reserves, avoid depressants of myocardial contractility. If regional, skeletal abnormality can make the block difficult to perform, and response to injection is unpredictable. In some cases, epidural space is obliterated and cannot be completely accessed. If local anesthetic toxicity, airway management can be difficult.

Maintenance
- With positive pressure ventilation, decrease tidal volume and increase rate. Consider pressure support ventilation.
- High ventilating pressure may predict large blood loss.

Extubation
- Awake is preferable.
- Airway edema is possible after extensive anterior osteotomy, decompression, and/or fusion. Compression of the airway from retropharyngeal hematoma is possible. Consider leak test before extubation, or maintaining the pt intubated and sedation for 12-24 h postop. Consider extubation over tube exchanger.

Adjuvants
- Ischemic optic neuropathy with prolonged procedures in the prone position

Postoperative Period
- Comfortable pt position and pain control without airway obstruction

Anticipated Problems/Concerns
- Airway control
  - The extreme distortion of the spine, especially the neck, may make intubating the trachea and ventilating the pt very difficult.
  - Any airway compromise or depression of ventilation can result in catastrophe.
  - Depression of ventilation with opiate analgesics can be dangerous.
- Pulm function
  - Owing to abnormal mechanics of the thorax and neck, the ability to ensure normal oxygenation during surgery and in the postop period can be a potential problem.
- Regional anesthesia
  - Placement of spinal, epidural, or caudal block could be technically very difficult. Action of local anesthetics in the central axis could be unpredictable. Consider preop x-rays of the lumbar spine to facilitate access for neuraxial block.
  - Strongly consider paramedian approach to central block.
- Prolonged postop intubation
  - Substantial blood loss, fluid/blood product administration, and the prone position make airway edema likely, requiring extended postop intubation. Pt should be informed preop to avoid panic postop.

Anomalous Pulmonary Venous Drainage

Roger A. Moore

Risk
- One percent of all congenital heart defects.
- TAPVD, the severe form, or PAPVD, the less severe form, exists when pulm veins drain into the venous circulation.
- M:F 4:1 in infradiaphragmatic type.

Perioperative Risks
- Rapid CV deterioration secondary to hypercapnia and resultant acidosis
- Sudden pulm Htn and RHF during hypoventilation
- Periop mortality: 2-20% depending on preop status

Worry About
- Air bubbles entering the venous circuit
- Endocarditis risk
- Concurrent pneumonia with hypoxemia or hypercarbia
- Polycythemic hyperviscosity attack with:
  - Periop dehydration
  - Cold OR environment

Overview
- TAPVD incompatible with life unless an ASD allows adequate R-to-L shunting of blood. TAPVD pts with small ASDs are more critically ill and often require balloon septostomy as a bridge to surgery. Some cyanosis, usually with O_2 saturations of 85-95%.
- Increased flow through pulm vascular beds results in pulm Htn.
- Four types of TAPVD:
  - Supracardiac: Pulm veins connect to the left innominate vein via an anomalous "vertical vein" or connect to the right SVC via an anomalous "short connecting vein," or connect to the left SVC (45%).
  - Cardiac: Pulm veins drain into the coronary sinus or directly into the right atrium (23%).
  - Infracardiac: Pulm veins drain into IVC, portal veins, hepatic veins, or ductus venosus (21%).
  - Mixed: Combined supracardiac, cardiac, and infracardiac connections (11%).

Etiology
- Embryologic atresia or malformation of the common pulm venous system resulting in persistence of abnormal connections

Usual Treatment
- Severe TAPVD with little systemic shunt needs immediate cardiac correction after birth. Most children with TAPVD require cardiac correction before 1 y of age.
- Cardiac correction of PAPVD may be postponed into childhood.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Hypoxemia	Snoring	Airway class	
CV	CHF Hypoxemia Monitoring problems	Decreased activity level Dyspnea Anomalous peripheral vessels	Rales Cyanosis Pulses and blood pressures in all four extremities	ECG: RVH, RAH ECHO, cath Cardiac consultation
RESP	Hypoxemia	Bronchospasm SOB Pulm edema Exertional cyanosis	Wheezing Tachypnea Clubbing	CXR Granular lung fields
HEME	Sludging DIC	Polycythemia Bleeding or bruising	Clubbing Bruises	Hgb PT PTT, bleeding time
CNS		Previous stroke	Complete neurologic evaluation	CT scan if neurologic findings
MS		Feeding difficulty Failure to thrive	Ht, wt, head circumference	Plot of growth curves

Key References: Müller M, Scholz S, Maxeiner H, et al: Efficacy of inhaled iloprost in the management of pulmonary hypertension after cardiopulmonary bypass in infants undergoing congenital heart surgery. A case series of 31 patients, *HSR Proc Intensive Care Cardiovasc Anesth* 3(2):123–130, 2011; Young TW: Anomalous pulmonary venous return. In Moodie DS, editor: *Clinical management of congenital heart disease from infancy to adulthood*, Minneapolis, 2014, Cardiotext, pp.77–92.

Perioperative Implications

Preoperative Preparation

- Desired hemodynamics: Preload, normal (CVP 10-12 mm Hg); afterload, low; PVR, normal; HR, normal to high; contractility, normal
- Liberal oral fluids preop
- Avoid premedication causing hypoventilation
- Subacute bacterial endocarditis prophylaxis

Monitoring

- Absolute air bubble precaution
- Arterial cath
- CVP cath; know specific anatomy, incl SVC variations
- TEE
- Others as per ASA routine

Airway

- Associated congenital syndromes with airway anomalies
- Cricoid ring limiting airway diameter
- Primary need to maintain airway and avoid increased $PaCO_2$
- PEEP, with pulm edema or elevated pulm blood flow

Induction

- If IV in place, use fentanyl or ketamine with pancuronium, vecuronium, or rocuronium.
- If no IV:
  - If unstable, ketamine IM.
  - If stable, slow inhalational induction with sevoflurane (avoid high sevoflurane levels until IV placed).
- Actively avoid hypoventilation and agents that produce myocardial depression.

Maintenance

- Use fluids judiciously to avoid RV overload.
- Positive pressure ventilation usually improves oxygenation.
- Use narcotics in conjunction with inhalational agents as tolerated.
- Avoid nitrous oxide.
- Use high FiO_2.
- Capnographic $ETCO_2$ will not accurately reflect $PaCO_2$.
- Prepare for hypothermic cardiac arrest during TAPVR repair.
- Avoid hypothermia before and after bypass.

Extubation

- Do not attempt deep or early extubation.
- Before extubation, assess adequacy of ventilation (with insp pressures of at least −20 mm Hg) and tidal volumes.

Postoperative Period

- Close monitoring of ventilation and pulse oximetry.
- Active warming with avoidance of shivering.
- Be prepared for immediate reintubation.

Adjuvants

- Inotropic support with dopamine or epinephrine

Anticipated Problems/Concerns

- If pulm hypertensive crisis occurs:
  - Hyperventilate.
  - 100% inspired O_2.
  - Consider iloprost, prostaglandin E_1, tolazoline, amrinone, isoproterenol, or nitric oxide.

Anorexia Nervosa

Russell T. Wall III

Risk

- Primarily in white adolescent females from middle- or upper-class families; 4% to 10% males.
- More common in models, ballet students, and professions demanding high achievement.
- Occurs in 5-10 per 100,000 population; mortality rate 5-10%.
- Bimodal peak age of onset: 14 and 18 y.

Perioperative Risks

- Predisposing conditions include:
  - CV dysfunction (bradycardia, hypotension, and dysrhythmias).
  - Acid-base abnormalities (both metabolic acidosis and alkalosis are possible), lyte abnormalities (decreased K, Mg, NA, and P)
  - Hematologic abnormalities (decreased Hgb, WBC, fibrinogen, and plt).
  - Hypothermia, delayed gastric emptying, and renal dysfunction (prerenal azotemia).
- Lyte/nutrient abnormalities associated with refeeding: most dangerous is hypophosphatasia (but also thiamine deficiency and decreased K. Mg, NA, and P).

Worry About

- Degree and duration of malnutrition (excess protein depletion = impaired cellular function)
- Degree of organ dysfunction
- Greater weight loss = greater risk
- Refeeding syndrome (severe hypophosphatasia occurred in 0.5% in largest modern study)

Overview

- Anorexia nervosa
  - Obsessive fear of obesity; pursuit of thinness
  - Dramatic decrease in food intake and excessive physical activity
  - Refusal to maintain weight above 85% IBW
  - Distorted body image
  - Amenorrhea for >3 mo
  - Radical restriction of caloric intake
  - Appears cachectic
  - Risk of death high if weight loss >40% of IBW
  - Of patients, 40% to 50% recover with treatment; 20% to 30% improve with treatment
- Bulimia
  - Means "ox hunger" or voracious appetite
  - Obsessive fear of obesity; overconcern with body shape and weight
  - Appears well nourished
  - Averages two binge-eating episodes each wk for at least 3 mo
  - Irresistible urge to overeat; loss of control in desire to eat
  - Wt control by self-induced vomiting, diuretic and laxative use, strict dieting/fasting, vigorous exercise
  - Greater percent of alcohol use, illicit drug use, stealing, self-mutilation, and suicide attempts than with anorexia
  - Of patients, 30% to 60% recover with treatment

Etiology

- Unknown, but possibly hypothalamic dysfunction or psychiatric cause

Usual Treatment

- No specific/definitive treatment
- Therapies offered:
  - Psychotherapy (individual, group, and family)
  - Behavior modification
  - Antidepressants (TCAs, MAO inhibitors, serotonin-uptake inhibitors) often prescribed but not consistently effective
  - Nutrition counseling (1500 to 2500 calories/d, metoclopramide or bethanechol for gastric emptying, benzodiazepine before meals)
  - Relaxation exercises
- If severe: Hospitalization stressing weight gain, with tube feedings or hyperalimentation as last resort

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Decreased response to SNS Hypovolemia		Bradycardia Orthostatic hypotension Hypotension (<70 mm Hg systolic)	ECG
	LV dysfunction (myocardial atrophy) Decreased LV wall thickness Decreased LV cavity size Decreased myocardial contractility	CHF symptoms	CHF	CXR ECHO
	MV prolapse		Murmur	
	Cardiomyopathy secondary to ipecac Conduction abnormalities		Dysrhythmias (tachydysrhythmia, AV blocks, nonspecific ST-T changes, low QRS amplitude, sinus bradycardia, prolonged QT)	ECG
	Hypercholesterolemia			Cholesterol, triglycerides
	Anemia			Hct
	Thrombocytopenia			Plts
	Hypofibrinogenemia			Fibrinogen
RESP	Aspiration pneumonia Resp insufficiency	Vomiting with decreased consciousness Dyspnea Muscle weakness	Hypoxia, tachypnea Bradypnea (<15/min)	CXR Decreased P
GI	Delayed gastric emptying, decreased motility	Early satiety, abdominal pain		
	Esophagitis, esophageal/gastric rupture	Vomiting with bulimia	Pneumomediastinum	CXR
	Hepatic insufficiency		Pneumoperitoneum Fatty infiltration of liver	Abdominal x-rays Increased LFTs
RENAL	Prerenal azotemia secondary to decreased volume	Starvation Dehydration, vomiting		BUN 60–70 mg/dL Lytes (K, Na, P, Mg)
	Renal insufficiency Renal calculi	Decreased GFR		Serum creatinine
	Polyuria	XS caffeine and water ingestion		
	Acid-base abnormalities (metabolic acidosis/alkalosis)	Vomiting		ABGs
	Lyte abnormalities (decreased K, Na, Mg, CA, and P)	Diuretics, laxative abuse		Lytes
	Hypoalbuminemia	Rhabdomyolysis	Peripheral edema	<3 g/dL is evidence of severe protein malnutrition
	ATN			CPK, LDH, aldolase
ENDO	Decreased BMR Hypothermia (<96.6° F rectally)		Vasoconstriction	
	Estrogen deficiency	Amenorrhea		Decreased WBC (leukopenia)
	Depressed immune function Hypophosphatemia Hypomagnesemia Hypoglycemia			
	Euthyroid sick syndrome		Bradycardia Hypothermia Cold intolerance Dry skin and hair Slow DTRs	Serum P Serum Mg Serum glucose TFTs
CNS	Brain atrophy with dilated ventricles	Starvation		
	Risk for Wernicke/Korsakoff if refed without thiamine treatment	Illicit drug and alcohol use		
	Depression			
PNS	Peripheral neuropathy			EMG changes
MS	Osteoporosis	Estrogen and IGF-I deficiency	Vertebral compression fractures Stress fractures	X-rays of back and extremities
	Cachexia (if anorexic)			
	Myopathy	Dieting		

Key References: Helgeson LE: Obesity and nutritional disorders. In Fleisher LA, editor: *Anesthesia and uncommon diseases,* ed 5, Philadelphia, 2006, Saunders, pp 216–218; Rubin RT: Anorexia nervosa, bulimia nervosa, and other eating disorders. In DeGroot LJ, Jameson JL, editors: *Endocrinology,* ed 5, Philadelphia, 2006, Saunders, pp 877–886.

Perioperative Implications

Preoperative Preparation

- Evaluate degree and duration of malnutrition.
- Assess degree of organ damage (especially cardiac, pulm, renal, and hepatic).
- For emergency surgery, severely malnourished pts have significantly increased morbidity and/or mortality.
  - Delay elective surgery until pt is medically stable and nutritional status is improved.
  - Optimize hemodynamics, volume status, acid-base status, lytes (Na, K, P, and Mg), and glucose.
- Treat severe anemia if present.
- Consider metoclopramide to promote gastric emptying.

Monitoring

- ABGs, lytes.
- A-line, CVP, and PA cath may be indicated.

Airway

- Induction
  - Consider rapid-sequence induction (decreased GE sphincter tone and gastric emptying)
  - Cautious dosing because of possible LV dysfunction and hypovolemia
  - Antibiotics

Maintenance

- Aggressively avoid hypothermia.
- Cautious use of potent inhalation agents to avoid hemodynamic depression.
- Excess fluids may precipitate pulm edema and CHF.

Extubation

- Consider awake extubation.

Adjuvants

- Cautious use of muscle relaxants (decreased muscle mass, lyte and acid-base abnormalities)

Anticipated Problems/Concerns

- Temperature control
- Hemodynamic stability
- Acid-base and lyte management
- Whether pt's metabolic reserve is adequate to accommodate intraop and postop surgical stress and/or demands of wound healing and combating infection

Anticoagulation, Preoperative

Jerrold H. Levy

Risk

- Pts with mechanical heart valves, atrial fibrillation, pulm embolism, or recent venous thrombosis.
- Oral anticoagulant therapy (warfarin, oral Xa inhibitor-rivaroxaban, apixaban, and edoxaban) and direct thrombin inhibitor (dabigatran) and use of low-molecular-weight heparin, fondaparinux may increase potential risks in elective or emergency surgery.
- Other populations include pts who receive heparin IV before vascular or cardiac surgery and pts undergoing cardiac surgery with extracorporeal circulation.

Perioperative Risks

- Balance between risk of bleeding versus thromboembolic complication is a major periop risk.
- Risk is greater with major and emergency versus elective surgery.

Worry About

- Excessive allogeneic transfusions, either to correct effects of anticoagulation or for risk of excessive bleeding.
- In pts with valvular heart disease, concomitant hepatic dysfunction due to HF may produce abnormal PT and/or thrombocytopenia.
- Heparin-induced thrombocytopenia can be associated with heparin therapy due to acute administration or prolonged use (~5 d).

Overview

Heparin (Standard Unfractionated)

- For preventive therapy and acute management, cofactor antithrombin III binds to thrombin and factor X to inhibit their effects.
- Variability in response to heparin depends on:
  - Prep of heparin administered.
  - Individual characteristics of pts.
  - Duration of therapy (due to decreased antithrombin III levels).
- Duration of action depends on dose and method of administration.
  - 100 U/kg: $T_{½}$ 56 min.
  - IV: 60 min.
  - 400 U/kg: $T_{½}$ tripled.
  - SQ: 3 h.
- Depolymerized in endothelial cells.
- Eliminated in urine.
- Heparin resistance (many proteins neutralize anticoagulant therapy; prolonged therapy can lower antithrombin III levels).
- Monitoring of the anticoagulant effect: PTT or ACT.

Heparin (LMWH)

- $T_{½}$ 4 to 7 h
- Higher and more predictable bioavailability: 100%
- Removed by renal filtration; accumulates with renal failure
- Not reversed with protamine; no current reversal therapy except time

Heparin Reversal Treatment

- Protamine reversal according to the ratio heparin:protamine 1:1.3 (or start with 50 to 100 mg and check the ACT)
- Monitoring: ACT in cardiac surgery

Warfarin

- Oral anticoagulant.
- Member of the coumarin family.
- Vitamin K antagonist causing inactivation of factors II, VII, IX, and X and anticoagulants C/S.
- Used for thromboembolic complication prevention.
- Peak plasma concentration reached 1-4 h after ingestion.
- $T_{½}$: 36 to 42 h.
- INR required: 2-3.
- Stop for surgery: bridge with heparin, but new data questions this.

Warfarin Reversal Treatment

- Vitamin K: 10-20 mg PO, lower doses IM, or IV, but takes several days for normalization of INR
- Fresh frozen plasma starting with 2 U but higher doses required, Tx reactions common or circulatory overload, and lowest INR ~1.5
- Purified protein concentrates of II, VII, IX, and X with protein C/S (KCENTRA in US); Beriplex and Octaplex outside of US

Novel Agents Approved in Other Countries Not Yet Available in the United States

- Rivaroxaban, apixaban and edoxaban are oral Xa inhibitors.
- Dabigatran is an oral thrombin inhibitor.
- These agents studied in periop DVT prophylaxis and AF treatment.
- For dabigatran reversal, idarucizumab, a monoclonal antibody Rx, at 5 g, completely reverses its effects (Praxbind).
- For Xa reversal, andexanet is under investigation, but growing data about use of PCCs in this setting.

Assessment Points

System	Effect	Assessment by Hx
ENDO	Risk of protamine reactions is 10- to 30-fold higher in diabetics receiving protamine-containing insulin	Hx of insulin use

Key References: Levy JH, Spyropoulos AC, Samama CM, et al: Direct oral anticoagulants: new drugs and new concepts, *JACC Cardiovasc Interv* 7(12):1333–1351, 2014; Douketis JD, Spyropoulos AC, Kaatz S, et al: Perioperative bridging anticoagulation in patients with atrial fibrillation, *N Engl J Med* 373(9):823–833, 2015.

Perioperative Implications

Preoperative Preparation

- Elective surgery/warfarin therapy.
  - Stop warfarin 5 d before surgery.
  - Depending on situation, potentially replace with heparin in checking INR, PTT, and platelet count.
  - Stop heparin a minimum of 2-3 h before surgery.
  - Recent evidence (BRIDGE Trial) suggests that bridge therapy may result in increased bleeding without reduction in thromboembolic benefits in patients on anticoagulant therapy for AFIB.
- Reversal for emergency surgery.
  - Warfarin therapy can be acutely reversed with PCC, and heparin therapy can be reversed with protamine; dabigatran can be reversed with idarucizumab.
- Consider avoiding regional anesthesia.
- Approach anticoagulation reversal cautiously in the anticoagulated patient.

Postoperative Period

- Restart heparin therapy immediately after surgery (PTT, plt count, blood cell count, and bleeding).

Anticipated Problems/Concerns

- Introduction of epidural or spinal anesthesia requires minimum 60-120 min between stopping and restarting heparinization; consider removing cath at least 120 min after stopping heparinization and complete restoration of normal clotting time. Longer times are required with other longer-acting anticoagulation agents.

Antithrombin III Deficiency

Ellise Delphin | Vasanti Tilak

Risk

- Incidence in USA: 1:2000-5000 (may be higher)
- Men and women equally affected and no racial or ethnic difference

Perioperative Risks

- Risk of postop thromboembolic phenomena; 40% to 70%, most common (in descending order): DVT, pulm embolus, mesenteric thrombosis, cerebral venous, and retinal thrombosis; highest risk in those with antithrombin III (AT III) levels <50% of normal
- Risk of pregnancy-related venous thromboembolism may be >50% in untreated pts
- Heparin resistance is common

Worry About

- Hypercoagulable state periop
- Thrombus formation on indwelling cath
- Pulm emboli or DVT with immobility
- Mesenteric, inferior vena cava, or CNS thrombosis
- Withdrawal of warfarin sodium preop, as pts may be heparin resistant
- Timing of neuraxial anesthesia in anticoagulated pts

Overview

- AT III is an α_2-globulin and a serine protease inhibitor, capable of inactivation of thrombin and factor Xa in blood.
  - It has antiinflammatory properties via interactions with the endothelium.
  - AT III deficiency results in an unusual susceptibility to thromboembolic disease.
- Heparin resistance may be problematic during surgery.
- Massive thromboembolism can occur periop with AT III levels <50.

Etiology

- Genetic: Reduced AT III synthesis inherited as an autosomal dominant trait, manifests as thromboembolism in late teens to early 30s
- Acquired: Secondary to consumption of AT III due to massive thromboembolic disease, DIC, renal disease with proteinuria (especially nephrotic

syndrome), chronic liver disease, prolonged heparin therapy, and increased protein catabolism
- Conflicting data about role of oral contraceptive use, pregnancy, and CAD

Usual Treatment

- Medical therapy: LMWH, unfractionated heparin, sodium warfarin, or combination of oral anticoagulants
- Periop: FFP, cryo-precipitate, AT III concentrate (plasma derived or recombinant), and heparin (heparin resistance can be treated with FFP).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CAD		Angina, dyspnea	ECG, CXR, angiography
PVS	DVT Arterial occlusion		Gangrene, absent pulses	
RESP	Pulm embolus	Dyspnea Exercise tolerance decreased	SOB	CXR V/Q scan
GI	Mesenteric artery/vein occlusion Decreased AT III	Abdominal pain Chronic liver disease symptoms	Rectal bleeding, jaundice, hepatomegaly	Serum albumin, AT III level
HEME	Bleeding and thrombosis	DIC	Petechiae, purpura, thrombosis	FDP, PT, PTT, plt count, AT III level Anti-Xa assay
GU	Decreased albumin and AT III levels	Nephrotic syndrome, proteinuria	Edema	Urinalysis, serum albumin
CNS	CVA	Sudden onset; Hx of other embolic disease	Seizure, loss of vision/motor function	CT scan, angiogram

Key References: Maclean PS, Tait RC: Hereditary and acquired antithrombin deficiency: epidemiology, pathogenesis and treatment options, *Drugs* 67(10):1429–1440, 2007; Paidas MJ, Forsyth C, Quere I, et al: Perioperative and peripartum prevention of venous thromboembolism in patients with hereditary antithrombin deficiency using recombinant antithrombin therapy, *Blood Coagul Fibrinolysis* 25(5):444–450, 2014.

Perioperative Implications

Preinduction/Induction/Maintenance

- Assess whether congenital or acquired; if acquired, treat primary disease if possible.
- Weigh risks of thromboembolic phenomenon versus excessive bleeding.
- Stop oral anticoagulation and substitute FFP or AT III concentrate to bring AT III level to 80% to 120% normal.
- Heparin to provide PTT of >1.5 times control.
- Provide mechanical and pharmacologic thromboprophylaxis.

Monitoring

- Careful attention to temp
- Volume status and resp variables
- PTT, AT III levels, and anti-Xa activity assay

General Anesthesia

- No special concerns with airway, induction, or adjuvant drugs.
- Maintain normothermia to avoid hyperviscosity.
- Maintain intravascular volume.
- IV heparin effect should be monitored.
- Careful evaluations of hypotension or change in $ETCO_2$.

Regional Anesthesia

- Neuraxial techniques require meticulous attention to the timing of
  - Neuraxial anesthesia in relation to the last dose of anticoagulant.
  - First postop dose of anticoagulant in relation to the placement of neuraxial block and/or removal of indwelling cath.
- For plexus and peripheral blocks, follow ASRA guidelines for anticoagulated pts.

Postoperative Period

- Consider ICU for monitoring.
- Continue anticoagulation.
- Early mobilization.
- Remove indwelling cath ASAP.
- Oral anticoagulation might be reintroduced ASAP.

Anticipated Problems/Concerns

- Embolic phenomena can occur intraoperatively
- Monitoring lines may be foci for thrombus formation
- Perioperative thromboembolic events' major concern; continuous anticoagulation is required, as is operative prophylaxis with AT III concentrate (plasma derived or recombinant), FFP, and heparin

Anxiety Disorders

Misako Sakamaki

Risk

- Lifetime prevalence approximately 30% in USA
- Gender: Female (2× more likely compared with male)
- Environmental: Traumatic or stressful events
- Age: Often develop in childhood and early adulthood; however, may occur any time after a stressful event
- Medical conditions: Chronic mental or physical illness
- Genetics: Family psychiatric history

Perioperative Risks

- Generalized anxiety disorder leads to chronic autonomic hyperactivity with increased risks for CAD and Htn.
- Uncontrolled anxiety and fear may predispose pts to greater risk for acute postop pain and postop N/V.
- Increased risk of periop complications due to impaired response to stress.

Worry About

- Inadequately treated anxiety disorders affecting pt's decision-making and communication capacities, which may complicate medical courses
- Altered drug anesthetic requirements and drug metabolisms associated with psychiatric medications
- Systemic side effects from psychiatric medications
- Potential medication interactions with anesthetics
- Signs/symptoms may overlap with other medical conditions (e.g., hyperparathyroidism) and drug-induced causes (e.g., alcohol, caffeine, nicotine, withdrawal), which could be life-threatening.

Overview

- Types
  - Generalized anxiety disorder
  - Panic disorder
  - Social anxiety disorder
  - Specific phobias
  - PTSD
  - OCD
- Characterized by excessive apprehension, physical tension, physiologic symptoms, dissociative anxiety, and fear leading to significant distress or impairment
- Comorbidity with major depression (60%), other mental disorders, and substance abuse
- Associated with a variety of chronic medical conditions

Etiology

- Genetics: ↑ norepinephrine metabolites, ↓ GABA level, ↓ postsynaptic alpha-2 adrenergic receptor sensitivity, and ↓ benzodiazepine binding sites on platelets and lymphocytes; altered central processing involving amygdala and nuclei of basolateral complex that play central roles in fear and anxiety responses
- Stress
- Drugs: Caffeine, alcohol, nicotine, and withdrawals

Usual Treatment

- Lifestyle changes (e.g., regular exercise, reduce caffeine/alcohol/nicotine intake)
- Psychotherapy
- Pharmacotherapy
  - SSRI/SNRI
  - Benzodiazepines
  - Beta-blockers (for phobias)
  - Adjuvants therapy: TCAs, MAOIs, antipsychotics, buspirone, and pregabalin
- Alternative remedies: Kava-kava, valerian root, and passion flower
- Deep brain stimulation (OCD)
- Surgery: Cingulotomy (OCD)

Assessment Points

System	Effect	Assessment/PE	Test
CV	CAD, HTN, increased, dysrhythmias	Decreased exercise tolerance, diaphoresis, palpitations, angina, CHF symptoms	ECG and/or invasive testing if indicated
RESP	Obstructive lung disease, OSA	Decreased exercise tolerance	Generally not needed
GI	Irritable bowel syndrome	Nausea, diarrhea	
ENDO	Increased cholesterol		
CNS	Migraines Insomnia Hyperarousal state	Headaches, fatigue, tremor, sweating, restlessness	
MS	Muscle tension	Headaches and skeletal muscle pain	
IMMUNO	Altered immune response to stress and environment	Hay fever, hives	

Key References: Grant BF, Stinson FS, Dawson DA, et al: Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions, *Arch Gen Psychiatry* 61(8):807–816, 2004; Clarke H, Kirkham KR, Orser BA, et al: Gabapentin reduces preoperative anxiety and pain catastrophizing in highly anxious patients prior to major surgery: a blinded randomized placebo-controlled trial, *Can J Anesth* 60(5):432–443, 2013.

Perioperative Implications

Preoperative Preparation

- Discuss the periop needs and benefits of psychiatric intervention with surgeons and psychiatrists.
- Continue outpatient medications; abrupt cessation may cause withdrawal.
- Treat acute anxiety with benzodiazepine or beta-blockers if indicated.
- Alpha-2-delta blockers such as gabapentin and pregabalin may be effective in reducing preop anxiety and postop pain.
- Assess cardiovascular status: HR, cardiac rhythm, and BP.
- Review pt's medications, which may have significant interactions with periop medications.

Monitoring

- Myocardial ischemia, cardiac dysrhythmias, and BP control
- Altered temperature regulations; hyperpyrexia

Induction

- Sudden reduction of autonomic hyperactivity may cause BP and HR fluctuations.

Maintenance

- Altered drug metabolism and anesthetic requirements and potential drug interactions with intraop medications, incl:
  - SSRIs: CYP450 inhibitor (fluoxetine) associated with serotonin syndrome (tramadol, dextromethorphan, pethidine, and pentazocine)
  - TCAs: ↑MAC, ↑response to indirect-acting vasopressors and sympathetic stimulations, increased response to indirect-acting vasopressors (e.g., ephedrine) and sympathetic stimulation
  - MAOIs: Orthostatic hypotension, tyramine-induced hypertensive crisis, excessive effects of sympathomimetic drugs and sympathetic stimulation and serotonin syndrome (meperidine)
  - Antipsychotics: Orthostatic hypotension, increased QT and PR intervals, decreased BP under GA, extrapyramidal side effects (typical antipsychotics), decreased seizure threshold, abnormal temperature regulation, sedation, and neuroleptic malignant syndrome
  - Benzodiazepine: Diazepam, clonazepam, and midazolam are metabolized via CYP-mediated oxidation: Increased duration of effect with liver impairment; synergistic effects among benzo, hypnotics, and opioids
  - Kava-kava: Decreased SVR, increased effects of CNS depressants, abnormal platelet aggregation, and liver toxicity

Extubation

- Confusion and combativeness
- Prolonged narcosis

Postoperative Period

- Continue psychiatric medications to avoid acute relapse.
- Consider early psychiatric intervention.

Anticipated Problems/Concerns

- Anticipate enhanced postop acute pain and PONV.
- Anticipate complications related to substance abuse (e.g., alcohol withdrawal).
- Anticipate and treat postop delirium.
- Anticipate prolonged hospital course.
- Be cautious before introducing any new medications for potential drug interactions.

Aortic Regurgitation

Robert B. Schonberger | Paul G. Barash

Risk

- There are on the order of 100,000 aortic valve surgeries each year, with approximately 18,000 of them performed annually in the USA.
- Of aortic valves, 20% to 30% have isolated regurgitation at time of replacement.
- At time of replacement, 12-30% of aortic valves have combined regurgitation and stenosis.
- M:F ratio: 3:1.
- Racial predominance: None known.

Perioperative Risks

- Left ventricular failure
- Right ventricular failure
- Subendocardial ischemia
- Splanchnic ischemia

Worry About

- Underlying causes of acute aortic regurgitation including aortic dissection, a malfunctioning valve prosthesis, or endocarditis
- Hypertension, which increases aortic regurgitation and decreases cardiac output
- Bradycardia, which increases aortic regurgitation and decreases cardiac output
- When going onto bypass, avoid LV distention from fibrillatory arrest before aortic cross-clamping (frequently occurs during cooling on pump) until LV decompression is immediately achievable

Overview

- Long latency period between onset of hemodynamic changes and symptoms with the exception of acute aortic regurgitation (~20-30 y)
- Myocardial ischemia uncommon
- Bicuspid valve +/– ascending aortic aneurysm frequently associated with aortic regurgitation
- Abdominal pain a manifestation of splanchnic ischemia

Etiology

- Congenital bicuspid valve
- Damage to leaflets
- Aortic root dilatation
- Loss of commissural support

Treatment

- Medical: Control of systolic hypertension via vasodilators (e.g., ACE inhibitor), calcium channel blockers, and diuretics.
- In Marfan syndrome, which is often accompanied by aortic regurgitation and root dilation, angiotensin receptor blockers are a promising treatment to prevent or slow the progression of aortic dilation.
- Surgical: Aortic valve replacement.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Aortic valve dysfunction	Dyspnea with exercise	High-pitched, early diastolic, decrescendo blowing murmur Mid-diastolic low-pitched murmur (Austin Flint) Widened arterial pulse pressure (water-hammer) To and fro bobbing of head (de Musset sign)	CXR ECHO Cardiac MRI
	LV dysfunction	Dyspnea with exercise Nocturnal dyspnea	Displaced posterior MI S_3	ECG CXR ECHO Cardiac MRI Cardiac cath
RESP	CHF	Dyspnea Nocturnal dyspnea	Rales S_3	CXR
GI	Splanchnic ischemia	Abdominal pain	Distended abdomen	

Key References: Nishimura RA, Otto CM, Bonow RO, et al: 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 129(23):2440–2492, 2014; Wilson W, Taubert KA, Gewitz M, et al: Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group, *Circulation* 116(15):1736–1754, 2007.

Perioperative Implications

Preoperative Preparation

- Consider optimizing LV performance with vasodilators, inotropes, and diuretics.
- Avoid reduction in aortic diastolic pressure, and be vigilant regarding low mean arterial pressures despite apparently normal systolic pressures.
- Emergent procedures (acute aortic regurgitation); full-stomach precautions.

Monitoring

- Arterial cath.
- ECG leads II/V5 and ST-segment analysis.
- Consider pulmonary artery cath and transesophageal ECHO.

Preinduction/Induction

- Elective: Avoid hypertension, hypotension, hypoxemia, and bradycardia; nondepolarizing muscle relaxants may be preferred over succinylcholine due to their lack of bradycardic effects.
- Emergency (acute aortic regurgitation with aortic dissection): Weigh the aspiration risk against the danger of acute increases in aortic wall tension and avoidance of bradycardia and consider rapid-sequence technique.
- Decreased aortic diastolic pressure combined with elevated LV diastolic pressures can lead to decreased coronary perfusion and subendocardial ischemia.
- Bradycardia and elevations in SVR increase regurgitant fraction and decrease cardiac output.

Maintenance

- Hemodynamic goals remain to avoid bradycardia, increases in SVR and decreases in diastolic blood pressure.
- Pulmonary capillary wedge pressures may underestimate LVEDP due to premature closure of the mitral valve.
- Pulmonary capillary wedge pressures may overestimate LVEDP in pts with combined aortic regurgitation and mitral regurgitation.

Extubation

- Consider extubation for patients undergoing valve replacement in the intensive care unit after respiratory and hemodynamic criteria are met.

Postoperative Period

- Consider augmenting preload to maintain and preserve filling volume of a still-dilated LV cavity.
- Inotropic support may be required to maintain cardiac output if inadequate intraop myocardial preservation was achieved.
- Evaluation for neuro injuries secondary to embolism during valve replacement. Meticulous de-airing maneuvers will lessen gaseous microembolization.

Anticipated Problems/Concerns

- Prolonged Trendelenburg position may be poorly tolerated during central venous cath insertion.
- Intraaortic balloon counterpulsation contraindicated before valve replacement.
- Atrial fibrillation or other SVTs may be poorly tolerated and may require aggressive treatment.
- Retrograde cardioplegia (not anterograde) may be required for myocardial protection.
- Associated diseases may present difficult intubation (e.g., rheumatoid arthritis, Marfan syndrome, trauma from acute aortic dissection).
- On separation from cardiopulmonary bypass, complete ECHO exam is recommended to examine the integrity of the replacement, as well as unanticipated iatrogenic injuries to other cardiac structures.

Aortic Stenosis

Jared Feinman

Risk

- Most common valvular heart disease; prevalence only 0.2% among adults aged 50-59 y, but increases to almost 10% after age 80 y.
- Calcific aortic stenosis: Major risk factors are increasing age, LDL, diabetes mellitus, smoking, hypertension, and bicuspid valve anatomy. Less common risk factors include disorders of calcium metabolism, renal failure, and history of mediastinal radiation.
- Bicuspid aortic valve is present in 1-2% of USA population and accounts for 60% of AVRs in pts under age 70 y and 40% over 70 y.
- Rheumatic aortic stenosis: Late sequela of streptococcal infection, more common in developing countries and often involves other valves.

Perioperative Risks

- Hypovolemia and/or vasodilation from anesthetic drugs lead to hypotension due to lack of preload reserve necessary to overcome systolic pressure gradient in pts with severe AS
- Risk of myocardial ischemia is elevated due to increase in LVED pressure (reducing coronary perfusion gradient) and LVH (associated with structural coronary abnormalities)
- Bicuspid valve associated with ascending aortic aneurysm and dissection, with a lifetime risk of about 6%

Worry About

- Drop in SVR and preload leads to reduced stroke volume through stenotic valve.
- Reduced SVR and stroke volume leads to hypotension, which reduces coronary perfusion and may lead to myocardial ischemia.
- Tachycardia poorly tolerated.
- Diastolic dysfunction very common.
- Atrial fibrillation; atrial kick provides up to 40% of LVED volume in AS pts, and its loss can lead to profound hypotension.

Overview

- Normal valve area (AVA) 2.6-3.5 cm^2; AS classified as mild (AVA >1.5 cm^2), moderate (AVA 1-1.5 cm^2), and severe (AVA <1 cm^2).
- Stenosis at the aortic valve leads to development of pressure gradient from LV to aorta.
- Increase in LV systolic pressure increases wall tension, producing LV hypertrophy.
- LV hypertrophy and augmented preload are primary means of maintaining adequate stroke volume and cardiac output in severe AS.
- Hypertrophy decreases LV compliance and diastolic dysfunction may ensue, making atrial contraction critical for maintaining adequate LV filling and stroke volume.
- Preload reserve generally exhausted in severe AS, so hypovolemia and reduced SVR are poorly tolerated.
- Elevated LVED pressure and alterations in coronary microcirculation associated with LV hypertrophy reduce coronary perfusion.
- Angina, dyspnea, and syncope are common presenting symptoms.
- Diagnosis of AS is made using ECHO or in the cath lab by assessing pressure gradient and valve area.
- Mean and peak pressure gradients across the valve also are used to classify severity.

- Pressure gradients may be low despite severe AS in pts with reduced EF (low-flow/low-gradient AS) or small ventricular volumes (low-flow/low-gradient AS with preserved EF).

Etiology

- Congenital bicuspid (and rarely unicuspid) aortic valve
- Rheumatic aortic stenosis
- Calcific degenerative disease

Usual Treatment

- Early in the disease process, medical therapy is indicated, including lifestyle modification (e.g., smoking cessation, exercise), and judicious use of antihypertensives.
- In severe AS, medical therapy does not prolong life, and AVR is the only effective treatment.
- AVR is a Class I indication in pts with
  - Symptomatic severe AS.
  - Asymptomatic severe AS with a LVEF <50%.
  - Asymptomatic severe AS in pts undergoing other cardiac surgery.
- AVR is a Class IIa indication in pts with:
  - Asymptomatic severe AS and low surgical risk.
  - Asymptomatic severe AS and decreased exercise tolerance or fall in BP with exercise.
  - Symptomatic low-flow/low-gradient severe AS.
  - Moderate AS in pts undergoing other cardiac surgery.
- TAVR is now a commonly used alternative to open AVR in pts who pose a high surgical risk due to age, comorbidities, and/or previous cardiac surgery.
- Balloon valvuloplasty may be used as a bridge to definitive surgical treatment with open AVR or TAVR.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Severe aortic stenosis Myocardial ischemia Diastolic dysfunction Arrhythmias	Angina, dyspnea, syncope Angina Dyspnea Palpitations, syncope	Systolic murmur Rales, edema, wheeze Rales, edema, JV distention Irregular pulse on exam	ECHO, cardiac cath, and dobutamine stress ECHO in suspected low-gradient AS ECG, ECHO, coronary angiography CXR, ECHO ECG, Holter
CNS	Syncope	Syncope		ECG, Holter, ECHO

Key References: Rashedi N, Otto C: Aortic stenosis: changing disease concepts, *J Cardiovasc Ultrasound* 23(2):59–69, 2015; Cook D, Housmans P, Rehfeldt K: Valvular heart disease: replacement and repair. In Kaplan J, editor: *Kaplan's cardiac anesthesia: the echo era,* ed 6. St. Louis, 2011, Elsevier, pp 570–584.

Preoperative Preparation

- Adequate premedication to reduce preop tachycardia due to anxiety.
- Ensure adequate preload but beware of administering large amounts of volume rapidly due to diastolic dysfunction.
- Pts with severe symptomatic AS may benefit from postponement of elective surgery until after AVR is performed.

Monitoring

- ECG for ST segment analysis.
- Preinduction invasive arterial pressure monitoring.
- Pulm artery cath may be useful in major surgery with large fluid shifts to better assess LVED pressure and volume status.
- Transesophageal ECHO warranted when blood loss or volume shifts are anticipated and an experienced echocardiographer is available.

Airway

- None

Preinduction/Induction

- Narcotic heavy induction is beneficial due to bradycardia, maintenance of SVR, and blunting of sympathetic response to laryngoscopy.
- Alpha agonist like phenylephrine should be used to treat hypotension with induction.
- Judicious use of propofol (and co-administration of an alpha agonist) is warranted to limit drop in SVR. Etomidate may also be useful for this reason.
- Laryngoscopy only after sufficient sympathetic attenuation.

Maintenance

- Intraop fluid management should aim for maintaining already elevated left-sided filling pressures with adequate replacement of blood loss and insensible losses.
- Balanced anesthetic using narcotics, muscle relaxant, and a lower dose of volatile agent is preferred.
- Higher doses of volatile agents may depress cardiac function, increase risk of arrhythmia-induced hypotension, and drop SVR, leading to hypotension and myocardial ischemia.
- Caution with agents that decrease preload and afterload (e.g., nitroglycerin, nitroprusside), or any agent with significant histamine release.
- Caution with agents that directly or indirectly increase heart rate (e.g., pancuronium, atropine).
- Early electrical cardioversion for intraop atrial fibrillation.
- Generally, avoid neuraxial anesthesia (especially spinal) due to hypotension from sympathectomy. Epidural anesthesia may be used with extreme caution in laboring pts and other cases where its benefit is strong, but must be carefully dosed for a gradual onset of block with minimal drop in SVR, while simultaneously augmenting preload and administering vasoconstrictors when needed.

Extubation

- Minimize sympathetic stimulation and tachycardia.

Postoperative Period

- Aggressive pain control
- Maintenance fluids as appropriate to maintain adequate preload

Anticipated Problems/Concerns

- Myocardial ischemia with intraop hypotension.
- Diastolic dysfunction.
- Dysrhythmias can lead to precipitous hypotension and ischemia and should be treated aggressively until a return to sinus rhythm is achieved or hemodynamics stabilize.

Apert Syndrome (Acrocephalosyndactyly Type 1 and 2)

Andrea Johnson

Risk

- 15:1,000,000 live births
- Equal M:F ratio

Perioperative Risk

- Aspiration
- Bronchospasm
- Resp depression
- Airway obstruction

Worry About

- Difficult mask, airway, or IV access
- Elevated intracranial pressure, temperature dysregulation, and seizures
- Corneal abrasions (due to exophthalmos)
- PACU and perioperative monitoring for apnea
- Cardiac anomalies (10% of cases)
- Anatomic anomalies (regional/neuraxial anesthesia)

Overview

- Apert syndrome is a disorder identified by synostoses of the cranium, vertebral bodies, and digits. It is caused by a mutation in the FGFR-2 gene.
- Two major manifestations are bicoronal synostosis and maxillary hypoplasia. High-arched V-shaped palates and cleft palates are common.
- Strabismus, syndactyly, and conductive and neuronal hearing loss are common manifestations.
- Cognitive delay (IQ <70) see in 67% of pts.

Etiology

- Autosomal dominate disorder; however, most cases are sporadic mutations of the FGFR-2 gene.
- Sporadic mutations are associated with paternal age >40 y.

Usual Treatment

- Craniosynostosis release: Frontoorbital advancement usually around 6 to 8 mo of age
- Midface advancement: Correction of brachycephaly, orbital dystopia, or midface hypoplasia
- Correction of hypertelorism: Interorbital bone resection
- Mandibular and maxillary advancement and orthodontics: Usually conducted after cranial maturation to enhance cosmetic appearance

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	CNS malformations Ventriculomegaly Hydrocephaly Elevated intracranial pressure Thermoregulatory disorders Cognitive delay	Developmental delay, nausea/vomiting, headache	Papilledema	CT/MRI
HEENT	Craniosynostosis, midface hypoplasia, nasopharyngeal, and palatal anomalies	Dyspnea Difficulty phonating	Early fusion of cranial sutures Hypertelorism Cleft or V-shaped palate	Radiologic studies
CV	Atrial septal defect/ventricular septal defect Patent foramen ovale Overriding aorta	Dyspnea Lethargy	Heart murmur	ECHO
RESP	Central/obstructive sleep apnea Aspiration Bronchospasm Increased airway secretions	Daytime somnolence Snoring Witnessed apnea Coughing Wheezing	Wheezing Course breath sounds Increased oral secretions	Sleep study
MS	Cervical spine abnormalities (usually fusion at C5-C6) Syndactyly	Limb abnormalities	Decreased cervical ROM	Radiographic studies

Key References: Niraj K, Shubhangi A, Ashish B, et al.: Anesthetic management of craniosynostosis repair in patient with Apert syndrome, *Saudi J Anaesth* 8(3):399–401, 2014; Losee JE, Gimbel ML, Rubin J, Plastic and reconstructive surgery. In Brunicardi F, Andersen DK, Billiar TR, editors: *Schwartz's principles of surgery*, ed 10, New York, 2014, McGraw-Hill.

Perioperative Management

Preoperative Consideration

- Review imaging to assess for increased ICP and cardiac and airway anomalies.
- Preoperative warming measures.
- Minimize risk of bronchospasm; consider antisialagogue and beta-2 agonist.
- Anticipate difficult IV scenario.
- Discuss with surgical team the risk for admission, especially with a history of sleep apnea.

Monitoring

- Standard ASA monitors
- Arterial line if indicated
- Core temperature when possible

General Anesthesia

- Maintain normothermia.
- Multimodal approach to pain management to minimize opiates.
- Consider intermittent gentle suctioning through ETT to prevent mucus plugs.

Regional Anesthesia

- Due to anatomic anomalies with bone and soft tissues, consider performing all regional techniques under ultrasound.
- Exercise caution with regional techniques known to interrupt innervation of the diaphragm or cough reflexes.

Postoperative Period

- Anticipate prolonged postop ventilation.
- Exercise caution with sedating medications for pain control.
- Monitor and treat for bronchospasm or laryngospasm in PACU.

Anticipated Problems/Concerns

- Anticipate prolonged monitoring or hospitalization for pts with history of sleep apnea.
- Anticipate bronchospasm, especially during periods of light of anesthesia.
- Suction airway and ETT judiciously before extubation and weigh risk/benefit of deep extubation.

Apnea of the Newborn

Shanique Brown Kilgallon | Alan Jay Schwartz

Risk

- Full-term infants with an underlying pathology (i.e., neurologic disorders, metabolic derangements)
- Premature infants, with or without an underlying pathology
- Infants less than 60 wk post conceptual age
- Underweight infants <1000 g
- Anemia

Perioperative Risks

- More prone to apnea during local or neuraxial anesthesia or when additionally administered IV sedative
- More prone to apnea after general anesthesia

Worry About

- Unexpected apnea in recovery room
- Unexpected apnea in hours after outpatient procedures
- Unexpected apnea on ward hours after inpatient procedures

Overview

- Apnea is defined as pauses that last >20 sec without physiologic derangement or that last >10 sec with physiologic derangement (i.e., bradycardia, oxygen desaturation).
- Apnea in term infants is never physiologic.
- Apnea in preterm infants may signal CNS disorder or developmental immaturity.
- Sudden onset of apnea in any infant may also reflect a new-onset sepsis or hypoglycemia.
- Utility of pneumogram screening controversial.
- Indications for home apnea monitoring controversial.

Etiology

- Term or preterm infants:
  - CNS disorders (seizures, bleeds, and structural changes)
  - Systemic disorders (hypoglycemia, sepsis, and GE reflux)
- Preterm infants:
  - Same as term infants
  - If full evaluation is negative, physiologic apnea of prematurity diagnosed

Usual Treatment

- Theophylline or caffeine
- O_2
- Transfusion
- CPAP

Assessment Points

System	Effect	Assessment By Hx	PE	Test
CV	Congenital heart disease leads to desaturation PDA may cause CHF	CHD, PGE_1 treatment	Murmur; cyanosis	ECHO
RESP	Children with bronchopulmonary dysplasia may be prone to apnea	Hx of hyaline membrane disease or other parenchymal lung disorder	Abnormal pulm compliance or O_2 requirement	CXR, ABGs, O_2 sat
GI	GE reflux may cause vagal overload	Hx of reflux	None obvious	pH study, barium swallow
CNS	Seizures may cause apnea; structural abnormalities may create ineffective respiratory drive	Hx of seizures or change in neurologic development	Exam for seizures or neurologic change	EEG, head US, CT, MRI

Key References: Henderson-Smart DJ, Steer P: Postoperative caffeine for presenting apnea in preterm infants, *Cochrane Database Syst Rev* (2):CD000048, 2000; Balain M, Oddie S: Management of apnoea and bradycardia in the newborn, *Paediatr Child Health* 24(1):17–22, 2014.

Perioperative Implications

Monitoring
- Routine

Airway
- Not usually a problem; obstructive apnea may occur but is rare.
- Bronchospasm may occur in infants with bronchopulmonary dysplasia.

Maintenance
- Usually no problem during procedure; vigilance required postop

Extubation
- Watch for intermittent inadequate respiratory effort for hours.

Adjuvants
- No special concerns

Anticipated Problems/Concerns

- Consider scheduling elective procedures after 60 wk post conceptual age.
- Periop not complex; vigilance regarding care and assessment in postop period.

Appendicitis, Acute

Gaurav Malhotra

Risk

- One of most common abdominal emergencies
- Possible at any age but most common during an individual's teens and 20s
- 11 in 10,000 individuals will experience appendicitis
- M:F ratio 1.4:1
- Most common reason for nonobstetric surgery during pregnancy; Occurs in 1 out of every 800 to 1500 pregnancies; slightly more common during second trimester; incidence of perforation highest during third trimester (70%)

Perioperative Risks

- Risk of intraabdominal perforation or abscess; risk increases with delay in diagnosis and treatment.
- Ileus.
- Sepsis.
- Fecal fistula.
- Mortality is 2-3% for perforated versus 0.1% for nonperforated appendicitis.
- Mortality for perforated appendicitis higher in elderly and pregnant pts.
- In pregnant pts, fetal mortality of approximately 35% for perforated appendicitis compared with 1.5-3% for uncomplicated appendicitis.

Worry About

- Airway and aspiration risk because pt may have full stomach with symptomatic nausea and vomiting
- Tachycardia due to pain, dehydration, or sepsis
- Hypotension due to dehydration or sepsis (poor PO intake, vomiting, diarrhea, or intra-abdominal abscess)
- Preop IV antibiotics
- Appendicitis in pregnancy
  - Possible delay in diagnosis due to atypical symptoms, as well as hesitation in performing imaging and diagnostic studies out of concern for the fetus
  - Awareness of anatomic and physiologic changes of the parturient
  - Avoidance of teratogenic agents and risk factors for intrauterine fetal asphyxia

Overview

- One of the most common abdominal emergencies in children, adults, and pregnant women.
- Increased risk of perforation if diagnosis delayed over 24 h.
- Increased morbidity/mortality with perforation.
- Pts may present with right-lower-quadrant or diffuse abdominal pain, nausea and vomiting, diarrhea, anorexia, malaise, fever, or mild leukocytosis.

Etiology

- Primarily due to appendiceal obstruction (80%); obstruction most commonly due to fecaliths, hyperplasia of lymphoid follicles (commonly in pediatric pts), stones, or tumors.
- Obstruction of the appendix causes increased intraluminal pressure, which leads to thrombosis and occlusion of blood vessels and lymphatics supplying it: this causes organ inflammation and ischemia, which can further progress to perforation, intraabdominal abscess, and peritonitis.
- Appendiceal inflammation leads to bacterial proliferation, most commonly anaerobic and gram-negative organisms.

Usual Treatment

- Appendectomy is standard of care. Pt should be taken to OR as soon as possible to avoid perforation or disease progression.
- Periop antibiotics may need to be continued postop, especially in cases of perforation.
- Laparoscopic or open appendectomy performed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia; hypotension	Vomiting; signs of dehydration	Vital signs; orthostatic signs	BP and HR ECG as indicated by H&P
RESP	V/Q mismatch	Dyspnea; tachypnea	Splinting due to abdominal pain, diminished breath sounds	Pulse oximetry and RR, increased A-a gradient
GI	Ileus, perforation, abscess	Abdominal pain, vomiting, diarrhea	McBurney point tenderness, abdominal guarding Peritoneal irritation: rebound tenderness; Rovsing and psoas signs	Abdominal x-ray, CT, US, barium enema WBC count
RENAL	Dehydration, electrolyte disturbances	Oliguria	Vitals signs; orthostatic signs	UA, BUN, creatinine

Key References: Backius M, McGrath B, Monk J, et al.: Changing epidemiology of acute appendicitis in the United States: study period 1993–2008, *J Surg Res* 175(2):185–190, 2012; Gadalla F: Appendectomy for a pregnant patient. In Yao F, Malhotra V, Fontes MI: *Yao and Artusio's anesthesiology: Problem-oriented patient management,* ed 7, Philadelphia, 2012, Lippincott Williams & Wilkins, pp 778–792.

Perioperative Implications

Preoperative Preparation

- Isotonic fluid replacement to correct fluid deficits and electrolyte abnormalities
- Aspiration prophylaxis: H_2 antagonist, nonparticulate antacid, and nasogastric tube placement
- Antibiotics with adequate gram-negative and anaerobic coverage
- Opiate premedication for abdominal pain
- Baseline fetal heart rate tracing in parturient

Monitoring

- Standard.
- Urinary catheter.
- Consider invasive monitors if septic.
- Consider fetal heart rate monitor if fetus is viable and obstetrics team is immediately available.

Airway

- Full stomach precautions

Induction

- Rapid sequence induction with cuffed ETT.
- Anticipate hemodynamic instability with induction in septic or dehydrated pts.
- In parturient, avoid supine hypotension syndrome by positioning in left uterine displacement.
- Can consider regional anesthesia if pt is cooperative, hydration is adequate, systemic sepsis is absent, and high abdominal exploration is unlikely.

Maintenance

- Standard maintenance with adequate muscle relaxation.
- Evacuate stomach with oral-gastric or nasogastric tube.
- If using laparoscopic approach, anticipate hypotension with abdominal insufflation causing decreased venous return and cardiac output.
- In parturient, ensure fetal well-being by maintaining adequate maternal oxygenation, hemoglobin content, and hemodynamics.

Extubation

- Extubate when pt is fully awake and regains laryngeal reflexes.

Postoperative Period

- Pain control with PCA, oral opioids, and NSAIDs.
- PONV; Treat with ondansetron, metoclopramide, or promethazine.
- Continue antibiotics for 3-5 d for perforated appendicitis.
- Monitor for sepsis.
- In parturient:
  - Fetal heart rate monitor to ensure fetal well-being.
  - Consider tocolytic medication to prevent premature labor (22% of women in third trimester go into labor within 1 wk of surgery).

Adjuvants

- Laparoscopic versus open appendectomy: Laparoscopic approach tends to have shorter hospital stay, decreased postop pain, and decreased wound infection rate; however, it also tends to have a higher rate of intraabdominal abscess and hospital costs.

Anticipated Problems/Concerns

- Aspiration risk
- Hemodynamic instability due to dehydration and possible sepsis

Arnold-Chiari Malformation (Chiari Malformation Type II)

Jason D. Walls | R. Alexander Schlichter

Risk

- Arnold-Chiari malformation (Chiari Malformation type II or CMII) is found exclusively in pts with myelomeningocele.
- Myelomeningocele occurs in 0.6 of 1000 live births.

Perioperative Risks

- Vocal cord paralysis
- Respiratory distress
- Apnea
- Neurogenic dysphagia and pulmonary aspiration
- Hydrocephalus and increased ICP
- Congenital heart defects (37% of pts with myelomeningocele) including atrial septal defect, ventricular septal defect, anomalous pulmonary return, tetralogy of Fallot, bicuspid aortic valve, coarctation of the aorta, and hypoplastic left heart syndrome

Worry About

- Any symptoms of possible brainstem compression (stridor, hoarse voice, or difficulty swallowing) in a child less than 2 y with CMII must be urgently evaluated as a neurosurgical emergency.
- Nearly 21% of children with myelomeningocele will development hindbrain, cranial nerve, or spinal cord compression by 3 mo of age, increasing to 33% by age 5 y.
- Of pts with symptomatic CMII, 15% die by 3 y of age.
- Mortality rate has improved with emergent surgical treatment in symptomatic pts.

Overview

- CMII is characterized by herniation of the cerebellar vermis, brainstem, and fourth ventricle through the foramen magnum in the setting of myelomeningocele.
- Commonly associated with hydrocephalus (90%) and syringomyelia (20-95%).
- Other variable abnormalities associated with CMII include dysplasia of the corpus callosum, enlargement of mass intermedia, abnormalities of the white and gray matter, hippocampal dysplasia, elongation of the pons, beaking of the midbrain tectum, and defects of the falx and tentorium.
- Symptomatic CMII is the leading cause of death in pts less than 2 y old with myelomeningocele.
- Symptoms differ relative to age of onset, with neonates presenting as a neurologic emergency and older children presenting with more subtle findings of hyporeflexia weakness, or headache.

Etiology

- Pathophysiology not completely understood
- Multiple theories of embryologic origin, including primary malformation or secondary abnormalities related to altered cerebral spinal fluid dynamics

Usual Treatment

- Early closure of myelomeningocele, usually within 72 h after birth, proven to cause upward movement of hindbrain herniation but does not appear to prevent lifetime occurrence of symptomatic CMII.
- Treatment of hydrocephalus more important than surgical decompression to prevent CMII symptoms, and, in any symptomatic CMII pt, physician must first rule out and treat hydrocephalus.
- Of pts, 20% will need surgical treatment including brainstem decompression via posterior cervical laminectomies at all involved segments and possible duraplasty.
- Unlike Chiari Malformation type I, suboccipital craniotomy often not necessary due to already enlarged foramen magnum.
- Intrauterine myelomeningocele repair shows evolving benefits of possibly preventing CMII and decreasing overall severity.
- Intrinsic brainstem dysfunction cannot be treated surgically.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Hindbrain herniation Hydrocephalus Increased ICP	Occipital headache, weak cry, irritability	Opisthotonus posturing, quadriparesis, hypotonia, ataxia, and down-beat nystagmus Increased head circumference; bulging anterior fontanelle	MRI Shunt evaluation
SPINAL CORD	Cervical myelopathy Syringomyelia	Altered dexterity, handwriting change, unable to provide self-care	Upper extremity weakness, spasticity, ataxia, hand muscle atrophy, scoliosis, back pain, and loss of sensorimotor function	MRI, SEP/ MEP
HEENT	Cranial nerve X dysfunction	Stridor (must evaluate to rule out neurologic cause; do not assume viral upper-respiratory infection)	Vocal cord paralysis; altered gag reflex	Laryngoscopy (direct; fiberoptic)
RESP	PEAC Central and obstructive breathing disorders	Snoring, apnea, daytime sleepiness, daytime attention deficit	Cyanosis, bradycardia, death during painful experience	PSG, ENT evaluation
GI	Neurogenic dysphagia, aspiration, nutritional deficiency	Choking, regurgitation, prolonged feeding time, weight loss	Muscle wasting; aspiration pneumonia	Swallow study; direct laryngoscopy

Key References: Messing-Jünger M, Röhrig A: Primary and secondary management of the Chiari II malformation in children with myelomeningocele, *Childs Nerv Syst* 29(9):1553–1562, 2013; McClain CD, Soriano SG, Rockoff MA: Pediatric neurosurgical anesthesia. In Cote CJ, Lerman J, Anderson B, editors: *A practice of anesthesia for infants and children,* ed 5, Philadelphia, 2013, Elsevier, pp 510–532.

Perioperative Implications

Preoperative Preparation

- Present for multitude of procedures including myelomeningocele closure, cerebral spinal fluid shunt placement, shunt revision, brainstem decompression, and scoliosis correction.
- Assess for latex allergy (increased risk in pts with myelomeningocele).
- Preoperative evaluation including assessment of concurrent comorbidities and active medications, as well as a focused physical exam to assess level of consciousness, motor and sensory function, cranial nerves, and ICP.
- Laboratory evaluation including hemoglobin, type and cross, and electrolytes.
- Review of relevant imaging studies, including CT scans, ECG, and chest plain films.

Monitoring

- Standard ASA monitors with invasive arterial blood pressure.
- Monitor urinary output.
- If central venous access deemed necessary due to pt disease or limited peripheral IV access, avoid neck veins to decrease risk of altering cerebral blood flow or venous drainage.
- Consider TIVA to facilitate neurophysiologic monitoring when applicable.

Airway

- Endotracheal intubation required (naso, oro, or tracheostomy)
- Limit neck flexion during intubation in pts with brainstem compression

Preinduction/Induction

- Use opioids carefully because of their respiratory depressant effects and possible deleterious effects on ICP.
- Sedatives including midazolam appear safe under the direct supervision of the anesthesiologist.
- IV induction with propofol preferred over inhalational induction.
- Avoid hypoxia, hypercarbia, and coughing to limit further increases in ICP when elevated.
- Position pts with myelomeningocele carefully to avoid direct pressure on neural tube defect.

Maintenance

- General anesthesia with controlled ventilation.
- Consider TIVA for benefits of improved neurophysiologic monitoring and favorable effects on cerebral blood flow, cerebral metabolic rate, and ICP.
- When in the prone position, pt's head is rigidly fixed with pins or placed in a cerebellar head frame when pinning contraindicated. Avoid excess neck flexion.
- Carefully evaluate blood loss and management of IV fluid administration, and attempt to limit cerebral edema while maintaining hemodynamic stability.
- Carefully manage known exaggerated heat loss secondary to the disproportionately large head of the neonate.

Extubation

- Prepare for the need for postop mechanical ventilation.
- During emergence and extubation, carefully avoid large fluctuations in ICP and blood pressure.

Postoperative Period

- 24-h monitoring in ICU

Anticipated Problems/Concerns

- Problems related to surgery including hemorrhage, infection, vascular injury, nerve injury, and persistent symptoms of brainstem compression
- Apnea or airway obstruction due to respiratory center or cranial nerve damage
- Secondary cervical instability or kyphosis following cervical laminectomy
- Venous air embolism

Aspiration, Perioperative

Onur Demirci | Paula A. Craigo

Risk

- Risk of aspiration: Approximately 3 per 10,000 anesthetics, 11 per 10,000 emergency and/or after-hours cases, and 29 per 10,000 emergency cases in ASA IV and V pts
- Loss of protective reflexes and sphincter function
- Obstructed or abnormal GI motility
- Increased gastric fluid volume; decreased pH
- Inadequate anesthesia leading to coughing and straining during airway manipulation or induction
- Trauma, emergency/night surgery, pregnancy, difficult airway, advanced age, long-standing diabetes mellitus, pain, analgesics, and ASA status >2
- Obesity: not an independent risk factor

Perioperative Risks

- Mortality after aspiration: 5%; higher if ASA >2 or if mechanical ventilation required for >24 h after the aspiration event

Worry About

- Of pts who aspirated, 20% had no risk factor: of these, 66% had difficult intubation
- Rapid-sequence induction may have deleterious effects on heart rate and blood pressure
- Clinical worsening may be delayed up to 24 h after the inciting aspiration event

Overview

- Prevention of aspiration best because there is no definitive treatment.
- Vast majority of pts with risk factor(s) do not aspirate.
- Consider aspiration in differential diagnosis of bronchospasm with hypoxemia.

Etiology

- Loss of protective reflexes: Sedation, neuromuscular disorders/relaxants, and altered mental status
- Obstructed or abnormal motility: Achalasia, gastroparesis, pain, and opioids
- Increased GI contents: Bleeding, obstruction, and feeds

Usual Treatment

- Suctioning or bronchoscopy if obstructing particles present
- Lavage and steroids not helpful; surfactant investigational
- Empiric antibiotics: Consider if pt is compromised, with fulminant course, or suspected high bacterial load due to bowel obstruction

Assessment Points

System	Effect	Assessment by History	Physical Examination	Test
HEENT	Awake intubation in difficult airway; cricoid pressure may distort anatomy and obstruct ventilation	Hx difficult airway, head and neck surgery/radiation	Airway exam	X-ray, CT scan, OR records as available
CV	Rapid-sequence intubation may lead to ischemia with tachycardia, hypertension/hypotension, or myocardial depression	Anginal Sx, exercise intolerance, Hx CHF, CAD age, sex, risk factors	S3, rales; displaced PMI	ECG and ECHO in selected patients
RESP	Rapid-sequence intubation may lead to bronchospasm	Hx pulm disease, wheezing with URI, smoking	Wheezing; prolonged expiratory phase	CXR, continuous pulse oximetry
GI	Abnormal sphincters, motility, acidity	Hx peptic ulcer disease, reflux Sx, diabetes, scleroderma, bowel obstruction	Abdominal exam for distention	
NEURO	Increased ICP leads to vomiting; depressed protective reflexes; muscle weakness		Neurologic exam	

Key References: Marik P: Aspiration pneumonitis and aspiration pneumonia, *N Engl J Med* 344(9):665–671, 2001; Tasch MD, Langeron O: Aspiration prevention and prophylaxis: preoperative considerations. In Hagberg CA, editor: *Benumof and Hagberg's airway management*, ed 3, Philadelphia, 2013, Elsevier, pp 265–279.

Perioperative Implications

Preoperative Preparation

- NPO status:
  - Adults: 6-8 h for solids depending on fat content and 2 h for clear liquids
  - Infants: 6 h for formula, 4 h for breast milk, and 2 h for clear liquids
- Pharmacologic prophylaxis in selected pts:
  - Increase gastric pH: Nonparticulate antacid, H_2 blockers, and proton pump inhibition
  - Decrease GI contents: prokinetics
  - Increase lower esophageal sphincter pressure: β-antagonists and metoclopramide
- Preinduction gastric emptying:
  - Preexisting orogastric or nasogastric tube to wall suction; might not remove particulate matter but will empty liquid contents
  - Proven not to cause/worsen gastroesophageal reflux

Monitoring

- Routine

Airway

- Protect airway with cuffed ETT or maintain protective reflexes.
- Awake intubation in difficult airway.
- LMA not protective against aspiration.

Preinduction/Induction

- Regional anesthesia can result in aspiration if seizures or hypotension decrease alertness.
- GA: Risk at induction and extubation.
- Denitrogenation with 100% O_2.
- Check optimal pt position, table height, drugs and tools available, and suction at hand.
- Rapid-sequence induction; cricoid pressure until ETT placement assured by $ETCO_2$.

Maintenance

- Care with depth of sedation during sedation/regional cases

Extubation

- Return of muscular strength/coordination/consciousness adequate to protect airway if emesis occurs.
- If emesis occurs, position pt with head-down or right-side tilt and thoroughly suction the oropharynx and trachea.

Postoperative Period

- If no symptoms in 2 h, significant aspiration extremely unlikely.
- If pneumonitis occurs, initial postop CXR may be normal, proceeding to white-out in a few to 24 h.
- PEEP redistributes lung water and improves oxygenation; higher PEEP may decrease cardiac output and ventilation.
- Maintaining low cardiac filling pressures may limit lung fluid accumulation but may worsen negative effects of PEEP.

Adjuvants

- Muscle relaxants must be dependably rapid acting.
- Regional anesthesia in high-risk pts: Avoid oversedation (loss of protective airway reflexes) hypotension (can cause nausea and vomiting).
- Drug interactions between anesthetic drugs and 1 or 2 doses of aspiration prophylaxis not significant.

Anticipated Problems/Concerns

- Must balance concern for aspiration risk against airway quality, cardiopulmonary reserve, and feasibility of regional techniques

Asthma, Acute

Puneet Sayal | T. Anthony Anderson

Risk

- Prevalence in USA: 25 million people; nearly 5% for persons age 5-34 y
- Increased prevalence and severity in African Americans, adult females, and atopic individuals

Perioperative Risks

- Risk related to degree of preop control of symptoms and optimization of medication regimen
- Morbidity due to bronchospasm and laryngospasm

Worry About

- Bronchospasm
- Hyperinflation of lungs
- Medication side effects (e.g., β-agonists causing tachycardia and hypokalemia)
- Adrenal insufficiency (chronic corticosteroid use)

Overview

- Characterized by chronic bronchial wall inflammation, reversible expiratory airflow obstruction, airway hyperreactivity, wheezing, dyspnea, and cough.
- Type I exacerbation: "slow-onset, late arrival," slow and progressive obstruction.
  - Inadequate asthma control, treatment, and/or compliance; preventable with better preoperative control (e.g., adding an inhaled corticosteroid).
  - Often overusing bronchodilators, maximally relaxed smooth muscle, inflammation undertreated, and airway edema present.
  - Additional beta-2 agonists not helpful, present with secretions and mucous plugging and eosinophilic infiltration; slower response to treatment.
  - Majority of asthma fatalities.
- Type II exacerbation: "Sudden-onset, fatal asthma," rapid and in response to an allergen.
  - Little airway inflammation, predominantly neutrophilic infiltration.
  - Reaction is typically in response to a specific allergen.
  - Rapidly respond to bronchodilators.
  - Respiratory arrest, acidemia, and altered mental status more likely than with type I.
  - More likely to improve with appropriate treatment

Etiology

- Pathophysiology is a combination of the release of inflammatory mediators by IgE antibody activation and the abnormal autonomic nervous system regulation of airway function.

Usual Treatment

- Manual bag-mask ventilation, bronchodilators, anti-inflammatories, deepen anesthesia, and alter ventilation settings (I:E ratio).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachyarrhythmias, possible pulm Htn	Palpitations, HR	Tachycardia, irregular rhythm, loud P_2	ECG, ECHO
RESP	Airflow obstruction, decreased lung elastance, hyperinflation, hypoxemia, hypercapnia, variations in peak flow	Dyspnea, cough, wheeze, chest tightness, nighttime awakenings, symptoms induced by exercise, allergens	Prolonged I:E, decreased breath sounds, wheezing, pulsus paradoxus	PFT, CXR, ABG
ENDO	Steroid-induced hyperglycemia; adrenal insufficiency (prior <1 y steroid users)	Polyuria, polydipsia, weakness	Hypotension in adrenal insufficiency	Glucose, lytes, cortisol, ACTH, stimulation test
MS	Steroid myopathy; steroid-paralytic myopathy	Difficulty climbing stairs or rising from chair; difficulty weaning mechanical ventilation	Proximal muscle weakness in steroid myopathy; possible quadriplegia in steroid-paralytic myopathy	Measurement of inspiratory muscle force, CPK, EMG, muscle biopsy

Key References: Applegate R, Lauer R, Lenart J, et al: The perioperative management of asthma, *J Aller Ther* S11:007, 2013; Bateman ED, Hurd SS, Barnes PJ, et al: Global strategy for asthma management and prevention: GINA executive summary, *Eur Respir J* 31(1):143–178, 2008.

Perioperative Implications

Preoperative Preparation

- History: Inquire about Hx and degree of control of asthma symptoms, any recent flare requiring corticosteroids, increased use of β_2-agonist medication (or continued use through the periop period), emergency room or hospital visit for asthma, allergies, recent URI, history of periop bronchospasm/pulm complication, and tobacco use or environmental exposure
  - Consider rescheduling elective procedures for 2-3 wk after resolution of URI
  - Consider course of oral corticosteroids in poorly controlled asthmatic pts before operation
- Physical examination:
  - Lung auscultation may reveal wheezing
  - Visual inspection may demonstrate accessory muscle use
  - Assess vital signs (hypercapnia, hypoxemia, hypotension, and tachyarrhythmias)
- Testing: Usually unnecessary; consider arterial blood gas, spirometric evaluation, or eosinophilic cationic protein in patients with severe asthma; measure and compare the peak expiratory flow rate to prior data points during an exacerbation

Perioperative Management
- Ensure adequate premedication and consider benzodiazepines.
- Airway instrumentation: Important trigger for bronchospasm; avoid unnecessary airway instrumentation (e.g., consider supralaryngeal airway and deep extubation).
- Consider IV medication (e.g., IV lidocaine) to depress airway reflexes.
- Avoid histamine-releasing medications (e.g., atracurium, mivacurium, morphine), and when possible consider avoiding muscle relaxant reversal agents that cause increased airway hyperreactivity (e.g., neostigmine, physostigmine).

Intraoperative Signs/Symptoms of Airway Hyperreactivity
- Wheezing: Auscultation of lungs can provide qualitative information regarding amount of airflow.
- Air trapping/Auto-PEEP: Secondary to decreased expiratory airflow → dynamic hyperinflation, reduced dynamic compliance of lungs → hypotension by decreased venous return, pneumothorax, subcutaneous emphysema, and cardiac arrest secondary to right ventricular failure; consider a 30- to 60-sec apnea trial.
- Hyperinflation: Signified by increased plateau pressure (goal: P_{plat} <30 cm H_2O), can be reduced by decreasing minute ventilation and shortening inspiratory time/lengthening expiratory time.
- Hypercapnia: Secondary to increased dead-space ventilation, made worse by hyperventilation.
  - Acute rise in Pco_2: Increases cerebral blood flow, increases intracranial pressure, decreases intracellular pH, and decreases cardiac contractility.

Differential Diagnosis
- Ventilator malfunction
- Endotracheal tube obstruction
- Endobronchial intubation
- Pneumothorax
- Pulmonary embolus

Treatment
- Switch to manual bag ventilation; allows direct qualitative assessment of pulmonary compliance and release of trapped gas.
- Remove trigger.
- Bronchodilators (e.g., β_2-agonist), consider combining with anticholinergic (e.g., ipratropium).
- Anti-inflammatories (e.g., corticosteroids, cromolyn, leukotriene inhibitors).
- Deepen anesthetic to depress airway reflexes, reduce bronchospasm, and resultant bronchodilation: inhalational anesthetic, intravenous anesthetic (e.g., propofol, ketamine), and neuromuscular blocker (e.g., rocuronium).
- Consider epinephrine, magnesium sulfate, heliox, bronchoscopy to remove mucus plug, noninvasive positive pressure ventilation to decreased work of breathing (if not intubated), and extracorporeal life support.

Postoperative Period
- Pain may trigger bronchospasm/laryngospasm: Prevent pain and treat promptly; consider regional anesthesia when possible.
  - Neuraxial blockade improves postop lung function due to improved pain therapy and diaphragmatic function.
- Close observation for postop bronchospasm/laryngospasm.

Atherosclerotic Disease

Marc B. Royo

Risk
- Over 100 million USA adults age 20 y or older have a total cholesterol >200 mg/dL.
- Cardiovascular disease accounts for approximately 1 of every 3 deaths in USA (31.3%).

Perioperative Risks
- Cardiovascular disease increases risk of periop major adverse cardiac events (cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest).
- Approximately 3% of pts undergoing noncardiac surgery will experience a periop cardiac complication.

Worry About
- Increased risk of end-organ hypoperfusion (e.g., myocardial, cerebral, renal)
- Increased risk of embolic events from unstable plaque rupture
- Association with aneurysm formation and increased risk of dissection
- Coexisting diseases and behaviors such as Htn, DM, and tobacco smoking
- Possible link with increased risk of postop delirium

Overview
- Lipid deposition and eventual calcification of coronary, cerebral, and peripheral arteries
- Integral in the pathogenesis of coronary artery disease, carotid artery disease, peripheral arterial disease, and some forms of chronic kidney disease

Etiology
- Multifactorial
- Risk factors: dyslipidemia, Htn, DM, endothelial dysfunction, smoking, and male sex

Usual Treatment
- Primary prevention include modification of risk factors (diet, physical activity, and smoking)
- Pharmacologic options for prevention includes antithrombotics (e.g., aspirin) and lipid-lowering agents
- Coronary artery disease: Antianginal treatment (nitrates, β-blockers, and calcium channel blockers), angioplasty, stenting, and CABG surgery
- Carotid artery disease: carotid endarterectomy or stenting
- Cerebrovascular insufficiency: extracranial-intracranial bypass is sometimes performed
- Peripheral vascular insufficiency: angioplasty, stenting, or revascularization

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, ventricular dysfunction (systolic and/or diastolic), coronary artery stenosis, myocardial ischemia	Angina, exercise intolerance, dyspnea, usually asymptomatic	Split S_2, S_3 and/or S_4; murmur; cardiomegaly	Vital signs, ECG, treadmill exercise testing, pharmacologic stress test, coronary angiography, and ECHO; may consider perioperative troponin screening in high-risk individuals
RESP	COPD (many are smokers)	Smoking history, dyspnea on exertion, sputum production	Decreased breath sounds, prolonged expiration, wheezing, signs of right heart failure	ABG, PFTs, CXR
CNS	Cerebrovascular insufficiency/infarction	History of syncope, TIA, CVA	Carotid bruit; focal neurologic deficits	Carotid US ultrasound or angiogram
PERIPH ARTERIES	Limb blood flow supply/demand imbalance, aneurysm formation	Claudication; may be asymptomatic; rest pain	Decreased pulses, pulsatile abdominal mass, nonhealing peripheral wounds	Ankle-brachial systolic pressure index, angiogram, and MRI
GI	Intestinal ischemia	Abdominal pain; occult blood in stool/gastric contents	Abdominal exam may be paradoxically normal	CBC, amylase, and mesenteric angiography

Key References: Hansson GK, Libby P, Tabas I: Inflammation and plaque vulnerability, *J Intern Med* 278(5):483–493, 2015; Halub ME, Sidwell RA: Cardiac risk stratification and protection, *Surg Clin North Am* 95(2):217–235, 2015.

Perioperative Implications

Preoperative Preparation
- Consider risk stratification tool (RCRI) and AHA/ACC clinical practice guideline to direct preop evaluation.
- Optimize cardiac symptomatology.
- Continue antianginal Rx (nitrates, β-blockers, calcium channel blockers, aspirin, and statins).
- Attention to and stabilization of coexistent diseases (HTN, DM, and COPD).

Monitoring
- Cardiovascular
  - ECG with appropriate lead placement; ST trending.
  - Consider intra-arterial catheter.
  - Consider CVP catheterization to monitor volume status.
  - Consider TEE in high-risk pts (cardiac surgery, recent MI, CHF, and unstable angina).

- Cerebrovascular
  - Stump pressure, EEG, and SEPs have been used in carotid endarterectomy.
  - CSF pressure and drainage in thoracoabdominal aneurysm repair.

Airway
- None

Preinduction/Induction
- Avoid extreme or prolonged changes in heart rate or blood pressure.
- Treat HR and BP changes aggressively.

Maintenance
- No one anesthetic agent or technique is superior; maintaining HR at a low level and hemodynamic stability are more important.
- For peripheral vascular surgery, regional anesthesia in combination with postop epidural analgesia may decrease the incidence of graft thrombosis (see also Peripheral Vascular Disease).
- For carotid endarterectomy, maintaining cerebral perfusion pressure is an important goal.
- For abdominal aortic surgery, optimizing loading conditions, and detecting and treating myocardial ischemia and ventricular dysfunction are important, particularly around aortic clamping/unclamping.

Extubation
- Same concerns as during induction
- Rapid emergence to allow neurologic assessment after carotid endarterectomy

Adjuvants
- β-blocking agents and other antihypertensives are useful in hyperdynamic situations.
- Prophylactic nitroglycerin and Ca^{2+}-channel blockers used to treat myocardial ischemia have not been conclusively proven effective.
- Use vasoconstrictors, such as α-adrenergic agonists, with caution, to increase BP in cases of heart failure.

Anticipated Problems/Concerns
- High risk of periop myocardial ischemia (often silent).
- Avoid postop hypothermia (increases oxygen demand).
- Periop volume status important for pts with history of heart failure.
- Concern for reocclusion with peripheral revascularization procedures.
- Risk of renal dysfunction and neurologic injury in cases of aortic surgery.

Atrial Fibrillation

Sheela Pai Cole

Risk
- Isolated atrial fibrillation affects >1% of those >60 y of age.
- Overall incidence is 0.4% of adult population.
- In the postcardiac surgical population, the incidence can be as high as 27-40%.
- No racial predominance.
- Prevalence increases with older age.
- Independent risk factor for stroke.
- In pts presenting for cardiac surgery, the incidence of postop atrial fibrillation increases with increasing left atrial size, as well as in the presence of valvular abnormalities.

Perioperative Risks
- Rapid ventricular response in CHF
- May be a sign of impending or ongoing myocardial ischemia
- Embolization if persisting beyond 48 h without anticoagulation

Worry About
- Decreased cardiac output due to loss of atrial kick, especially in the presence of left ventricular hypertrophy, aortic stenosis, or diastolic dysfunction
- Myocardial ischemia secondary to increased myocardial O_2 demand
- Increasing embolization risk with increased duration

Overview
- Develops over 2 decades in 2% of pts >30 y of age.
- Related to left atrial size, underlying heart disease, and abnormal electrophysiology.
- Incidence increases with age.
- Most affected persons have underlying cardiac disease.
- Common after cardiac surgery, particularly valve surgery.

Etiology
- CAD
- RHD
- Cardiomyopathy; heart failure
- Mitral stenosis; mitral regurgitation especially with left atrial enlargement
- Htn and associated left ventricular hypertrophy
- Pericarditis
- Resp insufficiency including hypoxia and hypercarbia
- Hypercatecholamine states such as hyperthyroidism
- Subarachnoid hemorrhage
- Sarcoidosis/amyloidosis
- Idiopathic

Usual Treatment
- Cardioversion for hemodynamic instability in the first 48 h
- Amiodarone increases the chances of spontaneous conversion to sinus rhythm, especially if cardioversion is required
- Digitalis
- β-blockers
- Calcium antagonists
- Quinidine (with digitalis)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CHF Angina Stroke	Palpitations Chest pain Dyspnea Orthopnea	Variation in intensity of first heart sound; absence of A waves in jugular venous pulse; irregularly irregular ventricular rhythm	ECHO (if indicated)
RESP	CHF Pulm embolism	Dyspnea Orthopnea Chest pain Tachypnea	S_3 Rales Wheezing	CXR, V/Q scan (if suspicion of pulm embolism)
GI	Ischemic bowel from low flow or embolization	Abdominal pain	Acute abdomen	ABGs/lytes
RENAL	Decreased renal perfusion	Decreased urine output		BUN/Cr
CNS	Syncope, fatigue	Stroke	Neurologic deficit	Head CT

Key References: Mitchell LB, Crystal E, Heilbron B, et al: Atrial fibrillation following cardiac surgery, *Can J Cardiol*, 21(Suppl B):45B–50B, 2005; Prystowsky EN, Padanilam BJ, Fogel RI: Treatment of atrial fibrillation, *JAMA*, 314(3):278–288, 2015.

Perioperative Implications

Preoperative Preparation
- Search for precipitating causes: new onset may signify acute disease process, which may delay surgery
- Control ventricular response or perform synchronized cardioversion to normal sinus rhythm if unstable
- If AFIB has been present for longer than 48 h, presence of clot in left atrium needs to be ruled out before cardioversion

Monitoring
- ECG with ST-segment analysis
- Additional monitoring such as use of arterial line or pulm artery catheter should be predicated on type of surgery, additional comorbidities, or hemodynamic instability

Airway
- None; consider intubation if shock present

Preinduction/Induction
- Avoid excessive sympathetic stimulation.
- Maintain oxygenation/ventilation.

Maintenance
- Monitor oxygenation, maintain normocarbia, and correct electrolyte imbalances.
- Control ventricular response.

Extubation
- Avoid excessive sympathetic stimulation.

Adjuvants
- Amiodarone may potentiate hypotension when administered along with anesthetic agents.
- Digitalis has little effect on anesthetic agents.
- Ca^{2+} antagonists can decrease AV conduction and increase NM blockade.
- β-blocker agents can cause decreased AV conduction.
- Addition of β-blockers and Ca antagonists such as diltiazem may potentiate refractory bradycardia.
- Quinidine (with digitalis) can increase NM blockade.

Postoperative Period
- Maintain adequate analgesia.
- New onset may require prompt treatment based on hemodynamic status.
- If duration is greater than 48 h, anticoagulation may need to be instituted.

Anticipated Problems/Concerns
- Rapid ventricular response may result in significant fall in cardiac output.
- DC synchronized cardioversion establishes sinus rhythm in >90%.
- Pretreatment with amiodarone increases chances of remaining in sinus rhythm.

Atrial Flutter

Megha Parekh | Marek Brzezinski

Risks
- AFLT occurs <1/10 as often as AFIB.
- Usually occurs in elderly pts with structural heart disease (those with LV dysfunction, RV dysfunction, pulm vascular disease, RHD, or CHD).
- Other risk factors include COPD, hypertension, obesity, and male sex.
- Occurs with relative frequency after cardiac surgery (peaks on postop d 2 to 4) but seldom after noncardiac surgery.

Perioperative Risk
- Circulatory insufficiency or myocardial ischemia from extremes of heart rate, especially in pts with CHD
- Increased risk of thromboembolism
- Associated disease, especially adequacy of CV and pulm function

Worry About
- Heart rate-related: Hemodynamic instability, myocardial ischemia, Pulmonary edema, or heart failure
- Thromboembolism-related: Stroke, MI, or bowel ischemia
- Increased proarrhythmia risk with drugs for pharmacologic cardioversion

Overview
- Mechanism is atrial macro-reentry; circuit is usually in the right atrium.
- Type I or typical AFLT: Most common form is characterized by regular atrial rates of 240 to 340 bpm with fixed (often 2:1) AV conduction.
- Type II or atypical AFLT: Less commonly presents with regular atrial rates of 340 to 450 bpm, with variable or fixed AV conduction that may result in irregular QRS complex and pulse; re-entry is usually around previous atrial scars.

Etiology
Usual Treatment
- Goals include restoring and maintaining normal sinus rhythm, control of ventricular rate, and anticoagulation to prevent systemic embolization depending on risk of thromboembolism and length of time in AFLT (if sinus rhythm is not restored).
- Cardioversion can be accomplished pharmacologically (flecainide, dofetilide, propafenone, IV ibutilide, or amiodarone) or with direct current cardioversion. External pacing may be required in pts receiving rate-controlling medications.
- Consider emergency R-wave synchronized DC-cardioversion if pt is hemodynamically unstable.
- Ventricular rate control strategies include β-blockers, nondihydropyridine Ca^{2+}-channel blockers such as diltiazem and verapamil (alone or in combination). When unsuccessful or contraindicated, digoxin or amiodarone can be considered. Pts with chronic AFLT who failed pharmacologic rate control may benefit from AV nodal ablation with permanent ventricular pacing (not a treatment for acute AFLT).
- Anticoagulation should be considered for AFLT lasting >48 h or sooner if at high risk of thromboembolism (e.g., high CHA_2DS_2-VAS_c score, impaired renal function, or low cardiac output).
- Although warfarin remains the most commonly used anticoagulant (target INR of 2.5), the new oral anticoagulants (dabigatran, rivaroxaban, and apixaban) offer a reasonable alternative in patients without a prosthetic heart valve, severe renal impairment, or risk of GI bleed. Use of aspirin may be considered in pts with CHA_2DS_2-VAS_c score of 1.
- Prophylactic amiodarone, diltiazem, and β-blockers lower the risk for AFLT after cardiac surgery.

Assessment Points

System	Effect	Assessment by PE	Exercise	Test
CV	Atrial flutter, left ventricular function, coronary disease severity	Palpitations, dizziness, weakness, lethargy, orthopnea, cough dyspnea, exercise intolerance, symptoms of angina	Irregular pulse/pulse deficit, S_1–S_2 intensity rales, and wheezes	ECG, Holter monitoring, EP studies, ECHO, exercise ECG, MRI, cardiac cath, stress ECG, dipyridamole scintigraphy, angiography
RESP	CHF COPD	Dyspnea, orthopnea, cough Dyspnea, wheezing	S_3, rales, wheezes	CXR, PFTs
GI	Decreased perfusion	GI distress, diarrhea		
RENAL	Decreased perfusion	Polyuria (nocturnal)		BUN/Cr
NEURO	Ischemia or stroke	Syncope, mental changes, paresis/paralysis, dementia	Mental deficits Neurologic exam	See CV

Key References: January CT, Wann LS, Alpert JS, et al: 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society, *Circulation* 130(23):e199–e267, 2014; Frendl G, Sodickson AC, Chung MK, et al: 2014 AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures, *J Thorac Cardiovasc Surg* 148(3):e153–e193, 2014.

Perioperative Implications
Preoperative Preparation
- Adequate ventricular rate control (80 to 100 bpm) with β-blockers or Ca^{2+}-channel blockers with AV conduction-slowing properties.
- Treat CHF if present; otherwise, optimize cardiopulmonary function.
- If acute onset (<48 h), consider cardioversion.
- When AFLT is of >48-h duration, intracardiac thrombus must be excluded before cardioversion (e.g., TEE) or the pt should receive a course of anticoagulation before and after cardioversion.
- Consider prophylactic amiodarone, diltiazem, or β-blockers to lower the risk for AFLT after cardiac surgery.

Monitoring
- ECG with ST–T trending and strip-chart recorder for documentation of new arrhythmias or myocardial ischemia.
- Consider extended monitoring, including direct arterial catheter, cardiac output monitoring, and TEE in the presence of concomitant left ventricular dysfunction depending on the type of procedure.

Anesthesia Induction
- Left ventricular dysfunction and AFLT increase risk for hypotension during induction with agents such as thiopental or propofol.
- Desflurane, ketamine, and pancuronium may accelerate ventricular rate.

Maintenance
- Expect increased circulatory instability and less tolerance of large fluid shifts or blood loss.
- No anesthetic drugs are especially contraindicated; caution should be used with drugs that speed conduction.
- Optimize electrolyte levels.
- Limit use of catecholaminergic inotropic agents.

Tracheal Extubation
- Possible increased risk for thromboembolism with hyperdynamic circulatory state.
- Sympathomimetic or antimuscarinic drugs may accelerate ventricular rate.

Atrial Septal Defect, Ostium Primum

Elizabeth Laverriere | Todd J. Kilbaugh

Risk

- Ostium primum ASD is a variant of AV canal defect. Classified as an ASD, it is actually an endocardial cushion defect.
- Less common than secundum ASDs, this defect comprises 0.5-1% of all congenital heart defects, and 15-20% of ASDs.
- Approximately 50% of pts with primum ASD are female.
- Ostium primum is most commonly associated with the genetic defect trisomy 21 (Down syndrome). It is also associated with Holt-Oram and Noonan syndrome.

Perioperative Risks

- Periop mortality rate: 1.5-6%, lower mortality if repair is done before onset of pulm Htn.
- Late in clinical course of unrepaired, clinically significant ASDs; CHF is common with a L-to-R shunt.
- Increased risk of atrial dysrhythmias, heart block, and air embolus with surgical repair.
- Significant risk of mortality if Eisenmenger syndrome (eventual reversal of the shunt into a cyanotic R-to-L shunt) has occurred. Surgical repair is often not recommended at this point.

Worry About

- AV valves, which are usually abnormal
- Abnormal conduction axis
- CHF and Eisenmenger syndrome

Overview

- Failure of inferior atrial septum to close at the level of the tricuspid and mitral valves.
- Symptoms present earlier, are more severe than in secundum ASD, and include dyspnea, fatigue, atrial arrhythmias, recurrent respiratory infections, and failure to thrive.
- L-to-R shunt increases pulmonary blood flow and right-sided volume overload.
- Progression of clinical course: CHF (more common than in secundum pts) and shunt reversal (R-to-L flow across ASD).
- Frequently associated with mitral regurgitation with a cleft in the anterior mitral leaflet (can cause left-sided volume overload) and/or tricuspid regurgitation.
- Diagnosis by ECHO; characteristic appearance: Absence of the lower atrial septum.
- Cardiac catheterization may be required to assess PVR and pulm Htn in large shunts.

Etiology

- Failure of septum primum to fuse with endocardial cushion to close ostium primum

Usual Treatment

- Asymptomatic pts require no medications.
- Diuretics are used for CHF.
- ACE inhibitors may be used for afterload reaction in the presence of mitral regurgitation.
- Antiarrhythmics are occasionally needed for atrial dysrhythmias.
- Percutaneous closure is not possible because the rim of the inferior atrial tissue is inadequate to prevent the device from impinging on the valves.
- Surgery is the definitive management, usually between 2-5 y, but it may be earlier if there is mitral regurgitation, CHF, or failure to thrive. The incision is median sternotomy, submammary, lateral thoracotomy, or transxiphoid. The defect is closed under direct visualization using CPB. Endocarditis prophylaxis is indicated for 6 mo after repair. Persistent AV valve abnormalities may require long-term prophylaxis.
- Consult a geneticist if syndromic.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult intubation	Down syndrome	Down syndrome facies	
CV	Atrial dysrhythmias, right-sided heart failure L-to-R shunting, hypertrophic RA and RV Mitral regurgitation	Palpitations SOB, frequent fatigue Cyanosis if shunt reversal	Irregular rate and rhythm Right heart enlargement Normal S_1, wide, fixed splitting of S_2, and soft systolic ejection murmur; diastolic rumble	ECG (tall P wave, RBBB + RVH) CXR—cardiomegaly ECHO Cardiac catheterization Dye dilution study
RESP	Increased pulm blood flow Increased PVR	SOB, frequent URIs	Rales; wheezing	CXR—increased pulm vascular markings
GI	Feeding difficulty Hepatic dysfunction if severe CHF	FTT Jaundice	Hepatomegaly	LFTs; PT/ INR
CNS	Embolic stroke from chronic AFIB	Various neurologic changes		Head CT, cardiac ECHO
RENAL	Renal dysfunction if severe CHF			Cr and BUN

Key References: Rivenes SM: Ostium primum atrial septal defects. *eMedicine* <http://emedicine.medscape.com/article/890880-overview>, 2015 (Accessed 10.03.16.); Wasnick JD, Hillel Z, Kramer D, et al: Anesthesia for patients with congenital heart disease. In Wasnick JD, Hillel Z, Kramer D, et al editors: *Cardiac anesthesia and transesophageal echocardiography.* New York, 2011, McGraw-Hill.

Perioperative Implications

Preoperative Medications

- Oral or IV midazolam before procedure
- Antibiotic prophylaxis

Monitoring

- Routine monitors, arterial line, CVP; intraop TEE to assess anatomy before CPB, AV valve regurgitation, and function, ventricular function and to check for air and residual shunt after CPB; central and peripheral temp monitoring

Induction

- IV or inhalational: IV induction theoretically slowed by L-to-R shunt because of increased pulmonary blood flow; inhalational induction speed is increased; may place an epidural with loss of resistance to saline technique to avoid air embolism; must be placed 1 h before heparinization

Maintenance

- Balanced anesthetic: Combination of opioids, inhalational agent, and muscle relaxants.
- Reduced fraction of oxygen to maintain PVR and decrease L-to-R shunt.
- Avoid nitrous oxide to minimize size of air bubbles.
- Watch for shunt reversal with hypoxemia, hypercarbia, and hypothermia.

Extubation

- If intraop course is uneventful, then pt may be extubated at the end of the procedure.
- Control BP with milrinone, nitroprusside, or nitroglycerin.
- Keep mechanically ventilated if the repair has been complex or arrhythmias are present.

Adjuvants

- Watch for supraventricular dysrhythmias and AV conduction defects; must have pacing wires during surgical repair.

Postoperative Period

- Adequate analgesia for sternotomy or thoracotomy pain; pacemaker available for transient heart block

Anticipated Problems/Concerns

- Air emboli with vascular access.
- Dysrhythmias: SA node or AV node dysfunction.
- Depressed systolic function; Inotropic support, diuretics, and afterload reduction may be helpful.
- Third-degree AV block with repair of low-lying defects.
- Residual pulmonary Htn, which can lead to tricuspid regurgitation and right ventricular failure.
- Residual mitral valve insufficiency may remain or worsen.
- Endocarditis, especially with a residual cleft mitral valve.
- Pts with left ventricular outflow tract obstruction are at higher risk for reoperation.

Atrial Septal Defect, Ostium Secundum

Jeffrey D. Roizen

Risk

- Incidence in USA: 140,000 with ostium secundum ASD (70–80% of ASDs).
- Accounts for 7% of all congenital cardiac defects but roughly one-third (30–40%) of congenital cardiac defects in pts older than 40 y.
- Gender prevalence: Females >males, with a 2:1 ratio in isolated ASDs.
- Familial incidence: Significant if associated with P-R prolongation or forearm and hand abnormalities (Holt–Oram syndrome).
- Increased incidence in high altitude.

Perioperative Risks

- Periop mortality rate 1%
- Later in course, associated with atrial dysrhythmias, pulm Htn, and right heart failure
- Increased risk of atrial dysrhythmias, heart block (rare), and air embolus with surgical repair

Worry About

- Risk of infections endocarditis and paradoxical air embolization with IV access.

Overview

- Failure of closure of midseptal fossa ovalis.
- Usually asymptomatic early in life.
- 15% incidence of associated noncardiac anomalies.
- Associated with mitral valve prolapse (10–20%).
- L-to-R shunt increases pulm blood flow (shunt fraction proportional to ASD size).
- Late in course: Pulm Htn, right heart failure with possible shunt reversal, supraventricular arrhythmias.
- Uncorrected defect carries a mortality rate of 6% per y > age of 40.
- Diagnose by echocardiography and Doppler color flow echocardiography.
- >80% spontaneous closure in the first year of life for small defects.

Etiology

- Failure of septum secundum to fuse with septum primum secondary to defective formation or resorption of the septum primum, shortening of the septum secundum, or a combination of the three

Usual Treatment

- Digitalis and diuretics for child with CHF.
- Antiarrhythmics occasionally needed for atrial dysrhythmias.
- Surgery or transcatheter closure is indicated when Qp:Qs ratio ≥1.5:1 in pts between 3–5 y.
- Surgery indicated if ASD >25 mm diameter or if anomalous pulm venous return is present.
- Endocarditis prophylaxis not indicated after successful simple surgical closure; indicated for 6 mo after repair using a prosthetic device.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Atrial dysrhythmias, right-sided heart failure, L-to-R shunting	Palpitations, SOB, DOE	Irate and rhythm, right heart enlargement, loud S_1, fixed S_2, and crescendo-decrescendo systolic murmur	TEE with color Doppler flow, four-chamber view, bicaval view, angiography, dye dilution study
RESP	Increased pulm blood flow Increased PVR	SOB, frequent URIs	Rales, wheezing	CXR
GI	Hepatic dysfunction if severe CHF	Jaundice	Hepatomegaly	LFTs, PT
RENAL	Renal dysfunction if severe CHF			Cr, BUN
CNS	Embolic stroke from chronic AFIB	Various changes		Head CT, cardiac ECHO if suspected emboli
MS			Holt-Oram syndrome Large left costal cartilage	

Key Reference: Findlow D, Doyle E: Congenital heart disease in adults, *Br J Anaesth* 78(4):416–430, 1997.

Perioperative Implications

Perioperative Preparation

- Narcotics and anticholinergics.
- Antibiotic prophylaxis.
- Continue digoxin if used for rate control.

Monitoring

- Routine monitors, arterial line, and CVP; TEE indicated for assessing anatomy before CPB and evaluating for air and residual shunting after CPB; central and peripheral temp monitoring

Induction

- IV induction is theoretically slowed by left to right shunt; inhalational induction is not significantly affected.
- Epidural with loss of resistance to saline technique to avoid air embolism.

Maintenance

- Avoid nitrous oxide to minimize size of air bubbles; inhalational, TIVA, or a combination of techniques are appropriate; watch for shunt reversal with hypothermia, hypercarbia, and hypoxemia.

Extubation

- In isolated lesions, pts can be extubated at the end of case if hemodynamically stable.

Adjuvants

- Watch for dysrhythmia from hypokalemia if pt is on digoxin and diuretics; maintain potassium of 4.0 or higher.

Postoperative Period

- Adequate analgesia for sternotomy or thoracotomy pain

Anticipated Problems/Concerns

- Paradoxical air emboli with vascular access
- Dysrhythmia (5–10% if no prerepair dysrhythmia)
- Heart failure
- Heart block after CPB (rare)
- Sternal infection (rare)
- Endocarditis

Atrioventricular and Bifascicular Heart Block

Joshua Knight | Dennis Phillips | David G. Metro

Risk

- Prevalence: First degree (0.65–1.6%); second degree (0.003% in young adults; higher in organic heart disease); third degree (overall 0.02%; congenital 1:20,000 live births); increases with age presumably because of small vessel disease
- Inferior MI: Carries low mortality even if associated with high-degree AV block
- Anterior MI: If high-degree AV block results, then mortality approaches 80%

Perioperative Risks

- Progression of benign heart block to second degree type II or third degree
- Heart failure, myocardial and global ischemia, shock, and pacemaker failure

Worry About

- Autonomic changes influencing the degree of blockade
- Pacemaker failure or electrocautery interference
- Intracardiac wire or PA catheter placement leading to third-degree block
- β-blockers, calcium channel blockers, digoxin, and anticholinergics influencing the degree of heart block

Overview

- AV blocks: First degree (PR interval >0.20 sec). Block site =AV node. Usually benign. Associated with anterior MI, digitalis, and certain neuromuscular diseases.
- Second-degree type I (Mobitz I or Wenckebach): Increasingly prolonged PR interval until QRS has dropped. Block site =AV node (normal QRS). Usually benign. Usually does not progress over time to

second-degree type II or third degree. May progress acutely with anesthesia, autonomic influences, or intracardiac catheters/wires.
- Second-degree type II (Mobitz II): Fixed PR interval with occasional dropped QRS. Block site = usually infranodal (wide QRS) and permanent. The larger infranodal block site yields a slower ventricular rate and symptoms. It commonly progresses to third degree. High mortality is associated.
- Bifascicular block: Three "fascicles"/bundles" of nerves conduct via the ventricles: Right bundle branch, left anterior fascicle, and left posterior fascicle. When two of three are blocked, it is termed *bifascicular*. When third fascicle is blocked, pt is in third-degree heart block.
- Third degree: Atria and ventricles have separate pacemakers. Any atrial rhythm (e.g., AFIB/flutter) could be present. Ventricular rate/rhythm depends on the site of the blockade. The more infranodal block yields a slower ventricular rate. If only upper AV node is blocked, the patient may have junctional rhythm (normal QRS) and be more stable. If entire AV node is blocked, then the ventricular rate will be 20 to 40 bpm, and perfusion is compromised.

Etiology

- First degree: Usually benign or associated with anterior MI, digitalis
- Second-degree type I: Benign (athletes and children) from high vagal tone or from myocarditis, mononucleosis, Lyme disease, amyloidosis, sarcoidosis, β-blockers, calcium channel blockers, digitalis, and volatile anesthetics
- Second-degree type II and bifascicular blocks: Anterior MI
- Third degree: Inferior MI (usually more stable HR >40); anterior MI with necrosis of bundle branches (unstable HR <40); severe hyperkalemia, hypermagnesemia; concurrent use of calcium channel and β-blockers; digitalis; high doses of volatile anesthetics, opiates, anticholinesterases; increased vagal input (laryngoscopy, esophagoscopy/TEE, peritoneal retraction, and ocular pressure); or congenital

Usual Treatment

- Dual chamber pacing is preferred pacing method in the AV block (level of evidence C)
- Class I indications for permanent pacing (all level of evidence C except as noted)
- 3rd, Type II 2nd degree AV block associated with the following:
  - Symptomatic or permanently drug-induced bradycardia
  - Ventricular arrhythmias
  - Exercise
  - Asymptomatic bradycardia with the following:
    - Asystole episodes >3 sec
    - Escape rhythms <40 bpm
    - Atrial flutter with bradycardic pauses >5 sec
    - Wide QRS (level B)
    - Isolated right-bundle block (level B)
    - Cardiomegaly and/or LV dysfunction (3rd degree only, level B)
- Neuromuscular disease (level B)
- SA nodal catheter/operative ablation

Bifascicular
- Intermittent 3rd degree (level B), Type 2 2nd degree (level B), and alternating bundle branch blocks

Class IIa recommendations
- Asymptomatic 3rd degree with escape rhythm >40 bpm
- Asymptomatic 2nd degree at intra/infra-His levels (level B)
- First/second degree block with hemodynamic compromise (level B)
- Bifascicular w/ syncope or HV interval >100 ms, nonphysiologic infra-His block (level B)

Class IIb recommendations
- Any AV block due to a drug that may have persistent effects (level B), or any AV block (level B) or bifascicular block (level C) due to neuromuscular disease

Class III recommendations
- Asymptomatic 1st degree (level B) or Type 1 supra-His 2nd degree
- Any degree due to medications or transient conditions expected to resolve (level B)
- Any asymptomatic bifascicular block without some degree of concomitant AV block (level B)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Heart failure	Syncope, SOB, DOE, "skipped beats," last pacemaker battery replacement, fatigue	Bradycardia, JVD	ECG, ECHO, BNP
RESP	Pulm edema, hypoxia	Cough, pink sputum, orthopnea	Rales, tachypnea, wheezing, cough	CXR, pulse ox
RENAL	Prerenal failure, fluid retention	Oliguria, edema, fatigue, N/V	Edema, impaired mentation	BUN, Cr, FENa, lytes
NEURO	Poor cerebral perfusion	Lightheadedness, N/V	Impaired mentation	CT head

Key References: Stone ME, Salter B, Fischer A: Perioperative management of patients with cardiac implantable electronic devices, *Br J Anaesth* 107(S1):i16–i26, 2011; Epstein AE, DiMarco JP, Ellenbogen KA, et al: 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society, *J Am Coll Cardiol* 61(3):e6–e75, 2013; Gillis AM, Russo AM, Ellenbogen KA, et al: HRS/ACCF expert consensus statement on pacemaker device and mode selection, *J Am Coll Cardiol* 60(7):682–703, 2012.

Perioperative Implications

Preinduction/Induction/Maintenance

- Ascertain indication for and type of pacemaker, as well as functionality.
- Consider changing pacemaker to asynchronous mode if electrocautery is to be used.
- Have external and/or intravenous pacemaker and magnet available.
- Consider preinduction arterial catheter.
- Anticipate medication influences on autonomic nervous system balance (i.e., vagolysis from pancuronium, glycopyrrolate).
- Avoid intracardiac placement of central line wire.
- Consider using bipolar electrocautery; ensure proper electrocautery return pad placement away from the pacer.

Monitoring

- Low SaO_2 and high peak airway pressures can signify pulm edema.
- Low $ETCO_2$ may indicate low cardiac output.
- Arterial waveform: Diminished rate of rise may indicate poor cardiac output.
- Ensure adequate and constant ECG tracing with special attention to PR interval, QRS width, and AV association.

General Anesthesia

- Anticipate the effects of laryngoscopy, intubation, and TEE placement.
- Avoid rapid increases in volatile anesthetic concentration.
- Avoid high-dose opiates.
- Use β-blockers or calcium channel blockers carefully; use short-acting agents.
- Retraction or insufflation of vagal mediated structures can worsen bradycardia.
- Surgeon may need to stop the offending maneuver until pt is stabilized.
- Monitor and maintain normal serum electrolyte concentration.

Regional Anesthesia

- High thoracic spinal block will result in bradycardia even without preexisting heart block.
- Preexisting heart block may worsen after sympatholysis.
- Atropine ineffective if heart block is below the AV node; use direct-acting agents.
- Use epinephrine immediately.
- Verify or induce euvolemia.

Postoperative Period

- Obtain ECG to verify preop baseline and cardiology consult.
- Pacemaker interrogation by electrophysiology and return to previous mode.
- Perform physical exam looking for signs of heart failure.

Anticipated Problems/Concerns

- If heart block is at the AV node then:
  - AV conduction is worsened by increased vagal input, peritoneal insufflation, esophageal manipulation (intubation, TEE, and esophagoscopy), β-blockers, calcium channel blockers, high-dose opiates, and anticholinesterases.
- AV conduction is improved by vagolysis (antimuscarinics), exercise, and isoproterenol.
- If the heart block is infranodal, then autonomic influences are opposite of the above.
- Development of a slow ventricular response rate <40–50 bpm is concerning.
- Ensure transcutaneous and/or transvenous pacemaker availability and practitioner knowledge.
- Have direct-acting sympathomimetics available.

Autoimmune Diseases, Cold

Joseph L. Seltzer | Lee A. Fleisher

Risk

- Rare
- Autoimmune hemolytic anemias occur in 1 of 80,000 persons; of these, 17.3% are due to cold antibodies.

Perioperative Risks

- Acute hemolysis due to cold
- Hemoglobinemia
- Hemoglobinuria
- Rarely, vascular occlusion

Worry About

- Cooling to 28–31° C will cause hemolysis.
- These temperatures can be reached in extremities during cardiopulmonary bypass.

Overview

- In two circumstances antibodies will react in the cold to produce hemolysis:
  - IgG antibodies associated with mononucleosis, mycoplasmal pneumonia.
  - IgM antibodies found in the idiopathic form of the disease and in lymphoproliferative disease.
- Hemolysis usually occurs at temp below 31°C.

Etiology

- Idiopathic
- Lymphoid (B-cell) malignancy
- Infections: mycoplasmal pneumonia, mononucleosis, cytomegalovirus, varicella, EBV

Usual Treatment

- Keep warm; administer folic acid.
- For severe cases, chlorambucil or cyclophosphamide.
- Plasmapheresis.
  - Rituximab.
  - Prednisone.

Assessment Points

System	Effect	PE	Test
HEME	Mild to moderate anemia		Hgb, blood bank antiglobulin tests
GU	Hemoglobinuria		
CV	Dyspnea on exertion if anemia is severe		
DERM	Agglutination of RBCs in cold	Acrocyanosis	

Key References: Young S, Haldane G: Major colorectal surgery in a patient with cold agglutinin disease, *Anaesthesia* 61(6):593–596, 2006; Bratkovic K, Fahy C: Anesthesia for off-pump coronary artery surgery in a patient with cold agglutinin disease, *J Cardiothorac Vasc Anesth* 22(3):449–452, 2008.

Perioperative Implications

Preoperative Preparation

- Determine risks of operating vs. not operating.
- Plasmapheresis—may be used, but no more than 2 d before surgery.

Monitoring

- Temp
- Urine output

Maintenance

- Keep pt warm, including extremities.
  - Consider forced-air warming.
  - Warm all fluids.
- Normothermic cardiopulmonary bypass.
- No preferred agent or technique.
- Consider hemodilutional autologous transfusion or other techniques to avoid homologous transfusion and formation of new antibody.

Postoperative Period

- Warm fluids and extremities.
- Monitor for manifestations of cold agglutinin disease.

Anticipated Problems/Concerns

- Hemolysis if temperature falls.
- Renal dysfunction due to hemoglobinuria.
  - Molting or cyanosis of the skin can occur.

Autonomic Dysreflexia

Kieran A. Slevin

Risk

- AD occurs with greatest frequency in pts with spinal cord injury at T6 or above.
- Occurs with highest frequency following urologic or lumbar and thoracic spine procedures.
- Tetraplegic pts develop AD if cystoscopy and lithotripsy are performed without anesthesia.
- The higher the injury level, the greater clinical manifestations of CV dysfunction.
- Risk of AD greater with complete (91%) versus incomplete (27%) cord transections.
- AD more often a delayed finding in chronic SCI; minor clinical evidence seen in first d/wk.

Perioperative Risks

- AD most commonly triggered by irritation and/or manipulation of urinary bladder or colon, as well as in labor.
- Severe increased BP and increased or decreased HR is associated with stimulation below level of transection.
- Objectively, increased SBP >20-30 mm Hg is considered a dysreflexic episode. However, be aware that the usual resting ABP in these pts is 15-20 mm Hg less than in non-SCI subjects.
- Awake pts may complain of HA; anxiety; sweating, piloerection; and flushing above injury level; and dry, pale skin below. In anesthetized pts, SBP rising to up to 300 mm Hg heralds onset of severe, life-threatening AD.

Worry About

- Untreated, uncontrolled hypertensive episodes, which can lead to intracranial hemorrhage, retinal detachment, seizures, and death.

Overview

- Physiologically, AD is caused by a massive sympathetic discharge triggered by a noxious or nonnoxious stimulus originating below the level of the SCI.
- Specifically, destruction of the vasomotor pathways results in a loss of inhibitory and excitatory supraspinal input to the sympathetic preganglionic neurons, thus causing labile BP.
- Also, changes in spinal sympathetic neurons and primary afferents underlie abnormal CV Δs.
- Symptoms are usually short-lived because of treatment or self-limiting nature of the episode.

Etiology

- Most common cause is traumatic interruption of the spinal cord.
- Can also occur due to infectious or oncologic processes causing destructive spinal lesions.

Usual Treatment

- Stop initiating stimulus as first-line therapy when possible.
- Can decrease or prevent AD by use of neuraxial blockade (spinal >>epidural).
- When signs of AD are evident, administer ganglionic blockers (trimethaphan), direct vasodilators (nitroprusside) or α-antagonists (phentolamine), GA, or spinal anesthesia.
- Level 1 evidence that intrasphincteric anal block with lidocaine limits the AD response in pts undergoing anorectal procedures; level 1 evidence that topical lidocaine does not.
- Level 1 evidence that prazosin is superior to placebo in prophylactic management of AD.
- Level 2 evidence that nifedipine can prevent BPΔs during cystoscopy in SCI pts with AD.
- Level 4 evidence that epidural anesthesia may be effective in pts with AD during labor and delivery.
- Centrally acting hypotensive agents (e.g., clonidine) are NOT effective in treating AD.
- Treat tachyarrhythmias with β-blockers in combination with antihypertensives.
- Nicardipine may be preferable in a pt with an upper spinal cord injury undergoing operation in the paralyzed area.
- Magnesium sulfate has significant beneficial effects on AD in labor in a pt with a high spinal cord injury.
- Complete bladder deafferentation does not abolish AD during bladder urodynamic studies.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway	C-spine trauma/surgery H/O; difficult intubation	↓ C-spine ROM ↓ Mouth opening	Airway exam
CV	Orthostatic hypotension Baseline relative hypotension (15–20 mm Hg)	H/O dizziness when going from supine to upright position	↓ BP, orthostasis, tachycardia, bradycardia, AFIB	Orthostatic BPs ECG
RESP	Decreased resp volumes, atelectasis, pneumonia, hypoxemia Impaired cough reflex	SOB Difficulty w/secretions	Tachypnea Cyanosis Decreased/unequal BS	CXR ABG evaluation
GI	Full stomach status due to GI atonicity	Complaints of reflux		
RENAL	UTI, renal stone disease, renal failure	Flank pain	Chronic Foley catheter	UA and BUN/Cr
CNS	Bowel and bladder dysfunction Chronic and central pain states Altered MS (if severe head trauma)	Incontinence Chronic opioid therapy Adjuvant pain meds	Hyperreflexic below level of transection Babinski sign positive	Hyperalgesia Allodynia
PNS	Insensate below level of transection Pain at level of transection	Skin-color changes	Flushing/piloerection above Dry, pale skin below	
MS	Paralysis, muscular atrophy below Sacral decubiti	Paraplegia or quadriplegia	Muscle atrophy Sacral decubiti	

Key References: Krassioukov A: A systematic review of the management of autonomic dysreflexia after spinal cord injury, *Arch Phys Med Rehabil* 90:682–695, 2009; Liu N: Iatrogenic urological triggers of autonomic dysreflexia: a systematic review, *Spinal Cord* 53(7):500–509, 2015.

Perioperative Implications

Preoperative Preparation

- Nifedipine can be used for prophylaxis; given 30 min before procedure, likely to trigger AH.
- Attention to CV and pulm function, volume status, and airway exam.

Monitoring

- Consider preinduction invasive monitoring (arterial and CVP/PA catheters) if volume changes are expected and in setting of poor cardiac reserve (high lesions) and renal insufficiency.

Airway

- Be prepared for fiberoptic intubation.

Induction

- Use nondepolarizing muscle blockers when relaxation is necessary.
- IV nicardipine can be used to treat AD.
- Succinylcholine can cause severe K^+ release and hyperkalemia in chronic lesions.
- Consider nitroprusside before induction.

Maintenance

- GA with volatile agent superior to nitrous-narcotic technique for prevention/treatment of AD.

Regional Anesthesia

- Anesthetic technique of choice when possible.
- Spinal anesthesia highly effective in preventing AD precipitated by surgery.
- Ensure careful assessment of level of spinal blockade in SCI pts due to sensory deficits below injury: avoid unnecessarily high or inadequate blocks.
- Epidural anesthesia effective in preventing AD in laboring pts.

Extubation

- May be difficult due to resp insufficiency in pts with high-level spinal lesions

Adjuvants

- Muscle relaxants required in abdominal surgery due to diffuse increase in muscle tone

Postoperative Period

- AD can occur postop in setting of unrecognized or untreated distended bladder or rectum.
- Consider intracerebral hemorrhage protocol in the setting of unexplained delayed emergence with increased BP.

Becker Disease

Pikulkaew Dachsangvorn

Risk

- Prevalence is approximately 1:50,000

Perioperative Risks

- Myotonia

Worry About

- Myotonic episode leading to a difficult to ventilate/intubate situation

Overview

- Genetic disease that results in muscle membrane hyperexcitability and delayed relaxation
- Recessively inherited form of MC
- Initial symptoms start around 4–12 y of age, with generalized myotonia and moderate to pronounced muscular hypertrophy from chronically increased muscle activity
- Signs include muscle stiffness after voluntary contraction that improves with repetitive movement ("warm-up" phenomenon) and worsens after prolonged rest
- Many experience transient weakness (<1 min) upon initiating movement; history of clumsiness, dropping objects, impaired postural control, or uncontrolled falling upon standing
- Rarely, can have atrophy in the forearms and painful muscle cramps
- Most have normal life expectancy without significant handicap
- Aggravating factors: dietary insufficiencies, sleep deprivation, prolonged physical activity, and emotional stress
- Menstruation, pregnancy, and hypothyroidism may alleviate or worsen symptoms in some individuals
- No involvement in smooth and cardiac muscles, no extramuscular manifestations
- It is important to differentiate this from myotonia with dystrophy, which is a multisystem disorder
- Diagnosis:
  - Characteristic symptoms (described previously)
  - "Percussion myotonia": reflex hammer produces obvious dimpling or fasciculation in prominent muscles, such as thenar eminence or thighs, that lingers for several seconds
  - Objective evidence: electromyography
  - Molecular genetic testing is commercially available, although not sensitive for less common mutations

Etiology

- Impaired functioning of skeletal muscle ClC-1
- Skeletal muscle chloride channels serve to stabilize membrane potential at the resting level; impaired ClC-1 leads to sarcolemmal excitability and delayed muscle relaxation
- More than 120 mutations have been described; most mutations are unique to individual families or isolated cases

Usual Treatment

- Most pts prefer to minimize their symptoms by avoiding triggers.
- Pharmacologic therapies include quinidine and quinine, which are effective and well tolerated in low-dose, short-term use; however, continued administrations can lead to toxicity affecting vision, hearing, gastrointestinal, central nervous systems, and possibly causing death.
- Other drugs with variable success include procaine, tocainide, mexiletine, carbamazepine, and phenytoin, by use-dependent blockade of voltage-gated sodium channels.

- Directed pharmacologic approach to increase chloride conductance of skeletal muscle includes taurine and clofibric acid; however, the effect is modest.
- Other interventions include optimizing pt's emotional state and relaxation techniques. Some subjects have shown improvements with alcohol use. Exercises that improve flexibility and decrease muscle strains can be helpful.
- Gene therapy to introduce a functional copy of the normal gene has been considered; however, this may not be effective in disorders caused by a dominant-negative mechanism.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
No effects on CNS, CV, RESP, GI, GU, ENDO, HEME/ID systems because BD only affects skeletal muscle membranes.				
HEENT	Blepharospasm (myotonia of the eyelids)			
MS	Delayed muscle relaxation that is resistant to NDMR and DMR	Obtain full Hx regarding symptoms and aggravating factors	Upper-extremity atrophy Muscular hypertrophy in other areas of the body Reflex hammer test	EMG

Key References: Bandschapp O, Iaizzo PA: Pathophysiologic and anesthetic considerations for patients with myotonia congenital or periodic paralyses, *Pediatr Anesth* 23(9):824–833, 2013; Dunø M, Colding-Jørgensen E: Myotonia congenita. In Pagon RA, editor: *GeneReviews*. Available at <http://www.ncbi.nlm.nih.gov/books/NBK1355/>. (Accessed 23.02.16.)

Perioperative Implications

Preoperative Preparation

- Keep pt normothermic throughout pre-/intra-/and postop periods because shivering can trigger myotonic episode.
- DMR, NDMR, and regional anesthesia are ineffective in minimizing myotonic contractions because the defect lies within the muscle membrane.
- Regional anesthesia with peripheral nerve stimulation in combination with fentanyl and midazolam sedation for shoulder surgery has been used successfully without complication.

Monitoring

- Neuromuscular monitoring is mandatory.
- Core temperature monitoring is recommended.

Airway

- Can be difficult to ventilate/intubate if myotonia was elicited during induction/extubation.

Preinduction/Induction

- Consider administering IV lidocaine prior to propofol induction as pain associated with propofol injection can lead myotonia.
- Avoid depolarizing muscle relaxant (succinylcholine), as it has been shown to provoke severe generalized muscle stiffness, including masseter spasm and decerebrate posturing, making intubation and ventilation difficult to impossible.
- Response to NDMR appears to be normal; however, consider reducing the dose of NDMR in pts with associated muscle wasting.

Maintenance

- Consider short-acting NDMR and allow pt to recover fully from muscle relaxant without reversal because anticholinesterase can precipitate myotonia.
- Currently, there are no data on reversal of rocuronium by sugammadex for MC pts.

Extubation

- Consider avoiding anticholinesterase use.
- Avoid coughing on extubation.

Postoperative Period

- Continue to maintain normothermia and adequate pain control.

Anticipated Problems/Concerns

- No association with malignant hyperthermia as previously suggested.
- In rare cases, epinephrine or selective beta-adrenergic agonists in high doses may aggravate myotonia. Beta-antagonist propranolol has also been reported to worsen myotonia.

Beckwith-Wiedemann Syndrome

Arlyne K. Thung | Lee A. Fleisher

Risk

- 1 per 13,700 individuals.
- No gender predilection, although with monozygotic twins it is seen more in females than males.
- Conceptions from IVF have a 3–5 times increased risk of BWS.

Perioperative Risks

- Acute airway obstruction; difficult mask ventilation and intubation secondary to macroglossia
- Hypoglycemia due to islet cell hyperplasia and hyperinsulinemia
- Cardiac malformations

Worry About

- Persistent hypoglycemia, which may cause CNS damage; therefore intraop infusion of a glucose-containing solution and frequent glucose checks are required.
- Difficult airway management.

Overview

- Commonly known for the triad of EMG.
- Other clinical features include anterior earlobe creases, posterior helical pits, facial nevus flammeus, hemihyperplasia, renal anomalies, embryonal tumors, cardiac malformations, and hypoglycemia.
- 7.5% estimated risk for embryonal tumor development, which occurs in the first 10 y of life. Most common tumors are Wilms tumor and hepatoblastoma but may also include rhabdomyosarcoma, adrenocortical carcinoma, and neuroblastoma.
- Cardiac involvement often limited to mild cardiomegaly, although other cardiac defects have been reported (atrial and ventricular septal defects, tetralogy of Fallot, hypoplastic left ventricle, cardiomyopathy, cardiac tumors, and valvular disease).
- Hypoglycemia due to islet cell hyperplasia and hyperinsulinemia occurs in 50% of BWS pts, is often responsive to medical therapy, and usually regresses during the first 4 mo of life. Persistent hypoglycemia refractory to medical management may require pancreatectomy.

Etiology

- Clinically and genetically heterogeneous.
- May be genetically transmitted (15%) or occur sporadically (85%).
- Variety of mutations in chromosome 11p15.5 region.
- Mutation near gene for IGF-II.

Usual Treatment

- Prenatal detection of polyhydramnios, omphalocele, placentomegaly, macrosomia, macroglossia, and renal anomalies on fetal US may prompt genetic testing and counseling if BWS is suspected.
- Screening for hypoglycemia in the first few days of life if BWS is suspected. Surgical intervention if hypoglycemia persists despite medical management.
- Surgical repair of omphalocele.
- Possible reduction of macroglossia in the first year of life to avoid complications of airway obstruction, feeding, and speech difficulties.
- Infants with hypoglycemia and severe oral intolerance due to macroglossia may require gastrostomy tube placement as a temporizing measure until regular feeds become possible after glossal resection.
- Orthopedic follow-up to monitor leg-length discrepancies due to hemihyperplasia.
- Tumor surveillance (abdominal US, alpha-fetoprotein).
- Surgical resection of operative tumors.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Macroglossia	Hx of difficult mask ventilation and intubation	Determine extent by physical inspection and oral palpation, previous anesthesia Hx	No testing
CV	VSD, ASD, TOF, valvular disease, hypoplastic LV, cardiac tumor and cardiomegaly (most common) possible	SOB, DOE	Cardiac exam for murmurs	ECHO CXR
ENDO	Hypoglycemia Hypothyroidism	Shaking, lethargy		Glucose Thyroid function tests
RENAL	Renal medullary dysplasia Nephrolithiasis	Hx of renal tumors/previous resections, chronic UTIs	Palpate for masses, Flank pain	US BUN/Cr

Key References: Weksberg R, Shuman C, Beckwith JB: Beckwith–Wiedemann syndrome, *Eur J Hum Genet* 18(1):8–14, 2010; Eaton J, Atiles R, Tuchman JB: GlideScope for management of the difficult airway in a child with Beckwith–Wiedemann syndrome, *Paediatr Anaesth* 19(7):696–698, 2009.

Perioperative Implications

Preoperative Preparation

- Coordinated care with endocrinology and an ENT specialist to assist in the management of hypoglycemia and difficult airway.
- Discussion with ENT for planned tracheostomy if significant airway edema and swelling is anticipated following glossal resection.
- Review of lab results (hypothyroidism, polycythemia, hypocalcemia, and hyperlipidemia have been reported in pts with BWS in addition to hypoglycemia).
- Review cardiac workup if available.
- Pretreatment with antisialagogue (glycopyrrolate or atropine) if intubation is planned.

Monitoring

- Standard monitoring appropriate for surgical procedure
- Frequent glucose checks

Airway

- Assume difficult mask ventilation due to macroglossia.
- Nasal intubation may be more easily performed than oral intubation in pts with significant macroglossia. Pretreat with a nasal decongestant and dilate with nasal trumpets if nasal intubation is considered.
- Assistance with glossal manipulation if direct laryngoscopy is performed.
- Backup airway devices (e.g., fiberoptic, glidescope, LMA) and surgical support (ENT) if conventional laryngoscopy fails.
- Age-appropriate ETT.

Induction

- Inhaled induction with sevoflurane versus awake intubation with sedation/topicalization.
- Clinicians should be aware that administration of IV anesthetics and muscle relaxants may cause pt's tongue to fall backward, causing acute airway obstruction.

Postoperative Period

- After meeting strict extubation criteria, pts should be monitored in ICU or recovery area with immediate backup for management of airway issues and hypoglycemia.

Anticipated Problems/Concerns

- Difficult airway
- Hypoglycemia

Behçet Disease

Anurag Gupta

Risk

- Affects age group between 20–40 y
- Nations along Silk Route have higher incidence
- Males and females are equally affected

Perioperative Risks

- Increase in IOP during intubation in pts with uveitis complicated by glaucoma
- Pulmonary embolism
- Difficult airway due to oral inflammation

Worry About

- Difficult airway
- Hyperreactive skin
- Pulmonary aneurysm
- Intracranial Htn
- Concurrent anti-inflammatory medications

Overview

- Multisystem inflammatory disorder of unknown etiology characterized by relapsing episodes of oral aphthous ulcers, genital ulcers, other skin lesions, and ocular lesions.
- For diagnosis of BD, an international study group proposed the presence of oral aphthous ulcers and any two other manifestation among the following:
  - Recurrent genital ulceration.
  - Skin lesion.
  - Papulopustular lesions.
  - Ocular involvement.
  - Positive pathergy test: Hyperreactivity of skin leading to sterile pustule and erythematous papule formation after intracutaneous injection or needle prick.
- Ocular and vascular involvement increases morbidity.
- Major vessel disease and neurologic involvement are the major cause of death.
- Newer drugs have shown good improvement in resistant cases of BD, but further studies are needed to reinstate their efficacy.
- Extracutaneous ulcers, which heal by scarring, may be found in children.
- Erythematous nodosum-like lesions may occur mostly in females; the lesions are more erythematous and edematous, and they heal within a week, leaving hyperpigmentation after healing.

Etiology

- Although exact etiology unknown, BD is found to be mostly associated with HLA-B51.
- Other genes implicated are HLA-26, PSOR1C1, HLA-Cw1602, GIMAP, UBAC2, IL-10, and IL-23.

Treatment

- Mucocutaneous BD: Thalidomide, dapsone, TNF-α inhibitor (Etanercept), IFN-α, and colchicine
- Ocular involvement: Azathioprine, cyclosporine, IFN-α, and methotrexate
- Vascular involvement: Azathioprine, cyclophosphamide, and cyclosporine
- Joint involvement: Colchicine and NSAIDs
- GIT: Azathioprine
- CNS: Anticoagulants, infliximab, IFN-α, and adalimumab
- Corticosteroids: Severe, life-threatening disease in ocular, vascular, GI, and neuro BD (as advised by an expert committee report)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Recurrent oral aphthous ulcers Airway edema	Frequent attacks >3 times/y Ulcers may be single/ multiple After local trauma/dental extraction	Minor ulcers: <1 cm; heal without scarring in 4-14 days Major ulcers: >1 cm; heal with scarring Site involves gingival, buccal, labial mucosa, soft and hard palate Airway edema Erythematous border around ulcers	PCR CBC Tzanck smear HPE Vit B12 Iron Folate
	Relapsing uveitis Glaucoma Cataract Loss of vision	Presents 2-3 y after oral lesions Frequent attacks leads to complications	Blurred vision Lacrimation Floaters Periorbital global pain Hyperemia	Intraocular fluid: • Culture • PCR • Immuno-histochemical study
RESP	Pulmonary artery aneurysm Vena cava thrombosis Pleural effusion Pulmonary infarct Pulmonary fibrosis	Previous history of oral and ocular involvement Hemoptysis Chest pain	Superior vena cave syndrome Stony dullness on percussion ↓ breath sounds	CXR CT angiography
CV	Cardiac involvement is uncommon Myocarditis Valvular lesion Pericarditis Ventricular aneurysm	History of oral/ocular lesions	Dyspnea Fatigue Pulmonary edema Chest pain	ECG 2D-ECHO
	Vasculitis is common Venous > arterial Superficial thrombophlebitis Venous thrombosis	Tenderness over the peripheral vein Calf tenderness		Doppler study of deep veins
GI	Ileitis Colitis Intestinal perforation Acute abdomen	Positive previous history Pain in abdomen Diarrhea Dyspepsia Vomiting Dysphagia Retrosternal chest pain Hematemesis	Abdominal tenderness Rigidity and guarding	GI endoscopy • Round and oval ulcers • No granulations
GU	Genital ulceration	History of aphthous ulcers Involvement of scrotum, glans or shaft in males Involvement of labia in females	Larger and deeper lesion with irregular border Heals with scar	
CNS	Meningoencephalitis Stroke in young pt Movement disorder Dural sinus thrombosis Arterial vasculitis Aseptic meningitis Intracranial and extracranial aneurysm	Headache Seizure Brain stem syndrome Ataxia Aphasia Pseudobulbar palsy Cranial nerve palsy Pyramidal tract sign		CSF examination • Increased protein • Increased cell count • Normal glucoseMRI Diffusion weighted image: Increased diffusion coefficient in BD HPE: Perivascular lymphatic infiltration with area of necrosis

Key References: Saleh Z, Arayssi T: Update on the therapy of Behçet disease, *Ther Adv Chronic Dis* 5(3):112–134, 2014; Kokturk A: Clinical and pathological manifestations with differential diagnosis in Behçet's disease, *Pathol Res Int* 2012:690390, 2012.

Perioperative Implications

Preoperative Preparation

- Avoid multiple sticks for IM sedation and IV cannulation.
- Concomitant steroid therapy and the necessity of stress dose should be considered.
- Prophylactic antibiotic therapy because the pt may be on immunosuppressant therapy.
- Prophylaxis against thromboembolism.

Monitoring

- Consider brain function monitoring.
- Arterial catheter as indicated.

Airway

- Oral ulcers, erythema, edema around the lesion, and previous scarring may make airway difficult.
- Use maneuver to reduce pressor response to intubation.
- Avoid airway blocks.

Preinduction/Induction

- Premedication through IV routes.
- Avoid depolarizing muscle relaxant to prevent rise in IOP.

Maintenance

- Depth of anesthesia between 40 and 60 BIS value
- Fluid as per 4:2:1 rule
- Adequate padding of pressure points

Extubation

- Check for any airway trauma or bleeding oral surface.

Postoperative Period

- Pain management by infusion of opioids/suppository

Anticipated Problems/Concerns

- Vasculitis and thrombus formation in larger vessels increases the risk of pulmonary embolism; therefore, initiation of thromboembolic prophylaxis is helpful in such cases.

Bernard-Soulier Syndrome

Miguel A. Yaport | Lee A. Fleisher

Risk

- Estimated to be <1 in 1 million persons, but may be higher due to misdiagnosis and underreporting
- Rare: Approximately 100 cases reported in literature

Perioperative Risks

- Severe hemorrhage out of proportion to plt count
- Transfusion reactions

Worry About

- Severe periop hemorrhage
- Limited availability of blood products
- Concurrent medical conditions (e.g., uremia, liver disease) or medications (NSAIDs, heparin, and antiplatelet agents) contributing to bleeding

Overview

- Coagulopathy characterized by defects in plt number and function due to an absence or abnormality in plt membrane glycoprotein receptor complex GPIb-IX-V, a four-protein complex responsible for initiating plt adhesion at sites of vascular injury and binding Von Willebrand factor
- Defect in primary hemostasis; mucocutaneous bleeding; often, the bleeding is more severe than expected for the pt's particular plt count
- Clinical phenotype severity varies; manifestations range from easy bruising, purpura, epistaxis, gingival bleeding, and menorrhagia to hematuria, GI bleeding, and fatal hemorrhage
- Severe bleeding associated with menses, trauma, and certain surgical procedures (e.g., tonsillectomy, appendectomy, splenectomy, dental extraction)
- Diagnosed by prolonged bleeding time, presence of a small number of very large plt on blood smears (macrothrombocytopenia), reduced plt counts (20,000–100,000), and absence of RIPA

Etiology

- Autosomal recessive inheritance pattern; a wide spectrum of clinical manifestation based on the degree of glycoprotein complex dysfunction.
- Individual genes have been identified for each of the proteins in the complex and may be the target for future therapy: 17p12 (GPIba), 22q11.2 (GPIbb), 3q29 (GPV), and 3q21 (GPIX).

Usual Treatment

- Bleeding prophylaxis including lifestyle modifications (e.g., personal safety, avoidance of trauma, avoidance of antiplatelet medications [aspirin], adequate dental hygiene, use of contraceptives in females at puberty)
- Bleeding treatment: Plts, PRBCs, and EACA
- Refractory bleeding: DDAVP, gamma globulin, corticosteroids, and recombinant factor VIIa

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral/mucosal friability	Epistaxis and gingival and cutaneous bleeding	Sores, stomatitis, erythema	See HEME
CV	Vascular access: potential hemorrhage			
GI	GI bleeding	Melena, hematochezia		Stool guaiac, endoscopy
HEME	Coagulopathy: Primary hemostasis, mucocutaneous bleeding Severe hemorrhage Antibodies to blood products	Bleeding gums, bruising easily, menorrhagia, epistaxis Hx of transfusion family Hx of periop bleeding	Petechiae, bruises, gingival hyperemia	PT/ INR, PTT, plt count, blood smear, plt function assay, ristocetin cofactor activity Type and screen, crossmatch, and antibody analysis

Key References: Kostopanagiotou G, Siafaka I, Sikiotis C, et al: Anesthetic and perioperative management of a patient with Bernard-Soulier syndrome, *J Clin Anesth* 16(6):458-460, 2004; Lanza F: Bernard-Soulier syndrome (hemorrhagiparous thrombocytic dystrophy), *Orphanet J Rare Dis* 1:46, 2006.

Perioperative Implications

Preoperative Preparation

- Collaboration with hematology and blood bank.
- Ensure availability and adequacy of blood products.
- Assess and optimize coagulation (coagulation factor analysis, dialysis if uremic, and FFP/vitamin K if increased INR).

Monitoring

- Standard monitors.
- Risk-benefit assessment to evaluate more access or invasive monitoring (A-line or CVP) versus unnecessary or failed attempts leading to sources of potential bleeding.
- Urine output for new-onset hemoglobinuria as first sign of transfusion reaction.
- Avoid undue tension on soft tissues and provide adequate padding of pressure points and mucosal surfaces.
- Consider intraop thromboelastogram.

Airway

- Avoid nasal manipulation.
- Use extreme caution with friable oral and pharyngeal mucosal surfaces.
- Consider video laryngoscopy to ensure first-attempt success.

Induction

- No specific recommendations

Maintenance

- Avoid hemodilution.
- Meticulous surgical hemostasis.
- Normothermia promotes coagulation.
- Analyze clot formation via thromboelastography and transfusion as needed.
- Controlled hypotension may reduce potential blood loss; however, avoid in anemic pts.

Extubation

- Care of mucosal membranes, gentle orotracheal suction under direct visual guidance, and avoid coughing

Adjuvants

- Neuraxial anesthesia is relatively contraindicated in these pts. Individual risk-benefit assessment based on severity of disease and plt function (e.g., thromboelastography).

Postoperative Period

- Continue monitoring coagulation status.

Anticipated Problems/Concerns

- Severe intraop and postop hemorrhage
- Transfusion-related reaction and increased likelihood of infectious bloodborne diseases

Bilirubinemia of the Newborn

Kha M. Tran

Risk

- A common problem in neonates.
- Some types pathologic and some physiologic.
- Bilirubin may be unconjugated or conjugated; differentiating important for diagnosis.
- If pathologic, varying effect on management (e.g., sepsis, Rh incompatibility, GI obstruction, Gilbert, AVM, sickle cell, biliary atresia).
- Clinical, epidemiologic, and genetic risk factors associated with significant hyperbilirubinemia include preterm gestational age, exclusive breastfeeding, glucose-6-phosphate dehydrogenase deficiency, Rh/ABO incompatibility, East Asian or Native American ethnicity, any jaundice observed in the first 24 h of life (hemolysis until proven otherwise), cephalohematoma or significant bruising after delivery, and Hx of a previous sibling treated with phototherapy.

Perioperative Risks

- Risks specific to a primary pathologic cause of bilirubinemia
- Acute bilirubin encephalopathy (unconjugated bilirubin may penetrate brain cells and cause dysfunction in either pathologic or physiologic states)
- Kernicterus (chronic and permanent sequelae of bilirubin neurotoxicity)

Worry About

- Factors that increase blood-brain barrier permeability to unconjugated bilirubin (hypoxia, hypercarbia, acidosis, hyperosmolality, hypertension, seizure activity, and sepsis)
- Drugs (e.g., sulfonamides, ceftriaxone, ampicillin, salicylates, furosemide, contrast dye) that displace bilirubin from albumin, which can increase free fraction of unconjugated bilirubin in the blood

- Conversely, binding of some drugs to albumin may be altered in the presence of hyperbilirubinemia in the neonatal period
- Physiologic states (dehydration, hypercarbia, and acidosis) may displace bilirubin
- Surgery may increase load of heme to be degraded (e.g., hematoma absorption)
- Primary pathology

Overview

- Bilirubin is derived from the catabolism of proteins that contain heme, usually, from the breakdown of hemoglobin from RBCs.
- Heme is oxidized to biliverdin and then reduced to bilirubin, which is unconjugated, nonpolar, and lipid soluble.
- Unconjugated bilirubin circulates bound to albumin in equilibrium with its unbound fraction that readily crosses the blood-brain barrier and can cause neurotoxicity.
- Bilirubin is conjugated in the liver cell microsomes by the enzyme (UDP)-glucuronyl transferase, to form the polar, water-soluble glucuronide of bilirubin.
- Most of the conjugated bilirubin is excreted as bile, which is metabolized by intestinal flora and excreted in the feces.
- The danger of unconjugated hyperbilirubinemia is bilirubin-induced neurologic dysfunction.
- Bilirubinemia peaks in term infants between 3–5 d; preterm infants 5–6 d
- Clinical features of bilirubin encephalopathy are lethargy, anorexia, nausea, vomiting, and opisthotonic posturing.
- The ability of anesthetic agents to displace bilirubin from albumin has not been well studied.

Etiology

- Nonpathologic, physiologic jaundice due to immature hepatic glucuronyl transferase
- Pathologic hyperbilirubinemia due to many causes (isoimmunization, erythrocyte biochemical defects, erythrocyte structural defects, infection)
- Excess bilirubin production from RBC breakdown (intravascular hemolysis or polycythemia, extravascular bruising or cephalohematoma)
- Decreased removal of bilirubin through gut (decreased meconium evacuation and increased enterohepatic recirculation; decreased bile flow due to liver disease or cholestasis)
- Breastfeeding jaundice (occurs in first wk after birth and implies inadequate hydration or caloric intake)
- Breast-milk jaundice (unidentified factors in normal mature human milk that cause increased reabsorption of UB from gut) can last for 3–4 wk up to 3 mo

Usual Treatment

- Goal of therapy is to prevent indirect-reacting bilirubin–related neurotoxicity.
- Phototherapy and exchange transfusion (for severe cases) remain the primary treatment modalities used to keep the maximal total serum bilirubin below the dangerous levels.
- Phototherapy bypasses the hepatic system and produces photoisomers of bilirubin that are more water-soluble and can be cleared directly in bile or urine without conjugation in the liver.
- Exchange transfusion removes infants' sensitized and destroyed RBCs and circulating antibodies; double-volume exchange replaces 85% of circulating RBC volume, decreases bilirubin level by 50%, and corrects anemia.
- AAP guidelines for healthy term infant: Phototherapy when serum bilirubin >12–15 mg/dL; exchange transfusion >20–25; premature or ill term-infants have lower threshold for starting therapy.
- Several factors are important when determining the bilirubin level above which kernicterus is possible (gestational age, degree of illness, evidence of hemolysis, rate of rise, albumin level, and physiologic stress).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Jaundice resulting from accumulation of unconjugated, nonpolar, lipid-soluble bilirubin pigment in the skin		Jaundice progresses in cephalocaudal direction (face, approximately 5 mg/dL; abdomen, approximately 15 mg/dL)	
RESP	Pleural effusion, pulm edema	Maternal prenatal history	Resp distress	CXR
HEME	Hemolysis	Rh/ABO maternal-fetal incompatibility	Anemia, bruising, cephalohematomas hepatosplenomegaly, jaundice	Maternal ABO and Rh typing Cord blood type, Rh and direct Coomb CBC, diff, retic, and blood smear Fractionated bilirubin, LFTs, ammonia, PT/PTT, blood and urine cultures
CNS	Bilirubin toxic to CNS cells	High levels of bilirubin	Abnormal posture, tonicity, reflexes	

Key References: Kaplan H, Wong RJ, Sibley E, et al: Neonatal jaundice and liver diseases. In Martin RJ, Fanaroff AA, Walsh MC, editors: *Fanaroff and Martin's neonatal-perinatal medicine,* ed 10, Philadelphia, 2015, Elsevier, pp 1618–1673; Bhutani VK, Wong RJ, Stevenson DK: Hyperbilirubinemia in preterm neonates, *Clin Perinatol* 43(2):215–232, 2016.

Perioperative Implications

Preoperative Preparation

- Determine reason for hyperbilirubinemia.
- Weigh risks and benefits of surgery if bilirubin levels are high.
- Ensure adequate intravascular volume.
- Active efforts to lower bilirubin levels.
- Address coexisting disease states.

Monitoring

- Blood sampling may be indicated.

Airway

- Neonatal airway concerns

Induction

- Maintain normal hemodynamics.

Maintenance

- No one agent or technique preferred.
- Few data reflecting effects of anesthetic agents on bilirubin levels.
- Avoid hypoxia, hypothermia, and acidosis.

Extubation

- Standard criteria

Postoperative Period

- Apnea/bradycardia risks.
- Monitor bilirubin levels.

Anticipated Problems/Concerns

- Ultimate goal of therapy and management is to prevent bilirubin encephalopathy and kernicterus.

Bipolar Disorder

Alan David Kaye | Martin J. Carney | Rachel J. Kaye

Risk

- Lifetime prevalence within USA 4%
- Vast majority of pts younger than 25 y
- Suicide rates are 20 times higher than that of general population

Perioperative Risks

- Risk of disregard for self care within manic phases, especially in the setting of enhanced stress
- Exacerbation of the disease if certain medications
- Anesthetic considerations focused on drug-drug interactions and altered dosing (e.g., lithium decreases MAC requirements)

Worry About

- Depressed, irrational, irritable pt behavior
- Increased morbidity and mortality due to overlapping medical conditions (e.g., diabetes mellitus, cardiovascular disease, obesity)
- Drug interactions and side effects
  - Extrapyramidal side effects (EPS) (e.g., akathisia, tardive dyskinesia, muscle rigidity)
  - Cardiac effects such as QT prolongation and orthostatic hypotension
  - Rash including Stevens-Johnson syndrome and toxic epidermal necrolysis
  - Lithium risk during pregnancy, thyroid, parathyroid, and diabetes insipidus

Overview

- Bipolar disorder made up of four subtypes that differ in the intensity of mania, as well as the presence or absence of depression.
- There can be a reduced need for sleep, racing thoughts, impulsivity, and mood swings.
- Strong link to family history, as well as heightened illicit drug usage and alcohol abuse.
- Treatment often includes a mixture of antipsychotic medication, as well as mood stabilizers (e.g., lithium, anticonvulsants).
- Typical antipsychotics utilize dopamine antagonism and are plagued with EPS (e.g., tardive dyskinesia).
- Atypical antipsychotics utilize serotonin antagonism with less dopamine effect, leading to fewer EPS manifestations.
- EPS can be treated with anticholinergics such as benztropine 2 mg or diphenhydramine 50 to 100 mg.
- Neuroleptic malignant syndrome is a rare but fatal sequelae of large doses of antipsychotics.
- Mood stabilizers such as lithium uniquely cause thirst, polyuria, weight gain, and the gambit of side effects following diabetes insipidus.

Etiology

- Clear genetic association within first-degree family members.
- Environmental factors play into the epigenetic realm of manic breaks in the disease, including stressors, altered sleep cycle, and substance abuse.
- Disruption in neurotransmitters such as serotonin and norepinephrine likely play a role.

Usual Treatment

- Aimed at managing acute manic events, depressive symptoms, and long-term mood stabilization.
- Lithium, the most commonly used mood stabilizer, is dosed at 900 to 1800 mg orally per day, with the second most common being valproate dosed at 1000 to 3000 mg orally per day.
- Additionally, antipsychotic medications added to mood stabilizers for superior effects versus monotherapy alone.
- Most effective drugs for controlling acute manic episodes: Haloperidol (typical), risperidone, olanzapine, and quetiapine (atypical).
- Behavioral and cognitive psychotherapy.
- Electroconvulsive therapy: the treatment of choice for pts with severe mania refractory to pharmacotherapy.
- Indicated when rapid recovery is required.

Assessment Points

System	Effect	Assessment by Hx	PE
CV	QT prolongation Orthostatic hypotension	Dizziness Dizziness	Orthostatic hypotension Postural BP changes
GI	Liver dysfunction	Alcohol and medication use	Bleeding and jaundice
HEME	Agranulocytosis	Frequent infection	Mild fever
ENDO	Diabetes insipidus Hyperlipidemia	Polydipsia, polyuria	Signs of dehydration
NEURO	EPS	Typical antipsychotic usage	Dystonia, bradykinesia,akathisia, tardive dyskinesia
GENERAL	NMS	Medication usage or change	Hyperthermia, rigidity, autonomic instability, cardiac arrhythmia
	Stevens-Johnson syndrome Toxic epidermal necrolysis	Carbamazepine or lamotrigine use	Fever, rash, blisters

Key References: Price AL, Marzani-Nissen GR: Bipolar disorders: a review, *Am Fam Physician* 85(5):483–493, 2012; Geddes JR, Miklowitz DJ: Treatment of bipolar disorder, *Lancet* 381(9878):1672–1682, 2013.

Perioperative Implications

Preoperative Preparation

- Mental status must be assessed in preop planning.
- Mood stabilizers and antipsychotic regimen should remain the same with lithium level; check if concerned.

Monitoring

- Routine

Airway

- Standard protocol

Preinduction/Induction

- Variable outcomes by institution; standard approach needed

Maintenance

- Thermodysregulation risks: monitor temperature and treat symptoms.
- Adequate, but not excessive urine output.
- Hypotension, tachycardia, and arrhythmia.

Extubation

- Standard practice

Anticipated Problems/Concerns

- Polypharmacy is regularly practiced to control bipolar disorder, and these drugs must be carefully titrated and monitored in the preop and postop settings.
- Psychiatric and mental assessment should be regularly performed to monitor compliance and understanding.
- Cardiac arrhythmia, BP instability, and neuropsychiatric symptom exacerbation.
- Hypothyroidism and diabetes insipidus.
- Regional not a good choice with this disorder.
- Postop adherence and medication changes.

Blebs and Bullae

Trent Bryson

Risk

- Prevalence of blebs as high as 6% of young, healthy adults, although spontaneous rupture occurs only in 7.4 to 18 per 100,000.
- Incidence of ruptured bulla is 26 per 100,000.
- Increased incidence of primary disease in young males.
- Increased prevalence with smoking (Hx, including tobacco and illicit substances), COPD, chronic bronchitis, cystic fibrosis, lung cancer, staphylococcal pneumonia, tuberculosis, Marfan syndrome, Ehlers-Danlos syndrome, alpha-1 antitrypsin deficiency, sarcoidosis, fiberglass pneumoconiosis, and BMI <22.

Perioperative Risks

- Pneumothorax
- Bronchopleural fistulae
- Caval compression of nonruptured giant bulla
- Pulm Htn and RV failure
- COPD

Worry About

- CV collapse from tension pneumothorax
- Expanded dead-space ventilation
- Inability to adequately ventilate due to bronchopleural fistula
- Inadequate venous return from caval compression
- Expansion of bulla leading to compressive effects or rupture

Overview

- *Bleb* usually refers to a collection of air caused by ruptured alveoli within the visceral pleura without any other lining that is <1 cm in size.
- Bullae >1 cm in size and arise from various sources, which cause destruction of lung parenchyma.
- Nitrous oxide is contraindicated, and positive pressure ventilation should be avoided if possible.
  - Nitrous oxide 35 times more soluble than nitrogen in blood. Because of this, nitrous oxide readily diffuses into any gas-filled cavity much more rapidly than nitrogen is absorbed, which leads to rapid expansion of pneumothoraces.

- In spontaneous ventilation, bullae are more compliant than normal lung tissue and preferentially fill. At higher pressures and volumes, bullae are much less compliant than normal lung and therefore have much higher peak pressures than normal tissue and are prone to rupture.

Etiology

- Primary: Unknown but may be genetic; more common in young males
- Secondary: Emphysema, smoking, lung cancer, cystic fibrosis, pneumonia, and tuberculosis

Usual Treatment

- No treatment for asymptomatic, incidental blebs
- First-time rupture of a bleb is treated conservatively, depending on size of pneumothorax; Varies from 100% O_2 to chest-tube placement
- Surgical treatment: indicated for ruptured blebs in those in high-risk occupations that involve frequent changes in barometric pressure or recurrent spontaneous pneumothorax
- Surgical treatment of bullae done for increasing SOB or recurrent pneumothorax
- Surgical approach: Usually VATS, but may require thoracotomy or median sternotomy; laser ablation and mechanical pleurodesis may be utilized

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CAD, pulm Htn, RV failure	Angina, DOE	Signs of RV failure (palpable PA, peripheral edema)	ECG, stress test, ECHO
RESP	Expiratory obstruction and air trapping V/Q mismatch Hypoxia, hypercarbia Pneumothorax	Exercise tolerance, cough	Pursed-lip breathing, tachypnea	CXR, ABGs, chest CT, V/Q scan
ENDO	Possible steroid use			Glucose
MS	Barrel-chested			

Key References: Bansal S, Surve RM, Venkatapura RJ: Anesthetic management of a paraparetic patient with multiple lung bullae, *J Neurosurg Anesthesiol* 26(1):85–86, 2014; Slinger PD, Campos JH: Anesthesia for thoracic surgery. In Miller RD, Eriksson LI, Fleisher LA, et al., editors: *Miller's anesthesia,* ed 7, Philadelphia, 2010, Churchill Livingstone, pp 1819–1888.

Perioperative Implications

Preinduction/Induction/Maintenance

- Optimize oxygenation and deliver bronchodilators if necessary.
- Regional or neuraxial anesthesia is preferential over general endotracheal anesthesia.
- Some associated conditions may have significant mucus plugging; fiberoptic bronchoscope with suction and irrigating capabilities may be useful.
- Careful attention to hemodynamic monitors and ventilator peak pressures and volumes is essential.
- Have a surgical team available during induction because this is most common time for pneumothorax to occur.
- Recent chest x-ray evaluation for severity of disease and progression is also essential.

Monitoring

- Routine
- Consider arterial line to recognize more rapidly signs of CV collapse from pneumothorax or caval compression

General Anesthesia

- Maintaining spontaneous ventilation through induction can minimize complications. Avoid the use of paralytics or consider mask induction or awake fiberoptic intubation techniques.
- Consider ketamine induction to maintain ventilation for IV induction.
- If disease is unilateral and positive pressure required, a double lumen endotracheal tube can allow you to isolate the diseased lung and not expose it to increased pressure.
- If positive pressure ventilation needed, pressure control ventilation at low pressures with higher rate may be useful, but beware of breath stacking.
- Allow adequate exhalation times to avoid breath stacking (auto-PEEP) by appropriately setting I:E ratio.
- Do not use nitrous oxide under any circumstance.
- Consider use of isoflurane because it is the most bronchodilating-inhalation agent; it may decrease pressure requirements or obstruction in COPD pts.
- Careful attention to spontaneous ventilatory rate and volumes before extubation.
- Avoid high airway pressures from fighting the ventilator.
- If pt paralyzed, assure full reversal before attempt to extubate.
- COPD pts may retain CO_2, so be careful not to drive $ETCO_2$ too low and prolong emergence.

Regional Anesthesia

- Preferred technique if possible for most cases.
- Optimize volume status.
- Watch for resp distress from loss of accessory resp muscles from neuraxial anesthesia.
- Epidural may be preferable to spinal to avoid loss of accessory muscles by slowly raising the level by interval dosing.
- Pleurodesis is exquisitely painful and often requires a thoracic epidural to control pain and assure adequate chest excursion during recovery.

Postoperative Period

- Beware of CO_2 narcosis in those who retain CO_2.
- Spontaneous rupture can occur at any time. Continue adequate monitoring and watch for sudden dyspnea, desaturation, and loss of unilateral breath sounds.

Anticipated Problems/Concerns

- Rupture of bleb or bulla will cause a pneumothorax, which may rapidly progress to tension.
- Treatment of choice for tension pneumothorax is needle thoracostomy in second to third intercostal space in midclavicular line (in line with the nipple of a male pt). Most failures of needle thoracostomy occur from placement of needle too medial into the mediastinum.
- Obstructive pulmonary pathology includes bronchoconstriction and accessory muscle use even in the spontaneously breathing pt.
- Positive pressure ventilation is to be avoided, and nitrous oxide is absolutely contraindicated.

Bleomycin Sulfate Toxicity

John F. Rompala

Risk

- Pts with a history of germ cell tumors, lymphomas, squamous cell carcinomas, Kaposi sarcomas, and cervical cancers treated with BLM
- Incidence of BLT is 10–40%; mortality is 1–2%
- Risk of BLT increases with total dose >400 unit, glomerular filtration rate <80 mL/min, or advanced tumor stage at time of diagnosis
- History of concurrent thoracic irradiation cisplatin administration
- Age greater than 40 y
- History of smoking or exposure to high FiO_2s

Perioperative Risks

- Exposure to high FiO_2 may increase risk of developing pneumonitis and potentially lethal ARDS in periop setting.
- Preexisting lung pathology in combination with low FiO_2 may result in hypoxia.
- Risk of pulm injury is greatest within about 8 mo of administration, but BLM likely confers an elevated lifetime risk of BLT.
- Pulm adverse events rarely related to the intrapleural or intralesional administration of BLM.

Worry About

- Periop exposure to high FiO_2s (>30%)
- Periop hypoxia
- Fluid overload, transfusion of red cells, and prolonged operative time
- Intrapleural administration of BLM, which has been associated with local pain and hypotension requiring symptomatic treatment

Overview

- Antibiotic with antitumor properties isolated from the fungus *Streptomyces verticillus* is used primarily to treat testicular cancers and lymphomas, as well as some head and neck tumors.
- BLM is also effective for treatment of malignant and recurrent pleural effusions.
- BLM is inactivated by the enzyme BLM hydrolase. Lungs and skin have the lowest levels of BLM hydrolase and thus are more susceptible to injury.
- Cleared by renal excretion. $T_{1/2}$ 4 h.

Etiology

- BLM binds both Fe^{2+} and DNA. The Fe^{2+} is oxidized to Fe^{3+}, resulting in free radicals, which damage DNA, leading to cell death.
- Oxidative damage to cell membranes and fatty acids likely initiates an inflammatory response resulting in myofibroblast proliferation and ultimately pulmonary fibrosis.
- Early reports demonstrated a link between administration of BLM/exposure to high FiO_2s and subsequent development of lung toxicity and fibrosis.

Assessment Points

System	Effect	Assessment by Hx	PE	Tests
RESP	Pulm fibrosis ARDS with O_2 exposure	Dyspnea, dry cough	Frequently normal Earliest sign is fine rales	CXR: Bilateral infiltrates progressing to consolidation and honeycombing High-resolution CT scan: Ground-glass opacities and fibrosis Decreased O_2 sat PFTs: Restrictive pattern/decreased DLCO
MUCOCUT	Inflammation, dermal fibrosis	Itching, burning, skin tenderness	Stomatitis, alopecia, scleroderma-like skin changes	
HEME	Minimal bone marrow toxicity			CBC

Key References: Reinert T, Baldotto C, Nunes F, et al.: Bleomycin-induced lung injury, *J Cancer Res*, 2013. <http://dx.doi.org/10.1155/2013/480608/>. (Accessed 24.02.16.); Aakre BM, Efem RI, Wilson GA, et al.: Postoperative acute respiratory distress syndrome in patients with previous exposure to bleomycin, *Mayo Clin Proc* 89(2):181–189, 2014.

Perioperative Implications

Preoperative Preparation

- In pts with Hx of testicular, squamous cell cancer, or lymphoma, inquire about exposure to BLM, as well as Hx of other risk factors.
- Any pt with abnormal PFTs, or who is clinically symptomatic, should be considered at high risk for development of ARDS.
- Pts receiving BLM within 8 mo of surgery are at higher risk, but BLM exposure most likely confers elevated lifetime risk of BLT.

Intraoperative Management

- Use of low FiO_2 has been mainstay of BLT prevention. Some studies call this practice into question. It is best to maintain FiO_2 below 30%, but perhaps not at expense of hypoxia.
- Utilize protective lung ventilation strategies.
- Maintain neutral fluid balance with preference toward colloids. Avoid transfusions if possible. Consider invasive monitoring to guide fluid therapy.
- In high-risk pts, pretreatment with corticosteroids (1 mg/kg prednisone) may be helpful in limiting postop ARDS.

Postoperative Period

- Provide adequate oxygenation with the lowest possible inspired FiO_2.
- Observe carefully for 3–5 d after surgery, for signs of dyspnea, hypoxia, cough, or rales.
- Use PEEP or CPAP to treat postop hypoxia.
- Add methylprednisolone up to 1 mg/kg/d if developing ARDS, and diuretics if clinically indicated.

Anticipated Problems/Concerns

- Pts who had previously received BLM and have received supplemental oxygen are susceptible to lung toxicity and ARDS.
- Maintaining adequate oxygenation with the lowest possible FiO_2 can be difficult.
- Neutral fluid balance and avoidance of transfusions if possible. Invasive monitoring may be useful for guidance.

Blindness

Stanley W. Stead

Risk

- Eye injuries represent 4% of claims analyzed in the ASA Closed Claims Project.
- Majority of entries in the ASA POVL Registry are associated with cardiac and spine cases, with a reported incidence as high as 4.5% and 0.2%, respectively. Other surgical procedures with POVL reported including head and neck, liver transplants, thoracoabdominal aneurysm resections, peripheral vascular procedures, and prostatectomies.
- In the Registry, POVL is most often associated with ION 89% of the time and CRAO 11% of the time.
- Blindness can result from injury to the eye, its surrounding structures (eyelid and conjunctiva), blood supply, and optic nerve.
- Blindness may be transient (glycine absorption), prolonged, or permanent (ION, CRAO, traumatic, and central ischemic events).

Perioperative Risks

- ION: Bilateral blindness in spine procedures in the prone position, cardiopulmonary bypass, head and neck dissections, complex instrumented spinal fusion surgery, where there is significant facial swelling and venous hemodynamics may be altered (highest incidence: Pts <18 y)
- CRAO: Periocular trauma and rarely bilateral blindness.
  - Procedure dependent factors: improper head positioning, use of a horseshoe headrest when placing the eye in contact with the headrest, anemia, blood loss greater than 1 L, systemic hypotension, and procedure duration greater than 6 h
- Intraocular procedures, procedures around the eye, prone position with padding around the face and eyes, exophthalmos, or ophthalmic nerve blocks
  - 1.5% glycine irrigation during TURP as well as transurethral bladder procedures and hysteroscopic procedures in women

Worry About

- Pressure on the globe or contact with eye by foreign objects or solutions
- Positioning of pt, especially prone
- Low blood-flow states: Systemic hypotension, anemia, and venous drainage impairment of the head and neck
- Operations in physical proximity to the eyes
- During ophthalmic surgery:
  - Movement of pt under either MAC or GA during intraocular surgery
  - Trauma to optic nerve, retinal artery, or vein during orbital or sinus surgery
  - Coughing or substantial Valsalva maneuvers by pt following intraocular surgery
- During ophthalmic nerve block:
  - Perforation of globe
  - Trauma to the optic nerve, retinal artery, and vein

Overview

- Unless associated with glycine irrigating solution, blindness is often an irreversible complication following anesthesia and surgery.
- Blindness is most often associated with injury to the eye, its surrounding structures (eyelid and conjunctive), blood supply, and optic nerve.

Etiology

- Conditions that can result in blindness following anesthesia include: Corneal abrasion, vitreous loss, hemorrhage, movement of pt while operating on or in the eye, chemical injury to the cornea or conjunctiva from cleaning materials on the anesthetic mask, spillage of prep solution into the eye, and direct trauma to the eye due to OR table padding, needle used in retrobulbar block, anesthetic mask pressure on the globe, or foreign body falling into the eye. Additionally, prone position, hypoxemia following cardiac arrest, prolonged hypotension, CRAO, increased intraocular pressure, and embolization, occlusion, thrombosis, or spasm of the retinal artery.
- Blindness may occur following absorption of glycine irrigating solution during TURP (glycine distribution similar to that of γ-aminobutyric acid, an inhibitory neurotransmitter; levels of glycine >143 mg/L associated with transient blindness).

Usual Treatment

- In the case of glycine, supportive treatment is indicated until plasma glycine levels <143 mg/L.
- ION: There is no effective treatment and most lost vision is not recovered.
- CRAO: Immediate lowering of intraocular pressure with acetazolamide and topical medications; hyperbaric O_2 therapy may be beneficial if begun within 2–12 h of symptom onset.
- Consider stated spine procedures on high-risk pts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL	Retinal artery occlusion	Migraines, coagulopathies, hemoglobinopathies, and oral contraceptives increase IOP	Pale ischemic retina with pathognomonic cherry-red spot and afferent papillary defect	
HEENT	Ischemic retinopathy	Hypotension Hypoxemia Shock	Funduscopic: Normal retina but optic nerve head is swollen and ischemic. Eventual optic nerve pallor	
	Orbital pressure		Funduscopic: Edematous retina with dilated arterioles and engorged veins	
GU	Transient blindness during or after TURP	TURP with glycine irrigating solution	Normal papillary response to light and accommodation; Fundus normal	Plasma glycine level (nml 13–17 mg/L)

Key References: Lee LA, Roth S, Posner KL, et al.: The American Society of Anesthesiologists Postoperative Visual Loss Registry: analysis of 93 spine surgery cases with postoperative visual loss. *Anesthesiology* 105:652–659, 2006; Shen Y, Drum M, Roth S: The prevalence of perioperative visual loss in the United States: a 10-year study from 1996 to 2005 of spinal, orthopedic, cardiac and general surgery. *Anesth Analg* 109:1534, 2009.

Perioperative Implications

Preinduction/Induction/Maintenance

- Proper positioning essential.
- If pt is prone, adequate padding so no pressure is transmitted to either globe or nasal bridge.
- When the face is completely draped, consider use of a metallic Fox shield to protect eye from inadvertent pressure.

Monitoring

- Eye checks frequently during the procedure to ensure no pressure on the globe
- Ensure adequate venous drainage without increased venous pressure or increased intracranial pressure, particularly when venous outflow may be compromised by position or procedure.

General Anesthesia

- Anesthetic masks may injure eye, either through inadequate drying and application of cleaning solution to eye or through direct pressure.
- Hypotension and hypoxemia implicated in cases of CRAO.
- Hypotension, anemia, and prolonged procedures are implicated in ION.

Regional Anesthesia

- In ophthalmic nerve blocks, needle does not enter globe or retinal artery, vein, or nerve. Avoid excessive volume of local anesthetic, which increases IOP and may compromise vascular supply of the globe.

Postoperative Period

- When pt is recovering in the prone position, ensure there is no pressure on orbit or globe.

Anticipated Problems/Concerns

- Absorption of glycine from 1.5% glycine irrigation fluid may be significant.
- ION usually occurs without any other evidence of vascular injury.
- Optic nerve may be very vulnerable to hemodynamic changes in the prone position.

Botulism

Debra E. Morrison

Risk

- Infant botulism.
- Wound botulism.
- Foodborne botulism.
- Adult intestinal toxemia.
- Injection botulism.
- Biological warfare/inhalational botulism (Category A biological threat).
- Incidence
  - In USA, approximately 145 cases are reported each year: infant botulism 65%, wound 20%, and foodborne 15%; adult intestinal colonization and iatrogenic botulism rare.
  - Foodborne outbreaks of two or more persons occur most years, and are usually caused by home-preserved foods with low-acid content (pH ≥4.6, although toxin will not be formed in acidic foods, low pH will not degrade any preformed toxin). Foods implicated differ between countries, reflecting local eating habits and food preservation procedures. Improper handling of commercially prepared foods has also been implicated (canned, fermented, salted, and smoked), including unrefrigerated infused cooking oils, baked potatoes wrapped in foil and left sitting out before eating, and ready-to-eat foods in low-oxygen packaging. Low temperature, high salt, and low pH prevent growth of bacteria and toxin formation. Food samples associated with suspect cases should be sealed, stored, and sent to labs.

Perioperative Risks

- Dx late, incorrect or missed
  - Differential Dx: For adults, myasthenia gravis, Eaton-Lambert, Guillain-Barre, virus attacking brain/spinal cord, CVA, organophosphate exposure, tick paralysis, other neurotoxin; may need brain scan, spinal fluid examination, and EMG, tensilon test to rule out other causes; for infants, sepsis, failure to thrive, dehydration, encephalitis, and metabolic disease
  - Nonspecific history and physical findings: classic adult symptoms include double vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, muscle weakness; infants appear lethargic, feed poorly, are constipated, and have a weak cry and poor muscle tone—if untreated, symptoms may progress to cause paralysis of the respiratory muscles, arms, legs and trunk; fever and loss of consciousness are not associated symptoms
  - Onset of foodborne botulism: usually 12-18-36 h after eating contaminated food, but can be as early as 4 to 6 h or as late as 8 to 10 d
  - Laboratory result takes d to wk and should be used only as confirmation; treat before confirmation; tests are performed at some state health department labs and at CDC
  - Triad: Bulbar symptoms, resp compromise, and dilated pupils
- Prolonged weakness requiring prolonged support
- Enteral nutrition: Desired but problematic due to gastroparesis and bowel paralysis
- Aspiration risk
- Elevated potassium if immobile in ICU

Worry About

- Arrhythmias
- Hyperkalemia, arrhythmias, and then cardiac arrest
- Prolonged weakness necessitating prolonged intubation and leading to nosocomial infection
- Skin breakdown

Overview

- Botulism is a rare but serious neuroparalytic illness caused by a nerve toxin (BoNT) produced by the rod-shaped gram-positive bacterium *Clostridium botulinum* (and sometimes by strains of *Clostridium butyricum* and *Clostridium baratii*), commonly found in soil. *C. botulinum* grows best in low-oxygen conditions; spores survive in a dormant state until exposed to conditions that support growth. Seven types of toxins (A to G), but only A, B, E, and rarely, F cause illness in humans; three different intracellular protein targets; and different durations.
- In infant between 2 wk and 1 y old, occurs by ingestion of spores, which grow in intestine and release toxin, usually by honey ingestion, or associated with parent who works with soil or with living in rural areas.
- Occurs in wounds of IV/skin popping drug users (or any traumatized tissue contaminated with organisms) in which there is local infection and absorption of produced toxin. There is increased incidence over the last several years in IV drug users (black tar heroin), especially in California.
- Foodborne: Improperly preserved or cooked food, even properly cooked food left at improper temperature, allows germination and toxin production by contaminating spores; consumption of food with preformed toxin results in absorption of potent neurotoxin; with education and control of food industries, now uncommon in USA; ingestion of infected inadequately cooked wildlife poses at least potential risk. Foodborne botulism can be a public health emergency.
- Intestinal: Spore colonization possible in adults as well if normal gut flora has been altered by surgery or antibiotic therapy.
- Cosmetic injections (black market toxin, Botox overdose, or spread beyond injection site) or cerebral palsy (Botox overdose or spread beyond injection site) are a cause.
- Inhalational: Genetically engineered toxin, development of biological warfare (at-risk locations). Concern is inadequate stocking of antidotes worldwide and inadequate preparation and medical support. Biological warfare in Iraq has led to organization of task forces such as Scorpio at the national/regional level to stockpile antidotes. Median lethal dose for humans has been estimated at 2 nanograms/kg, approximately three-times greater than in foodborne cases. If inhalation exposure is suspected, additional exposure must be prevented by removal and storage of clothing in plastic until it can be washed, as well as immediate showering and decontamination of those exposed.
- Waterborne: Could theoretically result from ingestion of water contaminated with preformed toxin, but risk is low if common water treatment processes are used (boiling and disinfection with 0.1% hypochlorite bleach solution).

Etiology

- Botulinum toxin binds irreversibly to synaptic membrane of cholinergic nerves and prevents release of acetylcholine but not its synthesis and storage.

Usual Treatment

- Supportive; may be on ventilator for wk to mo and require intense medical and nursing care.
- Nutritional support; enteral preferred (basic maintenance plus need to keep bowels moving to eliminate spores), but parenteral also required.
- Early antitoxin treatment shows better outcome; antitoxin blocks action of circulating toxin and prevents patients from worsening, but recovery still takes many wk/up to several mo. Long-term effects may include fatigue and shortness of breath for y, requiring long-term therapy and with implications for later anesthetics.
- Efforts may be made to remove toxin from the gut by inducing vomiting and using enemas. Avoid cathartic agents containing magnesium because of the theoretical concern that increased magnesium levels may enhance the action of botulinum toxin.
- Equine-derived antitoxin for adults (risk of serum sickness/anaphylaxis); skin testing and desensitization instructions provided with antitoxin; more broad-spectrum antitoxins associated with increase in hypersensitivity; available from the CDC.
- Presently trivalent antitoxin preparation is available for adults (10 mL vial with 7500 IU type A, 5500 IU type B, and 8500 IU type E): available from the CDC.
- BabyBIG (human botulism immune globulin) used for infant botulism came out in 1990; more in use since 2003: available from state public health departments.
- Vaccine exists but rarely used because effectiveness has not been fully evaluated and negative side effects have been demonstrated.
- Botulism reportable to CDC or state health department and requires report to obtain antitoxin.
- Antibiotics for secondary infections.
- Avoid aminoglycosides and clindamycin, which may potentiate or exacerbate neuromuscular blockade.
- Guanidine increases the release of acetylcholine from nerve terminals and appears to be useful in mild cases.
- Modern clinical practice and early antitoxin treatment: mortality reduced from 50% to 60% to 3% to 5%; worldwide mortality cited as 5% to 10% by WHO.

Assessment Points

System	Effect	Assessment by Hx	PE	Tests
RESP	Pharyngeal constrictor and genioglossal hypotonia, paralysis of resp musculature Infection Atelectasis	Drooling Poor feeding Decreased resp effort Increased secretions Tracheal secretions Poor resp effort Poor color	Poor head control Absent gag Weak cough Fever Rhonchi Rales Cyanosis	Diagnosis of elimination; electrophysiology studies are fastest diagnostic tool to rule out other causes; EEG and neuroimaging are normal as long as there is no hypoxic insult; edrophonium test to rule out myasthenia gravis shows no improvement Blood, urine, CSF analysis and culture, and metabolic and hepatic profiles are generally within normal limits Stool samples are difficult to collect due to constipation; can use sterile water enema Serum testing possible if stool is unobtainable but has low sensitivity compared with stool testing (negative serum test does not exclude possibility of infant botulism) Samples injected into mice; look for signs of botulism Laboratory result takes d to wk and is used as confirmation Tests only performed at some state health department labs and CDC; samples must be collected sterilely, refrigerated, and shipped with cold packs
GI	Constipation	No bowel movement Irritability	Palpable stool Abdominal distention	
RENAL	UTI	Foul-smelling urine		
CNS	SIADH Seizures Cranial neuropathies	Infrequent urination Twitching Altered consciousness Ptosis Expressionless face Feeble cry	Diminished urine flow Seizure activity Fixed and dilated pupils Facial palsy Poor cough and gag	
PNS	Spinal neuropathies	Limp limbs	Hypotonia	

Key References: Centers for Disease Control and Prevention (CDC); National Center for Emerging and Zoonotic Infectious Diseases: Botulism: general information. <http://www.cdc.gov/nczved/divisions/dfbmd/diseases/botulism/>. (Accessed 24.02.16.); World Health Organization; Nantel AJ: *Clostridium botulinum*. International programme on chemical safety. Poisons Information Monograph 858 Bacteria. *Geneva*, 1999. <http://www.who.int/csr/delibepidemics/clostridiumbotulism.pdf/>. (Accessed 24.02.16.)

Perioperative Implications

- Early diagnosis, treatment, and optimization
- Continue supportive resp care
- Sepsis from secondary infections
- Avoid resp depressants and paralytics
- Aspiration risk
- Pts may require feeding tube (jejuna better than gastric to minimize aspiration risk) and/or parenteral nutrition
- Likely to OR/IR/GI for wound debridement, feeding tube, tracheostomy, and central line
- If possible, avoid airway manipulation, unnecessary medications, and those that are resp depressants
- Avoid narcotics because of their effect on bowel; consider alvimopan before narcotics are given if they are necessary

Preoperative Preparation
- Recommend pt receives antitoxin before wound debridement so additional toxin release does not cause further paralysis
- Low threshold for treatment if suspecting botulism
- Manage preop electrolytes
- Botulism does not affect endocrine, hematologic, hepatic, or renal function (except for neurogenic bladder)
- Continue antibiotics
- CXR to help assess status
- Aspiration prophylaxis
- If pregnant, parturient can safely be given as antitoxin (intrathecally in severe cases); consider early tracheostomy to avoid sequelae of resp depression; botulism is not known to cause direct fetal risks only those associated with mother's ventilatory compromise, because the molecule is too large to pass through placental barrier

Monitoring
- Standard ASA monitors.
- If pt unstable in ICU, consider arterial cannulation for management of autonomic dysfunction; infants may see motor function return before autonomic system function returns.

Airway
- Aspiration risk
- May already be intubated or have tracheostomy

Induction
- Avoid succinylcholine.
- May not require paralytic.

Maintenance
- May not require paralytic throughout treatment

Extubation
- Likely unable to extubate.
- Continue supportive care postop.

Adjuvants
- Avoid resp depressants if possible.
- Consider regional procedures and nonnarcotic pain medications rather than narcotics for pain control in wounds.

Postoperative Period
- Continued supportive care
- Manage electrolytes

Associated Problems/Concerns
- Aspiration pneumonia
- Sepsis from wound
- Missed diagnosis
- Malnutrition
- Biological warfare: Limited information on effectiveness of antitoxin success with inhalational botulism; amount of neutralizing antibody in presently available formulation may not be enough for treatment of genetically engineered toxin
- Travel: food preservation techniques vary according to local custom. WHO supports efforts to detect and respond to botulism, through INFOSAN, which links national authorities in charge of managing food safety events in member states; INFOSAN is managed jointly by FAO and WHO.

Brain Death

Jessica L. Shanahan | T. Anthony Anderson

Risk
- Number of pts awaiting organ transplantation is much greater than the number of available solid organs
- Medical management affects the viability of organs for transplant

Perioperative Risks
- Cardiovascular collapse
- Pulmonary edema
- Endocrine dysfunction
- Metabolic imbalance
- Coagulopathy
- Hypothermia

Worry About
- Cardiovascular collapse and metabolic derangement limiting organ viability

Overview
- Brain death is a clinical diagnosis in a comatose pt who has suffered terminal neurologic insult with confirmation of irreversibility and lack of confounding variables (e.g., hypothermia, severe electrolyte disturbances, endocrine disturbances, drug intoxication, acid-base abnormalities).
- Brainstem function is absent.
- Ancillary testing such as EEG, cerebral angiography, or transcranial Doppler may be used to support the diagnosis but is not required.
- An initial catecholamine surge occurs after brain death (initial increased HR with potential arrhythmias, increased SVR, and increased BP).
  - Associated myocardial injury may arise from increased SVR and result in LV failure and decreased CO.
  - Neurogenic pulmonary edema may result.
- After several h, loss of sympathetic tone may occur, causing hypotension and limiting organ viability if untreated.
- Endocrine dysfunction occurs due to pituitary infarction, causing DI, hypothyroidism, and hyperglycemia.
  - DI further exacerbates hypovolemia/hypotension.
- ICU care can affect the viability of organs for transplantation.

Etiology
- Elevated ICP, anoxic brain injury, and trauma

Usual Treatment
- Treatment protocols may improve organ viability, increasing the number of transplanted organs and the long-term function of the transplanted organs.
- Replete DI losses, maintain BP to allow adequate organ perfusion, use a lung-protective ventilatory strategy, control endocrine abnormalities with insulin and vasopressin (consider thyroxine/T3 and corticosteroids, especially if low ejection fraction or hemodynamic instability), transfuse to maintain oxygen delivery to organs, and correct coagulopathy if ongoing bleeding.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pulmonary edema ARDS/ALI	Low PaO_2 Increased peak airway pressures		ABG CXR
CV	Myocardial injury Loss of vascular tone Hemodynamic instability Hypovolemia	Hypotension		BP +/– CVC +/– PAC +/– Cardiac catheter +/– TEE
HEME	Coagulopathy, may progress to disseminated intravascular coagulation Anemia			Coagulation studies HCT
ENDO	DI Hypothyroid Hyperglycemia Hypernatremia			Lytes Low urine specific gravity Elevated UOP Glucose
CNS	Lack of cerebral and brainstem function Poikilothermic	Hx of drug ingestion, metabolic encephalopathy, and/or hypothermia excluded	Absent brainstem reflexes (apnea test)	Toxicology screen Temp monitor +/– EEG, cerebral angiography, brain imaging
MS	Reflex somatic movements mediated by spinal reflexes		Neurologic exam	

Key References: Anderson TA, Bekker P, Vagefi PA: Anesthetic considerations in organ procurement surgery: a narrative review, *Can J Anest* 62(5):529–539, 2015; Cross R: Brain death. In Fleisher LA, Roizen MF, editors: *Essence of anesthesia practice,* ed 3, Philadelphia, 2010, Elsevier, p 49.

Perioperative Implications

Monitoring
- Temp
- A-line
- CVP +/– PAC
- UOP
- ABG

Airway
- Lung-protective ventilation: TV 6-8 mL/kg of ideal body weight; PEEP 8-10 cm H_2O
- Judicious IV fluid (CVP <10)

Maintenance
- Correct metabolic derangements (acidosis, hypoxemia, and hypercarbia) and electrolyte abnormalities (hypernatremia and hyperglycemia).
- Evidence suggests volatile anesthetics are best for long-term organ outcome.
- Restore intravascular volume, replacing DI urinary losses and evaporative losses.
- Consider vasopressin to support hemodynamics and control polyuria (Vasopressin 1 U IV bolus, 2.4 U/h IV infusion).
- Use other vasopressors as necessary to maintain adequate organ profusion (norepinephrine and dopamine).
- "Lung-protective" ventilatory strategy: TV 6 to 8 mL/kg of predicted body weight; PEEP 8 to 10 cm H_2O.
- Maintain SBP >100 mm Hg, MAP >70, HR 60 to 120 bpm, and CVP 4 to 8 (<10) mm Hg.
- Insulin infusion to maintain serum glucose <180 mg/dL.
- Consider hormone replacement with thyroxine or T3 infusion (thyroid hormone (tetraiodothyronine) 20 lg IV bolus, 10 mcg/h IV infusion) and corticosteroids (methylprednisolone 15 mg/kg IV q24h).
- Transfuse for Hgb <7 or 8 g/dL.
- Correct coagulopathy with clotting factors or platelets if evidence of ongoing bleeding.
- Maintain skeletal muscle paralysis.
- Keep normothermic.

Extubation
- Not done
- Ventilation discontinued when aorta cross-clamped

Adjuvants
- Heparin per procurement team

Anticipated Problems/Concerns
- Increased HR and BP on incision do not obviate the criteria for brain death.
- Removal of CVC or PAC during heart procurement may be requested.
- Lung recruitment maneuver may be requested with the lungs held open with 10 cm H_2O continuous airway pressure before lung procurement.

Brain Injury, Traumatic

Mitchell L. Weinstein

Risk
- Incidence in USA: 1.7 million TBIs per year as of 2010, resulting in more than 280,000 hospitalizations and over 50,000 deaths.
- TBI is responsible for about 30% of all deaths due to injury.
- TBI, primarily from falls, has increased more than 50% in geriatrics from 2001 to 2010.

Perioperative Risks
- Brain herniation
- Coagulopathy, DIC
- Metabolic derangement

Worry About
- Occult cervical spine injury
- Other preexisting medical conditions
- Neurogenic pulm edema
- Subclinical seizures

Overview
- TBI is a major cause of death and disability with increasing rates among senior citizens.
- Care is focused on avoiding secondary injury to the brain.
- Normal saline without glucose should be used instead of colloid or albumin. Hypertonic saline can be used with appropriate caution.
- Brief moments of hypocapnia may occur to urgently lower ICP, otherwise normocapnia.
- Avoid hyperthermia. There is no consensus on therapeutic hypothermia.
- Antiseizure prophylaxis with phenytoin to levetiracetam for high-risk pts.

Etiology
- External trauma causing brain contusion, laceration, diffuse axonal, injury, or hematoma.
- Spontaneous bleeding from cerebral vessels may occur, subarachnoid or intracerebral.
- GCS ≤8 is severe TBI; 9 ≤GCS ≤12 is moderate TBI.

Usual Treatment
- Emergent decompressive craniectomy usually occurs in TBI from a stroke.
- Keep ICP <20 by elevating HOB and extraventricular draining of CSF.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Facial fractures; cervical spine injury, oropharyngeal injury	Mechanism of injury	Periorbital or mastoid ecchymosis; epistaxis; blood or vomitus in mouth	CT head; skull X-ray
RESP	Neurogenic pulm edema	Sudden onset of dyspnea	Tachypnea, tachycardia, pink frothy sputum	ABG, CXR
CV	Neurogenic stunned myocardium	ECG changes	Cardiac dysrhythmias, decreased CO	Cardiac enzymes, TEE
METAB	Hyponatremia/hypernatremia Hypoglycemia/hyperglycemia	Mental status changes Changes in urine output		Blood lytes, glucose
CNS	Seizures	Decreased mental status, failure to improve with treatment	Seizure activity may be subclinical	EEG

Key References: Wijayatilake DS, Jigajinni SV, Sherren PB: Traumatic brain injury: physiological targets for clinical practice in the prehospital setting and on the neuro-ICU, *Curr Opin Anaesthesiol* 28(5):517–524, 2015; Sharma D, Vavilala MS: Perioperative management of adult traumatic brain injury, *Anesthesiol Clin* 30(2):333–346, 2012.

Perioperative Implications

Preoperative Preparation
- Early intubation if GCS <8 or cannot maintain airway.
- Evaluate other injuries.
- Mannitol (0.25–1 g/kg body weight) if ICP >20 mm Hg and no severe hypovolemia.
- FFP, platelets, and 2 units PRBC typed and crossed.

Monitoring
- Arterial line is mandatory.
- Consider CVP.
- ICP monitor.
- Urine output.
- Consider monitoring cerebral oxygenation, blood flow, or metabolism if available.

Airway
- Manual in-line stabilization.
- Avoid nasal intubation.

Preinduction/Induction
- Aspiration risk; use a rapid sequence induction; use succinylcholine if concerned about difficult airway and sugammadex is not available.
- Avoid hypoxia (PaO_2 <60 mm Hg or SpO_2 <90) and hypercarbia.
- Avoid hypotension (SBP < 90 mm Hg).

Maintenance
- Keep pt normocarbic, normoglycemic, and normothermic.
- Maintain cerebral perfusion pressure between 50–70 mm Hg by either lowering ICP, raising MAP, or both. Keeping CPP >70 can increase risk of ARDS.
- Low-dose inhaled agents or propofol for maintenance.

Extubation
- Consider extubation if airway reflexes are intact and can maintain $PaCO_2$ 35–45 mm Hg.
- Avoid coughing or agitation.

Postoperative Period
- Avoid significant hypertension to prevent rebleeding.
- Keep head of bead elevated at 30 degrees and set ICP monitor appropriately.
- Continue to follow blood chemistry and coagulation.
- Deep sedation to reduce cerebral metabolism, if needed.

Anticipated Problems/Concerns

- Frequently these pts are taking meds that affect platelets or coagulation in addition to having a traumatic injury that increases the risk of a coagulopathy or DIC. Be aggressive to avoid progressive hemorrhagic injury.
- Adverse changes in neuro function may occur. Be alert for posttraumatic hydrocephalus or new bleeding.
- Potential for seizures, SIADH, and DI.
- Neurogenic pulm edema can occur within minutes of the CNS injury or be delayed 12–24 h.
- Concern with neurogenic stunned myocardium.

Bronchiectasis

Matthew Hart | Jeffrey R. Kirsch

Risk

- Incidence in USA <1:10,000 hospital admissions.
  - Cystic fibrosis is the single largest cause of bronchiectasis in industrial nations.
  - A subgroup of Native Americans of Alaskan decent has a four-fold increase in the incidence of bronchiectasis over the general population. Ciliary deformities have been shown in a Polynesian population.
- No gender prevalence.
- Socioeconomic prevalence: Inbreeding and primitive health care, particularly lack of immunization and poor treatment of childhood bronchitides, increase the prevalence.
- Occasionally seen in children:
  - Bronchial cartilage deficiency (Williams-Campbell syndrome)
  - Tracheobronchomegaly (Mounier-Kuhn syndrome)
  - Inherited immunoglobulin deficiencies, impaired phagocytosis, and complement deficiency
  - α_1-Antitrypsin deficiency
- Occasionally seen in adults with acquired γ-globulin deficiency:
  - Cystic fibrosis
  - RA
  - Pulm ciliary dyskinesias (Kartagener syndrome)

Perioperative Risks

- Spillage of infected secretions from bronchiectatic regions to normal lung leads to pneumonitis and retention of secretions
- Risk from bacteremia, after manipulation
- Risk of secondary acute resp failure
- Massive hemoptysis
- Pneumothorax

Worry About

- Exacerbation of asthma
- Amount of sputum produced and its nature
- Fever and hemoptysis: Acute pulm infection
- Right heart function
- Check frequency of cough and daily sputum volume; culture and smear for composition; check body temp and WBC count for acute infection
- Exercise tolerance will indicate associated impairment or disability
- Postop pulmonary decompensation

Overview

- Abnormal widening or dilatation of one or more branches of the bronchial tree, generally caused by permanent damage or destruction to the corresponding segments muscular wall, resulting in a decreased elasticity; widened segments commonly fill with purulent secretions; mucosa is swollen and inflamed and may be ulcerated with granulation tissue exposed; and extensive collateral flow occurs in these chronically inflamed bronchi (3–12% of CO).

Etiology/Pathogenesis

- Exact etiology for acquired form remains unclear but often involves necrotizing infection in tracheobronchial wall. Five mechanisms may predispose pts:
  - Bacterial, viral, or fungal bronchopulmonary infections, including TB, pertussis, and measles
  - Bronchial obstruction
  - Immunodeficiency states, including IgG deficiency, IgA deficiency, and leukocyte dysfunction
  - Hereditary defects in ciliary-mucosal clearance, including Kartagener syndrome, α_1-antitrypsin deficiency, and cystic fibrosis
  - Miscellaneous disorders, including recurrent aspiration, inhaled irritants, Young syndrome, and bronchiolitis obliterans following heart-lung transplantation

Usual Treatment

- Medical therapy: Postural drainage, chest physiotherapy, antibiotics for cultured infection, bronchodilators, and steroids for symptomatic treatment
- Surgical therapy: Resection indicated for uncontrolled hemoptysis; or lobar closely confined disease, age >20 y; bronchopulmonary lavage under GA with divided airway (double-lumen tube)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Sinusitis	Postnasal drip Stuffiness, headache	Translucency	X-ray, US, bright lights
CV	Clubbing, cyanosis CHF (cor pulmonale) Kartagener syndrome	Exercise tolerance Pulm Htn, edema Chronic sinusitis	Situs inversus	ABG Loud P_2 Right heart studies Immotile spermatozoa
RESP	Bronchiectasis	Cough with sputum Hemoptysis Wheezing	Rhonchi CXR: 93% tram lines; 7% normal	Smear, culture, high-resolution CT, bronchogram Bronchoscopy PFTs
HEME	Immunodeficiency Infection	IgG, IgA, WBC Guided antibiotic therapy		
CNS	Brain abscess	CT/MRI		

Key References: O'Brien C, Guest PJ, Hill SL, et al.: Physiological and radiological characterization of patients diagnosed with chronic obstructive pulmonary disease in primary care, *Thorax* 55:635–642, 2000; Nikolaizik WH, Warner JO: Aetiology of chronic suppurative lung disease, *Arch Dis Child* 70(2):141–142, 1994.

Perioperative Implications

Monitoring

- Routine for majority of cases
  - Consider PA catheter for cor pulmonale or CHF.
  - Arterial line for longer/invasive procedures.

Airway

- Careful frequent suctioning and humidification of inspired gases

Induction

- Consider preop pulmonary optimization: Chest physiotherapy and bronchodilator treatment.
- May consider increase steroids if on chronic therapy.
- Consider regional anesthesia when possible.

Maintenance

- Routine

Extubation

- Depends upon degree of pulm and cardiac dysfunction.
- Consider extubation and immediate recovery in sitting position.

Adjuvants
- Routine

Postoperative Period
- Use stir-up regimen and monitor for retained secretions and resp failure.
- Have postop plan for chest physiotherapy.
- Pt may need to continue course of antibiotics.
- Supply supplemental oxygen and monitor SpO_2.
- Check for platypnea-orthodeoxia if right atrial pressures become elevated.

Anticipated Problems/Concerns
- Retained secretions and secondary resp failure
- Right heart decompensation if hypoxemia persists
- Bacteremia from airway manipulations

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Bronchiolitis Obliterans Syndrome

Yiliam F. Rodriguez Blanco | Eellan Sivanesan

Risk
- Incidence in USA: 1:40,000
- Racial predilection: None
- Occurs primarily after lung and hematopoietic stem cell transplantation
- Industrial workers exposed to inhalants who have presented with BOS: nylon-flock, battery workers, manufacturer of flavorings (diacetyl butter-like flavoring), and textile workers

Perioperative Risks
- Hypoxemia and severe periop airway obstruction.
- Pulm infection, sepsis, and pulm edema post transplant.
- Injury to tracheal anastomosis due to ETT placement.
- Prolonged intubation (increased sensitivity to medications including muscle relaxants, pulm functions, renal impairment, and pulm edema).
- Complications of immunosuppression (infection, hemorrhage, and renal impairment).
- Preop focus must differentiate between active invasive pulm infection and ongoing chronic rejection with colonization, as well as maximizing medical condition and stratifying risk.

Worry About
- Pulm functions
- Differentiating BOS from untreated invasive pulm infection and other disorders
- Side effects of immunosuppression including infection with invasive techniques, hemorrhage, and renal failure with cyclosporine
- Airway and vascular allograft denervation (physiologic and pharmacologic side effects)
- Other effects of etiologic agents

Overview
- Delayed-onset allograft dysfunction and continual decline in FEV_1 not due to other etiologies of transplant dysfunction; it frequently occurs with signs of airflow obstruction.
- Because BO is difficult to confirm histologically (transbronchial biopsy of larger airways with sporadic involvement often provides insufficient samples and has a high false-negative diagnostic rate), the International Society for Heart and Lung Transplantation proposed a staged clinical definition of BO termed BOS (stages 0 to 3 defined by changes in pulm functions, and based on spirometry, rather than histology).
- BOS clinical staging is important to the clinician because it indicates allograft function.

Etiology
- The mechanism involved in the etiology of BO remains poorly understood.
- Two forms of BOS with inflammation and fibrosis: Rejection-related and non-rejection related.
- After transplant, the syndrome reflects small airway obliterations caused by "chronic rejection."
- Several risk factors, including primary graft dysfunction, lymphocytic bronchiolitis, ischemia-reperfusion injury, acute cellular rejection, mismatches at HLA loci, autoimmunity (collagen V sensitization), persistent neutrophil influx and sequestration (bronchoalveolar lavage neutrophilia), GE reflux with resultant aspiration, loss of cough reflex due to denervation, complication of prematurity (bronchopulmonary dysplasia), toxicant inhalation ("popcorn lung"), and exposure to infectious agents (bacterial, viral, and some atypical organisms including mycoplasma, chlamydia, and fungi) (BO with organizing pneumonia [BOOP]).
- BOS is described after lung, heart-lung, bone marrow, renal, pancreas, and liver and hematopoietic stem cell transplantation; BOS remains the leading cause of death for those who survive beyond 1 y after lung transplantation.

Usual Treatment
- Varies depending on whether or not BOS is rejection related
- Rejection-related BOS: Mainly treated with augmented immunosuppression (systemic corticosteroids, cyclosporine, tacrolimus, and azithromycin) and supportive care, including O_2, bronchodilators, and chest physical therapy
- Non-rejection related BOS is treated with supportive care, anti-infective agents, and medical antireflux therapy, and may respond to steroids (especially toxic fumes and other environmental exposures)
- Newer treatments for rejection-related conditions: Extracorporeal photopheresis, aerosolized cyclosporine, antithymocyte globulin, IV immunoglobulin, statins, bortezomib, interleukin subtype specific antagonists, and montelukast
- Referral to surgeon for potential fundoplication of the GE junction if GE reflux is confirmed
- Severe cases often require lung transplant or even retransplant, with an accompanying increased risk of recurrent BOS and graft dysfunction

Assessment Points

Use previous classification to determine the possible cause of BO, including posttransplantation or environmental exposure(s).

System	Effect	Assessment by Hx	PE	Test
GENERAL	Active infection	Fever and non-rejection related change in status	Increased temp, tachycardia with infection	Increased WBC
RESP	Loss of lung functions (% FEV_1)	Recent change in functional capacity, invasive lung infections, meds, lung colonization (resistant bacteria), risk factors, BOS staging; environmental exposure (e.g., diacetyl production)	Tachypnea, wheezes, cough, fever, cyanosis, pulm edema	CXR, high-resolution computed tomography, PFTs (decreased FEV_1, decreased O_2 saturation hypoxia) bronchoscopy for endobronchial biopsy, culture, bronchoalveolar lavage, lung biopsy (diagnosis)
RENAL	Loss of function due to immunosuppression	Change in status, dialysis	A-V fistula (avoidance for procedures), fluid overload, pulm edema, increased weight	Decreased renal functions, tachycardia, peripheral edema, SOB
HEME	Thrombocytopenia due to medications	Prolonged bleeding	Bruising	CBC with decreased platelets, increased bleeding time

Key References: Meyer KC, Raghu G, Verleden GM, et al.: An international ISHLT/ATS/ERS clinical practice guideline: diagnosis and management of bronchiolitis obliterans syndrome, *Eur Respir J* 44(6):1479–1503, 2014; Feltracco P, Falasco G, Barbieri S, et al.: Anesthetic considerations for nontransplant procedures in lung transplant patients, *J Clin Anesth* 23(6):508–516, 2011.

Perioperative Implications

Preoperative Preparation

- PFTs for BOS staging and resp status and bronchoscopy for biopsy and culture.
- Treat active infections aggressively.
- Evaluate renal functions and adjust periop medications where appropriate.
- Continue anti-infective and immunosuppressive therapy during the periop period and adjust dosing to keep within the indicated therapeutic range.
- Strict aseptic techniques due to immunosuppression.
- Premedication useful due to excessive secretions, but avoid excessive resp depression.
- Reflux prophylaxis.
- Corticosteroids supplementation especially for long, invasive, and stressful procedures.
- Watch for increased sensitivity to opioids, hypercarbia, resp acidosis, bronchial hyperresponsiveness (bronchoconstriction), V/Q mismatch, GE reflux, hyperkalemia, and hypomagnesemia.
- Most common side effect of immunosuppressive drugs: Cyclosporine and tacrolimus (Htn, diabetes, neurotoxicity, and renal failure), glucocorticoids (hyperglycemia, weight gain, osteoporosis, and adrenal insufficiency), and azathioprine (anemia and thrombocytopenia).

Monitoring

- Routine.
- Consider arterial line placement if hypoxic, acidotic, or O_2 saturation is inadequate: invasive monitoring must be carefully weighed against the possibility of infection from intravascular catheters.
- TEE or other continuous CO monitoring systems may be helpful in assessing cardiac function in post heart-lung transplant pts, and when there is evidence of pulm edema and pulm Htn.
- CVP insertion recommended (when necessary) on side of native lung (one-lung transplant).

Airway

- ETT cuff placement should avoid tracheal anastomosis.
- Oral intubation is preferred over nasal intubation (due to infection and thrombocytopenia).
- Anticipate difficult intubation if on chronic corticosteroids due to Cushingoid (moon face) features and limited atlanto-occipital joint mobility.
- Use aseptic tracheal suction technique.

Induction

- Short-acting agents preferred; adjust doses to pt status and to avoid prolonged CV depression.

Maintenance

- Avoid fluid overload; renal dysfunction due to immunosuppressants and disruption of lymphatic drainage in posttransplant pts can lead to pulm edema with fluid overload.
- Significant reductions of cyclosporine or tacrolimus blood levels can be caused by dilution with IV fluids.
- Adjust neuromuscular blocking dosage due to interactions with immunosuppressive agents and adjust dosage if renal impairment. (Cyclosporine enhances the effect of muscle relaxants producing a prolonged block.)
- NSAIDs can cause further renal toxicity in addition to immunosuppressants.
- Prevent additional mechanical obstruction (ventilator-induced disease and excessive tidal volumes) and employ ventilator with capability for variable inspiratory and expiratory ratios.
- Lateral decubitus position may aggravate V/Q mismatch.
- Hyperventilation during mechanical ventilation should be avoided because seizure threshold in pts taking immunosuppressive agents may be lowered.
- Use shorter-acting agents to avoid prolonged CNS, CV, and resp depression to facilitate a swift recovery of functions and timely extubation.

Extubation

- Delay until adequate ventilation is assured (sustained tetanus on monitoring).
- The lack of cough reflex below the tracheal anastomosis makes pts unable to clear secretions, unless they are awake, increasing the risk of silent aspiration.

Adjuvants

- Consider regional technique because it allows opioid sparing, but dense intercostal blockade can delay extubation in pts with poor respiratory reserve.

Postoperative Period

- Monitor for and aggressively treat resp depression, infection, and fluid overload.

Anticipated Problems/Concerns

- Many pts with resting hypoxia and marginal compensated lung functions come to OR for diagnostic lung biopsy. A thoracoscopic technique may be impossible owing to adhesions post heart/lung transplantation or pt's inability to tolerate one-lung ventilation.
- Anticipate further perioperative resp decompensation after open-lung biopsy.
- Arrange postop disposition (monitored bed and ventilator support) depending on preop functional status and the potential for periop complications.

Acknowledgment

We thank Dr. Roy Levitt for his previous contributions to this chapter.

Bronchitis, Chronic

C. William Hanson III

Risk

- Incidence in USA: 14 million
- Race with highest prevalence: Caucasian
- M:F ratio 1:2
- Smoking, second-hand smoke, occupational exposure to pulm toxic substances (radon, coal, silicates, and asbestos)

Perioperative Risks

- Bronchospasm

Worry About

- Airway stimulation at light levels of anesthesia
- Laryngospasm (due to secretions and hyperreactivity)
- Hypoxia
- Hypercarbia

Overview

- Chronic productive cough with periodic exacerbations (most d for at least 3 mo and for at least 2 consecutive y)
- Enlargement of the mucus-secreting glands in the airways with excessive sputum production
- Obstruction of expiratory airways
- Derangement in V/Q relationships
- Chronic hypoxia with right heart failure
- Exacerbations with intercurrent bacterial or viral infections

Etiology

- Acquired, usually due to smoking
- May also be due to asthma or frequent childhood resp infections

Usual Treatment

- Avoidance of environmental irritants such as cigarette smoke (preferably >8–10 wk before elective surgery)
- Antibiotics for acute exacerbations; inefficacious for prophylactic treatment
- Oral glucocorticoids: appropriate for acute exacerbations but not for maintenance therapy
- Periop stress dose glucocorticoid (methylprednisolone, dexamethasone, and hydrocortisone) administration: may be appropriate in pts on prolonged (>3 wk) high dose (≥20 mg prednisone per day) oral steroids
- Short-acting bronchodilators, such as beta agonists or anticholinergics, for acute exacerbations and long-acting beta agonist bronchodilators plus inhaled steroids for long-term maintenance therapy; pts on inhalers may be treated with preintubation inhalation of a beta agonist

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Short, fat neck			
CV	Right heart failure	Exercise tolerance	RV heave Dependent edema	ECG ECHO
	Pulm Htn			PA catheter
RESP	Airways obstruction	Smoking Hx (current, recent, emote) Number and severity of recent exacerbations	Cyanosis	PFT, DLCO, ABGs
MS			Clubbing of fingers	

Key References: Kim V, Criner GJ: Chronic bronchitis and chronic obstructive pulmonary disease, *Am J Respir Crit Care Med* 187: 228–237, 2013; Yamakage M, Iwasaki S, Namiki A: Guideline-oriented perioperative management of patients with bronchial asthma and chronic obstructive pulmonary disease, *J Anesth* 22:412–428, 2008.

Perioperative Implications

Preoperative Preparation
- Smoking cessation
- Antibiotics to decrease sputum production
- Resp conditioning

Monitoring
- Consider arterial line to monitor blood gases
- Consider pulm artery catheter for large fluid-shift operations

Airway
- Often, truncal obesity (especially with corticosteroids); may have redundant soft tissue in airway or a short, fat neck

Preinduction/Induction
- Avoid stimulating the airway while pt is in light levels of anesthesia because it may precipitate bronchospasm (although less likely than with asthma).
- Regional anesthesia may be preferable.

Maintenance
- Frequent suctioning of ETT
- Limit narcotic administration (danger of periop CO_2 retention)
- Adjuvant regional anesthesia for postop pain management in procedures that affect resp mechanics (e.g., intercostal nerve blocks, epidural analgesia)

Extubation
- Administer intratracheal bronchodilator in responsive pts before extubation.
- Consider IV lidocaine before extubation.

Anticipated Problems/Concerns
- Postop resp complications (secretions, mucus plugging, atelectasis, pneumonia, and prolonged requirement for mechanical ventilation)

Bronchopulmonary Dysplasia

Marissa G. Vadi | Ryan E. Lauer

Risk
- Incidence in USA: 10,000-15,000 infants annually
- Risk increases with decreasing gestational age and birth weight
- Affects at least one-quarter of infants with birth weights <1500 g
- No race or gender predilection

Perioperative Risks
- Bronchospasm
- Pulm Htn
- Cor pulmonale

Worry About
- Airway obstruction and hyperreactivity
- Pulm Htn and cor pulmonale
- "BPD spells": Acute cyanotic events caused by increases in central airway resistance
- Tracheomalacia and/or bronchomalacia
- Recurrent pulm infections

Overview
- Chronic lung disease associated with premature birth and positive pressure mechanical ventilation, the clinical definition of which has evolved over time
  - "Classic BPD": Associated with characteristic radiographic changes and four stages of lung injury: exudative → necrosis → pulm fibrosis → severe cystic changes, and cor pulmonale
  - "New BPD": Seen after introduction of surfactant therapy, antenatal steroid administration, and improved neonatal ventilator strategies; mild respiratory distress syndrome and continued need for supplemental oxygen; and lung development is uniformly arrested, with simplified alveolar structures and dysmorphic capillaries
- Disease severity (mild, moderate, or severe) determined by the gestational age of the infant, oxygen dependency at 36 wk postconceptual age, total duration of oxygen supplementation, and positive pressure requirements
- Chronic airway obstruction and hyperreactivity present in long-term survivors
- High risk of periop morbidity if pulm Htn present

Etiology
- Multifactorial; arrest of pulm development ± inflammation
- Major risk factors: premature birth, respiratory failure, oxygen supplementation, and mechanical ventilation
- Impaired angiogenesis, which reduces alveolar-capillary gas exchange, leading to hypoxemia and increased PVR

Usual Treatment
- Supplemental oxygen
- Inhaled bronchodilators (e.g., β-agonists)
- Pulm vasodilator therapies (e.g., sildenafil, calcium channel blockers, bosentan) if pulm Htn present

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible tracheomalacia	SOB Stridor	Retractions Audible stridor	Bronchoscopy for severe cases
CV	PulmHtn Cor pulmonale	Exertional dyspnea Syncope Cyanosis, esp. during feeds Supplemental O_2 dependence	Hypoxia Cyanosis ± clubbing Rales Peripheral edema Elevated JVP	ECG ECHO Cardiac cath
RESP	Possible bronchomalacia Decreased tidal volumes Increased airway resistance Decreased dynamic lung compliance Hypoxia Hypercapnia	SOB Cyanotic spells Supplemental O_2 dependence Asthmalike symptoms Recurrent respiratory infections	Tachypnea Retractions Cyanosis ± clubbing Expiratory wheezing Rales	CXR ABG
GI	Failure to thrive	Poor feeding	Low BMI	Generally not needed

Key References: Jensen EA, Schmidt B: Epidemiology of bronchopulmonary dysplasia, *Birth Defects Res A Clin Mol Teratol* 100(3):145–157, 2014; Lauer R, Vadi M, Mason L: Anaesthetic management of the child with co-existing pulmonary disease, *Br J Anaesth* 109(21):i47–i59, 2012.

Perioperative Implications

Preoperative Preparation
- Determine room-air oxygen saturation and baseline supplemental oxygen requirements.
- Obtain electrolytes (if pt receiving chronic diuretic therapy); ABG (if oxygen requirements recently increased); and ECHO (if clinical markers concerning for pulm Htn).
- Avoid general anesthesia for elective procedures during acute respiratory infection.
- Avoid spinal anesthesia in patients with severe pulm Htn; decreased venous return and bradycardia may precipitate right heart failure.
- Consider preoperative nebulized β_2 agonist and/or steroid administration.
- Administer premedication cautiously in pts with pulm Htn.

Monitoring
- Standard ASA monitors.
  - Monitor pulse oxygen saturation, end-tidal carbon dioxide, and body temperature closely. Abnormalities may worsen pulm Htn.
- Consider arterial cannulation for invasive blood pressure monitoring and central venous line placement for inotrope administration in pts with pulm Htn.

Airway
- No particular association with difficult tracheal intubation
- Risk for subglottic stenosis, airway granulomas, and pseudopolyps if prolonged tracheal intubation occurred during infancy; may require smaller tracheal tubes

Induction
- Induction agents of choice: Sevoflurane (mask induction) and propofol (IV induction). Consider IV ketamine if pt is hemodynamically unstable.
- Ensure deep level of anesthesia before airway manipulation.
- Avoid histamine-releasing neuromuscular blocking agents.

Maintenance
- Treat bronchospasm with inhaled beta-agonists. Use IV terbutaline or epinephrine for refractory wheezing.
- Avoid hypoxia, hypercarbia, and hypothermia (increase PVR).
- Avoid high peak inspiratory pressures; provide longer inspiratory times.
- Consider inhaled nitric oxide for pulm hypertensive crisis.

Postoperative Period
- Continuous pulse oximetry
- May require prolonged postop ventilation
- Pain management strategy may affect postop resp status

Anticipated Problems/Concerns
- Respiratory insufficiency and postop ventilation
- Worsening pulm Htn
- Pain control

Buerger Disease (Thromboangiitis Obliterans)

Jeongae Yoon

Risk
- Current or recent chronic tobacco/nicotine exposure
- Ashkenazi Jewish ethnicity; prevalence much greater in Eastern Europe, Southeast Asia, and India
- Age <45, male gender (M:F ratio: 10–100:1)
- Incidence in USA: Progressively decreasing in association with decreasing smoking prevalence; <8–10/100,000

Perioperative Risks
- Similar to any pt with chronic tobacco exposure
- Risks to already compromised perfusion of distal extremities

Worry About
- Coexisting pulm disease in tobacco smokers
- Abnormal Allen test result in a young (<45 y) male smoker with leg ulcerations (classic clinical scenario for Buerger)
- All extremities because TAO is never confined to a single limb

Overview
- Inflammatory vasculitis of small and medium arteries and veins in extremities.
- Classic distribution is infrapopliteal or distal to the brachial artery.
- Results in extremity ischemia leading to claudication of calf, foot, forearm, or hands.
- Severe ischemia results in ulcerations and gangrene progressing to necrosis and eventual amputation of ischemic extremity.
- Olin (2000) criteria:
  - Age <45 y.
  - Current or recent history of tobacco use.
  - Presence of distal-extremity ischemia indicated by claudication, rest pain, ischemic or gangrenous ulcers, and documentation by noninvasive vascular testing.
  - Exclusion of autoimmune diseases (scleroderma, CREST, sclerodactyly, and telangectasia), hypercoagulable states (antiphospholipid syndrome or homocysteinemia), or DM.
  - Exclusion of proximal embolic source by ECHO or angiography.
- Diagnosis confirmed with biopsy of active lesion showing a highly cellular thrombus formation with neutrophils, giant cells, and microabscesses but intact internal elastic lamina: differentiates from other vasculitis conditions.
- Antiendothelial antibody titers may allow tracking of disease progression and severity.
- Lesions occasionally occur in coronary, mesenteric, and cerebral vasculature but always present initially in extremities.

Etiology
- Autoimmune reaction against vascular endothelial cells potentiated by nicotine exposure.
- Antiendothelial antibodies trigger immune reaction and microabscesses and thrombosis formation.
- Impaired endothelium-mediated vasodilation in peripheral vasculature, which results in ischemia.
- Angiographic evidence of disease exists before clinical presentation in unaffected limbs.

Usual Treatment
- Complete tobacco and/or nicotine cessation, including nicotine patches/gum and avoidance of passive smoking; all other treatments are palliative.
- Prostaglandins analogue (e.g., IV iloprost), cilostazol, and bosantan, which has shown efficacy in symptom management and disease progression.
- Aspirin and clopidrogel used for secondary prevention.
- Surgical revascularization usually not possible given distal and diffuse nature of vascular lesions.
- Sympathectomy provides palliative short-term pain relief, but no long-term benefit; spinal cord stimulators can provide pain relief.
- Amputation is ultimate treatment option for affected distal digit and/or extremity for nonhealing ulcerations or gangrene.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Coronary lesions consistent with ischemia	Angina, MI, CHF SOB	Third heart sound, regular rhythm, or no rales	ECG, ECHO, coronary angiography
RESP	Consistent with chronic tobacco exposure, COPD, chronic bronchitis	SOB, cough, increased sputum	Findings consistent with chronic smoker	CXR, PFT results consistent with obstructive pattern
HEME	Carboxyhemoglobin	Smoking Hx		Blood gases with co-oximetry
CNS	Vascular lesions, leading to cerebral ischemia	Syncopal episodes, TIA, CVA	Carotid bruit	Carotid US, CT angiogram
GI	Mesenteric ischemia	"Intestinal angina"	Abdominal bruit	Mesenteric angiography
EXTREMITIES	Distal ischemia, gangrene	Claudication, rest pain, nonhealing ulcers, prior amputations	Cool extremities, poor capillary refill, hair loss, thrombosis, migraines, ulcerations/gangrene	Allen test, Doppler US, angiography with evidence of "corkscrew collateral" revascularization

Key Reference: Olin JW, Shih A: Thromboangiitis obliterans (Buerger's disease), *Curr Opin Rheumatol* 18(1):18–24, 2006.

Perioperative Implications

Preinduction/Induction/Maintenance
- Carefully document locations/extent of distal-extremity ulcerations and thrombosis migraines.
- Optimize preinduction pulmonary status.
- Pay special attention to padding and protection of distal extremities.
- Prevent hypothermia in the entire periop phase by keeping extremities warmed and covered.

Monitoring
- Consider risks versus benefits of distal arterial catheter
- Femoral arterial catheterization would be a viable option for invasive monitoring.
- Pulse oximetry may be more accurate in a proximal location, such as the ear lobe.

General Anesthesia
- Avoid hypothermia (OR ambient temperature and forced-air warmer).
- Maintain intravascular volume and avoid alpha agonists if possible.
- Regional anesthesia can be performed safely.
- Avoid epinephrine in local anesthetic solutions to limit risk of vasospasm.

Postoperative Period
- Keep distal extremities warm; 40% of pts have concurrent Raynaud phenomenon.

Anticipated Problems/Concerns
- Excellent opportunity to reiterate importance of smoking cessation.
- If no critical limb ischemia, smoking cessation will prevent amputation.
- Long-term prognosis for major amputation: 11% at 5 y; 21% at 10 y; and 23% at 20 y.

Bulimia Nervosa

Ronda R. Flower | Christopher J. Cullom | Alan David Kaye

Risk

- Prevalence ranges from 3–30% among women aged 15–30 y.
- Bulimic symptoms can be part of the anorexia nervosa syndrome.
- The bulimic type is more damaging than anorexia nervosa as the combination of vomiting, laxative abuse, and malnutrition can lead to global organ dysfunction.

Perioperative Risks

- Increased risks (which have not been quantified) of hypotension, cardiac arrhythmias, hypothermia, aspiration of gastric contents, and metabolic abnormalities and their consequences.

Worry About

- Reduced cardiac muscle mass with a decrease in chamber size, impaired myocardial contractility with decreased cardiac output, and relative hypotension
- Mitral valve prolapse, arrhythmias, and severe bradycardia
- Starvation, dehydration and electrolyte abnormalities (hyponatremia, hypokalemia, hypoalbuminemia, hypomagnesemia, hypocalcemia, hypophosphatemia)
- Alterations (hypofunction) in autonomic nervous system function and a hypervagal state
- Abnormal temp regulation
- Decreased gastric emptying, gastric dilatation, diminished GE sphincter tone, aspiration of gastric contents, gastric rupture, and accompanying peritonitis
- Compensatory hypoventilation due to chronic metabolic alkalosis from recurrent vomiting and laxative abuse
- Mallory-Weiss tear or esophageal rupture leading to acute mediastinitis
- Liver and kidney dysfunction
- Osteoporosis and irreversible dental/gingival disease

Overview

- Eating disorder characterized by binge-eating episodes followed by self-induced vomiting, fasting, and abuse of diuretics or laxatives.
- Greatest periop risks are associated with low cardiac output and cardiac arrhythmias.
- Hx is characterized by denial and is often unreliable. Pts may report exercise intolerance, cold intolerance, weight fluctuation, and syncope.

Etiology

- Unknown; thought to be largely emotional

Usual Treatment

- SSRIs, such as fluoxetine (Prozac), have been found to be the most effective pharmacotherapy. The second line of pharmacologic treatment is with tricyclic antidepressants.
- Cognitive behavioral therapy.
- K^+ supplements.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Cardiomyopathy, mitral valve prolapse, arrhythmia, ipecac cardiomyopathy	Exercise intolerance, syncope	Heart sounds, BP, pulse	ECG, ECHO
RESP	Bradypnea		Vitals, auscultation	ABGs
GI	Gastric dilatation, diarrhea Gastric rupture/peritonitis Hepatic dysfunction Inanition	Usually unreliable Projectile vomiting	Skin turgor, pulse, BP, abdomen	Lytes CT scan, ABGs, CBC Hepatic enzymes Serum glucose
ENDO	Decreased T3 and T4, decreased norepinephrine, decreased vasopressin secretion, abnormal temp regulation	Cold intolerance		
HEME	Pancytopenia	Bruising, infections	Skin	CBC, plt
RENAL	Decreased GFR on basis of dehydration			BUN/Cr
CNS	Depression, decreased CSF norepinephrine Decreased pain sensitivity		Subconjunctival hemorrhage	
DERM	Dry skin/mucous membrane		Callus formation on dorsum of hand	
ORTHO	Decreased bone mass			X-ray, DEXA scan
GYN	Amenorrhea	Menstrual cycle alteration		LH, FSH
MS	Muscle mass, myalgias	Marked weight fluctuation	Cachectic	

Key References: Suri R, Poist ES, Hager WD, et al.: Unrecognized bulimia nervosa: a potential cause of perioperative cardiac dysrhythmias. *Can J Anaesth* 46(11):1048–1052, 1999; Seller CA, Ravalia A: Anaesthetic implications of anorexia nervosa. *Anaesthesia* 58(5):437–443, 2003.

Perioperative Implications

Preoperative Preparation

- Assess cardiac status, electrolytes, hepatic enzymes, volume status, and UPT.
- Consider urine toxicology screen to rule out comorbid substance abuse.

Monitoring

- Routine.
- Arrhythmia, volume status, myocardial function.
- Temp monitoring is important.

Airway

- May have increased risk of aspiration of gastric contents; consider NG tube.

Induction

- Hypovolemia, myocardial dysfunction, and ANS dysfunction may make for CV instability.
- Sodium citrate and H^+ blocker administration, plus utilization of rapid-sequence induction.
- Lower doses of nondepolarizing neuromuscular blocking drugs, as decreased K and Ca augment the blockade.
- Careful positioning, as these pts are susceptible to nerve palsies and other musculoskeletal injuries from severe cachexia and osteoporosis.

Maintenance

- CV instability, volume and lyte status, as well as temp should dictate anesthetic regimen.
- Avoid older agent halothane, as arrhythmia threshold decreases with use of this gas.

Extubation

- Awake extubation because of GI motility dysfunction.
- Autonomic hypofunction may lead to sudden postop collapse.

Adjuvants

- Vary if lyte, renal, or hepatic dysfunction exists.

Anticipated Problems/Concerns

- Gastric volume changes may increase risk of aspiration
- Volume status, lyte, CV, and ANS changes increase risk of hypotension, arrhythmia, and sudden postop collapse
- Habitus and metabolic changes may predispose to hypothermia
- Menstrual irregularities. UPT advised.

Burn Injury, Chemical

Shawn Banks | Albert J. Varon

Risk

- From 1999 to 2008, 3% of all reported burn injuries.
- Risk increases with age: 1% of burn injuries from birth to age 16; 3.7% from 20–30; and 5% from 30–50, according to the National Burn Repository Report on Data from 1999 to 2008.
- Majority of chemical exposures occupational, occurring in men of working age, whereas assaults with caustic chemicals are more likely to occur against women.
- American Association of Poison Control Centers reports approximately 130,000 exposures to caustic substances in 2007.

Perioperative Risks

- Morbidity varies by exposure type and substance. Surface burns may be regarded like thermal burns after decontamination.
- Caustic ingestion may result in perforation and/or bleeding, and respiratory compromise from upper-airway edema.

Worry About

- Identify injury setting, chemical(s) involved, areas of exposure, and duration before decontamination.
- Airway compromise may arise from face/ingestion exposures; develop an airway management plan early.
- Occupational exposures may have associated traumatic injuries (from explosions, fire, falls, etc.).
- Chemical burns may produce more tissue necrosis than their initial appearance would suggest.

Overview

- A large number of different chemicals can potentially cause injury, including acids, bases, and organic and inorganic compounds.
- Acid burns generally produce coagulative necrosis; depth may be limited by formation of coagulated proteins at base of burn.
- Bases typically generate liquefactive necrosis; depth often much deeper than in acid burns.
- Organic compounds cause direct heat production and chemical reactions that disrupt skin.
- Inorganic compounds bind directly to the skin and create salts that damage skin integrity.
- Severity of burn is related to a variety of factors including the pH, concentration, volume, physical form, and contact-time duration of the offending agent.

Etiology

- Surface burns: Most commonly work-related injury and accidental; upper limbs are more commonly injured because these substances are usually handled or carried; injuries to the lower limbs and face can occur through splashing
- Ingestions: Pediatric most commonly accidental; adults most frequently a suicidal gesture

Usual Treatment

- Remove contaminated clothes.
- Early decontamination with water or saline irrigation for surface exposures; elemental metals (potassium, lithium) should not be exposed to moisture due to strong exothermic reaction.
- Prevent contaminated irrigation solution from running onto unaffected skin.
- After initial decontamination, pt is treated as a typical burn pt.
- Ensure adequate fluid resuscitation for large BSA burns.
- Take measures to prevent complications (e.g., hypothermia, infection, rhabdomyolysis).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Face and airway burns; eye injuries	Dysphonia, odynophagia, dysphagia Visual changes	Denuded or inflamed oral mucosa and conjunctivitis	Endoscopy, ophthalmologic evaluation
RESP	Chemical pneumonitis, ARDS	Dyspnea	Hypoxemia, possible rales or evidence of edema, auscultation may be normal	CXR, ABG
CV	Arrhythmias, hypovolemic shock	Palpitations Chest pain Dyspnea	Tachycardia or irregular rhythms	ECG, CXR
GI	Esophagogastritis, perforated viscus	Odynophagia/dysphagia, hematemesis, epigastric pain	Abdominal tenderness/guarding	Endoscopy, contrast CT scan, x-ray
RENAL	Electrolyte disturbances, RF, acute tubular necrosis	Deep or large surface area burns. Associated crush injuries	Myoglobinuria, oliguria	Basic metabolic profile (BUN/Cr), urine myoglobin
MS	Rhabdomyolysis, compartment syndromes	Deep or large surface area burns; associated crush injuries	Evolving loss of motor/sensory function	Serum myoglobin, compartment pressure monitoring

Key References: Seth R, Chester D, Moimen N: A review of chemical burns, *Trauma* 9:81–94, 2007; Diez C, Varon AJ: Anesthetic management of the burn patient, *Curr Anesthesiol Rep* 6:16–21, 2016.

Perioperative Implications

Preinduction/Induction/Maintenance

- Review history of the current injury, including the amount of associated TBSA burn and time elapsed since injury.
- Reliable vascular access is essential for adequate fluid resuscitation.
- Normalize electrolytes, if possible.
- Preop medication should be used to alleviate anxiety, reduce pain, and facilitate pt comfort during transfer and transport.

Monitoring

- Adequate intraop monitoring is essential due to the potential for extensive blood loss, frequent changes of position, and duration of surgery.
- Placement of surface monitors can be difficult due to location of burns.
- Try to place invasive lines away from injury, not through damaged skin.
- Consider arterial line placement for extensive debridements/grafting to allow beat-to-beat monitoring and frequent sampling of arterial blood.
- Presence of an arterial line should not preclude placement of NIBP cuff (backup if arterial line fails during procedure). Negotiate with surgeon the best location for NIBP cuff.

General Anesthesia

- Most surface chemical burns that proceed to OR are extensive enough to be treated as thermal injuries.
- Choices for induction and maintenance of general anesthesia depend on associated hemodynamic instability and airway status.
- Muscle relaxants; avoid succinylcholine after acute phase (first 24 hours); resistance to non-depolarizers may evolve after acute phase.
- Narcotic tolerance may be higher in chronic phase.
- Transfusions may be required in extensive debridement procedures.
- Epinephrine-soaked pads may be applied by surgeon to decrease bleeding. This may result in tachycardia and a falsely stable BP that deteriorates after removal of pads.
- Thermoregulation is impaired. Warm OR as much as possible. Apply forced-air heating blankets. Administer warmed fluids and blood products.
- Extubation in the acute phase should be carefully considered if there is suspicion of airway edema or difficult reintubation.

Regional Anesthesia

- No contraindication in small or peripheral injuries.
- Placing block through intact skin preferable.
- Excision and grafting procedures may be accompanied by large fluid shifts and blood loss, in which case, the loss of sympathetic tone resulting from a neuraxial block may be undesirable.

Postoperative Period

- Acute, extensive injury may require ICU care.
- Pain management can be challenging in chronic phase.

Anticipated Problems/Concerns

- Early, goal-directed resuscitation and correction of electrolyte abnormalities.
- Careful monitoring of airway and early airway intervention, if needed.
- Maintain normothermia.

Burn Injury, Electrical

Christian Diez | Albert J. Varon

Risk

- Low-voltage burns (<1000 V) commonly occur in children at home.
- High-voltage burns (≥1000 V) are more common in adults and characteristically occur in outdoor environments near power sources and lines.
- Lightning electrical burns carry highest rate of mortality and usually have energy >30 million volts.

Perioperative Risks

- Pts with an acute burn or a history of burns may present an additional challenge to securing the airway. Fluid resuscitation in acutely burned pts may cause severe facial and airway edema; pts with a history of burns, especially facial, may have limited mouth opening and neck extension.
- Difficult IV access is a common problem. Two large-bore IVs are commonly needed for major burn surgery; however, depending on length of stay and surface area burn, central access and intra-arterial monitoring of blood pressure may be necessary.

Worry About

- Arrhythmias and cardiac arrest from direct electrical energy or metabolic derangements.
- Respiratory failure and edematous airway; respiratory failure may occur from tetany of respiratory muscles or cerebral injury.
- Blunt injuries, fractures, and dislocations if patients were jolted from electrical shock or fell from high structures.
- Compartment syndrome: Delayed exploration and decompression may result in increased amputation rates along with increased organ failure and mortality.
- Rhabdomyolysis and myoglobinuria from muscle injury leading to acute kidney injury.
- Hypothermia remains a serious concern despite that electrical injuries may not result in a large surface area burn.
- Acute hyperkalemia due to large muscle destruction and cellular breakdown.

Overview

- Severity of electrical burn depends on current, route taken by the current, and the duration of contact with the electrical source.
- Entry wounds occur often in the hands, with a leathery, charred appearance. Exit wounds are often explosive.
- Extent of injury may be misleading, as the visibly burned area is often small. Large amounts of destroyed tissue may be present under normal-appearing skin, leading to under resuscitation.
- Signs of electrical injury include loss of consciousness, extremity mummification, loss of pulses in an extremity, myoglobinuria, elevated serum creatinine kinase, and cardiac arrest.
- The electrical current in most households is between 110–220 V, which may produce a low-voltage burn and dysrhythmias. High-voltage burns often cause immediate cardiac arrest and/or respiratory paralysis.
- Direct lightning strikes are rarely survivable.

Etiology

- Of all burns, 3–5% are electrical.
- Causes vary greatly from electrical appliances in water to work-related accidents.
- Children may be involved in low-voltage burns at home. One cause is chewing electrical cords, causing oral mucosa burns.

Usual Treatment

- If ventricular fibrillation or asystole is present, CPR must be immediately initiated. If initial dysrhythmias are present, continuous cardiac monitoring is required because most serious dysrhythmias occur within 24 h. If dysrhythmia not present on arrival and no cardiac arrest occurs at the scene, further cardiac monitoring is not necessary.
- Secure airway if needed and obtain appropriate IV access.
- If myoglobinuria present, maintain urine output >2 mL/kg/h with generous hydration. Consider sodium bicarbonate infusion to alkalize urine and mannitol or furosemide to help maintain urine output.
- Escharotomy and fasciotomy may be required for vascular or nerve decompression.
- Indications for surgical decompression include progressive neurologic dysfunction, vascular compromise, increased compartment pressure, and systemic clinical deterioration from suspected ongoing myonecrosis.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Burn injuries, edema, compartment syndrome	Prehospital information, mechanism of injury	Remove all clothing to determine nature and extent of injury; check peripheral pulses	Measurement of compartment pressures (fasciotomy when >30 mm Hg, diastolic pressure minus tissue pressure <30 mm Hg)
CV	Arrhythmias, hypovolemia	Arrest in the field, ventricular fibrillation, high-voltage burn	Hypotension, bradycardia, or tachycardia	ECG
RESP	Paralysis, edema	Lightning or high-voltage injury	Signs of hypoxia	ABG, pulse oximetry
HEME	Hemolysis, vascular thrombosis, dehydration	Extensive tissue injury	Edema, extensive burns	Hematocrit
RENAL	Acute kidney injury	More frequent in high-voltage injuries	Large muscle destruction and tissue necrosis	Urine myoglobin, BUN/Cr, FEN_a, serum electrolytes
NEURO	Peripheral and central neuropathies	Injury that crosses midline, limb compartment syndrome	Neurologic deficits	MRI, nerve-conduction studies

Key References: Lovich-Sapola JA: Anesthesia for burns. In Smith CE, editor: *Trauma anesthesia,* ed 2, Cambridge, 2015, Cambridge University Press, pp 666–688; Bittner EA, Shank E, Woodson L, et al: Acute and perioperative care of the burn-injured patient, *Anesthesiology* 122:448–464, 2015.

Preoperative Implications

Preinduction

- Burn pts have increased metabolic rate; NPO time should be kept to a safe minimum. Consider continuing enteral feeds shortly up to surgery if the airway is secured and no airway invention is planned.
- Discuss with surgeon the extent of surgery to anticipate amount of blood loss.
- Maintain careful airway evaluation due to increased risk for airway edema and skin or muscle rigidity because of burns.
- Labs, including blood gases, K^+, and blood type and cross-match.
- Large-bore IV access may be needed in cases of complex debridement/grafting. Ultrasonography is recommended for obtaining central venous access.

General Anesthesia

- Selected for most large skin graft procedures
- Many pts already receiving ventilation support
- Recommended for cases in which large blood loss anticipated

Monitoring

- Use standard ASA monitors. It may be difficult to place monitors on burned surfaces. Use of staples and/or sutures to secure ECG leads or catheters may be required.
- Arterial monitoring may be necessary for extensive procedures or for pts receiving prolonged ventilatory support. Ultrasonography can facilitate arterial cannulation.
- Maintaining normothermia is a major challenge. Ambient temperature in OR must be raised. Use of fluid warmers and sterile forced-air warmers may be required.

Induction

- Induction agents such as ketamine may be useful in pts not already receiving ventilatory support. However, as with any of the other induction agents, it can result in myocardial depression in the catecholamine-depleted pt.
- In thermal burn pts, succinylcholine is contraindicated after 24–48 h from their injury. One must be cautious in electrical burn injury because severe muscle destruction may result in hyperkalemia. In this scenario, succinylcholine is contraindicated even at the injury's outset. Larger than usual doses of nondepolarizing muscle relaxants are frequently required for adequate muscle relaxation.

Maintenance

- Choice of inhaled anesthetic does not alter outcome.
- Larger doses of narcotics may be needed because burn pts often develop tolerance to opiates. The analgesic properties of ketamine make it a good choice for induction. Preop opioid infusions may be continued during surgery, with adjunct boluses for increased analgesic requirements.
- Lung-protective ventilatory strategy with tidal volumes ≤6 mL/kg (predicted body weight) and PEEP should be used. Increased respiratory rate and permissive hypercapnia may be required.

- Use crystalloids, red blood cells, and fresh frozen plasma judiciously to maintain normal blood volume and composition and avoid worsening edema.

Regional Anesthesia

- Can be used for analgesia after determining cause and extent of any neurologic sequelae and excluding possibility of a compartment syndrome
- May be used for anesthesia during minor procedures; donor sites are more painful than grafted sites and should be blocked preferentially

Postoperative Period

- Standard extubation criteria should be followed, paying special attention to total fluids given and the possibility of airway edema.
- Increased analgesic demands. Consider physical ability to activate PCA before instituting it.
- Monitor carefully during transport, especially in critically ill pts.

Anticipated Problems/Concerns

- Minimize the possibility of renal failure by maintaining adequate urine output and alkalinizing the urine.
- Monitor edema during surgery because the tracheal tube tape may become a facial tourniquet or the tube may migrate outside glottis.
- Pts who develop sepsis or multiorgan failure have worse outcomes.
- Burn pts have an increased incidence of infection. Therefore, meticulous aseptic care during line placement, intubation, and all invasive procedures is essential.

Burn Injury, Flame

Shawn Banks | Albert J. Varon

Risk

- Flame injuries accounted for 43% of all burn cases from 2003 to 2012.
- 70,000 flame injuries requiring treatment over same 10-y period.
- Approximately 70% of injuries are accidental and nonwork related.
- Approximately 70% of injuries occur at home.

Perioperative Risks

- Major predictors of mortality include BSA >40%, age >60, and presence of inhalation injury.
- Predicted mortality is 0.3%, 3%, 33%, or 90%, depending on presence of zero, one, two, or three of the above-mentioned risk factors.
- Up to one-third of pts with inhalation injury will develop acute airway obstruction.
- Other incidental traumatic injuries may be present.

Worry About

- Airway protection and ventilation
- Hypovolemia with early goal-directed volume resuscitation as the single most important therapeutic intervention
- Hypothermia

Overview

- Direct thermal energy produces direct cellular destruction and coagulative necrosis.
- Systemic microvascular integrity is lost in massive inflammatory response; proteins are lost into interstitial space.
- Significant shift of fluids, electrolytes, and proteins into the interstitium occurs with rapid equilibrium of intravascular and interstitial compartments.
- Changes reflected by massive edema formation and loss of circulating plasma volume, hemoconcentration, decreased urine output, and depressed CV function.
- Cardiac output is reduced due to hypovolemia, decreased contractility, and increased afterload.
- Most edema occurs at the burn site and is maximal at 24 h after the injury. Edema results in tissue hypoxia and increased tissue pressure with circumferential injuries.

Etiology

- American Burn Association stratifies thermal injury etiologies as fire, hot liquids, contact with hot objects, and electrical sources. Flame burns are the most lethal of all thermal injuries.

Usual Treatment

- Most important points of initial phase are assessment of current (and prediction of subsequent) airway patency and documentation of the presence or absence of inhalation injury.
- Early intubation likely if pt has face/inhalation injury or if BSA injured requires aggressive fluid resuscitation.
- Provide supplemental O_2 and monitor O_2 saturation in burn pts with significant injury. Most pts with large burns will require prompt ET intubation and mechanical ventilatory support.
- Prompt establishment of large-bore IV access and rapid initiation of fluid resuscitation. Parkland or "Universal" formula is most commonly used (4 mL/kg/BSA% over 24 h, with first half given over first 8 h).
- Insert urinary catheter early to monitor urine output as guide for volume status.
- Evaluate all extremities and chest wall for potential compartment syndrome requiring fasciotomy or escharotomy for urgent release.
- Multiple skin grafting procedures may be necessary during admission.
- Early debridement of eschar is performed to minimize infection; dead tissue readily supports bacterial growth.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Face and airway burns	Dysphonia, dysphagia Reports of fumes or extraction from enclosed space	Singed facial or nose hair, carbonaceous sputum, facial burns	Oral inspection, laryngoscopy, bronchoscopy
CV	Arrhythmias, hypovolemic shock, myocardial depression	Palpitations, dyspnea Loss of consciousness, depressed mental status	Tachycardia or irregular rhythms, hypotension	ECG
RESP	Pneumonitis, ARDS, restrictive disease from eschar, carboxyhemoglobinemia	Cough, dyspnea, stridor	Hypoxemia, circumferential chest eschar	ABG, co-oximetry, chest radiograph
RENAL	Acute renal failure, ATN, electrolyte disturbances	Large BSA burns, crush injuries	Myoglobinuria, oliguria	Electrolyte profile (BUN/Cr), urine myoglobin, urinalysis
CNS	Hypoxemia	Loss of consciousness, confusion	Focused neurologic exam	ABG, co-oximetry
MS	Tissue destruction, rhabdomyolysis, compartment syndrome	Large BSA burns, overadministration of fluids	Evolving loss of motor and/or sensory function	Serum myoglobin, compartment or bladder pressure monitoring

Key References: Snell JA, Loh NH, Mahambrey T, et al: Clinical review: the critical care management of the burn patient, *Crit Care* 17(5):241, 2013; Bittner EA, Shank E, Woodson L, et al: Acute and perioperative care of the burn-injured patient, *Anesthesiology* 122(2):448–464, 2015.

Perioperative Implications

Preoperative Preparation

- Thermoregulation is impaired. Warm OR as much as possible before pt arrives. Use forced-air warming blankets and fluid warmers intraop.
- Anesthesia services may be requested for bedside debridement and other procedures.
- Assess location and adequacy of venous access.
- Document presence of other invasive devices (e.g., arterial catheter, ET or tracheostomy tubes, feeding tubes) and ventilatory settings.

Monitoring

- Standard monitors may be difficult to apply to extensive burns.
- Arterial line is advisable for extensive grafting procedures that can be long and involve significant blood loss.
- Central venous access may be necessary if peripheral access sites are burned. Lines should be preferentially placed through intact skin.

Airway

- Intubate with largest feasible ETT to aid pulm toilet, minimize mucus plugging, and decrease work of breathing. Need for postop mechanical ventilation is common.

Preinduction/Induction
- Succinylcholine should be avoided after acute phase (first 24 h after injury).
- Gastroparesis and high residual gastric volumes are common after injury; use aspiration precautions.
- Induction agent doses should be adjusted in the context of hypovolemic shock.

Maintenance
- Requirements for neuromuscular blockers usually increased; attributed to the increased binding sites at extrajunctional receptors.
- Pts may need significantly increased narcotics.
- Keep the OR room temperature at ≥85° F to minimize heat loss and decrease metabolic rate.
- Communicate decreases in core body temperature to surgeons; case may be shortened to prevent severe hypothermia.

Extubation
- Consider extubation in early stages of management cautiously. Emergent reintubation may be very difficult due to edema.

Anticipated Problems/Concerns
- Most common complications include pneumonia, UTI, resp failure, cellulitis, and sepsis.
- Ventilator-associated pneumonia may develop in 70% of pts with inhalation injury.
- Pain management is usually challenging. Opioid doses often significantly exceed recommended standard dosing guidelines. Autograft donor sites are very painful; regional analgesia may be useful.
- ACS is a life-threatening complication caused by high-volume resuscitation. Extremity compartment syndromes can also result from extensive edema formation.
- Incidence of DVT in burn pts is increased (1-23%). Therefore, DVT chemoprophylaxis is routinely used.

Calcium Deficiency/Hypocalcemia

Erin Treasy | Henry Liu

Risk
- Common in critically ill pts and may be as high as 88% in ICU pts

Perioperative Risks
- Neuromuscular instability leading to seizure, laryngospasm, bronchospasm, or resp arrest
- Impaired cardiac function causing heart failure, hypotension, and dysrhythmias

Worry About
- Symptomatic hypocalcemia

Overview
- Normal serum calcium content: 8.5–10.5 mg/dL.
  - With 40–50% bound to plasma proteins (albumin).
  - With 45–50% ionized (physiologically active).
  - With 10–15% nonionized, bound to inorganic anions such as phosphate, citrate, and sulfate.
- Total calcium level related to albumin level and acid-base status affects the ionized calcium level.
- Ionized calcium level is the preferred measurement (normal: 4.75–5.3 mg/dL [1.19–1.33 mol/L]).
- The physiologic role of calcium:
  - Neuromuscular signaling and muscle contraction.
  - Hormone secretion.
  - Cardiac contractility.
  - Blood coagulation.
  - Cell growth.
  - Transport and/or secretion of fluids.

Etiology
- Hormonal
  - Hypoparathyroidism (intentional or unintentional surgical removal, hypomagnesemia, and "hungry bone syndrome")
  - Pseudohypoparathyroidism (decreased response to PTH)
  - Decreased vitamin D production/activity (decreased sunlight, hyperphosphatemia, and anticonvulsants)
- Ca^{2+} chelation (massive transfusion, cell lysis and phosphate release, and pancreatitis)
- Osteoblastic metastasis (prostate and breast cancers)
- Alkalosis (increased calcium binding to proteins)
- Congenital and autoimmune disease
- Most common causes of acute intraop hypocalcemia: Acute hyperventilation (resp alkalosis) and massive infusion of citrated blood products (>1.5 mL/kg/min)
- Can occur with persistent diarrhea and hypomagnesemia due to PPI treatment in a small number of pts

Usual Treatment
- Treat based on ionized calcium, not total calcium level.
- Asymptomatic hypocalcemia rarely requires treatment.
- Symptomatic hypocalcemia requires emergent treatment.
  - IV calcium chloride (300–500 mg) or calcium gluconate.
  - Follow with continuous replacement if needed.
  - Administered slowly because venous irritation can occur, with central venous administration preferred because calcium chloride can cause tissue necrosis if extravasated from a peripheral vein.
- Hypocalcemia often concurs with hypomagnesemia/hyperphosphatemia. Treat as needed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Involved in cardiac pacemaker activity and generation of cardiac action potential	Hx of dysrhythmia SOB (or other symptoms of heart failure)	Prolonged QT Hypotension Pulmonary vascular congestion	ECG Continuous cardiac monitoring CXR
HEME	Citrate in stored blood products chelates calcium	Massive transfusion of citrated blood products (>1.5 mL/kg/min)		Ionized calcium level
GI	GI smooth muscle spasm	Abdominal cramping		
RESP	Resp smooth muscle contraction/tetany	SOB Laryngospasm Bronchospasm	Hypoxia Stridor Wheezing Resp arrest	Pulse oximetry
NEURO	Essential for all muscular movement Involved in the muscular excitation/contraction coupling	Muscle spasm Seizure Depression Psychosis Neuromuscular irritability Circumoral numbness Tingling in fingers/toes	Facial grimacing Seizure Papilledema (secondary to increased intracranial pressure) Irritability	Chvostek sign (twitch of circumoral muscles with tapping of the facial nerve anterior to the ear) Trousseau sign: Carpal spasm induced by inflation of BP cuff to 20 mm Hg above systolic BP for 3 min
DERM			Dry, scaly skin Brittle nails	

Key References: Khosla S: Hypercalcemia and hypocalcemia. In Kasper D, Fauci A, Hauser S, et al, editors.: *Harrison's principles of internal medicine,* ed 19, New York, 2015, McGraw-Hill; Edwards MR, Grocott MPW: Perioperative fluid and electrolyte therapy. In Miller R editors: *Miller's anesthesia,* ed 8, Philadelphia, 2015, Elsevier, pp 1767–1810.

Perioperative Implications

Preinduction/Induction/Maintenance
- Correct symptomatic hypocalcemia preop.
- Goal of treatment to eliminate symptoms, not necessarily return calcium levels to normal range.

Monitoring
- Serial ionized calcium measurements
- Continuous ECG monitoring

General Anesthesia
- Negative inotropic effects of anesthetic medications may become more pronounced.

Regional Anesthesia
- Hypocalcemia results in increased neuronal membrane irritability/tetany.
- Paresthesia a common finding.

Postoperative Period

- Acute hypocalcemia may develop after thyroidectomy/parathyroidectomy.
- During liver transplantation, especially during anhepatic stage.

Anticipated Problems/Concerns

- Risk of hypocalcemia with massive transfusion of citrated blood products (>1.5 mL/kg/min) may be more severe with hepatic dysfunction due to impaired citrate metabolism.
- Alkalosis increases Ca^{2+} binding to proteins, thereby decreasing ionized calcium.
- Very low levels of ionized calcium may impair coagulation.

Cancer, Bladder

Ashish C. Sinha

Risk

- Primary risk factor is smoking; smokers are more than twice as likely to get bladder cancer compared with nonsmokers.
- Incidence: males 37 per 100,000; females 9 per 100,000.
- No associated increased risk with alcohol or caffeine consumption.
- Median age of diagnosis: 73 y.
- Greater for Caucasian than for African Americans.
- Quitting smoking decreases risk over time (baseline in 5–8 y).
- Incidence on a decline since 1999.

Perioperative Risks

- Risks vary based on surgical procedure and coexisting disease
- Chemotherapy: Pulm fibrosis and renal and cardiac dysfunction
- Fatty infiltration of liver in those with poor nutritional status
- Protein-calorie malnutrition resulting from cancer, metabolism, anorexia, anemia, hypoalbuminemia and dehydration

Overview

- Transitional cell cancer generally a systemic disease at time of Dx; 60% of patients will die of metastatic complications.
- Pts are typically elderly with long Hx of smoking, thereby promoting concurrent diseases: COPD, lung CA, atherosclerosis, angina, CAD, CHF, and Htn.
- Chemotherapy/radiation therapy may be used preop, thus complicating periop period.

Survival and Stage

- Relative survival (%) of 5 y:
  - In situ (only in the layer of cells in which it began): 96.6%
  - Localized (confined to primary site): 73.3%
  - Regional (spread to regional lymph nodes): 36.1%
  - Distant (cancer has metastasized): 5.6%

Worry About

- Significant blood loss (type and cross blood products and large-bore IV access).
- Hyperextension of lumbar spine/pelvis and compression of iliac veins results in reduced venous return of blood volume.
- Adequate padding of peripheral nerves (upper and lower extremities).
- Maintenance of neutral neck position in flexed body position.
- Monitoring of UO difficult after ligation/division of ureters.
- Overall postop morbidity between 30–64%.

Etiology

- Exposure to aromatic amines (arylamines): β-naphthylamine in cigarette smoke causes bladder cancer in mice.
- Work-related exposure: β-naphthylamine and benzene in the manufacture of rubber products, arylamines in synthetic textile and hair dyes, and paint pigments.
- Drivers of diesel trucks are affected.
- "Slow acetylators" (homozygous and autosomal recessive) may be at higher risk; *N*-acetyltransferase may detoxify aromatic amines.

Usual Treatment

- Chemotherapy
- Doxorubicin/bleomycin/cyclophosphamide/cisplatin/methotrexate; 5-fluorouracil/vinblastine/teniposide
- Radiation therapy
- Transurethral fulguration
- Radical cystectomy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Doxorubicin (Adriamycin) toxicity: Cardiomyopathy	>550 mg/m^2, prior or concurrent mediastinal radiation therapy	Signs of CHF	Endomyocardial biopsy, serial ECHO, radionuclide angiography, DLCO ECG
	5-Fluorouracil: Myocardial ischemia (rare)	Angina		ECG
	Cyclophosphamide: Pericarditis with effusion	CHF	Signs of CHF	ECHO
RESP	Smoking-related injury	Cough, sputum, infections	Wheezes, rhonchi, barrel chest	CXR PFT
	Bleomycin or cyclophosphamide toxicity: Pulm fibrosis	>500 mg (bleomycin), cough, dyspnea	Rales, fever	CXR
	Methotrexate: Inflammation		Pulm edema, effusions, infiltrates	CXR
RENAL	Cisplatin: ATN Methotrexate: Renal failure	Occurs 3–5 d after course		BUN, Cr, proteinuria, hyperuricemia Hematuria, proteinuria
HEPATIC	Methotrexate: Fibrosis			SGPT
CNS	Methotrexate: Encephalopathy	Confusion, somnolence, ataxia, tremors, and focal signs		

Key References: Patel HR, Cerantola Y, Valerio M, et al: Enhanced recovery after surgery: are we ready and can we afford not to implement these pathways for patients undergoing radical cystectomy? *Eur Urol* 65(2):263–266, 2014; Friedrich-Freksa M, Schulz E, Nitzke T, et al: Performing radical cystectomy and urinary diversion in regional anesthesia: potential risk reduction in the treatment of bladder cancer, *Urol Int* 91(1):103–108, 2013; Cerantola Y, Valerio M, Persson B, et al: Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS®) society recommendations, *Clin Nutr* 32(6):879–887, 2013.

Preoperative Implications

Preoperative Preparation

- Consider rehydration after bowel preparation.
- Use two large-bore IVs or one peripheral IV plus a central line.

Monitoring

- Consider arterial catheterization.
- Renal perfusion difficult to judge after division of ureters. Consider CVP or PAC or TEE.
- Standardize anesthesia technique: no bowel prep, no preop fasting, epidurals (T9-T11), PONV, and DVT prophylaxis.
- Consider combined general-epidural anesthesia to treat postop incisional pain and to reduce blood loss and fluid requirements for cystectomy, as well as less risk of postop ileus.

Induction
- Watch for hypotension due to volume depletion from prep and/or decreased systolic function from cardiotoxic chemotherapeutic agents.

Maintenance
- Avoid high concentrations of O_2 in pulm fibrosis.
- Goal-directed fluid therapy (based on euvolemia and pulsus paradoxus).
- Avoid N_2O (bowel surgery).
- Maximize efforts to prevent hypothermia.

Postoperative Considerations
- Consider overnight ventilation if procedure is long, and prepare for significant blood loss/fluid resuscitation. An epidural catheter can optimize pulmonary toilet and recovery.
- Fluids shifts occur during first 48 h.
- Early oral nutrition, ambulation, and drain removal.
- EBT of TURBT about 200 mL; cystectomy between 500–1000 mL.
- Pain score of 7–9 (cystectomy) expected.

Acknowledgement

I wish to thank Dr. Andrew Dziewit for his work on this chapter in an earlier edition of this book.

Cancer, Breast

Vincent S. Cowell

Risk
- 100 times more common in women than men.
- Besides skin cancer, most common cancer in USA for women; 1 in 8 women develop breast cancer; a man's lifetime risk is about 1 in 1000.
- Most significant risk factors for breast cancer are gender and growing older. About 2 out of 3 women with invasive breast cancer are 50 y or older when the cancer is found.
- Racial predilection: non-Hispanic whites > African Americans > Asians, Hispanics, and Native Americans.
- African Americans are more likely to die of breast cancer because their cancers tend to be more aggressive and of a more advanced stage that is diagnosed at a younger age.
- Of breast cancers, 5–10% are directly due to inherited mutations of the *BRCA1* and *BRCA2* gene, which tend to occur more often in younger women.
- Increased with family Hx among close blood relatives; personal Hx increases the risk of developing a new cancer in the same or other breast.
- >85% are diagnosed in women with no family Hx (genetic mutations secondary to aging and life in general rather than inherited).
- Associated with increased risk: Obesity, aging, high alcohol consumption, estrogen exposure, and long-term heavy smoking.

Perioperative Risks
- Mortality: very rare
- Lymphedema of arm following axillary node dissection
- Ipsilateral brachial plexus injury from extensive abduction of the arm, or iatrogenic
- Injury to long thoracic and/or thoracodorsal n. during surgical dissection of axilla
- Rare incidence of unrecognized pneumothorax
- Breast surgery is associated with postop N/V, with incidence as high as 60%
- Neuropathic pain, postmastectomy pain syndrome (up to 20–30% may develop symptoms)

Worry About
- Systemic or regional effect of metastasis to lungs, brain, or bones.
- High incidence of postop N/V
- NMB and identification of major nerves.
- Access to an upper extremity may be restricted or limited
- Potential adverse effects of chemotherapeutic drugs and chest radiation therapy

Overview
- Two types of invasive breast cancer, which account for 95%: invasive ductal carcinoma at around 80% and invasive lobar carcinoma at around 10%.
- Abnormal growth of adenomatous tissue that results in systemic symptoms and metastasizes to the liver, bones, lungs, and brain.
- Early detection of breast cancer offers a greater range of treatment options, increasing survival time.
- Mammography: reduces the risk of dying from breast cancer by 15–20%
- Physical exam and mammography are complementary
- Needle biopsies provide histologic diagnosis.
- Presurgical needle localization may be necessary for nonpalpable lesions.
- Most breast biopsies yield benign diagnosis.

Etiology
- Exact cause of most breast cancers is still unknown.
- Inherited and acquired genetic mutations increase the risk of developing breast cancer.

Usual Treatment
- Noninvasive breast cancer: Lumpectomy or partial mastectomy rarely with sentinel node Bx and/or axillary node dissection with radiation and/or hormonal therapy (e.g., tamoxifen and toremifene)
- Invasive breast cancer: Lumpectomy, partial mastectomy with sentinel lymph node Bx, possible ALND or radiation, possible chemotherapy, and possible hormonal therapy
- Radical mastectomy: Rarely performed
- Of women who undergo mastectomy, 20–40% elect to have breast reconstruction, with either an implant, a tissue flap, or a combination of the two.

Prognosis
- In USA, about 40,730 women will die from breast cancer in the year 2015, making it the second-most lethal cancer in women (lung cancer is the leading cancer killer in women).
- Relative 5-y survival rate for women diagnosed with cancer is 89%. The 10-y survival rate is about 83%; after 15 years, it is 78%. Unfortunately, women in lower social and economic groups still have significantly lower survival rates than women in higher groups.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CHEST	Lung lesions	Nipple discharge Chest pain or discomfort	Breast asymmetry Nipple discharge, erythema, crusting, or erosion Nipple retraction Skin dimpling	Physical exam Mammography Fine-needle aspiration biopsy CXR
GI	Liver metastasis	Fatigue, abdominal pain	Enlarged or nodular liver	Liver US or CT scan
HEME	Bone metastasis	Lethargy, SOB	Anemia, pancytopenia	CBC
CNS	Brain metastasis	Change in mental status, seizures	Neurologic exam	Head CT
MS	Bone metastasis Pathologic fractures	Severe pain Immobility Arm swelling	Deformities Pain on palpation Axillary adenopathy	Bone scan X-rays Physical exam

Key References: Andreae MH, Andreae DA: Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis, *Br J Anaesth* 111(5):711–720, 2013; Wu J, Buggy D, Fleischmann E, et al: Thoracic paravertebral regional anesthesia improves analgesia after breast cancer surgery: a randomized controlled multicentre clinical trial, *Can J Anaesth* 62(3):241–251, 2015.

Perioperative Implications

Preoperative Preparation
- Optimal preop preparation, in response to associated anxiety, which can be achieved through both pharmacologic and nonpharmacologic means

Monitoring
- Routine with attention to placement of ECG leads
- IV site and BP cuff on contralateral arm

Airway
- Table arrangements may warrant a secure airway.
- Nasal O_2 or LMA may be appropriate.

Induction
- Thoracic epidurals, intercostal nerve blocks, and local infiltration have successfully been administered as primary anesthetics and adjuvants to GA.
- There is speculation that regional anesthesia and analgesia techniques might help to maintain perioperative immune competence thus modulating the risk of recurrence or metastasis.

Maintenance
- Consideration for the high incidence of postop N/V.
- Incision over operative breast that can also include axilla.
- Dissection can include breast areolar tissue, muscle down to chest wall, and extension into axilla.
- Identification of thoracodorsal and long thoracic nerve often requires stimulation that contraindicates presence of NM blocking agents.
- Surgical field will be in view and allow for monitoring of active blood loss.
- Surgical team leaning on chest can affect ventilatory performance.

Postoperative Considerations
- Pain score: 2–6.
- Pain adequately managed with Toradol, acetaminophen, narcotic PCA, or regional block.
- Communicate with PACU that no venous sticks or BP measurements should be performed on arm of operative side when axillary lymph node dissection is involved.

Anticipated Problems/Concerns
- Anxiety associated with the fear of breast cancer and altered body image can be quite significant.

Cancer, Esophageal

Dawn P. Desiderio | Alessia Pedoto

Risk
- Incidence in USA: 4.39:100,000 in white men, 2.0:100,000 in white women, 8.63/100,000 in African-American men, and 4.2:100,000 in black women.
- Adenocarcinoma more common in white men, while SCC highest in black men.
- Overall mortality rate is 4% (white) to 8% (black).

Perioperative Risks
- Reflux as a risk of aspiration.
- Malnutrition with dehydration due to dysphagia.
- Periop arrhythmias occur in 20–60% of cases.
- Anastomotic leak most frequent surgical complication (9–10%).

Worry About
- Pulm compromise (25%) due to lung injury from preop chemo-/radiation therapy, chronic aspiration, extensive tobacco use, and ventilator-induced lung injury
- Airway protection during induction and postop
- Arrhythmia
- Alcohol withdrawal syndrome
- Hydration status/malnutrition

Overview
- Primarily either SCC from the esophageal squamous epithelium or adenocarcinoma of gastric origin.
- Median age of diagnosis is 67 y, with a long-standing Hx of tobacco and alcohol intake.
- Dysphagia and weight loss are initial symptoms, often present for 3–4 mo.
- Extensive local growth and lymphatic involvement before becoming widely disseminated.

Etiology
- SCC (mainly localized in the upper one-third of the esophagus) is associated with achalasia for >25 y, tobacco use, alcohol, and lack of aspirin and statin use.
- Adenocarcinoma (mainly at GE junction) is associated with GERD, esophagitis (Barrett esophagus), and obesity.
- Nutritional factors (red meat, poor vegetable intake, hot liquids) have been implicated.

Usual Treatment
- Treatment depends on extent of disease and pt's medical status.
- Radioablation or photodynamic therapy is reserved for esophageal dysplasia.
- Surgery with or without chemotherapy the only curative option (open or minimally invasive [MIS]).
- Radiation is reserved for pts with unacceptable surgical risks or advanced disease.
- Palliative placement of internal esophageal stents facilitates swallowing of liquids and secretions.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Alcohol abuse–induced cardiomyopathy and arrhythmias	DOE Exercise tolerance		ECG ECHO, stress test
RESP	Tobacco abuse Chronic aspiration Radiation/chemotherapy	Pneumonias, RV Htn Cough, DOE Sputum	Wheezing RV heave	CXR PFTs, DL_{CO} ABG
GI	Obstruction Reflux Malnutrition	Dyspnea, orthopnea, weight loss	Debilitated	EGD
CNS	Alcohol abuse Delirium tremens	Last EOTH ingestion and amount		
MS	Weakness	Poor nutrition	Muscle wasting	Serum albumin
RENAL	Dehydration	Limited intake		Lytes, Cr, BUN

Key References: Ng JM, Carney A: Anesthesia for esophagectomy, *Anesthesiol Clin* 33:143–163, 2015; Carney A, Dickinson M: Anesthesia for esophagectomy, *Anesthesiology Clin* 33:143–163, 2015.

Perioperative Implications

Preoperative Preparation
- Sedation should be minimized to prevent aspiration in pts at risk.
- Antisialagogue (atropine 0.4 mg or glycopyrrolate 0.2 mg) may be used.
- May premedicate with H_2 blockers for acid aspiration prophylaxis plus metoclopramide to promote gastric emptying.
- Steroids given if recently used.
- Placement of thoracic epidural or paravertebral cath for postop pain control.
- Gabapentinoids to prevent chronic pain.
- Cisplatinum-based chemo can lead to CRF.
- Fasting for 6-8 h for solids and 2 h for carbohydrate-rich drinks has been suggested (ERAS) if no dysphagia.

Monitoring
- Monitor arterial line for ABG and BP.
- Employ goal-directed therapy techniques for fluid management.

Airway
- Rapid-sequence induction or awake FOB intubation may be necessary for symptomatic pts.
- Lung isolation DLT, bronchial blocker or a Univent tube properly positioned) may be necessary to accommodate one-lung ventilation.

Induction
- Hypovolemia often results in BP fluctuations.
- Risk of aspiration.

Maintenance
- No one agent or technique is shown to be superior.
- Hypotension can occur due to mediastinal compression, blood loss, and initial dehydration. Maintain "balanced" fluid management. Role of vasoconstrictors is controversial on anastomosis perfusion. Low-dose dopexamine may be beneficial.
- Oxygenation concerns during one-lung ventilation, the use of 100% O_2, prior pulm disease due to tobacco history, and volu-baro-atelectrauma during mechanical ventilation.
- Lung-protection advocated during mechanical ventilation; lower tidal volumes 5–6 mL/kg recommended with/without PEEP, using either volume or pressure modes of ventilation to maintain adequate oxygenation with plateau inspiratory pressures <25 cm H_2O.
- Hypothermia is a concern in long procedures.
- Placement of NG tube with surgical guidance can decompress the stomach (thus decreasing risk of aspiration and dehiscence).

Extubation
- Continuing risk of aspiration.
- Aim for early extubation either in the OR or within a few hours of surgery. This decreases the need for postop sedation with less fluid requirements and requires presence of good regional techniques.
- Use caution with obese and sleep apnea pts.
- If postop ventilation required, the DLT should be changed to a single lumen tube or bronchial blockers removed.
- A tube exchanger (Cook airway exchanger cath) is indicated if reintubation is deemed difficult (possible edema and fluid shifts) or in case of residual muscle paralysis. DLT is withdrawn over the tube exchanger and a single lumen tube is threaded over. Laryngoscope can be used to move soft tissue that may impede placement.

Adjuvants
- Acetaminophen can be used to supplement analgesia. NSAIDs may increase risk for anastomotic leak.
- Postop metoclopramide should be used with caution due to increased motility and possible anastomosis damage.

Postoperative Period
- Epidural/paravertebral analgesia is beneficial for open procedures. Regional techniques (intercostal blocks) should be used to supplement IV narcotics for MIS.
- Increased risk for supraventricular tachycardia and atrial fibrillation (25%). Rate control is recommended by the AHA, initially with IV amiodarone (class 2A) or diltiazem (class 2B) if BP tolerates. Beta-blockers should be continued in the postop period.
- Pneumonia and anastomotic leak are the other two most common complications.

Anticipated Problems/Concerns
- Airway management concerns: Aspiration risk, reintubation, and extubation criteria.
- Volume status in a dehydrated pt undergoing a lengthy surgical procedure with mediastinal compression and a thoracic epidural.
- Arrhythmias in the postop period; use prophylatic amiodarone.

Cancer, Lung Parenchyma

Roger A. Moore

Risk
- Lung cancer is the primary cause of cancer death.
- Asbestos exposure increases risk 5-fold.
- Smoking increases risk 15-fold.
- Radon exposure increases risk 2-fold.

Perioperative Risks
- Associated CAD
- Pulm insufficiency following lung tissue resection

Worry About
- Optimization of preop pulmonary status
- Issues secondary to metastatic spread, such as superior vena caval syndrome
- Myasthenic syndrome (Eaton-Lambert) with oat cell carcinoma
- Massive hemoptysis with cancer invasion of bronchial arteries
- Active pneumonia in pulm parenchyma distal to obstructed bronchioles
- Development of postop ARDS, pneumonia, or respiratory failure in 15–20%; higher in elderly
- Development of cardiac complications in 10–15%; higher in elderly

Overview
- Four primary types of lung cancers: squamous cell, or bronchogenic; adenocarcinoma (most common); large cell carcinoma; and small cell carcinoma.
- 70% of pts with COPD need extra postop pulm care.
- Pts often nutritionally depleted.
- Many pts have alcohol abuse history.
- Preop pulm state may limit option of lobectomy.
- Hormonal imbalances common due to hormone secreting tumors:
  - 3% of pts are Cushingoid.
  - 70% of pts with bronchogenic carcinomas have increased ACTH or pro-ACTH.
  - Up to 60% of pts with lung cancer have inappropriate ADH.
- Myasthenic syndrome occurs owing to decreased release of nerve-ending acetylcholine, leading to increased sensitivity to all muscle relaxants.

Etiology
- Environmental factors important (smoking, asbestos exposure, radon exposure).
- Higher incidence in areas located near oil refineries.

Usual Treatment
- Oat cell cancer frequently treated with radiation and chemotherapy (need good renal function).
- Lobectomy or pneumonectomy are common approaches in other types of lung cancers; DLCO of <60% predicts 75% mortality; >100% predicts 100% survival.
- Lobectomy increasingly performed using VATS, while pneumonectomy still primarily performed with a thoracotomy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia, arrhythmia, cor pulmonale	Angina SOB Palpitations SOB	S_3 gallop Irregular pulse Distended neck veins	Exercise stress test ECG Cath ECHO
RESP	Pneumonia, bronchospasm, COPD	Productive cough, wheezing, SOB, dyspnea	Rhonchi-rales, wheezes, decreased BS, clubbing	CXR; PFTs: MBC, MMEFR, DLCO; ABGs
ENDO	SIADH	Lethargy, increased weight, decreased urine Thin skin, poor wound healing Weight gain, striae	Hypometabolic	Lytes Elevated urine sodium (rarely needed)
	Increased ACTH		Cushingoid, increased BP	Cortisone level (rarely needed)
NM	Eaton-Lambert (myasthenic)	Decreased muscle weakness	Decreased muscle strength with exercise	EMG (rarely needed)
NUTRITION	Wasting DTs	Weight loss, alcohol abuse	Cachexia, BMI change, increased liver size	Liver function tests (especially albumin)

Key References: Lohser J, Slinger P: Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung, *Anesth Analg* 121: 302–318, 2015; Chappell D, Jacob M, Hofmann-Kiefer K, et al: A rational approach to perioperative fluid management, *Anesthesiology* 109:723–740, 2008.

Perioperative Implications

Preoperative Preparation

- Resp optimization with bronchodilatation, antibiotics, pulm hygiene, and smoking cessation
- Correction of lyte imbalances

Monitoring and Operative Care

- Routine monitors include temperature monitoring with active warming devices.
- Intra-arterial line and possible pulm cath, but if a PA cath is used, be alert to it being caught in the surgical pulm incision.
- Neuromuscular blockade monitor.
- Thoracic epidural is key for postop pain control.

Airway

- Double-lumen tube or bronchial blocker needed—usually left-sided, unless left pneumonectomy.
- Fiberoptic bronchoscope should be available for positioning of endobronchial tube.

Induction

- Anesthetic choice dependent on associated medical problems.
- Light or no premedication to decrease CO_2 retention.
- When right-sided double-lumen tube used, ensure right upper lobe ventilation (easiest with fiberoptic bronchoscope).

Maintenance

- Nerve damage with lateral position
  - Use axillary roll.
  - Brachial plexus injury with arm hyperextension
  - Pad all pressure points.
- Substantiate pulse oximetric and capnographic readings with ABGs.
- If O_2 saturation falls during one-lung ventilation, PEEP on dependent lung may help. If not, CPAP on nondependent lung may help.
- Intraop fluid restriction, including use of blood and blood products, can significantly decrease postop resp failure.
- With one-lung ventilation, use TV of 4–5 mL/kg ideal body weight and 10 of PEEP in typical patient.

Extubation

- If postop ventilation required and double lumen tube has been used, it needs to be switched to single-lumen tube.
- Extubation should be determined by adequacy of resp variables.

Adjuvants

- Bronchodilators for intraop use, inotropes for myocardial depression, antiarrhythmics for post-lobectomy-pneumonectomy arrhythmias (some advocate prophylactic digoxin—but conflicting reported results)

Postoperative Period

- If pneumonectomy performed, there is a significant risk for postop ARDS.
- Adequate pain management usual for recovery of pulm function:
  - PCA or use of intercostal blocks can be effective.
  - Thoracic epidural most efficacious.
- Be watchful for DTs, inappropriate ADH, and decreased neuromuscular strength.

Anticipated Problems/Concerns

- Intensive pulm toilet postop.
- Employ careful suctioning of bronchial stump because of possibility of rupture.
- Bronchopleural fistula and tension pneumothorax are possible concerns.

Candidiasis

Ashish C. Sinha

Risk

- Risk occurs in pts with suppressed immune systems from diseases like AIDS, chemotherapy drugs, and extended steroid therapy.
- Risk factors include current and recent broad-spectrum antibiotic therapy.
- Diabetes, leukemia, and neutropenia also increase risk.
- IV hyperalimentation and prolonged ICU stay increase risk.
- Risk increased via breaches of protective epithelial barrier: Surgical trauma, burn injury, long-term indwelling IV, or bladder catheters.
- Even in healthy individuals, candida can be cultured from the oral cavity in a third to more than half; this increases with chronic illness and duration of hospitalization.
- As systemic bacterial infections have declined with aggressive antibiotic use, systemic fungal infections have correspondingly increased.
- Candida is fourth most common organism recovered from blood cultures.

Perioperative Risk

- Candidemia with septic shock is infrequent in non-immunocompromised pts but has a very high mortality rate, ~30% higher than bacteremic septic shock, and a high likelihood of MOF, along with delayed recovery from this organ failure.
- Pts more likely to have compromised renal function at baseline.

Worry About

- Disseminated candidemia and associated organ dysfunction
- Candidemic septic shock
- Side effects of azole, nystatin, or amphotericin-B therapy

Overview

- Candidemia occurs in 30 cases per 100,000 admissions (in USA) and is associated with ~14.5% increase in mortality, 10-day increase in hospital stay, and ~$40,000 increase of charges.
- ~50 cases per 1000 pts per y; of these, 10% develop candidemia, with an attributable mortality of 25%.
- ~1% of pts colonized on wards.
- Incidental culture positive to fatal candidiasis.

Etiology

- Among isolated species, ~ 60% *C. albicans*, ~20% *C. tropicalis*, with the rest in decreasing order, including *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *Candida* spp.
- Can result from antibiotic therapy, because normal flora that keeps fungal growth in check is eliminated with antibiotics.

Usual Treatment

- Oropharyngeal: Oral itraconazole and fluconazole
- Esophageal: Oral and IV fluconazole, oral itraconazole, low-dose IV amphotericin B
- Vulvovaginal: Topical and oral azole agents
- Systemic infections: IV amphotericin B, high dose fluconazole (echinocandin in pts with neutropenia)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Thrush Endophthalmitis	Dysphagia Visual changes	White oral plaques Ophthalmic lesions	Bleed on scraping Fundoscopic and field of vision
CV	Endocarditis Septic shock	SOB Refractory hypotension	Cardiac murmurs Fever	Auscultation CVP, CO, PCWP
RESP	Pneumonia ARDS	SOB, cough, tachypnea, decreased exercise tolerance	Rapid shallow breathing, hypoxemia, consolidation	PFT, ABG, CXR
CNS	Meningitis Brain abscess	Altered mental status, signs of increased ICP, nausea, vomiting, headache, seizures, loss of appetite	Mental status exam, neck stiffness, photophobia, confusion	CT, MRI, blood cultures, CSF cultures
RENAL	Renal abscess Cystitis	Dysuria, polyuria, low back pain, hematuria	Costovertebral tenderness on affected side	Urine culture, cystoscopy, CT
MS	Fungal osteomyelitis	Tenderness over bone, skin breakdown over infected bone	Moderate to severe bone pain, limited range of motion	X-ray, culture and sensitivity, bone scan
GI	Inflammation through GI tract, intra-abdominal abscess	Dysphagia, abdominal pain, diarrhea	Abdominal tenderness, signs of peritoneal irritation, hepatomegaly, splenomegaly	CT or MRI, endoscopy, abdominal ultrasound

Key References: Pfaller M, Neofytos D, Diekema D, et al: Epidemiology and outcomes of candidemia in 3648 patients: data from the Prospective Antifungal Therapy (PATH Alliance) registry, 2004–2008. *Diagn Microbiol Infect Dis* 74(4):323–331, 2012; Bassetti M, Righi E, Ansaldi F, et al: A multicenter study of septic shock due to candidemia: outcomes and predictors of mortality, *Intensive Care Med* 40(6):839–845, 2014.

Perioperative Implications

Preoperative Preparation
- Continue antifungal therapy.
- Evaluate for septic shock.
- Rule out infected lines or catheters; change if indicated.

Monitoring
- If septic, A-line, CVP ± PA catheter, along with standard monitoring.

Airway
- Be careful not to aggravate oral lesion at intubation.

Preinduction/Induction
- Choose drugs based on septic signs and symptoms.
- Worry about hypotension and hypoxemia at induction.

Maintenance
- Choose drugs based on hemodynamic status.
- Choose ventilatory modes based on presence of ARDS.

Extubation
- May have to be delayed if ARDS or septic state requires hemodynamic support.

Adjuvants
- In the presence of compromised renal or hepatic function, modify anesthetic drugs accordingly.

Anticipated Problems/Concerns
- Candidemia presents with a diverse clinical picture, from low-grade fever to fulminant septic shock. There is higher periop mortality in this group of pts.

Carbon Monoxide Poisoning

Peter H. Breen

Risk
- CO is the predominant toxic gas in smoke. (COHb can reach 10% in tobacco smokers.)
- CO poisoning is a major cause of death (early symptoms may be only headache and dizziness).
- CO is produced by all internal combustion engines, incomplete oxidative combustion (e.g., house fires, charcoal and gas grills, malfunctioning butane/propane stoves), and endogenous sources (e.g., by the liver from exogenous exposure to paint stripper).
- No odor, taste, or color and causes no irritation.
- Toxicity potentiated by low inspired O_2 concentration (e.g., smoke inhalation).
- To minimize CO in circle circuit carbon dioxide absorbers, use fresh soda lime, use sevoflurane, and minimize drying (lower FGF and stop FGF during use).
- During GA, use semiclosed circuits, especially when machine has not been used for 2–3 d (e.g., Monday morning).

Perioperative Risks
- Main target organs: Heart and brain
- Heart: Effect can resemble ischemia; potentiated by CAD.
- Brain: Acute loss of consciousness; after initial improvement (lucid window), up to 30% risk of secondary syndrome: chronic psychiatric dysfunction and cerebral and cerebellar syndromes.

Worry About
- Seek other smoke inhalation injury.
- Consider concomitant cyanide poisoning, which potentiates CO toxicity.
- Be alert for CO poisoning in donor for organ transplantation.

Overview
- CO, a colorless, nonirritating, odorless gas, is a natural byproduct of combustion.
- CO binds avidly to Hgb (>200 times more than O_2) to form COHb, which carries no O_2 and causes a left shift in the oxyhemoglobin dissociation curve (decreases O_2 off-loading to tissues).
- CO binds to intracellular hemoproteins such as myoglobin and cytochrome aa_3 (esp cardiac) to inhibit O_2 uptake and metabolism.
- "Classic" cherry-red complexion rarely observed (need COHb >40%; may be obscured by coexistent hypoxia and cyanosis).
- COHb level correlates poorly with clinical condition (symptoms with "normal" COHb).
- Treatment should be guided by symptoms and signs, not by blood COHb concentration.

Etiology
- CO produced by incomplete oxidative combustion (e.g., house fires, malfunctioning butane/propane stoves, home heaters, all internal combustion engines)
- Suicide attempts

Usual Treatment
- Normobaric O_2: $T_{½}$ of COHb decreases from 3.5 hr (air breathing) to 0.75 hr (O_2 breathing).
- Treat clinical symptoms, not just increased COHb.
- General supportive care, especially for other aspects of smoke inhalation injury.
- Hyperbaric O_2 (2.5 atm) decreases COHb $T_{½}$ to 20 min, increases dissolved plasma O_2, and has been shown to decrease the likelihood that delayed neurologic complications will develop. For pts with neurologic Sx (including impaired consciousness), evidence of myocardial ischemia, fetal distress (if pregnant), poisoning in pediatric pts, or other Sx of significant exposure (e.g., COHb >25%), hyperbaric O_2 within 6–8 h of exposure if feasible is recommended.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Thermal/toxic upper airway injury	Fire exposure/smoke inhalation	Perioral burns Airway edema	Laryngoscopy/bronchoscopy
RESP	CO diffuses rapidly into blood, leading to COHb	Dyspnea, tachypnea		Cooximetric COHb: PO_2 usually normal CXR
	Thermal/toxic airway and parenchymal injury		Bronchoconstriction and pulm edema	Bronchoscopy
CV	Lower O_2 content in blood and lower O_2 unloading in tissue	Possibly angina or evidence of heart failure, tachycardia	Cardiac failure	ECG: Ischemic ST-T changes CXR
METAB	Tissue hypoxia leading to acidosis			Lactic acidosis
CNS	Coma, cerebral edema	Temporal headache, N/V, restlessness	Muscle weakness, altered mental status	Abnormal neuropsychometric testing
	Neuropsychiatric syndrome	Cerebral, cerebellar		Can occur after initial recovery

Key Reference: Breen PH, Isserles SA, Westley J, et al.: Combined carbon monoxide and cyanide poisoning: a place for treatment?. *Anesth Analg* 80(4):671–677, 1995.

Perioperative Implications

Preoperative Preparation
- Continuous 100% O_2.
- Document CNS status.
- Consider hyperbaric O_2 if mental status altered or pt has myocardial ischemia or is pregnant.

Monitoring
- Routine monitors (if no lung injury and thus no decreased PaO_2, there may be no tachypnea)
- SpO_2 does not distinguish between O_2Hb and COHb. Thus SpO_2 overestimates O_2Hb during CO poisoning.
- Newer SpO_2 monitors (Masimo Corp., Irvine, CA) can discriminate between O_2Hb and COHb (and metHb).
- Mixed venous oximeter catheters overestimate O_2Hb in presence of COHb.
- Arterial cannulation for frequent blood sampling.
- Venous and arterial COHb levels are almost identical.

Airway
- Airway injury and edema often occur during smoke inhalation, which may require emergent airway management.

Induction
- Avoid cardiac depressant agents.

Maintenance
- 100% O_2 (no N_2O)
- Assess muscle weakness to guide dosage of muscle relaxant.

Extubation
- Ensure CNS status permits natural airway maintenance and protection.

Adjuvants
- Consider treatment for concomitant cyanide poisoning.

Postoperative Period
- Maintain 100% O_2.
- Consider hyperbaric O_2.

Anticipated Problems/Concerns
- Heart and brain affected most.
- Follow CNS function carefully.
- Seek concomitant smoke inhalation injury and cyanide toxicity.
- CO toxic in trace quantities (breathing 0.1% inspired CO for 1 h results in significant toxicity, with COHb ~30%); CO not detectable with conventional gas analysis instruments (e.g., capnographs, mass spectrometers).
- Standard pulse oximeters do not specifically measure COHb, and SpO_2 measurements are only minimally affected, even by severe CO poisoning.

Carcinoid Syndrome

Stanley H. Rosenbaum | Ranjit Deshpande

Risk
- Carcinoid is the most common GI endocrine tumor.
- 15 cases in 1 million population per y.
- Seen in fewer than 20% of pts with carcinoid.

Diagnosis
- Urinalysis for 5-HIAA and serotonin levels
- Platelet serotonin levels
- Serum chromogranin A
- CT scan and MRI
- Octreoscan and MIBG

Perioperative Risks
- Associated with pt's ability to tolerate abrupt hemodynamic change and/or bronchospasm

Worry About
- Abrupt Htn or hypotension with stress
- Right-sided valvular heart disease

Overview
- Endocrinologically active tumor from GI mucosa
- May release histamine-like substances, leading to hypotension and bronchospasm, or may release serotonin, leading to hypertensive reactions (and hypovolemia)
- Commonly found in ileum or rectum; less so in pancreas and lung
- Systemically active when metastatic to liver, or when released substances avoid metabolism by liver (carcinoid syndrome)
- Left-sided cardiac disease in 10% of pts if there is a pulmonary carcinoid

Etiology
- Acquired disease.
- Electrolyte disturbances (due to intestinal secretion of sodium, potassium, and water)
- Bronchospasm
- May be associated with other ectopic humoral tumors, such as MEN 1 syndrome.

Usual Treatment
- Surgery or arterial embolization to reduce tumor burden.
- Histaminic effects blocked only partially by H_1 and H_2 blockers, mainly H_2.
- Somatostatin analogues octreotide and lanreotide block humoral release.
- Interferon α (alpha) and cytotoxic agents may control symptoms.
- Surgical treatment can play a role in metastasis to the liver.
- No specific medical Rx for established valvular heart lesions.
- Catecholamines may increase humoral release and worsen symptoms.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Cutaneous flushing, lacrimation Pellagra-like skin lesions	Episodic flushing induced by stress, eating, alcohol consumption	Hyperkeratosis, hyperpigmentation	
CV	Histamine-induced hypotension Serotonin-induced Htn Endomyocardial fibrosis, especially in right heart	Sx of right-sided CHF	Murmurs of pulmonic stenosis, tricuspid regurgitation, ascites, edema	ECHO Cardiac cath
RESP	Bronchospasm Endobronchial tumor with obstruction	Episodic asthma poorly responsive to medication Focal wheeze at site of obstructing tumor	Wheezing associated with episodes of flushing	
GI	Diarrhea Obstructing tumor	Episodic watery diarrhea		Bowel films, hepatic CT, ultrasound, angiograms
ENDO	Serotonin secretion			Urinary 5-HIAA levels elevated in most pts Occasionally need to measure plasma histamine
RENAL	Dehydration from chronic vasospasm or diarrhea			BUN/Cr, lytes
CNS	Hemodynamic instability, vasodilation	Hypertensive headache Syncope with flushing		
MS	Cutaneous flushing, lacrimation Pellagra-like skin lesions	Episodic flushing, induced by stress, eating, alcohol consumption	Hyperkeratosis, hyperpigmentation	

Key References: Mancuso K, Kaye AD, Boudreaux JP, et al.: Carcinoid syndrome and perioperative anesthetic considerations, *J Clin Anesth* 23(4):329–341, 2011; Poell B, Al Mukhtar A, Mills GH: Carcinoid: the disease and its implications for anesthesia, *Contin Educ Anaesth Crit Pain* 11(1):9–13, 2011.

Perioperative Implications

Preoperative Preparation
- Assess adequacy of electrolyte and fluid balance.
- Assess right-sided valvular status.
- Somatostatin analogue (octreotide) available; its use has dramatically decreased hazards of anesthesia for pts with carcinoid syndrome.

Monitoring
- Expect rapid fluctuation of BP.
- Central venous pressures may not correlate well with fluid volumes.

Airway
- Risk of stress-induced wheezing (Rx: somatostatin analogue)

Induction
- Chronic vasoconstriction and diarrhea may cause hemodynamic instability.

Maintenance
- Volume assessments complicated by changing vascular tone
- Cardiac function limited by right-sided valvular lesions

Extubation
- Possible stress-induced hemodynamic instability (Rx: Somatostatin analogue)

Adjuvants
- Caution: Catecholamines may increase humoral release and worsen symptoms.
- Somatostatin analogue for hypotension or hypertension or bronchospasm has dramatically decreased anesthesia risk for pts with carcinoid syndrome.

Postoperative Period
- Humoral effects of hemodynamically active metastatic carcinoid usually not eliminated by surgery

Cardiac Tamponade

Mark J. Baskerville

Risk

- Overall incidence: 2 pts per 10,000 population
- 2% incidence due to trauma in penetrating injuries
- Post-cardiac surgery: Greater incidence after valve replacement (0.6%), compared to CABG (0.2%)

Perioperative Risks

- Early diagnosis and prompt treatment are crucial in mitigating mortality and morbidity.
- Effusion can irritate myocardium, causing atrial and ventricular dysrhythmias.
- Regional cardiac tamponade is more common after cardiac surgery, where a localized effusion or hematoma compresses a single chamber.
- Sudden death from cardiac tamponade typically presents as a PEA arrest.

Worry About

- Sudden deterioration in hemodynamics
- Catastrophic cardiac collapse upon anesthetic induction and/or mechanical ventilation
- Uncontrolled bleeding
- End-organ injury from poor perfusion
- Rebound hypertension after release of tamponade

Overview

- Pericardial effusion is the anatomic diagnosis, whereas tamponade is the pathophysiologic diagnosis resulting in obstructive shock.
- Pericardial sac normally contains ~20 mL of fluid. It is the duration of time that an effusion accumulates that determines the likelihood of an acute tamponade.
- The pericardial pressure-volume curve is exponential in that once the effusion exceeds the limit of pericardial stretch, small increments of fluid create a steep rise in pressure.
- Transmural pressure = P_{in}(chamber) – P_{out}(pericardial), such that when the transmural pressure becomes negative, the chamber collapses.
- A compensatory sympathetic response leads to tachycardia and systemic vasoconstriction in order to maintain cardiac output and BP. Loss of endogenous sympathetic tone (e.g., induction of anesthesia) can lead to cardiovascular collapse.
- As the stroke volume becomes fixed, cardiac output becomes dependent on heart rate.
- Ventricular interdependence occurs when the septum shifts during the respiratory cycle due to the external constraint of the tightening pericardial sac. During inspiration, the septum shifts to the left, decreasing the LV stroke volume. During expiration, the septum shifts to the right, decreasing RV filling. However, the opposite occurs in positive-pressure ventilation.
  - Pulsus paradoxus: An exaggerated drop in systolic BP (>10 mm Hg) with spontaneous inspiration.
  - Beck's triad: Hypotension/JVD/muffled heart tones.
  - CXR: Cardiomegaly with globular heart.
  - ECG: Sinus tachycardia, low voltage, PR depression, diffuse ST elevations, and electrical alternans.
  - CVP tracing: The y descent is abolished due to an increase in intrapericardial pressure, preventing diastolic filling of the ventricles.
  - PA catheter: Equalization of diastolic pressures across chambers.
  - ECHO: RV can collapse in early diastole and RA can collapse in late diastole. LA collapse is rare, but highly specific for tamponade. One may see the heart swinging within effusion. IVC dilation without respiratory variation correlates with elevated right atrial pressure in tamponade. Doppler study may demonstrate substantial variation in transvalvular flow velocities with respiratory cycle.
- Be suspicious of localized clot in post–cardiac surgery that may not be evident on transthoracic ECHO.

Etiology

- Post cardiac surgery (valves > vessels)
- Thoracic aortic dissection
- Traumatic mediastinal injury
- Pacemaker lead perforation
- Malignant effusion (especially breast and lung)
- Mediastinal radiation
- ESRD (uremic effusion)
- Post MI (Dressler syndrome, ventricular wall rupture)
- Infectious (viral, fungal, TB)
- Myxoedema
- Collagen vascular disease (lupus, rheumatic disease)

Usual Treatment

- Pericardiocentesis
- Percutaneous balloon pericardiotomy
- Pericardial subxiphoid window
- Mediastinal exploration

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension Tachycardia Poor perfusion	Lethargy Pleuritic chest pain	Distant heart tones JVD Friction rub	ECG ECHO
RESP	Dyspnea	Orthopnea Poor exercise tolerance	Rales Cyanosis	CXR
RENAL	Oliguria Metabolic acidosis	Weight gain	Edema	Creatinine Lactic acid

Key References: Spodick DH: Acute cardiac tamponade, *N Engl J Med* 349:684–690, 2003; O'Connor CJ, Tuman KJ: The intraoperative management of patients with pericardial tamponade, *Anesthesiology Clin* 28:87–96, 2010.

Perioperative Implications

Preoperative Preparation

- Ensure adequate preload with cautious volume administration.
- Vasopressors and inotropes readily available.

Monitoring

- Routine ASA monitors.
- Arterial line
- CVP +/– PA catheters advantageous, but not mandatory
- TEE ideal

Airway

- Full stomach precautions with emergent procedures

Preinduction/Induction

- "Full, Fast, and Tight."
- Ketamine is an ideal induction agent, since it increases heart rate, contractility, and systemic vascular resistance, while maintaining spontaneous ventilation.
- Maintain spontaneous ventilation; consider inhalational induction.
- Decompression of tamponade via subxiphoid cardiac window under local anesthesia prior to induction of general anesthesia may be necessary.

Maintenance

- If mechanical ventilation is necessary, use low tidal volumes and minimize PEEP until tamponade is relieved.
- May need to quickly deepen anesthetic to overcome sympathetic surge after pericardium is decompressed.
- Coagulopathy and anemia should be treated promptly with transfusion of blood products.

Extubation

- Low threshold to keep pt intubated until stability confirmed

Adjuvants

- Vasodilators and beta blockers readily available to treat residual sympathetic surge.

Postoperative Period

- Vigilance for recurrent effusion/tamponade.
- Postdrainage pulm edema more common after large-volume drainage.
- ICU care generally warranted.

Anticipated Problems/Concerns

- Sudden cardiovascular collapse with transition to positive pressure ventilation.
- Rebound hypertension/tachycardia after relief of tamponade.
- Atrial fibrillation may necessitate emergent cardioversion.
- Myocardial ischemia or stunned myocardium.

Cardiomyopathy, Alcoholic

Gregory H. Botz | Marian E. Von-Maszewski

Risk

- Incidence in USA: 15–20 million chronic heavy ethanol users.
- As much as 50% of dilated cardiomyopathy may be ethanol-related.
- Population at risk: Unclear; likely includes chronic ethanol users with at least 90 g of daily ETOH for at least 5 y (1 standard drink =12 g ETOH).
- Gender: Male predominance.

Perioperative Risks

- Alcohol withdrawal
- CHF
- Dysrhythmias common: AFIB, PAC, PVC
- Hypomagnesemia and hypokalemia common

Worry About

- Myocardial ischemia: Supply < demand (CAD rare).
- Abnormal systolic and diastolic function.
- Chronic alcohol use alters myocardial response to inotropes, especially epinephrine.
- Alcohol withdrawal symptoms.

Overview

- Insidious onset; Sx uncommon unless severely stressed until late in course.
- Dilated cardiomyopathy: Ventricular hypertrophy early, chamber dilation later.
- Low-output cardiac failure (as compared with high-output failure in cirrhosis and beriberi).
- Malnutrition often coexists.

Etiology

- Direct myocardial damage by ethanol and its metabolites
- Progressive chamber dilation and ventricular hypertrophy; microscopic fibrinoid deposition
- Possible intracellular calcium dysregulation
- Possible muscle excitation-contraction impairment

Usual Treatment

- Abstinence: Ventricular function improves markedly after abstinence.
- Pharmacologic management: Digitalis, diuretics, beta-blockers, and ACE inhibitors.
- Address nutritional deficits, thiamine, folate, and multivitamins.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Plethora, reflux, esophageal varices, friable mucosa	Reflux Sx Hematemesis	Spider angiomata	Endoscopy
CV	LV dysfunction CHF Myocardial ischemia Dysrhythmia	Fatigue, orthopnea PND Rare angina Palpitations	Narrow pulse pressure Cardiomegaly S_3, S_4, murmur JVD, peripheral edema	ECG ECHO Stress testing
RESP	Pulm edema	Dyspnea Cough	Rales	CXR
GI	Hepatic congestion	Poor appetite, distention	Hepatomegaly	PT, albumin, LFTs
HEME	Coagulopathy, Anemia	Abnormal bleeding	Pallor ecchymosis	CBC, PT/PTT, plt
RENAL	Decreased renal perfusion	Oliguria		Cr, FEN_a
CNS	Poor perfusion Cerebral atrophy	Confusion	Abn mental status	
MS	Proximal muscle weakness Peripheral neuropathy		Proximal limb weakness and muscle atrophy	

Key References: George A, Figueredo VM: Alcoholic cardiomyopathy: a review, *J Card Fail* 17(10):844–849, 2011; Fox CJ, Liu H, Kaye AD: The anesthetic implications of alcoholism, *Int Anesthesiol Clin* 49(1):49–65, 2011.

Perioperative Implications

Preoperative Preparation

- Pharmacologic management of CHF.
- Correct electrolytes.
- Consider neuraxial anesthesia, if appropriate, to reduce afterload.

Monitoring

- ECG with ST-segment analysis.
- Consider arterial pressure cath, pulm artery cath, TEE depending on surgery, and ventricular function.

Airway

- NG tube placement risky in presence of varices

Preinduction/Induction

- Pt may have intravascular volume depletion.

Maintenance

- Avoid tachycardia and increased sympathetic activity.
- Avoid depression of myocardial contractility.
- Prevent increases in afterload to maintain cardiac output.

Extubation

- Routine

Postoperative Period

- Consider monitoring in critical care unit.
- Observe for ethanol withdrawal.
- Effective pain management avoids increases in SVR and heart rate.

Adjuvants

- Multivitamins, thiamine, B_{12}, and folate.
- Consider benzodiazepines, α_2 agonists for prophylaxis against withdrawal symptoms.
- Volume of distribution may be increased; consider adjusting drug dosages.

Anticipated Problems/Concerns

- Postop ventricular dysfunction and CHF can occur.
- Alcohol withdrawal symptoms can develop.

Cardiomyopathy, Dilated

Andrew Oken

Risk

- Accounts for approximately ~10,000 deaths and ~46,000 hospitalizations per year in USA; idiopathic DCM is one of the primary indications for cardiac transplantation.
- Often ages ~20–60 y old but can affect older and younger pts as well.
- African-Americans > Caucasians; males > females

Perioperative Risks

- CHF and dysrhythmias and hemodynamic instability.
- Morbidity and mortality directly related to severity of cardiomyopathy and complexity of surgery.

Worry About

- Compromised myocardial function and hemodynamic instability.
- Management strategies periop include pharmacologic and mechanical support options.
- Dysrhythmias and management of CRT/ICD devices..
- Meticulous assessment and management of periop volume status.

Overview

- DCM is characterized by myocyte death and fibrosis, leading to impaired myocardial contraction, chamber dilatation, and LV and/or RV failure.
- Dilation and diminished systolic function (EF <40%) lead to heart failure, often manifesting initially with dysrhythmias or sudden cardiac death.
- Presentation and clinical course varies tremendously, but pts are commonly found to have symptoms of heart failure with diminished exercise tolerance and dyspnea, orthopnea, and PND.

- Discovery of cardiomegaly on physical exam or CXR or ECHO may also lead to the diagnosis or may present with dysrhythmias, conduction delays, or sudden death.
- Sx are often gradual in onset and initially underappreciated until cardiac function is notably compromised, although it may present more acutely depending on etiology.
- The clinical course is variable from gradual deterioration to rapid decline.
- Diagnostic evaluation begins with a thorough history and physical exam and progresses to include lab testing and ECG, ECHO, coronary angiography, and endomyocardial biopsy.
- Assessment of myocardial function and reserve are important in guiding periop management.

Etiology

- 50% of cases are idiopathic, ~9% myocarditis, and ~7% ischemic; others include infiltrative, peripartum, Htn, HIV, connective tissue disease, toxins including substance abuse, ETOH, doxorubicin, endocrinopathies, genetic diseases, and multiple others, although in lesser frequency. Interestingly, genetic abnormalities are being increasingly recognized.

Usual Treatments

- The molecular complexity of DCM affords limited focused disease-modifying interventions or therapies.
- Nevertheless, attempt to identify and address remediable causes (e.g., ETOH and other toxins or exposures, ischemia).
- Treat any associated comorbidities that may be contributing to clinical decline (e.g., ischemia, Htn, anemia, toxins, DM, deconditioning, obesity).
- Standard appropriate therapies for heart failure should already be established and have been initiated and optimized preoperatively, including ACE inhibitors or ARBs, beta-blockers, diuretics, aldosterone antagonists, and so forth.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Depressed myocardial function Dysrhythmias CHF	Fatigue, decreased exercise capacity DOE, PND Orthopnea	Cardiomegaly, elevated JVP, S_3, abdominojugular reflex, peripheral edema, pulsus alternans	ECHO, ECG, CXR Stress test, cardiac cath
RESP	Pulmonary congestion and edema	Dyspnea Cough	Rales and pulmonary congestion, diminished breath sounds, Cheyne-Stokes breathing	PFTs, CXR, ABGs
GI	Visceral engorgement Hepatic congestion Coagulopathy	Weight loss, bloating, fullness, easy bruisability	Ascites, hepatic congestion	Liver enzymes, liver synthetic function (albumin, PT/INR, LFTs)
RENAL	Decreased renal perfusion	Changes in urinary frequency, oliguria	Peripheral edema	BUN/Cr, Na+/K+
CNS/PNS	Diminished perfusion	Cool extremities and confusion	Mental status assessment	Consider carotid US, head CT

Key References: Jefferies JL, Towbin JA: Dilated cardiomyopathy, *Lancet* 375(9716):752–762, 2010; Mann, Zipes DP, Libby P, Bonow RO: DL: *Braunwald's heart disease: a textbook of cardiovascular medicine,* ed 10. Philadelphia, PA, 2015, Elsevier.

Perioperative Implications

Preoperative Preparation

- Determine stability of Sx and whether heart failure is appropriately optimized and compensated.
- NYHA classification and functional assessment helpful to assist in guiding periop management planning and strategy.
- Optimization of heart failure therapy and volume status; consider preop admission to facilitate.
- Continue pharmacologic regimen, especially maintenance therapies and inotropes.
- CRT/ICD devices should be interrogated, and perioperative management strategies understood and coordinated among services (i.e., cardiology, ICU, anesthesiology, and surgical teams).
- Considerations for invasive monitoring, inotropic support, possible postop ICU management, and ventilator support.

Monitoring

- Routine standard ASA monitors
- Considerations for invasive monitoring (arterial line, CVP and/or PA cath) and intraoperative TEE dictated by myocardial reserve
- Focus on early recognition and treatment of anticipated hemodynamic instability
- TEE and/or PAC for assessment of continuous volume and myocardial function

Airway

- Routine

Preinduction/Induction

- Anticipate diminished myocardial performance and reserve and hence intolerance of myocardial depressant effects and vasodilatory effects of medications/anesthetics at time of induction and anesthetic maintenance.
- Periop volume status and fluid management are paramount.
- Attempt to minimize myocardial depressants and maintain physiologic baseline filling pressures (i.e., afterload and preload status; assumes pt hemodynamically optimized preop).

Maintenance

- Minimize myocardial depressants and optimize fluid management with vigilant surveillance of volume status.
- Narcotic-based anesthetic to minimize myocardial depression of potent inhalational agents.
- Optimize myocardial contractility and afterload reduction, PVR, and preload.
- Caution regarding RV failure and precipitants of elevated PVR (e.g., hypoxia, hypercarbia, acidosis, catecholamines).

Adjuvants

- Consider neuraxial or regional anesthetic techniques.
- Immediate availability of therapeutic options for treatment of pulm Htn (e.g., consider iNO, prostacyclin, or nebulized iloprost).
- Inotropes for LV and RV support, vasoconstrictors, and vasodilators; often includes combinations of dobutamine, epinephrine, milrinone, amrinone, norepinephrine, and/or vasopressin, as indicated by hemodynamic status.
- Periop pharmacologic inotropic support often includes combinations of dobutamine, epinephrine, milrinone, amrinone, norepinephrine, and/or vasopressin, as indicated by hemodynamic status.
- Depending on the procedure and the clinical status and degree of myocardial decompensation, patient may require periop mechanical support (e.g., IABP, impella, VAD).

Extubation

- Routine with the caveat that potential for periop hemodynamic instability must be considered in decision making for timing of extubation.
- Cautiously manage emergence hemodynamics.
- May be delayed given cardiopulmonary insufficiency.

Postoperative Period

- Possible ICU management, including ongoing ventilator and hemodynamic support particularly for large volume shifts, complex procedures, and/or preop decompensation
- Meticulous ongoing volume assessment and management

Anticipated Problems/Concerns

- Diminished physiologic reserve, CHF, dysrhythmias, and hemodynamic instability; RV and LV failure and pulm Htn

Cardiomyopathy, Hypertrophic

Stavroula Nikolaidis

Risk

- Relatively common inherited disorder; 0.2% or 1 in 500 Americans are affected. It is equally distributed between males and females and has no racial group predominance. The median age of clinical manifestation is 35 years, but it can manifest in any age.
- The clinical presentation is variable, reflecting a diverse genetic background. Pts may be totally asymptomatic or present with MI, CHF, arrhythmias, or even sudden death. HCM is not an infrequent cause of SCD in young athletes.
- Pts with the disorder may be asymptomatic (20–25%) or undiagnosed at the time of anesthetic. Anesthesia may "unmask" HCM.

Perioperative Risks

- Dynamic LV outflow obstruction (either at rest or provoked) is present in approx 60% of pts with HCM, which is a risk of hemodynamic instability.
- Risk for heart failure and pulm edema from impaired relaxation and diastolic dysfunction from a hypertrophic and noncompliant LV.
- Risk for myocardial ischemia and injury, even in the absence of obstructive CAD, due to increased myocardial O_2 demand (LVH, high intraventricular pressure) and limited supply (impaired coronary reserve, due to dysfunction of the coronary microvasculature).
- Supraventricular (atrial fibrillation) and ventricular dysrhythmias.

Worry About

- Factors that aggravate or trigger dynamic outflow obstruction can cause hemodynamic compromise, such as decreased preload and afterload, decreased end diastolic volume, increased sympathetic activation (from pain, surgical stimulation, medications), increased LV contractility, and tachycardia.
- Myocardial ischemia (even with "normal" coronary angiogram or radionuclide imaging).
- Diastolic dysfunction; heart failure difficult to control with traditional diuresis (caution with volume depletion).
- Arrhythmias: Supraventricular and ventricular dysrhythmias may cause hemodynamic instability, increase the risk of embolic stroke (AFIB), and cause shortness of breath or CHF (diastolic dysfunction).
- Pts with HCM who undergo noncardiac surgery bear a higher risk for periop MI, death (4.2%), and higher incidence of periop complications.

Etiology

- Genetic disease with autosomal dominant inheritance and extremely heterogeneous genotype. Over 1400 mutations have been identified in at least 11 genes. This is most likely the reason for the extremely variable genetic expression or phenotype. Mutations that encode for the myosin heavy chain (MYH7) and myosin-binding protein C3 account for 70%–80% of sarcomeric mutations. Genetic testing is recommended for pts and their first-degree relatives.

Overview

- Synonyms: HCM has replaced the following older terms: muscular subaortic stenosis, idiopathic hypertrophic subaortic stenosis, hypertrophic obstructive cardiomyopathy, and asymmetric septal hypertrophy.
- Definition: Hypertrophied and abnormally thickened LV, nondilated (except at end stage), often asymmetrical, in absence of other cardiac or systemic causes for LVH (e.g., AS or Htn), associated with myocardial disarray.
- Pathophysiology: The structural cardiac abnormalities in HCM are
  - Histopathologic picture consists of myocytes that are not aligned parallel but form a disorganized pattern (myocardial disarray).
  - Through the disease process, the myocardial microvasculature develops increased vessel wall to lumen ratio, which leads to dysfunction. Thus over time, affected myocardium with microvascular dysfunction can develop ischemia, injury, and chronic fibrosis.
  - Remodeling changes start and evolve before onset of symptoms.
- Clinical presentation: Clinical manifestations of HCM relate to
  - Diastolic heart failure (dyspnea, fatigue, exercise intolerance);
  - Ischemia (angina, MI, often in the absence of obstructive CAD);
  - Arrhythmias (dizziness, palpitations, syncope/sudden death);
  - LVOT obstruction (dizziness, hypotension, shortness of breath, syncope); or
  - Mitral regurgitation (SOB, CHF, pulm edema, pulm Htn).

  There is a wide clinical spectrum of presentations that varies from totally asymptomatic to severely symptomatic. Approximately one-third of pts with HCM do not have LVOT obstruction at rest or with provocative maneuvers (peak gradient <30 mm Hg); a third do not have LVOT obstruction at rest but will develop with provocative maneuvers (Valsalva, inhalation of amyl-nitrate a potent vasodilator or sympathetic stimulation, administration of catecholamines, exercise, tachycardia, hypovolemia, post PVC); and a third of HCM pts have LVOT obstruction at rest (peak gradient >30 mm Hg), which worsens with provocative maneuvers.
  - Morphologic characteristics, a mechanism of LVOT obstruction, include:
  - LV wall thickness—The majority of the patients have LVH with normal systolic function and LVEF in the 70% range, with almost obliteration of the LV cavity at end systole. Disproportionately thick intraventricular septum is seen in approximately 90% of cases (>13 mm, >15 mm in hypertensives), with septal wall thickness to posterior wall thickness ratio >1.3. The risk of sudden death is significantly elevated: 18/1000 person-years when wall thickness is >30 mm. Patients with mid septal thickening, which is the most prevalent type, are symptomatic at a younger age and have a larger LV mass, which is associated with a higher incidence of sudden death and worse symptoms (NYHA 3 or 4 symptoms and grade 3 or restrictive diastolic dysfunction by ECHO).
  - The mitral valve—The specific morphologic characteristics of the mitral valve apparatus in HCM plays an important role in the development of dynamic LVOT obstruction. More specifically, (1) the anteriorly positioned papillary muscles that support the leaflets of the mitral valve, (2) elongated or redundant mitral valve leaflets, (3) thickened intraventricular septum, and (4) normal or hyperdynamic LV systolic function contribute to narrowing of the LVOT and most likely predispose to abnormal systolic anterior motion of the anterior mitral valve leaflet (SAM) toward the intraventricular septum. SAM further narrows the LVOT, which results in generation of the dynamic systolic flow gradient across the LVOT. SAM is the main mechanism of MR in HCM, with LVOT obstruction in the absence of intrinsic mitral disease. A posteriorly and laterally directed MR jet is generated, which peaks in mid- to late systole. It is a dynamic jet that improves as the gradient across the LVOT decreases with appropriate management and worsens with provocative maneuvers.
  - Mechanism of LVOT obstruction: Recent studies have shown that the mechanism of SAM is not the venturi forces generated from the high-velocity flow through the LVOT as we used to believe. It is rather a flow-drag phenomenon: as the LV diastolic inflow (normally directed posteriorly) passes via the anteriorly displaced mitral valve, it forms an anteriorly directed jet that hits the intraventricular septum. Then, as blood flow is directed posteriorly, it forms the outflow jet, directed from the posterior wall toward the LVOT, and drags the mitral valve leaflets even more anteriorly toward the LVOT in a flow-drag phenomenon.

    Risk factors for SAM and LVOT obstruction are anteriorly placed mitral valve and papillary muscles, posterior mitral annular calcifications, mid septal hypertrophy, mitral leaflet c-sept <2.5 cm, anterior to posterior mitral valve leaflet ratio <1.3, and normal LV systolic function with small ventricular cavity.
  - In cases of severe HCM with small ventricular cavity, in the absence of LVOT obstruction or aortic stenosis, significant systolic intraventricular outflow gradient may be generated from the severely thickened myocardium.
  - In 10–20% of cases, significant intrinsic mitral valve disease coexists. In such cases, the mitral regurgitation does not improve, despite significant decrease of the LVOT gradient with appropriate management.
  - Approximately 10% of cases progress to terminal stages with advanced fibrosis, significant LV dilation, and decreased LVEF. This resembles dilated cardiomyopathy and has poor prognosis.
- Diagnostic modalities: Because the clinical presentation resembles that of fixed AS, or coronary artery disease, the following diagnostic modalities aid in the differential diagnosis:

  ECG: Indicates changes associated with LVH, not specific to HCM: SR or supraventricular arrhythmias like AFIB, pathologic Q waves, poor R wave progression in the precordial leads, S in V_1 >35 mm, R in V_5 >35 mm, intraventricular conduction delay with QRS duration >0.12 ms, left axis deviation, left anterior fascicular block, LBBB, characteristic deep T-wave pattern in more than 2 leads, ST depression.
  - ECHO: 2D, 3D, and Doppler ECHO, via TTE or TEE route, are extremely helpful in diagnosis and assessment of the severity, differential diagnosis and risk stratification of HCM. ECHO measurements are also used to tailor management in the chronic or perioperative setting (particularly identifying whether there is LVOT obstruction and the severity of), assess the effectiveness of intervention, identify additional pathology, or risk stratify and determine the prognosis. Typical findings are LVH, LVEF >60–70%, +/−LVOT gradient at rest or with provoking maneuvers, SAM, MR, or other mitral valve abnormalities.
  - Newer developing ECHO modalities, TDI and Strain, are more sensitive in identifying contractile dysfunction or impairment of the lusitropic ability of the myocardium while the LVEF is still normal and before changes appear on ECG. These techniques may be utilized to differentiate between LVH from chronic Htn and HCM. The presence of SAM is not pathognomonic for HCM. SAM has been noted to happen occasionally after mitral valve repair and has also been observed in elderly pts with chronic Htn, normal LVEF, sigmoid septum, and calcified mitral valve leaflets in the presence of provocative conditions such as hypovolemia and hypotension.

- Cardiac cath: Frequently performed to exclude CAD and confirm the diagnosis, or "localize" the gradient (differentiate from AS) when ECHO images are suboptimal.
- Cardiac MRI and CT scan: MRI and CT scan images provide great description of the anatomy helpful if surgery is planned but no information regarding the hemodynamics. MRI images with late gadolinium enhancement are indicative of myocardial fibrosis which is associated with higher incidence of cardiovascular events.
- Other tests such as Holter, exercise stress ECHO, and myocardial biopsy may be used on an individual basis to provide additional information.
- Treatment: The therapeutic goal is to alleviate symptoms with agents and techniques that improve the diastolic dysfunction and decrease the LVOT gradient and MR. Prophylactic AICD is placed in high-risk pts. Arrhythmia management with cardioversion, EP study/ablation, and antiarrhythmic medications are often needed. Pacemaker or resynchronization therapy helps improve symptoms in cases of branch block and needed in complete heart block.
  - Pharmacologic: Agents that decrease the heart rate and contractility, such as beta blockers and Ca^{2+}-channel blockers, as well as antiarrhythmics (disopyramide), are commonly used.
  - Surgical: Septal myomectomy is the gold standard for the correction of LVOT obstruction in pts with disproportionately thickened septum who are refractory to medical management. It may need to be combined with mitral valve repair or replacement. Complications include VSD (high risk if preop septal wall thickness is <20 mm), heart block, severed septal perforator coronary artery, and AI. Mortality rate is 1–2% in experienced high volume centers.
  - Percutaneous intervention: Septal ablation by alcohol injection is reserved for pts with intraventricular septum thicker than 16 mm, who are not surgical candidates and do not have mitral valve pathology. Complications include RBBB in 50% of cases, MI, ethanol injection in the wrong artery, ventricular septal rupture, heart block, and coronary dissection.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia	Angina	Worse with nitrates (avoid)	ECG, exercise tests, coronary angio (may be "normal"), cardiac MRI
	LVOT obstruction	Dyspnea, syncope, dizziness	Systolic murmur accentuated by Valsalva	ECHO
	Mitral regurgitation	Dyspnea	Holosystolic murmur	ECHO
	Dysrhythmias	Syncope, sudden death, palpitations	Rales, wheeze, edema	ECG, Holter
	Diastolic dysfunction	Dyspnea		ECHO, CXR
RESP	Pulm congestion Secondary pulm Htn	Dyspnea, orthopnea	Rales, wheeze	CXR Right heart cath
CNS	Syncope	Syncope, presyncope		Negative CNS work-up

Key References: Pollack LC, Barron ME, Maron BJ: Hypertrophic cardiomyopathy, *Anesthesiology* 104(1):183–192, 2006; Hensley N, Dietrich J, Nyhan D, et al.: Hypertrophic cardiomyopathy: a review, *Anesth Analg* 120(3):554–569, 2015.

Perioperative Implications

Preoperative Preparation

- Avoid physiologic changes that reduce LV cavity size (maintain preload and afterload; avoid tachycardia).
- Ensure adequate preload, and replace any preop volume depletion.
- Continue beta-blocker, Ca^{2+}-channel blocker, and antiarrhythmic.
- Also note disopyramide (used preop in severe HCM) has anticholinergic activities.
- Sedate adequately to prevent anxiety-induced sympathetic stimulation.
- SBE prophylaxis is not recommended for HCM pts with severe MR unless after surgery, septal myomectomy, or mitral valve repair or replacement.
- ICD/pacemaker interrogation

Monitoring

- Aside from the ASA standard monitors, the decision that additional monitors should be used depends on the surgical procedure, the severity of HCM, presence of CHF, and the pt's condition, in addition to other comorbidities. Invasive arterial pressure monitoring, CVP and/or PA cath, or even the noninvasive PPV could be used as needed for optimal pt management. Transesophageal ECHO is very useful, especially in the event of major blood loss, volume shifts, or sympathetic stimulation are anticipated.

General Anesthesia

- When choosing an induction agent, avoid drug-induced vasodilation or sympathetic activation; etomidate may be advantageous over ketamine or propofol. Ketamine in smaller dosages, as part of a balanced anesthetic, can provide hemodynamic stability in such pts. Ketamine should be avoided in larger doses because of sympathetic stimulation and tachycardia. Propofol should be used with caution; it can be used in incremental doses, but the provider should be ready to promptly correct the blood pressure with alpha agonist. Profound vasodilation caused by large bolus of propofol may be poorly tolerated.
- Phenylephrine infusion (alternatives: vasopressin, norepinephrine) should be immediately available, as worsening dynamic LVOT obstruction is anticipated with any anesthetic provoked decrease in BP and SVR or surgery provoked increase in sympathetic stimulation.
- Avoid prolonged laryngoscopy, as it may induce sympathetic stimulation.
- Insertion of CVP/PAC may be helpful to manage the pt particularly if significant blood loss is anticipated; invasive monitoring may induce atrial or ventricular dysrhythmias.

Maintenance

- Volatile agents that decrease LV contractility without severe vasodilation are desirable. Halothane is the classic example. Likewise, sevoflurane is preferable over isoflurane or desflurane.
- Avoid agents that decrease preload and afterload (e.g., nitroglycerin, nitroprusside) or increase contractility (inotropes), as well as agents associated with significant histamine release.
- Avoid agents that directly or indirectly increase HR and contractility (e.g., pancuronium, atropine, epinephrine, ephedrine).
- Promptly treat hypotension with volume expansion (avoid anemia; promptly replete blood loss) or pure alpha-adrenergic agonist (e.g., phenylephrine).
- Consider early electrical cardioversion for atrial fibrillation. Defibrillator available in OR.
- Consider beta-blockade or Ca^{2+}-channel blockade to prevent and treat tachycardia, LVOT obstruction, or ischemia.
- Although pulm edema from diastolic dysfunction and MR is difficult to treat (use diuretics very judiciously), patients with severe LVH and diastolic dysfunction are prone to develop CHF easily from volume overload. Careful fluid balance is necessary.
- Secondary PHT from HCM with MR worsens with "conventional" pulm vasodilators (increase LVOT obstruction). MR will improve with relief of LVOT obstruction.
- It is advisable to maintain minute ventilation by using higher rates and lower tidal volumes (higher tidal volumes with lower rates will decrease venous return).

Extubation

- Avoid sympathetic stimulation. Ensure adequate analgesia.
- Utilize beta-blockade or Ca^{2+}-channel blockade to abolish sympathetic response during emergence of anesthesia.

Neuraxial Anesthesia

- Although spinal and epidural anesthesia can be performed in pts with HCM, for the reasons mentioned previously, a slow controlled titration of medication via epidural is preferred.

Postoperative Period

- The goal should be aggressive postop pain management for avoidance of sympathetic stimulation from pain. Nerve blocks are preferred. Some pts without severe disease might tolerate epidural, as long as the anesthetic is titrated slowly. Epidural narcotic analgesia can be used when indicated.

Cardiomyopathy, Ischemic

Cory D. Maxwell | Jonathan B. Mark

Epidemiology

- Approximately a 1:1000 incidence per y, increasing with age.
- M:F incidence ratio: 2:1.
- Most common cause of heart failure; accounts for 40% of all cases.

Perioperative Risks

- CHF exacerbation
- Hypotension
- Pulmonary edema
- Myocardial ischemia/infarction
- Acute renal failure
- Malignant arrhythmias/pacemaker management with electrocautery
- LVEF, which is important for prognosis and periop complications but may not correlate with symptoms or exercise tolerance

Worry About

- Acute heart failure (hypoventilation → hypercarbia → increased PVR → right heart failure)
- Inability to extubate (cardiac instability, pulmonary edema)
- Periop cardiac event (MI)
- Fluid management (balance optimizing preload with volume overload, minimizing fluid shifts)
- High risk for arrhythmia (PAC, PVC, AFIB, Vtach, VFIB)
- Postop ICU care (CCU versus SICU [severity of heart disease versus magnitude of surgery])

Overview

- Severe impairment of LVEF leading to CHF; instances arising from myocardial ischemia and infarction have extremely poor prognoses, with a 30–50% 2-*y* mortality.
- Pts will benefit from optimization of medical therapy for underlying ischemia (nitrates, beta-blockers, calcium antagonists, aspirin), CHF (ACE inhibitors/angiotensin-II receptor blockers, hydralazine, digoxin, aldosterone antagonists, loop diuretics), prevention of cardiac thrombus formation (warfarin), and HR control for atrial fibrillation (digoxin, beta-blockers).
- An ICD for secondary prevention of SCD is likely. A mortality benefit exists, especially if LVEF <35%.
- CRT with biventricular pacing improves symptoms in pts with prolonged QRS duration with low LVEF.

Etiology

- Acquired disease with genetic predisposition.
- Risk factors include hypertension, diabetes, hyperlipidemia, tobacco, advanced age, obesity, and peripheral vascular disease.

Usual Treatment

- Medical therapy: ACE inhibitors, beta-blockers, aldosterone antagonists, and continuous IV infusions (end-stage only → milrinone, dobutamine)
- Cardiac rehabilitation: Improved symptoms and functional capacity
- Electrophysiology optimization: AICD insertion and CRT with biventricular pacing
- Associated cardiac surgery: Valvular surgeries, LV aneurysmectomy, and CABG.
- PCI: Only in cases of (1) severe symptoms, (2) exacerbation, (3) failed medical therapy, (4) high risk coronary anatomy, and (5) worsening LV dysfunction
- LVAD: Destination therapy or a bridge to transplantation
- Cardiac transplantation
- Other interventions: Transmyocardial laser revascularization if angina after all of the above
- Possible future therapy: Stem cell and autologous myoblast transplantation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia Arrhythmias CHF	Angina Dyspnea, PND palpitations	S_3, S_4, loud P_2 Narrow pulse pressure Displaced point maximal impulse	ECG Stress testing ECHO Stress ECHO MRI Myocardial contrast ECHO Cardiac catheterization
RESP	Pulm congestion/edema	Dyspnea on exertion Orthopnea Cough	Rales Wheezes	CXR
GI	Ascites	Abdominal distention	Shifting dullness Fluid wave Hepatomegaly	Liver function tests PT Albumin
CNS	Embolic stroke due to thrombus or atheroembolism	Weakness Vision problems Confusion	Altered mental status Focal deficits	CT (early → rule out SAH) MRI (late → confirm ischemia)
MS	Peripheral edema	Swollen ankles Weakness	Pitting edema	
RENAL	Insufficiency (prerenal)	Oliguria		Cr, BUN Excreted fraction of filtered sodium

Key References: Fihn SD, Blankenship JC, Alexander KP, et al.: 2014 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: executive summary, *J Am Coll Cardiol* 64(18):1929–1949, 2014; Hensley NB, Hogue CW*: Anesthesia for non-cardiac surgery in patients with ischemic heart disease*, Waltham, MA, 2015, UpToDate.

Perioperative Implications

Preoperative Preparation

- Pharmacologic control of myocardial ischemia and CHF

Monitoring

- ECG (V_5 or multilead) with ST-segment analysis
- Arterial catheter (close BP monitoring, ABGs) → possibly preinduction
- PA catheter or TEE for major operations and/or poor medical condition

Airway

- None

Preinduction/Induction

- Avoid tachycardia and increased afterload to minimize myocardial oxygen demand.
- Greatest stress for developing myocardial ischemia or LV dysfunction, especially if hypoventilation occurs.
- Relative hypovolemia may result from diuretic therapy.

Maintenance

- Limited ability to increase cardiac output in response to stress; this may require exogenous catecholamines.
- Attention to fluid balance; monitor PAWP to avoid pulmonary edema or low cardiac output.
- Avoid cardiac depressants, including high-dose inhaled anesthetics, high-dose opiates, and alpha-2 agonists.

Extubation

- Another time of significant stress for developing myocardial ischemia or LV dysfunction.
- Consider postop mechanical ventilation if a large fluid resuscitation was required intraop.

Adjuvants

- Extensive preop medical therapy may have circulatory consequences.
- Preop anticoagulation (for CAD or AFIB) may preclude regional anesthesia.

Postoperative Period

- When possible, epidural pain management techniques may minimize sympathetic tone.
- Intensive care and invasive hemodynamic monitoring for major procedures.

Anticipated Problems/Concerns

- Periop myocardial ischemia, arrhythmia, and CHF exacerbation remain paramount concerns.

Cardiomyopathy, Peripartum

Unyime S. Ituk

Risk

- Exact incidence unknown
- Incidence in USA: About 1:3000 to 1:4000 live births
- Incidence higher in African-Americans compared to Caucasians
- Highest incidence in Haiti and parts of Africa

Perioperative Risks

- CHF
- Arrhythmias; atrial and ventricular
- Pulm and systemic thromboembolism

Worry About

- Increased myocardial oxygen demand with progression of pregnancy may exceed myocardial oxygen supply resulting in myocardial ischemia.
- Autotransfusion associated with uterine contractions during labor and involuted uterus after delivery may significantly increase preload resulting in pulm edema.
- Anticoagulation may contraindicate neuraxial anesthesia.
- Inadequate pain control during labor will increase sympathetic drive resulting in increased afterload and worsening of cardiac function.

Overview

- A type of DCM.
- All of the following must be present for a diagnosis: cardiac failure in the last mo of pregnancy or within 5 mo postpartum, no identifiable cause of cardiac failure, absence of heart disease prior to the last mo of pregnancy, ECHO evidence of LV systolic dysfunction.
- Symptoms and signs of heart failure will often develop insidiously and must be discriminated from normal physiologic changes of pregnancy.
- Pt complaints include dyspnea, orthopnea, cough, hemoptysis, malaise, chest or abdominal pain.
- Physical findings include peripheral edema, jugular venous distension, crackles on chest auscultation, a third heart sound, and a new onset regurgitant murmur.
- CXR will reveal cardiomegaly and pulm edema, while ECG may show arrhythmias with nonspecific ST and T wave changes. Dilated hypokinetic ventricles are seen on ECHO.

Etiology

- Exact etiology is unknown.
- Possible etiologies include viral or autoimmune myocarditis, abnormal cytokines, and selenium deficiency.
- Abnormal cleavage product of prolactin inducing apoptosis has also been implicated.
- African-American ethnicity, advanced maternal age, multiple gestation, and hypertensive diseases of pregnancy are contributing factors.

Usual Treatment

- Treatment is mainly supportive and aims to restore normal hemodynamic indices, avoiding further worsening of cardiac function and complications of heart failure.
- Sodium and fluid intake restriction is essential if the pt presents with signs of pulm edema. Diuretics are administered to decrease preload.
- Vasodilators (nitrates or hydralazine) may be useful in reducing afterload if the pt's systolic blood pressure is in an acceptable range.
- In pts with low cardiac output state despite initial therapy, inotropic agents (dobutamine or levosimendan) are indicated.
- Beta-blockers are indicated once pt is clinically stable.
- Anticoagulation is recommended in parturients with LVEF <35%.
- Pts are best managed by a multidisciplinary team.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway edema	Pregnancy	Airway exam	
RESP	Pulm edema	Dyspnea Cough	Tachypnea Rales/rhonchi	CXR
CV	LV dysfunction CHF Myocardial ischemia Arrhythmias	Fatigue, orthopnea PND Chest pain Palpitations	Narrow pulse pressure Cardiomegaly JVD, peripheral edema S_3, S_4, murmur	ECG, BNP CXR, ECHO Troponin
GI	Hepatic congestion	Abdominal pain	Tender hepatomegaly	LFTs, PT, albumin
OB	Decreased placental perfusion		FHR—absent variability	NST, BPP Doppler velocimetry
HEME	Anemia	Fatigue	Pallor	CBC

Key References: Sliwa K, Hilfiker-Kleiner D, Petrie M, et al.: Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy, *Eur J Heart Fail* 12(8):767–778, 2010; Dennis AT: Heart failure in pregnant women: is it peripartum cardiomyopathy? *Anesth Analg* 120:638–643, 2015.

Perioperative Implications

Antepartum management

- Pharmacologic management of congestive heart failure following established guidelines
- ACE inhibitors should be avoided during pregnancy.
- Supplemental oxygen to maintain oxygen saturations ≥95%.

Monitoring

- ECG with ST-segment analysis
- Intra-arterial blood pressure monitoring is indicated
- Consider a CVP or PA cath if patient is in acute heart failure or pulm edema
- TEE is useful for assessing ventricular and valvular function if general anesthesia is used for delivery

Airway

- Airway edema can make management potentially difficult.
- Cautious instrumentation of airway because oral and pharyngeal mucosal surfaces are friable.
- Be prepared for an emergent airway.

Preinduction/Induction

- Combined spinal epidural or epidural analgesia/anesthesia with slow titration of low concentrations of local anesthetic has the advantages of decreasing preload and afterload provided normal blood pressure is maintained.
- The neuraxial block also provides excellent pain control and attenuates the sympathetic response to pain and its effects on the heart.
- If general anesthesia is indicated, the goal is to maintain a low to normal heart rate and avoid hypotension or hypertension.
- An opioid-based induction of anesthesia will avoid the myocardial depression and hypotension associated with large doses of propofol or thiopental.
- Etomidate has also been used for induction of anesthesia.
- Neonatal resuscitation will be required if high-dose opioid is used for maternal induction of anesthesia.
- Avoid aortocaval compression.

Maintenance

- The same principles during induction apply; avoid tachycardia, hypotension, hypertension and depression of myocardial contractility
- Low concentration of inhalational agent <0.75 MAC
- TIVA using remifentanil and propofol has also been reported.
- Cautious use of oxytocin after delivery because of its potential CV adverse effects.

Extubation

- Extubate awake; risk of pulm aspiration of gastric contents.

Postoperative Period

- Consider close hemodynamic monitoring in the critical care unit.
- Medical management of heart failure should continue and addition of ACE inhibitors or ARBs to reduce afterload should be considered.

Anticipated Problems/Concerns

- Acute pulm edema.
- Tachyarrhythmias.
- Pulm and systemic embolism.
- Hemorrhage.

Cardiomyopathy, Restrictive

Pankaj Jain | Andra E. Duncan

Risk

- About 5% of all primary cardiomyopathies.
- Idiopathic type is rare, and may be familial.
- 50% of pts with AL-type amyloidosis are affected.
- Endomyocardial fibrosis is endemic in Africa, Asia, and Central and South America.

Perioperative Risk

- Diastolic dysfunction and low cardiac output state.
- Right heart failure with ascites and congestive hepatomegaly.
- Left heart failure with pulmonary edema.
- Cardiac arrhythmias, especially atrial fibrillation, ventricular arrhythmias, and AV block.

Worry About

- Thromboembolic complications
- Valvular insufficiency
- Autonomic neuropathy causing hemodynamic instability
- Respiratory, renal, CNS, and airway manifestations of underlying disease.

Overview

- Heterogeneous group of diseases characterized by restrictive cardiac physiology and diastolic dysfunction.
- Cardiac amyloidosis is a disorder of extracellular deposition of proteinaceous material in the myocardium and other organs.
- Endomyocardial fibrosis is a restrictive obliterative cardiomyopathy associated with eosinophilia.
- Pathophysiology: Increased stiffness of the myocardium that leads to restrictive ventricular filling with elevated filling pressures and dilated atria.
- Left ventricular systolic function is usually normal.
- Cardiac valves may be affected by infiltrative conditions causing stenosis or regurgitation
- Cardiac amyloidosis has a poor prognosis, especially when LVH, reduced systolic function, and heart failure is present.

Etiology

- Primary restrictive cardiomyopathy includes idiopathic (unknown cause) and genetic causes (mutations of sarcomere proteins including troponin I and T).
- Secondary restrictive cardiomyopathy occurs as part of a multisystem disorder, which include infiltrative diseases (amyloidosis, sarcoidosis, Gaucher disease), storage diseases (hemochromatosis, Fabry disease, glycogen storage disease), autoimmune disease (scleroderma), endomyocardial disease (carcinoid, endomyocardial fibrosis), and as a sequelae of cancer therapy (radiation therapy, anthracycline).

Usual Treatment

- Loop diuretics reduce pulmonary and systemic congestion
- ACE inhibitors and angiotensin receptor blockers may counteract neurohormonal changes associated with heart failure
- Pts with AFIB require rate control with beta-blockers, electrical/pharmacologic cardioversion to restore normal sinus rhythm, and anticoagulation.
- Pacemaker may be required with high-grade A-V block.
- Heart transplantation may benefit pts with advanced disease.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible difficult airway and macroglossia secondary to amyloidosis Uveitis secondary to sarcoidosis Supraglottic granuloma secondary to sarcoidosis	Dyspnea Dysphagia Abnormal speech	Enlarged tongue Cervical lymphadenopathy Conjunctival/iris nodules secondary to sarcoidosis	Careful airway assessment Ophthalmologic evaluation
RESP	Cardiogenic pulmonary edema Pleural effusion Pulmonary hypertension Restrictive lung disease secondary to sarcoidosis	Dyspnea Cough Chest pain Hoarseness	Crackles Rhonchi Stridor	CXR CT chest Spirometry ABG
CV	Diastolic dysfunction Possible LV systolic impairment Bi-atrial enlargement Valvular abnormalities Conduction abnormalities and AV block Atrial/ventricular arrhythmia Small vessel disease secondary to amyloidosis	Dyspnea Orthopnea Edema Enlarged abdomen Syncope Angina	Irregular pulse Elevated JVP Kussmaul sign Hepatosplenomegaly	ECG ECHO Cardiac cath Cardiac MRI Endomyocardial biopsy BNP Holter monitor
RENAL	Nephrotic syndrome secondary to amyloidosis Nephrogenic DI Fanconi syndrome ESRD	Proteinuria Renal insufficiency	Edema Hypertension	BUN/Cr Urine analysis Renal Bx
NEURO	Autonomic/peripheral neuropathy secondary to amyloidosis Cranial neuropathy secondary to sarcoidosis Carpal tunnel syndrome secondary to sarcoidosis/amyloidosis	Paresthesias Weakness Incontinence Diarrhea	Orthostatic hypotension	Tilt table test
GI	Malabsorption (malnutrition) secondary to amyloidosis Ascites GI bleed Gastroparesis Pseudo-obstruction	Weight loss Diarrhea Nausea, vomiting Abdominal pain	Palpable liver and spleen Jaundice and icterus	LFT GI endoscopy and biopsy
HEME	Anemia Thrombocytopenia/thrombocytosis Eosinophilia Plasma cell dyscrasia/multiple myeloma	Bleeding Bruising	Purpura Pallor	CBC Bone marrow aspirate Serum protein electrophoresis Iron studies
ENDO/ METAB	DM in hemochromatosis Hypothyroidism/hypopituitarism secondary to sarcoidosis Electrolyte abnormalities			Basic metabolic panel Serum calcium Fasting blood sugar HbA1c Endocrine evaluation Thyroid function test
MS	Arthropathy/polyarthritis secondary to amyloidosis/sarcoidosis Compression fractures Myopathy secondary to amyloidosis	Bone pain Joint pain	Shoulder pad sign	Joint aspiration Imaging

Key References: Wexler RK, Elton T, Pleister A, et al.: Cardiomyopathy: an overview, *Am Fam Physician* 79:778–784, 2009; Fleisher LA, Fleischmann KE, Auerbach AD, et al.: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 130:2215–2245, 2014.

Perioperative Implications

Preoperative Preparation

- Assess myocardial function and signs of left and right heart failure.
- Evaluate volume status.
- Identify electrolyte abnormalities.
- Assess conduction disturbances and ensure recent pacemaker interrogation.
- Continue perioperative beta-blockade.

Monitoring

- Supplement standard ASA monitors with invasive intra-arterial blood pressure monitoring.
- Central venous access allows monitoring of right-sided pressures and administration of vasoactive and inotropic drugs.
- PA catheter may be useful for assessment of loading conditions and measuring cardiac output in pts with advanced disease.
- Intraop TEE monitoring may be considered when significant fluid shifts are expected and when valvular dysfunction or myocardial depression is present.

Airway

- Macroglossia and laryngeal tumors occur in pts with amyloidosis.
- Supraglottic lesions associated with sarcoidosis may complicate airway management.

Induction

- Maintain preload and adequate heart rate to ensure adequate cardiac output.
- Avoid medications that cause myocardial depression, bradycardia, or decrease venous return.
- Etomidate is suitable because of minimal impact on hemodynamics and myocardial function.
- Ketamine, despite intrinsic cardiodepressant properties, maintains SVR.
- Carefully titrate IV opioids such as fentanyl or sufentanil.
- Caution with neuraxial blockade because of reduced venous return and SVR.

Maintenance

- A balanced anesthesia technique with lower doses of inhaled volatile anesthetics supplemented with opioids can be used.
- TIVA may also be considered.
- Judicious fluid management guided by invasive pressure monitoring, urine output, and other indices of tissue perfusion.
- Maintain normal sinus rhythm with normal heart rate.
- Monitor for hypotension, especially with autonomic neuropathy.

Extubation

- Ensure hemodynamic stability, adequate respiratory drive, and complete neuromuscular reversal.

Postoperative Period

- Ensure adequate cardiac output and end-organ perfusion.
- Postop pain management with central neuraxial blockade entails risk of decreased venous return and reduced SVR.

Anticipated Problems/Concerns

- Management of postop right (hepatic congestion, peripheral edema) and left heart failure (pulm edema).
- Postop AV block and arrhythmias.

Carnitine Deficiency

Marjorie Brennan | Raafat S. Hannallah

Risk

- Rare (1:40,000 in Japan)

Perioperative Risks

- Hypoglycemia triggered by fasting
- Massive rhabdomyolysis and cardiac arrest described following GA and succinylcholine. (The response may be confused with malignant hyperthermia.)
- No evidence that susceptibility to malignant hyperthermia is associated with the carnitine palmitoyltransferase enzyme system

Worry About

- Periop hypoglycemia: Avoid prolonged fasting; IV glucose should be administered
- Neurologic and cardiopulmonary status: Determine if a cardiomyopathy is present

Overview

- CACT and CPT2 are essential cofactors in enzymatic transport of long-chain fatty acids into mitochondria, in which they are oxidized.
- When carnitine is deficient, peripheral tissues cannot use fatty acids for energy production, and the liver cannot adequately make ketone bodies as an alternative substrate.
- The tissues become glucose dependent, and their metabolism exceeds the liver's capacity for glucose production.
- This glucose dependency can lead to severe liver failure (increased hepatic enzymes, lactic acidosis, and encephalopathy) and hypoketotic hypoglycemia.

Etiology

- CACT resulting from mutations in the *SLC22A5* gene, which leads to the production of defective OCTN2 carnitine transporters
- CPT deficiency resulting in impaired transfer of fatty acids into mitochondria
- CPT deficiency associated with rhabdomyolysis and higher incidence of renal insufficiency

Usual Treatment

- Dietary supplementation with L-carnitine and high-carbohydrate diet to prevent hypoglycemia

Assessment Points

System	Effect	Assessment by Hx	Test
CV	Cardiomyopathy		ECHO
HEPATIC	Hypoglycemia Hepatomegaly with fatty infiltration	Lethargy	Blood glucose Bilirubin Liver function tests
HEME	Coagulopathy	Bleeding	Hypoprothrombinemia
CNS	Encephalopathy	Vomiting, diarrhea	Hyperammonemia
RENAL	Renal insufficiency	Recurrent myoglobinuria	BUN/Cr

Key References: Lucas M, Hinojosa M, Rodriguez A, Garcia Guasch R: Anaesthesia in lipid myopathy, *Eur J Anaesthesiol* 17(7):461–462, 2000; Lilker S, Kasodekar S, Goldszmidt E: Anesthetic management of a parturient with carnitine palmitoyltransferase II deficiency, *Can J Anaesth* 53(5):482–486, 2006.

Perioperative Implications

Preoperative Preparation

- Continue daily carnitine therapy.
- Glucose infusion preop.
- Avoid protracted preop fasting.
- For emergency surgery while pt is in metabolic crisis, rehydrate; correct glucose, acid-base, and electrolyte imbalances; use IV carnitine if necessary; treat hypoprothrombinemia with FFP.

Monitoring

- Routine

Airway

- Best to avoid succinylcholine for intubation

Maintenance

- IV glucose infusion and frequent monitoring of serum glucose level.
- Muscle weakness may be present and requires careful titration of muscle relaxant dosing.

Extubation

- No unusual concerns

Adjuvants

- Consider antiemetic prophylaxis to speed resumption of oral intake.

Anticipated Problems/Concerns

- Periop hypoglycemia and metabolic acidosis/decompensation.
- In the presence of carnitine deficiency, propofol may theoretically result in mitochondrial dysfunction and cellular hypoxia.
- Increased risk of bupivacaine-induced cardiotoxicity may be seen. Double-check before giving bolus epidural injections.

Carotid Sinus Syndrome

Benjamin H. Krasne | Christian Diez

Risk

- Male > female
- 9% of pts with recurrent syncope; history of falls
- Increased incidence with age, rarely below age 50 y
- Peripheral vascular disease
- Head and neck cancer

Perioperative Risks

- Presence of CSS does not increase rate of mortality, sudden death, or stroke more when compared with pts with similar age and risk factors.
- CSS does increase morbidity, secondary to injuries sustained during syncopal episodes.

Worry About

- Presence of comorbid conditions: CAD, carotid stenosis, and neck tumor
- Severity of CSS and frequency of syncopal episodes
- Hemodynamic compromise: Bradycardia and/or hypotension

Overview

- The carotid sinus reflex occurs with changes in transmural pressure of the baroreceptors at the carotid sinus.
- Reflex arc:
  - Afferent signals are sent via glossopharyngeal and vagus nerves to the nucleus tractus solitarius.
  - Efferent signaling occurs through sympathetic and vagus nerves to the heart and blood vessels.
- CSH is defined as an exaggerated response to baroreceptor stimulation.
- CSS occurs in pts with CSH when direct CSM or accidental neck stimulation produces symptoms such as dizziness/syncope or bradycardia and/or hypotension.
- Three types of CSS:
  - Cardioinhibitory type, which is due to vagal stimulation of SA and AV nodes, resulting in sinus bradycardia and may be treated with atropine.
  - Vasodepressor type, which results in hypotension due to inhibition of vasomotor sympathetic tone; differentiated with cardioinhibitory type by not responding to atropine treatment.
  - Mixed type, which results in bradycardia and loss of vasomotor tone.
- Diagnosis: Perform CSM in supine position and massage each carotid individually for 5 second. Test is positive if any of the three are true: asystole greater than 3 sec (cardioinhibitory type); decrease in SBP >50 mm Hg (vasodepressor type); and combination or mixed type. There have been some new suggestions that SBP ≤85 mm Hg may be more sensitive in correctly identifying vasodepressor type.

Etiology

- Afferent overshoot from external pressure due to internal atherosclerotic changes diminishing carotid sinus compliance
- Degenerative process of the nucleus tractus solitarius that occurs with age and is associated with sternocleidomastoid movement (head turning or looking down)
- Possible association with dementia, especially DLB
- Mechanical deformation from neck tumors

Usual Treatment

- Medication
  - Atropine or vasopressors for acute, symptomatic pt.
  - For vasodepressor type, midodrine has been used with moderate success, and fludrocortisone has been used with limited success.
- Permanent dual chamber cardiac pacing is effective for cardioinhibitory and mixed types of CSS in pts who are symptomatic (pacing is of no benefit in vasodepressor type).
- Surgical denervation of carotid sinus may be attempted to treat vasodepressor type or pts who remain symptomatic despite pacing.
- Blocking the afferent limb (glossopharyngeal nerve) of the reflex with ethanol ablation is controversial due to high complication rate.
- Surgical removal of neck mass causing carotid sinus compression.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Syncope	Dementia, DLB	CSM	MRI brain
RESP/HEENT	Potential for difficult intubation/ventilation Bradycardia and/or hypotension	Neck mass, neck surgery, symptoms with neck movement	Airway exam, tracheal deviation, carotid bruit	Carotid duplex CT/MRI neck
CV	Bradycardia and/or hypotension	Syncope with head turning or neck stimulation, CAD, PVD	CSM	CSM with ECG monitoring and A-line

Key References: Amin V, Pavri BB: Carotid sinus syndrome, *Cardiol Rev* 23(3):130–134, 2015; Solari D, Maggi R, Oddone D, et al.: Assessment of the vasodepressor reflex in carotid sinus syndrome. *Circ Arrhythm Electrophysiol* 7:505–510, 2014.

Perioperative Implications

Preoperative

- ECG, increased workup if advanced CAD
- CXR and/or CT scan to r/o tracheal compression if neck mass present
- Interrogate pacemaker, convert to DOO mode if unipolar cautery is to be used

Monitoring/Lines

- Consider arterial line for symptomatic pts (strongly encouraged if position other than supine or head turning is needed during surgery).
- If no pacemaker is present, have external pacer readily available.

Airway

- Minimize neck extension during laryngoscopy; inline immobilization may be used.
- Consider asleep fiberoptic if pt has frequent symptoms with neck movement.

Positioning

- Avoid turning pt's neck.
- Ensure that instruments or personnel are not causing pressure to pt's neck.

General Anesthesia

- Emergency drugs may be required based on type of CSS.
- General anesthesia may be preferred because inhalational agents have been shown to attenuate baroreceptor reflexes.
- Avoid hypotension on induction if coronary or carotid disease is present.
- Avoid long-acting beta-blockers or antihypertensive drugs.

Regional Anesthesia

- Glossopharyngeal nerve block for CSS treatment may be performed.
- As an adjuvant to general anesthesia, local anesthetic may also be injected around the carotid sinus before ipsilateral neck dissection to attenuate the baroreceptor response.

Postoperative Period

- Strict postop orders in PACU outlining no head turning or neck compression.
- If intraop asystole has occurred, anesthesiologist/surgeon may need to place a temporary transvenous pacer.

Anticipated Problems/Concerns

- Potentially difficult intubation.
- Assess pacemaker function if present.
- Pt may undergo profound hypotension or asystole at any time in the periop setting; emergency drugs should be readily available.
- Avoid neck stimulation/movement and maintain hemodynamic stability.

Carpenter Syndrome (Acrocephalopolysyndactyly Type II)

Ray Munroe | Lee A. Fleisher

Risk

- Extremely rare; global estimate: 1:1,000,000 births
- Over 100 reported cases

Perioperative Risks

- Airway obstruction
- Difficult mask ventilation and/or difficult intubation
- Increased ICP from craniosynostosis
- Coexisting congenital anomalies, especially cardiac

Overview

- Manifestation:
  - Craniosynostosis
  - Polysyndactyly
  - Cardiac defects
  - Obesity
  - Maxillary or mandibular hypoplasia
- Craniosynostosis usually with metopic and sagittal sutures (midline suture fusion)
- Cardiac defects in up to 50% of cases (tetralogy of Fallot, transposition of great vessels, pulm artery stenosis, VSD, and ASD)
- Other features: Brachydactyly, cognitive impairment, umbilical hernia, macrosomia, cryptorchidism in

males, molar agenesis, high-arched narrow palate, broad cheeks, shallow supraorbital ridges, hypertelorism, and genu valgum

Etiology

- Currently not elucidated
- Autosomal recessive
- Mutation in RAB 23 gene on chromosome 6P12.1-q12 shown in most cases; at least five different mutations in RAB 23 gene
- Some cases of mutation in MEGF8 gene

Usual Treatment

- Surgery is the only option to correct cranial or cardiac abnormalities

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Craniosynostosis Mandibular or maxillary hypoplasia		Acrocephaly Abnormal facies Overbite/underbite Restricted mouth opening	CT head
RESP	Obstructive sleep apnea	Daytime somnolence Hx snoring	Macroglossia, tonsillar hypertrophy, redundant soft tissue	Polysomnography
CV	Congenital cardiac defects		Varies with type of defect and Hx or repair	ECG, TTE, CBC
GI	None			
CNS	Increased ICP Cognitive delay		Acrocephaly	CT head
HEME	None			
METAB	Obesity	Highest percentile on pediatric growth charts	Central adipose deposits	BMP, lipid panel

Key References: Bissonnette B, Luginbuehl I, Marciniak B, et al.: Acrocephalopolysyndactyly syndromes. In Bissonnette B, Luginbuehl I (eds): *Syndro mes: rapid recognition and perioperative implications.* New York, NY, 2006, McGraw-Hill; Kadakia S, Helman SN, Healy NJ, et al.: Carpenter syndrome: a review for the craniofacial surgeon. *J Craniofac Surg* 25(5):1653–1657, 2014.

Perioperative Implications

Preoperative Preparation

- Equipment available for difficult airway
- Congenital heart disease: may warrant prophylactic antimicrobial therapy
- Increased ICP: may warrant avoiding preop sedation

Monitoring

- Arterial line if indicated
- CVP/PA catheter: Consider as indicated

Airway

- Equipment available for difficult airway
- Surgeon available if surgical airway required

Preinduction/Induction

- Risk for obstruction and difficult mask ventilation is increased.
- Potential for agitation in pt with cognitive impairment.
- Maintain spontaneous ventilation while securing airway if possible.

Maintenance

- Adjustments required if pt Hx of repaired cardiac defects.
- Adjustments required if ICP is increased.
- Judicious opioid use in setting of increased risk for postop airway obstruction.

Extubation

- Difficult airway precautions

Postoperative Period

- Increased risk for upper-airway obstruction

Anticipated Problems/Concerns

- Difficult airway in periop period
- Complications from increased ICP
- Complications from congenital heart defects

Central Neurogenic Hyperventilation

Sarah C. Fausel | Kirk Lalwani

Risk

- True CNH is exceedingly rare; the exact incidence is unknown.
- In pts with neurologic injury, it is most often associated with pulm dysfunction or shunting (aspiration, pneumonia, pulm edema, and baseline disease).
- Primarily seen in comatose pts.
- No association with age or gender.

Overview

- A diagnosis of exclusion in neurologic disorders and in cases of hyperventilation; life-threatening causes of hyperventilation (hypoxemia, ischemic bowel, and acidosis) must be ruled out.
- Primary diagnostic criteria are hyperventilation that persists during sleep; low $PaCO_2$, high PaO_2, and absence of drug or metastatic causes.
- Associated primarily with brainstem inflammation and brainstem tumors with inconsistent involvement of midbrain, pons, and/or medulla.
- CNS lymphomas and astrocytomas are the most common tumor types with gliomas, lymphomatoid granulomatosis, and medulloblastoma; also reported in metastatic tumors.
- May result from seizure activity that stimulates the ventilatory response.
- May be associated with acute intermittent porphyria.
- Effects of GA unknown.

Etiology

- Exact etiology and level of brainstem dysfunction not known.
- Probable etiology:
  - Uninhibited stimulation of inspiration and expiration centers in the medulla and/or loss of descending inhibitory control of ventilation by cerebral cortex with brainstem lesion.
  - Ultimate control of respiration, which may lie in the medulla (dorsal and ventral respiratory groups) with fine control from the pneumotaxic center of the pons with input from cerebral cortex, hypothalamus, chemoreceptors and mechanoreceptors, and vagal nerve.
  - Stimulation of most areas of cerebral cortex except motor/premotor areas, which inhibit respiration.
  - Has been associated with brainstem infarction and malignancy.
  - Tumor, which may reduce local pH in the brainstem and activating respiratory chemoreceptors located in the ventral brainstem at the junction of the pons and the medulla.
  - Destructive lesions of midbrain or pons in animal studies, which do not produce CNH. (It is unclear if animal models serve as an adequate model of the human brain in this instance.)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Tachypnea	Tachypnea that persists during sleep and is unpleasant to the conscious patient	Resp rate Normal inspiratory and expiratory excursion	ABG (all must be present to diagnose): PCO_2 (low) pH (alkalotic) PaO_2 (increased for age) Decreased bicarbonate Alveolar-to-arterial gradient not larger than normal
CNS		Pt cannot volitionally inhibit hyperventilation	Focal or nonfocal CNS findings	CSF pH may be normal CT/MRI

Key Reference: Tarulli AW, Lim C, Bui JD, et al.: Central neurogenic hyperventilation. A case report and discussion of pathophysiology, *Arch Neurol* 62:1632–1634, 2005; Kramer CL, Wijdicks EF: Central neurogenic hyperventilation, *Neurology* 83:376, 2014.

Differential Diagnosis for Hyperventilation

- Metabolic acidosis
- Bowel ischemia with acidosis
- Pulm pathology with hypoxemia (pneumonia, pulm embolus, pulm edema, and restrictive or obstructive lung disease)
- Drug toxicity (salicylates, theophylline, cyanide, and topiramate)
- Sepsis
- Encephalopathy/CNS lesions (glioblastoma, encephalitis, MS, brainstem lymphoma, brainstem glioma, brainstem infarction, and liver dysfunction)
- Anxiety
- Psychogenic
- Cardiac (CHF and valvular disease)
- High altitudes
- Hyperthyroidism
- Pregnancy
- Must exclude other etiologies for respiratory alkalosis with appropriate lab/Dx testing

Adverse Effects

- Respiratory alkalosis shifts oxyhemoglobin curve to the left.
- Hypocapnia is a potent cerebral vasoconstrictor, subsequently decreasing cerebral blood flow and volume, which may result in ischemic insults.
- Effect of severe hypocapnia in normal brains is less clear and may produce ischemia when combined with Bohr effect. (Hemoglobin's oxygen affinity is inversely related to the concentration of CO_2.)

Treatment

- No completely effective or consistent treatment currently known
- Narcotics may attenuate resp rate and improve blood gases but will not correct rate or alkalosis.
- Mechanical ventilation with neuromuscular blockade and sedation during treatment of tumor has been attempted.
- Treatment of tumor with steroids, chemotherapy, or radiation therapy is sometimes effective.
- Increasing dead space ventilation and administration of supplemental oxygen and benzodiazepines are not effective.

Outcome

- Death from progressive neurologic deterioration or other complications (aspiration, pneumonia) is likely.
- Pt may have improvement with treatment of tumor or long-term narcotics.

Cephalopelvic Disproportion

John Kissko III

Risk

- Occurs in 1–3% of the pregnant population

Perioperative Risks

- Increased maternal and fetal morbidity and mortality
- Protracted labor
- Arrested labor
- Uterine rupture
- Increased rate of cesarean section
- Increased rate of forceps- or vacuum-assisted delivery

Worry About

- Increased need for surgical delivery
- Increased incidence of fetal distress and need for emergency intervention

Overview

- Subset of fetopelvic disproportion.
- Methods of Dx include various clinical and radiographic estimations of fetal head size and pelvic capacity, none of which alone is an accurate predictor of increased risk of failed labor.
- Leads to abnormal labor pattern with increased likelihood of operative delivery.
- Operative delivery associated with higher incidence of morbidity and mortality in mother and fetus.
- Anesthesia necessities: Complete preop evaluation for possible emergency C-section, including airway exam and neuraxial anesthesia landmarks.

Etiology

- Maternal causes include contracted pelvis (inlet, midpelvis, or outlet), Hx of scoliosis, previous pelvic trauma (especially fracture with callous formation), and Hx of poliomyelitis.
- Fetal causes include macrosomia (often secondary to gestational diabetes), abnormal presentation, and hydrocephalus.

Usual Treatment

- Obstetric: Proper evaluation and planning before and during labor
- Anesthesia: Neuraxial anesthesia for pain relief during labor or operative delivery

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GYN	CPD	Failure to progress adequately in labor	Pelvic exam	Radiographic cephalopelvimetry

Key References: Cunningham F, Leveno KJ, Bloom SL, et al: Abnormal labor. In Cunningham F, Leveno KJ, Bloom SL eds: *Williams obstetrics*, ed 24, New York, NY, 2013, McGraw-Hill; Hillyard SG, Bate TE, Corcoran TB, et al: Extending epidural analgesia for emergency Caesarean section: a meta-analysis. *Br J Anaesth.* 107(5):668–678, 2011.

Perioperative Implications

- Labor usually more prolonged and painful in pts with CPD
- Epidural or CSE usually adequate to cover pain without significantly prolonging the course of labor
- Increased need for surgical delivery or C-section, many times in emergent fashion

Anesthetic Technique

- Labor epidural (PCEA): A low concentration of bupivacaine 0.125% or ropivacaine 0.10% is supplemented with an opioid (e.g., fentanyl) to help reduce motor block. Continuous infusion at 8–10 mL per h with pt-controlled boluses of 6–8 mL every 10 min can be used as needed. Programmed intermittent bolus with additional patient-controlled boluses is also an option.
- Labor CSE: In early first-stage labor (<4 cm cervical dilation), consider injection of 15 mcg fentanyl combined with 1 mL sterile saline followed by continuous epidural as with a PCEA. In late first-stage labor (>4 cm cervical dilation), intrathecal injection of local anesthetic (e.g., 1 mL of 0.25% bupivacaine) and opioid (e.g., 15 mcg fentanyl) is sometimes sufficient for the remainder of the first and second stages of labor, although a PCEA is usually started.

- Nonemergent C-section: For all C-sections regardless of level of immediacy, standard OR and anesthesia machine check, left uterine displacement to maximize uterine blood flow, and application of ASA standard monitors. For *elective C-section*, usually spinal anesthesia is used to achieve a T4 level to pain sensation. This can be accomplished by 1.8–2 mL of 0.75% bupivacaine injected at L3-L4 interspace, often combined with opioid (fentanyl and/or preservative-free morphine) and epinephrine. Maintain BP within normal limits using adequate IV hydration, and phenylephrine or ephedrine when necessary.
- Emergency C-section: Following labor *without* fetal distress (e.g., failure to progress) or labor *with* fetal distress (e.g., Category III fetal heart tracing), if pt has a reliable epidural block, epidural anesthesia is extended, using a higher-concentration local anesthetic (e.g., 3% chloroprocaine, 2% lidocaine, or 0.5% ropivacaine) if time permits. If pt does not have a functioning epidural catheter, then a spinal technique may be used (again, if time allows). Otherwise, general anesthesia with rapid sequence induction may be required.

Anticipated Problems/Concerns

- If there is no epidural catheter in place and a difficult airway is suspected, then consider spinal anesthesia or performing an awake intubation for general anesthesia. Emergency airway equipment (e.g., LMA, video laryngoscope, fiberoptic scope, jet ventilator) should be readily available.
- Neuraxial anesthesia should only be attempted while the fetus is not in imminent danger. The clinical situation must be discussed fully, effectively, and efficiently with the managing obstetricians to develop the safest plan for both the pt and fetus.

Cerebral Arteriovenous Malformations

L. Jane Easdown

Risk

- Cerebral AVMs are rare: 1–2% cause of CVA in a younger population; mean age of diagnosis is 31 y.
- 55% of pts are men.
- Symptomatic cases: 1:100,000 per y.
- Found in 4.3% of population at autopsy.
- Of those affected, 45–70% present with hemorrhage, 30% with seizures, 12% with persistent neurologic deficits, and 1% with headaches.
- Yearly risk of hemorrhage is 1–3%.

Perioperative Risks

- Risk of hemorrhage at embolization is 2–4%.
- Intraop blood pressure management is critical.
- Postop NPPB occurs as blood is diverted from the AVM to the surrounding brain, presenting risk of cerebral edema or hemorrhage.

Worry About

- Massive intraventricular or intraparenchymal hemorrhage
- Seizure
- New neurologic deficits
- Cerebral edema, hyperemia post resection, or endovascular embolization

Overview

- Localized arteriovenous shunt comprised of a tangle or "nidus" of abnormally walled vessels, which cause symptoms by rupture, ischemia, and diversion of flow or pressure on adjacent structures; many are detected on routine scans. The majority of AVMs will bleed at least once.
- 0% are supratentorial, and 4–10% are associated with aneurysms.
- Increased risk of rebleed of 6–33% within the first year.
- As the result of hemorrhage, 16% of pts are moderately or severely disabled. Hemorrhage leads to mortality in 10–30% of cases.
- Vein of Galen malformations are rare congenital lesions with connections between the intracerebral vessels and the great vein of Galen. This disorder in neonates or infants may result in high output CHF or increased ICP from hydrocephalus.

Etiology

- Although congenital in origin, no specific genetic defect has been determined. Sometimes AVMs are associated with hereditary hemorrhagic telangiectasia.

Usual Treatment

- Evidence-based neurosurgic management is based on the Spetzler-Martin grading scale. AVMs are graded 1–5, based on their size, location (eloquent or noneloquent brain), and pattern of venous drainage.
- Smaller and more superficial AVMs (grades 1–3) might be surgically resected for cure. Higher-grade AVMs may be treated with endovascular embolization or stereotactic radiotherapy. Multimodal therapy is common, especially embolization before surgical resection. Embolic materials include solid or liquid agents. Conservative management may improve outcomes in high-grade or unruptured AVMs.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway protection	Aspiration	Active gag reflex	
CV	CHF in children with vein of Galen AVM		S_3 and CHF	CXR, ECHO, ECG
CNS	Seizures, focal deficits, CVA, and raised ICP	Headaches, seizures, changes in mentation, and focal deficits	Neurologic exam	MRI, MRA, CT, cerebral angiography

Key References: Miller C, Mirski M: Anesthesia considerations and intraoperative monitoring during surgery for arteriovenous malformations and dural arteriovenous fistulas. *Neurosurg Clin N Am* 23(1):153–164, 2012; Bendok BR, El Tecle NE, El Ahmadieh, TY, et al: Advances and innovations in brain arteriovenous malformation surgery. *Neurosurgery* 74(Suppl 1):S60–S73, 2014.

Perioperative Considerations

Preoperative Preparation

- Endovascular embolization procedures usually require GA to ensure BP control and no pt movement during microcatheter placement.
- Craniotomy for resection requires preop preparation similar to aneurysm clipping.
- Neurologic exam with attention to focal deficits and raised ICP.
- Prior embolization/radiotherapy may have been performed.
- Carefully assess size and location of AVM.

Monitoring

- Invasive BP monitoring
- Central venous access for craniotomy procedures anticipating extensive blood loss.
- O_2 saturation monitor, which might be placed on the foot on the side of the femoral introducer to monitor arterial integrity during angiography
- Precordial Doppler for detection of air
- Jugular bulb venous O_2 monitoring (has been described)
- Intraop neuro monitoring, which may include EEG and SSEPS

Airway

- ETT for craniotomy and LMA or intubation for airway management for embolization

Induction

- Careful management of BP to prevent Htn (increased ICP or hemorrhage) or hypotension (ischemia)

Maintenance

- Manage BP and ICP carefully, especially with intubation, pinning, and incision.
- Surgeons may request burst suppression with propofol for brain protection if temporary clips are used during resection.
- Surgeons may request hypotension or hypocapnia.
- Control blood glucose.
- Maintain strict isotonic/hypertonic fluid.
- Perform angiography before emergence.
- Plan for arousal and neurologic testing immediately after operation.

Extubation

- Careful BP control: Labetalol and additional opioid
- Expected request for neurologic exam
- May keep intubated to control NPPB hyperemia

Adjuvants

- Cell saver and blood products immediately available
- BP control with nicardipine, NTG, NTP, and beta-blockers
- Phenylephrine infusion
- Propofol infusion for TIVA or burst suppression
- Steroids and mannitol
- Antiepilepsy medications

Postoperative Period

- Complete obliteration of a large AVM will lead to redistribution of CBF and hyperemia or NPPB. Until autoregulation returns, pt may require lower BP and control of CO_2 by intubation and ventilation.
- Postop ICU neurologic monitoring will be required.
- After arteriogram, the femoral cath site should be monitored for bleeding.

Cerebral Palsy

Alan David Kaye | Mark R. Jones | Carmen Labrie-Brown

Risk

- Leading cause of childhood motor disability: 2–2.5 per 1000 live births in developed countries.
- Incidence has not decreased despite improved perinatal care due to increased survival in premature neonates.
- Cerebral palsy pts undergo surgery at higher rates due to frequent comorbidities.

Perioperative Risks

- Dehydration
- Electrolyte imbalance
- Hypothermia
- Delayed recovery
- Hypotension
- Seizure

Worry About

- Difficult intubation
- GE reflux and aspiration
- Associated respiratory impairment and hypoxemia
- Drug interactions or hypersensitivity
- Latex allergy

Overview

- Any nonprogressive central motor deficit dating to events in the prenatal, perinatal, or postnatal periods
- Wide spectrum of symptoms
  - Cognitive impairment
  - Seizures
  - Sensory loss (visual and hearing)
  - Communication and behavioral disturbances
  - Respiratory, GI and orthopedic problems
- Normal intellect (especially dyskinetic group) often
- Classified as spastic (87%), dyskinetic (7%), ataxic (4%), and mixed (2%)

Etiology

- Mostly unknown and multifactorial
- Antenatal cerebral events causing complications at time of delivery (e.g., periventricular hemorrhage, genetic disorder, infection)
- Postnatal events such as trauma and infection
- All causes: Result in damage to the CNS during early brain growth

Usual Treatment

- Anticonvulsants, antispasmodics (benzodiazepines, baclofen, and dantrolene), antidepressants, antireflux agents, laxatives, and anticholinergics
- Often intramuscular botulinum toxin injections and orthopedic procedures (tendon releases and osteotomies), fundoplication for reflux, gastrostomy tube placement, tracheostomy, major spine surgery, and dental rehabilitation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Tongue thrusting Poor dentition Salivary drooling	Difficulty swallowing	Dental malocclusion Dental caries	Formal airway assessment usually difficult
RESP	Restrictive defect Aspiration pneumonia Recurrent chest infections	Cough Dyspnea (difficult to detect if mobilization limited)	Often normal Reduced air entry Bronchial breathing Wheeze	Pulm function tests, ABG CXR
CV	Right-sided heart failure from restrictive lung disease	Often normal Dyspnea	Tachycardia S_3 or S_4 Distended JVP Hepatomegaly	ECG ECHO
GI	GE reflux Esophageal dysmotility	Poor swallowing Night wakening	Dehydration Pallor Malnutrition	CBC Lytes ± Endoscopy
MS	Spasticity Dyskinesia Ataxia	Muscle pain and spasms	Increased muscle tone Contractures Tremor	Gait analysis performed before major orthopedic surgery
CNS	Epilepsy (30%) Visual and hearing defects	Tonic-clonic and complex-partial seizures	Myopia Visual field defects Strabismus	Not usually relevant
HEME	Iron-deficiency anemia	Fatigue	Pallor	CBC, differential
METAB	Electrolyte imbalance Hypovolemia	Laxative use Fatigue Never thirsty	Dehydration Malnutrition	UA Albumin

Key References: Wongprasartsuk P, Stevens J: Cerebral palsy and anaesthesia. *Paediatr Anaesth* 12:296–303, 2002; Wass CT, Warner ME, Worrell GA, et al: Effect of general anesthesia in patients with cerebral palsy at the turn of the new millennium: a population-based study evaluating perioperative outcome and brief overview of anesthetic implications of this coexisting disease. *J Child Neurol* 27(7):859–866, 2012.

Perioperative Implications

Preoperative Preparation

- Pts can have normal intellect. (One-third have mental retardation.)
- Involve parents in management because parents have good insight into periop care.
- Avoid unfamiliar faces if possible.
- Optimize respiratory status (bronchodilators, antibiotics, and physical therapy).
- Optimize nutrition and fix electrolyte imbalance and hypovolemia.
- Continue medical Rx, especially anticonvulsants.
- Pts may need antireflux, antisialagogue, or sedative premedication (cautious doses of sedatives).
- Topical local anesthetic for venipuncture.
- Discuss periop analgesia (often a regional technique for lower-limb surgery).

Monitoring

- Core temp (susceptible to hypothermia)
- Neuromuscular blockade
- Airway pressures

Airway

- ETT is better sized to age, not weight.
- Salivary secretions may make ventilation difficult.
- Overbite may make intubation difficult.

Induction

- Rapid sequence may be required but is often impractical.
- IV access often difficult.
- Inhalation sometimes favored (in semisitting position if concerns of reflux exist).

Maintenance

- Position pt carefully and check frequently.
- Consider antiemetics, especially when opioids are administered.
- IV fluids.
- MAC may be lower in cerebral palsy as much as 20% and up to 30% if pt is on anticonvulsants.
- Use warming devices.
- Consider regional (epidural) techniques for lower-limb surgery.

Other Intraoperative Challenges

- Bleeding:
  - Anecdotal evidence that pts with neuromuscular scoliosis bleed more than pts with idiopathic scoliosis.
  - Poor nutritional/nonambulatory status.
  - Borderline low platelet count and function due to anticonvulsants.
  - Subnormal clotting factor level.
- Temp:
  - Pediatric pts with severe CP may be unable to regulate temp.
  - Pts may have little subcutaneous fat.
  - Some arrive to OR with temp <35° C.
  - Warm room until pt is draped, and use warming blanket/gases/fluids.

Extubation

- Awake if prone to reflux

Drug Considerations

- Baclofen should not be stopped abruptly; however, it may cause postop bradycardia and hypotension.
- Resistance to nondepolarizing NMB may occur (but is probably not clinically significant).
- Ketamine and methohexital may be avoided in epileptic pts.
- N_2O and opiates may worsen nausea.

Postoperative Period

- Ensure aggressive respiratory care and frequent aspirations.
- Maintain normothermia.
- Pts susceptible to N/V.
- Avoid/treat muscle spasms (IV diazepam and epidural clonidine).
- Facilitate early mobilization.

Anticipated Problems/Concerns

- Latex allergy
- Hypothermia
- Prolonged recovery time
- Postop N/V (worse with opiates)
- Postop muscle spasms
- Retention of secretions and postop chest infection

Cerebrovascular Transient Ischemic Attack

Zirka H. Anastasian | Eric J. Heyer

Risk

- Overall incidence in USA: Approximately 1.1 per 1000.
- Risk related to demographic factors: Age, gender, and race.
- Estimated prevalence of TIA in men is 2.7% versus 1.6% in women ages 65–69 y, and 3.6% in men versus 4.1% in women ages 75–79 y. The overall prevalence is estimated to be 0.4% among adults 45–64 y.
- African Americans and Hispanics at higher risk than Caucasians.

Perioperative Risk

- Pts with Hx of TIAs at increased risk of postop stroke.
- Risk of periop stroke increased in pts with medical Hx of cerebral vascular disease, peripheral vascular disease, hypertension, diabetes, chronic renal insufficiency, COPD, and atrial fibrillation.
- Pts with CAD for CABG have a high incidence of carotid stenosis (50% with some; 20% with stenosis >50%).
- Likewise, pts with carotid stenosis have high incidence of CAD (over 50%).
- Risk of periop stroke increased in pts with planned surgery: CABG (3–6%), vascular (1%).
- Pts with Hx of stroke 9 mo or less ago at increased risk of major adverse cardiac events and mortality after elective, noncardiac surgery (even low- and intermediate-risk surgeries).

Worry About

- Crescendo TIAs
- Duration of symptoms >1 h
- Symptomatic or critical internal carotid artery stenosis
- Known cardiac source of embolus, such as atrial fibrillation
- Known hypercoagulable state

Overview

- TIA: Transient episode of neuro dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction. The end is biologic (tissue injury) rather than arbitrary (24 h).
- Risk of hospitalization for major cardiac event after TIA is 2.6% for first 90 days.
- ABCDD score for assessing risk of stroke after TIA.
  - A = Age (> 60 y = 1 point)
  - B = Blood pressure elevation when first assessed after TIA (systolic ≥140 mm Hg or diastolic ≥90 mm Hg = 1 point)
  - C = Clinical features (unilateral weakness = 2 points; isolated speech disturbance = 1 point; other = 0 points)
  - D = Duration of TIA symptoms (≥60 min = 2 points; 10 to 59 min = 1 point; <10 min = 0 points)
  - Diabetes (present = 1 point)
- Score interpretation:
  - Score 6 to 7: High 2-day stroke risk (8.1%)
  - Score 4 to 5: Moderate 2-day stroke risk (4.1%)
  - Score 0 to 3: Low 2-day stroke risk (1%)

Etiology

- Cerebral vessel disease: atherosclerosis, lipohyalinosis, inflammation, amyloid deposition, arterial dissection, developmental malformation, aneurysmal dilation, or venous thrombosis
- Remote disease: embolus formed from the heart or other circulation, which lodges in a cerebral vessel
- Blood flow–related: related: Inadequate cerebral blood flow due to decreased perfusion pressure or increased blood viscosity (hypotension, trauma, surgical compression, steal, and coagulopathy)

Usual Treatment

- Determine causing factor.
- For cerebral vessel disease: Antiplatelet therapy, anticoagulation, and revascularization (carotid endarterectomy, carotid stent, vertebral artery stent).
- In remote disease, investigate and treat causing factor (e.g., atrial fibrillation, valvular disease), and use antiplatelet therapy and anticoagulation.
- If blood flow–related, treat underlying cause and use antiplatelet therapy and anticoagulation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Neck trauma Compression			
CNS	Cerebrovascular disease Transient focal neuro deficit	Vision changes, language changes, weakness, sensory changes, ataxia Previous stroke	Carotid bruit Retinal exam (for ischemia)	Carotid Doppler Angiography: Carotid and vertebral artery CT/MRI
CV	CAD disease Atrial fibrillation Possible valvular disease	MI Angina Decreased exercise tolerance Risk factors for atherosclerosis	Irregular heart rate/rhythm Murmur	ECG Stress test Holter, TEE/ TTE
GI		N/V		

Key References: Easton JD, Saver JL, Albers GW, et al: Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists, *Stroke* 40(6):2276–2293, 2009; Anastasian ZH: Anesthetic management for acute ischaemic stroke, *Br J Anaesth* 113 (Suppl 2):ii9–ii16, 2014.

Perioperative Implications

Perioperative Preparation

- Determine blood pressure range that the pt normally experiences.
- Manage blood pressure with both cerebral perfusion and CAD in mind.
- Perform preop cardiac workup and medical stabilization and consider postponing surgery if nonemergency surgery.
- Conduct preop neuro exam to identify any baseline deficits.
- Avoid excessive premedication (pt can be more sensitive).
- Avoid long-acting intraop agents that can obscure postop neuro exam.

Monitoring

- Use ECG monitoring for ischemia and arrhythmia.
- Consider arterial line and central line/PA catheter if extensive CV disease is present.

Airway

- Avoid extreme neck manipulation and pressure on the carotid artery during ventilation and intubation.

Preinduction/Induction

- Maintain pressure to allow for sufficient cerebral perfusion (rightward shift in cerebral autoregulation in Htn).
- Titrate medication because patient requirements can decrease.

Maintenance

- Pts can be more sensitive to medications.
- Avoid long-acting agents if neuro exam is to be performed postop.
- Isoflurane theoretically neuroprotective allows lowest cerebral blood flow before EEG symptoms of ischemia.

Extubation

- Ensure pt is awake, following commands, and able to protect the airway.
- Ensure pt does not have a large neuro deficit that would lead to swelling and respiratory insufficiency postop.

Postoperative Period

- Period of greatest risk for stroke is after general surgery.
- Resume antiplatelet therapy and anticoagulation as soon as possible.

Cervical Disk Disease (Cervical Spine Disease)

Andrew D. Rosenberg

Risk

- Incidence in USA: 12,000 deaths/y; 70 million with cervical disk disease, spondylosis, or trauma
- Disk disease a consequence of aging (3rd-5th decades)
- Present in RA, ankylosing spondylitis, and other rheumatic disorders
- Trauma, especially motor vehicle accidents
- M:F ratio: 3:2

Perioperative Risks

- Mortality (acute) 1–5% (depending on associated injuries)
- Spinal cord damage with C-spine movement
- Difficulty intubating or reintubating postextubation
- Swelling or hematoma after neck surgery, which can cause obstruction of airway
- Steroid-induced complications

Worry About

- Airway management; C-spine movement during or after intubation
- Exacerbating or causing spinal cord damage with neck motion
- Osteoarthritis with osteophytes impinging on nerve roots

Overview

- Neck pain: Present in 30% of adults in USA
- Can cause radiculopathy, which can be aggravated by neck extension
- Root:
  - C3: Unusual
  - C4: Numbness rare; pain at root of neck
  - C5: Numb over shoulder to lateral aspect of upper arm ("epaulet" area)
  - C6: Second-most common radiculopathy; pain across top of neck, along biceps muscle into tips of thumb and index finger, as well as biceps muscle weakness
  - C7: Most common herniation, resulting in pain across back of shoulder triceps and into middle finger, as well as loss of triceps reflex
  - C8: Numb small finger; weak interossei

Etiology

- Disk disease is a process of aging.
- Inflammatory arthropathy or trauma; in trauma, can have fractures, dislocations, or ligamentous damage causing spinal cord paralysis; can get swelling of soft tissues of the neck.

Usual Treatment

- Neck should be stabilized, not forced into position; any movement can cause damage.
- In pts with atlantoaxial subluxation, avoid flexion. Pts can have superior migration of the odontoid as well as subaxial subluxation.
- Stabilization and time to heal and repair.
- Shoulder and strap muscle-strengthening exercises.
- Epidural steroids for recent disk disease.
- Steroids for acute spinal cord injury based on local recommendations.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Numbness and pain in RA: Superior migration of odontoid, atlantoaxial subluxation, ADI increased (>4 mm unstable), subaxial subluxation, cricoarytenoid arthritis, airway abnormalities, trauma, swelling	Hoarseness, snoring	In RA: TMJ problems, hypoplastic mandible	In RA: Neck x-ray flexion and extension (measure ADD) Evaluate bones, ligament alignment, soft tissue swelling, motion
CV	Trauma: Possible cardiac contusion/injury spinal shock		Heart sounds distant Unstable BP	ECG, ECHO
RESP	Rheumatologic disorders: Fibrosis, honeycombing Ankylosing spondylitis: Restrictive pattern Trauma: Diaphragm function (C3–C5), pneumothorax, hemothorax, contusion, aspiration, rib fractures	SOB	In trauma: Dyspnea, paradoxical ventilation, flail chest, and breath sounds absent with pneumothorax	CXR and ABG
GI	Ulcers secondary to aspirin for RA			
HEME	RA: Anemia secondary to medications		Trauma: Look for signs of bleeding	Hgb
CNS	Vertebral artery compression: Dizziness, vertigo, nausea, blurred vision			

Key References: MacDonald D: Intraoperative motor evoked potential monitoring: overview and update. *J Clin Monit Comput* 20(5):347–377, 2006; Schwartz D, Sestokas A, Dormans JP, et al: Transcranial electric motor evoked potential monitoring during spine surgery: is it safe? *Spine* 36(13):1046–1049, 2011.

Perioperative Implications

- Assess neck in disk disease, rheumatic diseases, and trauma.
- Consider intubation with neck stabilized by an assistant to avoid flexion or extension or awake fiberoptic intubation.
- Consider intubating with fiberoptic intubation, Glidescope, AirTraq, LMA, light wand, or other airway-assistance device.
- Avoid medications (e.g., midazolam), including muscle relaxants if they are used for initial intubation, that might interfere with specialized spinal cord monitoring, SSEPs, or TCMEPs.

Monitoring

- Acute spinal cord shock may require arterial and PA cath or TEE to facilitate monitoring and treating hemodynamic disturbances.
- When using intraop TCMEPs, protect the tongue and ETT from the masseter and muscles of mastication contraction during stimulation. Remember, muscle relaxants cannot be used with TCMEPs.

Induction

- Consider not initiating irreversible steps (e.g., muscle relaxants) until airway is secured.

Extubation

- Consider not extubating until pt is able to maintain airway without threat of swelling or airway obstruction.

Adjuvants

- Steroids reduce injury in acute traumatic spinal cord injury: use local recommendations.

Postoperative Period

- Observe for neck swelling, hoarseness, and airway obstruction.
- Assess neurologic status.

Anticipated Problems/Concerns

- Anticipate difficulty intubating pts due to abnormal anatomy or limitation of motion. Prepare pt for fiberoptic intubation.
- Associated traumatic injuries including cardiac, brain, lung, abdomen, bladder, and long bones, as well their consequences.
- ARDS from aspiration in a preop traumatic event.
- Injury to tongue or ETT from biting down because of muscle contraction from TCMEP stimulation.

Chagas Disease

Tricia Desvarieux | Charles W. Hogue Jr. | Nanhi Mitter | Lee A. Fleisher

Risk

- 16–18 million people infected worldwide
- Rare in southern USA; chronic disease more likely in immigrants from endemic regions (South America, central Brazil prevalence 6–8%)
- More than 50,000 die each year; mortality estimated at 50% at 4 y secondary to heart failure
- Higher risk to laboratory workers and personnel exposed to blood products, travelers to endemic areas

Perioperative Risks

- Not defined.
- Most important prognostic factor is degree of myocardial dysfunction.
- Esophageal changes due to megaesophagus and reflux.

- Associated with myasthenia gravis.
- CNS symptoms: Meningoencephalitis (particularly in immunocompromised pts).

Worry About

- LV dysfunction and CHF: Chagas myocarditis, refractory heart failure. Most often biventricular in nature, right >left. Sudden cardiac death associated with 55–65% deaths; precipitated by exercise, VTach, VFIB, asystole, AVB.
- Conduction abnormalities (complete AV block, RBBB, LAFB)
- Ventricular arrhythmias (VT, AFIB)
- Ventricular aneurysms (posterolateral, inferior basal, apical)
- Megaesophagus, achalasia, risk of pulm aspiration
- Blood transmission and infections
- Thromboembolism, stroke

Overview

- Acute infection mostly in pediatric population; asymptomatic in two-thirds of pts, followed by chronic disease after latency of more than 2–3 decades.
- In endemic areas, mild forms of disease are common, with a benign course.
- Pathogenesis to chronic progressive end-organ disease poorly understood; autoimmunity, microvascular dysfunction, autonomic neuropathy implicated.
- Cardiac involvement most serious end-organ manifestation; colon and esophagus also affected.
- Mechanisms proposed for cardiac involvement unclear but include neurogenic mechanisms, parasite-dependent inflammation, microvascular disease, and immune-mediated injury.
- In USA, the diagnosis is usually not considered; presentation as CAD or dilated cardiomyopathy, or with AV heart block, CHF, ECG conduction abnormalities, sustained VTach.
- Serologic test for diagnosis based on hemagglutination, immunofluorescence, ELISA, PCR; these are usually negative during first wk. Therefore Dx depends on detection of circulating parasites.
- Continues to cardiac involvement: Decapillarization of the myocardium.
- Downregulation of the nicotinic Ach receptors and associated myasthenia gravis symptomatology.

Etiology

- Protozoan infection: *Trypanosoma cruzi*.
- Transmission to humans by reduviid bug, the "kissing bug."
- Transmission by blood transfusion, organ transplantation, vector, lab accident, reactivation of chronic disease during immunosuppression. Recently oral chagasic infection via food contamination (sugar and acai juices) also found possible, with more severe clinical course.
- Central and South America are endemic areas.

Usual Treatment

- Nifurtimox (limited efficacy, poor oral bioavailability) for acute disease; usefulness for indeterminate phase or chronic disease not established.
- Benzimidazole (similar efficacy as nifurtimox) second agent; not available in USA.
- Recent success with protriptyline in the acute and chronic forms.
- Allopurinol for the cutaneous form.
- No evidence that trypanocide drug therapy cures disease.
- Other treatment related to symptomology: Amiodarone for arrhythmias related to LV dysfunction; also sotalol. Invasive treatment modalities include surgical excision, cath ablation, aneurysmectomy, epicardial mapping.
- Pts at high risk for sudden cardiac death will have an ICD placed.
- Heart transplant, bone marrow cell transplant uncertain.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Conduction abnormalities, LV dysfunction and aneurysm	Syncope, DOE, orthopnea, fatigue, atypical angina	JVD, edema, rales, cardiomegaly Murmurs, TR, MR, wide split S_2, prominent diffuse apical thrust	ECG ECHO MUGA Cardiac cath CXR for possible cardiomegaly
	Ventricular arrhythmias	Syncope, palpitations	Biventricular enlargement	Holter electrophysiologic study, TTE, TEE
GI	Megaesophagus, megacolon	Dysphagia, GE reflux, constipation	Abdominal distention	Barium studies, CXR, endoscopy

Key Reference: Leckie RS, Leckie S, Mahmood F: Perioperative management of a patient with Chagas disease having mitral valve surgery, *J Clin Anesth* 21(4):282–285, 2009.

Perioperative Implications

Preoperative Preparation

- LV function optimization with diuretics, ACE inhibitors; consider beta-blockers and Ca^{2+}-channel blockers. Consider amiodarone in cases of VTach/VFIB.
- Prophylaxis against pulm aspiration
- Assessment of conduction abnormalities, arrhythmias.

Monitoring

- Dictated by degree of LV dysfunction and proposed procedure; consider PA cath or TEE. On TEE, may see biventricular enlargement, thinning of ventricular walls, apical aneurysm, intramural thrombus.
- ECG during entire periop period. Often seen is a long QT interval, AV block, bundle branch block. Pt may have VTach/VFIB.

Preinduction/Induction

- Consider temporary pacing if symptomatic AV block.
- Caution with negative inotropic drugs.
- Awake or rapid-sequence intubation.
- Consider judicious use of muscle relaxants.

Maintenance

- Technique dictated by preferences, procedure, degree of cardiac involvement.
- Avoid hypoxemia (facilitates ischemic myocardial changes on capillary level, which can further progress to wall thinning and aneurysm formation).

Postoperative Period

- Continued monitoring depends on preexisting LV dysfunction and operative procedure.
- ECG monitoring for ventricular arrhythmias and AV conduction block.

Charcot-Marie-Tooth Disease

Sylvia H. Wilson | Julie R. McSwain

Risk

- Incidence: 1:2500 people
- Peripheral disease severity varying from mild to severe autonomic, motor and sensory neuropathy

Perioperative Risks

- Potential for postop weakness, especially following nondepolarizing neuromuscular blocking agents

Worry About

- Resp insufficiency secondary to diaphragmatic or phrenic nerve dysfunction
- Preexisting vocal cord palsy or paralysis
- Secondary nerve entrapments or injuries with intraop positioning

Overview

- Peripheral neuropathy is caused by peripheral demyelination (altered myelin function or production) or axonal loss (altered axonal structure or function).
- Neuropathies can be autonomic, motor, sensory, or mixed.
- Distal weakness and sensory loss typically develop in the first 2 decades of life, followed by a slowing in disease progression with resultant skeletal deformities (more commonly in feet) and loss of DTRs.
- Most pts remain ambulatory with a normal life span, but quality of life is often affected.
- CMT is diagnosed by electrophysiologic and molecular genetic testing, occasional muscle biopsy.
- Management of the disease process is often multidisciplinary and should include neurologists, physical therapists, orthopedists, and geneticists, among others.
- Surgery aims to preserve or improve quality of life and functional independence.

Etiology

- Most common hereditary, peripheral, motor, and sensory neuropathy
  - Also known as HMSN
  - Over 70 genes identified with at least one CMT phenotype
  - Autosomal dominant and X-linked dominant inheritance more common
- Inheritance: Wide range of genetic heterogeneity
  - Majority of types are autosomal dominant (CMT1 and CMT2)
  - Over 20% of pts without known familial Hx for CMT
  - X-linked recessive and autosomal recessive less common
- Main subtypes
  - Type 1 (CMT1): Demyelinating (altered myelin function/production); autosomal dominant; slow nerve-conduction velocity; most predominant form in Western countries (in those of European descent)
  - Type 2 (CMT2): Axonal loss (altered axonal structure/function); autosomal dominant; preserved nerve-conduction velocity
  - Type 3 (CMT3): Severe early onset (Dejerine-Sottas disease)
  - Type 4 (CMT4): Demyelinating or axonal loss; autosomal recessive
  - X-linked CMT (CMTX)

Usual Treatment

- Effective treatment: None
  - Ascorbic acid (vitamin C): No benefit in clinical trials
  - Creatine supplementation: No benefit in clinical trials
  - Resistance exercise training: Minimal improvement in clinical trials
  - Accurate genetic diagnosis: Now important for accurate prognosis, potential future gene-targeted therapy, and potential antenatal counseling (especially because there is no specific effective treatment)
- Orthopedic surgical procedures: correct skeletal deformities but will not correct preexisting motor or sensory loss
- Surgical treatment to correct foot deformities, which may include soft tissue surgery (e.g., plantar fasciotomy, tendon transfers/releases), osteotomies, and joint fusions
- Supportive therapy such as rehabilitation, pain management, and physical therapy (may be useful and improve pt's mental and physical state, as well as improve quality of life)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	OSA Vocal cord palsy Ocular/bulbar dysfunction	Symptoms of OSA Voice changes Vision changes, dysphagia	Airway exam Hoarseness, stridor, dysphonia Nasal speech, drooling, absent gag reflex	Sleep study Fiberoptic airway exam, laryngeal EMG studies Gag reflex
RESP	Respiratory insufficiency, restrictive lung disease Pneumonia Phrenic nerve palsy	Dyspnea Fever, dyspnea Dyspnea, orthopnea	Tachypnea Lung field consolidation Decreased breath sounds	PFT, ABG CXR, WBC PFT, CXR, conduction studies
CNS	Central sleep apnea Autonomic dysfunction	Daytime somnolence Syncope	None Orthostatic hypotension	Sleep study Tilt table test, Valsalva
PNS	Sensory loss in UE and LE	Numbness, tingling	Neuro exam	EMG
MS	Progressive distal weakness Muscle atrophy of LE Skeletal deformities of LE Scoliosis	Progressive weakness Progressive weakness Gait abnormalities Gait abnormalities	Neuro exam, DTRs Thin distal muscles Pes cavus Spine examination	EMG None Radiologic evaluation Radiologic evaluation
CV	Cardiomyopathy (rare) Arrhythmias (rare)	Dyspnea, chest pain Palpitations, syncope	Crackles, LE edema Irregular heart rate	ECG, ECHO ECG

Key References: Aboussouan LS, Lewis RA, Shy ME: Disorders of pulmonary function, sleep, and the upper airway in Charcot-Marie-Tooth disease. *Lung.* 185(1):1–7, 2007; Pareyson D, Marchesi C: Diagnosis, natural history, and management of Charcot-Marie-Tooth disease. *Lancet Neurol.* 8(7):654–667, 2009.

Perioperative Implications

Preoperative Preparation

- Screen for concomitant diseases (DM, thyroid disorders, and vitamin deficiencies).
  - Concurrent DM associated with more severe neuropathy.
  - Cardiac disturbances (arrhythmias, AV block, and cardiomyopathy) reported but rare.
- Avoid medications that may induce neuropathy when possible: Chemotherapeutic agents, antibiotics (metronidazole), amiodarone, and colchicine.
- Document pt symptoms and preexisting neuro (sensory and motor) deficits.

Regional Anesthesia

- Case reports describe successful use without evidence of disease exacerbation.
  - No controlled studies
  - Neuraxial: Numerous case reports describe successful use
  - Peripheral nerve blocks: Case reports and series describe successful single injections and catheters; nerve stimulation, which may be unreliable; ultrasound guidance, which is recommended and may limit needle manipulations and inadvertent nerve trauma
- Consider decreasing local anesthetic dose because there have been reports of prolonged blockade.

Monitoring

- Neuromuscular blockade monitoring may be difficult or unreliable.
- Additional monitoring should otherwise be guided by other pt comorbidities.

Airway

- Severe forms associated with upper-airway dysfunction and restrictive lung impairment

Preinduction/Induction

- Safe use of succinylcholine reported (peripheral neuropathy, not myopathy); however, theoretical concern of hyperkalemia

Maintenance

- No definitive connection with malignant hyperthermia; however, cases reported.
- Mixed reports regarding duration of nondepolarizing neuromuscular blocking agents.
- Neuromuscular blockade monitoring may be difficult. Consider monitoring TOF at adductor pollicis because upper limbs are usually less affected than lower limbs.
- Neostigmine safe and does not appear paradoxically to worsen neuromuscular transmission.

Extubation

- If nondepolarizing neuromuscular blocking agent given, reversal agents and skeletal muscle strength assessment before extubation (underlying skeletal muscle weakness, including restrictive lung pathology).
- Preexisting vocal cord dysfunction (severe forms of CMT) may lead to airway compromise.

Postoperative Period

- Upper-airway dysfunction and restrictive lung impairment because rib cage changes and phrenic nerve and diaphragmatic involvement are associated with severe forms.
- Potential postoperative respiratory insufficiency and apnea (obstructive and central).
- Consider BiPAP or CPAP in the PACU if concern for upper-airway obstruction exists.

Anticipated Problems/Concerns

- Traditional monitoring of neuromuscular blockade after the use of nondepolarizing neuromuscular blockers may be difficult and/or misleading.
- Pts may be reluctant to accept regional anesthesia for fear of worsening their neuropathy; however, there are several case reports that describe successful use of regional techniques with no exacerbation of symptoms.

CHARGE Association

Pikulkaew Dachsangvorn

Risk

- Newborns: 1 in 10,000

Perioperative Risks

- Respiratory failure in the neonate (due to choanal atresia)
- Difficult airway (cleft lip and palate and tracheomalacia)
- Aspiration risk
- Congenital heart disease

Worry About

- If pt has respiratory insufficiency, consider subglottic stenosis.
- Postop respiratory failure.

Overview

- The term CHARGE was coined in 1981 to describe pts with coloboma, congenital heart defects, choanal atresia, retardation of growth and/or other development, genital anomalies, and ear anomalies with deafness.
- Traditionally diagnosed clinically, using Blake or Verloes criteria; now diagnosis can be confirmed by molecular genetic testing.
- In the past, CHARGE was an association. However, it is now accepted as a genetic syndrome.
- It shares many clinical features with velocardiofacial (22q11 deletion syndrome) and Kallmann syndrome.
- Major features (features that are more specific to CHARGE):
  - Coloboma of the iris and/or retina, with or without microphthalmia.
  - Choanal atresia or stenosis.
  - Characteristic CHARGE ear deformity.
  - External ear: Cup-shaped ear with absent ear lobes.
  - Middle ear: Stapes abnormalities and cochlear anomalies.
  - CN dysfunction (oculomotor dysfunction, weak chewing, facial palsy, hearing difficulties, and swallowing problems).
- Minor features (significant, but less specific for diagnosis of CHARGE):
  - Hypothalamo-hypophyseal dysfunction, congenital diaphragmatic hernia, tracheoesophageal fistula, brain anomalies, hypotonia, developmental delay, kidney anomalies, genital hypoplasia, and lacrimal duct atresia.
  - Characteristic face: Broad forehead, square face, and facial asymmetry.
  - Scoliosis, obstructive sleep apnea, and webbed neck.
- Rare features: Immune deficiency, limb anomalies, epilepsy, and anal atresia.
- Four features almost always present with CHD7 mutation: external ear anomalies, cranial nerve dysfunction, semicircular canal hypoplasia, and delayed milestones.
- Congenital heart defects present in 76% of CHD7-positive pts and 85% of clinical diagnosis of CHARGE syndrome.

Etiology

- CHD7 gene mutation
- De novo mutations in almost all cases, with parent-to-child transmission only seen occasionally (autosomal dominant with variable expression)

Usual Treatment

- Multidisciplinary care, including genetic counseling
- Cardiac assessment with possible medical treatment or surgical correction of congenital cardiac anomalies
- Tracheostomy as indicated
- Surgical correction of choanal atresia as needed
- Feeding therapy and speech therapy
- Gastrostomy in pts who fail traditional feeding therapy
- Renal, endocrine, and immunologic evaluations
- Hearing aids and possible deaf-blind services
- Psychologic evaluation because some pts may need assistance in coping with developmental and behavioral management

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Choanal atresia Cleft lip +/– palate Micrognathia	Dyspnea	Can be unilateral, failure to pass NGT	
CV	Conotruncal anomalies (tetralogy of Fallot, truncus arteriosus, interrupted aortic arch), AV canal defects, ASD, VSD, PDA	Activity level Cyanosis Weight	Murmurs	ECHO
RESP	Aspiration pneumonitis Airway obstruction below choanae in 70% of patients (laryngomalacia—40%, tracheomalacia—20%, subglottic stenosis—10%) TEF	Dyspnea Cyanosis Review prior records Snoring	Rales, wheezing	
GI	Swallowing difficulties, FTT			
CNS	CN dysfunction (facial palsy, hearing loss, dysphagia) Hypotonia Developmental delay	Variable		Swallowing study IQ <70 in over 70%
GU	Renal insufficiency, Polyhydramnios Cryptorchidism and micropenis/hypoplastic labia			BUN, Cr
ENDO	Hypogonadotropin deficiency Short stature, delayed puberty			LH, FSH
HEME/ID	Immunodeficiency (lymphopenia, SCID)			CBC+diff

Key References: Hsu P, Ma A, Wilson M, et al: CHARGE syndrome: a review, *J Paediatr Child Health* 50(7):504–511, 2014; Bergman JE, Janssen N, Hoefsloot LH, et al: CHD7 mutations and CHARGE syndrome: the clinical implications of an expanding phenotype, *J Med Genet* 48(5):334–342, 2011.

Perioperative Implications

Preoperative Preparation

- Premedication with midazolam can be helpful because many pts with CHARGE syndrome have developmental delay and autistic-like behaviors.

Monitoring

- Standard as indicated by coexisting disease(s) and surgical procedure

Airway

- Anticipate difficult airway. Rarely, airway becomes more difficult as CHARGE pts age. Case reports exist for failed direct laryngoscopy, failed laryngeal mask airway, and failed Glidescope intubation. Therefore multiple airway adjuncts must be immediately available.
- May need PEEP to help with ventilating pts with OSA and tracheomalacia.
- Anticholinergic may be helpful with excessive salivation.
- Consider requesting ENT surgeon in the room for known difficult airway pts.

Preinduction/Induction

- Inhalational or intravenous induction. Maintain spontaneous ventilation until proven that airway can be managed safely.

Maintenance

- Routine

Extubation

- Residual muscle relaxant may worsen preexisting hypotonia.
- Anticipate airway obstruction especially if pt was difficult to ventilate during induction.
- Be prepared to reintubate.

Postoperative Period

- Postop airway events occur in 35% of CHARGE pts. Risk factors include cardiac, GI, or airway procedures.

Anticipated Problems/Concerns

- Desaturation needing intervention
- Excessive secretions
- Aspiration
- Arrhythmias or other heart rate abnormalities
- Stridor
- Failed extubation

Cherubism

Daniel Siker | Lee A. Fleisher

Risk

- >250 cases in world literature
- Cherubs have a 40% chance of having a cherub offspring

Perioperative Risks

- Swelling of lower face causing airway obstruction
- Displacement of ocular orbit and lower eyelid, causing visual changes
- Excessive blood loss from curettage of vascular lesions
- Association with Noonan syndrome

Worry About

- Pulm valve stenosis (Noonan syndrome)
- Undiagnosed hyperparathyroidism
- Convex, V-shaped hypertrophied hard palate
- Small mouth opening and mild trismus

Overview

- Progressive symmetric fullness of cheeks and jaw, with retraction of lower eyelids exposing an inferior rim of sclera.
- Onset age: 2–12 y.
- These round-faced, upwardly gazing infants look like Renaissance art cherubs.
- Diagnostic biopsy of mandible shows multinucleated giant cells.
- Associated problems with speaking, breathing, swallowing, chewing.
- Pathognomonic x-ray of jaw demonstrates radiolucent lesions.

Etiology

- Mutations in the *SH3BP2* gene cause cherubism.
- Familial: Autosomal dominant.
- Penetrance: 100% for boys, 50% for girls.
- Etiology unknown, but alternative names include familial fibrous dysplasia, bilateral giant cell tumors, and familial multilocular cystic disease.
- Multilocular cystic malformation of mandible and maxilla with painless submandibular lymphadenopathy.

Usual Treatment

- Operative curettage, removal of displaced teeth, cortical reshaping of mandible
- Selective embolization with operative excision of vascular lesions
- Bone grafts
- For hyperparathyroidism: Normalization of 25(OH) D, Ca, K, and iPTH

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Orbits shifted Enlargement	Loss of binocular vision Photo review by age	Upward gaze Painless jaw swelling Lymphadenopathy	Jaw series
	Poor opening	Moderate trismus	Soft tissue swelling Concave palate	
	Malocclusion	Absence of third molar	Loose teeth	X-ray
CV	If associated with Noonan syndrome	Pulmonic valve disease	Pulm valve stenosis	ECHO
RESP	Generally unaffected	Obstructive airway	Sleep study	
ENDO	Rule out hyperparathyroidism	Onset at older age	Normal Ca^{2+}, K^+	
CNS	Midparental intelligence	No developmental delay except with Noonan syndrome		
MS	Long bone lesions		Humerus, anterior ribs, femoral neck	

Key References: Monclus E, Garcés A, Artés D, et al.: Oral to nasal tube exchange under fibroscopic view: a new technique for nasal intubation in a predicted difficult airway, *Paediatr Anaesth* 18(7):663–666, 2008; Papadaki ME, Lietman SA, Levine MA, et al.: Cherubism: best clinical practice, *Orphanet J Rare Dis* 7(Suppl 1):S6, 2012.

Perioperative Implications

Preoperative Preparation

- Rule out parathyroid disease.
- Ensure available blood for curettage replacement.

Monitoring

- Routine

Airway

- Difficult airway protocol.
- Oral intubation using a laryngeal mask technique has been reported. Fiberscopic control of the exchange and the introduction of a Cook exchange catheter into the trachea through the oral tube before withdrawal permits oxygenation of the pt and acts as a guide for oral tube reintroduction if required.

Preinduction/Induction

- Spontaneous ventilation
- Laryngeal mask airway

Maintenance

- Consider hypotensive technique for minimizing blood loss.

Extubation

- May require ICU admission for prolonged intubation.

Adjuvants

- Routine

Postoperative Period

- Extubation awake with confirmation of no bleeding

Anticipated Problems/Concerns

- Nasal intubation for oral procedures may be problematic, similar to Pierre Robin, Goldenhar, and Treacher Collins syndromes. As mandibular rami approach midline, no space for visualization of airway.

Chiari Malformations

R. Alexander Schlichter | Jason D. Walls

Risk

- 1:1000 live births
- Increased use of MRI leading to greater diagnosis
- Chiari malformation types I and II: Most common pediatric hindbrain abnormality
- Chiari type II always accompanied by myelomeningocele (which occurs in 0.6 of 1000 live births)

Perioperative Risks

- Respiratory and gastrointestinal dysfunction
- OSA, which has been targeted as an independent risk factor in perioperative morbidity, regardless of type of procedure
- Herniation

Worry About

- Increased ICP
- Herniation
- Hydrocephalus
- Syringomyelia
- Respiratory and cardiac center dysfunction
- Neurogenic dysphagia
- Rapid neuro deterioration in Chiari type II

Overview

- Group of hindbrain abnormalities ranging from herniation of cerebellar tonsils to cerebellar agenesis
- Often complicated by syringomyelia, a cavity fluid collection of the spinal cord
- Classification of Chiari malformations: Types I to IV (also type 0 and 1.5):
  - I: Herniation of cerebellar tonsils through foramen magnum into upper cervical spinal canal, disrupting normal CSF flow; not typically associated with hydrocephalus, but often complicated by syringomyelia (30–70%); referred to as adult-type secondary to delayed diagnosis
  - II (Arnold-Chiari): Herniation of cerebellar vermis, brainstem, and fourth ventricle through foramen magnum in the setting of myelomeningocele; commonly associated with both syringomyelia (20–95%) and hydrocephalus (90%)

- III: Very rare, extreme malformation (<1%) in which cerebellum and brainstem herniate into posterior encephalocele; associated with poor prognosis, severe neurologic deficits, respiratory insufficiency, developmental delay, and hydrocephalus
- IV: Cerebellar hypoplasia or aplasia without associated herniation (extremely rare)
- 0: Syringomyelia without tonsillar herniation that resolves with posterior fossa decompression
- 1.5: Similar to type I but other brainstem components are herniated, in addition to cerebellar tonsils

Etiology

- No unifying pathophysiologic mechanism between different types
- Multiple hypothesis to explain various malformations
- Syringomyelia may have a common origin between different Chiari malformations related to altered CSF dynamics
- Slightly more prevalent in female gender and European ethnicity

Usual Treatment

- No known medical treatment
- Posterior fossa decompression via suboccipital craniotomy with or without duroplasty to re-establish normal CSF flow from posterior fossa to cervical subarachnoid space
- Associated abnormalities, including hydrocephalus, syringomyelia, or scoliosis, which might dictate varied surgical treatment pathways
- Syringomyelia rarely needs direct surgical drainage and typically collapses following successful posterior fossa decompression

Assessment Points

System	Effect	Assessment by Hx	PE	Test
		Chiari I Malformation		
CNS	Brainstem compression	Headache and nonradicular occipital/cervical worsens with activity or Valsalva Dysphagia Severe snoring and OSA Respiratory dysrhythmias	C2 dysthesia Downbeat nystagmus Hoarse voice Tongue atrophy, fasciculations Dysarthria Facial numbness	MRI/cine-MRI CT X-ray (total spine, flex/ex)
	Spinal cord dysfunction (Syringomyelia)	Spasticity Urinary incontinence Arm/hand weakness	Scoliosis Loss of pain/temp sensation Extremity/trunk dysesthesia Arm/hand wasting	Urodynamic testing
	Cerebellar compression	Ataxia	Nystagmus	
		Chiari II Malformation		
CNS	Brainstem compression	Dysphagia, poor suck Aspiration pneumonia Gastroesophageal reflux Opisthotonus Sleep apnea Breath holding Weak cry Prolonged hiccups	Nasal vocalization Palatal weakness Tongue fasciculation/atrophy Inspiratory wheeze Cranial nerve VI palsy Lack of response to inspired CO_2 Tracheal anesthesia Depressed/absent gag	MRI CT
	Spinal cord dysfunction(syringomyelia)	Upper-extremity spasticity Upper-extremity weakness	Persistent cortical thumbs Loss of pain and temperature Upper-extremity weakness and muscle wasting Scoliosis	
	Cerebellar compression	Truncal ataxia	Nystagmus	

Key References: Cesmebasi A, Loukas M, Hogan E, et al.: The Chiari malformations: a review with emphasis on anatomical traits, *Clin Anat* 28(2):184–194, 2015; Tubbs RS, Hankinson TC, Wellons JC: The Chiari malformations and syringohydromyelia. In Ellenbogen RG, Abdulrauf SI, Sekhar LN, editors: *Principles of neurological surgery,* ed 3, Philadelphia, PA, 2012, Saunders, pp 157–168.

Perioperative Implications

Preoperative Preparation

- Assess for increased ICP, brainstem compression, and spinal cord dysfunction.
- Assess any other associated neurologic abnormalities and comorbidities.
- If history of recurrent aspirations, consider chest plain films and ABG analysis.

Monitoring

- Dictated by intended case, ranging from posterior fossa decompression to labor analgesia.
- For posterior fossa decompression, routine ASA monitors with invasive arterial monitoring.
- Central venous access not typically indicated.
- Foley catheter.
- Prepare for neurophysiologic monitoring.

Airway

- Endotracheal intubation while minimizing neck extension; use of in-line traction, fiberoptic bronchoscopy, Bullard laryngoscopy, and video laryngoscopy
- Special precautions in pts with myelomeningocele to avoid undue pressure on the defect

Preinduction/Induction

- Routine IV induction unless dictated by coexisting conditions.
- Consider rapid sequence induction if full stomach, dysphagia, uncontrolled gastroesophageal reflux, or recurrent aspiration are present.

Maintenance

- For posterior fossa decompression, total IV anesthesia may facilitate certain neurophysiologic monitoring modalities if employed.
- Prone positioning.
- Maintain rigid head fixation using Mayfield pin system (in pts >5 y old).
- In neonates, maintain strict temperature and glucose control.
- For obstetric analgesia and anesthesia, weigh risks and benefits of the anesthesia type provided for cesarean and vaginal delivery in parturients with Chiari malformations. Assess for signs and symptoms of increased ICP or neurologic deficits. In asymptomatic pts, spinal and epidural techniques appear safe in pts with Chiari I malformations. Imaging can help target levels that do not have syringomyelia for spinal or epidural placement.

Extubation

- Routine extubation with the goal of rapid emergence for neurologic evaluation and protection of airway reflexes
- Prepare for postop mechanical ventilation when indicated based on neuro deficits

Postoperative Period

- ICU for postop monitoring.
- Possible need for transport to remote locations to obtain postop imaging studies (CT scan).
- Prognosis: 90% of pts with Chiari type I have improvements or stabilization of symptoms. Syrinx typically resolves within 3 mo.

Anticipated Problems/Concerns

- Surgical complications include vascular or neuro injury, pseudomeningocele, CSF leak, meningitis, postop hemorrhage, occipital-cervical instability, hydrocephalus, brainstem compression, cranial nerve palsy, stroke, or persistent syringomyelia.
- Increased ICP management including mild hyperventilation, mannitol, or IV anesthesia.
- Brainstem compression leading to cardiovascular collapse, resistant hypotension, and dysrhythmias.
- Venous air embolism.

Churg-Strauss Syndrome

Rob Tanzola | Rebecca M. Gerlach

Risk

- Rare: 2–5 new cases/million/y
- Average age of onset: 35–50 y
- Male = female

Perioperative Risks

- Necrotizing eosinophilic vasculitis involving respiratory (100% of pts), cardiac (30–60% of pts), neurologic, GI, renal, and integumentary systems

Worry About

- Respiratory complications from severe asthma exacerbations
- CV collapse from coronary artery vasculitis, myocarditis, or cardiac tamponade; represents the major cause of mortality
- Peripheral and central neurologic defects (mononeuritis multiplex and cerebral infarcts)
- GI vasculitis (abdominal pain and bleeding)
- Effects of the standard treatments (steroids and immunosuppressants)

Overview

- Syndrome includes (1) a history of late-onset asthma, (2) eosinophilia, and (3) systemic vasculitis in two or more organ systems.
- Most pts have generalized symptoms, but respiratory effects such as asthma and pulmonary infiltrates are a core clinical feature.
- Affects all major organ systems to varying degrees.
- Delayed diagnosis is common because the first manifestation is usually synonymous with asthma and allergic rhinitis.
- Diagnosis should be considered in pts with asthma and an increased blood eosinophil count or pulmonary infiltrates.
- Prognosis: Remission can be obtained in >80% of pts, but relapse does occur.
- 5-y survival is 80%.
- Asthmatic symptoms usually persist despite recovery from vasculitic symptoms requiring chronic steroid use.

Etiology

- Attributed to an immune reaction to inhaled allergens, but the cause is unknown.
- Possible link to leukotriene receptors antagonist use.
- Three successive phases: (1) asthma and allergic manifestations → (2) blood eosinophil and tissue eosinophil infiltration → (3) systemic phase with subsequent necrotizing vasculitis.
- Clinical features tend to divide into two phenotypes: A vasculitic type with manifestations caused by small-vessel vasculitis (purpura, mononeuritis, and renal), and an eosinophilic type, where organ damage is a result of eosinophil infiltration (pulmonary and cardiac involvement). ANCA-positive pts tend to have the vasculitic type.

Usual Treatment

- Corticosteroids +/− immunosuppressant, depending on severity of organ involvement
- Pulse steroid with long-term wean if possible
- IVIG or plasma exchange for refractory cases

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Sinusitis	Headache Nasal discharge	Facial tenderness	CBC, differential, CT scan
RESP	Asthma Eosinophilic pneumonia/infiltrates	Dyspnea Fever Cough	Wheezing Lung field consolidation	CXR, CT scan, PFT ABGs, bronchoscopy ± Bronchoalveolar lavage, biopsy
CV	Coronary artery vasculitis Endomyocarditis Pericarditis Pericardial effusion/tamponade	Chest pain Dyspnea	Tachycardia, S_3 Pericardial rub Muffled heart sounds Elevated JVP	ECG, angiogram Cardiac MRI, angiogram ECHO
GI	GI vasculitis	Abdominal pain Diarrhea Melena/hematochezia		Endoscopy
CNS	Peripheral neuropathy/mononeuritis multiplex Cranial nerve palsy Cerebral ischemia/hemorrhage	Weakness Sensory deficits	Power assessment	EMG CT
RENAL	Focal segmental glomerulonephritis	Weight gain Foamy urine	Leg edema Hypertension	BUN, Cr Urinalysis
HEME				CBC, eosinophil count ANCA
DERM	Skin lesions		Palpable purpura Cutaneous nodules	Skin biopsy
METAB	Insulin resistance secondary to long-term steroid use	Polyuria Polydipsia		Glucometer, HbA^{1C} Oral glucose tolerance test

Key Reference: Pagnoux C, Guilpain P, Guillevin L: Churg-Strauss syndrome, *Curr Opin Rheumatol* 19:25–32, 2007.

Perioperative Implications

Preoperative Preparation

- Assess asthma control, optimization of bronchodilators, and treatment with inhaled or oral corticosteroids.
- Rule out significant cardiac involvement +/− treatment for heart failure.
- Assess immunosuppressive and steroid-induced side effects.
- Stress-dose steroids if significant surgical stress is anticipated and adrenal suppression suspected.

Monitoring

- Arterial line if significant respiratory or cardiac compromise.
- Consider CVP, PA cath, or intraop ECHO as indicated.

Airway

- Airway hypersensitivity: avoid instrumentation if possible.

Preinduction/Induction

- Regional/neuraxial anesthesia if possible
- Induction with agents that minimize airway reactivity (propofol) or have bronchodilator properties (ketamine)
- Supraglottic airway device if possible to avoid precipitating bronchospasm
- Possible link with pseudocholinesterase deficiency, although not definite

Maintenance

- Volatile anesthetics with bronchodilator properties (avoid desflurane, which can lead to coughing and bronchospasm)
- Avoid histamine-releasing medications (e.g., morphine, atracurium)
- Ventilator parameters: Low tidal volume (6–8 mL/kg), longer expiratory time, avoidance of PEEP, and peak end-inspiratory plateau pressures <30 cm H_2O

Extubation

- Period prone to airway sensitivity and bronchospasm; consider deep extubation.
- Use neostigmine, which can cause bronchospasm, with caution.

Postoperative Period

- Monitor respiratory status given postop decreases in VC and FRC.
- Have an adequate plan for analgesia with consideration for epidural analgesia if appropriate.
- Manage steroid use.

Anticipated Problems/Concerns

- Severe bronchospasm

Cigarette Smoking

Magnus K. Teig | Kevin K. Tremper

Risk

- Smoking is the most common cause of preventable death. Half of cigarette smokers die of a smoking-related disease; on average, smokers lose at least 10 y of life expectancy.
- In USA, incidence of smoking is 17.8%: 42.1 million smokers (2013). Consumption in USA peaked in 1965 at 42%. Worldwide consumption still rising, with 5.8 trillion cigarettes smoked per y; fastest consumption growth is in China.
- Native Americans/Alaskan Natives have highest rate of smoking in USA at 26% followed by African Americans at 25.5%.
- Frequency increased with a lower level of educational attainment (24.2% without high school diploma; 41.4% with GED; 5.6% of those with a graduate degree) and poverty; true even in low- to middle-income countries.
- Male:female ratio: 4:3, with young women the fastest-growing group.

Perioperative Risks

- Increased risk of CAD × 2 that of nonsmokers of the same age
- Postop pulm complications up to × 6 that of nonsmokers
- COHb increased (up to 15%)
- Hyperreactive airway
- No increased risk of pulm aspiration
- Reduced risk of postop N/V
- Increased rate of death (odds ratio 1.63) and postop complications in elective surgery and major joint, spine, and neurosurgery

Worry About

- CAD, COPD, PVD, productive cough, and reactive airways
- Increases physiologic age by 8 y (30 packs per y) relative to nonsmokers
- Decreased tolerance to pain, requiring increased doses of analgesics
- Increased rate of postoperative delirium
- Pediatric passive smoking and reactive airways and increased rate of SIDS

Overview

- Addictive habit: Cigarette smoke contains >4000 identifiable constituents, many of which are pharmacologically active, toxic, or have tumorigenic effects. Acute effects relate to CO and nicotine.
- 90% of tobacco smoke is gaseous, consisting of nitrogen, O_2, and carbon monoxide along with gaseous irritants and carbon monoxide. Particulate matter consists of nicotine, tar, and other volatile organics.
- Nicotine stimulates the sympathetic ganglia, causing release of catecholamines from the adrenal medulla and sympathetic nerve endings, increasing BP, HR, and SVR, that persists for 30 min after one cigarette.
- Associated with decreased MAO and increased dopamine levels in the brain.
- Inhaled CO produces up to 5–15% COHb, compared with 0.3–1.6% in nonsmokers. Combined effects of nicotine and COHb put diseased myocardium at risk.
- Irritates the pulm system, increasing mucus production while decreasing ciliary activity and mucus flow, markedly impairing tracheobronchial secretion clearance.
- Chronic use associated with CAD, Htn, COPD, peripheral vascular disease, and numerous cancers.
- Smoking also increases all blood cell lines, platelet reactivity, and fibrinogen.
- Cessation for 3–4 hours results in insignificant hemodynamic side effects from nicotine, and it improves myocardial O_2 supply to demand.
- Cessation of smoking the night before surgery will reduce the COHb and nicotine levels to that of nonsmokers. Cessation 4–6 d will result in a return of ciliary activity.
- Cessation for less than 4 wk has same rate of respiratory and wound healing complications as found in active smokers (OR 1.2); smokers should stop at least 4 wk before surgery.
- Cessation for 2 y reduces risk of MI to that of the nonsmoking population.
- Smoking is the cause of 1 of every 5 deaths in USA and is the leading cause of preventable mortality (480,000 preventable deaths/y).

Etiology

- Habituation and addiction

Usual Treatment

- Nicotine patch and clonidine, varenicline, bupropion, Smokers Anonymous, or self-withdrawal

Treatment

- Cessation for a minimum of 12–24 h decreases COHb and nicotine levels.
- Cessation for ≥4 wk will reduce postop pulm complications.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral, pharyngeal, and head and neck cancers		Lesions on exam or intubation	Usually not needed
CV	Increased HR, SVR, and coronary vascular resistance Myocardial ischemia Increased PVR Increased blood viscosity	Exercise tolerance, angina (see Coronary Artery Disease)	Two-flight walk	ECG
RESP	Increased COHb and COPD Decreased FEV_1FVC Increased secretion Decreased clearance Increased airway reactivity	Exercise tolerance, chronic productive cough, character of sputum	Auscultation	CXR if symptomatic Hct, sputum

Key References: Moores LK: Smoking and postoperative pulmonary complications, *Clin Chest Med* 21:139–146, 2000; Barrera R, Shi W, Amar D, et al.: Smoking and timing of cessation: impact on pulmonary complications after thoracotomy, *Chest* 127(6):1977–1983, 2005.

Perioperative Implications

Preoperative Preparation

- Cessation overnight will decrease COHb and nicotine.
- Cessation for 4 wk will decrease postop pulm complications. Cessation for <4 wk does not increase the rate of pulm complications.
- Preop nicotine replacement therapy 4–8 wk before surgery and counseling may reduce postop complication rate and increase the rate of long-term smoking cessation; 60% 3–6 mo abstinent.
- Scheduling of elective surgery should be considered an opportunity to quit smoking.
- If chronic productive cough, consider antibiotic treatment at time of surgical scheduling.

Monitoring

- Routine monitoring.
- SpO_2 monitoring may falsely read higher SpO_2 than actual if COHb is present (SpO_2 = % HbO_2 + % COHb).
- Consider invasive monitoring if symptomatic pulm or cardiac disease.

Airway

- Potential laryngeal hyperreactivity

Premedication/Induction

- Consider deep induction if Hx of reactive airway disease.

Maintenance

- Routine maintenance unless symptomatic cardiac or pulm disease.
- Avoid light depth of anesthesia to reduce potential bronchospasm. Desflurane has a similar rate of bronchospasm as sevoflurane.

Extubation

- Consider deep extubation if severe reactive airway disease but easy to intubate and ventilate, with no aspiration risk.

Adjuvants

- Routine; smoking increases metabolism of theophylline, and it decreases the half-life from 265 to 180 min.

Postoperative Period

- Epidural analgesia may be beneficial in decreasing complications of hypercoagulability, CAD, or COPD.

Anticipated Problems/Concerns

- Long-standing Hx of smoking with symptomatic pulm disease leads to a high risk of developing postop pneumonia due to increased mucus production and decreased ciliary function. Cessation for at least 4 wk is recommended.
- Airway reactivity significantly increased in smokers; abstinence for 24 h does not change this reactivity. Reactivity starts reducing after 24–48 h and reduces to near the level of nonsmokers after 10 d of abstinence.
- Risk of MI decreases after 2 years of cessation; 15 years cessation is required to reduce risk to that of someone who never smokes.

Cigarette Smoking Cessation

Nathan G. Orgain

Risk

- In USA, approximately 21% of adults smoke tobacco; prevalence varies inversely with socioeconomic class; men > women (26% vs. 15%).
- Minorities more likely to smoke and less likely to quit.
- Prevalence among adults and teens declining, but growing evidence that teens using electronic cigarettes may be more likely to try other tobacco products.

Perioperative Risks

- Current smokers at increased risk of pneumonia, sepsis, unplanned intubation, mechanical ventilation, cardiac arrest, MI, stroke, and death.
- Increased periop morbidity and mortality related to smoking-associated diseases.
- Probability of morbidity and mortality increase with number of packs smoked per year.

Worry About

- Undiagnosed or poorly treated smoking-related disease (CAD, COPD, cerebrovascular, and peripheral arterial disease) that may affect a safe anesthetic plan
- Propensity for bronchospasm, coughing, decreased pulm reserve, and mucus plugging
- Decreased O_2 content secondary to high COHb levels
- Increased heart rate and BP secondary to nicotine in pts who have smoked just before anesthesia
- Home exposure to second-hand smoke and increase risk of periop pulm complications in children (laryngospasm and asthma)

Overview

- Smoking results in acute changes in cardiopulmonary function, even in otherwise asymptomatic patients. With long-term use, smoking causes chronic changes in cardiopulmonary function that eventually culminate in irreversible cardiopulmonary disease.
- Acute changes include carbon monoxide-mediated decreases in O_2 content and nicotine-induced increases in heart rate and BP. Nicotine-mediated effects are relatively short-lived, whereas COHb persists for many hours.
- Chronic changes include a gradual decline in lung function, consisting of decreases in FEV_1, mucociliary activity, gas exchange, and pulm macrophage activity.
- Associated diseases including CAD, COPD, cerebrovascular disease, and numerous cancers (lung, laryngeal, oral, stomach, bladder, and others).

Etiology

- Acquired behavior that is generally viewed as addiction (both physical to components of tobacco, e.g., nicotine, and psychological/social)
- Risk factors: low education level, low socioeconomic status, and early age of smoking onset

Usual Treatment

- During periop period, pts may be more open to and successful in quitting, and anesthesiologists have a role in urging pt to quit.
- Counseling by anesthesiologists, surgeons, and other counselors.
- Group therapy (e.g., a "12-step" program).
- Pharmacologic adjuncts (e.g., nicotine replacement gum/patch/pill, bupropion, varenicline).
- Referral to quitting resources (e.g., Quit Line phone resource, hospital counselors, state health programs) if possible during periop visits.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral/laryngeal cancer	Hoarseness	Oral exam (and inspection during direct laryngoscopy)	
CV	CAD (±LV function) Cerebrovascular disease	Exertional chest pain, dyspnea, poor exercise tolerance, orthopnea, paroxysmal nocturnal dyspnea	S_3 gallop, dysrhythmia, carotid bruit	ECG, stress test, ECHO, angiography
RESP	COPD	Dyspnea, poor exercise tolerance	Tachypnea, rales, wheezing and pursed-lip breathing	CXR, ABG
OTHER	Increased carboxyhemoglobin (with recent smoking)	Dyspnea	Tachycardia, tachypnea, hypoxia	ABG with co-oximetry (measure CoHb %)

Key References: Gronkjaer M, Eliasen M, Skov-Ettrup LS, et al.: Preoperative smoking status and postoperative complications: a systematic review and meta-analysis, *Ann Surg* 259(1):52–71, 2014; Lee SM, Landry J, Jones PM, Buhrmann O, Morley-Forster P: Long-term quit rates after a perioperative smoking cessation randomized controlled trial, *Anesth Analg* 120(3):582–587, 2015.

Perioperative Implications

Preoperative Preparation

- Advise smoking cessation for at least 12 h before operation (COHb levels fall to near-normal).
- Advise that a longer period of cessation (i.e., ~2 mo) may be necessary to achieve a decrease in postop pulm morbidity. Cessation may rarely be worthwhile in pts with severe pulm disease undergoing a major procedure.
- Suggest that now is an excellent time to quit smoking (reduce future disease risk, improve postsurgical wound healing, recovery, and reduce smoking-related aging).
- Evidence suggests that both the anesthesiologist's reinforcement and in-hospital tobacco cessation programs consisting only of a brief education and counseling visit, self-help take-home materials, and a follow-up phone call are cost-effective in promoting cessation.
- Employ "5 A's": Ask, Advise, Assess, Assist, and Arrange for tobacco cessation

Monitoring

- Routine monitoring
- Most SpO_2 monitors do not distinguish between COHb and oxyhemoglobin. Significant levels of COHb may exist without decrease in SpO_2 reading (obtain ABG with cooximetry if concern exists).

Airway

- Smokers vulnerable to bronchospasm or mucus plug obstruction anytime.
- Children with second-hand smoke exposure may be at increased risk of laryngospasm.

Induction

- Avoid instrumentation of airway until deep level of anesthesia achieved.
- Provide complete preoxygenation because pts have lower tolerance of apnea.

Maintenance

- Follow routine and ensure adequate depth of anesthesia to avoid bronchospasm.

Extubation

- Consider deep extubation if other considerations permit to avoid bronchospasm (e.g., empty stomach, easy laryngoscopy)
- Well-timed IV opioid aids in cough suppression.

Postoperative Period

- Monitor for respiratory complications (e.g., pneumonia, bronchospasm).
- Continue to encourage permanent smoking cessation.
- Ensure pt does not attempt to smoke in presence of supplemental O_2.

Anticipated Problems/Concerns

- Propensity for bronchospasm and mucus plugging.
- Decreased O_2 content secondary to high COHb levels.

Cleft Palate

Brenda C. McClain

Risk

- 1 per 800 live births
- Frequently associated with cleft lip
- Gender predominance: Cleft lip/palate more common in males (2:1); isolated cleft palate more common in females (3:1)

Perioperative Risks

- Morbidity and mortality extremely low; only five life-threatening cases of postop airway obstruction described in the literature.

Worry About

- Difficult airway with associated anomalies of head and neck as in syndromes such as Shprintzen, 4P, or Pierre Robin
- Submental obstruction of airway during mask ventilation; view on laryngoscopy obstructed by tongue

- Laryngospasm on anesthetic induction and airway obstruction due to chronic URIs, chronic otitis media, and/or tongue becoming wedged in the cleft
- Difficult intraop oxygenation due to chronic aspiration syndrome
- Increased risk for transfusion if anemic due to poor ability to feed
- Intraop airway obstruction and extubation by Dingman gag
- Intraoperative dysrhythmias caused by surgical infiltration of epinephrine
- Postop airway obstruction by forgotten pharyngeal packs and severe lingual edema
- Undiagnosed associated congenital heart and renal diseases

Overview

- Congenital condition occurs by 7th-12th wk of intrauterine life and is multifactorial, but it can be associated with a single cause such as benzodiazepine usage.
- Cleft palate repair at 12–18 mo; cleft lip closed at 3 mo if also present; single to multiple stage methods employed dependent on type of defect(s).
- Usually not associated with severe blood loss.
- Postop airway obstruction may occur more frequently in prolonged procedures.
- A tongue stitch is often placed at end of surgery for management of possible airway obstruction, and it is removed the next day.

Usual Treatment

- If child is in otherwise good health, a palatoplasty is performed electively.
- All children with cleft palate should have repair by 18 mo to ensure:
  - Normal speech development
  - Appropriate social integration
  - Normal growth of maxilla

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Otitis media Clear rhinorrhea Difficult airway	Ear pain Snore, grunt	Temporomandibular exam Airway exam (micrognathia)	
CV	Associated congenital heart disease	SOB, cyanosis, poor growth	CV exam, club foot	ECG, ECHO
RESP	URI Aspiration	Cough, fever Congestion SOB, cyanosis	Chest exam Chest exam	CXR
GI	Impaired deglutition Malnutrition	Nasal regurgitation Poor growth		Observe feeding
HEME	Anemia	Malnutrition	Pallor	Hgb/Hct
RENAL	Associated congenital defects	UTI	Club feet	UA, BUN/Cr

Key References: Chiono J, Raux O, Bringuier S, et al.: Bilateral suprazygomatic maxillary nerve block for cleft palate repair in children, *Anesthesiology* 120(6):1362–1369, 2014; Steward DJ: Anesthesia for patients with cleft lip and palate, *Semin Anesth Periop Med Pain* 26(3):126–132, 2007.

Perioperative Implications

Preoperative Preparation

- Recognize possibility of multiple future procedures and attempt to minimize stress during induction. Consider oral premedication.

Anesthetic Technique

- GA, usually induced via a mask and using increasing concentrations of volatile agent in O_2, to avoid paralysis until airway is secured.
- Oral airway or gauze packing of cleft may help manual ventilation by preventing tongue from lodging in cleft.
- Intubation, often with RAE ETT secured to mandible, because access to airway may be severely limited.

Monitoring

- Precordial stethoscope, pulse oximeter, and noninvasive BP measurement.
- Maintain normocapnia if epinephrine injection is used.

Postoperative Considerations

- Significant risk for airway obstruction due to edema
- Often obligate mouth breathers
- Judicious use of opioids in a monitored setting; rectal acetaminophen is helpful, especially in combination with suprazygomatic maxillary nerve blocks

Anticipated Problems/Concerns

- Airway difficulty during induction and intubation, especially when associated with other facial anomalies
- Postop airway obstruction due to forgotten pharyngeal pack, severe lingual edema, or obligate mouth breathing

Coagulopathy, Factor IX Deficiency

Thomas M. McLoughlin Jr.

Risk

- Within USA, approximately 4000 persons are affected (20% of all hemophiliacs): incidence: 1:25,000–30,000 males; 75–100 are people born with the disease in USA each year.
- No racial prevalence.
- Highest prevalence overwhelmingly in males.

Perioperative Risks

- Increased risk of hemorrhagic complications from any procedure.
- Of affected individuals, 60% have severe disease (<1% normal circulating factor IX).
- Of carrier females, 10% have abnormal hemorrhage risk.

Worry About

- Excessive and/or uncontrollable hemorrhage
- Tendency for recurrent hemorrhage after initial control
- Expansive deep and soft-tissue hematomas
- Increased risk if hepatic dysfunction from prior plasma product transfusions

Overview

- Inherited; also called hemophilia B or Christmas disease.
- Very similar to hemophilia A (classic hemophilia), but with somewhat less severe bleeding frequency and severity.
- Hemarthrosis accounts for 75% of bleeding episodes. Chronic debilitating arthritis is a common development.
- Soft-tissue hematomas and hematuria also common.
- Intracranial hemorrhage is most common fatal complication.
- Disease severity proportional to circulating factor IX activity (<1% normal activity = severe disease; >5% = generally mild disease).
- Modern maintenance factor replacement treatment results in normal life expectancy.

Etiology

- Sex-linked recessive disorder.
- 70% of cases inherited; 30% result from spontaneous mutation.
- Acquired factor IX deficiency associated with liver disease.
- Adult levels may not be reached in healthy newborns until 6 mo of age.

Usual Treatment

- Restoration of circulating factor IX activity; biological half-life is 18–24 h.
- Plasma-derived pooled factor IX concentrates (AlphaNine SD, Mononine).
- Recombinant factor IX concentrates (BeneFIX [Pfizer], Rixubix [Baxter], and Ixinity [Emergent]) along with an extended half-life (approximately 86 h) recombinant product (Alprolix [Biogen]).
- Of patients in USA, >75% use recombinant products for maintenance therapy.
- In vivo effect of recombinant factor IX products is less than that of plasma-derived products.
- Rarely (3–5% of pts), acquired alloantibodies to administered factor IX substantially complicate treatment.
- Prothrombin complex concentrates and FFP are alternatives for life-threatening hemorrhage if concentrates unavailable.

Assessment Points

System	Effect	Assessment Hx	PE	Test
GI				LFTs if hepatitis Hx
HEME	Coagulopathy	Dental extractions, menses, lacerations, epistaxis	Ecchymoses, hematomas	Prolonged PTT; PT and platelet count usually normal
RENAL	Hematuria; eventual clot formation can obstruct collecting system	Discolored urine		BUN/Cr, urine dipstick or microscopic exam
CNS	Intracranial hemorrhage	Headache	Neurologic exam	
PNS	Discrete peripheral neuropathies	Hx of compressive hematoma	Sensory and motor exam	
MS	Hemarthrosis, chronic arthritis	Painful, warm joints	Decreased ROM	X-rays usually not necessary

Key References: Franchini M: Current management of hemophilia B: recommendations, complications and emerging issues, *Expert Rev Hematol* 7:573–581, 2014; Mensah PK, Gooding R: Surgery in patients with inherited bleeding disorders, *Anaesthesia* 70(Suppl 1):112–120, 2015.

Perioperative Implications

Preoperative Preparation

- Collaborate with consulting hematologist.
- Schedule surgery early in wk to allow optimal postop laboratory support of the assessment of hemostasis; if multiple procedures are contemplated in near future, schedule simultaneously.
- Assess preop factor IX activity; determine goal as guided by magnitude of hemostatic challenge (15–30% factor IX activity for minor lacerations/hematomas; 40–60% for hemarthrosis or major hemorrhage, 50–100% for periop coverage or life-threatening bleeding).
- Units of factor IX needed (plasma-derived) = (Weight in kg) (fractional increase in factor IX activity desired); once-daily dosing is sufficient for maintenance.
- Units of factor IX needed (recombinant) = (Weight in kg) (fractional increase in factor IX activity desired) (reciprocal of observed potency for product). BeneFIX demonstrates 0.8 IU/dL observed activity per administered unit; Rixubis demonstrates 0.9 IU/dL activity per administered unit; Alprolix demonstrates 1 IU/dL activity per unit.

Monitoring

- Confirm expected increase in factor IX activity after preop dose but before incision.

Airway

- Laryngoscopy to avoid tissue trauma; consider mask ventilation.
- Avoid blind oral instrumentation.
- Nasotracheal route is best avoided.

Maintenance

- Consider tourniquets and local cooling to minimize blood loss.

Extubation

- Avoid coughing on endotracheal tube.
- Caution with oropharyngeal suction; best done under direct vision.

Adjuvants

- Regional anesthesia not absolutely contraindicated, but consider with caution; successful brachial plexus blockade at the axilla has been described; no epidural hematoma from neuraxial technique reported when diagnosis of hemophilia B known in advance.
- Postop factor IX activity requirements following major surgery are 75-100% POD 0-3; 60-80% POD 4-6; and 40-60% POD 7-14.

Anticipated Problems/Concerns

- Excessive periop blood loss and hematoma formation
- Potential for delayed or recurrent bleeding after initial control
- Increased likelihood of infectious blood-borne disease (HIV, hepatitis), mostly in pts treated with plasma replacement products before the early 1990s

Coarctation of the Aorta

Thomas M. Chalifoux | Edmund H. Jooste

Risk

- Sixth most-common congenital heart defect: 4:10,000 live births
- Recognized in 5–8% of pts with CHD

Perioperative Risks

- Perioperative mortality: 1% when associated with no other cardiac anomalies in neonates, 10% when associated with a VSD, and 50% when associated with HLHS; children and adults: Less than 0.5%
- Postop risk of paraplegia: 0.5–1.5% (even lower risk if younger than 1 y of age)

Worry About

- Closure of the ductus arteriosus in neonates and infants, which can lead to acute LV failure and hypoperfusion distal to coarctation.
- Maintain adequate perfusion to the lower portion of the body during cross-clamping of the aorta to provide adequate perfusion to spinal cord and abdominal vital organs.
- Intraop systemic Htn proximal to the aortic cross-clamp.
- Acute hypotension and metabolic acidosis on release of aortic cross-clamp.
- Postop systemic Htn.

Overview

- Congenital narrowing of the aorta at or near the ductus arteriosus or ligamentum arteriosum, causing a hemodynamically significant pressure gradient
- Commonly associated defects in neonates and infants: Bicuspid aortic valve, mitral valve anomalies, PDA, aortic hypoplasia, VSD, AV canal defects, d-TGA, and single ventricle variants
- Usually an isolated defect in older children and adults
- Lifelong surveillance needed after repair

Etiology

- Several theories: Abnormal flow patterns in the developing fetal heart, which may cause decreased aortic flow resulting in aortic hypoplasia; ectopic ductal tissue in the aorta; or a combination of both
- Possibly a component of trisomy 13, trisomy 18, deletion of chr 22q11, Turner syndrome, Kabuki syndrome, or Takayasu arteritis

Usual Treatment

- Surgical repair for initial management, using several techniques, including subclavian flap aortoplasty, resection and end-to-end anastomosis, and prosthetic patch augmentation; left thoracotomy (common) and cross-clamp time should be minimized to 20 min, but repair of associated defects may require sternotomy and CPB with or without DHCA.
- Transcatheter balloon angioplasty used for initial management of native coarctation in older infants and young children and for management of recoarctation, which may include endovascular stent placement; also stent procedure of choice in older children and adults. Children with stents may require stent dilation as the child grows.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL	Failure to thrive	Poor feeding	Poor growth	Growth chart
NEURO	Intracranial aneurysm (child and adult)			
HEENT	Upper-body Htn (rare in neonate <5 d old)	Epistaxis Headache		Four extremity BP measurement
CV (general)			Systolic pressure and pulse gradient between upper and lower extremities (may not be present with PDA)	ECHO, ECG, CXR, MRI/MRA, cardiac cath with angiography
CV (neonate/infant)	CHF	Poor feeding	Tachypnea, cyanosis, hepatomegaly, metabolic acidosis	ABG, CXR
CV (child/adult)	Development of collateral circulation			CXR showing rib notching (a late finding)
PULM	CHF (neonate and infant)		Resp failure	CXR, ABG
RENAL	Renal failure secondary to poor perfusion (neonate and infant)			Lytes, BUN, creatinine, urine output and analysis
MS	Poor peripheral perfusion Spinal cord compression by dilated anterior spinal artery or branch compressing a nerve root	Claudication, lower extremity pain, paresthesia, muscle weakness	Diminished or absent femoral pulses	

Key References: Kenny D, Hijazi ZM: Coarctation of the aorta: from fetal life to adulthood, *Cardiol J* 18(5):487–495, 2011; Landsman IS, Davis PJ: Aortic coarctation: anesthetic considerations, *Semin Cardiothorac Vasc Anesth* 5(1):91–97, 2001.

Perioperative Implications

Preoperative Preparation and Induction

- Neonate/infant: Maintain PDA with PGE_1. PDA closure can lead to CHF, upper-body Htn, and lower-body hypoperfusion and shock.
- The presence of a VSD leads to significant left-to-right shunting and a further steal of the systemic blood flow. Do not decrease PVR further by hyperventilation or the use of 100% O_2.
- Right lateral decubitus position used for left thoracotomy. Good padding is important.
- Regular ETT used for neonates and infants, but consider bronchial blocker or double lumen ETT in older children and adults.

Monitoring

- Standard monitors, pulse oximeter × 2 (right upper and either lower extremity), and urinary cath.
- Right upper-extremity arterial cath (radial, ulnar, or axillary) or lower-extremity arterial cath if pressure gradient is high or a combination of arterial and NIBP monitoring in the RUE and a lower extremity.
- Central venous access required for infusion of vasoactive medications.
- SSEPs may be used to motor spinal cord perfusion during aortic cross-clamping (particularly if aortic gradient is high or there is little collateral circulation) in older children.

Maintenance

- To prevent spinal cord ischemia, passively cool to core temp 34–35° C, maintain normocapnia, and keep distal mean arterial pressure >40 mm Hg.
- Control Htn with titratable agents: Inhalation agent, sodium nitroprusside, esmolol, and nicardipine.
- If mean arterial pressure <40 mm Hg or there is significant change in the SSEP signal with aortic cross-clamp application, institute left heart bypass.
- Be prepared to treat a sudden drop in BP and acidosis following aortic cross-clamp release with fluids and sodium bicarbonate.

Postoperative

- Neonates and infants with CHF remain intubated and ventilated until condition improves.
- Children and adults may usually be extubated in the OR.
- Pain management: Opioids, dexmedetomidine, intercostal nerve block by surgeon, paravertebral cath, and epidural cath (must consider risk of epidural hematoma).

Anticipated Problems/Concerns

- Paraplegia likely secondary to spinal cord ischemia, particularly if clamp time >30 min
- Postcoarctectomy syndrome: Severe abdominal pain with tenderness, Htn, fever, vomiting, ileus, melena, and leukocytosis (occurs 2–3 d postop)
- Pulm Htn in neonates and infants with CoA and VSD (Rx: NO and milrinone)
- Stridor/partial airway obstruction at extubation secondary to recurrent laryngeal nerve injury
- Ventilatory compromise at extubation secondary to phrenic nerve injury causing hemidiaphragmatic paralysis
- Intraop and postop bleeding
- Aortic aneurysm, dissection, and rupture
- Neurologic symptoms from subclavian steal secondary to reduced perfusion of the left arm after subclavian flap angioplasty
- Chylothorax from thoracic duct injury
- Recoarctation (late complication)

Cogan Syndrome

Michael Carrigan | Jeffrey R. Kirsch

Risk

- Extremely rare: approximately 250 reported cases in the literature
- Mean presentation 30–40 y; however, cases in children and elderly reported
- No predilection for gender, race, or ethnicity
- Possible association with IBD

Perioperative Risks

- Hemorrhage
- Thrombosis and organ/limb ischemia
- Adrenal insufficiency and immunosuppression due to chronic treatment
- Postop N/V with vestibuloauditory dysfunction

Worry About

- Activity state of disease and hemorrhage/extension of pathologic vasculitis
- Coexisting vasculitis affecting cerebral, cardiac, mesenteric, and renal perfusion
- Sepsis with immunosuppression

Overview

- Heterogeneous presentation of nonsyphilitic interstitial keratitis and vestibuloauditory symptoms within 2 y of each other; note an atypical version allows exceptions to these criteria
- 10–15% of pts develop large cell vasculitis, usually aortitis
- Coronary involvement: often asymptomatic
- Typically sudden severe bilateral hearing loss; distinct from unilateral Meniere disease; deafness develops in ~50% of pts.
- Recurrent flares for majority of pts
- Mean long-term survival: 20+ y after diagnosis

Etiology

- No definitive cause, but an autoimmune process is suspected; often preceded by a viral prodrome.
- Proposed mechanisms include antibodies to an inner ear peptide, Cogan peptide, and HSP70.
- Rheumatoid factor and ANA are not consistently associated with diagnosis, but a small percent of pts are ANCA+.
- Approximately 50% have a history of daily smoking, and approximately 33% have or develop IBD.

Usual Treatment

- Topical steroids and mydriatic agents for isolated anterior chamber disease
- Systemic immunosuppressives for posterior chamber, inner ear, and vasculitis

- Typically high-dose steroids (1 mg/kg per d prednisone for 2–4 wk) until hearing improves, and then taper over 3–6 mo
- MTX, cyclophosphamide, azathioprine, leflunomide, tacrolimus, and rituximab all with case reports of effectiveness, usually reserved for severe organ or life-threatening presentations
- Surgical repair or bypass of diseased segments: favorable only when activity of the disease is under control with medical treatment
- Cochlear implant use: Very successful

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Inner ear dysfunction Interstitial keratitis	Dizziness, tinnitus Photophobia, redness, tearing, blurry vision, and oscillopsia	Slit lamp exam	Calorics and audiogram with sensorineural hearing loss
RESP	Pulmonary embolism Pneumonia (due to immunosuppression)	Dyspnea Cough	Tachypnea Lung field consolidation Wheezing	CXR, V/Q scan, CT scan Bronchoscopy BAL ABG
CV	Aortitis Coronary arteritis Limb ischemia AI, MR	Chest/back/abdominal pain Dyspnea Orthopnea	Tachycardia Hypotension Disparate limb BP Heart murmur	ECG, TTE CT scan Limb duplex scan Angiography
GI	Mesenteric ischemia	Post prandial abdominal pain N/V	Abdominal tenderness Splenomegaly	CT scan Angiography Abdominal US
CNS	Intracranial manifestations of vasculitis	Weakness Numbness Falling Incoordination Difficulty speaking	Gait instability Dysmetria Functional neurologic deficits	Head CT and MRI to R/O tumor/stroke Carotid duplex US
HEME	Pancytopenia	Easy bleeding and bruising Fatigue Fever	Petechiae Rash Pallor Lymphadenopathy	CBC and differential Reticulocyte count Peripheral smear
METAB/ ENDO	Iatrogenic Cushing syndrome	Poor wound healing Skin changes Body habits changes Emotional/psychiatric changes	Striae Buffalo hump Skin wounds Moon facies Htn Hirsutism	Electrolytes $HgbA_1C$
RENAL	Glomerulonephritis	Hematuria Oliguria Headache Edema	Htn Peripheral edema	BMP, albumin, UA

Key References: Singer O: Cogan and Behçet syndromes, *Rheum Dis Clin North Am* 41(1):75–91, 2015; Gluth M, Baratz K, Matteson E, Driscoll CL: Cogan syndrome: a retrospective review of 60 patients throughout a half century, *Mayo Clin Proc* 81(4):483–488, 2006.

Perioperative Implications

Preoperative Preparation

- Assess disease activity state and screen for concomitant vasculitic processes.
- Ensure adequacy of blood products and IV access.
- Severe neutropenia may warrant prophylactic antimicrobial therapy and reassessment of timing risk/benefit.
- Concomitant steroid therapy and necessity of stress doses should be considered.

Monitoring

- Consider awake arterial line in appropriate limb as indicated.
- Consider CVP, TEE, or PA cath as indicated for disease burden and procedure.
- Consider BIS if cerebral circulation is affected.

Airway

- Use caution with edematous airway mucosa.

Preinduction/Induction

- Tailor afterload and preload management to cardiac function and concomitantly affected organs including cerebral, renal, and mesenteric beds.
- Avoid hypotension in concomitantly affected organs.

Maintenance

- Judicious blood pressure management to preserve diseased organ bed perfusion

Extubation

- Avoid Htn with vascular repairs and aneurysmal burden.

Postoperative Period

- Continue monitoring of hemodynamics.
- Maintain vigilance for hemorrhage.
- Immunosuppressed patients have an increased susceptibility to infection.
- Watch for signs of adrenal insufficiency.

Anticipated Problems/Concerns

- Maintain a low threshold to evaluate the occult disease burden of other organ systems not identified preop.

Complement Deficiency

David Y. Kim | Marshall K. Lee

Risk

- C1 esterase inhibitor–deficiency incidence: 1:50,000-150,000 of the general population.
- Symptoms onset and diagnosis occur approximately at 20 y, and by 30 y approximately 98% of pts have symptoms.
- C2 deficiency incidence: <0.1% of the general
- Male versus female ratio: 1:6.
- Higher incidence (6%) in pts with autoimmune disease (see Immune Suppression).
- Incidence in pts with Hx of *Neisseria* meningitis: 15%.
- C3 and C5–C8 deficiencies have increased risk for infections.

Perioperative Risks

- Possible life-threatening airway compromise
- Increased risk of postop infection, particularly if the deficiency affects the early complement components
- Risk for inflammatory complications (e.g., glomerulonephritis, vasculitis)

Worry About

- Acute airway edema resulting from laryngeal or mucous membrane swelling, which can result in definitive airway obstruction; abdominal pain from intestinal edema, which may be an associated finding on exam
- Increased infectious risk

Overview

- Hereditary angioneurotic edema is associated with a complement deficiency of the enzyme C1 esterase inhibitor. It is a rare genetic deficiency that may lead to uncontrolled production of C2, C3, and C5 complement, resulting in acute noninflammatory, painless, nonpruritc, nonpitting edema. Initial inciting events are often the result of trauma, but may even be attributed to emotional stress.
- Any component of the classical pathway, alternate pathway, or terminal common pathway may be affected.
- Virtually all deficiencies show some ↑ risk of infection and/or autoimmune disease.
- Deficiencies in other complement components, C2 and C3, have also been associated with immunocompromised pts, resulting in recurrent life-threatening infections associated with a variety of organisms.
- Increased risk of autoimmune diseases.
- Deficiency in any of the terminal components C5–C8 show selective risk of recurrent neisserial infections, which usually are not life threatening.

Etiology

- C1 complement results from a heterozygous deficiency of C1 esterase inhibitor. The mediators of the angioedema response result from coagulation, complement, and the kinin pathway. C1 esterase inhibitor is a key regulator for Hageman factor, coagulation, plasmin, and plasma kallikrein. There have been more than 100 mutations on the C1 esterase gene in pts without hereditary angioedema, and 20% of those have been new mutations with no prior history.
- All complement proteins are inherited in an autosomal fashion, with the possible exception of properdin, which appears to be X-linked.

Usual Treatment

- Treatment modalities have included stanozolol, danazol, methyltestosterone, oxymetholone, aminocaproic acid, tranexamic acid, and cinnarizine. Mechanism of action for therapeutics is increased synthesis of C1 esterase inhibitor (for the steroids) and inhibition of plasmin activation (for the antifibrinolytics).
- Acute preop prophylaxis has consisted of fresh frozen plasma and epinephrine. However, caution must be taken because plasma provides substrates that may aggravate the scenario and worsen the edema. Purified concentrates of C1 esterase inhibitor given IV have also been used outside USA.
- Antibiotic treatment dictated by specific infection.

Assessment Points

System	Effect	Test
IMMUNO	Infectious risk for all systems	CH50 screening test for complement-mediated lysis of sheep erythrocytes; tests for specific complement components available at reference labs Assess other specific organs as indicated by autoimmune disease (e.g., renal for SLE)

Key References: O'Neil KM: Complement deficiency, *Clin Rev Allergy Immunol* 19(2):83–108, 2000; Wen L, Atkinson JP, Giclas PC: Clinical and laboratory evaluation of complement deficiency, *J Allergy Clin Immunol* 113(4):585–593, 2004.

Perioperative Implications

Preoperative Preparation

- In pts with C1 deficiency, consider preop administration of 2 units of FFP or C1 concentrate with appropriate consideration to risks and benefits of therapy.
- Sterile technique strictly observed.

Monitoring

- Routine.
- Coagulation profile.
- Minimize invasive lines.

Airway

- Airway management should minimize trauma. Tracheal intubation is acceptable, but preparation for an emergency tracheostomy should be made. Laryngeal mask airway use should be tempered by the concerns for upper-airway edema and resulting ineffective ventilation. Regional anesthesia is an acceptable alternative to prevent airway manipulation.

Induction

- Routine

Maintenance

- Routine

Extubation

- Extubate and remove all lines at earliest opportunity.

Postoperative Period

- Maintain sterile techniques.

Anticipated Problems/Concerns

- If emergency intubation is required, it is recommended that an otolaryngologist or surgical personnel be present for a possible tracheostomy or cricothyroidotomy.
- Ensure meticulous sterile technique to minimize risk of infection.

Congenital Methemoglobinemia

Bronwyn R. Rae

Risk

- Navajo Indians, Alaskan Indians, and people of Puerto Rican and Cuban ancestry
- Normal life span (except for RCM type II)

Perioperative Risks

- Oxidizing agents may increase MetHb to dangerous levels.
- Mild respiratory/cardiac depression may adversely affect pts with already limited reserve.
- Pregnancies not compromised.

Worry About

- Measurement of SpO_2
- Oxidant drugs (e.g., prilocaine, benzocaine, nitroglycerin, sulfonamides, phenacetin, and nitric oxide), which are contraindicated
- Myocardial ischemia due to decreased O_2 delivery
- Blood loss/anemia due to O_2-carrying capacity already reduced

Overview

- Enzyme deficiency: Shift of O_2 dissociation curve to the left leads to mild erythrocytosis (normal RBC life span).
- RCM type I defect restricted to red cell soluble cytochrome b5 reductase only. Cyanosis is sole clinical symptom. Homozygotes have compensatory increase in RBC mass. Heterozygotes may develop acute symptomatic methemoglobinemia after exposure to exogenous MetHb-inducing agents. Defect may be the cause of unexplained periop cyanosis.
- RCM type II: Defect occurs in all cells and involves both soluble and microsomal forms of cytochrome b5 reductase. Results include mental retardation, spasticity, opisthotonos, microcephaly, growth retardation, and death by 2–3 y of age.
- RCM type III: Nonerythroid enzyme deficiency, but CNS spared.
- HbM variations: Alpha chain variants affected from birth, and beta chain variants by 3–6 mo of age. Patients develop mild hemolytic anemia.

Etiology

- RCM types I, II, and III: Occur by autosomal recessive inheritance because of deficient reducing capacity of oxidized heme caused by NADH cytochrome b5 reductase (diaphorase) deficiency.
- HbM variants: Occur by autosomal dominant inheritance due to structural abnormality in globin moiety; amino acid substitutions create abnormal environment for heme residues, displacing the equilibrium toward the ferric state.

Usual Treatment

- RCM types I, II and III: Reducing agents (e.g., riboflavin 20–60 mg orally, methylene blue 1–2 mg/kg IV; the effect lasting 10–14 d) and ascorbic acid used for chronic management
- HbM variants: No available treatment. (In an emergency, hyperbaric O_2 therapy and exchange transfusion may be used.)

Assessment Points

System	Physical Examination	Test
RESP	Cyanosed but more "blue" than "sick"	15-30% MetHb
HEME	RCM types I and II: Mild erythrocytosis HbM variants: Mild hemolytic anemia	CBC
CV	May be unable to meet increased metabolic demand	ECG

Key References: Jaffe E, Hultquist D: Cytochrome b5 reductase deficiency and enzymopenic hereditary methemoglobinemia. In Scriver C, Beaudet A, Sly W, et al., editors: *The metabolic and molecular bases of inherited disease,* ed 3, vol. 3, New York, NY, 1995, McGraw Hill, pp 3399; Guay J: Methemoglobinemia related to local anesthetics: a summary of 242 episodes, *Anesth Analg* 108(3):837–845, 2009.

Perioperative Implications

Preoperative Preparation

- Can give reducing agents to pts with RCM type I, but no data exist on whether treatment is indicated before anesthesia.

Monitoring

- Pulse oximeter overestimates at low SpO_2 and underestimates at high SpO_2. In practice, it reads between 80–85%, regardless of true saturation.
- Use co-oximetry for SaO_2 and MetHb levels.
- Monitor ECG for ischemic changes.
- May see "chocolate brown" blood in the operative field or arterial cannula.

Airway

- None

Preinduction/Induction

- Adequate preoxygenation with 100% O_2 because O_2-carrying capacity is already decreased.

Maintenance

- Prilocaine, benzocaine, and EMLA cream are contraindicated. The literature is contradictory on lidocaine. The effects are probably due to respiratory/myocardial depression in patients with low reserve, rather than an increase in MetHb.
- Nitrous oxide, propofol, and volatile agents are okay.

Adjuvants

- None

Postoperative Period

- Avoid acetanilides, paracetamol, metoclopramide, and nitrites. Narcotics may be used.

Anticipated Problems/Concerns

- Avoid oxidant drugs in both homozygotes and heterozygotes.
- Pulse oximetry is inaccurate; use ABG with co-oximetry.
- May require supplemental O_2 postop.
- May have limited cardiac and respiratory reserve.

Congenital Pulmonary Cystic Lesions/Lobar Emphysema

Francine S. Yudkowitz

Risk

- Cause of cardiorespiratory compromise
- 10–15% associated with CHD

Perioperative Risks

- May develop worsening of cardiorespiratory status
- Contamination of unaffected lung by infected material from cyst

Worry About

- Associated congenital anomalies
- Tension pneumothorax
- Cardiorespiratory compromise

Overview

Congenital Pulmonary Cystic Lesions (Three Types)

- Bronchogenic: Abnormal budding and branching of tracheobronchial tree leading to resp distress, pneumonia, and atelectasis
- Dermoid: Lined with keratinized, squamous epithelium
- CPAM: Previously known as CCAM; similar to bronchioles but without alveoli, bronchial glands, and cartilage; overdistension because of gas trapping, which leads to resp distress

Congenital Lobar Emphysema

- Hyperinflation and air trapping result in expansion of affected lobe.
- Most commonly occurs in the left upper lobe, followed in frequency by the right middle, and then the right upper lobe.
- Preterm infants on mechanical ventilation develop emphysema in the right upper lobe.
- CXR shows emphysematous lobe crossing midline, mediastinal shift, and atelectasis in other lobes and possibly the contralateral lung. The presence of bronchovascular markings distinguishes this from pneumothorax and congenital cysts.

Etiology

- Congenital pulmonary cystic lesions may be bronchogenic, alveolar, or a combination of both, and anomalous development of the bronchopulmonary system occurs.
- Congenital lobar emphysema has extrinsic bronchial obstruction from abnormal vessels or enlarged lymph nodes and intrinsic bronchial obstruction from deficient bronchial cartilage, bronchial stenosis, or redundant bronchial mucosa.

Usual Treatment

- Surgical removal

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Decreased lung volume	Cyanosis, dyspnea, grunting, coughing	Tachypnea, retractions, wheezing, decreased BS, asymmetric chest expansion	CXR CT scan
CV	Mediastinal shift, decreased CO, VSD, PDA	Irritability, poor feeding	Decreased heart sounds Murmur	CXR, ECG, ECHO

Key References: Hammer G, Hall S, Davis PJ: Anesthesia for general abdominal, thoracic, urologic, and bariatric surgery. In: Davis PJ, Cladis FP, Motoyama EK, editors: *Smith's anesthesia for infants and children,* ed 8, Philadelphia, PA, 2011, Elsevier; Guruswamy V, Roberts S, Arnold P, Potter F: Anaesthetic management of a neonate with congenital cyst adenoid malformation, *Br J Anaesth* 95(2):240–242, 2005.

Perioperative Implications

Preoperative Preparation

- Assess the severity of cardiopulmonary compromise.
- Identify associated congenital anomalies.
- Optimize resp infection if pt is stable.
- Aspirate cyst before induction if there is cardiac compromise or airway obstruction.

Monitoring

- Arterial line for BP monitoring and blood gas analysis

Induction

- Avoid positive pressure ventilation until thorax is opened to avoid expansion of cyst or lobe.
- Avoid N_2O, which will expand the lobe or cyst.
- Inhalation induction with 100% O_2.
- Intubate without the use of muscle relaxants.
- Affected lung may need to be isolated. In small infants and children, this may be accomplished by using a bronchial blocker or doing a mainstem intubation.
- Surgeon should be available to open the chest immediately if deterioration should occur during induction of anesthesia.

Maintenance

- No one anesthetic preferred.
- Maintain spontaneous ventilation or assist with low airway pressures until thorax is opened.
- Once the pathology is removed, N_2O may be used.
- If Hx of repeated lung infections (cysts), there may be large blood losses.

Extubation/Postoperative Period

- Pt may be extubated after uncomplicated surgery and when cardiopulmonary function is adequate.
- Consider regional anesthesia (intercostal or epidural) for management of postop pain to decrease splinting and opioid use.

Anticipated Problems/Concern

- Pts with altered cardiopulmonary reserve before surgery may require postop intubation and ventilation.
- If pneumonectomy performed, there will be overinflation of the remaining lung, with a decrease in vital capacity. These children may have significant exercise intolerance for a prolonged period after surgery.
- Important that pt avoid postop atelectasis, coughing, and early ambulation or increase in activity.
- Altered pulm mechanics (decreased forced vital capacity and delayed forced expiration) may be present throughout childhood.

Congestive Heart Failure

Miklos D. Kertai

Risk

- Heart failure is a syndrome, not a disease.
- Incidence in USA: About 5.1 million, with more than 650,000 new cases diagnosed annually. Primary discharge diagnosis made in more than 1 million pts.
- 1-y and 5-y survival rates are 57% and 25% in men and 64% and 38% in women. Median survival after onset is 1.7 y in men and 3.2 y in women.

Perioperative Risks

- Heart failure occurs in 1–6% of pts after major surgery, and between 6% and 25%, in pts with existing cardiac conditions.
- EF <35% associated with increased operative risk.
- Single greatest risk factor for cardiac surgery. Use congestive heart failure score (CASS): Hx of CHF = 1; Rx digitalis = 1; Rales = 1; overt symptoms after treatment = 1; total 0–4. If score = 4, operative risk is 8× greater.

Worry About

- Ventricular dysfunction preop, which is associated with increased operative mortality.
- Pt with diastolic dysfunction may be asymptomatic at rest but sensitive to increases in heart rate, which may result in flash pulm edema.
- Dysrhythmias due to cardiac ischemia (sudden cardiac death).
- Associated acute or chronic mitral insufficiency.
- Volume status.
- Prolonged effect of ACE inhibitors.

Overview

- Different types of failure (left vs. right; acute vs. chronic; systolic vs. diastolic; low output vs. high output)
- Reduced contractility, decreased stroke volume, increased heart rate, and hypertrophy and ventricular dilatation
- Acute ischemia, which can lead to global diastolic dysfunction and CHF
- Papillary muscle ischemia, which may lead to severe mitral regurgitation and pulm congestion
- New York Heart Association classification: I, no limitation; II, slight limitation; III, marked limitation; IV, inability to carry out any physical activity; overall 1-year mortality for classes III and IV: 34–58%

Etiology

- Acquired, acute or chronic: CHD and MI; cardiomyopathy (idiopathic, hypertrophic, hypertrophic obstructive, congestive, and alcoholic). Valvular heart disease: Arrhythmias and severe hypertension.
- Congenital: Congenital heart disease, left-to-right shunts; intracardiac (ASD, VSD, and AV canal), and extracardiac (PDA and anomalous pulm venous connection). Obstructive (coarctation of the aorta and aortic stenosis). Complex (Ebstein anomaly).
- Multiple precipitating causes: Noncompliance with medications (digitalis and diuretics), excessive Na^+; excessive IV fluids; drugs (doxorubicin, corticosteroids, disopyramide, nortriptyline, NSAIDs, thiazolidinediones, metformin, cilostazol, PDE-5 inhibitors [sildenafil, vardenafil] androgens, and estrogens). Pulm embolism: High-output states (pregnancy, fever, hyperthyroidism, sepsis, AV fistula, and anemia).

Usual Treatment

- Chronic.
- Physical activity encouraged.
- Restriction of sodium intake.
- Chronic, well-titrated beta-blockade may lead to substantial clinical benefit (carvedilol and metoprolol).
- Inhibit RAAS (ACE inhibitors, angiotensin receptor blockers, and aldosterone inhibitors).
- Improvement in systolic heart failure (digitalis).
- Diuretics (hydrochlorothiazide, furosemide, and spironolactone).
- Vasodilators.
- Acute.
- Optimize preload and afterload before starting inotropes and vasodilators.
- Inotropes (dobutamine, epinephrine, milrinone, and amrinone).
- Vasodilators (nitroglycerin, nitroprusside, and nesiritide).
- Maintenance of beta-blocker therapy in acute exacerbation of systolic heart failure.
- Special measures
- Stimulation therapy (biventricular pacing + ICD)
- Surgical correction (CABG, CHD, valvular surgery, cardiomyoplasty, and cardiac transplantation)
- Assist devices (IABP, LV assist, and artificial heart)

Assessment Points

System	Effect	Assessment by Hx	Physical Examination	Test
CV	Inadequate cardiac output, congestion	Tachycardia, arrhythmias	Peripheral edema Facial edema (infants/young children), cardiomegaly, pulsus alternans, distended neck veins, Kussmaul sign, abdominojugular reflex	Exercise testing ECG, CXR Circulation time
RESP	Pulm congestion; decreased lung compliance, VC, TLC, pulm diffusion capacity	Breathlessness (exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea) Frequent resp infections	Rales and wheezes Pleural effusions Expectoration: Frothy blood-tinged sputum	PFT ABG CXR
GI	Hepatic and intestinal congestion	Nausea, bloating, fullness	Congestive hepatomegaly, ascites, icterus, cachexia	Liver enzymes
RENAL	Decreased GFR, activation RAAS	Nocturia, oliguria	Ankle edema	BUN/Cr, K^+, Na^+, proteinuria, specific gravity
CNS	Hypoperfusion	Confusion and impairment of memory	Mental status exam	
PNS	Increased sympathetic tone	Cool extremities	Peripheral vasoconstriction, pallor, diaphoresis, tachycardia, clubbing	

Key Reference: Hammill BG, Curtis LH, Bennett-Guerrero E, et al.: Impact of heart failure on patients undergoing major noncardiac surgery, *Anesthesiology* 108(4):559–567, 2008.

Perioperative Implications

Preoperative Preparation

- Stabilize pt by treating CHF before surgery.
- Continue inotropic support.
- Continue cardiac medications (ACE inhibitors may cause hypotension on induction).

Monitoring

- Consider arterial line.
- Consider CVP, PA cath, or TEE.
- CVP may be inaccurate in assessing volume.

Airway

- Frothy secretions may lead to difficult visualization.

Induction

- Preop therapeutic regimen (diuretics) causes hypovolemia, hypokalemia, and hyponatremia, which are potential problems before surgery.
- Replace volume judiciously (avoid dehydration and overhydration).

- Avoid myocardial contractility depressants (e.g., barbiturates).

Maintenance
- Maintain myocardial contractility, reduce afterload, and normalize PVR.

Extubation
- May be delayed owing to CV and pulm insufficiencies

Adjuvants
- Rx inotropes; digitalis and diuretics
- May be less responsive to catecholamines
- Regional anesthesia: Debated and not recommended by some (sympathectomy and volume status) or preferred (reduce preload) by others

Postoperative Period
- Inotropic support and mechanical assistance may be needed.
- Pulm edema develops in 2–16% of pts.

Anticipated Problems/Concerns
- Pulm edema may necessitate prolonged ventilation with high FIO_2.
- RV and/or LV failure in the postop period.

Constipation

Marc B. Royo

Risk
- Median prevalence of constipation in adults is 16% (studies range 0.7–79%); in adults aged ≥60 y, it is 33.5%.
- Prevalence may be higher in nonwhite and institutionalized populations.
- Male:female ratio: 1:1.5.

Perioperative Risks
- Increased risk of gastroparesis and N/V
- Increased intra-abdominal pressure
- Altered resp mechanics and delayed weaning from mechanical ventilation
- Poor nutritional status impairing wound healing

Worry About
- Risk of pulm aspiration on induction
- Increased peak and mean airway pressures, which may predispose to barotrauma
- Decreased chest wall compliance and tidal volumes, which promote atelectasis and increase shunt fraction and alveolar dead space (may cause hypoxemia and hypercarbia)
- Severe abdominal distension, which may decrease cardiac output (decreased venous return and ventricular compliance/contractility)
- Delayed enteral feeding

Overview
- A syndrome defined by difficult or infrequent passage of stool, hardness of stool, or a feeling of incomplete evacuation that occurs in isolation or secondary to another underlying disorder
- Classified into three groups: Normal transit constipation, slow transit constipation, and pelvic floor dysfunction/defecatory disorders
- Diagnosis made on clinical history (symptoms, comorbidities, and medications) and assessment of colonic transit and anorectal function

Etiology
- Slow colonic transit may reflect colonic motor dysfunction or inadequate caloric intake.
- Pelvic floor dysfunction/defecatory disorders may result from inadequate propulsive forces or increased resistance to evacuation.
- Secondary causes include endocrine or metabolic disorders (e.g., diabetes mellitus), neuro disorders (e.g., Parkinson disease), and medications (e.g., opioids, anticholinergics, antidepressants, calcium channel blockers).
- Nearly 50% of patients on long-term opioids experience constipation.

Usual Treatment
- There is no evidence that constipation can be treated by increased fluid intake unless there is evidence of dehydration.
- Increased physical activity is associated with less constipation.
- First-line therapy includes soluble dietary fiber and bulk-forming laxatives.
- Second-line therapy includes osmotic laxatives, stimulant laxatives, enemas, intestinal secretagogues, serotonin 5-HT_4 receptor agonists, and bile acid transporter inhibitors.
- Opioid-induced constipation may be treated with peripherally acting mu-opioid receptor antagonists.
- Surgical intervention is indicated only after nonsurgical measures have failed and symptoms compromise activities of daily living.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Decreased cardiac output (decreased ventricular compliance/contractility and venous return)	Severe cephalad movement of diaphragm	Abdominal distension, narrow pulse pressure	CXR, ECHO
RESP	Elevated diaphragm, atelectasis, hypoxemia, hypercarbia	Dyspnea, tachypnea, orthopnea If mechanically ventilated, increased peak and mean airway pressure	Rales, pleural effusions	ABG, CXR
GI	Decreased intestinal/gastric motility	Abdominal pain, N/V	Abdominal distension	Abdominal imaging

Key References: Bharucha AE, Pemberton JH, Locke GR 3rd: American Gastroenterological Association technical review on constipation, *Gastroenterology* 144(1):218–238, 2013; Webster LR: Opioid-induced constipation, *Pain Med* 16:S16–S21, 2015.

Perioperative Implications

Preoperative Preparation
- Assess volume status.
- Check lytes if receiving laxative therapies.
- Consider preop NG tube placement.

Monitoring
- Standard monitors

Airway
- Attention to airway pressures

Induction
- Consider rapid-sequence induction.

Maintenance
- Avoid nitrous oxide in pt with intestinal obstruction.
- Consider multimodal analgesic techniques and regional anesthesia to minimize use of opioids.

Extubation
- Consider preop resp status. Extubation to noninvasive positive pressure ventilation may be useful.

Anticipated Problems/Concerns
- Potential for prolonged wean from mechanical ventilation in the critically ill
- Risk of infection from bacterial overgrowth and gut translocation
- Delayed enteral feeding because of constipation

Conversion Disorder (Functional Neurologic Symptom Disorder)

Robert I. Cohen

Risk

- Reported prevalence varies widely (11–500"100,000). It may account for unexplained symptoms in as much as 1–14% of general medical/surgical pts and possibly as much as 20% of new outpatient neurology referrals.
- Possibly higher in rural populations, developing areas, lower socioeconomic groups, those less medically sophisticated, and following physical and sexual abuse and trauma.

Perioperative Risks

- Hx of conversion disorder may not increase periop morbidity or mortality per se, although the risk may increase for "failure to diagnose" if new symptom complexes are too quickly attributed to conversion disorder.

Worry About

- Presence of undiagnosed cognitive, neurologic, or general medical illnesses and adverse effects of a drug or treatment
- Periop appearance of conversion symptoms mimicking medical disturbances, drug effects, or anesthetic or surgically related complications
- Malingering disorder, factitious disorder, dissociative disorder, addiction, pseudoaddiction, and withdrawal

Overview

- DSM-V: Conversion disorder (functional neurologic symptom disorder)—in conversion disorder, a subclassification of Somatic Symptom and Related Disorders is a diagnosis of exclusion made when a pt demonstrates or reports motor or sensory symptoms unexplained by a medical condition.
- ICD-10 classifies conversion disorder among dissociative disorders and places more emphasis on disproving a factitious disorder.
- Following anesthesia, occurrence of seizures, generalized or focal weakness or sensory loss, and trouble with speaking or swallowing require careful workup even though may also be the presentation of conversion disorder. The amount of medical knowledge held by the pt may predict whether the presenting symptoms closely mimic known medical conditions and may affect the degree to which the pt accurately reproduces the symptoms on serial evaluation.
- Different from malingering and factitious disorders, the pt is not consciously generating false symptoms. In isolation, neither report of pain nor sexual dysfunction is sufficient to meet the criteria.
- Most common in the second through fourth decades, with initial symptom onset lasting up to 2 weeks, according to the DSM-V, loss of body movement, sight, or speech have better long-term outcome than symptoms of seizure or tremor.

Etiology

- Although the exact etiology is unknown, symptoms may occur as an unconscious solution to trauma or unresolved conflict.
- More common in pts with prior medical and psychiatric diagnoses.
- Possible genetic predisposition suggested in twin and familial studies.

Usual Treatment

- Confirm Dx with psychiatric consultant while excluding possible medical conditions.
- Reassure pt and family members that symptoms do not appear to represent a life-threatening condition and that investigation and treatment will continue.
- Optimize treatment of coexisting psychiatric (especially anxiety and depression) and medical conditions.
- Conversion disorder may respond to behavioral therapy, psychodynamic therapy, or psychoanalysis and may respond to psychopharmacologic treatment of comorbid anxiety and depression.
- There is no specific psychopharmacologic intervention for conversion disorder. Unless used to treat a comorbid condition, ECT is not indicated.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Four subtypes:			
	1. Motor: tremor, paralysis, localized weakness, aphonia, and difficulty with swallowing, balance, or coordination 2. Sensory: loss of touch or pain sensation, double vision, blindness, deafness, or hallucinations 3. Seizures or convulsions 4. Mixed presentation	Differential dx incl almost any medical condition (e.g., myasthenia gravis, MS, porphyria, diabetic neuropathy, hyperparathyroidism, tumors, idiopathic or substance-abuse dystonias)	Findings may not conform to known anatomic pathways or physiologic mechanisms; symptoms may be inconsistent (e.g., unacknowledged strength in antagonistic muscles; normal muscle tone, intact reflexes; equal difficulty swallowing solids and liquids; paralyzed extremity moves on its own with dressing [arm held over pt's head by examiner and dropped will not fall on the head]); stocking-glove anesthesia without proximal to distal gradient; equal loss of light touch, sharp-dull, and temperature discrimination at sharply demarcated anatomic landmarks rather than peripheral nerve or dermatome distribution	Absence of expected findings (including EEG, EMG, lumbar puncture, CT, MRI, SPECT scan, nerve conduction velocity, drug screen) suggests diagnosis
GENDER		Gender tendencies: Men—Antisocial personality and work-related or military injury Women—More common, especially on the left side of the body Children <10 years—Seizures and gait disturbances		

Key Reference: American Psychiatric Association: Somatic symptom and related disorders. In *Diagnostic and statistical manual of mental disorders,* ed 5, Arlington, VA, 2013, APA.

Perioperative Implications

Perioperative Preparation

- Carefully record pt's Hx and PE, documenting normal function, as well as any preexisting neurologic deficits.
- Confer with treating providers, (e.g., internist, neurologist, psychiatrist/psychotherapist).
- Consider possibility that the reason for surgeries in pt with multiple procedures may involve conversion symptoms.

Monitoring

- Routine

Airway

- None

Premedication/Induction/Maintenance

- Attempt to treat reported intense pain in holding area before titrating anxiolytic.
- Regional anesthesia not contraindicated.

Extubation

- None

Adjuvants

- Preop, do not omit psychiatric medication.

Postoperative Period

- Consider conversion disorder when neither neurologic evaluation nor workup of other possible medical conditions explains symptoms, especially in setting of trauma or unresolved stressors.
- Caution because apparent conversion symptoms may represent previously undiagnosed medical disease.

Anticipated Problems/Concerns

- Because conversion disorder is more common in pts with other psychiatric and medical diseases, clear documentation of these during the preop evaluation may prove of immeasurable value to the treating anesthesiologist in the postop period. If the pt develops new, otherwise unexplained symptom complexes, consider including conversion disorder in the differential diagnosis.

Cor Pulmonale

Paul Zanaboni

Risk

- RV failure is the third most common cardiac Dx after age 50 y.
- Of all CHF admissions, 10–20% have some aspect of right heart failure.
- Gender predominance is male > female.

Perioperative Risks

- Increased risk for respiratory failure, severe right heart failure (≥10% if cor pulmonale Dx made preop)
- Risk of prolonged postop ventilatory support

Worry About

- Increased PVR may cause systemic hypotension due to RV dysfunction, resulting in decreased LV filling
- Hypoxia, hypoxemia, hypercarbia, and acidosis intraop or in early postop period, which increase PVR
- Underlying CAD and LV dysfunction

Overview

- Alteration in RV structure (hypertrophy) and function (decreased)
- Most common cause: Long-standing LV dysfunction leading to RV failure, with other common causes including chronic pulmonary emboli and end-stage COPD resulting in increased PVR (secondary to chronic hypoxia and structural changes)
- Any disease that increases PVR chronically, which can induce RV changes, including idiopathic and toxin-induced pulm Htn, pulm fibrosis, severe obstructive sleep apnea, CHD with chronic RV overload, or RV outflow obstruction
- Prognosis: Favorable for those who can maintain a near-normal PaO_2; unfavorable for those with structural changes

Etiology

- LV heart failure
- COPD: Smoking or severe asthma
- Long-standing untreated OSA
- Acute or chronic pulm embolus
- CHD with RV volume overload (L-to-R shunt and long-standing pulmonic insufficiency) or afterload increase (pulm outflow obstruction)
- Primary pulm Htn or severe pulm fibrosis

Usual Treatment

- Use a lynchpin to optimize RV function by decreasing its afterload and PVR.
- Always optimize conditions to decrease PVR toward normal levels by treating hypoxia and hypercarbia.
- Vasodilators (only one-third of pts improve). Chronic treatments include oral medications such as calcium channel blockers; phosphodiesterase-5 inhibitors (sildenafil, and tadalafil); endothelian receptor antagonists (bosentan); inhaled or IV prostacyclin analogues such as epoprostenol, iloprost, and treprostenil; and IV or inhaled phosphodiesterase-3 inhibitors (milrinone). Acute treatments include inhaled nitric oxide, prostacyclin analogues iloprost, epoprostenol, or IV milrinone.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	RV failure Increased PVR Tricuspid regurgitation	DOE Effort-related syncope Chest pain	Accentuated pulm S_2 Diastolic or systolic murmur Dependent edema	CXR ECHO Right heart cath
RESP	COPD	DOEChronic cough, sputum	Hyperinflated lungsWheezing, rhonchi	CXR PFTs
GI	Passive congestion of liver or spleen		Hepatosplenomegaly	LFTs Albumin PT
RENAL	Impaired ability to excrete Na^+ and H_2O	Edema	Edema	Urinary Osm Urine-specific gravity
CNS	Stimulation of sympathetic nervous system secondary to hypoxia		Tachycardia	

Key References: Hosseinian L: Pulmonary hypertension and noncardiac surgery: implications for the anesthesiologist, *J Cardiothorac Vasc Anes* 28(4):1064–1074, 2014; Fox DL, Stream AR, Bullt T: Perioperative management of the patient with pulmonary hypertension, *Semin Cardiothorac Vasc Anest* 18(4):310–318, 2014.

Perioperative Implications

Preoperative Preparation

- Mortality risk in pts with primary pulm Htn and cor pulmonale high (2–20%); morbidity as high as 20–40%.
- Treat underlying infections.
- Maximize treatment of reversible airway disease.
- Avoid preop medications that will depress ventilation.
- Consider baseline ABG to assess PaO_2 and $PaCO_2$.

Monitoring

- Consider arterial line for beat-beat arterial pressure monitoring, noninvasive cardiac output measurement, and ABG collection.
- Consider intraop TEE to monitor RV function and RV dilation.
- Consider pulm arterial catheter to monitor PA pressures and CVP monitoring for evaluation of RV function for large fluid shift reoperations; remember that pts with pulm Htn have increased risk of pulm artery rupture.

Airway

- Potential for bronchospasm

Induction

- Try to increase SVR if pt has fixed increased PVR.
- Deep anesthesia for intubation may decrease incidence of bronchospasm and sympathetic stimulation, which increases PVR; however, caution must be used to avoid hypercarbia.

Maintenance

- Potent inhalational agents for bronchodilation.
- Consider avoiding nitrous oxide (which may increase PVR) and large doses of narcotics (which may cause postop hypoventilation and hypercarbia).
- Although positive pressure ventilation may increase PVR secondary to alveolar expansion (optimal TV around FRC), it can decrease PVR secondary to better oxygenation.
- Aggressively prevent hypercarbia, hypoxemia, and hypothermia, all of which may cause an increase in PVR.
- Hypovolemia and hypervolemia will influence RV function; TEE and CVP may be useful.
- Consider the use of inhaled NO or iloprost to treat increased PVR.
- Consider use of IV milrinone to decrease PVR (but beware of decreased SVR, which may require treatment with an α-adrenergic agonist).
- Consider the use of beta-adrenergic agents such as dobutamine or epinephrine to support RV cardiac output if faced with hemodynamic instability.

Extubation

- Bronchospasm may occur during emergence.
- Avoid hypoventilation and resultant hypercarbia.

Adjuvants

- Regional anesthesia is an option, but high level may decrease SVR in pts with a fixed increased PVR, leading to CV collapse.
- Inhaled NO or iloprost.
- Preop phosphodiesterase-5 inhibitors may accentuate effects of intraop vasodilators.

Postoperative Period

- Postop pain management with either low-dose epidural local anesthetics with low-dose opioids or low-dose intrathecal opioids can minimize resp depression.

Anticipated Problems/Concerns

- Increased PVR and RV dysfunction from hypoxia/hypercarbia or hypothermia

Coronary Artery Disease (Left Main and Non–Left Main Disease)

Timothy Heinke

Risk

- Incidence in USA: 15.5 million.
- Approximately 735,000 pts per y with CAD will have an acute MI and approximately 15% of these will die.
- CAD is responsible for approximately 1 of every 7 deaths in USA.
- Male predominance in pts <55 y old, but M = F in >55 y old.
- Risk factors include Htn, diabetes, smoking, familial incidence, hyperlipidemia, and high cholesterol.

Perioperative Risks

- Presence of disease by coronary anatomy is a good predictor of survival with CAD.
- Presence of left main disease with a high degree of stenosis is life threatening.
- Recent MI increases risk, but revascularization interventions protect pt.
- Impaired ventricular function, unstable anginal pattern, major surgery, and emergency surgery all increase risk.
- Pts at increased risk if undergoing reoperation for bypass surgery.
- Presence of a bare metal stent or drug eluting stent places pts at risk for a MI secondary to in-stent thrombosis (especially <1 mo after bare metal stent and <12 mo after drug eluting stent).

Worry About

- Myocardial ischemia, which can lead to MI
- Postop MI, which carries very high mortality (>50%) in noncardiac surgical pts
- Atherosclerosis in other vascular beds (CNS, renal, and mesentery)
- Increased bleeding during and after surgery if pt is taking an anticoagulant for the prevention of MI
- In-stent thrombosis with associated MI if pt discontinued antiplatelet medications (with up to 50% mortality)

Overview

- Atherosclerosis of vessels supplying blood to the heart results in decreased blood flow by limitation of flow due to anatomy or vasoactive dysfunction (e.g., spasm)
- Single greatest cause of death in USA population (approximately 370,000 deaths/y)
- Most prevalent form of CV disease; approximately 15.5 million pts in the USA population have CAD
- Leading cause of death in major noncardiac surgery

Etiology

- Atherosclerosis and obstructive deposits occur in the coronary artery.
- Involves the interaction of genetics, diet, and environment: Htn, cigarette smoking, and diabetes are three common predisposing factors.
- Myocardial O_2 delivery does not meet myocardial O_2 demands, and thus causes myocardial ischemia.
- Myocardial O_2 supply does not reach the myocardium after thrombosis of coronary artery, which causes MI.

Usual Treatment

- Medical: Nitroglycerin, beta-blockers, calcium-channel blockers (low dose and in vasospastic component), diet, antihyperlipidemia drugs, antiplatelet therapy, exercise, weight loss, and antioxidants
- Catheter-based interventional cardiology (indicated in ≤2-vessel CAD: PTCA has a 30% 3-mo closure rate), intracoronary stent (has good angiographic results and lower closure rates, but event-free survival is little different from PTCA)
- CABG surgery (indicated in ≥2-vessel CAD, left main disease, and diabetics)
- Coronary revascularization: indicated in pts with stable angina before noncardiac surgery in left main disease or three-vessel disease and in pts with high-risk unstable angina
- Surgery delay (if possible) of 1 mo after bare metal stent implantation and 12 mo after drug eluting stent implantation; during the periop period, continue antiplatelet therapy (if possible)

Assessment Points

Concern	Effect	Assessment by Hx	PE	Test
		Noncardiac Surgery		
Ischemia	Causes ventricular dysfunction and arrhythmias Can herald and/or cause MI	Angina Dyspnea on exertion		Holter monitor, ECG exercise radionuclide, treadmill stress ECHO
Infarction	Indicates severe CAD Causes death	Unstable angina		ECG, isoenzyme of CK creatine kinase with muscle and brain subunits, and troponin enzyme release
Impaired function	Heart failure, shock	Activity Hx Stair climbing Orthopnea	Orthopnea gallop Neck veins Rales Peripheral edema	EF (cath, ECHO, and radionuclide)
Stent thrombosis	Cardiogenic shock, death; increased risk if bare metal stent implanted <1 mo or drug eluting stent <12 mo	Antiplatelet regimen Type of stent (bare metal vs. drug eluting) Stent(s) location and date implanted		
		Cardiac Surgery		
Cardiac function	Best predictor of outcome	Activity Hx, stair climbing		Ventricular angiogram (EF >50% = good risk)
Coronary anatomy	Extent of disease and overall long-term survival			Coronary angiography
Renal function	Increased risk if impaired			Cr ≥1.4 mg/dL denotes increased risk
CNS	Increased risk of stroke Aortic atheromatous disease and prior stroke increase risk	Hx of TIA Amaurosis fugax	Carotid bruit	Carotid Doppler study and epiaortic ultrasound

Key References: Mozaffarian D, Benjamin EJ, Go AS, et al.: Heart disease and stroke statistics—2015 update: a report from the American Heart Association, *Circulation* 131:e29-322, 2015; Fleisher LA, Fleischmann KE, Auerbach AD, et al.: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 130:2215–2245, 2014.

Perioperative Implications

Preoperative Preparation

- Supportive preop interview to decrease stress and anxiety.
- Consider analgesics (opioid) for pain, or the likelihood of pain, before anesthesia.
- Give morning cardiac medications (especially beta-blockers and statins) and antiplatelets if pt has an intracoronary stent.
- Nitroglycerin at pt's bedside.

Monitoring

- Consider systemic arterial BP (invasive and continuous in unstable pts or in cases where BP swings are anticipated).
- Consider CVP and/or PA cath; in cardiac surgical pts, EF ≤30% should trigger consideration of central line or use of TEE.
- Consider TEE if pt is hemodynamically unstable.

Anesthesia

- Principle is to maintain O_2 supply and minimize myocardial O_2 consumption.
  - Maintain cardiac output, O_2 sat, and Hgb concentration (O_2 delivery).
  - Maintain diastolic BP (perfusion pressure).
  - Decrease HR, contractility, and wall tension (O_2 consumption).
- No outcome difference demonstrated among general anesthetics.
- Regional and conduction anesthesia with postop analgesia may be beneficial.
- Beware of neuraxial blocks in pts on anticoagulants.
- Transient periods of Htn are well tolerated; however, prolonged periods of hypotension, tachycardia, and anemia are not well tolerated.
- Maintenance of normothermia during noncardiac surgery may be beneficial.

Adjuvants

- Nitroglycerin, sublingual or (preferably) by continuous infusion (0.5–2 mcg/kg per min), can treat myocardial ischemia.
- Beta-blockers by bolus or infusion decrease HR and myocardial contractility and can prevent and treat ischemia.
- RBCs to maintain Hgb ≥8 g/dL.

Postoperative Period

- Second and third postop days are most common time for MI in noncardiac surgical pts; there is a high risk of ischemia intraop and in postop periods.
- Maintain good analgesia to decrease pt's stress response.
- Maintain cardiac medications (especially beta-blockers and statins).
- Consider use of aspirin or other medications to decrease coronary thrombosis in high-risk noncardiac surgical pts (especially pts with intracoronary stents).

Coronary Artery Spasm

Ferenc Puskas

Risk

- Disease affecting mostly middle- and old-aged men and postmenopausal women
- Gender difference: Higher incidence in women
- Periop CAS: Prevalent in elderly male pts with coronary risk factors
- Teenagers and young adults with illicit substance abuse, primarily cocaine
- Occurs in 1–5% of percutaneous coronary interventions
- Ethnic differences: Higher frequency in eastern populations
- Type A behavior pattern, severe anxiety, and panic disorder
- Age, smoking, and high sensitivity C-reactive protein (marker of inflammation)

Perioperative Risks

- Change of sympathetic activity: may trigger CAS
- CAS can lead to myocardial ischemia.
  - Chest pain and ischemic ST segment changes on ECG
- May be result of or associated with myocardial infarction
  - Coronary thrombosis: May trigger CAS, leading to acute MI, unstable angina, or ischemic sudden death

Worry About

- Cardiogenic shock: Decreased LV and RV compliance and decreased pump function
- In pts with CAS, tachyarrhythmias associated with anterior ST segment elevations, ventricular arrhythmias, and even ventricular fibrillation
- Bradyarrhythmias: More frequent with inferior CAS, potentially resulting in complete atrioventricular block, associated with hypotension and syncope

Overview

- Abnormal constriction of epicardial coronary arteries
- Classical CAS (Prinzmetal for variant or spastic angina):
  - Diagnosed if pt has severe chest pain, usually at rest, with concurrent ST segment elevation on ECG
  - Characterized by spasm of normal coronary arteries on arteriography
- Other forms of CAS:
  - Silent angina (without chest pain), diagnosed with Holter monitoring
  - CAS with concurrent atherosclerotic disease at the site or distant from the organic stenosis
  - Effort angina, unstable angina, or microvascular angina (female prevalence)
  - ECG changes, which may include either ST segment elevation, ST depression, or T wave abnormalities
  - Coronary arteriography: Can demonstrate normal or diseased coronary arteries

Etiology

- The exact mechanism of CAS is unknown. Several contributing factors are thought to play a role:
  - Change in sympathetic activity
  - Vagal withdrawal
  - Coronary thrombosis
  - Smooth muscle dysfunction
  - Compromised endothelium-mediated vasodilation
  - Increased Ca^{2+} sensitivity
  - Reduced endothelial NO activity
  - *eNOS* gene polymorphism
  - Signs of chronic low-grade inflammation
  - Oxidative stress

Usual Treatment

- Cessation of smoking
- Calcium-channel blockers (primary)
- Long-acting nitrates (short when symptomatic)
- Beta-blockers (when associated with fixed lesions)
- Magnesium supplementation (may have a preventive effect)
- Statin therapy (improving endothelial function)
- Coronary angioplasty (medically intractable)
- Coronary artery bypass surgery (medically intractable)
- Automatic defibrillator implantation (life-threatening arrhythmias)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL		Risk factor search: smoking and illicit drug use, especially cocaine		High sensitive C-reactive protein level
CV	Chest pain, myocardial ischemia, cardiogenic shock, ischemic sudden death, arrhythmias	Chest pain at rest or exertion, Hx of rapid heart rate, and Hx of syncope	Palpitations, cold sweat, nausea, vomiting, syncope, hypotension	Coronary arteriography with acetylcholine spasm provocation test ECG, ST segment analysis, Holter, exercise testing TEE or TTE—Wall motion abnormalities, cardiac biomarkers

Key Reference: Yasue H, Nakagawa H, Itoh T, Harada E, Mizuno Y: Coronary artery spasm: clinical features, diagnosis, pathogenesis, and treatment, *J Cardiol* 51(1):2–17, 2008.

Perioperative Implications

Preoperative Preparation

- Continue treatment medication until the morning of surgery.
- Ensure IV nitroglycerin, nicardipine, and beta-blockers are available.
- Have a plan for postop pain control.
- Consider regional or neuraxial techniques.

Monitoring

- Use two-lead (II and V5) ECG and ST segment analysis.
- Consider arterial line.

Airway

- Blunt intubation reflexes and avoid sympathetic surcharge on intubation.

Preinduction/Induction

- Cardio-stable induction
- Avoidance of hypotension and tachycardia

Maintenance

- Heart rate and BP control (maintain adequate diastolic BP).
- Avoid hypothermia.
- Maintenance of Hct.
- Optimization of supply/demand.

Extubation

- Smooth opioid wake up and extubation
- Heart rate and BP control
- Avoidance of hypercapnia and hypoxemia

Postoperative Period

- Adequate pain control
- Heart rate and BP control
- Treatment of shivering

Adjuvants

- Careful ST segment monitoring throughout periop period
- Immediate recognition and treatment of coronary ischemia by optimizing supply and demand, with special attention to adequate diastolic blood pressure

Anticipated Problems/Concerns

- Anticipate potentially life-threatening arrhythmias.
- Anticipate myocardial ischemia or infarction and LV and RV dysfunction
- Place defibrillator pads for high-risk pts.

Craniofacial Clefts

Jonathan M. Tan | John Fiadjoe

Risk

- Cleft lip and palates are the most common birth defects in USA.
- Cleft lip and/or palate incidence in USA is 1:600 newborns.
- Craniofacial clefts are rare, with incidence of 1:1000 births worldwide.
- Increased prevalence with Asians, Latinos, and Native Americans.
- Increased prevalence with exposure to radiation, infections (toxoplasmosis, rubella, and CMV), maternal age, maternal smoking exposure, and vitamin deficiencies.

Perioperative Risks

- Increased risk of airway obstruction, difficult airway management, and adverse airway events in the periop period
- Hemorrhage
- Seizures
- Associated congenital heart disease

Worry About

- Adverse airway events, including hypoxia, difficult intubation, airway obstruction, laryngospasm, bronchospasm, and accidental extubation
- Eating and speech problems

- Ear infections/hearing loss
- Choanal atresia

Overview

- Clefts can be cranial or facial in origin and are defined as a gap in soft tissue and/or bone.
- Significant variability in severity exists with craniofacial clefts and subsequent implications for surgical and anesthetic management.
  - Can be unilateral or bilateral with multiple clefts occurring at the same time.
  - Can be as minor as a cutaneous manifestation or as extreme as skeletal malformations.
- Classically, clefts were described and classified by Paul Tessier; his classification uses facial meridians to describe the location of clefts, with a clock-face analogy numbering (0–14) to describe the locations with midline as (0). Facial clefts are numbered from 0–7, and cranial clefts from 8–14, in a counter clockwise rotation.

Etiology

- Exact etiology is unknown, but most cases have associations to familial, genetic, and environmental factors.
- Possible theories include failure of the fusion process, failure of mesodermal growth/penetration, and/or disorder of migration of neural crest cells.
- Drug exposures in utero, including anticonvulsants, Accutane, and methotrexate, are associated with clefts.
- Infectious causes and exposure in utero.

Usual Treatment

- Definitive treatment with surgical repair with surgical type depending on craniofacial cleft manifestation and severity of disease

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Craniofacial cleft Craniofacial abnormality Hearing loss Chronic ear infections Difficult airway	Fevers, previous history of difficult airway	Thorough airway exam	
RESP	Airway obstruction	Dyspnea, poor feeding and weight gain	Tachypnea	CXR
CV	ASD/VSD	Dyspnea Lethargy	Heart murmur	ECG, ECHO
GI	Poor oral intake	Poor weight gain, malnourished, dry mucous membranes, poor skin turgor	Low weight for age Dry mucous membranes Sunken fontanels	Chemistry, serum albumin
CNS	Elevated ICP	Irritability, lethargy Headache, seizures, vomiting	Papilledema Bulging fontanels	Head CT, MRI
HEME	Anemia Coagulopathy	Age, nutrition status Bleeding gums, infections Easy bruisability Fatigue		CBC Type and screen/cross PT, PTT

Key References: Tessier P: Anatomical classification of facial, cranio-facial and latero-facial clefts, *J Maxillofac Surg* 4(2):69–92, 1976; Jackson O, Basta M, Sonnad S, Stricker P, Larossa D, Fiadjoe J: Perioperative risk factors for adverse airway events in patients undergoing cleft palate repair, *Cleft Palate Craniofac J* 50(3):330–336, 2013.

Perioperative Implications

Preoperative Preparation

- Assess for significant associated comorbidities such as elevated ICP and congenital cardiac disease.
- Particular attention to the airway examination.
- Assess for volume status because clefts can make feeding difficult, leading to malnourished and dehydrated pts.
- Communicate and coordinate with surgical teams on repair and surgical concerns.
- Weigh risks and benefits of premedication with anxiolytics because of risk of airway obstruction.

Monitoring

- Consider large vascular access for blood loss in extensive surgical repairs.
- Consider arterial line for hemodynamic monitoring in complex repairs.

Airway

- Conduct thorough airway examination and prepare in advance for a difficult airway.
- Mask ventilation and intubation can be difficult depending on severity and location of the craniofacial cleft.
- Airway devices including video scopes and flexible fiberoptic and laryngeal mask airways should be available.
- Consider presence of ENT surgeons during induction/airway management, especially if nasal passages are not patent or mouth opening is severely limited.

Induction

- Consider maintaining spontaneous ventilation during induction with either inhalation agents or IV agents.
- Difficult mask ventilation is uncommon, but difficult intubation can be anticipated based on location of the cleft.

Maintenance

- Be vigilant for accidental extubation and ETT obstruction or damage during the surgical repair.
- Monitor for blood loss and volume status and consider transfusion in complex craniofacial cleft repairs.

Extubation

- Ensure throat packs are removed (if used) and the oropharynx is clear of blood.
- Elevated risk for adverse airway events, including laryngospasm, bronchospasm, obstruction, accidental extubation, and subsequent hypoxia.

Adjuvants

- Infraorbital nerve blocks can provide postop analgesia for cleft lip repairs.
- Multimodal analgesia for postop pain control.

Postoperative Period

- Pts may require ICU monitoring postoperative, particularly pts with syndromic diagnosis.

Anticipated Problems/Concerns

- Monitor carefully for airway obstruction and postop bleeding in first 12–24 h.
- Monitor for blood loss and volume status.

Craniosynostosis

Francina Del Pino | Franklyn P. Cladis

Risk

- Occurs in 1:2000-2500 live births.
- May be spontaneous, syndromic, or familial, but it most commonly presents as an isolated abnormality; however, it can present as a component of a syndrome or genetic disorder in 15–40% of pts.
- Familiarity with associated head shapes can allow bedside diagnosis and differentiation from positional plagiocephaly. Rarely a CT scan will be required to differentiate plagiocephaly from synostosis.
- Craniosynostosis is diagnosed within the first months of life in most infants, but it can also present later.
- Surgical intervention should be performed during infancy, preferably in the first 6 mo of postnatal life, to prevent the further progression of the deformity and possible complications associated with increased ICP.

Perioperative Risks

- Precipitous hemorrhage can occur with inadvertent dural venous tears or disruption of large emissary veins.
- Venous air embolism: The incidence is high (83%); however, the vast majority is clinically silent and not associated with hemodynamic compromise. Incidence is much lower with endoscopic procedures (8%).
- Intracranial hypertension, which is usually diagnosed by ophthalmic examination (papilledema) or CT scan or by clinical symptoms such as headache in older children, is more commonly seen in syndromic craniosynostosis involving multiple sutures (47%).
- Avoid hypothermia.

- Position pt carefully. Supply eye protection because syndromic forms of craniosynostosis can have proptosis that may prevent full eyelid closure. Infants undergoing procedures in the prone position are placed in a horseshoe headrest.

Worry About

- Significant and rapid blood loss intraop
- Associated anomalies (if syndromic)
- Potential difficult airway (ventilation and possibly intubation)
- Monitoring for venous air embolism
- Management of increased ICP
- Difficulties upon extubation: OSA and significant airway edema

Overview

- A disorder of skull development that occurs because of the abnormal fusion of one or more cranial sutures, the observed deformity relates to the affected sutures.
- Virchow (1851) was the first to describe the arrest of skull growth that occurs in a direction perpendicular to the affected suture.
- Most commonly associated syndromes are Pfeiffer, Apert, and Crouzon.
- Untreated craniosynostosis can lead to elevated ICP and disturbances in intellectual and neurologic development.
- Bilateral coronal sutures are more commonly affected, and there is often associated extremity anomalies (syndactyly) and midface hypoplasia.
- From both a cosmetic and neurodevelopmental perspective, optimal outcomes are achieved when these procedures are performed before 1 y of age, and earlier surgical intervention may translate to a less extensive operation.

Etiology

- Biomechanical forces and genetically determined local expression of growth factors have been implicated. Spontaneous mutation of a syndromic gene is possible. The fibroblast growth-receptor pathway is most frequently involved.
- It can be inherited in an autosomal recessive or dominant pattern.

Usual Treatment

- Surgical intervention is usually done during infancy, preferably in the first 6 mo of postnatal life.
- Surgery is usually performed in a specialized hospital.
- Principles of surgical intervention are not only to excise the fused suture but also to attempt to normalize the calvarial shape.
- It is important to differentiate from posterior plagiocephaly, which is not associated with a risk of head-growth restriction or increased ICP, and the treatment is nonsurgical, usually with position changes.
- Current surgical techniques include open calvarial reconstruction, minimally invasive strip craniectomy with the use of a postop molding helmet, minimally invasive strip craniectomy with spring implantation, and cranial distraction.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
AIRWAY	Diff mask vent and/or intubation	Hx or previous mask ventilation or intubation	Facial symmetry Size of mandible Neck range of motion	Neck films may be indicated (Apert may have cervical fusion)
RESP	OSA	Apnea during sleep, snoring	Noisy breathing from the upper airway	Polysomnogram (apnea-hypopnea index) Overnight pulse oximetry Room air O_2 saturation
CV	CHD (ASD, VSD, tetralogy of Fallot)	Bottle feeds >30 min Diaphoresis with feeds Failure to thrive	Murmur	ECHO
MS	Diff IV access Diff a-line access		Syndactyly (Apert) Fused elbows (Pfeiffer)	
CNS	Increased ICP	Irritable, vomiting, somnolence (if acute)	Papilledema	Ophthalmology exam, VEPS
HEME	Anemia (nadir at 3 mo of age)			Preoperative Hct, type/cross

Key References: Haas T, Fries D, Velik-Salchner C, et al.: Fibrinogen in craniosynostosis surgery, *Anesth Analg* 106(3):725–731, 2008; Stricker PA, Fiadjoe JE: Anesthesia for craniofacial surgery in infancy, *Anesthesiol Clin* 32(1):215–235, 2014.

Perioperative Implications

Preoperative Preparation

- Laboratory testing should include CBC, type and screen, and coagulation profile. In open procedures also cross matching of blood.
- Midface hypoplasia and retrusion may cause OSA and postop airway obstruction such that postop mechanical ventilation may be indicated.
- Prepare for potential difficult airway. Children with severe airway obstruction may present with a tracheostomy.

Monitoring

- At least two peripheral IVs, 22 gauge or larger when possible
- Arterial line for immediate detection of hypotension and frequent blood sampling
- Central venous catheter: Some centers routinely insert it for complex cranial vault reconstruction procedures to measure central venous pressure to guide fluid and transfusion therapy; others reserve their use for children in whom adequate peripheral access is difficult to obtain
- Precordial Doppler for detection of venous air embolism

Airway

- Have several airway devices available, including LMA and videolaryngoscope if necessary.
- Consider using fiberoptic intubation for anticipated difficult airways, and even having a surgeon available in case an emergency tracheostomy is needed.
- Some anesthesiologists place a nasotracheal tube for infants in the prone position as a way to secure the airway better.

Positioning

- Craniofacial procedures can be lengthy, and careful attention to proper positioning is important.
- If pt is supine, some surgeons prefer the eyes not to be taped closed because they are within the surgical field. Ophthalmic ointment should be applied in these cases.
- If pt is prone, the head must be positioned on the horseshoe rest, ensuring no pressure on the orbits or other pressure points.

Induction

- An inhaled induction of anesthesia is most commonly performed. Children with signs or symptoms of significant acute ICP elevation may benefit from an IV anesthetic induction. Most elevation in ICP is chronic and asymptomatic.

Maintenance

- Administer general inhalational or IV maintenance with muscle relaxant.
- Maintain constant vigilance to guide fluid administration. This includes direct observation of the surgical field and directing close attention to the invasive blood pressure and waveform, central venous pressure, response to fluid challenges, urine output, hemoglobin measurements and blood gas assessments, and systolic pressure variation.
- Use active warming techniques such as forced-air convection blankets, circulating warm water mattresses, overhead radiant lights, and fluid warmers.
- Mannitol may be required before calvarial removal if increased ICP.
- Use isotonic solutions for maintenance IV fluids.

Extubation

- Most pts can be safely extubated at the end of the procedure.
- Infants who may require postop intubation and mechanical ventilation include those in the prone position for lengthy procedures with significant facial and tongue swelling and those with syndromic craniosynostosis who have significant preop obstructive sleep apnea.

Adjuvants

- Using antifibrinolytic drugs such as tranexamic acid has been shown effective in reducing blood loss and periop transfusion requirements.
- The off-label use of recombinant activated factor VII has been described as a rescue measure, but it has been associated with significant thrombotic complications; therefore, its use should be reserved for life-threatening situations in which all other methods of achieving hemostasis failed.
- Cell salvage may allow for reduction of transfusion.
- The use of preop recombinant erythropoietin has been described; however, its current use seems infrequent and limited to select pts. When administered, this technique is often combined with acute preop normovolemic hemodilution and other techniques to maximize efficacy.
- Blood products should be immediately available in the operating room at the beginning of the procedure.

Postoperative Period

- All children after open vault reconstruction are admitted to the ICU postop.
- Postop pain is usually not severe, and intermittent opioids together with acetaminophen provide satisfactory postop analgesia.

- Nearly all affected infants are extubated in OR upon completion of the procedure.
- Transfusion of blood products may be indicated postop.
- Postop hyponatremia is common (31% in one study), although direct complications from hyponatremia seem uncommon.
- Other postop concerns include CSF leak and infections.

Surgical Stages

- A bicoronal incision is made and the scalp and face are dissected to expose the calvarium.
- Calvarial removal may be partial or complete (neurosurgery).
- Supraorbital osteotomies are performed to mobilize the superior orbital rim, nasion, and lateral temporal bones.
- Calvarial vault remodeling and reconstruction with craniofacial plating system is performed.

Anticipated Problems/Concerns

- Difficult airway
- Massive blood loss and transfusion
- Hypothermia
- Possible postop intubation

CREST Syndrome

Ashish C. Sinha

Risk

- Pts with Hx of exposure to silica dust or PVC.
- Usual age group is 30–50 y.
- Fourfold to ninefold higher incidence in women than men; seen in all races.
- In USA systemic sclerosis has an estimated incidence of 19 cases per million and prevalence of 240 cases per million (range: 138–286).

Perioperative Risk

- Pts more likely to have compromised renal function at baseline
- Hypoxia from pulm Htn and/or restrictive lung disease
- Difficult intubation from narrow mouth opening

Worry About

- Reflux and thereby aspiration, renal crises, restrictive lung disease, CHF, pulm Htn, difficult intubation due to small mouth opening, and keeping patient warm to avoid Raynaud phenomenon

Overview

- **C**alcinosis, **R**aynaud phenomenon, **E**sophageal dysmotility, **S**clerodactyly, and **T**elangiectasia (CREST).
- Symptoms involved in CREST or limited cutaneous systemic sclerosis are associated with the generalized form of systemic sclerosis.

Etiology

- Exact etiology of systemic sclerosis is unknown; the following pathogenic factors are always present: Endothelial cell injury, fibroblast activation, and cellular and humoral immunologic derangement.
- Environmental factors, such as silica, industrial solvents, and radiation exposure, are all triggers or accelerators.
- CMV, HHV5, and parvovirus are possible viral accelerators.

Usual Treatment

- Glucocorticosteroid, immunosuppressive, chelating agents, endothelin receptor antagonist, PDE5 inhibitor, and peripheral vasodilators.
- Skin thickening with D-penicillamine and γ-interferon (not FDA approved).
- Pruritus with moisturizers, camphor and menthol, H_1 and H_2 blockers, tricyclic antidepressants, PUVA, UVA-1 phototherapy, and trazodone.
- Raynaud phenomenon with CCB, prazosin, PGE1, dipyridamole, aspirin, smoking cessation, and topical nitrates.
- GI symptoms with antacids, H_2 blockers, PPIs, prokinetic agents, and octreotide.
- Lung symptoms with CCB, PGs, cyclophosphamide, and high-dose corticosteroids.
- Renal involvement with ACE or angiotensin II inhibitors.
- Cutaneous telangiectasias can be treated by PDL and IPL; PDL has better cosmesis but more side effects.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM/HEENT	Sclerodactyly, few wrinkles or joint creases, decreased range of motion, hair loss, pruritus telangiectases	Observation	Tightness, indurations, hyperpigmentation or hypopigmentation	Airway examination
CV	Pericardial effusion, CHF, myocardial fibrosis, misconduction Cor pulmonale	Dyspnea, palpitation, irregular heart rate, chest pain from vasospasm	Rales and murmurs on auscultation	ECG, Holter monitoring, ECHO
RESP	Pulm Htn, aspiration pneumonia, dyspnea	SOB, cough, tachypnea, dec exercise tolerance	Dry rales	PFT, ABG, CXR, DLCO, HRCT
CNS	Carpal tunnel syndrome, trigeminal neuralgia (rare), entrapment neuropathies	Pain over wrist, other typical signs depending on nerve involved	Limited ROM	Conduction studies, CT
RENAL	Htn, oliguria	Headache, SOB, edema	Swelling of hands and feet	Check BP and UO and monitor serum Cr
MS	Raynaud phenomenon, arthralgias, myalgias, morning stiffness	Acroosteolysis, muscle weakness	Palpable tendon friction rubs, muscle wasting, flexion contractures	Increased serum CK and aldolase
GI	GE reflux, esophagitis, esophageal strictures, watermelon stomach, primary biliary cirrhosis, colonic diverticula, anal sphincter incompetence	Bitter taste, dysphagia, retrosternal and abdominal pain, diarrhea, self-soiling	Abdominal tenderness, decreased rectal sphincter tone	Barium swallow CT or MRI, endoscopy Abdominal ultrasound, antimitochondrial antibodies for PBC

Key References: Gabrielli A, Avvedimento EV, Krieg T: Scleroderma, *N Engl J Med* 360(19):1989–2003, 2009; Pritts CD, Pearl RG: Anesthesia for patients with pulmonary hypertension, *Curr Opin Anaesthesiol* 23(3):411–416, 2010.

Perioperative Implications

Preoperative Preparation

- Continue PPI, consider FOI, and evaluate for regional anesthetic techniques for pulm issues.

Monitoring

- If comorbidities dictate, arterial line (try to avoid due to Raynaud phenomenon, but difficult to get cuff pressure due to reduced flow; may need ABG)
- CVP ± PA cath if pulm Htn, along with standard monitoring

Airway

- Airway may be a challenge due to small oral opening,

Preinduction and Induction

- Worry about hypotension and hypoxemia at induction,

Maintenance

- Choose drugs based on hemodynamic status,
- Keep warm,

Extubation

- May have to be delayed if significant pulm compromise

Adjuvants

- In the presence of compromised renal, cardiac, or pulm function, modify anesthetic drugs accordingly

Anticipated Problems/Concerns

- Challenging airway, hypoxemia, CHF, renal function, and positioning challenges with contractures

Creutzfeldt-Jakob Disease

Astri M.V. Luoma | Surbhi Virmani

Risk

- Iatrogenic transmission (actual and theoretical)
  - Blood products: blood transfusion (3 reported cases). Greater risk with pooled products (since 1999 UK has imported blood fractions) or massive blood transfusion. Risk mitigated by deferral of recipients as donors (initiated: 1998 in France, 2005 in UK) and appropriate blood transfusion policies
  - Organ donation
  - Tissue grafts: Human dura mater (168 reported cases) or corneal grafts (3 reported)
  - Human pituitary hormones: 180 reported cases
  - Human gonadotrophin: 4 reported cases
  - Neurosurgical instruments
- Transmission via food chain (vCJD and BSE); causal link found through epidemiology, biochemical, and transmission studies
- Other transmission: Potentially through vaccines; however, bovine-derived products no longer in use

Perioperative Risks

- Risk of transmission through surgical instruments: through neurosurgical instruments (4–5 cases reported) or stereotactic intracranial probes (2 reported)
- Risk of transmission through blood transfusion: Pooled products pose a greater risk (3 cases reported)

Worry About

- Management of pts with dementia or neuropsychiatric issues
- Aspiration risk
- Nutritional status and frailty; resultant risk of poor wound healing and pressure sores
- Risk of transmission through surgical instruments

Overview

- Rare neurodegenerative disease
- Prion disease, also known as TSE
  - Four types: Sporadic (sCJD), inherited, iatrogenic, variant (vCJD)
  - Worldwide incidence 1-2:1,000,000 people per y
  - All are transmissible
- Fatal; treatment is supportive and management focused on preventing transmission
- Definitive diagnosis is histopathologic with 100% sensitivity and specificity

Etiology

- PrP^{c} occurs normally in human and animal cells; prion protein gene found on chromosome 20
- Prion disease results from accumulation of PrP^{Sc}, which may be by internal (inherited) or external (ingestion, iatrogenic) exposure
- PrP^{Sc} results in an autocatalytic process in which normal prion is converted to abnormal prion
- Animal forms of prior disease include scrapie and BSE (or "mad cow disease," resulting in vCJD, first diagnosed in 1996 in UK)

Usual Treatment

- Management is supportive for pt and family; no specific treatments exist, although various experimental options have been trialed

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Restricted mouth opening if PEG	Previous airway management problems	Airway examination	
CV	Risk of CJD as recipient of blood products	Blood transfusion history		
RESP	Recurrent pneumonia	Aspiration		CXR
GI	Swallowing difficulties Aspiration risk	Recurrent pneumonia	PEG in situ	
CNS	Psychiatric and behavioral problems (vCJD) Dementia, memory problems (sCJD > vCJD) Neurologic symptoms (vCJD > sCJD)	Psychiatric history, behavioral history from medical notes and carers Peripheral pain syndrome (vCJD) Previous human dura mater graft or human pituitary hormones/gonadotropin Family history of CJD	Neurologic examination: Ataxia Extrapyramidal and pyramidal signs Myoclonus Dysarthria Confusion	MRI: pulvinar or hockey stick sign (vCJD) CSF: positive for 14-3-3-protein, tau, S100 beta EEG: sharp wave complex (sCJD) General slowing (vCJD)
MS	Poor nutritional status Contractures		Frailty Contractures of limbs Weight/height and BMI	

Key References: Porter M, Leemans M: Creutzfeldt-Jakob disease, *Contin Educ Anaesth Crit Care Pain* 13(4):119–124, 2013; World Health Organization: Variant Creutzfeldt-Jakob disease. <http://www.who.int>, 2012.

Perioperative Implications

- Prevention of transmission is the focus; prion proteins cannot be destroyed by current sterilization techniques. WHO guidance should be adhered to.

Preoperative Preparation

- Early identification of at-risk pt and appropriate communication with and preparation of theater team.
  - Surgical procedure: Consider if there is a high risk of transmission and whether tissues to be handled are moderate or high infectivity risk. Of note, vCJD is found in lymphoreticluar tissues (e.g., tonsils), as well as cerebral and spinal tissues. This has implications for endoscopic procedures and instruments. Decide if single-use disposable instruments can be safely used for the procedure. Single-use instruments should be of the same standard and quality as multiuse instruments and cost effective.
  - Decide if surgical instruments can be safely destroyed.
  - Consider if new surgical instruments are required. In UK, children born after January 1, 1997, have a separate pool of surgical instruments.
  - Tracking system for all surgical instruments must be used.
  - When disease status is unknown or pt is considered at risk, and tissue of high risk of infectivity has been handled, surgical instruments should be quarantined until diagnosis is confirmed or excluded.
  - WHO surgical checklist can be used to highlight risk assessment.
  - System in place for linking pts with surgical equipment use.
- Decision on management of surgical instruments is based on risk of transmission.

Airway

- Prion protein may be found on lymphoreticular tissue.
  - Single-use laryngoscopes wherever possible.
  - Single-use disposable airway devices (e.g., supraglottic airways).
  - Fiber optic scopes: Single-use fiber optic scopes are now available and should be used. Where this is not possible, a tracking system should be in place so that all equipment is traceable.

Postoperative Period

- Pt isolation is not required.
- Both inhalation and IV induction and maintenance of anesthesia are appropriate and should be determined by pt-specific factors.
- Ventilators do not need to be quarantined, but single-use filters should be used as normal.
- Dispose of suction in the conventional manner.
- Sharps should be disposed of in the conventional safe manner.
- Routine postop management of pt, paying particular attention to prevention of pressure sores and maintenance of nutritional intake, as well as analgesia. Pts may not be able to express their needs.
- Pts who are identified to be "at risk" should have this communicated to them and their family with appropriate support services in place.

Anticipated Problems/Concerns

- Not correctly identifying a pt at risk and the possible iatrogenic transmission of CJD to other members of the public
- Postop confusion and delirium following general anesthesia
- Preop frailty and poor oral intake with resultant risk of pressure sores and surgical site infection

Cri Du Chat Syndrome (5p– Syndrome)

Klaus Morales dos Santos

Risk

- 1:15,000-50,000 live births
- Most common human chromosomal syndrome

Perioperative Risks

- Difficult airway management due to anatomic abnormalities of the airways.
- 30% can present with congenital heart disease.
- Aspiration risk.
- May require temp control.
- Cardiac events (pts may have cardiac abnormalities).

Worry About

- Difficult mask ventilation; airway obstruction secondary to hypotonia
- Difficult intubation
- Temperature regulation

Overview

- Microcephaly with profound mental retardation and hypotonia.
- Characteristic facies with micrognathia, low-set ears, facial asymmetry.
- Characteristic high-pitched cry may be due to laryngeal abnormalities (narrow diamond-shaped larynx, long floppy epiglottis) or neurogenic defect.
- CHD: Persistent ductus arteriosus, septal defects, or pulmonic stenosis.
- Behavioral features include repetition of movements, aggression, self-injury, and hypersensitivity to sound, among others.
- Repetitive respiratory infections are common.

Etiology

- Deletion of variable size of the short arm of chromosome 5 (5p–).
- Loss of the critical 5p15.2 region is responsible for most of the features.
- Most cases occur by spontaneous gene mutation (90%).
- 10% arise by unbalanced translocations.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Micrognathia	Respiratory distress in neonatal period; inspiratory stridor	Receding mandible	
CV	ASD, VSD, PDA, PS	SOB, cyanosis	Murmur, gallop	ECHO
RESP/GI	Pneumonia, chronic aspiration		Dyspnea, rales, rhonchi, wheezing	CXR
MS	Scoliosis			
CNS	Mental retardation, seizures		Hypotonia in infancy, hypertonia later	

Key References: Rodríguez-Caballero A, Torres-Lagares D, Rodríguez-Pérez A, et al.: Cri du chat syndrome: a critical review, *Med Oral Patol Oral Cir Bucal* 15(3):e473–e478, 2010; Santos KM, Rezende DC, Borges ZD: Anesthetic management of a patient with cri du chat syndrome. Case report, *Rev Bras Anestesiol* 60(6):630–633, 2010.

Perioperative Implications

Preoperative Preparation

- Difficult airway management

Monitoring

- Routine
- Pay particular attention to temp and neuromuscular blockade (fast-acting preferred).

Airway

- Laryngeal mask airway must be available.
- Fiberoptic bronchoscope ready to use before induction.
- Wide assortment of laryngoscope blades and ETT must be available.

Preinduction/Induction

- Presence of primary caregiver for uncooperative pts
- Sedation in monitored setting
- Warm OR for temp regulation

Maintenance

- Measures to actively warm the pt (forced-air warming blankets, warm IV fluids).
- Monitor neuromuscular blockade.

Extubation

- Preferably extubate awake.

Anticipated Problems/Concerns

- CHD may be present: Refer to cardiac assessment before anesthesia.
- Airway management may be difficult.
- Extubation may be difficult; pt may have airway obstruction postoperatively.

Crohn Disease

Mark C. Phillips

Risk

- Incidence of 3.1–14.6 cases per 100,000 person-years; prevalence of 26–201 cases per 100,000 persons.
- Incidence and prevalence are increasing worldwide; incidence is highest in North America and Northern Europe.
- Race: White >African American >Hispanic and Asian populations for risk.
- 3–4 times more common in ethnic Jews than non-Jewish whites.
- More likely to occur in those with a strong family history.
- Affects males and females equally.
- Peak occurrence between ages 15 and 25 y, with a second smaller peak between ages 60 and 80 y.

Perioperative Risks

- Aspiration
- Arrhythmias due to lyte disorders

Worry About

- Intravascular fluid volume and lyte imbalances.
- Chronic steroid use and need for perioperative supplementation.
- Nutritional status, chronic weight loss, and malnutrition.
- Difficult IV access due to chronic illness and frequent venipunctures.
- Higher risk of systemic thromboembolic events in comparison with control populations.
- Psychological mindset of the patient due to chronicity of the disease and relatively young age of pts. Depression is common.

Overview

- Chronic inflammatory disease of GI tract that can give rise to strictures, inflammatory masses, fistulas, abscesses, and hemorrhage
- Idiopathic, chronic relapsing immune-mediated disease
- May affect any portion of the GI tract from mouth to anus, most commonly affects small bowel and colon
- Pts often present with abdominal pain, persistent diarrhea, and weight loss
- Pt may develop bowel obstruction and perforation
- Pt may develop rectocutaneous fistulas, rectal fissures, and perirectal abscesses
- Pt may have anemia from several causes, including chronic disease, chronic blood loss, and folate and vitamin B_{12} deficiency
- Chronic malnutrition and weight loss
- Extraintestinal manifestations occur in approximately 25–30% of pts. These manifestations include uveitis and episcleritis, erythema nodosum and pyoderma gangrenosum, ankylosing spondylitis, and primary sclerosing cholangitis. When present, the extraintestinal manifestations can be more serious than the primary intestinal disease. These extraintestinal manifestations may precede, occur with, or manifest independently of the underlying bowel disease

Etiology

- Pathogenesis incompletely understood.
- Thought to arise from environmental priming and triggering events in a genetically susceptible pt.
- Smoking is a risk factor for Crohn disease and worsens the course of Crohn disease.

Usual Treatment

- Pharmacologic: Aminosalicylates; steroids; immunomodulating agents, such as azathioprine, 6-mercaptopurine, and methotrexate; antitumor necrosis factor therapy with infliximab, adalimumab, or certolizumab pegol.

- Surgical: Indications for surgery are failure of medical management, intestinal obstruction, intra-abdominal abscess, fistulas, fulminant colitis, toxic megacolon, massive hemorrhage, cancer, and growth retardation; 70–90% of Crohn disease patients will need surgical intervention at some point.
- Surgical procedures may include stricturoplasty, bowel resection, and abscess drainage.
- Main surgical principle is to preserve bowel length to avoid short bowel syndrome.
- Both medical and surgical management of Crohn disease are aimed at providing long-lasting symptomatic relief while avoiding excessive morbidity.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	Bowel prep, wt loss, diarrhea	Hypotension, tachycardia	Lytes, Hct
GI	Bowel perforation Malabsorption	Abdominal pain Diarrhea, weight loss	Abdominal tenderness, fever Cachexia	WBCs Albumin
MS	Ankylosing arthritis	Joint mobility	Decreased ROM of joints	

Key References: Baumgart DC, Sandborn WJ: Crohn's disease, *Lancet* 380(9853):1590-1605, 2012; Patel S, Lutz JM, Panchagnula U, et al.: Anesthesia and perioperative management of colorectal surgical patients—a clinical review (Part 1), *J Anaesthesiol Clin Pharmacol* 28(2):162–171, 2012.

Perioperative Implications

Preoperative Preparation

- Optimization of nutritional status preop can improve operative outcomes.
- Ensure volume status and lytes are normalized.
- If pt is on hyperalimentation preop, continue it during the case; monitor glucose.
- Assess current or recent steroid use and need for periop supplementation.
- Discontinue methotrexate at least 1 wk before surgery because it has been shown to decrease wound healing; resume after wound healing occurs.
- Pts with significant anemia should be transfused preop.
- Careful pt positioning and padding of extremities.

Monitoring

- Standard monitoring.
- Large-bore PIV access.
- Consider CVL if pt has difficult IV access or if patient is hypovolemic or large fluid shifts are anticipated.
- Consider arterial line if significant comorbidities exist.
- Foley catheter to monitor urine output.

Airway

- Aspiration risk if bowel obstruction present

Induction

- Rapid sequence induction in patients with gastric outlet or bowel obstruction.
- Consider preinduction placement of NG tube to suction gastric contents.

Maintenance

- Avoid nitrous oxide if bowel obstruction present.
- Abdominal relaxation with nondepolarizing muscle relaxants usually needed. If liver disease is present, avoid muscle relaxants dependent on hepatic metabolism.
- Check glucose regularly if on hyperalimentation.
- Consider need for significant fluid administration (open abdomen, long case).
- Maintain normothermia; fluid warmer and forced air warming device.

Extubation

- Awake extubation

Postoperative Period

- Consider epidural analgesia or IV PCA for pain control.
- Monitor fluid status carefully in the postop period.

Anticipated Problems/Concerns

- Possibly long surgery due to adhesions and multiple strictures
- May need aggressive fluid replacement due to hypovolemia and anemia worsened by third space losses
- May have severe nutritional deficiency, especially with short bowel syndrome from extensive resection
- Need for stress dose steroids if patient treated with steroids for medical management

Croup (Laryngotracheobronchitis)

Maurice S. Zwass | Jeffrey D. Roizen

Risk

- Children between 6 mo-6 y are at risk (6 mo–3 y at greatest risk).
- Children with underlying airway abnormalities (e.g., subglottic stenosis) or difficult intubations (e.g., micrognathia) and symptoms are at increased risk and require particular planning.

Perioperative Risks

- Difficulty with intubation because of very narrowed subglottic region
- Obstruction of the small tracheal tube because of airway secretions.

Worry About

- Risk of rebound tracheal edema several hours after racemic epinephrine treatment.
- Cardiorespiratory crisis in progressive or severe Sx, agitation, younger pts, difficulties with oxygenation or ventilation, failure to oxygenate.
- Bacterial superinfection of airway.

Overview

- Common childhood ailment with prodromal illness accompanied by a characteristic cough (which often sounds like seal barking).
- Sx and respiratory compromise from progressive swelling of subglottic region tracheal mucosa.
- Frequently present when inspiratory stridor and respiratory distress develop.
- Radiographs of the neck often demonstrate gradual progressive tracheal narrowing; most narrow just below level of vocal cords (referred to as steeple sign). Upper glottis on a lateral neck radiograph is normal.
- When obtained, evaluation of CBC is consistent with viral illness.

Etiology

- Viral agents are typical etiologies and include parainfluenza viruses (most common). Adenoviruses, influenza virus, RSV, and measles virus also associated.

Usual Treatment

- Cool mist often greatly improves Sx; supplemental O_2.
- If symptoms more severe, aerosolized racemic epinephrine can dramatically reduce airway swelling (rebound tracheal edema risk several hours after administration necessitates observation in hospital).
- Steroid administration controversial; may decrease severity of disease and decrease need for tracheal intubation or hasten improvement in first 24 h of illness.
- Small percentage of pts with this disease require tracheal intubation.
- Parenteral steroids (dexamethasone) and inhaled steroids (budesonide) have been used.
- Breathing helium-oxygen mixtures has been reported as helpful in some cases (lower density and viscosity).

Assessment Points

Differentiation Between Croup (Laryngotracheobronchitis) and Epiglottitis

	Croup	Epiglottitis
Age	3 mo–3 y	1–7 y
Onset	Gradual	More rapid (usually <24 h)
Fever	Low grade	High
Cough	Characteristic barking	None
Sore throat	Occasional	Frequently severe
Posture	Any	Frequently sitting forward, mouth open, drooling
Airway sound	Inspiratory stridor	Inspiratory stridor
Voice	Normal	Muffled
Appearance	Nontoxic	Toxic
Seasonality	Peak winter, epidemic	Year-round

Key References: Jenkins I, Saunders M: Infections of the airway, *Paediatr Anaesth* 19(Suppl 1):118–130, 2009; Tibballs J Watson T: Symptoms and signs differentiating croup and epiglottis, *J Paediatr Child Health* 47:77-82, 2011.

Perioperative Implications

Airway

- Airway support with good mask fit and positive pressure ventilation can generally overcome obstruction from swelling of airway.
- Identification of larynx is generally routine, but a tracheal tube 0.5–1.0 mm diameter smaller than usual may necessitate having available extra-long or micro-laryngeal tracheal tubes.
- Tracheotomy rarely needed as therapy for these pts with current management and reserved only for unusual cases.

Induction

- Induction common when IV access has already been obtained.

Anticipated Problems/Concerns

- Symptomatic pts who require intubation of trachea need tubes 0.5–1.0 mm smaller in diameter than pts without croup.
- Pts who require tracheal intubation usually require sedative management to tolerate ventilation; this is often followed for development of leaks around the tracheal tube as a sign of improvement of edema; most pts improve within 2–4 d. When leak is present at 20–25 cm H_2O of pressure, extubation can be considered; complicated cases and pts with prolonged courses may benefit from examination of airway in operating room at time of extubation.
- Although a viral illness, some pts may acquire bacterial superinfection of airways and require antibiotic therapy.

Crouzon Syndrome

Geoff Frawley

Risk

- Represents approximately 4.8% of cases of craniosynostosis at birth.
- Birth prevalence of 1.6:100,000 births.
- Estimated prevalence in general population of Europe is 0.9:100,000.
- No race predilection.

Perioperative Risks

- Difficult BMV, difficult intubation, massive blood loss, arterial gas embolism

Worry About

- Difficult airway
- Intraop blood loss
- Inadvertent dural sinus injury
- Postextubation subglottic edema
- External facial fixation devices

Overview

- Crouzon syndrome is an autosomal dominant disorder characterized by craniosynostosis causing secondary alterations of the facial bones and facial structure.
- Common features include hypertelorism, exophthalmos and external strabismus, parrot beak nose, short upper lip, hypoplastic maxilla, and a relative mandibular prognathism.
- Synonyms: Craniofacial dysostosis type II, FGFR deficiency.

Etiology

- Due to mutation in FGFR2 gene on chromosome 10.
- Normal function of FGFRs is to restrain limb growth. FGFR mutations are hypermorphic, causing excessive cranial bone formation.
- Inherited in autosomal dominant fashion, but de novo mutations account for 50% of cases.
- High penetrance but variable expressivity.
- Male to female preponderance of 3:1.

Usual Treatment

- In neonatal period tracheostomy for UAO or ventriculoperitoneal shunt for hydrocephalus may be required.
- Posterior vault expansion may be carried out in first 6 mo to achieve cranial decompression of intracranial venous hypertension.
- Fronto-orbital advancement to protect orbitae from subluxation at 6–12 mo.
- Complex hypoplasia of cranial vault, orbits, and midface may require frontofacial advancement (Le Fort III osteotomy) and/or distraction osteogenesis with application of RED frame.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	UAO secondary to septal deviation, choanal stenosis, and nasopharyngeal narrowing Ocular hypertelorism and proptosis Cleft lip or palate rarely	Sleep apnea snoring, daytime somnolence	Hypoplastic maxilla, relative mandibular prognathism Mallampati scoring difficult in toddlers Exposure keratopathy of cornea	3D cranial CT planning Polysomnography (sleep studies) or overnight oximetry
CV	FGFs involved in cardiac cushion proliferation and valvulogenesis	Exercise tolerance or arrhythmias	PDA or ASD murmurs	ECHO
RESP	Choanal atresia	OSA snoring		Nasoendoscopy
HEME	No known bleeding diatheses			
RENAL	Nil reported			
ORTHO	Cervical fusion (18%), usually C2-C3, occasionally C3-C4, C5-C6 Scoliosis Subluxation of the radial heads Ankylosis of the elbows.		Reduced range of movement of cervical spine	Cervical spine lateral x-ray or craniocervical CT
CNS	Chiari malformation Cerebellar tonsil herniation (73%) Progressive hydrocephalus (47%). Intracranial hypertension	Headaches Seizures	Gait disturbance Paresthesia	Craniocervical CT and MRI
PNS	Mild to moderate mental retardation	Developmental delay		
MS	Usually normal		Metacarpophalangeal shortening	Hand x-ray

Key References: Stricker PA, Shaw TL, Desouza DG, et al.: Blood loss, replacement and associated morbidity in infants and children undergoing craniofacial surgery, *Paed Anesth* 20(2):150–159, 2010; Hughes C, Thomas K, Johnson D, et al.: Anesthesia for surgery related to craniosynostosis: a review. Part 2, *Paediatr Anaesth* 23(1):22–27, 2013.

Perioperative Implications

Preoperative Preparation
- Caution with sedative premedication in presence of OSA or intracranial hypertension
- Cooperation limited in younger age groups

Monitoring
- Invasive pressure monitoring warranted for major craniofacial surgery

Airway
- Difficult BMV and intubation
- Mandibular hypoplasia more prominent postmaxillary advancement and may worsen glottic view

Induction
- Upper airway obstruction common on gas induction may require NPA

Maintenance
- Protection of orbits and corneas
- Reliable venous access mandatory
- Risk of excessive bleeding, dural tears, and gas embolism during vault surgery

Adjuvants
- Antifibrinolytics, surgical hemostasis with topical agents, and cell salvage have been described to reduce transfusion requirements

Extubation
- RED frame impedes access to upper airway. Wire cutters and spanner required to be with pt at all times.

Postoperative Period
- Increased risk of upper airway obstruction on emergence and in PACU
- Difficult BMV with RED frame in situ

Anticipated Problems/Concerns
- Multiple surgeries in first year of life to reduce risk of hydrocephalus or intellectual impairment
- Upper airway obstruction with postop facial edema; may require ICU/PACU care overnight

Cryptococcus Infection

Pierre Moine

Risk
- In general population: 0.4–1.3 cases per 100,000; AIDS pts: 2–7 cases per 1000.
- Impact of cryptococcosis: Approximately 625,000 deaths each year worldwide.
- Underlying immunocompromised conditions and risk factors: AIDS, systemic lupus erythematous, prolonged treatment with corticosteroids, organ transplantation, advanced malignancy, hematologic malignancy, diabetes, sarcoidosis, cirrhosis, idiopathic CD4 lymphocytopenia, or use of immune-modifying monoclonal antibodies (alemtuzumab, infliximab, etanercept, or adalimumab).
- More and more pts with cryptococcosis are described as immunocompetent.

Perioperative Risks
- Respiratory insufficiency, severe ARDS
- Elevated ICP

Worry About
- Underlying immunocompromised, genetic, or other conditions

Overview
- Systemic mycosis and third most prevalent disease in HIV-positive individuals
- *Cryptococcus neoformans*/*C. gattii* typically infect immunocompromised persons, essentially HIV and transplant-recipient pts, but also pts who do not have underlying HIV infection or are not transplant recipients. These pts tend to have a delayed diagnosis compared with the HIV and transplant groups and are remarkably currently the highest risk group for mortality in resource-available countries
- Wide range of clinical presentations from asymptomatic respiratory colonization to dissemination of infection into any organ. In severely immunosuppressed pts, involvement of multiple body sites. Common sites for infection are the lungs and CNS
- Pulmonary cryptococcosis/cryptococcal pneumonia: Mainly underestimated, not often recognized, multiple clinical presentations—asymptomatic solitary or multiple nodules, lobar infiltrates, interstitial infiltrates, cavities, endobronchial colonization or masses, mediastinal adenopathy, hilar adenopathy, miliary pattern, cavitary lesions, or pleural effusions/empyema, pneumothorax, and life-threatening pneumonia with ARDS
- Cryptococcal meningitis/meningoencephalitis: Primary life-threatening infection, most frequent and most severe form. Mortality rate approximately 12%. Other CNS clinical manifestations: Cryptococcomas (abscesses) of brain, spinal cord granuloma, chronic dementia (from hydrocephalus)
- Laryngeal cryptococcosis: hoarseness, cough, or acute airway obstruction

Etiology
- Seven species are described in the *C. neoformans* species complex: *C. neoformans*, *C. deneoformans*, *C. gattii*, *C. bacillisporus*, *C. deuterogattii*, *C. tetragattii*, and *C. decagattii*. *C. neoformans* and *C. gattii* are the agents highlighted in cryptococcal meningitis fungal infection. Other species, *C. laurentii* and *C. albidus*, are reported.
- Cryptococcus species are encapsulated heterobasidiomycetous fungi. The presence of a polysaccharide capsule is considered one of the reasons for the virulence of the yeast, increasing its invasiveness, pathogenicity, and conferring resistance to the host.
- Cryptococcus infection occurs by the inhalation of infectious cells and is considered a primary pulmonary infection, which may lead to a disseminated infection, with a special predilection for invading the CNS causing meningitis, encephalitis, or meningoencephalitis.
- Skin/subcutaneous, ophthalmic, bone, and prostatic disease also occur. Any pt with a diagnosis of cryptococcosis should be investigated for disseminated disease.

- No human-to-human transmission, except in cases of contaminated transplant tissue
- The most accurate diagnosis method is a LFA, which relies on antibody detection of the fungal glucuronoxylomannan in the capsule.

Usual Treatment

- An essential step in the treatment of cryptococcosis is first being able to make an accurate diagnosis and to so as quickly as possible.
- It has been shown that 89% of the pts with a relapse of cryptococcosis are reinfected by the original strain for a second time, raising concerns for gains in drug resistance (temporarily through heteroresistance or permanently through genetic mutations) or inefficiency of current drug regimens to clear fungus.
- Multiple challenges to effective antifungal treatment may include diagnosis, timing of treatment, cost of treatment, efficacy of the drugs, and availability of drugs.
- Cryptococcal meningitis/meningoencephalitis or CNS infection: The gold standard antifungal regimen is the combination of IV amphotericin B deoxycholate (polyene antifungal agent AMB) 0.7–1 mg/kg/day (or its liposomal derivatives, such as liposomal amphotericin B [AmBisome] 3–6 mg/kg/day with less nephrotoxicity) with 5-fluorocytosine (pyrimidine analogs 5-FC) 100 mg/kg/day for 2–4 wk. Adding flucytosine to amphotericin B reduces the rates of failure and relapse compared with amphotericin B monotherapy. Then fluconazole 400–800 mg/day for at least 8–10 wk. In HIV pts, maintenance fluconazole 200–400 mg/day PO therapy lifelong. Currently the issue of using azoles is developing resistance. Itraconazole is the second drug chosen for a maintenance dose. New-generation azoles (voriconazole, posaconazole) have demonstrated potent activity against *Cryptococcus* species.
- Despite the effectiveness of AMB, it has a high toxicity causing nephrotoxicity, hepatotoxicity, and myelotoxicity. In addition, 5-FC has hematologic toxicities.
- In resource-limited regions, fluconazole is the commonly used alternative therapy to AMB. However, fluconazole is fungistatic and not fungicidal and has been shown less effective than AMB-based therapy.
- Corticosteroids not recommended for the treatment of cryptococcal meningitis.
- Raised ICP is an extremely common complication of cryptococcal meningitis. Control of increased ICP (external drainage or CSF shunt, or surgical drainage of abscesses) to avert irreversible morbidity.
- Antiretroviral therapy in HIV pts or augmentation and restoration of host immunity through reversal of immunosuppression in other immunocompromised hosts.
- Pulmonary disease: fluconazole 400–800 mg/day for 6–12 mo.
- For more severe disease and immunocompromised hosts, treat like CNS disease.
- Echinocandins have no clinically useful activity against *Cryptococcus*.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
ENT	Laryngeal infection	Hoarseness, cough, or acute airway obstruction	Laryngeal edema and erythema, exophytic lesions	Laryngoscopy, stains, biopsy, cultures, serum cryptococcal antigen
RESP	Pneumonia	Fever, chest pain, cough, weight loss, dyspnea, sputum production	Signs of infection	ABGs, CXR, sputum culture, bronchoscopy, lung biopsy, serum cryptococcal antigen, LFA
CV	Endocarditis, myocarditis	Rare vascular instability		ECG, ECHO
HEME/IIMMUNO	Cryptococcemia		Signs of infection	Blood cultures, serum cryptococcal antigen, LFA
GU	Prostatitis, renal cortical abscess		Signs of infection	UA, urine cultures
CNS	Meningitis, abscesses, dementia	Headache, fever, nausea vomiting, cranial nerve palsies, lethargy, coma, seizures, or memory loss	Mental status, focal signs	CSF India ink stain, CSF cultures and cryptococcal antigen, LFA,CT, MRI

Key References: Perfect JR: Cryptococcosis (*Cryptococcus neoformans* and *Cryptococcus gattii*). In Bennett JE, Dolin R, Blaser MJ, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 8, Philadelphia, PA, 2015, Elsevier, pp 2934–2948; Idnurm A, Lin X: Rising to the challenge of multiple *Cryptococcus* species and the diseases they cause. *Fungal Genet Biol* 78:1–6, 2015.

Perioperative Implications

Preoperative Preparation

- Disposable anesthetic delivery circuits with bacterial filters.
- Protect and maintain airways for altered mental status, seizures, focal neurologic signs, and cranial nerve palsies.
- Organ system effects of HIV infection or underlying immunocompromised conditions.

Monitoring

- ARDS network low tidal volume protocol in severe ARDS patients.
- Consider monitoring increased ICP.

Airway

- None

Induction/Maintenance

- Anesthetic drugs associated with lower ICP and having neuroprotective qualities
- Possible interaction of antiretroviral drugs with the anesthetics and/or toxicity

Extubation

- Consider if can adequately protect airway.

Adjuvants

- None

Postoperative Period

- Careful observation for respiratory and neurologic compromise

Cushing Syndrome

Kathleen A. Smith | Justin L. Rountree

Risk

- Onset generally occurs in third and fourth decades.
- Approximately 3–5 times more common in women than men.
- 5-y mortality rate from adrenal carcinomas has been estimated to be >70%.

Perioperative Risks

- Lyte abnormalities
- Consequences of untreated Htn
- Hyperglycemia
- Cardiovascular disease more common

Worry About

- Challenges related to obesity, including airway management and IV access.
- Significant osteopenia secondary to impaired calcium absorption, making positioning difficult.
- Htn due to fluid retention.
- Increased risk of infection as a result of corticosteroids' immunosuppressive qualities.
- Hypokalemic alkalosis, commonly seen in ectopic ACTH production.
- Cushing syndrome may also occur with other disease states, including pheochromocytoma, sarcoidosis, pancreatic carcinoma, sarcoidosis, carcinoid lung tumors, and other neuroendocrine carcinomas.

Overview

- Most common cause of Cushing syndrome is iatrogenic administration of exogenous glucocorticoids.
- Spontaneous Cushing syndrome can result from adrenal gland hyperplasia secondary to increased ACTH production from a pituitary tumor or an ectopic nonendocrine ACTH tumor. Pituitary tumors may present with visual disturbances and have symptoms of increased ICP.
- Other causes include primary gland disorders, such as adrenal adenoma or carcinoma.
- Symptoms including Htn, hyperglycemia, increased intravascular volume, hypokalemia, abdominal striae, truncal obesity, telangiectasias, muscle weakness and/or wasting leading to thin extremities, osteoporosis due to impaired calcium absorption, depression, and insomnia.
- Severe metabolic alkalosis is often the first clinical manifestation of ectopic ACTH-secreting tumors and may result in significant hypoventilation, myocardial depression, arrhythmias, decreased cerebral blood flow, and neuromuscular excitability.

- A 24-h urine cortisol test can demonstrate elevated cortisol levels.
- Dexamethasone suppression test is used to aid in differentiating pituitary adenomas from adrenal tumors. Dexamethasone causes depression of cortisol and 17-hydroxycorticosteriod levels due to a negative feedback response, which is absent with ectopic ACTH or primary gland disease.
- ACTH plasma levels can also be tested directly.
- Radiologic evaluation including abdominal CT scan to evaluate the adrenal glands, pituitary MRI scan with gadolinium contrast to evaluate the pituitary gland, and a chest CT scan when ectopic ACTH is the suspected etiology.

Etiology

- ACTH dependent (excessive ACTH secretion, stimulating adrenal production of cortisol).
  - Pituitary microadenoma (Cushing syndrome) occurs in 70% of cases.
  - Ectopic ACTH production from a nonendocrine tumor (e.g., tumors of the lungs, pancreas, thyroid, or thymus).
- ACTH independent (excessive cortisol production by adrenals and suppression of ACTH production).
  - Adrenocortical adenoma or carcinoma (15%).
- Exogenous administration of glucocorticoids (e.g., treatment of asthma); these pts will likely need periop stress dose steroids.

Usual Treatment

- ACTH-dependent Cushing syndrome:
  - Transsphenoidal resection of pituitary microadenoma.
  - Radiation therapy.
  - Bilateral adrenalectomy in refractory cases.
- ACTH-independent Cushing syndrome:
  - Unilateral or bilateral adrenalectomy (laparoscopic is the preferred method).
  - Medical adrenalectomy.

1. Etomidate inhibits 17α-hydroxylase, 11α-hydroxylase, and 11-deoxycortisol β-hydroxylase, all of which are important in steroidogenesis.
   - Adrenal suppression may occur approximately 30 min following a single dose of etomidate and may last for 24 h.
   - Subhypnotic infusion of etomidate (0.03–0.1 mg/kg/h) can also be used to reduce cortisol levels to within normal limits in 24–48 h.
2. Other drugs that may be used to either inhibit steroidogenesis or prevent the release of glucocorticoids include ketoconazole, metyrapone, mitotane, or aminoglutethimide.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, hypervolemia	HA, visual disturbances		Noninvasive BP
FEN	Hypokalemia Metabolic alkalosis	Weakness, constipation, nausea, arrhythmias, potentiate neuromuscular blockade Hypoventilation	Decreased strength	Basic metabolic panel, flat T waves on ECG
RENAL	Fluid retention	Leg swelling	Peripheral edema	Serum/urine osmolarity
ENDO	Hyperglycemia	Thirst, frequency		Fasting blood glucose
MS	Muscle wasting Impaired calcium absorption	Proximal weakness Osteoporosis	Thin extremities Easy fracture	Difficulty rising from chair/climbing stairs Bone density scan
CNS	Pituitary adenoma	Elevated ICP	Somnolence, papilledema	CT scan

Key References: Heyn J, Geiger C, Hinske CL, et al.: Medical suppression of hypercortisolemia in Cushing's syndrome with particular consideration of etomidate, *Pituitary* 15(2):117–125, 2012; Domi R: Cushing's surgery: role of the anesthesiologist, *Indian J Endocrinol Metab* 15(Suppl 4):S322–S328, 2011.

Perioperative Implications

Preinduction, Induction, and Maintenance

- Prior to induction, normalize volume status, lytes, BP, and blood glucose levels. Spironolactone can be used to mobilize fluid and normalize potassium levels.
- Anxiety can cause increased secretion of cortisol. This response may be blunted by premedication.
- Make preparations to deal with a potentially difficult airway.
- Cortisol secretion is unlikely to be affected by the type of anesthesia used.
- Choice of anesthetic agents used for induction and maintenance of anesthesia are not affected by the presence of Cushing syndrome.
- Etomidate can be used at induction for its temporary suppression of the adrenal gland. This effect may be overcome by the significant cortisol release with surgical stimulation.
- Maintain blood glucose levels between 120–180 mg/dL; SQ insulin or infusion.

Monitoring

- Intraoperative monitoring should be based on the pt's current clinical state
- Arterial catheter may be indicated in cases of poorly controlled systemic Htn
- CVP monitoring is often used to aid in fluid administration, particularly in transsphenoidal tumor resections
- Intraop blood glucose levels and electrolytes

General Anesthesia

- GA is often the anesthetic of choice in pts with significant skeletal muscle weakness/wasting due to the need for mechanical ventilation
- Dose of muscle relaxant may need to be reduced in pts with skeletal muscle weakness
- Pneumoperitoneum, obesity, and lateral decubitus position may worsen hypoxia and hypercarbia
- The pneumoperitoneum should be kept as low as possible to decrease the risk of hemodynamic changes

Regional Anesthesia

- Regional anesthesia offers no significant advantage over general anesthesia in patients with Cushing syndrome

Postoperative Period

- Bilateral and unilateral adrenal resections require glucocorticoid and mineralocorticoid supplementation for life or until the remaining adrenal gland is able to compensate.
- Treatment doses start with 100 mg of IV hydrocortisone every 24 h, starting the day of surgery with titration over a week until a maintenance dose (20–30 mg/day) is reached. Hydrocortisone given in these quantities usually provides adequate mineralocorticoid activity.
- Bilateral adrenalectomy often requires the addition of fludrocortisone for mineralocorticoid supplementation.
- Close observation for pneumothorax when open adrenal resection is performed.
- Meningitis and transient DI are possible postop complications following a transsphenoidal microadenomectomy.
- Glucocorticoids decrease the tensile strength of healing wounds. Topical administration of vitamin A may improve wound healing in the face of increased glucocorticoids.

Anticipated Problems/Concerns

- Meningitis following microadenomectomy
- Obesity leading to a possible difficult airway
- Increased susceptibility to infection
- Hyperglycemia
- Increased risk of hypercoagulability and periop thromboembolic events
- Increased risk for intraop pneumothorax with open adrenal resection when compared with laparoscopic approach

Cyanide Poisoning

Peter H. Breen

Risk

- Potent rapid-onset toxin, especially with inhalation of HCN (volatile liquid).
- May be absorbed through mucous membranes; CN ingestion results in slower onset.
- Diffuses rapidly through body with high intracellular fixation to cytochrome aa_3 in cellular mitochondria to paralyze aerobic metabolism.

Perioperative Risks

- Main target organs: CNS and heart.
- Animal experiments: Apnea precedes cardiac collapse.

Worry About

- If CN toxicity resulted from fire or smoke exposure, consider also CO and other toxins.
- One third of pts with CO toxicity exposed to domestic fires also have increased CN.
- Be alert for CN poisoning in donors for organ transplantation.

Overview

- Major route of CN detoxification: Conversion to thiocyanate, which requires sulfane sulfur donor (e.g., thiosulfate) and enzyme (e.g., rhodanese); without renal excretion, increase in thiocyanate can cause CNS abnormalities.
- Minor route: Hydroxocobalamin (one form of vitamin B_{12}) chelates CN to form cyanocobalamin.
- metHb ferric ion has high affinity for CN.

Etiology

- Combustion product of natural and synthetic polymers
- Industrial chemistry (e.g., metals and plastics preparation)
- Plants: May contain cyanogenic glycosides
- Na nitroprusside: Overtreatment (>0.5 mg/kg/h within 24 h)
- Abuse (e.g., suicide, Chicago CN-laced-Tylenol murders [1982], terrorism, chemical warfare)

Usual Treatment

- Rescue victim from exposure.
- Intubation and ventilation with 100% O_2 (hyperbaric O_2, effective experimentally, is not practical).
- Gastric decontamination (if necessary).
- Weigh risks and/or benefits of drug therapy, since the half-life of CN is short (about 1 hr).
- Sodium thiosulfate (adult: about 150 mg/kg IV over 10 min) (minimal side effects, but thiocyanate requires renal excretion or hemodialysis); usually administered with sodium nitrite.
- Hydroxocobalamin (adult: 5–10 g IV over 20 min); safe and rapid.
- Methemoglobinemia induction (metHb, 30%) with sodium nitrite (adult: 300 mg IV over 10 min); slow and unpredictable; can be hazardous in presence of carboxyhemoglobin (from CO toxicity) because neither metHb nor COHb carries O_2; can be fatal in G6PD deficiency.
- Dicobalt EDTA (adult: 300 mg IV) followed by glucose infusion; potent and rapid but unsafe (especially due to arrhythmias, hypotension, and allergic reactions).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Decreased CNS depression leading to decreased airway maintenance/protection	Concomitant smoke inhalation injury	Perioral burns Airway edema	Laryngoscopy/bronchoscopy
CV	Stimulation at low CN concentration Depression at high CN concentration	Htn, tachycardia Hypotension, bradycardia	Increased cardiac output Decreased cardiac output, arrhythmias	ECG: Arrhythmias, especially decreased conduction, VTach, VFIB
RESP	Aerobic cellular respiration paralyzed			Increased blood PvO_2 and increased SvO_2 decreased VO_2, decreased VCO_2, decreased $PETCO_2$
	Thermal/toxic airway and parenchymal injury	Concomitant smoke inhalation injury	Bronchoconstriction and pulm edema	CXR Bronchoscopy
METAB	Cellular aerobic metabolism disabled	Combination of increased SvO_2 and lactic acidosis suggests CN toxicity	Blood CN level toxic above 0.2 mg/L	Lactic metabolic acidosis Whole blood CN levels (not available in all labs)
CNS	Stimulation at low CN concentration	Increased inhalatory CN intake Anxiety, dyspnea, headache Auditory/visual disturbances	Increased respiratory rate Confusion	
	Depression at high CN concentration		Apnea, convulsions, coma; Chronic sequelae possible	Funduscopy: Red retinal veins (increased SvO_2)

Key Reference: Breen PH, Isserles SA, Tabac E, et al.: Protective effect of stroma-free metHb during cyanide poisoning in dogs, *Anesthesiology* 85(3):558–564, 1996.

Perioperative Implications

Preoperative Preparation

- Continuous 100% O_2

Monitoring

- SpO_2 unreliable in presence of metHb (or COHb if coexistent CO poisoning)
- SvO_2 or PvO_2
- $PETCO_2$
- Measurement of VO_2 and VCO_2 helpful.

Airway

- Protect and maintain airway.

Induction

- Avoid CV depressant agents.

Maintenance

- 100% O_2 (no N_2O)

Extubation

- Ensure that CNS status permits natural airway maintenance and protection.

Adjuvants

- Consider treatment for concomitant CO poisoning (see Carbon Monoxide Poisoning).

Postoperative Period

- Maintain 100% O_2 breathing.

Anticipated Problems/Concerns

- Heart and brain are target organs.
- Prompt CPR (ventilation with O_2) determines outcome.
- Follow CNS function.
- Seek concomitant smoke inhalation injury and CO toxicity.

Cystic Fibrosis

Julie L. Huffmyer | Edward C. Nemergut

Risk

- Prevalence ranges from 1:2500 births in white population to 1:17,000 in African Americans; prevalence growing faster than incidence as median survival is increasing.
- For pts with CF, 50% of are older than 18 y of age; 30,000 affected in USA; 3000 affected in Canada; 20,000 affected in Europe.
- In white population, 2–5% are carriers,

Perioperative Risks

- Pulmonary:
  - Hypoxia and hypercarbia
  - V/Q mismatching

  - Pneumothorax
  - Airway obstruction with distal air trapping
- Pancreatic:
  - Glucose intolerance
  - Upper airway
  - Nasal polyps occlude nasal airways

Worry About

- Pneumothorax
- Atelectasis and air trapping
- Massive hemoptysis
- Copious, inspissated secretions
- Hypoxemia and hypercarbia
- Cor pulmonale

Overview

- Disease of the exocrine glands that affects the lungs, pancreas, and GI and hepatobiliary tracts.
- Pulmonary exacerbations are caused by airway obstruction with thickened mucus.
- Pulmonary infections are common, colonized with *Pseudomonas aeruginosa, Staphylococcus aureus, Haemophilus influenzae , Stenotrophomonas maltophilia, Burkholderia cepacia, Aspergillus fumigatus*.
- Pancreatic insufficiency leads to malabsorption of vitamins A, D, E, and K, nutritional deficiency, and CF-related diabetes mellitus.

Etiology

- Autosomal recessive trait due to mutation of gene on long arm chromosome 7, but 2000 disease-causing mutations known
- CFTR gene controls the transmembrane transport of chloride at the apical border of epithelial cells lining exocrine glands
- CFTR defect causes goblet cell hypertrophy, thickened mucous secretions, reduced mucociliary clearance and subsequent pulmonary inflammation, infection, and chronic hypoxia

Usual Treatment

- Goals: Control infection, promote mucous clearance, and improve nutritional status.
- Newer treatments include ivacaftor, a CFTR potentiator to improve lung function and reduce pulmonary exacerbations with class 3 mutations, and lumacaftor, which acts to restore chloride secretion as a result of the class 2 mutation delF508.
- Pulmonary: Chest physiotherapy, mucolytics (short term), bronchodilators, humidification, and antibiotics for infections.
- Pancreatic: Pancreatic enzyme replacement, vitamin supplementation, nutritional support, and glucose control.

Assessment Points

System	Effects	Assessment by Hx	PE	Test
HEENT	Frequent nasal polyps Sinusitis	Nasal obstruction Difficulty sleeping Fever, headaches	Nasal polyps Sinus drainage	Nasal endoscopy Sinus x-ray, culture
CV	Cor pulmonale Increased pulmonary vascular resistance, right ventricular hypertrophy	Dyspnea Orthopnea Cyanosis	Tachypnea Rales, rhonchi, wheezing Clubbing of fingers Cyanosis	ECG CXR
RESP	Bronchiectasis, atelectasis, pneumonitis, bronchospasm	Cough Dyspnea Exercise tolerance Orthopnea	Hyperinflation of lungs Poor ventilation, cyanosis Clubbing Cough, rales, rhonchi, wheezing	CXR PFTs A-a gradient
GI	Cholelithiasis, gallbladder dysfunction Pancreatic insufficiency Focal biliary cirrhosis, fatty liver Intestinal obstruction	Abdominal pain (may be asymptomatic) Poor fat absorption, glucose intolerance Abdominal pain, distention, N/V	Jaundice Abd rigidity	Liver ultrasound Cholangiography Glucose Liver function tests Abdominal x-rays
MS	Poor muscle development	Hx of poor nutrition, muscle weakness	Cachexia	

Key References: Huffmyer JL, Littlewood KE, Nemergut EC: Perioperative management of the adult with cystic fibrosis, *Anesth Analg* 109(6):1949–1961, 2009; Pittman JE, Ferkol TW: The evolution of cystic fibrosis care, *Chest* 148(2):533–542, 2015.

Perioperative Implications

Preoperative Preparation

- Hx and evaluation of baseline pulm status, exercise tolerance.
- CXR: Hyperexpansion indicated by flattened diaphragm.
- PFTs: Obstruction indicated by increased RV:TLC, decreased FEV_1 and $FEF_{25–75\%}$.
- ABG, lytes, blood glucose, liver function tests.
- Medications: Bronchodilators, antibiotics.
- Chest physiotherapy.

Monitoring

- Routine plus arterial pressure and/or central venous access as cardiopulmonary status and procedure indicates
- Blood glucose should be checked frequently in pts with pancreatic disease

Airway

- Oropharyngeal airway for upper airway obstruction due to possibility of nasal polyps

Induction

- IV induction faster than inhalation due to larger FRC, smaller tidal volumes, and V/Q mismatching.

Maintenance

- Volatile anesthetics useful as bronchodilators.
- Positive pressure ventilation may be necessary but should be used cautiously in light of pneumothorax risk.
- Warm and humidify gases.
- Suctioning of airway mucus and bronchiolar lavage may help to maintain oxygenation and ventilation.
- Muscle tone is important in maintaining patency of airways, so muscle relaxants should be used only when needed.
- Opioids are useful, but pain control must be balanced with adjunctive agents to minimize risk of respiratory depression.
- Regional anesthesia techniques particularly beneficial in minimizing instrumentation of the airways while providing postop pain control; careful with neuraxial anesthesia due to dependence on accessory breathing muscles.

Extubation

- Early extubation critical to avoid increase in pulmonary morbidity; provide lung recruitment maneuvers before extubation.
- Adjuvants.
- Bronchodilators, NSAIDs, ketamine, and IV lidocaine.

Postoperative Period

- Pain control key in encouraging coughing and deep breathing
- Chest physiotherapy and early activity

Anticipated Problems/Concerns

- Pneumothorax
- Postop respiratory insufficiency: consider BiPAP, requirement for oxygen
- Cor pulmonale
- Lyte disturbances (Na^+, Cl^-)

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Cytomegalovirus Infection

M. Veronica Dioverti | Stacey A. Rizza | Andrew D. Badley

Risk

- Seroprevalence increases with age and low socioeconomic status in USA: From 58.9% in those aged ≥6 y to 90.8% in those ≥80 y. Also higher in non-Hispanic blacks, Mexican Americans, and women.
- Severe disease from CMV is rare in immunocompetent individuals.
- Risk for CMV disease in transplant recipients: 10–40% with preventive measures.
- Risk for CMV disease in HIV-positive pts: 20–30% (increased risk with low CD4 count).
- Approximately 1:150 children is born with congenital CMV.

Perioperative Risks

- CMV transmission from tissue or blood products from a CMV-seropositive donor to a seronegative recipient
- Related to severity of CMV-induced organ dysfunction (if present): Pulmonary, CNS, hepatic, GI, cardiac, bone marrow, adrenal

Worry About

- Giving CMV-seropositive blood products to a CMV-seronegative immunocompromised host; filters that remove leukocytes from the blood can be used to prevent transmission of CMV if CMV-seropositive blood donors are used.
- Abnormal hepatic metabolism if CMV hepatitis is present may alter drug clearance.
- Elevated ICP if CMV encephalitis/meningitis.
- Abnormal oxygenation if CMV pneumonitis.
- Myocardial dysfunction or arrhythmias if CMV myocarditis.
- Perforated viscus secondary to colonic/gastric CMV.
- Bone marrow suppression resulting in abnormal bleeding from thrombocytopenia, anemia, and neutropenia.
- Adrenal insufficiency due to CMV adrenalitis.

Overview

- Double-stranded DNA betaherpesvirus; member of the *Herpesviridae* family—largest virus to infect humans.
- Vast majority of North American adults have had prior exposures and are CMV seropositive.
- Establishes latency after primary infection. Secondary infection occurs after reactivation of a latent virus in an immunocompromised host.
- Transmission through close contact, blood and blood products, organ transplantation, and sexually and perinatally.

Manifestations

- Immunocompetent host: Asymptomatic, heterophile antibody–negative mononucleosis-like syndrome
- Immunocompromised host: Symptomatic or asymptomatic viremia with or without organ involvement—retinitis, encephalitis, meningitis, myelitis, polyneuropathy, pneumonitis, esophagitis, gastritis, colitis, hepatitis, cholangitis, myocarditis, adrenalitis, vasculitis, and bone marrow suppression
- Neonates: Petechial rash, jaundice with hepatosplenomegaly; neurologic abnormalities, such as microcephaly and lethargy, eye involvement with chorioretinitis and optic nerve atrophy, prematurity and low birth weight, and sensorineural hearing loss

Diagnosis

- Serology: IgM has high rates of false positivity. Positive IgG indicates prior infection, which is useful for risk stratification in transplant recipients
- NAAT (in immunocompromised hosts)
- Viral cultures
- pp65 antigenemia (in immunocompromised hosts)

Usual Treatment

- Immunocompetent host: Supportive symptomatic management, antivirals not indicated
- Immunocompromised host: IV ganciclovir in moderate-to-severe infection; oral valganciclovir in mild infection. IV foscarnet or cidofovir for resistant virus. IV immunoglobulins as adjunctive therapy in refractory cases; other experimental drugs (brincidofovir, maribavir, letermovir)
- Surgical: For complications of end-organ damage, such as repair of GI perforation.

Prevention

- Oral valganciclovir in high-risk solid organ transplant recipients
- Preemptive monitoring with NAAT in stem cell, bone marrow, and umbilical cord transplant recipients

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Destruction of retina	Decreased visual acuity, blind spots	Funduscopy; white and red lesions	Ophthalmology evaluation
CV	Myocarditis; LV dysfunction	CHF symptoms, palpitations	Irregular rhythm, displaced PMI, S_3	ECG, ECHO, heart biopsy
RESP	Pneumonitis; impaired gas exchange	Dyspnea, nonproductive cough	Wheezes, crackles, hypoxemia	CXR, ABG, bronchoscopy + biopsy
GI	Viral infection of organ	Hepatitis/cholangitis: • Right upper quadrant pain • Jaundice, itching, acholic stools Esophagitis: Dysphagia, odynophagia Colitis: Diarrhea, abdominal pain Gastritis: Pyrosis, anorexia, epigastric pain	Signs of hepatic failure, fetor hepaticus, asterixis, jaundice, bruising, painful liver, nonspecific abdominal pain	Liver function tests, ERCP, EGD, US, NAAT, ± biopsy
HEME	Bone marrow suppression	Fever, fatigue	Petechiae, pallor, tachycardia	CBC with differential
CNS	Encephalitis	Motor or sensory abnormalities, altered mental status	Motor weakness, sensory abnormality, cerebellar ataxia, abnormal tests of cortical function	CT, MRI, lumbar puncture

Key References: Rafailidis PI, Mourtzoukou EG, Varbobitis IC, et al: Severe cytomegalovirus infection in apparently immunocompetent patients: a systematic review, *Virol J* 5:47, 2008; Crumpacker C: Cytomegalovirus. In Bennett J, editor: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 8, Philadelphia, PA, 2015, Elsevier, pp 1738–1753.

Perioperative Implications

Perioperative Preparation

- Evaluate for signs of pulmonary, cardiac, hepatic, CNS, bone marrow, and/or adrenal dysfunction.

Monitoring

- Routine
- May need drug dose adjustment if hepatic/renal dysfunction present

Airway

- May require high FIO_2 and PEEP if pneumonitis present

Preinduction/Induction

- Avoid tachycardia/hypotension.

Maintenance

- Follow CO, PCWP, SaO_2, and BP.

Extubation

- No special concerns

Postoperative Period

- Monitor for clinical signs of disease progression.

Adjuvants

- No special concerns

Dandy-Walker Syndrome

David Johnson | Lee A. Fleisher

Risk

- Multiple genetic factors; mostly sporadic with limited familial inheritance
- Range: 1:10,000-30,000 newborns

Perioperative Risks

- Variable phenotypic expression and organ involvement
- Increased incidence of additional developmental abnormalities
- Depend upon severity of disease and comorbidities, which may include elevated ICP; craniofacial, cardiac, and renal malformation; seizure disorder; respiratory depression; nausea; and vomiting

Worry About
- Hydrocephalus with elevated ICP and possible seizures
- Pt's ability to cooperate and follow commands
- Aspiration risk
- Ventilation challenges because of craniofacial abnormalities
- Postanesthetic respiratory depression
- Multiorgan disease resulting in cardiac and urogenital abnormalities

Overview
- Dandy-Walker complex represents a group of related congenital disorders of brain development, including Dandy-Walker malformation, mega cisterna, and Dandy-Walker variant.
- Includes congenital brain malformation involving a hypoplastic cerebellum with variable defects in formation of the cerebellar vermis, enlargement of the fourth ventricle, and cyst formation in the posterior fossa.
- Commonly associated conditions with variable severity include hydrocephalus, defects in corpus callosum formation, developmental delay, and abnormalities of the heart, urogenital tract, and bones. There may be associated developmental syndromes including PHACIES, spina bifida, and others, which may complicate management. Careful Hx and physical exam are required to identify comorbidities.
- ICP and seizure management are primary concerns.
- Rostral brain involvement may predispose pt to apnea following anesthetic.

Etiology
- Believed to be the result of multifactorial gene mutations. TUBA1A has been identified as a major driver, resulting from mutation of tubulin transport proteins. Inheritance is mostly sporadic, with a small familial association.

Usual Treatment
- Depends upon disease presentation. Hydrocephalus is often treated with ventriculoperitoneal shunt, medication for seizures, physical therapy for muscular involvement, occupational therapy, and education for learning disabilities.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Craniofacial abnormality, macrocephaly, micrognathia, macroglossia, occipital meningocele, nystagmus			
CV	Varied cardiac abnormalities, including Tetralogy of Fallot	SOB, poor exercise tolerance, "Tet spells"	Cyanosis, heart murmur	CXR, ECG, angiography
RESP	Medullary control of respiratory center		Apnea	
RENAL	Urogenital malformation	Urinary tract infections		UA
CNS	Intracranial pressure, developmental delay, CN palsy	N/V, seizure	Palsy, altered mentation	CT
MS	Abnormal vertebrae, prominent occiput, frontal bossing, cleft palate, truncal ataxia, muscle spasticity		Ataxia	CT

Key References: National Institutes of Health: Genetic and rare diseases information center. <https://rarediseases.info.nih.gov/gard/6242/dandy-walker-complex/resources/1>, 2016 (Accessed 12.04.16.); Shweta M, Rao S, Ladi SD, et al.: Dandy Walker syndrome: case report, *Innov J Med Health Sci* 4(1):309–311, 2014.

Perioperative Implications

Preoperative Preparation
- Identify organ involvement, aspiration risk, and anatomic defects.

Monitoring
- Standard monitoring
- Arterial line if cardiac dysfunction warrants

Airway
- Craniofacial abnormalities may compromise ventilation and intubation.
- Macrocephalus may be managed with a shoulder bag to improve positioning.
- Rapid sequence induction if aspiration risk exists.

Induction
- Avoid increased ICP with smooth induction, normocapnia, and muscle relaxants.
- Preop ventriculoperitoneal shunt may be needed before other surgeries.
- Succinylcholine may need to be avoided because of renal disease or elevated ICP.
- Cognitive impairment may render pt uncooperative.
- pt may have CV disease.

Maintenance
- Pt may have CV instability.
- Monitor for seizure activity; maintain normocapnia.

Extubation
- Anticipate challenges with reintubation.
- Pt may be at risk of apnea and delayed spontaneous ventilation due to diminished respiratory drive.

Adjuvants
- Shoulder bag, video laryngoscope, and fiberoptic laryngoscope

Postoperative Period
- Monitor respiratory status closely.
- Monitor for seizure activity; avoid increased ICP.

De Morsier Syndrome

Ashley R. Valentine | Jeffrey R. Kirsch

Risk
- For live births: 1:10,000; equal male to female prevalence
- Associated with younger maternal age
- May not be identified until later in life

Perioperative Risks
- Reduced cortisol stress response in undiagnosed or untreated pts. Hormone tests may be normal in nonstress conditions.
- Treatment of one hormone deficiency (e.g., hypothyroidism, or hypothyroidism and adrenal insufficiency) may unmask another or others (e.g., adrenal insufficiency, DI).

Worry About
- Unrecognized hypothalamic/pituitary axis deficiencies
- Neurocognitive disorders causing agitation, seizures, or confusion in periop period

Overview
- Highly phenotypically variable disorder diagnosed when at least two of three features are present: ONH, midline/CNS neuroradiographic abnormalities (may include absence of the septum pellucidum), and/or hypothalamic/pituitary abnormalities.
- ONH is third most common cause of any vision impairment in children <3 y in USA.
- ONH associated with other neuro abnormalities (e.g., developmental delay, autistic spectrum disorder, epilepsy, disrupted circadian rhythm).
- Hypothalamic/pituitary hormone abnormalities can develop at any age and may include growth hormone deficiency (most common), hypothyroidism, ACTH deficiency, and DI (least common).
- Limb abnormalities (e.g., syndactyly) and MSK abnormalities (e.g., spastic quadriparesis, hypotonia) also may be present.

Etiology
- Majority of cases are sporadic, and less than 1% have currently identifiable genetic mutation.
- Environmental risk factors may include antenatal drug/ETOH use and low socioeconomic status.
- Genetic mutations in HESX1, SOX2, SOX3, or OTX2 may be causal.
- See also Adrenal Insufficiency, Hypopituitarism, Hypothyroidism, and Seizure.

Usual Treatment
- Pts followed at least every 6 mo for growth and development
- At least annual vision evaluation and treatment as indicated
- Endocrine function followed for life because hypothalamic/pituitary abnormalities can develop at any age
- Supportive services tailored to individual pt's needs (e.g., occupational, speech, developmental, and/or physical therapy; neuropsychology; ophthalmology)
- Genetic counseling for families with identifiable genetic mutation
- May need surgical correction of associated strabismus or orthopedic deformities

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vision deficits, nystagmus, strabismus	History of abnormal vision, blindness, vision correction surgeries	HEENT exam	Evaluation by ophthalmologist
ENDO	Hypothalamus/pituitary abnormalities	Growth delay, precocious or delayed puberty, excessive thirst, excessive hunger, heat or cold intolerance, fatigue, constipation, weakness, history of treatment for known abnormalities	Vitals, puffy face, weakness	Endocrine hormones (TSH, T_3/T_4, GH, cortisol or cortisol stim test, glucose, IGF-1, IGFBP-3, LH, FSH
CNS	Cognitive delay, autistic spectrum disorder, behavioral disorder, epilepsy, sleep disorder, abnormal temperature regulation, hyperphagia or hypophagia, polydipsia	Stereotypical behaviors, not meeting developmental milestones, speech delay, seizures, abnormal sleep/wake cycles, temperature instability (unexplained fevers or frequent hospitalizations to rule out sepsis), insatiable appetite or food aversion, water-seeking behavior	General appearance, neuropsych exam	MRI, CT
MS	Weakness, spasms, motor delay, limb deformities	Not meeting developmental milestones, frequent falls, clumsiness	MSK exam NEURO exam	X-ray, CT, and/or MRI

Key References: Borchert M: Reappraisal of the optic nerve hypoplasia syndrome, *J Neuroophthalmol* 32(1):58–67, 2012; Sherlock DA, McNicol LR: Anaesthesia and septo-optic dysplasia: implications of missed diagnosis in the peri-operative period, *Anaesthesia* 42(12):1302–1305, 1987.

Perioperative Implications

Preoperative Preparation
- Evaluation and treatment of endocrine abnormalities (especially thyroid, ACTH, GH and deficiencies)
- Consider ONH if neonatal history of jaundice, hypoglycemia, and nystagmus/visual deficits
- Consider premedication for pts with cognitive delay.

Monitoring
- Standard monitors
- Neuromuscular (TOF) for recovery from muscle relaxants

Induction
- Consider avoiding succinylcholine in pts with severe weakness or immobility.
- Consider avoiding etomidate in pts with untreated secondary adrenal insufficiency.

Airway
- No special difficulty

Intraoperative Considerations
- Intraoperative CBG if history of hypoglycemia.
- Consider stress-dose steroids if secondary adrenal insufficiency.

Extubation
- No special difficulty but may need support for agitated pts

Postoperative Period
- Consider stress-dose steroids for secondary adrenal insufficiency.
- May have increased risk of postop delirium given vision/cognitive impairment.

Anticipated Problems or Concerns
- Abnormal temperature regulation may be difficult to differentiate from postop infection. Multidisciplinary supportive services may be needed postop.

Deep Vein Thrombosis

Sophia T. Cisler | Lee A. Fleisher

Risk
- Incidence in USA: 170,000–200,000 new cases; 90,000–100,000 recurrent cases.
- VTE is the third most frequent acute cardiovascular syndrome after MI and CVA.
- Half of all episodes are associated with recent surgery or hospitalization.
- VTE is recognized as the leading cause of preventable death in hospitalized pts.

Perioperative Risks
- Modified Caprini risk model can be used to predict risk in general surgical pts.
- Without prophylaxis, DVT develops in close to 30% of general surgical pts.
- With chemical prophylaxis, risk can be reduced to 8% for general surgical pts.
- Incidence of fatal PE: 0.1 (general surgery)–5% (total knee replacement).

Worry About
- Pulm embolism
  - Cardiac arrest, electromechanical dissociation
  - Increased A-a gradient, increased dead space, potentially leading to respiratory acidosis
- Increased bleeding risk, safety of regional anesthesia in anticoagulated pts
- Risks and benefits of discontinuing anticoagulation for surgery

Overview
- Classic symptoms of DVT: swelling, pain, and erythema of the involved extremity.
- GA associated with increase in tissue factor, vWF, tissue plasminogen activator, resulting in hypercoagulable/hypofibrinolytic state.
- Dx.
  - Contrast venography (gold standard); requires IV contrast exposure; 2–3% incidence of inducing thrombosis.
  - Compression/duplex ultrasonography of femoral/popliteal veins has sens/spec of 97% in symptomatic pts (less sens for more distal [calf] veins).
  - IP, also more sensitive in proximal (90%) than distal.
  - D dimer has high negative predictive value useul to rule out VTE).
- See also Pulmonary Embolism.

Etiology
- Pt-specific risk factors: age >40 y, immobility, obesity, malignancy, smoking, history of VTE, lower limb injury, inherited hypercoagulability
- Risk increased significantly by major surgery or critical illness
- Without prophylaxis, incidence is approximately 14% in gynecologic surgery, 22% in neurosurgery, 26% in abdominal surgery, and 45–60% in hip/knee surgery
- Risk decreased with regional anesthesia versus general, especially in LE orthopedic surgery

Usual Treatment
- Anticoagulation (UF heparin, LMW heparin, warfarin, or direct oral anticoagulants such as factor IIa or Xa inhibitors)
- Thrombolytics
- Thrombectomy, catheter or open surgical
- IVC filter for PE prevention in high-risk pts or if anticoagulation is contraindicated

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV			Tachycardia, RV strain	ECG, TTE/ TEE
RESP	PE	Chest pain, dyspnea, hemoptysis	Tachypnea, wheezing, hypoxemia	SpO_2, ABGs, $ETCO_2$
HEME				PT, APTT, Plt, Hgb, D dimer
DERM		Fever	Unilateral edema, erythema, warmth	
MS		Limb pain	Tenderness, Homans sign	Ultrasound, venography

Key References: Streiff MB, Agnelli G, Connors JM, et al: Guidance for the treatment of deep vein thrombosis and pulmonary embolism, *J Thromb Thrombolysis* 41(1):32–67, 2016; Krishnan KN: Deep vein thrombosis and pulmonary embolism—prevention, management, and anaesthetic considerations, *Indian J Anaesth* 54(1):8–17, 2010.

Perioperative Implications

Preoperative Preparation

- Consider preoperative placement of an IVC filter in high-risk pts.
- In high-risk procedure (e.g., hip surgery), neuraxial anesthetic may decrease DVT risk versus GA.
- For pts taking anticoagulant/antiplatelet drugs preoperatively:
  - Note the name, type, dosage, duration, and most recent dose.
  - Consider PT, PTT, and platelet count on day of surgery.
  - Confirm adequate blood product availability.
  - Explain risk and benefits of discontinuing medications perioperatively.
  - Consider and discuss with surgeon the role of reversal agents for urgent surgery or life-threatening bleeding.

Monitoring

- Noninvasive BP, ECG, SpO_2, $ETCO_2$.
- In high-risk pts, consider arterial line for serial ABGs, central line for CVP.
- Consider availability of TEE in high-risk pts or cases of suspected PE.

Airway

- None

Preinduction and Induction

- SCDs prevent venous stasis; may activate fibrinolytic system.
- When possible, administer SQ heparin before incision.

Adjuvants

- Depends on etiology; examine specific etiology (e.g., hypercoagulability).
- Heparin, warfarin, direct oral anticoagulants, and thrombolytics all increase perioperative bleeding diathesis. These agents may have effects on the pharmacokinetics of other drugs (verify specific effects).

Postoperative Period

- In high-risk pts, consider full anticoagulation postoperative as prophylaxis.
- If using SQ heparin, it should be administered every 8 h if possible.
- Continue SCDs, stockings until pt is ambulatory, but do not start in pts suspected of having DVT.

Anticipated Problems/Concerns

- PE represents life-threatening complication of DVT.
- Postthrombotic syndrome with chronic venous stasis, skin and wound effects.

Degenerative Disk Disease

John E. Tetzlaff

Risk

- Risk factors determined by spinal level
- Cervical spine: C3 and C4 most common; 10% of degenerative disk disease
- Thoracic: uncommon; can be related to trauma or tumor; 0.2–1.8% of disk disease
- Lumbar; very common; 85–90% of disk disease; third most common cause of chronic pain in USA

Perioperative Risks

- Difficult airway
- Spinal cord injury from airway manipulation or positioning
- Positioning injury from prone position
- Ischemic optic neuropathy

Worry About

- Cervical spine instability, nerve root entrapment, or chronic subluxation.
- Difficulty with intubation.
- Injury to the spinal cord, nerve roots.
- Pressure injuries or ventilatory difficulty with the prone position.
- Brachial plexus injury with the prone position.
- Optimum perfusion to the head. Ischemia, neck position, or venous congestion may contribute to ischemic optic neuropathy.
- Airway edema at the conclusion of surgery.

Overview

- Pain from herniation of an intervertebral disk with nerve root compression is the third most common chronic disease in USA and the most common indication for elective spine surgery.
- Incidence varies among spinal segments, being absent in sacral area; most common in lumbar area, next in cervical region, and uncommon in thoracic region.

Etiology

- Osteoarthritis
- Trauma
- Connective tissue diseases, such as rheumatoid arthritis or ankylosing spondylitis

Usual Treatment

- Conservative measures, including rest, exercise, physical therapy, heat, and traction.
- Symptoms are treated with analgesics and NSAIDs.
- During the acute phase, disk herniation can be treated with epidural steroid injection.
- Nonsurgical intervention, such as IDET.
- Surgery is performed to relieve compression on the spinal cord or specific nerve roots and to expand the space for nerve root exit from the spinal column.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway Visual acuity	Neck pain Patient report	Decreased ROM Patient report	Flexion/extension x-ray to detect instability Eye examination
RESP	Lung tumor can mimic symptoms of thoracic disk disease	Chest pain with chest excursion	Abnormal pulmonary auscultation	CXR, MRI
GI	GI malignancy can mimic symptoms of thoracic or lumbar disk disease	Truncal pain, abdominal pain	Abdominal mass	CT, MRI
RENAL	Pyelonephritis, cancer of prostate can mimic symptoms of lumbar disk disease	Lumbar pain, muscle spasm, fever/chills	Costovertebral angle tenderness to percussion	Urinalysis, prostate-specific antigen, lumbar spine x-ray, MRI, bone scan
CNS	Myelopathy, anterior spinal cord syndrome	Radiating pain, incontinence, sexual dysfunction, paraplegia	Long tract signs, abnormal reflexes, paresthesia, Babinski reflex	X-ray, MRI
PNS	Radiculopathy, absent deep tendon reflexes, peripheral nerve deficits	Sciatica, numbness, weakness of the extremities	Sciatic pain with ROM, motor deficits, Patchy sensory deficits	Electromyography
MS	Pain, decreased ROM, calcification	Pain, night pain, disability from work	Decreased ROM in spine	Spine x-ray, MRI

Key References: Rothman RA, Simeone FA: *The spine*, ed 54, Philadelphia, PA, 2011, Elsevier (Chapters 36–54); Popitz MD: Anesthetic implications of chronic disease of the cervical spine, *Anesth Analg* 84(3):672–683, 1997.

Perioperative Implications

Preoperative Assessment

- Evaluate coagulation if heavy aspirin or NSAID use, anticoagulants, or symptoms of bleeding.
- Airway assessment. If signs of cervical instability or other indicators of difficult airway management, flexion-extension x-ray of cervical spine.
- Antisialagogue if awake intubation.
- If spinal or epidural anesthesia planned, lumbar x-rays may be needed.
- Planned regional anesthesia may reduce minor complications, such as pain and nausea; intraop bleeding may be reduced.

Monitoring

- Potential for air embolism, greater with sitting position for posterior approach to cervical spine.
- Consider multilumen right atrial catheter; precordial Doppler if sitting position for cervical spine procedure.
- If large blood loss estimated, arterial line becomes indicated.

Airway

- If cervical spine not involved, then routine.
- If abnormal, choices include awake fiber optic intubation, asleep fiber optic intubation, inhalation

induction, and intubation with induction drugs and muscle relaxants with the head maintained in a neutral position, possibly with in-line stabilization.
- Increasing role for video laryngoscopy.

Induction
- If airway secured, induction dictated by other aspects of pt's health.
- If regional anesthesia, technical difficulty with placement due to anatomic abnormality of the spine.
- Consider paramedian dural puncture. Higher levels for dural puncture may result in a better block with spinal stenosis.

Maintenance
- Movement while prone with spinal cord exposed is dangerous. Avoid muscle relaxants after induction if motor evoked potential monitoring is planned.
- If regional anesthesia, be prepared to re-inject block if duration of surgery exceeds duration of action of local anesthetic injected.

Extubation
- Awake and supine are ideal.
- Rapid-emergence agents (propofol, sevoflurane) may facilitate neurologic exam in OR.

Adjuvants
- Injury in the prone position to eyes, lips, teeth, tongue, chin, brachial plexus, ulnar nerves, genitalia, peroneal nerves, skin of the patella, and ankles.
- Identify full neurologic function prior to extubation because reexploration for compressive hematoma could be indicated for major deficits.

Postoperative Period
- Neurologic checks to identify deficits; pain control.
- H_2-blocker therapy to prevent GI hemorrhage if large-dose steroid Rx chosen for nerve root swelling.
- Evaluate visual acuity.

Anticipated Problems/Concerns
- Difficult airway if cervical involvement.
- Air embolism: Avoid or withdraw N_2O if any symptoms.
- Transport bed availability and knowledge of how to remove frame, in case sudden transfer to supine position is necessary.
- Airway edema from prone position or anterior cervical dissection may present issues for immediate extubation. Consider leak test, and if in doubt, prolonged postoperative intubation with sedation may be indicated. Consider extubation over a tube exchanger.

Delirium (Postanesthetic) and Dementia

Marc B. Royo | Nabil M. Elkassabany

Risk
- Risk factors for the development of POD can be categorized as pt or procedure related.
- Pt-related factors:
  - Age >75 y.
  - Preexisting cognitive dysfunction or depression.
  - Male sex.
  - Preexisting severe illness.
  - Polypharmacy (>3 medications) and use of psychoactive medications.
  - History of substance abuse.
  - Laboratory abnormalities (anemia, hypoalbuminemia, sodium, potassium, glucose).
- Procedure-related factors:
  - Cardiac, orthopedic, and vascular procedures associated with highest incidence.
  - Emergent or urgent procedures.
  - Poorly controlled postop pain.
  - Periop administration of anticholinergics, antihistamines, benzodiazepines, and meperidine.
- Factors lacking association with risk of POD are operative time, type of anesthetic (general vs. regional), and mode of postop analgesia (regional techniques vs. systemic opioids).

Perioperative Risks
- POD associated with increased morbidity and mortality, prolonged hospitalization, higher rates of hospital-acquired complications, persistent functional and cognitive decline, and institutionalization following discharge
- Increased risk for falls, development of pressure ulcers, prolonged intubation/reintubation, and need for urinary catheterization
- Increased cost of hospitalization

Worry About
- Pt can demonstrate violent behavior that may place themselves or care providers at risk of harm.
- Rule out modifiable causes of delirium (metabolic abnormalities, progression of underlying disease, withdrawal).
- Drug-drug interactions can commonly precipitate changes in mental status.

Overview
- Dementia: Decline in cognition that represents a change from baseline level of function that interferes with independence and daily function.
- Delirium: Acute (h to d) change in baseline attention and awareness that fluctuates in severity during the course of a day and is accompanied by a disturbance in cognition. Three variants: hyperactive (psychomotor agitation, disturbed emotional state), hypoactive (decreased level of consciousness, apathy), and mixed.
- Incidence of POD is estimated to be 36.8%. It may be higher in pts >70 y of age.

Etiology
- The pathophysiology of POD is poorly understood and likely multifactorial. Current theories include the following:
  - Acute central cholinergic deficiency
  - Decreased GABA activity
  - Dopaminergic hyperactivity
  - Noradrenergic hyperactivity
  - Neuronal damage associated with inflammation (interleukins, interferon, TNF-α)
  - Global cerebral hypoperfusion
  - Surgical stress response

Usual Treatment
- Preventive measures:
  - Some evidence suggests benefit of early proactive geriatric consultation in elderly pts identified as at risk for POD.
  - Medications known to increase risk of POD (anticholinergics, antihistamines, benzodiazepines, opioids) should be replaced with alternatives that have minimal CNS effects whenever possible.
  - Medically optimize pt prior to surgery (comorbidities, electrolyte abnormalities, nutritional status, hemoglobin concentration).
  - Maximize environmental and situational awareness for pt through communication and room lighting appropriate for day/night.
- Treatment for established delirium:
  - Treat/remove reversible precipitating causes of delirium.
  - First-generation antipsychotics (haloperidol 1–2 mg PO q4h prn; decrease dose to 0.25–0.5 mg PO q4h prn for elderly).
  - Second-generation antipsychotics (olanzapine, risperidone) are equally effective but should be used with caution in elderly with dementia because use in this population has been associated with increased risk of stroke and death.
  - Midazolam/lorazepam for delirium associated with benzodiazepine withdrawal, alcohol withdrawal, or delirium associated with seizures.
  - Physostigmine 0.5–2 mg IM/IV prn for anticholinergic-induced delirium.
  - Consider one-to-one companion rather than applying physical restraints.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	POD	Preop: Baseline cognitive function, risk assessment, current medications Intraop: Pharmacologic agents used, significant intraoperative events Postop: Pain score, use screening tool (CAM)	Inattention, disorganized thinking, fluctuating altered level of consciousness, psychomotor agitation, emotional lability, hallucinations, violent behavior, apathy	O_2 saturation, ABG, CBC, electrolyte/blood glucose levels, CAM screening tool

Key Reference: Chaput AJ, Bryson GL: Postoperative delirium: risk factors and management: continuing professional development, *Can J Anaesth* 59(3):304–320, 2012.

Perioperative Implications

Preoperative Preparation
- Identify at-risk pts.
- Modify risk factors where feasible (medications, comorbidities, lyte abnormalities).
- Assess sensory impairments (visual and auditory) that may cloud postop picture.
- Consider proactive geriatric consultation.

Monitoring
- Standard monitors.
- Monitor acid-base status, lytes, and blood glucose level when clinically indicated.

Airway
- Maintain adequate oxygenation and ventilation.

Preinduction/Induction
- Avoid premedication with centrally acting anticholinergics and benzodiazepines.

Maintenance
- As dictated by the type of surgery.
- Careful titration of analgesics is critical to avoid oversedation or inappropriate pain control that may contribute to agitation.

Extubation
- Standard criteria for extubation. Avoid hypoxia and hypercarbia.

Anticipated Problems/Concerns

- Treatment agents associated with significant side effects:
  - First-generation antipsychotics (haloperidol): Greater incidence of extrapyramidal side effects, neuroleptic malignant syndrome, QT prolongation
  - Second-generation antipsychotics (olanzapine, risperidone): Lesser incidence of extrapyramidal side effects, more sedation, neuroleptic malignant syndrome, increased risk of stroke/death in elderly with dementia
- Psychologic stress on family members and caregivers should not be underestimated

Depression, Unipolar

Ashish C. Sinha

Risk

- Affects 2–4% of population; equal occurrence by gender; highest in 25–44 y.
- Lifetime risk 10–25% for women and 5–12% for men; at any point in time, 5–9% women and 2–3% of men suffer from this.
- Approximately 15% of pts with major depression commit suicide. Older than 55 y has fourfold increase in death rate.

Perioperative Risks

- Most periop issues arise from interactions between antidepressant medications and anesthetic agents. Withdrawal of antidepression medications can increase risk of suicide.

Overview

- Depression is the most common psychiatric disorder.
- Dx is clinical and based on persistent presence of 2 wk of symptoms.
- Distinguished from normal sadness and grief by severity and duration of disease.
- Medication and psychotherapy combination most effective; majority of pts recover.

Etiology

- Unknown pathophysiology, but suspect abnormalities of amine neurotransmitter (serotonin, dopamine, and norepinephrine) pathway
- Multifactorial; familial pattern thought to exist

Usual Treatment

- SSRI: Works by blocking reuptake of serotonin at presynaptic membranes with little effect on adrenergic, cholinergic, histaminergic, or other neurochemical system. Associated with fewer side effects.
- Tricyclic antidepressant: Inhibit synaptic reuptake of norepinephrine and serotonin. Also affect other neurochemical systems, including histaminergic and cholinergic systems, resulting in side effects, such as postural hypotension, prolonged QRS intervals (>0.1), cardiac dysrhythmias, and urinary retention.
- MAOI: Prevents breakdown of catecholamine and serotonin. Orthostatic hypotension is most common side effect observed. Significant systemic Htn associated with ingesting food containing tyramine or sympathomimetic drugs.
- ECT for pts who are resistant to antidepressant medications or with medical contraindication to antidepressants.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dehydration	Dry mouth, blurred vision	Glaucoma, retinal detachment decreased visual acuity	Fundoscopic exam
CV	AV conduction delays, bradycardia, tachyarrhythmia, hypertensive crisis, hypotension	Angina, symptoms of CHF, need for cardiac pacemaker, thrombophlebitis	Volume status, BP, S_3 gallop	12-lead ECG (± stress test), ECHO
RESP	Resp depression	CHF, severe pulmonary disease	S_3, rales, wheezing	CXR, ABGs
GI	Delayed gastric emptying	Reflux		Gastroendoscopy
ENDO	Variable catecholamine levels	Symptoms suggestive of pheochromocytoma	Unexplained severe Htn	VMA levels
RENAL	Urinary retention	Difficulty urinating		
CNS	MS, neuroleptic malignant syndrome, seizures, coma, ALS, CJD Alzheimer disease	Recent CVA, intracranial surgery, intracranial mass lesion	Neurologic deficits, symptoms of increase ICP	CT, MRI, neurologic exam, toxicology screen
MS AND COLLAGEN DISORDERS		Severe osteoporosis, major fractures, RA, SLE	Fractures, joint pain, and limited mobility	Skeletal x-rays, MRI

Key References: Sullivan PF, Neale MC, Kendler KS: Genetic epidemiology of major depression: review and meta-analysis, *Am J Psychiatry* 157(10):1552–1562, 2000; Uppal V, Dourish J, Macfarlane A: Anaesthesia for electroconvulsive therapy, *Contin Educ Anaesth Crit Care Pain* 10(6):192–196, 2010.

Perioperative Implications

- Serotonin syndrome
  - Potentially life-threatening drug reaction from interactions between SSRIs, atypical and cyclic antidepressants, MAOIs, opiates, and antibiotics, (e.g., phenelzine and meperidine, phenelzine and SSRIs, linezolid and citalopram)
  - Symptoms include agitation, delirium, autonomic hyperactivity, hyperreflexia, clonus, and hyperthermia
  - Treatment involves discontinuing the suspected agent(s), supportive measures, and control of autonomic instability, excess muscle activity, and hyperthermia.
  - In mild cases lorazepam, propranolol, or cyproheptadine (a 5-HT antagonist available only in oral form that binds to serotonin receptors) can be administered
- Fluoxetine
  - Potent hepatic cytochrome P-450 inhibitor, which increases plasma concentration of drugs that depends on P-450 for clearance.
  - Fluoxetine may increase the concentration of tricyclic antidepressants by twofold to fivefold.
  - Some cardiac antidysrhythmic and beta-blockers may also be potentiated as a result.
- Tricyclics
  - Anticholinergic effect causes CV abnormalities, such as orthostatic hypotension and cardiac dysrhythmias.
  - Due to increased availability of neurotransmitters in the CNS, anesthetic requirement may be increased. Likewise, increased availability of norepinephrine may cause exaggerated BP response in reaction to indirect-acting vasopressor, such as ephedrine.
  - Acute treatment with tricyclics (first 2–3 wk) is associated with potential significant Htn, whereas long-term treatment is associated with downregulation of receptors.
  - Tachydysrhythmias have been observed following administration of pancuronium, ketamine, meperidine, or local anesthetics containing epinephrine to pts who are also on imipramine.
- MAOIs
  - Anesthetic requirement may be increased due to increased concentration of norepinephrine in the CNS.
  - Serotonin syndrome from combining MAOI and meperidine has been noted.
  - Current belief is to continue MAOIs during the periop period, despite previous thought of discontinuing MAOIs 14 d prior to elective surgery.

- Benzodiazepine (midazolam) may be used to treat preop anxiety.
- Ketamine, a sympathetic stimulant, should be avoided.
- Serum cholinesterase activity may be decreased in pts on phenelzine, so the dose of succinylcholine may need to be reduced.
- The addition of epinephrine to local anesthetic solutions should probably be avoided.
- If hypotension develops, direct-acting drugs, such as phenylephrine, are preferred. The dose should also be decreased to minimize the likelihood of an exaggerated hypertensive response.

Anticipated Problems/Concerns

- In periop period, general rule is to try to continue antidepressant therapy.
- Be aware of potential interactions between anesthetic agents and antidepressants.
- Pts should be monitored for signs of serotonin syndrome.

Acknowledgment

I wish to thank Dr. Ian Yuan for his work on this chapter in the earlier edition of this book.

Dermatomyositis

Michael F. Roizen | Jeffrey D. Roizen

Risk

- Prevalence in USA: 3000–10,000.
- Group, demographics with highest prevalence include females, 2:1 relative to men, with a peak onset between 30–60 y of age.

Perioperative Risks

- Increased risk of respiratory failure and infections postop

Worry About

- Most case reports absolutely avoid depolarizing muscle relaxants and are careful with medications that have effects on muscle strength.
- Monitor muscle relaxant dosing and recovery.
- Valvular heart disease and cardiomyopathy: Cardiac muscle, though not severely involved, shows changes similar to skeletal muscles. Clinical manifestations are rare.

Overview

- Relatively rare diffuse connective tissue disorder of uncertain etiology characterized by idiopathic inflammatory myopathy with muscle involvement and weakness muscle and connective tissue involvement of skin and other organs. Valvular heart disease increases the risk of periop adverse cardiac events.
- Diagnosis is based on the clinical picture of muscle weakness and skin rash, myelography, raised serum CPK levels, and muscle biopsy.
- Respiratory system: Aspiration pneumonia may occur due to weakness of the muscle involved in swallowing. Progressive weakness of the intercostal and diaphragmatic muscles may result in respiratory insufficiency. Lung involvement may occur from the connective tissue disorder itself, which results in patchy infiltrates throughout both lungs, interstitial pneumonia, or fibrosis. Carcinoma of the bronchus or lung parenchyma is associated.

Etiology

- The lead theory regarding dermatomyositis involves a genetic predisposition to viral or immune destruction of muscles by viruses or other infectious agents. Dermatomyositis is considered a connective tissue diseases in the same category as lupus erythematosus or systemic sclerosis.

Usual Treatment

- Prednisone to control weakness and pain
- Various agents to control rash and calcinosis in skin

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Characteristic rash Raynaud phenomenon	Treatment with diltiazem or colchicine to reduce calcinosis Hydroxychloroquine may reduce the photosensitive rash Raynaud phenomenon may present.	Classic purple rash on eyelids and over bony prominences Children's skin can become thick and hard; rash appears on the back, knuckles, chest, shoulders, neck, and face.	Biopsy in past—look at results
HEENT	Possible regurgitation and swallowing difficulties	Symptoms of regurgitation	Test of swallowing with water	Usually not needed, neck x-rays in extension; GI swallow for motility
CV	Valvular heart disease Cardiac muscle, though not severely involved, shows changes similar to skeletal muscles. Clinical manifestations are rare, but heart failure and conduction defects reported.	Poor exercise tolerance Angina CHF symptoms	Two-flight walk Chest exam for signs of CHF BP lying and standing	ECG, ECHO for valvular disease
RESP	Decreased lung elastance; decreased FEV; decreased FVC Aspiration pneumonia due to weakness of the muscle involved in swallowing Potential progressive weakness of the intercostal and diaphragmatic muscles results in respiratory insufficiency.	Poor exercise tolerance		Generally not needed
GI	Esophageal motility disorders, gastroparesis, GI ulcers and infections	Early satiety		
RENAL	Nephropathy, if treatment for many years			BUN/Cr
ENDO	Insulin resistance from high dose prednisone treatment			FBS, lytes
CNS	Fatigue and weakness	Early satiety, impotence, N/V, orthostatic symptoms		Changes related to degree of type 2 diabetes from therapy
PNS	Proximal muscle weakness	Shoulder-girdle weakness	PNS exam, esp. if regional planned, which is recommended by most case reports	Abnormal muscle biopsy and MRI of proximal muscles
MS	Impaired mobility and strength	Muscle strength	Weakness, inability to get out of chair by self, decreased ROM of joints	Elevated muscle enzyme levels

Key References: Gunusen I, Karaman S, Nemli S, Firat V: Anesthetic management for cesarean delivery in a pregnant woman with polymyositis: a case report and review of literature, *Cases J* 2:9107, 2009; Shrestha GS, Aryal D: Anaesthetic management of a patient with dermatomyositis and valvular heart disease, *Kathmandu Univ Med J* 10(38):100–102, 2012.

Perioperative Implications

- May exhibit signs of some paraneoplastic disorder (e.g., polyneuropathy, subacute cerebellar degeneration, multifocal neuroencephalopathy, myasthenic syndrome).
- If on steroids for treatment, may benefit from periop steroids.
- If given cytotoxic drugs, hematologic status needs examination.

Preoperative Preparation

- Administer metoclopramide (10 mg/70 kg) in pts with esophageal motility problem or gastroparesis.
- Assess myocardial and volume status.

Monitoring
- Monitor for myocardial ischemia; can have CHF if volume overload and LV dysfunction present.
- Monitor blood sugar if on steroids.

Airway
- Due to impaired motility, swallowing dysfunction, and aspiration risk, many recommend regional anesthesia and only instrumentation of airway with awake fiberoptic techniques.
- Little information on the appropriate use of muscle relaxants. It is suspected that pts with dermatomyositis are sensitive to nondepolarizing muscle relaxants because of their diminished muscle mass. Muscle relaxants given with close monitoring.

Intraoperative Period
- If ventilatory status is marginal preop, then control ventilation. Airway protection and adequate ventilation are the two primary concerns.

Induction
- High incidence of swallowing and vocal cord dysfunction in these pts may lead to pooling of saliva in the pharynx and aspiration into the trachea.

Maintenance
- CV instability
- Narcotics used with caution to prevent any postop resp dysfunction

Extubation
- CV and pulm drive insufficiencies common with myopathies

Adjuvants
- No known adjuvant concerns except those that weaken muscular function.

Postoperative Period
- Respiratory insufficiency is the major postop complication. Due to the weakness of thoracic muscles, pts may have a diminished cough reflex, leaving them vulnerable to atelectasis.
- Weakness of pharyngeal muscles may make pts more vulnerable to aspiration pneumonia.
- A titrated analgesic regime or regional block for pain relief has been used in most of the anecdotal case reports.

Anticipated Problems/Concerns
- Increased risk of infections such as digestive and respiratory infections

Dextrocardia

Glyn D. Williams

Risk
- Birth prevalence of approximately 1:10,000; equal sex distribution
- 25% have PCD, an autosomal recessive disorder

Perioperative Risks
- Increased risk of cardiac decompensation, pulm Htn, resp failure, airway obstruction, sepsis, raised intracranial pressure, and death
- Increased likelihood of emergent open-heart or abdominal surgery

Worry About
- Heterotaxy syndrome (approximately 40% have dextrocardia)
- PCD (approximately 50% have dextrocardia)
- Distinguish from dextroposition—right cardiac displacement by extracardiac causes (lung, diaphragm, pericardium abnormalities)

Overview
- Dextrocardia results from embryologic anomalies. The heart is positioned in the right hemithorax, with base and apex of heart pointing caudally and to the right.
- Mirror-image dextrocardia can be asymptomatic incidental finding.
- PCD: Associated with:
  - Middle ear infections.
  - Paranasal sinusitis.
  - Lung disease (bronchiectasis, pneumonia).
  - Infertility.
  - Hydrocephalus.
  - Retinitis pigmentosa.
  - Situs inversus totalis.
  - Heterotaxy.
- Heterotaxy (1:6000 live births) is failure of usual R-L asymmetry: Associated with:
  - Congenital heart disease (many variants).
  - Brain (e.g., encephalocele).
  - Skeletal (e.g., spine deformities).
  - Facial (e.g., micrognathia).
  - Resp (e.g., tracheoesophageal fistula, PCD).
  - Gut (e.g., duodenal atresia, volvulus).
  - Pancreatic and liver hypoplasia.
  - GU tract (e.g., renal agenesis).
  - Other (e.g., diaphragmatic hernia).

Etiology
- The human fetal heart develops from a primitive cardiac tube, with sinus venosus, atrium, ventricle, bulbus cordis, and truncus arteriosus connected in series. With growth, the tube loops right or left. Dextrocardia can occur with abnormal looping.
- Heterotaxy and PCD result from abnormal structure and function of motile cilia. The ventral node, a transient midline structure present in early fetal life, has specialized monocilia that generate unidirectional extraembryonic fluid flow, which initiates normal R-L asymmetry. Abnormal flow leads to heterotaxy.

Usual Treatment
- PCD: Supportive pulmonary therapies, sinus surgery
- Heterotaxy: Surgical repair of congenital heart disease and medical management of cardiac failure, arrhythmia, antibiotic prophylaxis if immunocompromised

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway Aspiration risk	Snores Gags with feeding	Micrognathia, cleft palate Ear and sinus infection	CT sinuses CBC, differential
RESP	Pneumonia Bronchiectasis Poor secretion clearance	Dyspnea Chronic cough	Tachypnea Lung field consolidation Wheezing	CXR, CT scan PFTs, bronchoscopy
CV	One or two ventricle physiology Arrhythmia, heart failure Pulm Htn	Dyspnea Blue Syncope	Exercise intolerance Cardiac failure Cyanotic heart disease	ECG, Holter, CXR, TTE, MRI, CT, heart cath, SpO_2
GI	Obstruction, short gut syndrome, GERD, biliary atresia, pancreatitis	N/V, pain, distension Heartburn Yellow	Acute abdomen Hypoactive bowel sounds Jaundice	Abdominal x-ray, LFT Lytes, amylase Endoscopy
RENAL	GU anomalies	Urinary infections	Posterior urethral valves Hypospadias	BUN/Cr, lytes, CBC, US, MRI
CNS	Neurologic anomalies ICP high, meningitis	Irritability, lethargy Headache, seizures	Meningismus Papilledema	Lumbar puncture, head CT, MRI
MS	Sternum, spine, limb defects	Difficulty walking	Skeletal exam	X-ray
IMMUNE	Immunocompromised (asplenia/polysplenia)	Recurrent infections	Signs of infection	Ultrasound, MRI Immunology work-up

Key References: Rapoport Y, Fox CJ, Khade P, et al.: Perioperative implications and management of dextrocardia, *J Anesth* 29(5):769–785, 2015; Lobo LJ, Zariwala MA, Noone PG: Primary ciliary dyskinesia, *QJM* 107(9):691–699, 2014.

Perioperative Implications

Perioperative Preparation
- Congenital heart disease: Consult experts.
- PCD: Optimize pulmonary status.
- Immunocompromised: Choice of antibiotics.
- Consider reprogramming AICD/pacemaker.

Monitoring
- ECG, defibrillator: Reverse positions
- Heterotaxy: TEE, invasive hemodynamic monitoring
- Central lines: May have abnormal anatomy

Airway
- Possible difficult mask, difficult intubation.
- Avoid nasal intubation (sinusitis).

Induction
- Congenital heart disease concerns

Maintenance
- Humidify gases (PCD)
- Congenital heart disease concerns

Extubation
- Assess cardiopulmonary reserve.

Adjuvants
- Nitric oxide if pulm Htn

Postoperative Period
- Consider ICU if PCD or heterotaxy.

Anticipated Problems/Concerns
- Dextrocardia provides periop challenges ranging from minor (unusual ECG finding) to severe (life-threatening crisis). Pts with PCD may require additional pulmonary support during the periop period. Heterotaxy pts have high periop risk. Input from appropriate experts is recommended.

Diabetes, Type I (Insulin-Dependent)

Michael F. Roizen

Risk
- Incidence in USA: 1.25 million.

Perioperative Risks
- Risk of requiring a CABG is increased 5–10 times in presence of ESRD, CHF, or autonomic neuropathy; without these conditions, the risk is 1-1½ times that of a normal person.

Worry About
- Autonomic neuropathy, gastroparesis, and sudden postop death.
- Painless myocardial ischemia.
- Atlantooccipital joint immobility.
- Tight glucose control might be indicated in pregnant pts and those difficult to wean from bypass (in ECC as well as in the case of predictable global or focal CNS ischemia).

Overview
- Endocrinopathy assoc with ESRD or ophthalmic, myocardial, and neuropathic disease
- Blood sugar control per se not associated with increased periop risk in absence of
  - Hypoglycemia
  - Hyperosmolar coma
  - Ketoacidosis
  - CNS ischemia
  - Pregnancy
  - Extracorporeal circulation
- Type I diabetes leads to deranged autoregulation of the CNS (with blood sugar at 250 mg/dL), kidney function (with blood sugar at 225 mg/dL), and function of the blood vessels (with blood sugar at 100 mg/dL and concomitant increased BP).
- Need to control BP to decrease damage to these vessels and organs.
- Check pt's glucose log for degree of control.
- Variable control may predict periop hypoglycemic episodes.
- See also Diabetic Ketoacidosis.

Etiology
- Genetic predisposition to autoimmune destruction of glucose transporter on islet cells leads to increased blood glucose, which affects proteins via nonenzymatic glycosylation.
- Swollen cells (sorbitol is oncotically active).
- Increased viscous proteins (macroglobins), which impede blood flow.
- Increased substrate for anaerobic metabolism.
- Deranged autoregulation of blood flow.

Usual Treatment
- Insulin injections, lifestyle changes including stress management, diet, and exercise.
- Pancreatic and islet cell transplantation is an option in ESRD.
- Control of BP.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible atlantooccipital dislocation secondary to abnormal collagen glycosylation	Pain	Neck ROM, "prayer sign"	Usually not needed; x-rays of neck in extension
CV	Angiopathy, LV dysfunction (increased 4–10 times with Htn) Ischemic PVD	Poor exercise tolerance Angina, CHF symptoms	Two-flight climb Chest exam for signs of CHF BP lying and standing	ECG, CXR, coronary calcium score if indicated
RESP	Decreased lung elastance; decreased FEV; decreased FVC	Poor exercise tolerance		Generally not needed
GI	Gastroparesis	Early satiety		
RENAL	Nephropathy, especially with Htn	N/V, impotence; orthostatic symptoms Nonprotein foods		BUN/Cr
ENDO	Decreased insulin from islets			FBS, lytes
CNS	Autonomic dysfunction secondary to neuropathy	Early satiety, impotence, N/V, orthostatic symptoms		HRV on ECG BP change on standing
PNS	Stocking-glove neuropathy leading to infections		PNS exam, especially if regional anesthesia is planned	
MS	Impaired joint mobility secondary to nonenzymatic glycosylation of collagen	Joint mobility	Decreased ROM of joints	

Key References: Daneman D: Type 1 diabetes. *Lancet* 367(9513):847–858, 2006; Preiser JC, Devos P, Ruiz-Santana S, et al.: A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study, *Intensive Care Med* 35(10):1738–1748, 2009.

Perioperative Implications

Preoperative Preparation
- Metoclopramide (10 mg/70 kg) in pts with gastroparesis.
- Assess myocardial and volume status.

Monitoring
- Myocardial ischemia can indicate CHF if volume overload and LV dysfunction are present.
- Blood sugar.

Airway
- Atlantooccipital dislocation possible; see HEENT. Do prayer sign test; pt may have gastroparesis.

Induction
- Osmotic diuresis can lead to hypovolemia; ANS and CV dysfunction cause fluctuations in BP and HR.

Maintenance
- CV instability; volume status is key to avoiding renal and myocardial dysfunction with surgery; checking RR variation (HRV) to determine autonomic insufficiency likelihood still not widespread.

Extubation
- CV and pulm drive insufficiencies common with neuropathies.

Adjuvants
- Rx for tight control
- Regional: Diabetic nerves may be more prone to edema, especially if epinephrine has been used.

Reduce dose (e.g., lidocaine from 2.0% to 1.5%) for same effect.

Postoperative Period

- Sliding scale of insulin Rx based on blood glucose determinations every 1–3 h; tight control periop may decrease infections but side effects of hypoglycemia possibly negate benefit.

Anticipated Problems/Concerns

- Gastroparesis with presence of solid food 24 h after last meal if ANS dysfunction is present. Consider treating with metoclopramide 10 mg IM 1½ h prior to induction.
- ANS dysfunction is assoc with sudden death postop; pt can be kept in ICU/PACU overnight; vested adult who can measure blood glucose and call 911 if sent home postop.

Diabetes, Type II (Noninsulin Dependent)

Stanley H. Rosenbaum | Ranjit Deshpande

Risk

- Incidence in USA more than 25 million
- Highest prevalence: Hispanics and Native Americans
- Gender predominance: None
- Metabolic syndrome associated with obesity and sedentary lifestyle

Perioperative Risks

- Increased risk 5–10 times if end-stage renal disease, CV, CHF, or autonomic neuropathy; without renal, CV disease, or autonomic dysfunction, risk is 1–1.5 times normal.
- Metabolic abnormalities increased with perioperative insulin Rx.
- Unclear if same risks as for type I diabetes.

Worry About

- Autonomic neuropathy, gastroparesis, and sudden postop death.
- Myocardial ischemia; CV instability.
- Tight glucose control might be indicated in pregnancy (see Diabetes, Type III); difficult weaning from bypass (ECC), predictable global or focal CNS ischemia.
- Disordered autoregulation makes BP fluctuations dangerous.
- Fluid and electrolyte imbalance.
- Hyperosmolar hyperglycemic state and, less likely, diabetic ketoacidosis.

Overview

- Endocrinopathy that can cause same organ dysfunction as in diabetes type I: end-stage renal, myocardial, neuropathic disease, stiff joint syndrome, and retinopathy.
- Associated with deranged blood flow autoregulation to CNS (at blood sugar 250 mg/dL), renal (at blood sugar 200 mg/dL), and cardiac (at blood sugar 100 mg/dL) vessels.
- Ketosis is rare because there is some endogenous insulin.
- Primarily controlled by diet and/or oral agents, although insulin is more frequently used.
- Usually has high insulin levels for glucose level, but peripheral resistance to insulin effect. Can develop hyperosmolar nonketotic coma.
- Blood sugar control per se not associated with increased periop morbidity in absence of:
  - Hypoglycemia.
  - Hyperosmolar coma.
  - CNS ischemia.
  - Pregnancy.
  - Extracorporeal circulation.
- Preop HgBA1c levels (ideally <7%) indicate quality of recent blood sugar control. High levels correlate with chronic microvascular complications.

Etiology

- Familial predisposition with very high concordance in identical twins
- Autosomal dominant accentuated by conditions that increase peripheral insulin resistance (obesity, inactivity, hormones), increase glucose production or metabolic demands (glucocorticoids, pregnancy), or decrease insulin secretion (certain beta-adrenergic drugs)
- Increases nonenzymatic glycosylations
- Causes cell swelling
- Deranges autoregulation
- Increases viscous protein production
- Increases substrate for anaerobic metabolism

Usual Treatment

- Hypoglycemic agents (see oral hypoglycemic agents), diet, exercise, insulin
- BP control with ACE inhibitors being drugs of choice, especially in diabetic nephropathy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible atlanto-occipital dislocation Cataracts, glaucoma, retinopathy Periodontal disease	Pain	Neck ROM, prayer sign Loose decaying teeth	
CV	Premature CAD Hypertension Peripheral arterial disease Resting tachycardia, orthostatic hypotension	Angina Claudication Symptoms of CHF	Peripheral pulses	ECG CAD-related tests, as indicated
RESP	Decreased pulm elastance	Exercise tolerance		
GI	Gastroparesis Diarrhea	Early satiety		
ENDO	Hyperglycemia Osmotic diuretic–caused hypokalemia	Polyuria		Blood glucose, K^+
HEME	Infection from decreased WBC phagocytic function		Site of infections	
RENAL	Nephropathy Type 4 RTA	Asymptomatic although often associated with neuropathy		BUN/Cr, UA for protein
CNS	Cerebrovascular disease Medication-induced hypoglycemia	TIAs, CVAs, long-acting oral hypoglycemic agents	CNS exam	
PNS	Distal sensory and motor neuropathy Autonomic neuropathy	Impotence Foot infections	PNS exam, especially prior to regional anesthetic	
MS	Impaired joint mobility		ROM of joints	

Key References: Barash PG, Cullen BF, Stoelting RK, et al, editors: *Clinical anesthesia*, ed 7, Philadelphia, PA, 2013, Lippincott Williams & Wilkins; Kadol Y: Anesthetic considerations in diabetic patients. Part I: preoperative considerations of patients with diabetes mellitus. *J Anesth* 24(5):739–747, 2010.

Perioperative Implications

Preoperative Preparation

- Metoclopramide (5–10 mg) if gastroparesis.
- Assess myocardial, autonomic function, and volume status.
- Formulate recommendations for preop insulin and long-acting hypoglycemic agents.

Monitoring

- Blood sugar and metabolic abnormalities
- Painless myocardial ischemia can cause CHF if volume overload and LV dysfunction
- Peripheral vasculature and nerves vulnerable to pressure ischemia

Airway

- Atlanto-occipital dislocation possible: See HEENT, do prayer sign test

Induction
- Osmotic diuresis, autonomic nervous system, and CV dysfunction can make BP/HR fluctuate

Maintenance
- CV instability: Volume status and avoidance of hypertension key to avoiding renal and myocardial dysfunction periop

Extubation
- CV and pulm drive insufficiencies common with neuropathies

Adjuvants
- Regional: Diabetic nerves may be more prone to edema, especially if epinephrine used. Reduce dose (e.g., lidocaine from 2.0% to 1.5%) for same effect.
- Oral hypoglycemics may ablate preconditioning.

Postoperative Period
- Current ADA guidelines recommend IV administration of insulin for critically ill pts in ICU settings with a goal of maintaining plasma glucose concentration between 140–180 mg/dL.
- For noncritically ill pts, it is accepted to have targets below 140 mg/dL for fasting and <180 mg/dL postprandial.
- Debate as to whether control to tighter than 60–250 mg/dL is of value in absence of Htn.

Anticipated Problems/Concerns
- Autonomic nervous system dysfunction associated with sudden death postop; can monitor for resp function in ICU/PACU overnight; presence of adult at home who can measure blood glucose and call 911.
- Infections and end-organ risk substantially increased with blood sugar >250 mg/dL. Hypoglycemic symptoms hidden by autonomic nervous system dysfunction, effects of regional, sedative-narcotic, and beta-adrenergic blocking agents.

Diabetes, Type III (Gestational Diabetes Mellitus)

Kristen L. Lienhart | Danny Wilkerson

Risk
- Incidence of GDM approximately 5–6% of all pregnancies.
- Increased in African American, Hispanic, Asian, Native American, or Pacific Islander women.
- Risk factors:
  - Maternal age >25 y.
  - Previous delivery of macrosomic infant.
  - Glucosuria.
  - History of polycystic ovarian syndrome.
  - Previous unexplained fetal demise.
  - Previous pregnancy with GDM.
  - Strong immediate family history of NIDDM or GDM.
  - Obesity.
- Dx: Two-step approach:
  1. Fasting glucose >95 mg/dL or a glucose >130 mg/dL (identifies ~90% of women with GDM) 1 h after a 50-g OGTT.
  2. If initial screening meets or exceeds threshold, perform a 100-g, 3-h diagnostic OGTT on a separate day.

Perioperative Risks
- Increased frequency of gestational Htn, preeclampsia, and cesarean delivery
- Unlikely renal, ocular, neurologic, or orthopedic complications in GDM
- Hypoglycemia if insulin is used
- Fetal risk (if not controlled: Polyhydramnios or macrosomia [6 times normal])
- RDS (2–3 times normal); preeclampsia, neonatal hypoglycemia, prematurity

Worry About
- Hyperglycemia and hypoglycemia

Overview
- GDM is defined as a carbohydrate intolerance that occurs (or is first recognized) during pregnancy.
- Universal screening between 24-28 wk gestation.
- A glucose tolerance test is used to identify GDM. For details of the test, see the Key References.
- Maternal complications with GDM are few, but the fetus is at risk.
- Complications, such as fetal polyhydramnios, macrosomia (6 times normal), prematurity, birth trauma, RDS (2–3 times normal rate), neonatal hypoglycemia, or morbidity, are as common with type III diabetes (GDM) as with type I diabetes (insulin dependent).

Etiology
- Occurs in genetically susceptible individuals.
- Pregnancy, through secretion of substances from uterus, exerts diabetogenic effects.

Usual Treatment
- Many clinicians obtain a single HbA_{1c} level at 6–12 wk gestation. In pts with mildly elevated plasma glucose levels and normal concentration of HbA_{1c}, dietary modification alone and a modest increase in exercise are often sufficient to normalize plasma glucose levels.
- Use of insulin in GDM is now more common as tighter control seems beneficial.
- Insulin can be started if fasting glucose exceeds 95 mg/dL despite diet control.
- Glyburide and metformin are appropriate as first line therapy for diet failure in women with GDM.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible facial/pharyngeal edema	Snoring	Neck ROM, Mallampati exam	
CV	CV changes of pregnancy—Possible worse hypovolemia from osmotic diuresis		BP/HR with orthostatic maneuvers	
RESP	Resp changes of pregnancy, decreased FRC, etc.			
GI	Gastroparesis of pregnancy	Early satiety		
ENDO	Neonatal hypoglycemia if maternal hyperglycemia, obesity			Blood sugar, glucose levels, acid-base status of fetus, HbA_{1c} in mother
HEME	No change, unless type I diabetes			
RENAL	Decreased renal function			BUN/Cr
CNS	ANS dysfunction	Gastroparesis, early satiety	Orthostatic BP	Tilt table test
PNS	Neuropathy not present unless type I diabetes			

Key References: Cunningham FG, Leveno KJ, Bloom SL, et al, editors: *Williams obstetrics*, ed 24, New York, NY, 2014, McGraw-Hill, pp 1–40; Garrison A: Screening, diagnosis, and management of gestational diabetes mellitus, *Am Fam Physician* 91(7):460–467, 2015.

Perioperative Implications

Preoperative Preparation
- Full-stomach precautions: Nonparticulate antacid administration usual

Monitoring
- Blood sugar in maternal and umbilical vein blood

Airway
- Examine for edema.

Induction
- Regional anesthesia is preferred to general anesthetic due to risks of aspiration and failed airway attainment if C-section is performed.
- Osmotic diuresis can cause hypovolemia and increase BP and HR fluctuations.

Maintenance
- CV instability: Volume status is key to maintenance of uterine and other organ perfusion.

Extubation
- Ensure patient is awake before extubation.

Adjuvants
- Regional: Diabetic nerves may be more prone to edema, especially if epinephrine is used. Reduce dose (e.g., lidocaine reduced from 1.5% to 1%) for same effect.

Postoperative Period
- Usually GDM cured by delivery.
- Women with GDM need a follow-up GTT at 6–12 wk after delivery.

Anticipated Problems/Concerns
- Fetal dysfunction, especially hypoglycemia and acidosis, if maternal hypoglycemia present
- Rapid changes in maternal blood glucose can accompany the pain and/or exertion of vaginal delivery of fetus and accompany the endocrine changes of uterine delivery.

Diabetes Insipidus

Natalie F. Holt

Risk
- Hereditary/familial (rare):
  - Nephrogenic DI due to mutations in the AVP receptor gene, with X-linked recessive transmission; or AQP2, usually with autosomal recessive transmission, but autosomal dominant transmission also occurs; overall, males at greater risk than females
  - Central (hypothalamic) DI due to mutations of the AVP gene; usually manifests in childhood; males equal risk as females
  - May also be part of developmental syndromes (Wolfram syndrome, Laurence-Moon-Biedl syndrome) or congenital septo-optic dysplasia
- Acquired:
  - Trauma/surgery, infarction, inflammatory, infectious, infiltrative, or neoplastic process affecting the hypothalamic-neurohypophyseal region (>80% of vasopressin-secreting neurons must be destroyed before symptoms of DI manifest)
  - Renal disease (chronic renal failure, polycystic kidney disease, obstructive uropathy, renal transplantation)
  - Systemic conditions (multiple myeloma, sickle cell disease, sarcoidosis)
  - Lyte imbalances (hypokalemia, hypercalcemia)
  - Medications (lithium, demeclocycline, vinblastine, amphotericin B, sulfonylureas) or toxins (methoxyflurane, ethanol)
  - Idiopathic (may be associated with lung, breast, and slow-growing intracranial cancers)
  - Gestational due to pregnancy-induced acceleration of vasopressin metabolism by placental cysteine aminopeptidase
  - Primary polydipsia (dipsogenic DI) due to fluid intake in excess of renal free water excretion capabilities

Perioperative Risks
- Dehydration, hyperosmolarity, hypernatremia
- Altered mental status/seizures
- Hemodynamic instability
- Bladder distention, hydroureter

Worry About
- Fluid and lyte imbalance.
- Contributing drugs/toxins.
- Postop onset, especially following pituitary surgery (1–6 d postop: Classic pattern is surgery followed by early SIADH and then DI.

Overview
- Polyuria due to either insufficient production of vasopressin or inadequate renal tubular response to vasopressin.
- Polyuria, excessive thirst, polydipsia; dehydration rarely present in competent pts with access to water.
- Inadequate fluid replacement leads to hypernatremia, hyperosmolarity, and dehydration, causing fatigue, weakness, altered sensorium, hemodynamic instability, seizures, and possible death.
- In the periop context, fluid over-replacement plus treatment with DDAVP can lead to hyponatremia, hypo-osmolality, and overhydration, causing seizures and possible death.

Etiology
- Neurogenic (central/hypothalamic):
  - Inadequate release of vasopressin from posterior pituitary
  - Primary genetic or secondary acquired condition due to trauma/surgery (especially hypophysectomy and basal skull fractures), inflammation/infiltration, infarction, neoplasm
- Nephrogenic:
  - Inadequate renal tubular response to vasopressin
  - Primary genetic or secondary acquired due to medications/intoxications, chronic renal disease, systemic diseases (multiple myeloma, sickle cell disease), lyte imbalances (hypokalemia, hypercalcemia)

Usual Treatment
- Central DI: Synthetic vasopressin or vasopressin analogue (desmopressin) supplementation; older treatments (chlorpropamide, carbamazepine, clofibrate) that increase ADH sensitivity or stimulate ADH release not commonly used due to systemic side effects
- Nephrogenic DI: Diuretics (e.g., hydrochlorothiazide, amiloride), salt restriction, nonsteroidal anti-inflammatory drugs
- Primary polydipsia: Fluid restriction

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension Tachycardia Myocardial ischemia	Fatigue Weakness Reduced exercise tolerance	Orthostatic hypotension Dry mucous membranes, poor skin turgor (especially in infants)	ECG
ENDO	Anterior pituitary dysfunction	Pituitary surgery, neoplastic or infiltrative disease	Multisystem effects due to hormone deficiencies	Tests of anterior pituitary function, hormone levels
RENAL	Polyuria	Excessive production of dilute urine (urine osmolality 50–200 mOsm/kg; urine volume >3 L/day)	Urine volume and specific gravity	24-h urine collection; simultaneous measurements of plasma and urine osmolality; exclude hyperglycemia, hypercalcemia, hypokalemia
CNS	Altered sensorium Seizures Visual disturbance	Excessive thirst (particularly for cold drinks) Polydipsia History of head injury or cranial surgery	Neurologic function, including visual fields Papilledema Hyperreflexia Fever	MRI

Key References: Leroy C, Karrouz W, Douillard C, et al.: Diabetes insipidus, *Ann Endocrinol (Paris)* 74(5–6):496–507, 2013; Lacassie HJ, Muir HA, Millar S, et al.: Perioperative anesthetic management for Cesarean section of a parturient with gestational diabetes insipidus, *Can J Anesth* 52(7):733–736, 2005.

Perioperative Implications

Preoperative Preparation
- Recognition and appropriate treatment–water deprivation test; desmopressin trial; rule out metabolic causes, such as hyperglycemia, hypokalemia, and hypercalcemia.
- Assess lytes, serum osmolality, and volume status; replace water deficit over 48–72 h and do not lower sodium concentration by more than by more than 0.5-1 mEq/L per h depending on the duration of hypernatremia.
- Rule out additional hormonal deficiencies (e.g., cortisol).
- Discontinue provocative medications (e.g., lithium, mannitol).

Monitoring
- Urine output
- Serum lytes
- Intravascular volume

Airway
- Not affected

Induction
- Pts may have exaggerated hypotensive response due to hypovolemia
- Arrhythmias may occur as a result of lyte abnormalities

Maintenance
- Fluid and lyte monitoring and replacement.
- Invasive hemodynamic monitoring.
- Variable sensitivity to neuromuscular relaxants depending on concomitant lyte imbalances (e.g., hypercalcemia, hypokalemia).

Extubation
- Altered sensorium may impair airway protective reflexes.

Adjuvants
- Early consideration for initiating vasopressin replacement therapy.
- Administration of hypotonic IV fluids if oral intake inadequate to maintain normal plasma osmolality.
- Supplemental corticosteroid therapy if anterior pituitary deficiency present.
- Chlorpropamide treatment for DI may cause hypoglycemia.

Anticipated Problems/Concerns
- High-dose vasopressin therapy may cause vasoconstriction and precipitate myocardial ischemia in pts with preexisting CAD.
- Postop DI following pituitary surgery/traumatic brain injury usually manifests within 24–48 h but may be delayed.
- Vasopressin therapy will not increase urine osmolality in pts with nephrogenic DI and should not be used in pts with primary polydipsia.

Diabetic Ketoacidosis

Shamsuddin Akhtar

Risk
- Typically seen in pts with type I diabetes mellitus; can occur in pts with ketosis-prone type II diabetes.
- Stress related to acute infection, trauma, surgery, MI, pulm embolism, pancreatitis, alcohol abuse, stroke, emotional trauma, or drugs (steroids, thiazides, sodium-glucose transporter-2 inhibitors) can precipitate DKA in diabetic pts.
- Poor compliance with insulin therapy or inadequate outpatient insulin regimen.

Perioperative Risks
- CV collapse secondary to severe dehydration (diuresis, fluid deprivation, fever) and/or myocardial depression due to severe metabolic acidosis
- Cerebral edema and injury with rapid correction of DKA, especially in children
- ARDS and bronchial mucus plugging
- Worsening of preexisting renal dysfunction or periop MI in pts with preexisting CAD
- Malignant hyperthermia-like syndrome due solely to DKA (extremely rare)

Worry About
- Fluid deficit of 5–10 L in established DKA (100 mL/kg)
- Cardiac arrest, severe shock, or arrhythmias with onset of general anesthesia or regional anesthesia due to hypovolemia, acidosis, and lyte disturbances
- Severe lyte derangements and significant total body deficits of potassium (3–5 mEq/kg), sodium (7–10 mEq/kg), phosphate (5–7 mmol/kg), calcium (1–2 mEq/kg), and magnesium (1–2 mEq/kg)
- Necessity of surgical therapy to treat etiology of DKA (sepsis, abscess, gangrene)

Overview
- DKA is the most common acute metabolic emergency with significant mortality (3–5%).
- Two primary hormonal abnormalities: Absolute or relative deficiency of insulin; and glucagon excess, causing increased gluconeogenesis, increased breakdown of glycogen and decreased use of glucose by liver, muscle, and fat.
- Characterized by hyperglycemia (>250 mg/dL), ketosis (positive ketones in serum and urine), anion-gap metabolic acidosis (anion gap >10, HCO_3 <18, pH <7.3).
- Intensive periop hemodynamic and metabolic management essential for favorable outcome.

Etiology
- Type I diabetes with insulin deficiency caused by cessation or inadequate dosing of insulin therapy, with or without significant pathologic cause (infection, surgery) or emotional stress.
- Elevation of counter-regulatory hormones (glucagon, epinephrine, cortisol, and growth hormone) causes significant alteration in carbohydrate, fat, and protein metabolism and drive the catabolic and ketogenic state.
- Osmotic diuresis secondary to sustained hyperglycemia leads to volume and lyte depletion.
- Metabolic acidosis is a product of unrestrained free fatty acid release from adipose tissue and subsequent hepatic oxidation of fatty acids to ketone bodies (due to lack of insulin and glucagon excess).

Usual Treatment
- Search and treat initiating cause.
- Insulin, rehydration, correction of lyte derangements, and hemodynamic support.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	Duration of initiating event, postural symptoms	BP, HR, JVD, skin turgor, mucous membranes, tilt table test, orthostatic hypotension, shock	US, CVP, ABG
RESP	Hyperventilation (Kussmaul respiration)		Ventilatory rate and depth, fruity odor of acetone	ABG
GI	Anorexia, N/V	Appetite, N/V, abdominal pain	Abdominal distension, ileus, tenderness without rebound	
RENAL	Diuresis	Urinary frequency, thirst (polyuria, polydipsia)		UO, BUN/Cr, lytes (especially potassium), serum osmolality
ENDO	Insulin deficiency, glucagon excess during severe catabolic stress	Type I diabetes		Blood glucose ABG (anion gap) Ketones (urine, blood)
CNS	Confusion, drowsiness, lethargy to coma; late cerebral edema in children		Assess LOC Signs of increased ICP	ABG, serum osmolarity

Key References: Kamel KS, Halperin ML: Acid-base problems in diabetic ketoacidosis, *N Engl J Med* 372(20):1969–1970, 2015; Gosmanov AR, Gosmanova EO, Kitabchi AE: Hyperglycemic crises: diabetic ketoacidosis (DKA), and hyperglycemic hyperosmolar state (HHS). In De Groot LJ, Beck-Peccoz P, Chrousos G, editors: *Endotext* [internet]. South Dartmouth, MA, 2015, MDText.com, Inc. <http://www.ncbi.nlm.nih.gov/books/NBK279052/>.

Perioperative Implications

Perioperative Preparation
- Vigorous 0.9 normal saline infusion (15–20 mL/kg/h or 1–1.5 L in the first h) to restore hemodynamic stability, then 0.5 normal saline, especially if serum osmolality is >310 mOsm/L.
- Insulin Rx usually begins after first h of fluid therapy with 0.1 U of regular insulin/kg IV bolus (in adults) followed by infusion of 0.1 U/kg/h (as long as serum potassium is >3.3 mEq/L). Adjust insulin infusion to decrease glucose by 10% or 50–70 mg/dL per h. In children, fluid glucose content is adjusted prior to decreasing insulin infusion.
- Sodium bicarbonate not generally indicated, administer 100 mmol over 2 h if pH <6.9, hyperkalemia, or pt hemodynamically unstable with pH <7.1.

Monitoring
- Check glucose and lytes hourly (especially potassium); check pH frequently: Foley catheter to determine urine output reliably during periop period; CVP catheter for fluid management, possibly PA cath if pt has preexisting myocardial dysfunction or CAD; consider TTE/TEE in hemodynamically unstable pt

Airway
- Potential stiff joint syndrome with difficult intubation; at risk for aspiration

Induction
- Hemodynamic instability likely if intravascular volume depletion not corrected; pts frequently have preexisting autonomic neuropathy and CV dysfunction.

Maintenance
- Protect end organs, especially heart, renal, and CNS, because they are often compromised by DM.

Extubation
- Awake. May require mechanical ventilation and ICU admission if pH less than 7.2, compromised mental status, and/or high risk of aspiration.

Adjuvants
- Same as for diabetes

Postoperative Period
- Potential for hypoglycemic injury from rapid increase in insulin sensitivity when surgical cause of DKA corrected.
- Subsequent medical management should be continued by physician with expertise in diabetes.

Anticipated Problems/Concerns
- Hemodynamic instability from combined volume deficiency, acidosis, and pre-existing CV disease
- CNS dysfunction from metabolic and lyte abnormalities (hypokalemia, hypophosphatemia), both early and late

Diaphragmatic Hernia (Congenital)

N. James Halliday | Jibin V. Samuel

Risk
- Occurs in approximately 1 in 2500–5000 births; 12–25% have associated anomalies, in particular cardiac (20%), chromosomal (5–16%), and neurologic.
- Parents who have one child with isolated defect have 2% chance with next child.
- Usually left sided (90%) due to defect in foramen of Bochdalek and are more common in boys. Morgagni hernias (2–5%) located anterior are more common in girls. Remainder through esophageal hiatus.

Perioperative Risks
- 30–60% mortality despite improved diagnosis and management
- Degree of pulm hypoplasia and associated CNS and CV malformations affect mortality
- Timing of diagnosis associated with the prognosis

Worry About
- Hypoxemia and acidosis
- Pulm Htn and CHD
- Shock
- Tension pneumothorax

Overview
- Classified by site of herniation
  - Posterolateral defects (Bochdalek) are left sided (largest and associated with greatest degree of pulm hypoplasia). Morgagni hernias rare; parasternal, less symptomatic, and therefore diagnosed at later age
- Between 4–9 wk of age the pleuroperitoneal membrane forms with the left closing after the right. In Bochdalek and Morgagni, normal development of the diaphragm and digestive tract does not occur
- Degree of lung hypoplasia determined by time of defect during fetal development and amount of abdominal contents in chest. Although ipsilateral lung is most affected, both lungs are abnormal and result in decreased numbers and function of alveoli; hypoplastic lung with smaller pulm artery and decreased arterial branching causes high vascular resistance

Usual Treatment
- Initial treatment involves determining the severity of associated congenital anomalies and degree of illness.
- Goal is semielective surgery when pt is medically stable.
- Posterolateral defects require surgical repair (does not resolve the pulmonary dysfunction).
- Small defects closed primarily; larger defects use artificial diaphragm, which contributes to postop resp failure.
- In most cases, abdomen is closed primarily after correction but a silastic pouch may be used with increased intra-abdominal pressures.
- Fetal surgery has been accomplished in those severely affected with increased degree of pulm hypoplasia. FETO can be done to trigger lung growth. The Cochrane group reviewed two studies looking at a total of 97 women who underwent FETO and found insufficient data indicating improvement in perinatal mortality.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Mediastinal shift, associated ASD, VSD, coarctation, tetralogy of Fallot (23%)	Displaced cardiac impulse	CV exam	ECHO
RESP	Resp distress, pulm Htn	Decreased breath sounds on affected side Prominent ipsilateral chest	Pulm exam	CXR, ABG
GI	Malrotation, atresia (20%)	Scaphoid abdomen	Abdominal exam	
GU	Hypospadias		Inspection	
CNS	Spina bifida, hydrocephalus, anencephaly (28%)		Inspection and neurologic exam	US, CT
METAB	Acidosis, hypoxemia, hypercarbia			ABG

Key References: Aggarwal S, Stockmann P, Klein MD, et al.: Echocardiographic measures of ventricular function and pulmonary artery size: prognostic markers of congenital diaphragmatic hernia? *J Perinatol* 31(8):561–566, 2011; Crivell RM, Andersen C, Dodd JM: Prenatal treatments for babies with congenital diaphragmatic hernia, *Cochrane Database Syst Rev* 11:CD008925, 2015.

Perioperative Implications

Perioperative Management
- ECMO provides temporary support until perinatal circulation matures and less sensitive to vasoconstrictive stimuli (1–2 wk).

Preoperative Preparation
- Avoid triggers for pulm vasoconstriction.
- Goals include a PaO_2 >80, $PaCO_2$ 25–30, normal or elevated pH, and normothermia (hypothermia increases O_2 consumption).
- For pulm Htn, can also use nitric oxide 20–80 ppm, sildenafil.
- Avoid gaseous distension of stomach with early placement of NG tube.
- With compromised neonates, ET intubation, sedation, paralysis, and ECMO may be required if conventional or high-frequency ventilation fails.
- All neonates with resp distress require invasive monitoring using preductal right radial a-line. If severe, consider preductal and postductal A-line and pulse oximetry.
- IV access best in upper extremities to avoid possible IVC obstruction from increased intra-abdominal pressure.
- Watch for pneumothorax (sudden deterioration in BP or oxygenation); consider prophylactic contralateral chest tube; equipment needed should be available.

Anesthetic Technique
- Opioids well tolerated; inhaled halogenated anesthetics may cause significant hypotension; avoid N_2O, which distends gas-filled intestines.
- Avoid peak pressures more than 25 cm H_2O.
- High frequency, low tidal volume preferred.
- Continue nitric oxide if given preop.
- Lung mechanics change during surgery; may require hand ventilation.

Postoperative Period
- Continued muscle relaxation/opioids and ventilatory support.
- Once stable, assess need for continued resp support.
- If A-aDO_2 gradient >400 mm Hg or if cardiopulmonary deterioration, continue resp assistance.
- Persistent hypoxemia while on high FIO_2 suggests persistent pulm Htn with R-to-L shunting.
- Minimize ET suctioning, correct metabolic acidosis.
- Deliver adequate nutrition.
- High degree of neurologic problems, whether or not infants placed on ECMO; seizures, developmental delay, and hearing loss in 20–30%, but pulm outcomes are usually good.

Diarrhea, Acute and Chronic

Michelle Braunfeld

Risk

- Incidence in USA: 200–300 million new cases/y of acute, with >900,000 hospital admissions
- Chronic: 1–5% of population; increasing with age; female at greater risk than male
- Acute: Male and female equivalent

Perioperative Risks

- Hypovolemia with hemodynamic instability
- Electrolyte abnormalities, especially hypokalemia
- Acid-base abnormalities: May be non–anion gap acidosis or alkalosis, depending on underlying cause

Worry About

- Chronic
  - Underlying disease, especially iatrogenic (e.g., infection with antibiotic-induced diarrhea, end-stage liver disease with lactulose-induced diarrhea, or disaccharide [usually lactose] intolerance)
  - Hormone-producing tumors (e.g., carcinoid, VIPomas, gastrinomas)
  - Vitamin K malabsorption with coagulopathy
  - Extraintestinal manifestations of IBD (e.g., deforming arthritis, cholangitis)
  - Stress-steroid therapy in IBD
  - Psychologic symptoms in up to 50% of pts with IBS; often alternates with constipation
  - Postsurgical losses that may drain via ileostomy or fistula or may be due to inadequate bowel absorption secondary to resection (short bowel syndrome)
- Acute
- Viral, bacterial, or protozoan disease

Overview

- Acute: Abrupt onset of loose stools in healthy individual: Viral—Self-limited, 1–3 d, causing changes in small intestinal cells with a shortened transit time; bacterial—Tends to occur in groups of individuals (if within 12 h of a meal, usually due to preformed toxin); protozoan—Prolonged watery diarrhea from contaminated water supply in endemic area.
- Chronic: Too-frequent passage of stools that are too loose for too long; >200 g/day of stool for >4 wk.
- Multifactorial medical problem that requires supportive therapy and attention to the underlying etiology.
- Only one in a spectrum of medical problems associated with an underlying disease or with treatment of disease. Supportive therapy includes fluid and lyte repletion and attention to acid-base balance.
- Toxic megacolon: Extreme manifestation of inflammatory or infectious bowel disease is a surgical emergency. Pts often septic.

Etiology

- Chronic:
  - Osmotic: Laxatives, indigestible carbohydrates
  - Secretory: Hormone-producing tumors
  - Exudative: IBD, pseudomembranous colitis
  - Decreased mucosal contact/mixing: Short bowel syndrome, IBS, hypermotility secondary to vagotomy, diabetic neuropathy
  - Malabsorption: Pancreatic exocrine insufficiency, celiac disease, Whipple disease, small-bowel bacterial overgrowth
- Acute
  - Viral or bacterial (with or without toxin) or protozoan (see Overview)

Usual Treatment

- Volume and electrolyte replacement, including Na^+, K^+, $PO4^-$, Mg^{2+}.
- Although acid-base correction often follows above, may occasionally need replacement.
- Seek and treat underlying cause.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	Postural symptoms, quantitation of bowel movements	Orthostatic changes Narrow pulse pressure Tachycardia Dry mucous membranes	
	Dysrhythmia secondary to electrolyte abnormalities			ECG
RESP	Compensatory hyperventilation			ABG
METAB	Derangement dependent on underlying cause			Lab values include Ca^{2+}, Mg^{2+}, K^+, HCO_3^-; Na^+
RENAL	Prerenal azotemia			BUN/Cr
CNS	Profound electrolyte abnormality		Range from drowsiness to obtundation	
	Anemia—can be acute or chronic from acute GI losses or chronic disease state	Melena or hematochezia	Stool guaiac	Hct

Key References: Cataldo R, Potash M: Atropine as a treatment of diarrhea after celiac plexus block, *Anesth Analg* 83(5):1131–1132, 1996; DuPont HL: Persistent diarrhea. JAMA 315(24):2712-2723, 2016.

Perioperative Implications

Preoperative Preparation

- Assess volume status, lytes, and acid-base status.
- Repletion.

Monitoring

- Consider arterial and central venous cath (or some other fluid status monitor such as TEE) if significant hypovolemia and CV compromise present.

Airway

- May require full-stomach precautions

Induction

- Hemodynamic instability and decrease drug dosage if not repleted.
- Sympatholytic drugs and sympathectomy with regional anesthesia can shorten transit time and increase diarrhea.

Maintenance

- Tailor IV fluids to lyte and acid-base status (e.g., avoid normal saline if pt already has hyperchloremic acidosis).
- Continue lyte repletion if necessary.

Extubation

- Routine; dependent on underlying condition

Adjustments

- Acid-base status and lytes may affect muscle relaxant duration and ability of antagonists to reverse block.

Anticipated Problems/Concerns

- Most operations do not affect underlying condition; narcotics can make diarrhea less problematic, but use with caution in severe IBD because they may promote toxic megacolon.
- Regional anesthesia that causes sympathectomy leaves parasympathetic system unopposed, which can cause shortened transit time and increase diarrhea.

DiGeorge Syndrome

Andrea Johnson

Risk

- 1:4000 births with variable penetrance

Worry About

- Cardiac anomalies
- Immunodeficiency and poor wound healing
- Palatal anomalies
- Hypocalcemia
- Seizures
- Difficult mask/intubation

Overview

- Chromosome deletion 22q11.2.
- Classic triad: Conotruncal cardiac anomalies, hypoplastic thymus, and hypocalcemia.
- Clinical phenotype varies with mild-to-severe forms of immunodeficiency.
- Most cases are diagnosed in infancy, but Dx in adulthood is not uncommon.

Etiology

- Heterozygous versus homozygous deletion of 22q11.2
- Usually inherited from maternal genome

Usual Treatment

- Cardiac surgery
- Vitamin D (cholecalciferol and calcitriol), calcium supplementation
- Parathyroid hormone therapy
- BMT or thymic grafts (complete DiGeorge syndrome)
- Irradiated transfusion products
- IV Ig therapy
- Antibiotic prophylaxis

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Language and motor developmental delay	Failure to meet milestones	Speech or language delay	Physical exam
HEENT	Palatal laryngotracheal anomalies Facial dysmorphism	Difficulty feeding Nasal regurgitation	Cleft palate Hypotonia Hypernasal speech, micrognathia	CT Barium swallow study
CV	Conotruncal cardiac defects(interrupted aortic arch, truncus arteriosus, TOF, ASD, VSD, vascular rings)	Failure to thrive Cyanosis Dyspnea	Cyanosis, heart murmur, dyspnea, dysphagia	ECHO, CT
RESP	Asthma (atopic)	Dyspnea	Wheezing	PFT
MS	Scoliosis Rheumatoid arthritis	Asymmetric spine, painful joints	Asymmetry of spine, joint inflammation	Radiographs
HEME	Hypoplastic/aplastic thymus Immunodeficiency Severe combined immunodeficiency Autoimmune disease	Recurrent URIs, otitis media, opportunistic infections Thyroiditis Rheumatoid arthritis Recurrent bleeding	Symptoms of PNA, otitis media, sinus infections or severe immunodeficiency Symptoms of hypothyroid/hyperthyroid Symmetric degenerative joint disease	CXR Ig levels: Increased IgE, decreased IgA, decreased CD^{3+} Decreased or increased TSH, T^3,T^4 X-ray of affected joints CBC: Decreased platelets
ENDO	Hypocalcemia	Stiffness or twitching	Tetany	Increased phosphorus, decreased Ca^{2+} Decreased PTH

Key References: Seroogy CM: DiGeorge (22q11.2 deletion) syndrome: clinical features and diagnosis. Stiehm ER, TePas E, editors. Waltham, MA, 2015, UpToDate; Hauk PJ, Johnston RB, Liu AH, et al.: Immunodeficiency. In Hay WW Jr, Levin MJ, Deterding RR, et al, editors: *Current diagnosis & treatment: pediatrics, ed 22,* New York, NY, 2013, McGraw-Hill.

Perioperative Management

Preoperative Considerations

- BMP, Ca^{2+}, Phos, CBC, CD^{3+} count
- Type and cross irradiated blood products prn
- Review imaging and cardiac studies
- Reverse isolation precautions prn

Monitoring

- Standard ASA monitors.
- Arterial, central line prn.
- Consider preop calcitriol and intraop Ca^{2+}, as well as phosphate; premedicating with calcitriol and calcium can prevent intraop hypocalcemia.

General Anesthesia

- All IV, arterial, and central access placed under sterile technique
- Anticipate difficult mask/intubation scenario.

Regional Anesthesia

- Difficult neuraxial anesthesia placement due to scoliosis.
- Caution in pts with thrombocytopenia.
- Consider increased risk for developing infection at site of injection.

Postoperative Period

- Poor wound healing.
- Increased infection risk.
- Continue to monitor lytes; stress can precipitate a hypocalcemic crisis.

Anticipated Problems/Concerns

- High infection risk
- Lyte imbalances
- Airway/facial anomalies necessitating FO or video laryngoscopy
- Cardiac defects with shunting lesions

Dilated Cardiomyopathy

Frank W. Dupont

Risk

- DCM is a largely irreversible form of heart muscle disease, with an estimated prevalence of 1:2500; it is the third most common cause of CHF and most frequent cause for heart transplantation.
- DCM leads to progressive CHF, ventricular and supraventricular arrhythmias, conduction system abnormalities, thromboembolism, and sudden or heart failure–related death.
- Marked limitation of exercise capacity is a reliable predictor of mortality.

Perioperative Risks

- Increased periop morbidity and mortality, particularly in high-risk surgery cases:
  - CHF exacerbation
  - Renal failure
  - Systemic or pulm embolization from dislodged intracardiac thrombi

Worry About

- Autonomic instability
- Malignant tachydysrhythmias
- Worsening LV systolic and/or diastolic function, RV dysfunction

Overview

- Syndrome characterized by dilatation and impaired systolic function of left, right, or both ventricles with normal ventricular wall thickness
- LV systolic (decreased EF) and diastolic dysfunction (noncompliant ventricle), RV dysfunction; possibly pulm Htn and AV valvular regurgitation
- High risk of sudden cardiac death

Etiology

- Cause of idiopathic DCM remains unclear, but several pathophysiologic mechanisms have been implicated: genetic and familial factors, inflammatory and infectious factors, cytotoxicity, cell loss, and abnormalities in endogenous repair.

Usual Treatment

- Medical interventions primarily based on CHF treatment with diuretics, ACEI, ARB, vasodilators, and β-adrenergic receptor–blocking agents; anticoagulants for thromboembolic prophylaxis; ICD implantation for management of tachyarrhythmias and CRT for dyssynchrony
- Surgical treatment for refractory end-stage CHF: LVAD placement, heart transplant

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmias CHF Myocardial ischemia	Palpitations DOE Orthopnea PND Angina	Narrow pulse pressure, pulsus alternans Displaced PMI Systolic murmur (MR), S_3, S_4 JVD, ascites, pedal edema	ECG, EPS ECHO Stress test Coronary angiography
RESP	Pulm edema	Dyspnea	Rales, wheezes	CXR ABG
GI	Hepatic congestion	Abdominal distension	Hepatomegaly	LFTs, PT, albumin
HEME	Coagulopathy	Bruising		PT/ PTT
RENAL	Renal insufficiency	Oliguria		BUN/Cr, FEN_a
CNS	Cerebral infarcts	Stroke	Focal neurologic deficits	CT, MRI

Key References: Maron BJ, Towbin JA, Thiene G, et al.: Contemporary definitions and classification of the cardiomyopathies: an American Heart Association Scientific Statement from the Council on clinical cardiology, heart failure and transplantation committee; quality of care and outcomes research and functional genomics and translational biology interdisciplinary working groups; and Council on epidemiology and prevention, *Circulation* 113(14):1807–1816, 2006; Sumler ML, Andritsos MJ, Blank RS: Anesthetic management of the patient with dilated cardiomyopathy undergoing pulmonary resection surgery: a case-based discussion, *Semin Cardiothorac Vasc Anesth* 17(1):9–27, 2013.

Perioperative Implications

Preoperative Preparation
- Consider cardiology consultation to optimize pt's cardiac condition.

Monitoring
- ECG with ST-segment analysis.
- Arterial line dependent on invasiveness of surgery.
- Consider PA cath if anticipation of large fluid shifts in moderate- to high-risk surgery.
- TEE is the monitor of choice for the assessment of biventricular function and AV valve regurgitation in invasive surgical cases.

Airway
- None

Preinduction and Induction
- Anesthetic principles are based on afterload reduction, preload conservation, and prevention of tachycardia and myocardial depression.

Maintenance
- Higher doses of volatile anesthetic agents are often poorly tolerated; thus a narcotic-based anesthetic with low-dose volatile agents and/or benzodiazepine supplementation may be preferable.
- Fluid management should be conservative to prevent fluid overload and acute CHF exacerbation.
- Inotropic support may be necessary.

Extubation
- Beware of tachycardia and Htn and treat proactively.

Postoperative Period
- Consider ICU admission and mechanical ventilation if major intraop fluid shifts have occurred.

Adjuvants
- Regional anesthesia techniques are not contraindicated in the absence of coagulopathy and provided that hypotension is prevented.
- ICD management precautions should be taken if applicable.
- DCM predisposes to decreased blood flow to liver and kidney, which prolongs action of many drugs; also increased volume of distribution requires drug dose adjustments.

Anticipated Problems/Concerns
- CHF exacerbation, hemodynamic instability, tachydysrhythmias

Diphtheria

Pierre Moine

Risk
- Approximately 0.001 cases per 100,000 population in USA since 1980 (<5 cases a year).
- Endemic in developing countries.
- Still common in countries where mass immunization programs are not enforced.
- After political changes in Eastern Europe and Central Asia at the end of the 20th century, a resurgence in many vaccine-preventable diseases, including diphtheria, was reported across these countries.
- Risk factors for diphtheria outbreaks: older age (they are not up to date with booster immunization against diphtheria), lack of vaccination, alcoholism, low socioeconomic status, crowded living conditions, and Native American background.

Perioperative Risks
- Early (days after exposure): Respiratory compromise; respiratory arrest; airway obstruction and hemorrhage; conduction abnormalities, dysrhythmia, cardiogenic shock, CHF, myocarditis; shock, coma, and death
- Late (2–6 wk): Myocarditis and polyneuritis

Worry About
- Respiratory diphtheria early toxic manifestations: neck edema, pharyngitis, large pseudomembranes, massive swelling of the tonsils, bull-neck diphtheria (with massive edema of the submandibular and paratracheal region and foul breath, thick speech, and stridor), hoarseness, and difficulty breathing are associated with severe advanced disease/poor prognosis and with a significant early risk of total airway obstruction.
- Late toxic manifestations of diphtheria: polyneuropathy (resembles Guillain-Barré syndrome) and myocarditis (cardiac arrhythmias, conduction abnormalities, or CHF).
- Other complications: Septic arthritis, pneumonia, renal failure, endocarditis, encephalitis, cerebral infarction, and pulmonary embolism.
- Fatal pseudomembranous diphtheria typically occurs in pts with nonprotective antibody titers and in unimmunized pts. Death occurs in 5–10% of respiratory cases. Risk factors for death include bull-neck diphtheria, myocarditis with ventricular tachycardia, atrial fibrillation or complete heart block, an age of >60 y or <6 mo, alcoholism, extensive pseudomembrane elongation, and laryngeal, tracheal, or bronchial involvement, and delayed antitoxin administration.

Overview
- Diphtheria is caused by superficial infection of the respiratory tract or skin with toxin-producing strains of *Corynebacterium diphtheriae*. The pathogens multiply locally and produce diphtheria toxin. This results in necrosis of the mucosal cells and production of a thick, gray pseudomembrane containing fibrin, epithelial cells, bacteria, and neutrophils. Diffusion of toxin in the circulation causes toxic neurologic and myocardial complications.
- The major risk factor for *C. diphtheriae* infection continues to be travel to an endemic country (Indian subcontinent, Africa, or South East Asia).
- Prompt consideration of diphtheria: Severe pharyngitis, difficulty swallowing, respiratory compromise, or signs of systemic disease, including myocarditis or generalized weakness, and presence of a pharyngeal pseudomembrane or an extensive exudate.
- Respiratory diphtheria: Sore throat with low-grade fever and a strongly adherent pseudomembrane of the tonsils, pharynx, or nose. Occasionally weakness, dysphagia, headache, and voice change. The diphtheritic pseudomembrane is gray or whitish, sharply demarcated and tightly adherent to the underlying tissues. Respiratory diphtheria can progress to a swollen so-called bull neck, and the pseudomembrane can progress to cause airway obstruction. Attempts to dislodge the membrane may cause bleeding. Respiratory diphtheria remains the most common clinical presentation.
- Systemic toxin-mediated neurologic and cardiac toxicity of diphtheria: Neuritis and polyneuropathy

(cranial nerve involvement, respiratory and abdominal muscle weakness, generalized sensorimotor polyneuropathy and autonomic manifestations), and myocarditis (dysrhythmia of the conduction tract, dilated cardiomyopathy, congestive failure and circulatory collapse).
- Cutaneous diphtheria: Painful infected skin lesions and nonhealing or enlarging skin ulcers which lack a characteristic appearance. Cutaneous diphtheria has a low mortality rate, rarely associated with myocarditis or peripheral neuropathy.
- Invasive disease: Bacteremia, endocarditis, mycotic aneurysms, osteomyelitis, and septic arthritis.

Etiology

- Corynebacteria are Gram-positive rods (nonsporulating, nonencapsulated, and nonmotile Gram-positive bacillus). Many species from this genus are skin commensals and act only as opportunistic pathogens. Of the many *Corynebacterium* species, three can potentially produce a diphtheria toxin and cause diphtheria or diphtheria-like diseases: *C. diphtheriae*, *C. ulcerans*, and *C. pseudotuberculosis*.
- Historically the most commonly identified causative bacterium is *C. diphtheriae*. Human beings are the reservoir for *C. diphtheriae*, in particular children, and transmission of *C. diphtheriae* occurs from person to person, predominantly from the respiratory tract (via the aerosol route) but occasionally from cutaneous lesions or fomites. The incubation period for respiratory diphtheria is usually 2–5 d but occasionally is longer, with duration of up to 10 d reported.
- Two human isolate phenotypes: Nontoxigenic and toxigenic. *C. diphtheriae*, *C. ulcerans*, and *C. pseudotuberculosis* toxigenic strains express diphtheria exotoxin (mechanism of pathogenesis during human infection) that inhibits protein synthesis and kills susceptible cells. Toxin is produced in the pseudomembranous lesion and distributed to all organ systems through the blood. Toxigenic strains cause pharyngeal/respiratory and cutaneous diphtheria, and systemic diseases. The clinical and epidemiologic significance of nontoxigenic strains remains unclear. Nevertheless, cases caused by nontoxigenic strains have been reported in immunocompromised individuals.
- Laboratory diagnosis is by culture of an isolate of *Corynebacterium* species. qPCR assay identifies *Corynebacterium* species, plus the presence of the *tox* gene (diphtheria exotoxin) in DNA extracts from submitted isolates. If the *tox* gene is detected, the isolate goes to have an Elek test to detect expression of toxin.
- *C. ulcerans* is now more frequently reported and can also cause the same ranges of diphtheria-like illness. By contrast, the *C. ulcerans* reservoir is thought to be animals. It has been reported after consumption of raw dairy products and contact with cattle, pigs, and domestic pets. *C. ulcerans* diphtheria person-to-person transmission is proposed, but is not confirmed. *C. pseudotuberculosis* is also traditionally associated with farm animal contact and dairy products.

Usual Treatment

- Prompt hospitalization in respiratory isolation with close monitoring of cardiac and respiratory function. Cardiac work-up recommended. Airway management might be necessary and should be considered early in the course of disease.
- Determination of toxigenicity status of the strains of *Corynebacterium* is probably the most important aspect of laboratory investigation.
- Start treatments as soon as possible, even before confirmatory tests are completed, due to the high potential for mortality and morbidity.
- Equine DAT, the mainstay of treatment, is available in the USA only through the CDC. DAT neutralizes only non-tissue-bound circulating toxins and should therefore be given early in the course of the disease, on the basis of clinical suspicion rather than laboratory diagnosis. DAT reduces the extent of local disease, as well as the risk of complications of myocarditis and neuropathy. Rapid institution of DAT is associated with a significant reduction in mortality risk. The protective effect is described for both *C. diphtheriae* and *C. ulcerans*. DAT should be promptly administered after testing for sensitivity to DAT and without awaiting lab confirmation. DAT is based on horse serum and therefore severe, immediate anaphylaxis may occur.
- Macrolide antimicrobial therapy: Erythromycin remains the mainstay of therapy (erythromycin 500 mg IV q6h [for children, 40–50 mg/kg per day IV in 2 or 4 divided doses]/PO erythromycin 500 mg q6h daily to complete a 14-d course). Newer macrolides (azithromycin, clarithromycin) have shown minimum inhibitory concentrations similar to that for erythromycin.
- Erythromycin adverse effects include an association with prolonged QT syndrome and a theoretical concern of potentiation of myocarditis sequelae from diphtheria toxin. Therefore the appropriateness of erythromycin should be carefully considered.
- Main alternative therapy: Penicillins (procaine penicillin G 600,000 units [for children, 12,500–25,000 U/kg] IM q12h/PO penicillin V 125–250 mg q6h daily to complete a 14-d course)
- Alternative antimicrobial agents: Rifamycins (rifampin), lincosamides (clindamycin), tetracyclines (doxycycline), fluoroquinolones, third- (cefotaxime and ceftriaxone) and fourth-(cefepime) generation cephalosporins, glycopeptides (vancomycin, teicoplanin), lipopeptides (daptomycin), oxazolidinone (linezolid).
- Few cases of multidrug resistance to first-line antimicrobials have been reported. Antimicrobial susceptibility testing on all diphtheria toxin-producing *Corynebacterium* species is strongly recommended.
- Sustained routine campaigns for vaccination of children and adequate boosting vaccination of adults. Age-appropriate vaccination with diphtheria toxoid vaccines and timely decennial boosters should be encouraged to prevent diseases. Administration of diphtheria vaccine is recommended during convalescence because diphtheria infection does not always confer immunity.
- Respiratory diphtheria remains a notifiable disease in USA (national surveillance through the National Electronic Telecommunications System for Surveillance), whereas cutaneous diphtheria is not.
- Potential surgical debridement in cutaneous diphtheria.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Nasal, faucial or proximal pharyngeal, laryngeal diphtheria	Altered speech, pharyngitis, respiratory distress, croupy cough, hoarseness and stridor, chills, sore throat	Neck edema, fever, pharyngitis, large pseudomembranes, massive swelling of the tonsils, "bull-neck" diphtheria	Gram stain, nasopharyngeal swab, throat swab, culture of throat specimens/"membrane," indirect laryngoscopy
CV	Conduction abnormalities, dysrhythmia, cardiogenic shock, CHF, myocarditis	Dyspnea with minimal exertion, symptoms of CHF, palpitations	Tachycardia, ectopic beats, first-degree heart block, second-degree heart block, third-degree block, bundle branch block, atrial fibrillation, signs of CHF	ECG, CXR, serum troponin I, ECHO
RESP	Tracheobronchial diphtheria	Fever, tachypnea, dyspnea, presence of membrane, enlarged anterior cervical lymph nodes, edema of the surrounding soft tissue, "bull neck" appearance	Progressive respiratory compromise with partial to complete respiratory obstruction	Indirect laryngoscopy
HEME/IMMUNE	Systems compromised dependent on amount of toxin			CBC, blood cultures, PCR assays
GU	Proteinuria			UA
DERM/SOFT TISSUE	Cutaneous ulcers	Vesicles, "rolled edge" ulcers		Cultures, tissue biopsy for histopathologic examination
CNS	Interference with phonation, swallowing, respiration, resembles Guillain-Barré syndrome, peripheral polyneuritis	Symptoms depend on involved nerves: Cranial neuropathies, particularly ocular and bulbar palsies, limb weakness with reduced reflexes, limb paralysis, respiratory failure	Cranial nerves (most often III, VI, VII, X), peripheral nerves (motor >sensory)	Nerve conduction study

Key References: MacGregor RR: *Corynebacterium diphtheria* (Diphtheria). In Bennett JE, Dolin R, Blaser MJ, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases,* updated ed 8, Philadelphia, PA, 2015, Elsevier, pp 2366–2372; Moore LS, Leslie A, Meltzer M, et al.: *Corynebacterium ulcerans* cutaneous diphtheria, *Lancet Infect Dis* 15(9):1100–1107, 2015.

Perioperative Implications

Preoperative Preparation

- Initiate prompt treatments with diphtheria antitoxin and antimicrobial therapy.
- Assessment of respiratory distress/airway compromise.
- Assessment of cardiac toxicity (for early detection of rhythm abnormalities. Initiate electrical pacing for clinically significant conduction disturbance and provide pharmacologic intervention for arrhythmias or for heart failure).
- Assessment of neurologic toxicity.
- Assessment of immunization status of exposed healthcare workers.

Monitoring

- Maintain close monitoring of cardiac activity for early detection of rhythm abnormalities.
- Provide two large-bore IVs for pts with a toxic appearance; provide invasive monitoring and aggressive resuscitation for pts with septicemia.
- Initiate electrical pacing for clinically significant conduction disturbance and provide pharmacologic intervention for arrhythmias or for heart failure.
- Consider PA cath/noninvasive cardiac output monitoring or transesophageal echocardiography to assess degree of myocardial involvement.

Airway

- Secure definite airway for pts with impending respiratory compromise or the presence of laryngeal membrane (careful manipulation as membrane will bleed if manipulated).
- Early airway management allows access for mechanical removal of tracheobronchial membranes and prevents the risk of sudden asphyxia through aspiration.

Induction and Maintenance

- Compensate for problems of exotoxin shock and possible CHF, as well as cardiac arrhythmia.

Extubation

- Early: May need prolonged ventilation.
- Late: Cardiogenic shock/extensive polyneuritis may necessitate prolonged ventilatory support.

Adjuvants

- Cardiac pacemaker for arrhythmia control/complete heart block.
- Minimize use of sedative-hypnotics because development of respiratory difficulties may be obscured.

Postoperative Period

- Careful observation for respiratory, cardiac, and neurologic compromises

Anticipated Problems/Concerns

- Airway obstruction requiring tracheostomy/intubation
- Myocardial conduction problems that may necessitate electrical pacing
- Cardiogenic shock/CHF
- Neuritis that can present as a Guillain-Barré-like syndrome

Disseminated Intravascular Coagulation

Adrian Hendrickse

Risk

- Most common coagulopathy in the ICU.
- 1% of all hospital admissions.
- Evidence of a coagulopathy in the DIC spectrum approaches 90% in cases of severe sepsis.
- The most important initiator of DIC is sepsis, along with trauma (hypovolemic shock, extensive tissue damage, fat embolism, head injury); surgery (neurosurgery, CPB); obstetric emergencies (hemorrhage, preeclampsia, retained products, amniotic fluid embolism); malignancy (acute promyelocytic leukemia, disseminated metastases); and severe liver disease. Vascular abnormalities, immunologic reactions, toxins, and drugs can also cause DIC.
- Mortality: Dependent on the underlying condition and the severity of the coagulopathy.

Perioperative Risks

- Existing coagulopathy
- Organ failure

Worry About

- Excessive bleeding from surgical and anesthetic access sites
- Organ dysfunction and the need for supportive measures
- Coordinating the management of the coagulopathy

Overview

- DIC is a syndrome characterized by the pathologic imbalance of the coagulation, anticoagulation, and fibrinolytic processes, leading to systemic intravascular thrombosis and the deposition of fibrin in the microcirculation. DIC exists as a spectrum of clotting disorders, the two ends being acute (life-threatening) and chronic (subclinical).
- Acute DIC exists when there is a rapid activation of the coagulation system resulting in the consumption of platelets and the depletion of clotting factors at a rate greater than the body can compensate for, which can lead to excessive hemorrhage. Chronic DIC is a slower affair where the rate of consumption of platelets and clotting factors can be compensated for and where the clinical picture is generally that of microvascular thrombosis.
- Dx: There are no specific laboratory tests for DIC. DIC can be diagnosed clinically on the basis of the presence of a suitable risk factor, along with a selection of laboratory findings: a rapidly falling platelet count or a count $<100{,}000/mm^3$; prolongation of clotting times (APTT, PTT, INR); the presence of FDPs; a reduction in plasma concentration of coagulation inhibitors (ATIII, protein C); TEG analysis of clot formation and lysis.
- Serial testing showing temporal trends are invaluable.

Etiology

- DIC is initiated in one of two ways:
  - Systemic inflammatory response resulting in the activation of the complement pathway and the release of cytokines leading to systemic coagulation.
  - Activation of the extrinsic pathway of coagulation by the presence of increased concentrations of tissue factor.
- An impairment of fibrinolysis, which normally keeps coagulation localized, also plays its part in the progression of the syndrome.

Usual Treatment

- Primary goal is to treat the underlying condition.
- Mechanical ventilation, invasive monitoring, and hemodynamic support are often required.
- Surgery intended to remove the cause of DIC should not be delayed.
- Early involvement of a hematologist, serial coagulation testing, and communication with the transfusion laboratory to guide the use of blood products is recommended.
- Blood products:
  - PRBCs for significant hemorrhage.
  - FFP for clotting factor deficiencies.
  - Cryoprecipitate infusions to maintain fibrinogen >100 mg/dL.
  - Platelet infusions to keep level $>20{,}000/mm^3$ (in the absence of hemorrhage) or $>50{,}000/mm^3$ (with active bleeding or prior to surgery).
- Pharmacologic agents (limited, mixed, or poor evidence):
  - Heparin may be of benefit in cases in which thrombosis predominates but should be used in the critical care environment for venous thromboembolism prophylaxis .
  - ATIII, activated protein C, and thrombomodulin (if available) have all been used in the care of specific subgroups of hematologic and septic DIC cases with some success.
  - Antifibrinolytic agents (ε-aminocaproic acid, tranexamic acid, aprotinin) are generally not recommended but may be considered in pts with DIC who continue to bleed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Bleeding		Bleeding from minor sites of trauma	
CV	Sepsis Hypovolemic shock Microthrombi		Hypotension Signs of decreased organ perfusion	ECG PAC ECHO
RESP	Bleeding Microthrombi	Dyspnea Hemoptysis	Tachypnea	CXR ABGs
GI	Bleeding Microthrombi	Hematemesis		NG suctioning Stool sample, LFTs, clotting studies
GU	Bleeding Microthrombi	Hematuria PU/PV bleeding		Urine output, BUN, Cr
HEME	Bleeding Consumption of factors and platelets	Hemorrhage		Hb, Plt count, clotting studies, TEG, fibrinogen, D-dimer, ATIII, protein C, blood film
CNS	Bleeding Microthrombi		Neurologic deficits	CT
MS	Bleeding Microthrombi		Extremity infarcts	

Key References: Hunt BJ: Bleeding and coagulopathies in critical care, *N Engl J Med* 370(9):847–859, 2014; Levi M: Diagnosis and treatment of disseminated intravascular coagulation, *Int J Lab Hematol* 36(3):228–236, 2014.

Perioperative Implications

Preoperative Preparation

- Optimize the management of the precipitating cause.
- Correct coagulopathy.
- Liaise with laboratory to ensure blood product availability.

Monitoring

- Routine
- Invasive where indicated by severity
- Serial CBC, coagulation studies, and TEG

Airway

- Careful intubation to avoid trauma

Induction

- Be prepared for CV instability in sick pts.

Maintenance

- Use invasive monitoring and laboratory tests to guide interventions.

Extubation

- Organ dysfunction and/or failure may necessitate a protracted period of mechanical ventilation in an ICU.

Adjuvants

- Hepatic and/or renal failure increases the duration of action of most muscle relaxants.

Anticipated Problems/Concerns

- Periop management is best conducted in a critical care environment.
- Hemorrhage may continue into the postop period.
- Organ support may be prolonged.

Diverticulosis

Nancy C. Wilkes

Risk

- More prevalent in developed countries; common in the UK and other parts of northern Europe, North America, Australia, and New Zealand, but uncommon in southern Africa, the Middle East, the Far East, and the Pacific Islands.
- Prevalence in developing countries between 5–45%, depending on age of population and method of diagnosis; African and Asian countries with prevalence approximately 0.2%.
- Prevalence increases with age. In USA, seen in less than 5% of pts younger than 40 y; Approximately 30% by age 60 y and 65% by age 85 y.
- Low-fiber diet is the highest risk factor. High-fat and/or meat diets are high risk.
- Under age 50 y more common in men; over 50 y more common in women.
- Colonic motility disorders contribute.

Perioperative Risks

- Pts who present with diffuse peritonitis or fail nonoperative management of acute diverticulitis may require emergency surgery.
- Risks may include full stomach, obstruction, sepsis, and bleeding.

Worry About

- 15–25% of pts with diverticulosis will develop diverticulitis.
- Acute diverticulitis may be complicated by abscess, fistula, obstruction, or perforation.
- 15% of individuals with diverticular disease will develop acute GI bleeding. Of those, one-third will develop massive bleeding.
- Mortality rates of 22–39% reported for perforation and resultant fecal peritonitis.

Overview

- Multiple saclike herniations through weak points in the intestinal wall. Typically does not contain all layers of the wall but is a herniation of the mucosa and submucosa through the muscle layer.
- Vast majority (>90%) found in the sigmoid colon. Limited to the sigmoid in 65%, approximately 25% involving sigmoid and other segments.
- Of pts with significant diverticulosis, 70% remain asymptomatic and without related complications.

Etiology

- Not completely understood but thought to be related to low-residue diet with long transit time, as opposed to diets with high-fiber content with shorter transit time.
- Abnormalities of peristalsis and intestinal dyskinesis may contribute.
- With long transit times, intraluminal pressure increases, colon becomes distended, followed by acute and then chronic inflammation of diverticula.

Usual Treatment

- Dietary modification, high-fiber emphasis long term for diverticulosis.
- With the development of simple diverticulitis, 75% of cases are not associated with complications. Most are initially treated conservatively with medical therapy (low-residue diet and antibiotics); 85% respond quickly; 15% will require surgery.
- Severe abdominal pain, fever, and clinical signs of peritonitis and/or pelvic abscess require initial resuscitation, parenteral antibiotics, and operative intervention.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension Tachycardia Hemodynamic instability	Fatigue Weakness Angina	Auscultation	ECG BP Pulm artery cath
RESP	Hypoxemia	Tachypnea Dyspnea	Auscultation	SpO_2 ABGs CXR
GI	Perforation Obstruction Abscess Fistula Hemorrhage	Abdominal pain N/V Fever Abdominal rigidity Rectal bleeding	Diffuse abdominal tenderness Rebound Absent bowel sounds Abdominal rigidity	Free air under diaphragm if perforation CT scan Ultrasonography
HEME	Anemia, leukocytosis, DIC with sepsis			CBC with differential PT/ PTT, FSP, plt count, fibrinogen
RENAL	Colovesicular fistula	May pass air with urine if perforation into urinary bladder		Urinalysis Urine output
CNS	Disorientation with sepsis			

Key References: Young-Fadok TM, Sarr MJ: Diverticular disease of the colon. In Yamada T, Alpers DH, Kaplowitz N, et al., editors: *Textbook of gastroenterology,* ed 4, Philadelphia, PA, 2003, Lippincott Williams and Wilkins, pp 1843–1863; Tantawy H, Myslajek T: Diseases of the gastrointestinal system. In Hines R, Marschall K, editors: *Stoelting's anesthesia and co-existing disease,* ed 6, Philadelphia, PA, 2012, Saunders, pp. 301–304.

Perioperative Implications

Monitoring
- Routine, including urine output.
- With sepsis, monitor arterial pressure; consider PAC monitoring.

Maintenance
- Optimize intravascular volume and high O_2 content.

Postoperative Period
- Maintain intravascular volume.
- Continued monitoring of CV variables and urine volume.

Adjuvants
- Antibiotics
- Volume expanders
- Component therapy if DIC develops
- Vasopressor support if required; no interactions

Anticipated Problems/Concerns

- Condition is chronic so flare-ups may occur. Diverticulosis may progress to uncomplicated diverticulitis and evolve to the complicated form (abscess, perforation, obstruction, bleeding, fistula).
- Any surgical intervention and bowel resection would therefore have the anticipated side effects and complications expected from that procedure.

Do Not Resuscitate Orders

Alanna E. Goodman

Risk

- Violation of pt autonomy and self-determination if DNR orders are not reconsidered and honored for the periop period.
- Increasing numbers of pts have some form of advance directive.
- Approximately 15% of surgical pts have DNR orders.

Perioperative Considerations

- Resuscitation preferences can change based on pt status and prognosis.
- DNR orders do not become automatically suspended or continued when a pt goes to surgery.
- Intraop arrests tend to have better outcomes because they are witnessed, acted upon quickly, and are often due to reversible causes.
- Pts with DNR orders often undergo vascular access procedures, gastrostomy tube placement, tracheostomy, palliative procedures, repair of pathologic fractures, and surgery for emergent conditions (e.g., bowel obstruction, appendicitis).

Worry About

- Ethical and legal obligation to honor and follow pt's wishes and provide optimal medical care
- Appropriateness of the DNR order
- Delineation of anesthesia care and resuscitation
- Iatrogenic events
- Intraop deaths
- Liability

Overview

- The Patient Self-Determination Act (1990) was established to allow pts to avoid undesired medical interventions. It requires federally funded healthcare institutions to ask pts about advance directives when admitted and provide information about their right to have one (Medicare and Medicaid are federally funded).
- The 1983 Report of the President's Commission for the Study of Ethical Problems in Medicine justified the "favoring of resuscitation of hospitalized pts with unexpected cardiac arrest"— which conveys implicit pt consent for CPR.
- CPR is the only medical intervention that requires a MD order to be withheld.
- A DNR order is a limited advance directive that prevents resuscitative intervention in the event of a cardiopulmonary arrest..
- Many pts with DNR orders are terminally ill or have advanced disease.
- Policies should be set in place for reevaluation of DNR orders for pts requiring surgery. These policies should be institutional, written, unambiguous, and flexible to individual pt needs.
- Anesthesiologists should be familiar with their institution's policies, as well as state and federal laws.

Assessment Points

- What are the pt's wishes?
- When was the DNR order written/last updated?
- Why was the DNR order initiated?
- Did the pt have a terminal condition?
- Did the pt have correct prognostic information?
- Who discussed/wrote the DNR order with the pt?
- Did the physician influence the decision to have the DNR order?

Key References: *Ethical guidelines for the anesthesia care of patients with do not resuscitate orders or other directives that limit care,* Park Ridge, IL, 1993, American Society of Anesthesiologists; amended 1998; Waisel D, Burns JP, Johnson J, et al.: Guidelines for perioperative do-not-resuscitate policies, *J Clin Anesth* 14(6):467–473, 2002.

Perioperative Implications

- Review "required reconsideration" of the DNR orders.
- All changes to DNR status must be communicated to all members of the periop team and documented in the pt's medical record.
- Best if discussion of DNR orders can be done preop to develop a better pt-doctor relationship, avoid production pressure influences, and to allow time to contact all appropriate parties (surrogate, surgeon, primary care physician).
- This discussion should include what procedures are essential for the anesthetic and operation (e.g., intubation paralysis); iatrogenic arrest; and if the DNR order is modified, when and if it should be reinstated.
- The document for *Informed Consent for Anesthesia Care in The Patients with An Existing Do-Not-Resuscitate Order* created by The American Society of Anesthesiologists Committee on Ethics provides three resuscitation options during the periop period:
  - Full resuscitation.
  - Limited resuscitation: Procedure-directed, documents specific procedures the pt refuses.
  - Limited resuscitation: Goal-directed, allows resuscitation if the anesthesiologist and surgeon believe the adverse events are temporary and reversible. Allows resuscitation if the anesthesiologist and surgeon believe the resuscitation efforts support specified and documented goals of the pt.
- Consider consultation with an ethics expert if there is disagreement or concern about DNR orders and the surgery is not emergent.

Anticipated Problems/Concerns

- Anesthesiologists rarely have an established relationship with the DNR pt but must discuss and clarify resuscitation wishes.
- Aspects of anesthesia care (intubation, vasopressors, IV fluid therapy, transfusion, etc.) are resuscitative therapies.
- Medications used for anesthesia may cause cardiac depression, respiratory depression, and cardiac arrest.
- Anesthesiologists may be morally conflicted with the pt's desire for limited intervention. For a nonemergent case, the anesthesiologist can decide not to perform the anesthetic as long as there is another available physician and the change is not detrimental to the pt.

Double Aortic Arch

Anthony J. Clapcich

Risk

- Vascular rings account for <1% of cardiovascular malformations that require surgical correction. Double aortic arch is the most common form of complete ring that encircles both the trachea and the esophagus.
- Race/gender predilection: None.

Perioperative Risks

- Recurrent respiratory infections often aggravate chronic airway obstruction.
- Baseline dynamic tracheal compression can progress to complete airway obstruction upon induction and muscle relaxation.
- Persistent postop airway obstruction requiring prolonged mechanical ventilation and CPAP.

Worry About

- Esophageal obstruction: Dysphagia, choking, emesis, aspiration, FTT.
- Tracheal obstruction: Chronic cough, wheezing, barky-brassy cry, inspiratory/expiratory stridor; acute episodes of severe respiratory distress, apnea, cyanosis, and ALTE.
- Associated cardiac anomalies (10–20%): VSD, ASD, interrupted aortic arch, transposition of the great arteries, tetralogy of Fallot, truncus arteriosus, and complex univentricular lesions.
- Chromosome 22q11 deletion syndrome (20%): Genetic defect associated with syndromes, such as DiGeorge, velocardiofacial, CHARGE, and VACTERL; features include endocrine abnormalities (hypocalcemia, thyroid/parathyroid dysfunction, short stature), palatal and laryngotracheal abnormalities, developmental delay/neurologic abnormalities, renal tract malformations, thrombocytopenia, T-cell deficiencies, and autoimmune disorders.

Overview

- Vascular rings can be classified as complete or incomplete. Double aortic arch is the most common form of complete ring that encircles and compresses both the trachea and esophagus.
- Symptoms usually occur at birth or within the first 3 mo of life. The degree of tracheal and esophageal compression will dictate the severity of respiratory and GI perturbation.
- Initial work-up with CXR and upper GI can reveal tracheal deviation/narrowing and proximal esophageal distention/indentation. After the diagnosis is suspected, ECHO is used to examine arch anatomy and rule out other intracardiac anomalies. Both MRI and CT are very useful in further delineating vascular, airway, and GI anatomy. Cath is now reserved for assessing complex cardiac defects that require additional hemodynamic information. Bronchoscopy is often performed at the time of repair to evaluate the location, degree, and extent of airway obstruction, which may help to identify those pts at risk for postop respiratory compromise.

Etiology

- During normal human development, six branchial arches are sequentially formed and penetrated by six paired aortic arches that arise from the aortic sac and terminate in paired DA. These primitive arches largely regress (the fourth and sixth being the most persistent) and by the eighth week, the right DA largely involutes and forms the distal part of the right subclavian artery, leaving only the left DA to form the distal aortic arch and descending aorta. Failure of the right DA to involute results in a double aortic arch, whereby the ascending aortic arch divides into two arches, passes on each side of the trachea and esophagus, and joins posteriorly to form the descending aorta. The right carotid and subclavian arteries arise from the usually dominant, posterior right arch, whereas the left carotid and subclavian arteries arise from the smaller, anterior left arch.

Usual Treatment

- Medical therapy: None.
- Surgery: The goal is to relieve tracheal and esophageal compression by dividing the vascular ring and dissecting any fibrous bands. A thoracotomy is usually performed on the side ipsilateral to the minor arch. Right (posterior) arch is dominant in >75% of cases; thus left posterolateral thoracotomy is commonly used to expose the left (anterior) arch. Video-assisted thoracoscopic repair is also an effective option. Median sternotomy with cardiopulmonary bypass is reserved for cases that require concomitant repair of associated cardiac anomalies.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Chromosome 22q11 deletion features: Facial abnormalities Palatal abnormalities Velopharyngeal incompetence Congenital laryngeal web	Previous difficulties with anesthesia or intubation FTT Nasal regurgitation of formula; delayed speech/poor articulation (childhood) Noisy breathing, abnormal cry	Low set ears, short philtrum, hypertelorism, small mouth, small chin Cleft palate Hypernasal speech (childhood) Inspiratory/expiratory stridor, aphonia/weak high-pitched cry Hoarseness (childhood)	Flexible bronchoscopy Direct laryngoscopy/ bronchoscopy
CV	Depends on presence of associated cardiac anomalies (10–20% cases); None if *only* double aortic arch present	Cyanotic spells, CHF, dyspnea, diaphoresis, FTT	Murmur, cyanosis, four-limb noninvasive BP discrepancy, grunting, rales/wheezes, hepatosplenomegaly	Pulse oximeter, ECG ECHO Cardiac MRI Cardiac cath
RESP	Airway obstruction Recurrent respiratory infection	Dyspnea, apnea, intermittent cyanosis, ALTE Coughing, wheezing	Insp/expiratory stridor (± positional), hyper-extended head, brassy-barky cry, intercostal retractions, nasal flaring	CXR Bronchoscopy MRI CT
GI	Esophageal obstruction	Dysphagia, FTT		UGI Esophagoscopy

Key References: Licari A, Manca E, Rispoli GA, et al.: Congenital vascular rings: a clinical challenge for the pediatrician, *Pediatr Pulmonol* 50(5):511–524, 2015; Backer CL, Mongé MC, Russell HM, et al.: Reoperation after vascular ring repair, *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 17(1):48–55, 2014.

Perioperative Implications

Preoperative Preparation

- Oxygen therapy if decreased arterial oxygen saturation present
- Antibiotics for bronchopneumonia

Monitoring

- Bilateral upper extremity SpO_2 and Doppler probes are useful for assessing subclavian, carotid, and temporal pulses during temporary occlusion of the arch that is to be resected. Regional tissue oxygenation of the brain can be monitored via bilateral cerebral NIRS probes, which can reveal unilateral desaturation if carotid flow is compromised during arch manipulation and the patient's circle of Willis anatomy is not adequately providing collateral circulation.
- Potential for hemodynamic and respiratory instability warrant placement of arterial cath; presence of an aberrant subclavian artery may affect appropriate cath site.
- Large-bore IV access is essential; central venous line should be considered for pts with poor vascular access and those who require extensive repair on CPB.

Airway

- Dynamic and static airway obstruction likely; significant tracheal compression may require smaller ETT size than predicted.

Induction

- Inhalation induction without neuromuscular blockade until airway maintenance is documented by mask and/or ETT is placed distal to area of obstruction.
- Bronchoscopy during spontaneous ventilation allows for direct assessment of tracheal pathology and degree of dynamic airway collapse, thus identifying pts at risk for postop respiratory compromise.

Maintenance

- Balanced technique of narcotics and volatile agent is usually well tolerated.

Extubation

- Extubation at end of case if tracheomalacia and stenosis absent

Postoperative Period

- Good pain control essential for stable hemodynamics and avoidance of respiratory complications; IV opioids, rectal acetaminophen, intercostal nerve blocks, one-shot caudal, and caudal epidural cath have all been used with success.

Anticipated Problems/Concerns

- Despite surgical correction, persistent postop airway obstruction requiring prolonged mechanical ventilation and CPAP can occur secondary to edema, mucosal friability/reactivity, and long-segment tracheomalacia.

Down Syndrome

Stephanie Black

Risk

- Trisomy 21 is the most common autosomal aneuploidy; approximately 1:1000 live births.
- 80% of children with this condition survive beyond 1 y; average life expectancy 60 y.
- Increased incidence in mothers >35 y, but most are born to younger mothers, owing to higher fertility rates.
- Incidence decreased by elective termination of pregnancy from prenatal screening: high beta-hCG, low AFP, cell-free DNA, thickened nuchal fold, abnormal ductus venosus waveforms, absent nasal bone—cell-free DNA can now increase the sensitivity and specificity of these tests.

Perioperative Risks

- Airway obstruction
- Cardiac dysfunction due to CHD
- Cervical spine instability
- Immune and endocrinologic dysfunction

Worry About

- Airway obstruction:
  - Upper airway obstruction common immediately on induction of GA due to macroglossia, midface crowding, small mandible, short neck.
  - Subglottic stenosis in 20–25%; may cause postop stridor in children.
  - Obstructive sleep apnea in 30–50%. Central apnea also common.
    - Chronic hypoxemia may contribute to pulm Htn risk and increased opioid sensitivity.
- Congenital cardiac dysfunction:
  - 40% are born with CHD.
  - Most common: Complete atrioventricular canal defect (40%), VSD (25%).
  - Cyanotic CHD in 4% (usually tetralogy of Fallot).
  - Risk for pulm Htn because of pulm overcirculation.
  - May develop R-to-L shunting with profound hypoxemia.
  - Risk for paradoxical/systemic air emboli (coronary or cerebral vessels).
  - Bradycardia with inhalational induction with sevoflurane.
- Cervical spine instability:
  - Extension during intubation can cause neurologic symptoms (neck pain, arm pain, upper extremity weakness, torticollis) from atlanto-occipital instability.
- Generalized joint laxity; TMJ may sublux with jaw thrust.
- Endocrine: hypothyroidism (4–6% in children; 15–20% in adults), hypothermia.
- Immune dysregulation causes higher rates of certain cancers (ALL and AML) and respiratory infections.
- GI: Duodenal atresia in 4%; recurrent aspiration may cause pneumonia.
- Developmental delay:
  - May have fears of the unknown; can become physically resistant to entering OR.
  - Alzheimer disease and other mental illnesses (depression, psychosis) may coexist.

Overview

- Most common autosomal aneuploidy with an increasing life expectancy because of early interventions for multiple comorbidities
- Concerns for congenital cardiac disease, hypotonia, immune dysregulation, airway obstruction, recurrent pneumonia, oncologic predisposition, and GI disorders
- Physical exam findings: Midface hypoplasia, brachycephaly, epicanthal folds, simian crease, downward medial slant of eyes, high-arched palate, glossoproptosis, and murmur
- May require surgery for tympanostomy, strabismus, CHD repair, duodenal/esophageal atresia, marrow aspiration/biopsy, cervical spine fusion

Etiology

- Genetic: Trisomy 21

Usual Treatment

- Depends on penetrance and pathophysiology; may include the use of CPAP, thyroid hormone replacement, OT/PT

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Redundant tissue Midface hypoplasia Subglottic stenosis	Sleep apnea Intubation Hx Hearing deficit	Macroglossia Glossoproptosis "Down's facies"	Audiology Polysomnography
CV	CHD in 40% CAVC most common Tetralogy of Fallot in 4% Bradycardia on induction Risk for pulm Htn	Symptoms of CHF "Tet spells" Hx of CHD repair	Cyanosis Murmur Clubbing	ECHO ECG
ENDO	Hypothyroidism Metabolic syndrome	Thyroid hormone replacement Hypothermia	Obesity	Thyroid hormone levels
IMMUNE/ONC	Oncologic predisposition Immune dysregulation	Respiratory infections AML and ALL	Cough Lymphadenopathy	Auscultation Bone marrow biopsy/aspiration
MS	Hypotonia Subluxation of C1/C2	Upper motor neuron symptoms	Joint laxity	Cervical spine radiographs (controversy over whether these should be routine)

Key References: Arumugam A, Raja K, Venugopalan M, et al.: Down syndrome—a narrative review, *Clin Anat* 29(5):568–577, 2016; Maxwell LG, Goodwin SR, Mancuso TJ, et al.: Systemic disorders: down syndrome. In Davis PJ, Cladis FP, Motoyama EK, editors: *Smith's anesthesia for infants and children,* ed 8, Philadelphia, PA, 2011, Elsevier, pp 1172–1174.

Perioperative Implications

Monitoring

- Temperature (hypothermia).
- ECG (arrhythmias, ischemia); consider IM antimuscarinic drug to treat bradycardia from inhalational induction with sevoflurane, avoid hypercarbia and hypoxia to prevent PHTN.

Airway

- Have variety of devices available (e.g., oral and nasal airways, laryngeal mask, glidescope, fiberoptic) to manage airway obstruction.
- Avoid neck extension during laryngoscopy if possible.
- Smaller endotracheal tube may be necessary for narrowed subglottic space.

Vascular Access

- Allow more time for IV placement.
- Meticulously avoid injected air.

Patient Management

- Soft, warm, kind pt approach along with caregiver known to pt to help with initial management; warm, quiet OR

Anticipated Problems/Concerns

- Refractory hypoxia if R-to-L shunting develops
- Bradycardia with inhalational induction
- Resistance to separation from caregiver
- Life-threatening upper airway obstruction with difficult vascular access
- Spinal cord ischemia with neurologic damage

Drug Abuse, Lysergic Acid Diethylamide

Alan David Kaye | Burton D. Beakley

Risk

- "Hallucinogen" with primary effects of heightened or distorted mood, thought, and sensory perception. The hallucinogen class includes LSD, mescaline, phencyclidine, and psilocybin. These drugs cause tolerance and psychological drug dependence but not physical drug dependence or withdrawal.
- Initially marketed as an anesthetic agent; people began using it for recreational and spiritual purpose in the 1960s. LSD is still illegally used as a major hallucinogen worldwide.
- LSD use peaked in the late 1960s, and use has been declining since. The National Survey on Drug Use and Health reports more than 200,000 people using LSD for the first time yearly.
- LSD-related hospital visits remain low compared with those related to other major illicit drugs. In 2011, Drug Abuse Warning Network reported more than 1 million emergency department visits for nonalcohol illicit drug use; of these only 4819 were related to LSD.
- LSD is semisynthetic and produces psychedelic effects, including distortion of time and perceptions of colored visual patterns and abnormal movements. Psychological effects include dysphoria, euphoria, and changes in emotion and moods. LSD also causes multiple physical effects, including dilation of the pupils, salivation, dry mouth, loss of appetite, nausea, blurred vision, perspiration, hyperglycemia, Htn, tachycardia, and hyperthermia. The mechanism of action of LSD is thought to be predominantly by serotonin neurotransporter interactions. Hallucinogen persisting perception disorder, also known as flashbacks, and psychosis are two long-term effects that can be exacerbated by other drugs, such as sertraline, fluoxetine, and marijuana.

Perioperative Risks

- Acute intoxication produces a sympathomimetic effect, including mydriasis, increased body temperature, systemic Htn, tachycardia, anxiety, agitation, vomiting, aspiration, apnea, and unrecognized injuries.
- May prolong succinylcholine neuromuscular blockade and delay metabolism of ester local anesthetics (speculated inhibition of plasma cholinesterase).
- May potentiate analgesics.

Worry About

- Systemic: Htn, tachycardia, hyperthermia, hyperglycemia, salivation, nausea, vomiting, seizures, and apnea
- Serotonin syndrome: Triad of altered mental status, neuromuscular abnormalities, and autonomic hyperactivity
- Psychiatric: Hallucinations (visual, auditory, and tactile), labile mood, acute panic attacks, agitation, and hypertonia

Overview

- LSD is a semisynthetic odorless and colorless product of lysergic acid, a natural substance from the parasitic rye fungus *Claviceps purpurea*. It is also found naturally in several species of morning glory and Hawaiian baby woodrose plants.
- LSD is physiologically well tolerated; severe symptoms from recreational use are uncommon. Only in the setting of large ingestion (>400 mcg) has life-threatening toxicity occurred due to cardiovascular collapse and hyperthermia.
- There is high degree of psychological dependence but no evidence of physical dependence or withdrawal symptoms when acutely discontinued.
- Classified under Schedule I of the Controlled Substance Act.
- Psychological effects begin in 30–60 min and may last 8–12 h.

Etiology

- LSD displays both agonist and antagonist properties at the serotonin (5-HT) receptors, which are similar structurally with dopamine D2 receptors and have clinically related overlap.
- The most common route of exposure is via oral with rapid GI absorption.
- LSD is not associated with a physical or psychological addiction. Long-term use can result in persistent psychosis and hallucinogen persisting perception disorder ("flashbacks").

Usual Treatment

- Supportive reassurance; transfer pt to calm, quiet area with minimum external stimuli.
- Benzodiazepines seem to be the most effective agents for treating LSD psychosis and visual disturbances. If psychotic features persist after appropriate benzodiazepine treatment, then neuroleptics can be used as adjunct treatment.
- Rare cases require hemodynamic control, intubation, and ventilatory and supportive care.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT			Dilated, reactive pupils
CV	Sympathetic nervous system stimulation	Palpitations Sweating	Htn Tachycardia
RESP	No consistent changes	Diaphoresis	Tachypnea, apnea
ENDO	Hyperglycemia Mild hyperthermia		Elevated body temperature
CNS	Euphoria Anxiety, labile mood Tremors Visual hallucinations and illusions Synesthesia Distorted sense of time	Hx of drug ingestion	Altered mental status Hypertonia

Key References: Abraham HD, Aldridge AM, Gogia P: The psychopharmacology of hallucinogens, *Neuropsychopharmacology* 14(4):285–298, 1996; Passie T, Halpern JH, Stichtenoth DO, et al.: The pharmacology of lysergic acid diethylamide: a review, *CNS Neurosci Ther* 14(4):295–314, 2008.

Perioperative Implications

Preoperative Preparation

- Rule out associated traumatic injury.
- Hemodynamic control.
- Aspiration prophylaxis.
- Sedation if agitation is severe; benzodiazepines as first line treatment.

Monitoring

- Temperature
- Neuromuscular blockade

Airway

- Aspiration risk

Preinduction/Induction

- Salivation and N/V may justify the decision to utilize rapid sequence induction.
- Ketamine should be avoided, which may have synergic effects with LSD.
- Succinylcholine should be avoided.
- Exaggerated response to endogenous and exogenous catecholamines.

Maintenance

- Maintain normothermia.

Extubation

- At risk for aspiration.
- Continue supportive reassurance.

Adjuvants

- May have exaggerated response to sympathomimetic agents
- Potential for serotonin syndrome in pts taking concomitant serotonin precursors/agonist (SSRI, SNRI)
- Theoretical potential for ester local anesthetic toxicity due to inhibition of plasma cholinesterase activity
- Theoretical potential for prolongation of succinylcholine neuromuscular blockade due to inhibition of plasma cholinesterase activity

Anticipated Problems/Concerns

- Avoid injuries associated with agitation.
- Possible concomitant drug and/or alcohol use by pt.

Drug Overdose, Rat Poison (Warfarin Toxicity)

Michelle Braunfeld

Risk

- Major risk is hemorrhage, especially CNS or GI.
- Incidence: Risk of hemorrhage in 1–7.4% of pts chronically anticoagulated. Risk is dose-related and proportional to PT prolongation. Risk of hemorrhage doubles as INR increases from 2.0–2.9 to 3.0–4.4. It further quadruples as INR increases from 3.0–4.4 to 4.5–6.9. Age is associated with increased sensitivity to warfarin and increased incidence of bleeding complications.
- Rx for DVT, cerebral vessel atherosclerosis, prosthetic heart valves, mitral stenosis, and atrial fibrillation.

Perioperative Risks

- Bleeding
- Drugs that potentiate anticoagulant effects: Antibiotics (especially metronidazole, sulfonamides, cephalosporins), NSAIDs, phenytoin, cimetidine, barbiturates, alcohol

Worry About

- Bleeding complications of invasive procedures.
- Drug interactions.
- Transient protein C deficiency preceding effect on procoagulant levels at initiation of warfarin therapy leading to thrombotic complications.
- True poisoning with rodenticides (so-called superwarfarins) may result in prolonged clotting abnormality with abnormal PT values weeks to months post event because of the enormously long half-lives of these drugs.

Overview/Pharmacology

- Vitamin K antagonist.
- Cleared by hepatic and renal transformation and excretion. $T_{½}$ is approximately 40 h. Duration of action is 2–5 d.
- Onset of effect is delayed by 8–12 h because of time required to clear already synthesized clotting factors. For similar reasons, peak effect of a dose occurs 48 h post-administration.

Drug Class/Mechanism of Action/Usual Dose

- Blocks vitamin K–mediated carboxylation of factors II, VII, IX, X (procoagulants); protein C, protein S (anticoagulants).
- Carboxylation of coagulation factors oxidizes vitamin K. The vitamin K epoxide must be reduced to become active again. Coumarin anticoagulants block reduction of the epoxide. Thus large and/or repeat doses of vitamin K are needed for large overdoses or for long-acting forms.
- Chronically taken for systemic anticoagulation for DVT, CVA, prosthetic valves, and atrial fibrillation.
- Usual doses: Loading regimen varies, but maintenance dose is 2.5–10 mg/d.
- Alternatives: Other oral anticoagulation agents include the direct thrombin inhibitor, dabigatran, and the Xa inhibitors rivaroxaban and apixaban. Although these drugs all have the advantage of standardized dosing and none need lab monitoring, they also do not have established antidotes.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEME	Abnormal levels of factor II, IV, IX, X, and protein C, protein S	Easy bruising, prolonged bleeding time	Ecchymoses	PT

Key References: Holbrook A, Shulman S, Witt D, et al.: Evidence-based clinical practice guidelines: antithrombotic therapy and prevention of thrombosis, ed 9.: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, *Chest* 141(Suppl 2):e152S–e184S, 2012; Frumkin K: Rapid reversal of warfarin-associated hemorrhage in the emergency department by prothrombin complex concentrates, *Ann Emerg Med* 62(6):616–626, 2013.

Perioperative Implications

Possible Drug Interactions: Preoperative

- Increased effect: Antibiotics, NSAIDs, oral hypoglycemic, diazepam, cimetidine, diuretics, and phenytoin.
- Decreased effect: Methylxanthines, rifampin, antihistamines, corticosteroids, and barbiturates.
- Relatively minor surgical procedures may be performed without reversal of warfarin anticoagulation.
- Major surgical procedures warrant discontinuation of drug 1–3 d preop, with a target PT within 20% of nanoliter range. If discontinued, the need for bridging with low-molecular-weight heparin prior to surgery should be considered.
- For urgent surgery, pt may be given 10–20 mL/kg of FFP and 5–10 mg of vitamin K IV, with additional amounts of both given as needed.
- For emergent surgery, life-threatening bleeding, or the pt who cannot tolerate the volume of FFP for reversal, a four-factor PCC (KCentra in USA) is approved for use by the FDA. If a four-factor PCC is not available, evidence suggests effectiveness of a three-factor PCC (Bebulin, Profilnine, or FEIBA in USA) plus rVIIa or FFP. The value of rVIIa alone to reverse warfarin is unclear because, although it can normalize INR, the correlation of INR to clinical bleeding is not defined in that setting. This is because the PT is more sensitive to levels of VII and X than II or IX, and there is insufficient literature to evaluate a clinical effect. Regardless of what means are chosen, the need for repeat dosing should be considered and vitamin K IV should also be given since the effect of warfarin greatly exceeds the half-lives of these concentrates

Possible Drug Interactions: Adjuvants/Regional Anesthesia/Reversal

- Regional block: Relatively contraindicated without reversal of anticoagulation
- Peripheral block: Relatively contraindicated without reversal of anticoagulation

Anticipated Problems/Concerns

- It should always be kept in mind that the pt is chronically anticoagulated for an underlying thrombotic condition or risk. This should be balanced against the decision to reverse anticoagulation.
- All factor concentrates carry an inherent risk of thrombosis simply by their ability to disturb the balance of procoagulant and anticoagulants. Although such products as KCentra attempt to mitigate that by including heparin, antithrombin, protein C, and protein S, this is no guarantee against pathologic thrombosis.
- Because it contains heparin, KCentra is contraindicated in pts with a history of HIT.
- Hypothermia will potentiate anticoagulant effect.

Duchenne Muscular Dystrophy (Pseudohypertrophic Muscular Dystrophy)

Stephanie Black

Risk

- X-linked recessive; 1:3500 live male births; few known cases in females.
- Often undiagnosed until age 3–5 y; periop complications can occur before diagnosis.
- Deterioration through puberty to death usually before age 25 y.
- Periop risks may be present in female carriers.

Perioperative Risks

- Respiratory failure, prolonged mechanical ventilation
- Cardiac failure (CHF or arrhythmias)
- Hyperkalemia and rhabdomyolysis

Worry About

- Poor cardiac contractility, dilated cardiomyopathy, cardiac arrhythmias, pulm Htn from sleep apnea, MVP
- Poor respiratory function, restrictive lung disease from scoliosis, chronic pneumonia
- Aspiration risk from gastroparesis and dysphagia
- Possible hyperkalemic arrest with succinylcholine and volatile agents
- Associated with malignant hyperthermia-like syndrome unresponsive to dantrolene

Overview

- Most boys die from pneumonia, but heart failure is usually present by adolescence.
- Gradual onset of muscle wasting, replaced by fat/fibrosis, causing pseudohypertrophy.
- Hyperkalemic response to depolarizing NMBs may develop years before the onset of DMD symptoms; the prediagnosis infant may present with only mild gross motor delay.
- Increased sensitivity to nondepolarizing NM blockers.
- Use of Ca^{2+}-channel blocker (e.g., verapamil) may prolong or even cause NMB.
- Resting tachycardia common; cardiac involvement in 70% of cases, cardiac debilitation usually late.

Etiology

- X-linked recessive disease causing absence of dystrophin, destabilizing the sarcolemma
- Muscles (including myocardium) gradually replaced with fat and connective tissue

Usual Treatment

- Corticosteroids may increase strength and delay progression.
- Spinal rodding and fusion for scoliosis may increase comfort and ease of wheelchair use; pulmonary deterioration continues, and life may be only minimally prolonged.
- Tendon releases for contractures.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Conduction: heart block, SVT, prolonged QT Cardiomyopathy: Ventricular dilation or fibrosis, pHTN	Tachycardia CHF Sx: Orthopnea, DOE	Opening snap (MVP) CHF: crackles, JVD, edema	ECG ECHO Cardiac MRI
RESP	Decreased volume and flows Restrictive lung disease Sleep apnea Recurrent pneumonia/aspiration	SOB Snoring, apneic spells	Hypoxia Crackles Poor inspiratory effort	PFTs CXR SpO_2 on RA, polysomnogram
GI	Dysmotility, gastric dilatation, paralytic ileus			
GU	Bladder paralysis, impotence			
CNS	Decreased IQ		Mental status exam	
MS	Scoliosis, kyphosis Contractures Muscle destruction Macroglossia Poor IV access	Gross motor delay Progressive weakness Exercise intolerance	Pseudohypertrophy of calves, wheelchair dependence	Spine films Elevated CK levels (20–100× normal)

Key References: Birnkrant DJ, Panitch HB, Benditt JO, et al.: American College of Chest Physicians consensus statement on the respiratory and related management of patients with Duchenne muscular dystrophy undergoing anesthesia or sedation, *Chest* 132(6):1977–1986, 2007; Hayes J, Veyckemans F, Bissonnette B: Duchenne muscular dystrophy: an old anesthesia problem revisited, *Paediatr Anaesth* 18(2):100–106, 2008.

Perioperative Implications

Preoperative Preparation

- ECHO, ECG, and pulm function tests preop.
- Avoid or limit preprocedure sedation.

Monitoring

- Consider invasive cardiac monitoring based on EF and surgical procedure.
- Nerve stimulator.

Induction

- Succinylcholine contraindicated because of hyperkalemia risk.
- Limit volatile anesthetic exposure secondary to MH-like response.
- Avoid depressants of cardiac contractility; minimize arrhythmogenic medications.
- Consider regional technique to avoid the risks of GA.

Maintenance

- Variable response to NM blockers; titrate to effect.
- Consider using a "nontriggering" technique (MH precautions, TIVA, "clean" machine).
- Optimize regional or neuraxial blocks to minimize GA exposure.
- Avoid hypoxemia, large fluid shifts, and anemia to prevent uncompensated cardiomyopathy.

Emergence

- Potential for prolonged ventilator dependence greatest when vital capacity <30% of predicted.
- For GA cases, consider extubating directly to BIPAP and/or CPAP, weaning later.
- Outpatient surgery may be inadvisable due to late respiratory depression (cause unclear).
- Avoid postop shivering, which may cause rhabdomyolysis.

Anticipated Problems/Concerns

- Respiratory failure.
- Cardiomyopathy, CHF.
- Supraventricular tachydysrhythmias.
- Rhabdomyolysis, hyperkalemia, and cardiac arrest in response to succinylcholine and volatile agents have been described in boys years before clinical signs of DMD present.
- MH-like picture may be unresponsive to dantrolene.

Duodenal Atresia

Lynne G. Maxwell

Risk

- Incidence 1:5000–10,000 live births
- Male to female incidence is equal
- Trisomy 21 in 20–30%
- 45% are premature infants of pregnancy complicated by polyhydramnios
- Incidence of polyhydramnios 32–81%
- Mortality 3–5%; due not to duodenal atresia but to associated CHD or prematurity

Perioperative Risks

- Hypoxemia associated with immature lungs
- Hypoxemia due to CHD, persistent fetal circulation (pulm Htn)

Worry About

- Ventilation problems associated with prematurity.
- Other associated anomalies in 50% of cases: esophageal atresia (7%), other intestinal atresias, renal anomalies (5%), malrotation of the gut (30%), volvulus, imperforate anus (3%), annular pancreas (25%).

- CHD associated with trisomy 21 (ASD, VSD, AV canal).
- Aspiration on induction of anesthesia secondary to bowel obstruction.
- May be associated with cystic fibrosis.
- Late presentation can be associated with dehydration, hypovolemia, and hypochloremic alkalosis.

Overview

- Frequently premature infant of pregnancy complicated by polyhydramnios.
- Polyhydramnios may occur in the absence of premature birth.
- Diagnosis frequently made by prenatal ultrasound, allowing for parental counseling and planning for early repair; may not be detected until 28–32 wk gestation because of delay in development of proximal duodenal dilation.
- Vomiting after birth: May be copious and bile stained. If obstruction is proximal to ampulla of Vater, emesis is nonbilious.
- Flat abdomen.
- Dx is made by "double bubble" on abdominal x-ray (dilated stomach and proximal duodenum).
- Obstruction may be caused by partial obstruction: stenosis with perforated web or diaphragm rather than atresia; Dx may be delayed.
- Coexisting distal intestinal atresia is rare (<1%).

Etiology

- Unknown in sporadic cases
- More common in trisomy 21

Usual Treatment

- Fluid resuscitation with correction of any electrolyte abnormalities should precede surgery (especially in cases of prolonged vomiting).
- Surgical repair (duodenoduodenostomy) is curative; associated malrotation should be ruled out.
- Surgical technique may be open laparotomy or laparoscopic.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CHD—ASD, VSD, AV canal Persistent fetal circulation	Trisomy 21	Murmur Cyanosis	ECHO CXR Pulse oximetry
RESP	Respiratory distress syndrome of prematurity	Polyhydramnios Gestational age <36 wk	Tachypnea Retractions Flaring Grunting	CXR Pulse oximetry
GI	Duodenal obstruction Associated esophageal atresia	Bilious vomiting No gas in abdomen	Scaphoid abdomen	Abdominal x-ray Unable to pass OG tube
RENAL	Structural anomalies		Palpation of kidneys	Abdominal ultrasound

Key References: Aguayo P, Ostlie DJ: Duodenal and intestinal atresia and stenosis. In Holcomb III GW, Murphy JP, Ostlie DJ, editors: *Ashcraft's pediatric surgery,* ed 6, Philadelphia, PA, 2014, Elsevier, pp 414–429; Olsen M, Avery N, Khurana S, et al.: Pneumoperitoneum for neonatal laparoscopy: how safe is it? *Paediatr Anaesth* 23(5):457–459, 2013.

Perioperative Implications

Preoperative Preparation

- OG tube to decompress stomach and reduce gastric contents
- IV catheter placement with hydration (20 mL/kg NS) if Dx delayed beyond 24–48 h; correct electrolyte abnormalities.
- Surfactant for premature infants with significant lung disease.
- Confirm intramuscular vitamin K given as part of normal newborn care.

Monitoring

- Arterial monitoring for ABGs, electrolyte, and Hgb determination only in premature infants with significant lung disease, those with CHD, or those with extreme dehydration due to protracted vomiting; otherwise noninvasive BP sufficient as minimal blood loss expected.
- Temperature.
- Urinary catheter (small feeding tube) may be helpful in assessing adequacy of fluid resuscitation.
- Pulse oximetry, ECG, and end-tidal carbon dioxide and gas monitoring; preductal and postductal pulse oximetry in pts with congenital heart disease or persistent fetal circulation.

Anesthetic Technique

- Suction OG tube with infant supine and in left and right decubitus positions prior to induction and intubation.
- Awake intubation after preoxygenation only for actively vomiting, volume-depleted infants with abnormal airway anatomy.
- Rapid-sequence induction after preoxygenation for normovolemic pts with normal airway anatomy.
- Avoid N_2O to prevent intestinal distention.
- Nondepolarizing muscle relaxant helpful for surgical exposure.
- Second peripheral IV after induction.

Airway

- Precautions to prevent aspiration
- Abnormal airway anatomy unlikely

Preinduction/Induction

- Pt may be hypovolemic due to vomiting and/or poor feeding.
- Correct dehydration, hypochloremic alkalosis (failure to do so can shift oxyhemoglobin dissociation curve to left and reduce O_2 delivery to tissues).
- Debubble IV lines to prevent paradoxical air embolism.
- Type-specific blood available for transfusion (rarely needed).

Maintenance

- Mechanical pressure ventilation with rate 20–25, PIP 20–25, PEEP 2–5 to achieve adequate ventilation (tidal volume 8–10 mL/kg).
- Air/O_2 mixture to achieve O_2 saturation 92–96%, although some use 100% O_2 to provide reserve; data on retinopathy of prematurity due to operative exposure to 100% O_2 is not conclusive, and surgical retraction may restrict ventilation and cause atelectasis, which can cause desaturation.
- Surgical retraction/pressure on liver may decrease venous return and cause hypotension.
- Hemorrhage and/or air or carbon dioxide embolus has been reported prior to or after trochar insertion when laparoscopic technique is used; this may result in CV collapse, requiring CPR. Resuscitation drugs should be available.
- Cease insufflation of abdomen and evacuate gas from abdomen, left-side down/Trendelenburg position, 100% O_2, fluid administration, epinephrine bolus, cardiac compression if no cardiac output.
- Fentanyl or remifentanil/vecuronium or vecuronium/isoflurane or sevoflurane for premature infants.
- In full-term infants who may be immediately extubatable, consider caudal catheter threaded to low thoracic position. Dose with bupivacaine 0.25% (or ropivacaine 0.2%) with 1:200,000 epinephrine 0.5–0.75 mL/kg followed by continuous epidural infusion of 0.1% bupivacaine or ropivacaine at 0.2 mL/kg/h for postop pain relief.

Extubation

- May require postop ventilation if pt premature or has CHD.
- Full-term infants with effective epidural anesthetic and no or low-dose opioid administration may be extubated if effective spontaneous ventilation.

Anticipated Problems/Concerns

- Prematurity/respiratory distress syndrome/apnea.
- CHD.
- Hemorrhage, air, or gas embolus may occur at start of laparoscopic procedure.
- Risk of aspiration may continue postop; leave OG or NG tube in place.
- Later risk of GE reflux higher than normal (17%).
- Adequate fluid replacement.
- Other associated anomalies.

Ebstein Anomaly

Kavitha Pundi | Wanda C. Miller-Hance

Risk

- Incidence: Rare; <1:200,000 live births
- Accounts for <1% of congenital heart disease

Perioperative Risks

- Arrhythmias (approximately 20–25% incidence of accessory pathways)
- Intracardiac shunting
- Cyanosis and associated problems (e.g., polycythemia, hyperviscosity, altered vascular function, impaired cardiopulmonary performance)
- Ventricular volume overload
- Ventricular dysfunction

Worry About

- Delayed onset of action of IV agents due to blood pooling into dilated right-sided cardiac structures
- Rhythm disturbances: Atrial and ventricular
- Conditions that may allow for or enhance atrial level R-to-L shunting and increased hypoxemia
- Potential for paradoxical embolism
- Coexisting cardiac defects
- Increases in pulmonary vascular resistance
- Sequelae related to prior cardiovascular interventions

Overview

- Most common form of congenital TV disease.
- Primary congenital cause of TR.
- Results from incomplete delamination of the TV leaflets from the ventricular muscle during cardiac development.
- Wide morphologic spectrum and broad range of anatomic severity. Characterized by (1) downward displacement of septal and posterior TV leaflets attachments toward cardiac apex; (2) adhesion of leaflets to underlying RV myocardium; (3) redundancy of anterior leaflet ("sail-like"); and (4) dilation and thinning of "atrialized" portion of the RV with size reduction of functional chamber (RV myopathy).
- Pathophysiology: Primarily related to degree of TR, extent of RV contractile impairment and reduced compliance, and associated cardiac defects.
- Pts may present at any age.
- Extremely variable clinical spectrum ranging from no-to-minimal symptomatology, to intractable congestive heart failure; in the fetus it can be associated with marked cardiomegaly, arrhythmias, and hydrops.
- Interatrial communication (atrial septal defect or patent foramen ovale) frequently present, resulting in resting or exertional cyanosis due to bidirectional or R-to-L shunting.
- Associated pathology: Pulmonary stenosis or atresia (structural or functional), hypoplastic branch pulmonary arteries, RV outflow obstruction due to abnormal leaflets/chordal structures, ventricular septal defect, patent ductus arteriosus, abnormalities of the mitral and aortic valves, LV noncompaction, LV outflow tract obstruction, coarctation of the aorta.
- Ebsteinoid abnormality of the TV can be seen in association with congenitally corrected transposition of the great arteries.

Etiology

- Heterogeneous: Various genetic, pregnancy, and environmental risk factors implicated.
- Historic association with maternal lithium therapy during pregnancy.
- Most cases are sporadic with rare familial association.

Usual Treatment

- Highly dependent on clinical presentation, physiology, and coexisting cardiac malformations.
- Neonates with heart failure (secondary to severe TR and/or arrhythmias) or cyanosis (due to elevated pulmonary vascular resistance with an associated atrial level R-to-L shunt) may benefit from mechanical ventilation, diuretics, heart failure medications, inotropes, antiarrhythmics, alprostadil (PGE_1), oxygen/iNO, or other pulmonary vasodilators.
- Older children and adults with cyanosis, exertional dyspnea/decreased exercise tolerance due to progressive heart failure, or recurrent arrhythmias are managed with diuretics, antiarrhythmics, and heart failure medications.
- Cath or surgical ablation of atrial arrhythmias, maze procedure, pacemaker for AV block may be indicated.
- Surgery, when necessary, consists of TV repair with annuloplasty or valve replacement, plication of the atrialized RV, and closure of intracardiac communications. If a biventricular repair is not feasible, options include RV exclusion (Starnes procedure), "one and a half" ventricle repair (bidirectional Glenn connection to reduce venous volume load to the RV), or univentricular palliation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pulm hypoplasia (neonate) Pulm Htn (neonate)	Cyanosis Hypoxia	Tachypnea Resp failure, O_2 sat <90%	CXR, CT scan ABG/VBG, ECHO
CV	RV and/or LV dysfunction Arrhythmias R-to-L shunt	Dyspnea Palpitations Cyanosis at rest or exertion	Wide split S_2, S_3, murmur Tachycardia O_2 sat <90%	CXR, ECHO, MRI, cath ECG, Holter, EP study ABG/VBG, ECHO, cath, exercise test
GI	Liver congestion	Abdominal pain, edema	Ascites, jaundice, hepatomegaly, splenomegaly	Ultrasound/MRI/CT, LFTs (with INR), CBC, EGD
CNS	Paradoxical emboli Stroke	Headache Lethargy, seizures	Neurologic deficits	MRI or CT scan EEG
HEME	Polycythemia Iron deficiency	Headache, dizziness Fatigue	Clubbing Pallor	CBC Peripheral blood smear, ferritin, TIBC

Key References: Dearani JA, Mora BN, Nelson TJ, et al.: Ebstein anomaly review: what's now, what's next? *Expert Rev Cardiovasc Ther* 13(10):1101–1109, 2015; Ross FJ, Latham GJ, Richards M, et al.: Perioperative and anesthetic considerations in Ebstein's anomaly, *Semin Cardiothorac Vasc Anesth* 20(1):82–92, 2016.

Perioperative Implications

Preoperative Preparation

- Appropriate antibiotics for endocarditis prophylaxis.
- Large-bore peripheral IV access as required for planned procedure.
- Available emergency and antiarrhythmic drugs.
- Immediate access to cardioverter/defibrillator.
- Meticulous deairing of IV lines; consider the use of filters.

Monitoring

- Arterial line, CVP, PA cath as indicated; PA cath placement can be difficult and cardiac output measurements erratic.
- Close attention to the ECG.
- Careful monitoring of end tidal CO_2/pulse oximetry/blood gases.
- Urine output to assess renal perfusion.
- Consider the use of transesophageal echocardiographic monitoring in selected cases.

Airway

- Management based on the nature of the procedure
- Potential for bleeding of mucosal surfaces during instrumentation related to increased vascularity in chronic cyanosis

Preinduction/Induction

- Light premedication.
- Consider effects of anesthetic agents/mechanical ventilation on myocardial performance and hemodynamics.
- Potential hemodynamic compromise and rapid deterioration related to hypovolemia (diuretic/vasodilator therapy), myocardial depression, rhythm disturbances.
- Treat reductions in BP and rhythm problems as dictated by the hemodynamics.
- Consider risks and benefits of central neuraxial blockade as appropriate for the procedure.

Maintenance

- Maintain RV preload to provide adequate forward flow.
- Judicious use of fluids in the presence of ventricular dysfunction.
- Maintain a low pulmonary vascular tone to minimize RV afterload and enhance output.
- Normal to high heart rates to sustain forward flow and limit peripheral vascular congestion.
- Consider potential detrimental effects of the surgical procedure on preload/afterload leading to reductions in cardiac output (e.g., increased intraabdominal pressure associated with pneumoperitoneum during laparoscopic procedures).
- Optimize RV and LV function (inotropic support and vasoactive drugs as needed).

Extubation

- Pts may require postoperative mechanical ventilation.

Postoperative Period

- Close monitoring of volume status, UOP/perfusion especially in the setting of baseline ventricular dysfunction
- ECG monitoring for arrhythmias
- Adequate pain control

Anticipated Problems/Concerns

- Potential need for postprocedure/surgery ICU care
- Clinical presentation early in life associated with poor prognosis

Echinococcosis

Mark R. Jones | James M. Riopelle | Alan David Kaye

Risk

- Men approximately equal to women.
- *Echinococcus granulosus* causes cystic echinococcosis (hydatid disease) in people exposed to feces of dogs and other canids in endemic areas of nearly every continent.
- *E. multilocularis* causes alveolar echinococcus in people exposed to feces of infected foxes living in colder regions of the northern hemisphere. Cases of alveolar echinococcus continue to expand over the past 2 decades, despite increased awareness of the disease.
- *E. vogeli* and *E. oligarthrus* cause polycystic echinococcosis in people exposed to feces of infected dogs and wild carnivores in rural Central and South America.

Perioperative Risks

- Hydatid cyst rupture leads to anaphylaxis and spread of encapsulated organisms, which implant in exposed tissues (e.g., peritoneal cavity), later causing disseminated hydatidosis (bowel obstruction, cachexia, death)
- Failure to resect all echinococcal tissue due to microscopic or extensive disease extension
- Hemorrhage (if cyst attached to liver or major blood vessel)
- Systemic reactions to toxic agents instilled into cyst cavity; air embolism if cyst attached to a vein or hydrogen peroxide instilled into cyst cavity
- Postop jaundice, cholangitis, bacterial superinfection, vascular compression, and hepatic failure

Overview and Etiology

- Parasitic disease caused by organism classified as flatworm (adult stage). Parasite cycles through four different stages (adult tapeworm, egg, oncosphere, metacestode) each adapted to maximize survival in the two host organisms:
  - Definitive host: Carnivore; intestines contain adult flatworms releasing eggs into feces.
  - Intermediate host: Herbivore/omnivore (sheep, small rodents, man); ingests minute amount of feces of definitive host; eggs hatch in stomach and release oncospheres (first larval stage), which penetrate gut blood vessels and distribute to potentially any organ, especially liver and lung. Develop into slowly expanding fluid-filled cysts (metacestodes). Inner (germinal) layer of metacestode buds off tiny encapsulated protoscolices (Gk: juvenile heads) which accumulate to form hydatid sand.
- A definitive host eats infected organs of intermediate host; protoscolices are released into intestinal lumen; these evaginate; anterior parts attach to intestinal epithelium and become adult tapeworms.
- Adult *E. granulosus* (2–11 mm) inhabits small intestine of canid (dog, wolf, coyote, dingo, jackal); eggs distribute to grass eaten by sheep, goats, camels, yaks, cattle, pigs, horses, marsupials; man becomes infected via hand-to-mouth contact with fecally contaminated object. Cysts of volume up to 1000 mL form within intermediate host (or man—sometimes called dead end host), physically compromising organ function.
- Adult *E. multilocularis* (1–5 mm) inhabits small intestine of fox (occasionally dog, bush dog, rarely cat); intermediate host usually a rodent. Cysts become multiple and invade target organs.
- *E. vogeli* and *E. oligarthrus* rarely cause human disease (if present of polycystic type).

Usual Treatment

- *Echinococcus granulosus:*
  - Medical: Cyst instillation with nonspecific histotoxic solution (hypertonic NaCl, alcohol, silver nitrate, povidone-iodine, formaldehyde, hydrogen peroxide, chlorhexidine) in sequence of PAIR. Not appropriate if multiple cysts, cyst architecture subdivided into daughter cysts, or cysts balloon out via narrow passages to form satellite cysts. Increasing in popularity; complications include biliocutaneous fistula and bacterial superinfection of residual cyst cavity. Technique variants include percutaneous evacuation (sometimes using cutting-aspiration device), cyst catheterization/continuous irrigation.
  - Laparoscopic: Cystotomy, toxin irrigation, partial cystectomy (± use of aspirator-grinder); 77.16% of hydatid cyst surgeries are laparoscopic, regardless of location; cysts near major vascular structures require open technique.
  - Open: Complete resection for concealed, extensive, or invasive disease; attempt to avoid spilling contents; histotoxic solutions often used in conjunction.
- *Echinococcus multilocularis:*
  - Exhibits cancer-like growth behavior. Specific immunologic tests in combination with high-performance imaging techniques promise substantial improvements in early diagnosis of alveolar echinococcosis, which is essential for curative treatment, staging, and follow-up. Radical open surgical resection if possible; liver transplantation considered if disease confined to liver. Prevent recurrence by treating infected family companion animals with oral anthelmintic and praziquantel.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL		Pt from endemic area, fever, itching, family Hx	Fever (if high, possible superinfection)	US, CT, or MRI imaging of any part of body
GI	Liver mass (70%), biliary obstruction, Budd-Chiari	Abdominal pain dyspepsia, vomiting fatigue; previous surgery for same disease	Jaundice; signs of cirrhosis	Abdominal US, CT, or MRI; PT/ INR
RESP	Lung mass (20%) bronchial obstruction, pulm Htn	Chest pain, cough, SOB, hemoptysis	Fever (superinfection)	CXR; thoracic ultrasound, CT, or MRI; sputum microscopy for protoscolices
RENAL	Ureteral obstruction			Abdominal ultrasound, CT, MRI
HEME	Eosinophilia, antibodies	Duration of albendazole therapy (marrow toxicity)		CBC, eosinophil count; plt count; antibody-based tests (e.g., ELISA), newer DNA-based tests: problems with cross-reactivity, false negativity
CV	Obstruction, anaphylaxis			ECHO
GYN	Incidental occurrence	Last menstrual period	Signs of pregnancy	Blood or urine pregnancy test
CNS	Cyst (1.5%)	Seizure	Localizing neurologic findings, gait abnormality, hydrocephalus	Head CT, MRI

Key References: Gottstein B, Stojkovic M, Vuitton DA, et al.: Threat of alveolar echinococcosis to public health—a challenge for Europe, *Trends Parasitol* 31(9):407–412, 2015; Tuxun T, Zhang JH, Zhao JM, et al.: World review of laparoscopic treatment of liver cystic echinococcis—914 patients, *Int J Infect Dis* 24:43–50, 2014.

Perioperative Implications

Preoperative Preparation

- Review all imaging studies.
- Ensure entire surgical team aware of nature of disease.
- If liver disease, OR table capable of intraop cholangiography; if cirrhosis, normalize coagulation status (vitamin K, FFP); ensure intraop availability of PRBC (possibly FFP, plts, cryoprecipitate).
- Know anatomic extent of disease, proposed surgical approach (position, laparoscopy/incision); know backup plan if disease more extensive than thought.
- Pt to take oral benzimidazole anthelminthic (albendazole) 1 wk preop, 3 mo postop.

Monitoring

- Based on planned/potential procedure.
- Consider urinary catheter; if possibly extensive, consider invasive hemodynamic monitoring (art line, cent line), serial hct/coag/abg, precordial Doppler or TEE to diagnose embolism (air, CO_2, cyst contents), serial Na^+ if hypertonic NaCl used.
- Observe for SQ emphysema if laparoscopic approach.

Airway

- Tracheal intubation for laparoscopic or open procedure; double-lumen tube to protect nondiseased lung if pulm echinococcosis

Induction

- Rx choice based on general health status and concurrent diseases

Maintenance

- Large-bore venous access and fluid warmer(s) if hemorrhage risk.
- Consider gastric tube (whether laparoscopic or open).
- Immobile operative field essential, especially during portions of procedure where cyst spillage could occur.
- Have on-hand in case of anaphylactic or hemorrhagic shock: Epinephrine, vasopressin, other inotrope/vasopressor, $CaCl_2$, and $NaHCO_3$, adequate crystalloid/colloid/blood products.

- If gas embolism suspected, aspirate central line; if none, consider subcostal insertion of spinal needle attached to large aspirating syringe directly into RV.

Extubation

- Base on usual criteria, extent of operative procedure, pt's age and physical condition, and concurrent disease

Postoperative Period

- Base pain control plan on nature and extent of resection; regional anesthesia an option if coagulation status permits.
- Base monitoring on extent of resection, blood loss, and preop health status.
- Watch for pneumothorax, subphrenic abscess, pneumonia, bronchobiliary fistula, jaundice, hepatic failure, and septicemia.

Anticipated Problems/Concerns

- If the pt is being treated in a nonendemic area, surgical team may be unfamiliar with disease; anthelmintic medications may require special order well in advance of procedure.
- Consider *Echinococcus* in any pt from endemic area presenting for surgical excision of cyst; search for others using US imaging; consider ID consult and serologic testing.
- Cysts may eventually involute and degenerate, hence the conservative nature of treatment in nonemergent cysts.
- Arrange ultrasound imaging in family/neighbors/farm animals capable of being intermediate hosts.
- Examine stool of companion canids for eggs and segments.

Eclampsia

Emily Baird

Risk

- Incidence varies from 0.01–0.1% of pregnancies in developed countries.
- Occurs in 1–3% of pts with preeclampsia.
- Risk factors include age <20 y old, nulliparity, anemia, diabetes, and preexisting heart disease.

Perioperative Risks

- Eclampsia is a factor in approximately 10% of all maternal deaths in developed countries.
- Maternal complications include adult respiratory distress syndrome, acute renal failure, cardiopulmonary arrest, and CVA.
- Fetal complications include respiratory distress syndrome, small for gestational age, preterm birth, and intrauterine growth restriction.

Worry About

- Risk of pulm aspiration and hypoxemia with seizure
- Fetal bradycardia may occur during or following seizure
- 90% of women with eclampsia have manifestations of severe preeclampsia (Htn, proteinuria, renal insufficiency, pulmonary edema, coagulopathy)

Overview

- New onset of generalized, tonic-clonic seizures, and/or unexplained coma during the peripartum period in a woman without a preexisting neurologic disorder.
- Eclamptic seizures can occur during the antepartum (60%), intrapartum (20%), or postpartum (20%) period.
- Onset of eclampsia is generally preceded by signs of severe preeclampsia but approximately 10% occur without Htn.

Etiology

- Precise etiology is unknown, but two models have been proposed based on the central role of Htn in the majority of eclampsia cases.
  - Forced dilation theory: Htn exceeds the upper limit of cerebral autoregulation leading to hyperperfusion, endothelial dysfunction, and interstitial edema.
  - Vasospasm theory: Htn causes overactivation of cerebral autoregulation leading to vasoconstriction, hypoperfusion, localized ischemia, and cerebral edema.

Usual Treatment

- Establish patent airway and maintain maternal oxygenation.
- Maintain left uterine displacement.
- Seizure treatment/prophylaxis: Magnesium sulfate (4–6 g bolus over 20 min followed by 1–2 g/h infusion ± 2 g bolus over 10 min for recurrent seizure).
- Antihypertensive treatment for SBP ≥160 mm Hg and/or DBP ≥110 mm Hg: Labetalol (10–20 mg IV) and/or hydralazine (5–10 mg IV).
- Expeditious delivery via induction/augmentation of labor (preferred) or cesarean delivery (if persistent maternal or fetal distress).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn Reduced intravascular volume LV dysfunction (rare)	Dyspnea, peripheral edema	Htn, peripheral edema, decreased CVP	ECHO if suspect LV dysfunction
RESP	Airway edema Pulm edema	Snoring, stridor dyspnea, orthopnea	Tachypnea, dyspnea, hypoxemia, rales	CXR ABG
RENAL	Proteinuria Renal failure Decreased RBF Decreased GFR	Rapid weight gain, decreased urine output	Nondependent edema	24-h urine protein, BUN, Cr, uric acid
HEME	Thrombocytopenia Microangiopathic hemolysis DIC	Mucosal bleeding, easy bruising	Petechiae, bleeding from puncture sites	Hgb, Hct, plt, fibrinogen, and FSP
NEURO	Seizure Coma	Headache, visual disturbances	Hyperexcitability, hyperreflexia	CT/ MRI if focal deficits or prolonged coma
FETUS	Fetal distress IUGR Oligohydramnios			Fetal heart monitor Fetal ultrasound

Key References: Leffert LR: What's new in obstetric anesthesia? Focus on preeclampsia, *Int J Obstet Anesth* 24(3):264–271, 2015; Parthasarathy S, Kumar VR, Sripriya R, et al.: Anesthetic management of a patient presenting with eclampsia, *Anesth Essays Res* 7(3):307–312, 2013.

Perioperative Implications

Monitoring

- Standard maternal monitors including noninvasive BP, pulse oximetry, and UO.
- Indications for invasive BP monitoring: (1) BP poorly controlled; (2) frequent blood sampling; or (3) infusion of potent vasodilators (nitroprusside or nitroglycerin).
- Indications for invasive central venous monitoring: (1) infusion of potent vasoactive agents; (2) pulmonary edema; and (3) cardiomyopathy.
- Electronic fetal heart monitoring.

Regional Anesthesia for Labor and Delivery

- Benefits of an early epidural: (1) high-quality analgesia (attenuates hypertensive response to pain); (2) improvement in uteroplacental circulation; and (3) avoidance of general anesthesia if emergency cesarean delivery indicated.
- Assessment of coagulation status, as outlined previously, should be checked prior to both placement *and* removal of epidural cath.
- Avoid IV fluid boluses prior to neuraxial anesthesia because of the increased risk of pulm edema.

- Pts may display greater sensitivity to vasopressors; systemic and neuraxial administration of vasopressors should be used with caution.

General Anesthesia for Cesarean Delivery

- Neuraxial anesthesia preferable to general anesthesia for cesarean delivery.
- Potential for difficult intubation secondary to airway edema.
- Htn accompanying laryngoscopy increases the risk of cerebral hemorrhage and pulm edema.
- Induction with propofol increases seizure threshold and reduce $CMRO_2$ and CBF.
- Magnesium sulfate increases the potency and duration of depolarizing and nondepolarizing muscle relaxants.
- Avoid hypercarbia, which lowers seizure threshold.
- Maintain CPP (MAP – ICP) and avoid hypoxia, hyperthermia, and hyperglycemia to prevent further neurologic injury.

Postoperative Period

- Continue magnesium sulfate infusion for 24 h after delivery and/or last seizure.
- Increased risk of pulm edema as extracellular fluid is mobilized leading to increased intravascular volume.
- Most eclamptic pts have complete resolution of neurologic abnormalities.

Anticipated Problems/Concerns

- 10% will have recurrent seizures in the absence of prophylaxis with initial seizure.
- Eclamptic seizures can occur up to 4 wk postpartum.
- Cerebral hemorrhage accounts for 15–20% of deaths from eclampsia.

Ehlers-Danlos Syndrome

Christopher J. Cullom | Alan David Kaye

Risk

- EDS has an overall incidence of 1:10,000-25,000, with no ethnic predisposition.
- Six major subtypes, each with slightly different and unique phenotypes.
- Symptoms involve skin, ligaments, joints, and vessels.

Perioperative Risks

- Valvular abnormalities or major vessel dissection/aneurysm
- Unstoppable bleeding
- Pneumothorax from positive pressure ventilation or pneumoperitoneum
- Neuropathy or musculoskeletal injury from positioning
- Airway difficulty from atlanto-occipital instability

Worry About

- Musculoskeletal injury from positioning.
- Airway damage due to repeat intubations.
- TMJ luxation from intubation or mask ventilation.
- Postural orthostatic tachycardia syndrome possible in EDS; thus preop crystalloid and early use of vasopressors recommended.
- Initiate preop crossmatching of RBCs and use of cell-saver for major surgery. DDAVP improves bleeding time and transfusion requirement.
- Use ultrasound when performing central lines or arterials lines to avoid vessel dissection.
- Generally avoid neuraxial blockade due to risk of bleeding.

Overview

- EDS I, EDS II, and hypermobile type (EDS III) is found in 90% of cases.
- Vascular type (EDS IV) is found in 3–10% cases.
- Kyphoscoliotic (EDS VI), arthrochalasis (EDS VIIA/B), and dermatosparaxis (EDS VIIC) types are rare cases. Principal clinical features include tissue fragility, easy bruising, skin hyperextensibility, delayed wound healing, joint hypermobility, and atrophic scarring.
- Initial manifestation is usually easy bruising. Bleeding from gums after brushing or bleeding after minor trauma is common.
- Platelet count or bleeding time is normal, yet a Rumpel-Leede test may be positive.
- Cardiac manifestations include arterial aneurysms, arterial rupture, varicose veins, aortic regurgitation, mitral valve prolapse, or conduction disturbances.
- Other important manifestations include pneumothorax, diverticula of intestine, megaesophagus, or megacolon.
- EDS types I and II notably present with very soft, fragile skin.
- Frequent joint dislocations happen at shoulder, hip, and patella, typically with EDS III.
- EDS IV has the most severe presentation and only forms with increased risk of death due to cardiac pathology.
- EDS VI is recognized by kyphoscoliosis, muscle hypotonia, and joint hypermobility.
- Arthrochalasia type (EDS VII A/B) presents with joint hypermobility and congenital bilateral hip dislocation.
- Dermatosparaxis type (EDS VII C) presents with severe bruising, extreme skin fragility, large fontanels, and short stature.

Etiology

- Mutation in gene encoding for fibrillar collagen proteins or enzymes can be involved in modifications of these proteins.
- Type I collagen is the predominant type in body. Mutation in type I results in EDS VIIA/B. Mutation in type V collagen that is coexpressed with type I results in EDS I/II.

Usual Treatment

- No treatment for EDS; however, there are preventative guidelines.
- Protective pads for pressure points during positioning.
- Avoid antiplatelet drugs and use DDAVP for pts at high risk of bleeding.
- Baseline ECHO and ECG, especially for EDS type IV.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Mitral valve prolapse, aortic regurgitation, arterial aneurysm/rupture, conduction abn	Dizziness Palpitations Chest pain	Orthostatic hypotension Arrhythmia	ECG, ECHO
RESP	Pneumothorax, airway difficulty		SOB, wheezing	CXR
GI	Intestinal diverticula, megacolon			Abdominal x-ray
HEME	Bleeding propensity			CBC, Rumpel-Leede test
MS	Skin fragility, joint dislocations, TMJ dislocation		Skin fragility testing	X-ray of extremities
NEURO	Atlanto-occipital instability		Cervical spine eval	
HEENT	Retinal detachment		Visual acuity, ophthalmoscopic exam	

Key References: Weismann T, Castori M, Malfait F, et al.: Recommendations for anesthesia and perioperative management in patients with Ehlers-Danlos syndrome, *Orphanet J Rare Dis* 9(109):1–9, 2014; Johnston B, Occhipinti K, Baluch A, et al.: Ehlers-Danlos syndrome: complications and solutions concerning anesthetic management, *Middle East J Anaesthesiol* 18(6):1171–1183, 2006.

Perioperative Implications

Preoperative Preparation

- Genetic counseling and identification of EDS type
- Standardized bleeding history
- History of intubation difficulty
- Echo to exclude cardiac pathology
- Type and crossmatch of RBCs as well as avoidance of antiplatelet drugs

Monitoring

- Avoid invasive monitoring whenever possible due to bleeding risk.

Airway

- Atlanto-occipital instability creates airway difficulties.
- Use fiberoptic intubation to avoid multiple intubation attempts in the setting of fragile mucosa.

Preinduction/Induction

- Use of padding during position and appropriate tape to avoid shear forces and external tissue pressure
- Eye protection due to risk of retinal detachment

Maintenance

- No anesthetic or pharmacotherapy contraindications.
- BP control due to fragile vessels, particularly if there are undiagnosed aneurysms.
- Monitor for pneumothorax due to barotraumas.

Extubation
- Usual criteria

Postoperative Period
- Careful positioning and use of tape in PACU
- Early mobilization to avoid loss of strength
- Postop N/V prophylaxis to avoid esophageal tears

Regional Anesthesia
- Generally avoid due to potential risks.

Anticipated Problems/Concerns
- Cardiac pathology
- Hemodynamic instability and hypotension
- Airway difficulty
- Bleeding propensity
- Nerve and soft tissue injury due to positioning
- Tissue or vessel fragility
- Pneumothorax

Eisenmenger Syndrome

Inna Maranets

Risk
- 8% of all CHD pts.
- 11% of pts with intracardiac or aortopulmonary shunt, allowing continuous exposure of pulm vasculature to systemic arterial pressure.
- VSD is the most common lesion.

Perioperative Risks
- High risk of cardiovascular complications when undergoing noncardiac surgery; mortality reaching 30%.
- Severity of pulm Htn cyanosis, tricuspid regurgitation, and right ventricular dysfunction are important factors.
- Additional acquired cardiac and systemic diseases, such as CAD and renal dysfunction.
- Underlying pathology, urgency, duration of surgery, and anesthetic choice contribute to the risk.
- Bleeding due to platelet dysfunction.
- Mortality rate of pts with ES carrying pregnancy to viability is 27–30%, most often at delivery or postpartum.
- Fetal risks: Increased risk of preterm labor and intrauterine growth retardation; fetal demise of 75%.
- Cesarean section carries higher mortality: 70% versus 30% for vaginal delivery.

Worry About
- R-to-L shunt, pulm Htn, RV and LV ventricular failure, hypoxemia, polycythemia.
- Minor decrease in SBP can cause increase in R-to-L shunt, decreased pulm blood flow, hypoxia, and cardiovascular collapse.
- Increased blood viscosity can lead to thromboembolic phenomena, paradoxical emboli, hemoptysis.
- Arrhythmias, ventricular and supraventricular.
- May not tolerate positive pressure ventilation.
- Decreased systemic vascular resistance of pregnancy worsens R-to-L shunt.
- Inability to meet increased demand for O_2 with gestation and labor.
- Delivery produces autotransfusion with RV failure.
- Excessive bleeding with previous heparinization.
- Postpartum increase in PVR.

Overview
- ES is defined as pulm Htn at systemic level due to high PVR with reversed or bidirectional shunt through communication between the two circulations.
- Communication may be at aortic level (PDA, aortopulmonary window), intracardiac (ASD, VSD, AV canal, TAPVR) or single ventricle.
- Uncorrected L-to-R shunt leads to irreversible fixed pulm vascular obstructive disease.
- Characterized by pulm Htn, R-to-L shunt, and RV dysfunction.
- Overall poor prognosis; mean age at death: 25 y.
- Syncope, increased right-sided filling pressures, and systemic arterial desaturation below 85% indicate poor prognosis.
- 50% of pregnant pts die in association with pregnancy.
- Some pulm vascular reactivity may exist in the pulm vasculature of pregnant women; may be due to systemic hormonal changes of pregnancy.

Etiology
- Individuals with large unrestricted intracardiac or aortopulmonary communication have large L (systemic)-to-R (pulm) shunts.
- Uncorrected L-to-R shunt overloads pulm vasculature and RV.
- Continuous exposure to systemic pressure leads to pulm arteriolar medial hypertrophy, intimal proliferation, and fibrosis.
- Progressive pulm capillary and arteriolar occlusion leads to fixed increased PVR.
- As pulm pressure exceeds systemic, shunt reverses to R to L.

Usual Treatment
- Repair of intracardiac lesion is contraindicated.
- Supplemental oxygen to decrease PVR.
- Avoidance of medications that can cause hypotension, worsening cyanosis or hemorrhage (calcium channel blockers, antiplatelet agents, anticoagulants).
- Phlebotomy to treat hyperviscosity, extreme erythrocytosis (Hc >65%), and bleeding diathesis.
- Single or bilateral lung transplantation with repair of the primary cardiac defect.
- Combined heart-lung transplant in select pts.
- With expected high maternal mortality, pregnant pts with ES should initially be counseled to terminate pregnancy.
- For the pt who wishes to continue with pregnancy:
  - Hospital admission early in third trimester.
  - Anticoagulation with heparin: SQ heparin 5000–10,000 U bid.
  - Pts with O_2 sat <80% on room air should be fully anticoagulated.
  - O_2 Rx.
  - Monitor for preterm labor
  - Medical Rx: Diuretics, antiarrhythmics, inotropes

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	R-to-L shunt Right and left ventricular enlargement/failure	DOE, fatigue, syncope edema, orthopnea, anginal chest pain, arrhythmias	Elevated jugular venous pressure, increased intensity of S_2, split S_2 and S_3; decrescendo murmur of pulmonic regurgitation, holosystolic murmur of tricuspid regurgitation; rales; right parasternal heave	ECG CXR ECHO MRI Cardiac cath
RESP	Pulm Htn	Dyspnea, hemoptysis	Palpable pulm artery Cyanosis, clubbing	Pulse oximetry ABG, Hct (polycythemia)
NEURO	Neurologic abnormalities	Headache, dizziness, visual disturbances, CVAs	Neuro exam	CT scan, MRI
HEME	Polycythemia, Hyperviscosity	Headache, weakness, blurred vision, pruritus	Splenomegaly, facial erythema, bleeding gums	CBC

Key References: Ammash NM, Connolly HM, Abel MD, et al.: Noncardiac surgery in Eisenmenger syndrome, *J Am Coll Cardiol* 33(1):222–227, 1999; Bennett JM, Ehrenfeld JM, Markham L, et al.: Anesthetic management and outcomes for pts with pulmonary hypertension and intracardiac shunts and Eisenmenger syndrome: a review of institutional experience, *J Clin Anesth* 26(4):286–293, 2014.

Perioperative Implications

Preoperative Preparation
- Continue antiarrhythmic medications and withhold diuretics.
- Discontinuation of heparin; consider reversal with protamine.
- Endocarditis prophylaxis depends on the type of operation (AHA Guidelines).
- In pregnant pts avoid aortocaval compression at all times.
- IV lines must be carefully de-aired, consider placing air filters.

Monitoring
- Pulse oximetry.
- With uncorrected patent ductus arteriosus, use simultaneous right hand (preductal) and foot (postductal) pulse oximetry to estimate changes in shunt fraction.
- Arterial line for early recognition of sudden alteration of BP and repeated blood gas sampling.
- CVP line.
- PA cath use must be balanced against potential complications:
  - Difficult to position in PA.
  - High risk of arrhythmias, thrombi, paradoxical emboli, and PA hemorrhage.
  - Misleading data: Unreliable PCWP and measurement of CO with shunt.

Airway
- Preop administration of Bicitra, metoclopramide, and ranitidine if needed
- NPO for 8 h (if possible)

Preinduction/Induction
- No one best technique reported.
- Goal of any technique is to maintain both cardiac output and SVR.
- Combining short-acting IV narcotic (fentanyl), low-dose induction agent (sodium thiopental or ketamine), and inhalational agent (sevoflurane or isoflurane) with muscle relaxant devoid of cardiovascular effects (vecuronium or rocuronium).
- For labor:
  - Provision of effective analgesia prevents increased release of catecholamines, which increases PVR.
  - Coaxial technique: Initial intrathecal dose of narcotic.
- For cesarean section:
  - Regional: Slow induction of epidural anesthesia; counteract sympathectomy with vasopressor and maintenance of preload.
  - General anesthesia: Avoid rapid-sequence with risk of precipitating increase in PVR or inducing myocardial depression; maintain cricoid pressure through induction; avoid increase in PVR, decrease in SVR, hypoxia, hypercarbia, and myocardial depressants.

Maintenance
- GA: Narcotic, low-dose inhalational agent, muscle relaxant.
- Avoid hypotension (decrease SVR), acidosis, hypercarbia and hypoxia (increase PVR).
- For labor:
  - Epidural infusion with low-dose local anesthetic/narcotic solution.
  - Avoid Valsalva maneuver and pushing; delivery with vacuum or forceps.
- For cesarean:
  - High-dose narcotic technique.
  - Amnesia with benzodiazepine.
  - Avoid halogenated agents: Myocardial depression, decrease SVR.
  - Avoid nitrous oxide: Increase PVR, higher FIO_2.

Extubation
- High-dose narcotic technique may necessitate postop ventilation.

Adjuvants
- Avoid N_2O.
- Maintain SVR with dilute solution of phenylephrine.
- Inotrope, vasodilator for treatment of failure.
- Cautious use of oxytocin (systemic vasodilation).
- Avoid prostaglandin F (increase in PVR).
- Resume anticoagulation in postpartum period.

Postoperative Period
- Pain management is critical.
- In pregnant pts, death most often occurs at delivery or postpartum.
- Possible hemodynamic changes:
  - Excessive blood loss: Replace volume.
  - Autotransfusion: Treat with vasodilator, inotrope, judicious use of diuretic.
  - Arrhythmias: Sinus bradycardia, AV block, EMD.
  - Pulm emboli.
  - Postpartum increase in PVR; reason unknown.

Anticipated Problems/Concerns
- Unresponsive, increased PVR or decreased SVR with loss of oxygenation
- CHF

Emphysema

Amy C. Robertson | William R. Furman

Risk
- Incidence in USA: 4.7 million.
- Prevalence, incidence, and mortality increase with age.
- Higher in males than females.
- Higher in whites than nonwhites.

Perioperative Risks
- Intraop bronchospasm
- N_2O expansion of bullae
- Postop respiratory failure
- Postop pulm infection

Worry About
- Worsening of baseline pulm function, caused by:
  - Bronchospasm.
  - Acute bronchitis or pneumonia.
  - Pulm embolism.
- Worsening of baseline cardiac function caused by right heart failure.
- Most common comorbidities include ischemic heart disease, diabetes, skeletal muscle wasting, osteoporosis, and lung cancer.

Overview
- Anatomic: Destruction of interalveolar septa and loss of pulm elastic recoil, leading to formation of bullae and development of irreversible expiratory airflow obstruction.
- Remodeling of the small airway compartment and loss of elastic recoil result in progressive decline of FEV_1 and lead to static and dynamic hyperinflation.
- The "pink puffer" has dyspnea, hyperinflation, distant breath sounds, low diffusing capacity (decreasing D_LCO to <60% predicted).
- The "blue bloater" has chronic bronchitis, leading to hypoxemia, polycythemia, and CO_2 retention.
- Hypoxia, hypercarbia, and cor pulmonale are late developments.
- Mucociliary clearance is often worsened after inhalational anesthetics.
- Diaphragmatic mechanics are impaired by anesthetics, sedatives, NMBs, interscalene blocks, and supine positioning.

Etiology
- According to the elastase-antielastase hypothesis, the lung is normally protected from injury to its elastic tissues by antielastases, including API, which is also called a_1-antitrypsin. According to this theory, emphysema may be acquired or genetic.
- Acquired: Related to inhaled oxidants (cigarette smoke or other occupational exposures), which are believed to inactivate API, thus compromising lung matrix repair after injury.
- Genetic: Absent or abnormal API, also known as a1-antitrypsin deficiency, which accounts for a small fraction of cases.

Usual Treatment
- Smoking cessation (>6–8 wk may lessen anesthetic risk).
- Relief of symptoms by treatment of bronchospasm and infection.
- Most frequent cause of acute exacerbation is viral or bacterial infection. Treatment may consist of increased doses of bronchodilators plus systemic corticosteroids and antibiotics.
- In advanced cases, if hypoxia and cor pulmonale have developed, O_2 therapy may improve quality of life and survival.
- Lung volume reduction surgery may be considered for those with predominantly upper lobe disease and/or low exercise tolerance.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Tumors secondary to smoking	Voice change	Hoarseness, stridor, inspiratory obstruction	Flow-volume loops
CV	Cor pulmonale (late)	Edema, severe dyspnea	Signs of pulm Htn Hepatosplenomegaly Pedal edema, cyanosis, pleural effusions, usually without pulmonary edema	CXR ABG
	Pulm emboli	Episodic SOB Arrhythmias Hard to differentiate from course of underlying illness	May reveal DVT in legs	CXR High-resolution CT V/Q scan Pulm angiogram
RESP	Bronchospasm	Recent increase in dyspnea or decrease in exercise tolerance	Increased respiratory rate Increased expiratory time Increased accessory muscle use	Spirometry pre- and post-bronchodilators
	Pneumonia	Fever, dyspnea, increased sputum	Signs of pulm consolidation	CXR, WBC

Key References: Decramer M, Janssens W, Miravitlles M: Chronic obstructive pulmonary disease, *Lancet* 379(9823):1341–1351, 2012; Hausman MS, Jewell ES Engoren M: Regional versus general anesthesia in surgical patients with chronic obstructive pulmonary disease: does avoiding general anesthesia reduce the risk of postoperative complications? *Anesth Analg* 120(6):1405–1412, 2015.

Perioperative Implications

Preoperative Preparation

- Optimize bronchodilation.
- Eradicate any underlying bacterial infection.
- Encourage smoking cessation if this can occur >6 wk before surgery.
- Consider regional anesthesia where appropriate; associated with lower incidences of pneumonia, prolonged ventilator dependence, and unplanned postop intubation.

Monitoring

- Be cognizant of potential for increased gradient between $PETCO_2$ and $PaCO_2$.

Airway

- None, unless tumor present in airway

Preinduction/Induction

- If pt has airway reactivity, consider issues related to asthma/chronic bronchitis.
- Avoid N_2O when expansion of bullae is a risk.
- May avoid high concentrations of desflurane if airway reactivity is of concern.

Maintenance

- Recumbent positions impair chest wall muscle function, and abdominal muscle function usually needed for spontaneous ventilation.
- Ventilator settings: Avoid dynamic hyperinflation and development of intrinsic PEEP. Long expiratory times may be required; try to avoid high positive pressures (consider pressure controlled ventilation), especially if bullae are present.

Extubation

- Residual anesthetics may blunt the ventilatory response to CO_2, increasing the risk of postop respiratory failure.
- Pre-extubation bronchodilators.
- Unrelieved incisional pain, especially after abdominal or thoracic surgery, will impair breathing; consider postop epidural analgesia.
- Consider regional block and/or NSAIDs to lessen risk of respiratory depression.
- Pts may be semiconscious and combative owing to hypoxia and hypercarbia on emergence.
- Evaluate whether postop ventilation may be the safest approach until the residual anesthetic effects have dissipated. Extubation to NIPPV may be useful in such cases.

Adjuvants

- β-adrenergic agonists and anticholinergic agents for airway reactivity (may consider theophylline)
- Oral or inhaled steroids in selected pts

Anticipated Problems/Concerns

- Postop respiratory failure; consider NIPPV rather than reintubation in selected pts.
- Tension pneumothorax from ventilator-induced barotrauma.
- Airway plugging from secretions.

Encephalitis

Mary J. Njoku | David L. Schreibman

Risk

- Age; animal contact and occupational exposure to animals; ingestion of raw, partially cooked meat, fish, reptiles, or unpasteurized milk; insect contact; laboratory workers; healthcare workers; person-person transmission; recent vaccination and unvaccinated status; season (late summer/early fall, winter); travel and geographic exposure; immunocompromised state; transfusion and transplantation

Perioperative Risks

- Mental status alteration: Delirium, altered level of consciousness, clinical and subclinical seizures, increased ICP, and SIADH
- Unpredictable sedative and amnestic effects of anesthetics and adjunct drugs

Worry About

- Delayed awakening, postop delirium, clinical and subclinical seizures
- Hyperkalemic response to succinylcholine
- Transient myocardial dysfunction
- Paroxysmal sympathetic hyperactivity: Hyperthermia, tachycardia, hypotension, bradycardia
- Electrolyte abnormality secondary to SIADH and CPM with rapid correction of Na^+ abnormality

Overview

- Inflammation of brain parenchyma associated with clinical evidence of neurologic dysfunction.
- Manifestation of disease process or a component of another CNS or systemic illness.
- Organisms enter CNS via bloodstream or peripheral nerves.
- Symptoms: Altered mental status, altered consciousness, with or without focal neurologic abnormality, behavioral and personality changes in the presence of fever, irritability, changes in speech, changes in hearing, headache, photophobia, nuchal rigidity, vomiting, disorientation, lethargy, confusion, hallucinations, memory loss, clinical or subclinical seizures, myoclonus, coma.
- Dx is established by symptoms, epidemiologic Hx (exposure, season, geographic location), culture of blood/sputum/nasopharynx/stool, biopsy skin lesion/lymph node, serologic testing, CSF cells/protein/culture, CSF bacterial and viral antigens, CSF viral PCR, virus specific DNA sequencing, MRI, EEG, and CT scan (if MRI unavailable). Brain biopsy is rarely performed but should be early.

Etiology

- Unknown in most pts; manifestation of illness outside CNS
- Infectious:
  - Viral (most common): Herpes simplex, varicella zoster, CMV, EBV, influenza, RSV, enteroviruses, arboviruses, HIV, JC virus, rabies
  - Nonviral: Bacteria, prion, parasitic, fungal
- Noninfectious:
  - Postinfectious/immune mediated: ADEM immunologic response to antecedent antigenic stimulus
  - Paraneoplastic: Anti-NMDA receptor, which induces glutamatergic transmission impairment

Usual Treatment

- Empiric antibiotics: Acyclovir (important as viral etiology is most common infectious cause), ampicillin, ceftriaxone, vancomycin
- Doxycycline if rickettsial or ehrlichial disease suspected
- ADEM: Steroids, plasma exchange, chemotherapeutic agents
- Human rabies immunoglobulin infiltration of inoculation site immediately after bite
- Specific antimicrobial therapy according to culture and sensitivity
- Supportive care:
  - Intubate, ventilate, if dictated by mental status, airway reflexes
  - Hemodynamic support
  - Nutrition
  - DVT prophylaxis
  - GI prophylaxis
  - Physical therapy
  - Dx and treatment of extracranial infection
- Management of complications: Seizure, increasing ICP, SIADH, resp failure

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Virus access to CNS from nasal mucosa to olfactory bulb and olfactory tracts	Preceding URI		Nasopharyngeal swab Throat culture
CV	Autonomic dysfunction Neurogenic stunned Myocardium	Transient myocardial dysfunction	Labile BP, HR	ECG, troponin, CK, ECHO, left ventricular angio
HEME	Increased or normal WBC			CBC, WBC differential, serum antibody titers
RENAL	SIADH	Water intoxication Anorexia N/V Personality disorders Neurologic abnormality	No evidence of volume depletion Normal skin turgor Normal BP Mental status changes from lethargy to coma	Serum Na^+ and osmolality Urine Na^+ and osmolality BUN, Cr
CNS	Focal, global neurologic disturbances	Fever Headache Seizure Personality change Memory loss Confusion Weakness Sleep/awake abnormality Hearing, speech, visual changes	Focal neurologic deficits, altered mentation, papilledema, anisocoria; if spinal cord involvement: flaccid paraplegia, increased DTRs	CSF: Cell count (increased WBC, lymphocyte predominance), protein (increased), Gram stain, viral and bacterial culture, antibodies, antigens, viral PCR, viral DNA sequencing, MRI (temporal lobe involvement, hemorrhagic lesions, ±mass effect), EEG, CT

Key References: Tunkel AR, Glaser CA, Bloch KC, et al.: The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America, *Clin Infect Dis* 47(3):303–327, 2008; Pryzbylkowski PG, Dunkman WJ, Liu R, et al.: Case report: anti-*N*-methyl-D-aspartate receptor encephalitis and its anesthetic implications, *Anesth Analg* 113(5):1188–1191, 2011.

Preoperative Implications

Preoperative Preparation

- Document neurologic exam.
- Elicit Hx of increased ICP or seizure.
- If suspicion of anti-NMDA receptor encephalitis:
  - Concern for anesthetic interaction with a dysregulated NMDA receptor (i.e., propofol, midazolam, methadone, N_2O).
- If SIADH present, correct electrolyte and free water abnormality.
  - Sodium administration or fluid restriction depending on severity of hyponatremia.
  - Beware of central pontine myelinolysis with rapid correction of hyponatremia.

Monitoring

- Standard ASA monitors
- Invasive monitors when indicated; arterial line if ICP is an issue
- If EVD in use, continue monitoring ICP in the OR
- Lytes

Airway

- None

Induction

- Potential for hyperkalemic response to depolarizing NMBs if myopathy, paralysis, or prolonged immobilization; prefer use of nondepolarizing NMBs
- Autonomic instability and labile hemodynamics

Maintenance

- If pt is receiving seizure prophylaxis (e.g., phenytoin [Dilantin], carbamazepine [Tegretol], phenobarbital [Luminal], primodone [Mysoline], valproic acid [Depakote]) be aware of potentiation of sedative effects and alteration of hepatic metabolism of anesthetics and muscle relaxants.

Extubation

- Delayed awakening
- Seizures on emergence

Postoperative Period

- Delirium
- Other neurologic deterioration, including clinical or subclinical seizures

Anticipated Problems/Concerns

- Delayed emergence.
- SIADH, careful selection of replacement fluid.
- Hyperkalemic response to succinylcholine.
- Universal precautions for contact with infected materials; sterilization of reusable instruments.
- Use disposable instruments, specifically with JC virus disease.

Encephalopathy, Hypertensive

Shane V. Cherry | Christian Diez

Risk

- Chronic Htn, renal disease (particularly end-stage renal disease), malignancy, sympathomimetic drugs, and a history of transplantation and immunosuppressive therapies

Perioperative Risks

- Increased risk of myocardial ischemia, ventricular dysrhythmias, HF, aortic dissection, cerebral hemorrhage, coma, long-term neurologic disability, renal failure, or sudden death

Worry About

- Myocardial ischemia or infarction
- Aortic dissection
- HF
- Pulm edema
- Cerebral infarction (ischemic or hemorrhagic) or intracranial hemorrhage
- Acute renal failure
- Eclampsia in at-risk parturients
- Microangiopathic hemolytic anemia

Overview

- The most common clinical presentations of hypertensive emergencies are cerebral infarction (24.5%), pulm edema (22.5%), hypertensive encephalopathy (16.3%), and HF (12%).
- Hypertensive encephalopathy is by definition a hypertensive emergency and has recently come to fall under the umbrella term PRES.
- Hypertensive encephalopathy is a relatively rapidly evolving syndrome of severe Htn in association with (most commonly) seizures, headache, visual disturbances, altered mental status, vomiting, ataxia, and focal neurologic deficits that may become rapidly fatal.
- Occurs when the systemic BP is elevated beyond the cerebral autoregulatory threshold of MAP, typically greater than 160 mm Hg ("autoregulation breakthrough").
- Differential Dx: Ischemic or hemorrhagic stroke (particularly posterior circulation stroke), toxicology syndrome from drugs of abuse (e.g., cocaine), encephalitis, and venous sinus thrombosis.
- It is critically important to distinguish between ischemic stroke and hypertensive encephalopathy because the treatment for hypertensive encephalopathy is lowering of BP, whereas outcomes are improved with higher BPs after acute ischemic stroke and therefore antihypertensives are generally not recommended.
- Hypertensive encephalopathy can develop in pts with or without chronic Htn. However, because the cerebral autoregulation curve is shifted to the right in chronically hypertensive pts, it may take significantly higher BPs for these pts to develop signs of encephalopathy.
- As the name implies, PRES is usually reversible if diagnosed early and treated appropriately but can quickly become irreversible and fatal.
- Diagnostic test of choice is MRI, which will reveal symmetric reversible T2 high signal intensities located in the occipital and parietal lobes as a result of subcortical vasogenic edema. CT is not sensitive for the lesions of PRES and will often be normal.

Etiology

- The critical event is failure of cerebral autoregulation (for any reason) leading to cerebrovascular endothelial dysfunction and vasogenic edema that renders the pt encephalopathic.
- Leading theory of pathophysiology is that in the presence of increased cerebral perfusion pressure, the increased capillary hydrostatic pressure leads to vasogenic edema and may even disrupt the blood-brain barrier.
- Chemokines and cytotoxic agents may play a role in the endothelial dysfunction, as evidenced by the existence of PRES in normotensive and even hypotensive pts (e.g., undergoing chemotherapy or septic shock).
- Nonhypertensive causes and associations of PRES include:
  - Endocrine disorders: Pheochromocytoma, renin-secreting tumor, Cushing disease, and Conn syndrome.
  - Drug induced: Immunosuppressive therapy, chemotherapy, erythropoietin, MAOIs, abrupt discontinuation of antihypertensive drugs, sympathomimetic drugs, and drugs of abuse (e.g., cocaine, amphetamines, LSD).
  - AIDS.
  - Thrombotic thrombocytopenic purpura.
  - Status post CEA (CEA hyperperfusion syndrome).
  - Preeclampsia and eclampsia.
  - Acute intermittent porphyria.
  - Autonomic hyperreactivity, as with spinal cord lesions.

Usual Treatment

- Placement of arterial cath for beat-to-beat BP monitoring.
- Reduce MAP by 20% within the first h or to a target diastolic BP of 100–110 mm Hg, whichever value is greater.
- Parenteral antihypertensive agents: Most commonly used agent is sodium nitroprusside. Other common alternatives include labetalol, fenoldopam, nicardipine, enalaprilat, or hydralazine. Nitroglycerin has been reported to exacerbate symptoms and is contraindicated.
- In general, vasodilators, such as sodium nitroprusside, have a lesser effect on the cerebral circulation versus other vascular beds, making them primary choices for pts with hypertensive encephalopathy. Clonidine should be avoided because of its CNS depressant effects.
- Anticonvulsant therapy: Preferentially use agents that can be rapidly loaded, such as benzodiazepines or phenytoin/phenobarbital.
- Withdrawal of exacerbating factors (e.g., corticosteroids, immunosuppressive drugs).
- In eclampsia, delivery of the fetus and the placenta, as well as parenteral magnesium, are the mainstay of therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn Myocardial ischemia HF Aortic dissection	Htn Angina CHF Pain radiating to the back Preeclampsia	S_3 S_4 gallop JVD	ECG CXR BMP, CBC with peripheral smear Arteriogram
RESP	Pulm edema Decreased lung compliance Decreased FEV, FVC	Dyspnea Frothy sputum Orthopnea	Rales	CXR O_2 sat
GI	Vomiting	Abdominal pain	Abd mass	CT Plasma metanephrine levels
RENAL	Renal failure	Anuria		UA Measurement of UO
CNS	Cerebral infarction or intracranial hemorrhage Seizures Severe headache Visual disturbances Focal deficits Stupor, coma	Mental status exam	Altered mental status Retinal arteriolar spasm on ophthalmoscopy Papilledema May have a normal fundoscopic exam Neck stiffness Pronator drift	MRI

Key References: Granata G, Greco A, Iannella G, et al.: Posterior reversible encephalopathy syndrome—insight into pathogenesis, clinical variants and treatment approaches, *Autoimmun Rev* 14(9):830–836, 2015; Vaughan CJ, Delanty N: Hypertensive emergencies, *Lancet* 356(9227):411–417, 2000.

Preoperative Implications

Preinduction

- Determine home medications, compliance with antihypertensive regimens, and adequacy of BP control.
- Evaluate for end-organ damage.

Monitoring

- Arterial cath.
- Central venous cath or PA cath may be used if extensive surgery is planned or there is evidence of other end-organ damage (e.g., left ventricular dysfunction, renal failure).

General Anesthesia

- Volatile anesthetics are useful in attenuating sympathetic nervous system pressor responses; there is no evidence to suggest one volatile agent over another for control of intraop Htn.
- Nitrous oxide-opioid technique can be used be used for maintenance of anesthesia in pts with labile pressure while under GA; a volatile agent may be needed during periods of abrupt changes in surgical stimulation.
- Antihypertensive agent by continuous infusion is frequently a more effective means of controlling BP when compared with titrating volatile agent to BP.

Induction

- Induction of anesthesia may produce an exaggerated decrease in BP, particularly in the presence of diastolic Htn (intravascular volume depletion).
- Direct laryngoscopy and tracheal intubation can produce significant Htn; limit the duration of laryngoscopy and consider the use of opioids, lidocaine, beta blockers, and vasodilators to blunt the autonomic response.

Maintenance

- Control BP and minimize wide fluctuations because overly aggressive treatment of Htn may worsen other end-organ function.
- Monitor for myocardial ischemia.

Regional Anesthesia

- Epinephrine-containing solutions may place the hypertensive pt at risk or worsen an existent hypertensive crisis (e.g., epidural in a preeclamptic parturient).

Postoperative Period

- Extubate with careful BP control.
- Continue parenteral antihypertensive therapy and monitoring of invasive BP and mental status during transport and recovery.
- Maintain monitoring for other end-organ morbidity, such as myocardial ischemia, cardiac dysrhythmias, HF, stroke, and bleeding.

Anticipated Problems/Concerns

- Particular caution is necessary with the elderly, as well as pts with chronic Htn; overaggressive reduction in BP may worsen mental status and cause stroke.

Encephalopathy, Metabolic

Charles Weissman

Risk

- 3.4– 11% of medical ICU admissions
- 12–33% of multiple-organ dysfunction pts

Perioperative Risks

- With predisposing conditions (e.g., hepatic insufficiency), risk of developing or exacerbating metabolic encephalopathy
- Increasing severity of preexisting encephalopathy

Worry About

- Worsening hepatic insufficiency causing hepatic encephalopathy
- Diabetics becoming hypoglycemic or with DKA/hyperosmolar coma
- Postop hyponatremia
- Deteriorating renal insufficiency leading to uremic encephalopathy
- Preexisting encephalopathy may be exacerbated by anesthetics (e.g., benzodiazepines) in hepatic encephalopathy
- Postpartum, especially with preeclampsia, eclampsia; PRES
- Undiagnosed sepsis, hypothermia, high fever, CNS-acting drugs, including overdose
- CNS cause: Brainstem CVA, meningitis, occult head trauma, encephalitis, brain tumor

Overview

- Altered sensorium, stupor, or coma without any other explanation in the setting of a metabolic disturbance.
- Process affects global cortical function by altering brain biochemistry.
- Distinguished from structural lesions by a nonfocal neurologic exam.
- EEG shows diffuse background slowing, triphasic waves in hepatic encephalopathy.
- Increased spontaneous motor activity: Restlessness, asterixis, myoclonus, tremors, rigidity.

Etiology

- Hypoglycemic encephalopathy: Most commonly caused by accidental or deliberate overdosing with insulin or oral hypoglycemic agents or prolonged ethanol intoxication
- Hepatic encephalopathy: Acute or chronic hepatic insufficiency, Reye syndrome
- Uremic encephalopathy: Renal failure. After dialysis, disequilibrium syndrome caused by acute fluid and electrolyte shifts
- Encephalopathy due to fluid and electrolyte abnormality: Hyperosmolar state, hyponatremia (acute decrease to <120 mEq/L), hypernatremia, hypercalcemia associated with hypoparathyroidism (<4 mEq/L)
- Pulm encephalopathy: Combination of hypoxia and hypercarbia
- Drug overdose; sepsis; severe acute pancreatitis

Usual Treatment

- Uremic encephalopathy: Dialysis.
- Hepatic encephalopathy: Lactulose (oral or rectal), neomycin.
- Hypoglycemic encephalopathy: IV glucose.
- Septic encephalopathy: Treatment of underlying infection.
- Hyperosmolar/hypoosmolar state: Slow and careful restoration of electrolyte balance.
- Pulm encephalopathy: Quickly improve ventilation and oxygenation, mechanical ventilation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Sudden elevation $PaCO_2$(>65 mm Hg)	COPD, drug overdose	Hypoventilation, periodic breathing, papilledema	Pulse oximetry and end-tidal capnography, or ABG
GI	Hepatic insufficiency	Liver disease, cirrhosis, alcoholism, portosystemic shunt	Asterixis, jaundice, ascites	AST, ALT, bilirubin, ammonia PT (INR)
ENDO	Diabetes	Use of insulin or oral hypoglycemic agents	Blood glucose	
	Apathy Thyrotoxicosis	Hyperthyroidism	Tachycardia Fever, sweating	T_4, T_3
	Hypothyroidism	Hypothyroidism	Hypothermia Pretibial edema	TSH
	Hypercalcemia	Hyperparathyroidism Malignancy		Serum Ca^{2+}, PTH
	Hypernatremia Hyponatremia	Dehydration, diabetes insipidus SIADH, water intoxication		Serum Na^+
RENAL	Uremia Prerenal azotemia	Renal disease, ingestion of nephrotoxins (e.g., drugs)	Asterixis	BUN/Cr, serum lytes Toxicology screen
CNS	Altered sensorium, stupor, coma, seizures	Rule out head trauma	Nonfocal neurologic exam, altered mental status	EEG, CT Lumbar puncture
MS	Multifocal myoclonus, rigidity		Myoclonus, asterixis, rigidity, tremors	

Key References: Ravin PD: Metabolic encephalopathy. In Irwin RS, Rippe JM, editors: *Intensive care medicine*, ed 7, Philadelphia, PA, 2012, Wolters Kluwer/Lippincott Williams & Wilkins, pp 1760–1768; Kiamanesh D, Rumley J, Moitra VK: Monitoring and managing hepatic disease in anaesthesia, *Brit J Anaesth* 111(S1):i50–i61, 2013.

Perioperative Implications

Preoperative Preparation

- Assess and document preop mental status and neurologic function.
- Uremic encephalopathy: Preop dialysis, if possible.
- Hyperthyroidism, hypothyroidism: Initial treatment, if possible.

Monitoring

- Routine.
- In hyperosmolar states, uremia and liver failure with ascites may need central monitoring.

Preinduction/Induction

- Benzodiazepines should be avoided in hepatic encephalopathy. Propofol can be used.
- Increased potential for aspiration; consider rapid sequence.

Maintenance

- Carefully titrate anesthetics to avoid overdosing.
- Careful attention should be paid to intravascular volume status, blood glucose, and lytes.
- During and after TURP and hysteroscopy, sodium concentrations and volume status should be monitored.
- Correction of hypernatremia and hyponatremia should be gradual.
- In renal and hepatic failure, appropriate drugs and doses should be used. Long-acting drugs should be avoided. May be increased bleeding.
- Diabetics: Monitor intraop blood glucose to avoid hypoglycemia. Too rapid correction of hyperglycemia can lead to cerebral edema.

Extubation

- Extubate only if the pt is able to protect airway and maintain adequate ventilation.

Anticipated Problems/Concerns

- Poor mental status at the conclusion of surgery may require continued intubation.
- Hyponatremia is a cause of postop metabolic encephalopathy.

Encephalopathy, Postanoxic

Charles Weissman

Risk

- After successful prehospital cardiac resuscitation: 59–65% of pts remain comatose.
- 0–5% of successful resuscitations result in chronic vegetative state.

Perioperative Risks

- Worsening of neurologic status; blindness most common residuum.
- Postpone surgery in all but emergency situations.
- Do what is necessary to treat precipitating cause and to decrease sequelae (e.g., treat elevated ICP).

Worry About

- Repeat of events that initially caused encephalopathy (e.g., arrhythmias leading to cardiac arrest)
- Hypotension, hypercapnia, hypoxia, and sepsis that can exacerbate encephalopathy

Overview

- Brain injury resulting from prolonged period of insufficient cerebral oxygenation.
- Clinical picture ranges from mild confusion to brain death.
- Chances for acceptable neurologic recovery: 1% with continued coma after 24 h and lack of two of the following reflexes: Pupillary, corneal, and oculovestibular.
- Absence of brainstem function 72 h after event associated with irreversible coma.
- Therapeutic hypothermia (especially after cardiac arrest with initial VFIB or VTach) improves neurologic outcome.
- Good prognosis seen in 50% of pts awakening within 24 h of insult.
- Seizures occur in 25% of pts.
- Anoxic damage may have been sustained by other organs (e.g., MI, shock liver, acute renal failure, stress ulcers, ARDS).
- DI is poor prognostic sign.

Etiology

- Caused by inadequate O_2 delivery to CNS due to inadequate cardiac output, resp dysfunction, severe anemia, and/or increased ICP
- Most often secondary to primary cardiac (MI or arrhythmia) or pulm (asthma, pulm embolism) event
- May also be result of CO poisoning, suffocation, and cyanide poisoning

Usual Treatment

- Prevent recurrence of inciting event.
- Ventilatory and hemodynamic support as needed.
- Therapeutic hypothermia to 32–34° C for 12–24 h.
- Stress ulcer prophylaxis.
- Treatment of seizures (with anticonvulsants, e.g., phenytoin) and myoclonus.
- BP should be maintained at normotensive or mildly elevated levels in normotensives and higher in hypertensives.
- Treat fever promptly with antipyretic drugs.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	MI	Assess if cardiac disease was cause of arrest		ECG, other cardiac assessment Troponins, CK
RESP	ARDS	Assess if resp disease was cause of arrest Resp failure	Wheezing, stigmata of COPD	Pre-arrest PFTs ABGs
GI	Shock liver Stress ulceration	Hx of GI bleeding	Jaundice	AST, ALT, bilirubin, alkaline phosphatase Hct NG output
RENAL	Renal failure	Assess if lyte abnormality or acidosis caused initial event	Urine output	BUN/Cr
CNS	Altered mental status, diffuse and focal neurologic abnormalities	Changes in neurologic signs since hypoxic event, seizures	Neurologic and mental status exams, apnea test, brainstem reflexes	CT scan/CT angiography, MRI/MRA EEG SSEP, BAER
MS	Myoclonus, posturing Contractures	Abnormal movements, posturing Prolonged immobility	Decerebrate or decorticate postures, myoclonus Contractures	

Key References: Lippa CF, Moonis M: Generalized anoxia/ischemia of the nervous system. In Irwin RS, Rippe JM, editors: *Intensive care medicine*, ed 7, Philadelphia, PA, 2012, Wolters Kluwer/Lippincott Williams & Wilkins, pp 1768–1771; Topjian AA, Berg RA, Taccone FS: Haemodynamic and ventilator management in patients following cardiac arrest, *Curr Opin Crit Care* 21(3):195–201, 2015.

Perioperative Implications

Preoperative Preparation

- Assess and document neurologic function and mental status.
- Review cause of anoxic event.
- Assess damage to other organs.
- If pt hypothermic, beware of possible increased blood loss.

Monitoring

- If arrest was due to cardiac arrhythmias or MI/ischemia or if pt is hemodynamically unstable, may need specialized monitoring

Airway

- Assess potential for aspiration: Gag reflex and ability to cough and clear secretions.

Induction

- Avoid succinylcholine.

Maintenance

- Must consider that pts may have pain perception and will require analgesia.
- Do what is appropriate to decrease sequelae (e.g., treat increased ICP); therapeutic hypothermia.
- If being treated with therapeutic hyperthermia drug, clearance is reduced.

Extubation

- If unable to maintain patent airway or sustain adequate minute ventilation, pt should remain intubated.

Adjuvants

- Avoid long-acting anesthetics so that neurologic status can be assessed soon after surgery.
- Avoid drugs that decrease seizure threshold.

Anticipated Problems/Concerns

- Repeat of events (e.g., arrhythmias) that initially led to anoxic encephalopathy.
- Worsening of neurologic condition during periop period.
- Seizures and myoclonus.
- Postpone all but emergency surgery if fluctuating neurologic deficits or acute encephalopathic condition exists.

Endocardial Cushion Defect (Atrioventricular Canal)

Julie K. Freed | Paul S. Pagel

Risk

- 4% of all congenital heart disease and 0.3–0.4:1000 live births
- 40–50% of AV canal defects are associated with trisomy 21

Perioperative Risks

- Paradoxical air embolism
- Shunt reversal (from left to right to right to left) because of vasodilating volatile and IV anesthetics (reduced systemic vascular resistance)
- Endocarditis; prophylactic antibiotics for pts with a complete repair or a jet lesion
- Arrhythmias after AV canal repair
- Reactive pulmonary vasculature and PAH

Worry About

- Bradycardia
- PAH, RV failure, and shunt reversal
- Atrial arrhythmias resulting from atrial enlargement

Overview

- AV canal is associated with atrial and ventricular septal defects manifested by a variety of abnormal communications between the left and right heart structures.
- Categorized into atrial septal defects and partial or complete AV canal defect.
- Main hemodynamic problems include AV valve dysfunction, interatrial shunting, and interventricular shunting.
- L-to-R shunting results in RV or LV dysfunction or failure, frequent resp infections, and failure to thrive.
- Chronic L-to-R shunt causes increased pulmonary vascular resistance and shunt reversal (Eisenmenger syndrome), which may preclude surgical intervention.
- Diagnosis includes chest radiograph (enlarged heart), physical exam findings (murmur), prolonged electrocardiogram PR interval, and ECHO.

Etiology

- AV canal defects arise from abnormal endocardial cushion development between 4–5 wk gestational age.
- Failure of endocardial cushion fusion results in deficiencies in the interventricular septum that can form a common AV valve, common AV valve annulus, or interatrial communication.

Usual Treatment

- Medical management (before repair) directed to improve cardiac function and overall health (digitalis, diuresis, positive inotropic drugs, afterload reduction, adequate nutrition).
- Surgical management is definitive; includes repair of the septal defects and AV valves.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Feeding difficulties	Failure to thrive	Decreased weight/height for age	Compare with ideal weight/height
CV	CHF PAH	Fatigue, dyspnea, diaphoresis, coughing Dyspnea, tachypnea	Murmur, wheezing, rales, hepatosplenomegaly Increase in CHF Sx	CXR, TEE, cardiac cath TEE, cardiac cath
RESP	CHF, pneumonia	Dyspnea, tachypnea	Wheezing, rales	CXR
RENAL	Renal insufficiency			Cr, BUN
MS	Exercise intolerance			

Key References: Wenink AC, Zevallos JC: Developmental aspects of atrioventricular septal defects, *Int J Cardiol* 18(1):65–78, 1988; Bergin ML, Warnes CA, Tajik AJ, et al.: Partial atrioventricular canal defect: long-term follow-up after initial repair in patients ≥40 years old, *J Am Coll Cardiol* 25(5):1189–1194, 1995.

Perioperative Implications

Preoperative Preparation

- Midazolam (0.05–0.1 mg/kg) to reduce anxiety and facilitate cooperation.
- Anxiolytics not recommended for children <1 y of age.
- Use caution as anxiolytics may cause hypoventilation, hypercapnia, increased PVR, and shunt reversal.

Monitoring

- Standard ASA monitors; arterial and central venous cath
- CVP monitoring in the setting of PAH
- TEE if not contraindicated

Airway

- Anticipate difficulty when trisomy 21 is present

Induction

- Meticulous exclusion of air from IV tubing to avoid paradoxical air embolism.
- Inhalation induction time is minimally affected by L-to-R shunt but may be prolonged in R-to-L shunt.
- Choice of IV anesthetic for induction based on severity of heart failure.

Maintenance

- Decrease in afterload due to IV or volatile anesthetics may worsen R-to-L shunt.
- Adjuvant opioids to allow use of lower volatile anesthetic concentrations.

Extubation

- Extubation feasible in the operating for partial AV canal defects without heart failure or PAH.
- Airway obstruction or hypoventilation after extubation may increase PVR, requiring subsequent hyperventilation, increased FIO_2, or inhaled nitric oxide, or ECMO.

Adjuvants

- Positive inotropic drugs to enhance myocardial contractility
- Inhaled nitric oxide or prostaglandin I_2 to reduce PVR

Postoperative Period

- Closely monitor and reduce pulm artery pressures in pts with preop PAH.
- Reduced cardiac output may occur as a result of RV or LV dysfunction or LV outflow tract obstruction.
- May require temporary transvenous pacing or develop postop arrhythmias.

Anticipated Problems/Concerns

- Presence of arrhythmias, reduced cardiac output, moderate or severe mitral regurgitation, and elevated PVR is associated with greater risk of mortality

Endocarditis

Brendan T. Wanta | Daniel R. Brown

Risk

- Incidence: 3–10:100,000 population.
- Rheumatic heart disease is a key risk factor in lower-middle income countries.
- Valvular and cyanotic heart disease, DM, cancer, and IV drug use are risk factors in higher income countries.

Perioperative Risks

- Septic embolization to other organs (CNS, renal, and lung) is seen in 25–50% of pts.

Worry About

- Acute heart failure (valvular regurgitation or obstruction), stroke, and metastatic infection (i.e., epidural abscess/osteomyelitis)
- AV or bundle branch blocks due to infection extension

Overview

- IE is an infection of the heart, most commonly seen in pts with structural heart disease (i.e., CHD, mitral valve prolapse).
  - Acute infections commonly caused by *Staphylococcus aureus* and *S. epidermidis*.
  - Subacute infections commonly caused by *Streptococcus viridans* or HACEK group organisms (*Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species).
  - *S. aureus* bacteremia is highly associated with IE, and ECHO should be obtained with all *S. aureus*-positive blood cultures.
- Non-IE can be seen with systemic inflammatory disorders, such as SLE (Libman-Sacks endocarditis).
- Left-sided valves (mitral, aortic) are most commonly affected, except in IV drug users, in whom right-sided valves (tricuspid > pulmonary) predominate.
- IE diagnosed by the modified Duke criteria and presentation can be variable and nonspecific.

Etiology

- Autoimmune activity or bacterial colonization leads to endothelial injury and valvular damage.
- *S. aureus* is the most common bacterial isolate in high-income countries.
- Oral viridans group is the most common bacterial isolate in lower-middle income countries.
- Group D streptococci is classically seen in pts with colonic tumors.

Usual Treatment

- Empirical antibiotics (often combination therapy with focus on Gram-positive bacteria) started after blood cultures obtained when suspicion for IE exists
- Antibiotic treatment for at minimum 4 wk
- Surgery indicated in severe valvular dysfunction, with uncontrolled infection, and to prevent stroke/other embolic process

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Roth spots (retinal hemorrhage)	Visual disturbance	Retinal exam	Dilated funduscopic exam
RESP	Pulmonary edema	Dyspnea	Crackles Wheezing	CXR
CV	New or changed murmur Left ventricular or right ventricular failure Conduction abnormality	Dyspnea Orthopnea Light headedness/ syncope	Exam for signs of CHF (left or right sided, depending on lesion)	ECHO (TEE more sensitive than TTE) ECG
GI	Mesenteric ischemia Splenomegaly	N/V Pain	Acute abdomen Hypoactive bowel sounds	Contrasted CT Lactate
CNS	Stroke	Focal neurologic deficit(s)	Detailed neurologic exam	Head CT, MRI
RENAL	Hematuria Glomerulonephritis Pyuria	Urgency Pain Urine discoloration	CVA tenderness	UA
MS	Osler nodes Janeway lesions Splinter hemorrhages	Fever Night sweats Malaise	Skin and nailbed exam	ESR/CRP Rheumatoid factor

Key References: Cahill TJ, Prendergast BD: Infective endocarditis, *Lancet* 387(10021):882–893, 2016; Methangkool E, Howard-Quijano K, Ho JK, et al.: Infective endocarditis: the importance of intraoperative transesophageal echocardiography, *Anesth Analg* 119(1):35–40, 2014.

Perioperative Implications

Preoperative Preparation

- Assess cardiac status.
- Optimize volume status.
- CT head for baseline study and to rule out embolic stroke.

Monitoring

- Large bore central venous access
- Arterial pressure monitoring
- Noninvasive and invasive cardiac monitoring as indicated

Airway

- Potential for laryngeal involvement (i.e., edema, ulceration, VC paralysis) in pts with SLE.

Induction

- Consider etomidate, ketamine, and/or opioids to avoid SVR reduction.
- Awake arterial line may be beneficial.

Extubation

- Assess and manage postop cardiac dysfunction.
- Consider extubation to NIPPV in pts with continued signs of CHF.

Adjuvants

- Prophylaxis for dental procedures and respiratory tract procedures with biopsy recommended for pts with:
  - Prosthetic heart valves.
  - Unrepaired CHD.
  - Heart transplant with valvular disease.
- Prophylaxis not recommended for bronchoscopy (without biopsy) and GI or GU procedures.

Postoperative Period

- Early postop neurologic exam to assess for CNS embolization

Anticipated Problem/Concerns

- Embolization (intracranial, coronary, mesenteric) can lead to secondary infection.
- Ischemic stroke not a contraindication to surgery, but hemorrhagic stroke requires surgical delay of at least 1 mo.

Epidermolysis Bullosa

Sumita Bhambhani

Risk

- 1:17,000, 50% dystrophic form
- Racial distribution equal

Perioperative Risks

- Difficult IV access, airway, intraop positioning, reflux, steroid dependence, intraop hemorrhage, sepsis, iatrogenic corneal abrasion, blister formation, and airway obstruction

Worry About

- Problems similar to those found in pts with severe skin burns; severely compromised pts
- Difficult intubation (23%) secondary to microstomia
- Establishing monitoring and IV access
- Dehydration and malnutrition
- Anemia, hypoalbuminemia, electrolyte imbalance, and thrombocytosis
- Septicemia
- Renal and adrenal dysfunction

Overview

- Characterized by epithelial blistering resulting from minor trauma by lateral shearing forces, not pressure, because of absence of normal intracellular bridges caused by collagen abnormality
- Four types: SEB, JEB, DEB, and Kindler syndrome
- Associated conditions: Growth retardation, pyloric stenosis, esophageal stricture, pseudosyndactyly, enamel hypoplasia, muscular dystrophy, squamous cell carcinoma, and malignant melanoma
- SEB: Most common form; intraepidermal blisters on the soles and palms only in Weber-Cockayne form, generalized in Kobner form, generalized herpetiform in Dowling-Meara form, and generalized in association with muscular dystrophy in the MD form
- JEB: Blisters formed in the intralamina lucida and in intertriginous areas in the inversa form, which are generalized with growth retardation in the Herlitz form, generalized without growth retardation in the non-Herlitz form, and generalized with pyloric atresia
- DEB: Blisters formed in the sublamina densa and in intertriginous areas in the inversa form, on ankles in the pretibial form, on arms and legs in the pruriginous form; generalized blisters in the non–Hallopeau-Siemens form and with growth retardation and severe extracutaneous involvement in the Hallopeau-Siemens form, and aggressive squamous cell carcinomas (very commonly)
- Kindler syndrome: Blisters formed at multiple levels, intralamina lucida and sublamina densa; Kindler syndrome (previously considered as poikilodermatous photosensitivity disease); skin findings including atrophic scarring and nail dystrophy; possibly associated with severe colitis, esophagitis, urethral strictures, and ectropions; squamous cell carcinoma (can develop)

Etiology

- SEB: Inherited autosomal, usually dominant, mutation producing abnormal keratin intermediate filament proteins 5 or 14, which weaken the epidermal architecture; in the MD form abnormality, plectin (cytolinker protein) is the cause.
- JEB: An inherited autosomal recessive mutation produces abnormal laminin 5, abnormal type XVII collagen, and abnormal $\alpha_6\beta_4$ integrin.
- DEB: An inherited autosomal dominant or recessive mutation produces abnormal type VII collagen.

Usual Treatment

- Treatment is supportive, similar to initial burn treatment, with silver impregnated creams and collagen allografts.
- Retinoids and growth-stimulator factors are used to induce wound-repair keratin 6, 16, and 17, which form a more normal epidermis.
- An emerging treatment uses isothiocyanate sulforaphane which induces keratin 16 and 17 and occurs naturally in broccoli sprouts.
- Pts receive steroids and supportive treatment, such as nutritional support, wound care, contracture release, esophageal dilation, oral surgery, and treatment of skin cancers.
- Future treatment is expected to involve gene therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Enamel hypoplasia: Blisters, microstomia, ankyloglossia, supraglottic ulceration or narrowing,corneal erosion, ectropion	Delayed eruption and caries of teeth; painful perioral and intraoral lesions; hoarseness and respiratory obstruction; painful swallowing, spasm, food impaction	Poor oral hygiene and malocclusion; tongue atrophy; obliteration of vestibular sulci, stricture, webs, and vocal cord lesions	Airway assessment, endoscopy
GI	Bullae Perianal blisters, poor absorption, diarrhea	Esophageal stricture Anal pain, tenesmus, constipation	Reflux, regurgitation Anal fissure or stricture	Endoscopy
GU	Blisters	Urinary diversion	Obstruction, sepsis	Renal function
MS	Contractures, growth retardation	Movement limitations, stature	Flexion contracture, pseudosyndactyly	
DERM	Blisters	Age at onset, Hx of remissions and infections	Scars, milia, nail dystrophy, cancer	Skin biopsy

Key References: Lin YC, Golianu B: Anesthesia and pain management for pediatric patients with dystrophic epidermolysis bullosa, *J Clin Anesth* 18(4):268–271, 2006; Saraf SV, Mandawade NJ, Gore SK, et al.: Epidermolysis bullosa: careful monitoring and no touch principle for anesthetia management, *J Anaesthesiol Clin Pharmacol* 29(3):390–393, 2013.

Perioperative Implications

Preoperative Preparation

- Careful planning of monitoring, IV placement, positioning in the OR, prevention of reflux, and airway management

Monitoring

- No contraindication to pulse oximeter use.
- Protect blisters on the face with foam adhesive inverted to pad mask.
- Pad automated BP cuff heavily and limit intervals.
- Cut off adhesive from ECG leads and hold in place with defibrillator jelly pads.
- Suture invasive monitoring and IVs or wrap in place with petrolatum gauze.
- Esophageal stethoscope may damage mucosa.
- Avoid excessive heat or sweating, which increases the risk of blisters.

Induction

- Regional anesthesia encouraged; use spray antiseptics or pour prep solutions; no intradermal local anesthetics.
- No GA or muscle relaxant specifically contraindicated.

Airway

- All airway management techniques are reported successful.
- The mask (or nasal mask) should be lubricated and padded with petrolatum gauze; pad the chin under fingers; bullae occurred in 1:50.
- LMA one size too small, heavily lubricated, cuff soft with audible leak, extubated deep to prevent trauma; lingual bulla occurred in 1:57.
- Intubation is less frequent; use blind nasal, fiberoptic, and oral techniques; a heavily lubricated small tube and laryngoscope; cricoid pressure without lateral movement is permissible; 66% are class I or II view of larynx and 7–23% have difficult airway incidence; use soft lubricated gauze to prevent tube movement in the mouth; do not allow lateral forces on the corners of the mouth by the tube and do not use tape; the trachea is lined with columnar epithelium and, therefore, is less likely to blister.

Emergence

- Aim for a quiet emergence.
- No suction on intraoral mucosa.

Anticipated Problems/Concerns

- Positioning is performed by the pt if possible; lateral shear forces from lifting cause blisters.
- Corneal abrasion can occur because of poor eyelid retraction; use ointment generously and protect the eyes in while pt is in prone position.
- Treat hemorrhage with epinephrine or a thrombin-soaked sponge.
- Avoid sweating and warming devices, but if unavoidable, the device should be no warmer than skin temperature.
- Extremity tourniquets, IM or rectal medications and EMLA can be used.
- Common procedures include release of syndactyly, dressing change, squamous cell carcinoma, esophageal dilatation, and dental surgery.

Epiglottitis

Maurice S. Zwass | Jeffrey D. Roizen

Risk

- Prevalent in children 1–7 y; sometimes called supraglottitis, it does occur in adults (decreasing incidence in children >3 y related to vaccines against *Haemophilus influenzae* type B, but still found, particularly if pt is not immunized).
- Adult incidence remains constant with organisms group A *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*.

Perioperative Risks

- Acute deterioration of airway patency resulting in complete obstruction worse in children
- Difficulty in tracheal intubation due to severe edema of epiglottis and arytenoids

Worry About

- Airway compromise in children who appear toxic, with increasing distress, drooling, and hypoxemia. The acute risks of airway compromise (of concern in small children) appear to be less critical in adults, most likely because of larger airways.
- Loss of airway control and aspiration.

Overview

- An acute, potentially life-threatening cause of upper airway obstruction (etiologic agents may include bacteria other than *H. influenzae* type B).
- Produces inflammatory edema of epiglottis and other supraglottic structures.
- Onset is usually rapid; progression to severe obstruction can occur in several hours.
- High fever, sore throat, and dysphagia are frequently so severe that swallowing is inhibited and drooling results.
- Differential diagnosis also include retropharyngeal abscess (a bacterial infection), which can have the same presentation. It can be differentiated from epiglottitis by the presence of torticollis and trismus and with radiographic studies (contrast CT). Treatment is with antibiotics and surgical drainage.

Etiology

- *H. influenzae* type B is most often traditional associated pathogen, although this can be caused by β-hemolytic streptococci, group A *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Klebsiella pneumonia*.

Usual Treatment

- Antibiotic therapy against bacterium (usually *H. influenzae*) and airway support, which generally requires tracheal intubation.
- Because of high incidence of ampicillin-resistant strains, administer ampicillin plus a β-lactamase inhibitor (such as sulbactam) and/or chloramphenicol, cefuroxime, ceftazidime, or another penicillinase-resistant antibiotic as indicated by blood and epiglottis culture results.
- Tracheal intubation is classically performed in OR in a controlled fashion with surgical support for possible tracheotomy or cricothyrotomy present and gowned.

Assessment Points

Differentiation Between Epiglottitis and Croup (Laryngotracheobronchitis)

	Croup	Epiglottitis
Age	3 mo–3 y	1–7 y
Onset	Gradual	More rapid (usually <24 h)
Fever	Low-grade	High-grade
Cough	Characteristic barking	None
Sore throat	Occasional	Frequently severe
Posture	Any	Frequently sitting forward, mouth open, drooling
Airway sound	Inspir stridor	Inspiratory stridor
Voice	Normal	Muffled
Appearance	Nontoxic	Toxic
Seasonality	Peak winter, epidemic	Year-round

Radiographic studies may be helpful, because AP view of trachea appears normal but lateral neck view usually shows a markedly swollen, edematous epiglottis ("thumb-printing").

Key References: Jenkins I, Saunders M: Infections of the airway, *Paediatr Anaesth* 19(Suppl 1):118–130, 2009; Tibballs J, Watson T: Symptoms and signs differentiating croup and epiglottis, *J Paediatr Child Health* 47:77–82, 2011.

Perioperative Implications

Preoperative Preparation

- With suspected epiglottitis, other personnel on pt care team can set up care (e.g., OR, ICU). Radiographs can be obtained, but a team member capable of monitoring and securing the airway should be present.
- Allow pt to remain in a position of comfort (often sitting with parent). Direct exam of oropharynx is generally avoided, as are attempts to secure vascular access, because these may cause agitation leading to acute tracheal obstruction.
- Humidified O_2 should be delivered as tolerated.
- Aerosol therapy with racemic epinephrine may provide slight improvement of symptoms, but not definitive. If Dx is confirmed, pt is taken to the location for intubation (most commonly OR).

Airway Management

- For anesthesia, sevoflurane or halothane and O_2, maintaining spontaneous ventilation.
- IV cath should be placed after induction of anesthesia, followed by direct laryngoscopy.
- Large, swollen epiglottis can make identification of airway structures difficult, but once the epiglottis is identified, arytenoids and larynx are immediately below and tracheal tube can be inserted.
- Because of upper airway swelling, a tracheal tube 0.5–1 mm smaller in diameter may be needed (tracheal tube of adequate length can be made available).
- Rarely is emergency tracheotomy necessary, but surgeons are "gloved" until airway is secured.
- Frequently the orotracheal tube is changed to a nasotracheal tube for ease of securing and pt comfort.

Post-Airway-Management Plans

- Once the airway secured, cultures of blood and epiglottis are obtained, antibiotic therapy is initiated, and sedation plans are instituted.

Anticipated Problems/Concerns

- Respiratory support often for 24–72 h until swollen epiglottis returns to normal.
- Pts usually require sedative management to facilitate tolerating mechanical ventilation.
- Many pts (~25%) have assoc pneumonia that requires treatment.

Fabry Disease

Rohesh J. Fernando

Risk

- Genetic disease with reported annual incidence of approximately 1:100,000, but rarity may lead to underestimation of true prevalence
- Panethnic

Perioperative Risks

- Autonomic instability, particularly with neuraxial anesthesia
- Cardiovascular instability from conduction abnormalities and structural heart disease
- Periop stroke in those with cerebrovascular disease

Worry About

- Poor respiratory function, particularly in smokers
- Renal impairment
- Sudden swings in blood pressure
- Pain control in pts with chronic pain
- Abnormal temperature regulation

Overview

- Second most common lysosomal storage disorder.
- Disease process begins as early as fetal development but clinical symptoms are often not evident until after age 3 y, occurring a few years later in girls versus boys.
- Classically, homozygous young males are severely affected.
- Disease affects multiple organ systems but most notably affects the cardiac, cerebrovascular, renal, respiratory, and peripheral nervous systems.
- Risk of end-organ damage increases with age.

Etiology

- X-linked inherited lysosome storage disorder due to deficiency of lysosomal alpha-galactosidase A, leading to accumulation of glycosphingolipids throughout the body

Usual Treatment

- Enzyme replacement therapy can reduce symptoms and complications.
- Conventional medical treatment for disease-related morbidities.
- Transplantation, particularly renal and cardiac, may be necessary.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Deafness Corneal and lenticular opacities Vertigo Mucosal lesions	Difficulty hearing Light sensitivity Dizziness Nausea (vertigo)	Impaired pupillary constriction, hearing loss, oropharyngeal mucosal lesions	Audiometry, ophthalmologic exam including slit lamp, visual acuity, and fields
RESP	Obstructive ventilatory defect Exercise intolerance Airway obstruction (bronchospasm)	Dyspnea Cough	Tachypnea Wheezing	CXR Spirometry Oximetry Treadmill exercise testing
CV	LVH, RVH, aortic dilation Diastolic dysfunction LVOT obstruction Mild valvular insufficiency Coronary artery stenosis	Palpitations, angina, dyspnea	Irregular heartbeat, heart murmur	ECG ECHO Stress imaging Holter monitor
GI	Difficulty gaining weight Delayed gastric emptying Achalasia	Postprandial abdominal pain, N/V, early satiety	Smaller height and weight compared with unaffected siblings	Endoscopic or radiographic evaluations
CNS	TIA/stroke Mild dementia (late finding) Autonomic dysfunction Acroparesthesias	Pain in extremities, cold/heat intolerance, joint pain, stroke symptoms	Neurologic exam, pain inventory, hypohydrosis, orthostatic hypotension	Brain CT or MRI with T1, T2, and FLAIR images
HEME	Abnormal vascular reactivity Prothrombotic state	Angina, stroke, DVT	Thrombophlebitis	Proteins C & S, factor V Leiden, prothrombin G20210A, ATIII, lupus anticoagulant, anticardiolipin antibody
RENAL	Renal failure Proteinuria Impaired concentration ability	Fluid retention	Edema	Electrolytes, BUN, creatinine, GFR, 24-h urine for total protein/Cr
MS	Angiokeratomas, osteopenia, osteoporosis	Osteoporotic fractures	Raised skin lesions	Bone mineral density

Key References: Eng CM, Germain DP, Banikazemi M, et al.: Fabry disease: guidelines for the evaluation and management of multi-organ system involvement, *Genet Med* 8(9):539–548, 2006; Woolley J, Pichel AC: Peri-operative considerations for Anderson-Fabry disease, *Anaesthesia* 63(1):101–102, 2008.

Perioperative Implications

Preoperative Preparation

- Cardiac evaluation with ECG and echocardiogram should be obtained. Consider noninvasive cardiac stress imaging in pts older than 30 y and with concerning symptoms.
- Consider sodium citrate for gastric prophylaxis in pts with symptoms of achalasia.
- Consider preop sedation to avoid excessive activation of abnormal autonomic nervous system.
- Obtain baseline visual exam to differentiate from new deficit after surgical positioning or hemodynamic instability.
- Recurrent pain in extremities may be a relative contraindication for regional anesthesia.

Monitoring

- Consider arterial line given potential autonomic instability and cardiac history.
- Consider CVP or PA cath as indicated.
- Temperature monitoring is especially important.

Airway

- Risk for difficult direct laryngoscopy as a result of TMJ stiffness leading to limited mouth opening.
- Inspect airway for oropharyngeal lesions.
- Risk of bronchospasm.

Preinduction/Induction

- Be prepared for BP swings.
- Anticipate need for bronchodilators and avoid drugs that may cause histamine release when possible.

Maintenance

- Monitor ECG vigilantly given risk for arrhythmias and conduction abnormalities.
- Vasoactive medications should be ready to treat both hypotension and Htn.
- Avoid nephrotoxic medications and administer judicious IV fluids accounting for any renal impairment.
- Warming and cooling equipment should be available given autonomic instability.
- If taking carbamazepine for pain control, increased amounts of nondepolarizing neuromuscular blockade may be required.

Extubation

- Pts with achalasia or delayed gastric emptying should be considered at risk for aspiration.
- Ensure neuromuscular blockade not prolonged from renal insufficiency.
- Anticholinergics may exacerbate hypohidrosis.

Postoperative Period

- Analgesia plan critically important for those with chronic pain

Anticipated Problems/Concerns

- Dose medications appropriately in those with renal impairment.
- Amiodarone can exacerbate lysosomal abnormalities and should be avoided.

Factor V Leiden Mutation

S. Nini Malayaman | Henry Liu

Risk

- Most common hereditary thrombophilia
- Autosomal dominant inheritance pattern
- Heterozygous form in 5% of white population in USA (up to 15% in Europe), 2% of Hispanic Americans, 1% in both African and Native Americans
- Homozygosity in white population 1:5000
- May account for 85–95% of pts with APC resistance
- Relative risk of venous thrombosis sevenfold in heterozygous and 80-fold in homozygotes

Perioperative Risks

- VTE: DVT most likely; lower risk of PE
- Risk of arterial thrombosis unknown

Worry About

- Hypercoagulability
- DVT
- Recurrent fetal loss (twofold to fivefold increased relative risk)
- Conflicting data regarding association with placental abruption, severe preeclampsia, IUGR
- Cerebral vein thrombosis
- Renal transplant rejection
- Risk of thrombosis increased by protein S deficiency, prothrombin 20210 gene mutation, hyperhomocysteinemia, OCP use, pregnancy, increasing age, immobilization, and obesity

Overview

- Factor Va is a procoagulant that is inactivated by APC, with protein S as cofactor, causing less thrombin generation during the propagation phase.

- FVL is resistant to inactivation by APC so thrombin generation is allowed to continue and subsequent clot formation.
- FVL paradox describes the higher prevalence of FVL in pts with DVT compared with FVL pts with pulmonary embolism.
- In CPB, FVL pts found to have less blood loss and need less blood transfusion during hospital stay.
- Testing in FVL is the same as other causes of thrombophilia: Venous thrombosis and age <50 y; unusual sites of thrombosis (hepatic, mesenteric, cerebral); recurrent venous thrombosis; venous thrombosis with strong history of thrombotic disease, venous thrombosis in pregnant women taking oral contraceptives, relatives of pts who had venous thrombosis <50 y, MI in female smokers <50 y.
- Screening test: Modified APC resistance functional assay (sensitivity and specificity for FVL close to 100%).
- Confirmation test: DNA test. In liver transplant pts, DNA test positive, plasma FVL negative. In bone marrow transplant pts, DNA test negative, but plasma shows APC resistance.

Etiology

- SNP 1691 G >A on factor V gene that predicts a single amino acid substitution Arg >Gln.
- The mutated factor V protein is resistant to inactivation by APC.

Usual Treatment

- Treat acute thrombosis event according to standard guidelines.
- Long-term anticoagulation not recommended for heterozygotes if no prior thrombosis.
- Prophylactic anticoagulation (heparin, warfarin) considered for high-risk clinical setting.
- Newer oral anticoagulants (dabigatran [Pradaxa], rivaroxaban [Xarelto], apixaban [Eliquis]) may be considered for prophylaxis.
- Consider minimizing other risk factors for VTE: Stopping oral contraceptives (progesterone) in women with VTE, encouraging obese pts to lose weight, and minimize extended travel.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Cerebral vein thrombosis	Headache Abnormal vision Seizures	Stroke signs, weakness	CT/MRI with contrast
RESP	Pulm embolus	Chest pain Shortness of breath	Tachypnea	ABG, CXR, CT scan
HEME	Thrombosis	Pain at site of thrombosis		Prolonged aPTT, PTT
GU	Renal vein thrombosis	Flank or lower back pain	Hematuria, oliguria	Ultrasound, CT scan
MS	DVT most common Upper extremity thrombosis	Calf pain	Calf pain with DVT	Venography, compression ultrasound of legs
OB	Miscarriage Postpartum thrombosis	Bleeding, spotting		Ultrasound, FHR (Doppler)

Key References: Kujovich JL: Factor V Leiden thrombophilia, *Genet Med* 13(1):1–16, 2011; Van Cott EM, Khor B, Zehnder JL: Factor V Leiden, *Am J Hematol* 91(1):46–49, 2016.

Perioperative Implications

Preoperative Preparation

- Preop screening not recommended if asymptomatic.
- Anticoagulation should follow standard guidelines.
- In FVL heterozygotes, risk of bleed from warfarin is greater (1–3%) than risk of thrombosis (<1%).
- Avoid CVC if possible. FVL heterozygotes have twofold to threefold increase in CVC-related thrombosis.
- Sequential compression devices may decrease incidence of DVT.
- Consider consultation with hematology; may require temporary treatment with anticoagulation during periods of high-risk settings: surgery, cast, immobilization, pregnancy, etc.

Monitoring

- If arterial line indicated, use cautiously in homozygous pts.

Airway/Induction/Maintenance/Extubation

- No special precautions

Postoperative Period

- Standard anticoagulation protocols if no prior history of VTE
- Target INR 2.5 effective anticoagulation even in homozygous pts

Anticipated Problems/Concerns

- No need to alter periop management if asymptomatic.
- Confirmation test is a genetic test, so implications for pt and family members should be discussed.
- Aprotinin, an inhibitor of APC, has been used safely in FVL pts undergoing cardiac surgery without increased risk of thrombosis, although caution is often advised.

Familial Dysautonomia (Riley-Day Syndrome)

Thomas J. Ebert | Craig E. Cummings

Risk

- Autosomal recessive transmission
- Complete penetrance, marked variability in expression
- Predominantly affects Ashkenazi Jewish population (incidence 1:10,000–20,000; carrier frequency 1:27-32)

Perioperative Risks

- Intraop: Primarily cardiovascular with hemodynamic variability
- Postop: Primarily cyclic vomiting and pulmonary complications

Worry About

- Paroxysmal dysautonomic crisis triggered by physiologic or psychologic stress characterized by intractable vomiting, Htn, tachycardia, diaphoresis, erythematous macular rash
- Resp status compromised by dysfunctional swallowing, leading to repeated aspiration pneumonias, and restrictive lung disease secondary to scoliosis
- QTc prolongation and dysrhythmias, including bradycardia and asystole
- Insensitivity to hypoxemia and hypercarbia, including apnea to mild hypoxia
- Increased sensitivity to acetylcholine and catecholamines

Overview

- HSAN type III
- Differentiated from other HSAN types by profound autonomic dysfunction, Htn, orthostatic hypotension, and excessive or decreased sweating
- Characterized by recurrent pulmonary infections, esophageal dysmotility, spinal abnormalities, and thermal dysregulation
- High morbidity and mortality, with only 50% of newborns expected to reach age 40 y

Etiology

- Mutations of gene coding IKBKAP on chromosome 9q31
- Incomplete neuronal development and progressive neuronal degeneration in the peripheral and autonomic nervous systems
- Symptoms due to denervation of peripheral blood vessels and dysfunctional parasympathetic nervous system, baroreceptors, and chemoreceptors

Usual Treatment

- Dysautonomic crisis: Benzodiazepines are first-line therapy.
- Hemodynamic instability: Managed with hydration and direct-acting vasoactive therapies.

Assessment Points

System	Effect	Assessment by Hx	PE	Diagnostic Test
CV	Orthostatic hypotension QTc prolongation Arrhythmias	Dizziness, syncope Palpitations	Orthostatic vital signs	Autonomic function ECG
RESP	Pneumonia Bronchiectasis Restrictive lung disease	Pleuritic chest pain Productive cough SOB	Abnormal breath sounds, digital clubbing	CXR Pulm function
GI	Poor swallowing Aspiration pneumonia	Drooling, vomiting Paroxysmal crisis		Swallow study
GU	Dehydration Glomerulosclerosis	Nocturia, diaphoresis	Dry mucosa, skin turgor	BMP
CNS	Seizure Developmental delay	Seizure		EEG
MS	Scoliosis		Spinal curvature	Plain films

Key References: Ngai J, Kreynin I, Kim JT, et al.: Anesthesia management of familial dysautonomia, *Paediatr Anaesth* 16(6):611–620, 2006; Weingarten TN, Sprung J, Burgher AH: Perioperative management of familial dysautonomia: a systematic review, *Eur Jour Anaesth* 24(4):309–316, 2007.

Perioperative Implications

Preoperative Preparation

- Consider regional or neuraxial anesthesia as primary anesthetic or combined with general anesthesia to improve analgesia; poor thermal discrimination may affect assessment of blocks.
- Diminished laryngeal reflexes and dysphagia leading to abundant secretions: treat with antisialagogues.
- H_2 blockers can decrease gastric volume and acidity.
- Prevent dysautonomic crisis with anxiolytics; treat crisis with benzodiazepines or clonidine.
- Avoid medications that interact with the autonomic nervous system.
- Correct chronic dehydration secondary to dysphagia and emesis to reduce intraop hemodynamic instability. Maintenance requirements may be higher due to increased insensible losses from excessive sweating and drooling.
- Minimize narcotics as premedication because of the impaired ventilatory response to hypoxia and hypercarbia.
- Lines can often be placed without sedation given insensitivity to superficial pain.

Monitoring

- Standard monitors.
- Arterial line.
- Consider processed EEG monitor.
- Consider noninvasive cardiac output monitoring.

Induction

- Rapid sequence induction.
- Titrate induction agents carefully to minimize risk of hypotension.
- Use of nondepolarizing neuromuscular blocking drugs balanced against risk of postop hypotonia and unpredictable effect of reversal agents on the autonomic nervous system.
- Lubricate eyes to avoid corneal abrasions secondary to alacrima and corneal insensitivity.

Maintenance

- Consider mechanical ventilation with lung protective strategies, especially with restrictive lung disease.
- Consider total IV anesthesia.
- Titrate volatile anesthetic using processed EEG monitor plus minimum alveolar concentration to minimize autonomic compromise.
- Fluid management and judicious use of direct acting vasopressors and inotropes guided by noninvasive cardiac output monitoring.
- Aggressively treat blood loss.
- Vigilant temperature monitoring and correction.

Emergence

- Titrate analgesics for pain control.
- Spontaneous ventilation may be delayed. Chemoreceptor dysfunction makes $PaCO_2$ levels a poor trigger.
- Unpredictable response to reversal agents due to increased sensitivity to acetylcholine.
- Aggressive pulm toilet to decrease atelectasis and bronchiectasis.

Postoperative Care

- Multimodal analgesic regimen. Visceral and peritoneal sensations remain intact despite abolishment of peripheral pain sensation.
- Judicious use of opioids given abnormal ventilator response to hypoxia and hypercarbia.
- First-line treatment for cyclic vomiting with benzodiazepines.
- Optimization of resp function with assisted ventilation, deep suctioning, inhalational therapies, and chest physiotherapy.

Familial Periodic Paralysis

Oliver Bandschapp

Risk

- Rare; hyperPP approximately 1:200,000 and hypoPP approximately 1:100,000
- HyperPP with childhood onset; hypoPP with teenage onset

Perioperative Risks

- In hyperPP, succinylcholine may provoke severe myotonia, provide no relaxation, and cause hyperkalemia (resulting postop muscle weakness over days and rhythm disturbances).
- HypoPP associated with supraventricular or conduction defect-type cardiac arrhythmias; weakness may be enhanced by β-adrenergic blocking drugs, and postop resp muscle weakness may occur.
- Hypermetabolic crises (necessitating dantrolene use) reported in hypoPP pts.

Worry About

- Cold can trigger attack in both types of PP.
- K^+ and glucose have opposite effects in the two disorders; in hyperPP, K^+ triggers attacks and glucose is cure, whereas in hypoPP, glucose-induced hypokalemia triggers attacks and K^+ is cure.
- Cardiac complications (dysrhythmias) due to severe dyskalemia during attack.
- Respiratory insufficiency during attack.

Overview

- Channel defects in the sarcolemma lead to aberrant depolarization in the presence of dyskalemia, which inactivates sodium channels and renders muscle fibers inexcitable.
- Autosomal dominant conditions; hypoPP with reduced penetrance in females.
- HyperPP with frequent (daily) episodic attacks for minutes (to hours); episodes of weakness generalized, rarely bulbar and resp muscles involved in severe paralysis; hyperkalemia (in approximately 50%) during attacks; triggered by K^+ intake, rest after exercise, or cold; often additional EMG myotonia.
- HypoPP with less frequent but more severe episodic attacks for hours (to days); weakness may be focal or generalized, usually sparing facial and resp muscles; invariably hypokalemia during episode; triggered by carbohydrates, cold, stress, specific medications (e.g., beta-agonists, corticosteroids, insulin); no myotonia.
- Fixed proximal weakness often develops with increasing age in both types.

Etiology

- HyperPP caused by mutations in the voltage-gated sodium channel $Na_v1.4$ gene (*SCN4A*). Mutant channels (inactivation defect) lead to persistent sodium influx and depolarization, muscle membrane becomes inexcitable.
- HypoPP either caused by mutations in the *CACNAS* gene (encodes α_{1s}-subunit of dihydropyridine receptor) (type 1 hypoPP) or in approximately 10% by mutations in the *SCN4A* gene (type 2 hypoPP). Introduction of new accessory ion conduction pathways independent of normal conduction pathways, leads to paradoxical membrane depolarization in low potassium conditions causing inexcitability.

Usual Treatment

- Both types: In case of prodrome keep moving
- HyperPP: Salbutamol spray, glucose, thiazide diuretics, or carbonic anhydrase inhibitors
- HypoPP: K^+ salts, carbonic anhydrase inhibitors, or K^+-sparing diuretics

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Inadequate	Noticeable SOB	Respiratory rate high	ABG
MS	Weakness	Exercise, fatigue	Limb tone Hypoactive muscle stretch reflexes	HyperPP: Ictal serum K^+ level (elevated in approximately 50%) EMG myotonia (in approximately 75%) HypoPP: Low ictal serum K^+ level Exclusion of secondary causes (TSH, fT4 fT3 levels) Glucose/insulin or ACTH infusion induces paralysis attack Plasma biochemistry after attack: elevated myoglobin, creatine kinase Muscle fiber conduction velocity may be slower than normal No EMG myotonia

Key References: Suetterlin K, Männikkö R, Hanna MG: Muscle channelopathies: recent advances in genetics, pathophysiology and therapy, *Curr Opin Neurol* 27(5):583–590, 2014; Bandschapp O, Iaizzo PA: Pathophysiologic and anesthetic considerations for patients with myotonia congenita or periodic paralyses, *Paediatr Anaesth* 23(9):824–833, 2013.

Perioperative Implications

Preoperative Preparation

- HyperPP: carbohydrate loading during fasting period; consider 24-h furosemide for K^+ depletion
- HypoPP: avoid large glucose and salt loads; 24-h acetazolamide if not already given; only glucose-free solutions IV; if Hx of frequent instability, prepare infusion with K^+; reduce pt's anxiety

Monitoring

- Both types: Temperature (esophageal) (keep warm); ECG (detection of dyskalemia); NM monitoring mandatory (minimize relaxant dose)

Airway

- Both types: no special difficulty, but may need support

Preinduction/Induction

- Both types: Regional techniques are appropriate; relaxation with short-acting nondepolarizing agents as indicated.
- HyperPP: Avoid ketamine; no succinylcholine (severe myotonia, hyperkalemia with resulting postop muscle weakness over days).

Maintenance

- Both types: Use warming blankets and keep normothermic; warm all IV fluid.
- HyperPP: Use glucose 5% as maintenance, avoid hypoglycemia; do not give K^+-containing solutions, maintain normokalemia (use glucose/insulin if needed).
- HypoPP: Use MH trigger-free anesthetic methods; glucose-free solutions as maintenance, avoid hyperglycemia; give solutions containing K^+, aim for K^+ 4–5 mEq/L; ventilation during anesthesia should be normocarbic to avoid K^+ shifts.

Extubation

- HyperPP: Evidence of muscle weakness should be treated with IV calcium gluconate or chloride 10% 10 mL slowly over 5 min; anticholinesterase drugs may worsen/trigger myotonic symptoms.
- HypoPP: Evidence of muscle weakness should be treated with IV potassium chloride; normal reversal as indicated clinically; maintenance by IPPV if evidence of weakness in postop phase; severe postop weakness may be aggravated by Ca^{2+}.

Adjuvants

- Both types: Anticipate usual analgesic requirements for age and surgery; regional techniques are appropriate.
- HyperPP: Some experimental evidence suggests that condition (e.g., postop weakness) may be helped by phenytoin or by salbutamol.
- HypoPP: Ca^{2+}-channel blockers do not appear to be contraindicated in pts with concomitant CV disease.

Anticipated Problems/Concerns

- Both types: Cold triggers attack.
- HyperPP: Succinylcholine may not give relaxation, and therefore intubation may be difficult; severe myotonia may create resp difficulty; hypoglycemia and K^+ can trigger hyperkalemic attack; hyperkalemia can cause cardiac arrhythmia.
- HypoPP: May have associated supraventricular or conduction defect arrhythmias; resp muscle weakness may occur postop; must maintain serum K^+ above 4.0 mEq/L.

Fanconi Syndrome

Rayhan A. Tariq | Henry Liu

Risk

- FS can be inherited, acquired, or caused by exogenous factors.
- Incidence is sporadic. Exact incidence in USA is not clear.
- Most diseases associated with FS are inherited in an autosomal recessive pattern.
- Cystinosis is the most common cause in pediatric pts.

Perioperative Risks

- Potential for hypotension secondary to hypovolemia
- Renal failure, proximal renal tubular dysfunction
- Lyte imbalance (especially hypokalemia causing tachyarrhythmias)

Worry About

- Polyuria, polydipsia, and the resulting dehydration
- Type 2 renal tubular acidosis (defect in the reabsorption of bicarbonate in the proximal tubule)
- Hypokalemia-induced ventricular arrhythmogenicity
- Hypophosphatemia and associated osteomalacia and loss of bone density
- Hypokalemia may cause muscular weakness
- May be part of a genetic syndrome, such as Lowe syndrome (oculocerebrorenal syndrome)

Overview

- Disease of the proximal convoluted tubules in which glucose, amino acids, uric acid, phosphate, and bicarbonate are passed into urine, not being reabsorbed.
- Signs and symptoms reflect the tubular abnormality, including polyuria, polydipsia, and acidosis due to bicarbonate loss.
- Pts are very likely to have renal failure at the time of surgery.
- Muscle weakness due to hypokalemia.
- Renal phosphate wasting presents as osteomalacia or rickets.
- Most pts have proteinuria, although it is often minimal.
- Severe photophobia might be present with cystinosis (cystinosis is the most common cause of inherited form of FS).
- FS is different from Fanconi anemia characterized by progressive pancytopenia.

Etiology

- May be hereditary or acquired.
- Common hereditary causes are cystinosis (most common cause in children), Wilson disease, Lowe syndrome, galactosemia, glycogen storage diseases, and hereditary fructose intolerance mitochondrial cytopathies.
- Can be acquired via exposure to heavy metals (lead) and medications such as tetracycline (particularly when outdated), cisplatin, tenofovir, adefovir, rifampin, deferasirox, and aminoglycoside antibiotics.
- Dysproteinemias, such as multiple myeloma, amyloidosis, light-chain nephropathy, and benign monoclonal gammopathy may cause FS in adults.

Usual Treatment

- Mainstay of treatment is replenishment of lytes and fluids lost in urine.
- Metabolic acidosis due to bicarbonate loss is corrected by the administration of HCO_3^-, (usually 3–10 mg/kg/d of sodium bicarbonate in divided doses).
- Addition of a thiazide diuretic (1–3 mg/kg per d) of hydrochlorothiazide may be necessary to avoid volume expansion, which amplifies the excretion of bicarbonate by lowering the renal threshold (also need K^+ supplementation to account for extra K^+ lost in the urine with the use of TZD diuretic).
- For preventing bone disease, phosphate and vitamin D supplementation are necessary in addition to correction of metabolic acidosis.
- Losses of glucose and amino acids are not usually symptomatic and do not require treatment.
- Kidney transplantation in pts with renal failure due to cystinosis.
- Liver transplantation in case of Wilson disease.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmogenicity due to electrolyte disturbances, hypovolemia	Assess for clinically symptomatic bradycardia, heart block, CHF	Auscultation of heart sounds, ECG	Continuous ECG monitoring
RENAL	Metabolic acidosis, polyuria, K^+, Mg^{2+}, Ca^{+2}, PO_3^- loss in urine	Assess GFR and residual renal function.	Assess for dehydration	ABG, UA, BMP
CNS	Lyte imbalance, hypoglycemia may cause confusion/ disorientation and/or seizures; rarely muscle weakness	Evaluate pt compliance	Lung sounds: rales, edema of extremities	Neurologic assessment

Key References: Klootwijk ED, Reichold M, Unwin RJ, et al.: Renal Fanconi syndrome: taking a proximal look at the nephron, *Nephrol Dial Transplant* 30(9):1456–1460, 2015; Pandey R, Garg R, Chakravarty C, et al.: Lowe's syndrome with Fanconi syndrome for ocular surgery: perioperative anesthetic considerations, *J Clin Anesth* 22(8):635–637, 2010.

Perioperative Implications

Preoperative Concerns

- Existence of any other coexisting genetic/metabolic disorder should be ruled out by thorough Hx, physical exam, and special test(s).
- Preop ABGs, ECG.
- Preop electrolytes level (K^+, Mg^{2+}, Ca^{+2}, PO_3^-) and glucose in the morning of surgery.
- Correction of electrolyte imbalances (K^+, Mg^{2+}, Ca^{+2}, PO_3^-).
- Metabolic acidosis corrected by administering $NaHCO_3^-$ preop to maintain plasma bicarbonate levels at about 20 mEq/L.

Induction/Maintenance

- During laryngoscopy, special attentions to avoid overextension and pt positioning to prevent injury to the rickety bones
- Closely monitoring acid-base and fluid-electrolytes imbalance during the surgery
- Monitoring volume status by UO and CVP

Postoperative Period

- Postop labs of urine analysis, serum lytes, calcium, phosphorous, glucose, BUN, creatinine, albumin, and hematologic profile are used to guide postop care
- ECG monitoring in PACU (hypokalemia)

Anticipated Problems/Concerns

- Lyte imbalances warrant monitoring and correction periop
- Potential hypovolemia
- Other coexisting metabolic/genetic disorder(s)

Fat Embolism

Shamsuddin Akhtar

Risk

- Long bone fractures and pelvic fractures:
  - 80–100% fat embolism
  - Less than 1–30% FES
- Male-female ratio: 4:1
- Adult greatly increased over pediatric
- Multiple fractures >single fractures
- Pathologic fractures >traumatic fractures
- Total hip, total knee replacement, intramedullary nailing:
  - 27–100% fat embolism
  - Unknown incidence FES
- Unusual causes: Liposuction, fat injection, bone marrow harvest and/or transplantation, vertebroplasty, cardiopulmonary bypass, CPR, burns, pancreatitis, sickle cell disease, osteomyelitis, fatty liver, soft tissue injury

Perioperative Risks

- FES: <10% mortality
- Preexisting FES: Respiratory failure/ ARDS, RV dysfunction, shock, coagulopathy, neurologic dysfunction
- Intraop fat embolism: Shock, hypoxemia

Worry About

- Preexisting FES: Hypoxemia, reduced pulm compliance, pulm Htn, RV failure, hypotension, cardiac arrest, coagulopathy
- Intraop embolism: Hypotension, RV failure, hypoxemia, paradoxical embolization, stroke, neurologic dysfunction (delirium to coma, postop)

Overview

- Fat particles (globules of marrow fat) traveling into blood and lung.
- Must distinguish fat embolism, from FES (triad of hypoxemia, petechiae, and neurologic abnormalities). Fat embolism is more common than FES.
- FES can produce mild pulm dysfunction to severe ARDS.
- Pulm Htn and acute RV failure may occur in severe cases of FES.
- Typically the onset of signs and symptoms of FES happen 12–72 h following injury.
- Fat embolism occurs commonly during femoral reaming and cementing in hip arthroplasty.
- FES is confounded with cement reaction during arthroplasty.

Etiology

- Most frequently follows orthopedic trauma with release of marrow fat into venous circulation
- Pathology produced by mechanical obstruction by intravascular fat passing into the pulm and systemic arterial circulation and by production of endogenous inflammatory mediators

Usual Treatment

- Early fracture fixation to decrease embolization.
- Use of noncemented prosthesis or venting of femoral shaft may reduce embolization during hip arthroplasty.
- Unreamed nailing for fracture fixation to reduce embolization.
- O_2 therapy to maintain SaO_2 >90%.
- Low tidal volume ventilation strategy with PEEP as for ARDS.
- Aggressive hemodynamic support with fluid and/or inotropes for shock and/or RV failure.
- Factor replacement for coagulopathy with bleeding.
- Corticosteroids, heparin, ethanol, dextran, aspirin, and prophylactic vena caval filter are of unproven benefit.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Intravascular fat	Fever		Fat staining of blood Bronchoalveolar lavage, macrophage staining
	Hypoperfusion Pulm Htn RV failure	Syncope Dyspnea	Hypotension Tachycardia Oliguria Vasoconstriction Mental status changes	TTE/ TEE, CVP, PA cath Lactic acidosis
RESP	ARDS Hypoxemia	Dyspnea	Tachypnea Cyanosis Rales	Pulse oximetry CXR, ABGs Pulm compliance (on mechanical ventilation)
HEME	Thrombocytopenia DIC Anemia	Bleeding	Bleeding (rare)	CBC Plts PT, PTT D dimer Fibrinogen
DERM	Capillary fat embolism		Petechiae (60%) Axilla, chest Base of neck Conjunctiva Oral mucous membranes	
CNS	Neurologic injury Cerebral edema	Mental status changes	Delirium Confusion, agitation Focal deficits (rare) Seizure (rare) Coma (rare)	MRI

Key References: Akhtar S: Fat embolism, *Anesthesiol Clin* 27(3):533–550, 2009; Kwiatt ME, Seamon MJ: Fat embolism syndrome, Int J Crit Ill Inj Sci 3(1):64-68, 2013.

Perioperative Implications

Preoperative Preparation
- Avoid sedatives and/or narcotics if hypoxemic and not mechanically ventilated or with obtundation.

Monitoring
- Arterial cath
- TTE/TEE, CVP, and PA cath to diagnose and manage RV failure and/or pulm Htn

Airway
- May have ARDS; decreased FRC and O_2 reserve and limited tolerance for apnea.
- May already be intubated and ventilated in severe cases.

Induction
- Minimize myocardial depression.
- Avoid increases in PA pressures (hypoxemia, hypercarbia, acidosis).

Maintenance
- CV: Anticipate decrease in BP with femoral reaming/cementing: anesthetic reduction, fluid, vasopressors; pts with RV dysfunction may require longer-term inotropic support.
- Resp: Pts with ARDS may require increased FIO_2 and PEEP; use lung protective strategy, ARDSnet protocol.
- Heme: Factor replacement for coagulopathy with bleeding.

Extubation
- Maintain intubation and mechanical ventilation in hemodynamically unstable pts and those requiring increased FIO_2, PEEP or with reduced compliance.
- Pts with CNS involvement may have a prolonged or exaggerated response to anesthetics and narcotics and may require intubation postop for airway protection/patency.

Anticipated Problems/Concerns
- Embolism during femoral reaming, prosthesis cementing.
- FES may be delayed by up to 72 h following fat embolism.
- Pts with ARDS may be difficult to ventilate and oxygenate.
- Hypotension is due to RV dysfunction and pulm Htn.

Foreign Body Aspiration

Ahmed Alshaarawi | Jeffrey R. Kirsch

Risk
- Most prevalent in children ages ≤3 y.
- In adults, elderly are most susceptible to FB aspiration. Risk factors include Alzheimer disease or dementia, stroke, loss of consciousness due to trauma, alcohol intoxication, or drug overdose.
- Foods are most commonly aspirated foreign objects.

Perioperative Risks
- Hypoxemia due to FB obstruction
- Fragmentation of the FB and distal dislodgement during retrieval
- Severe inflammation due to presence of high oil contents in a FB, leading to bulky granulation resulting in bronchial stenosis, bronchiectasis, pneumonia, and lung abscess

Worry About
- Exacerbation of hypoxemia due to ineffective ventilation during either diagnosis or treatment secondary to sedation or prolonged periods of apnea during extraction of FB
- Prolonged extraction of FB, airway swelling, and bleeding, which may lead to further respiratory compromise

Overview
- Pts with FB aspiration may present with cough, stridor, wheezing, throat pain, drooling, dysphagia, respiratory distress, and hypoxemia (oxygen saturation <90%).
- Subglottic FBs are often aspirated into the right main bronchus, likely due to the less acute angles of the right bronchus.

Usual Treatment
- Flexible and rigid bronchoscopy.
- Bronchotomy or lung resection may be performed in rare occasions, especially when the FB aspiration is diagnosed late (>1 wk).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Hypoxemia	Choking, coughing	Dyspnea, dysphagia, respiratory distress	Pulse oximetry, radiographic imaging, bronchoscopy

Key References: Won C, Michaud G, Kryger MH: Upper airway obstruction in adults. In Grippi MA, Elias JA, Fishman JA, et al., editors: *Fishman's pulmonary diseases and disorders*, ed 5, New York, NY, 2015, McGraw-Hill Education; Duan L, Chen X, Wang H, et al.: Surgical treatment of late-diagnosed bronchial foreign body aspiration: a report of 23 cases, *Clin Respir J* 8(3):269–273, 2014.

Perioperative Implications

Preoperative Preparation

- Provide supplemental oxygen and monitor oxygenation levels (pulse oximetry).
- Avoid manipulation of airway to prevent further dislodgement of FB.
- Discuss with surgeon plan of anesthetic (MAC with topical anesthesia vs. GA) and agree on ventilation plan (spontaneous, controlled, or jet ventilation).
- Topical anesthesia with aerosolized 4% lidocaine may be beneficial, especially if using spontaneous ventilation technique.

Intraoperative Management

- Preoxygenate.
- Rapid sequence induction is likely necessary; however consider effect of fasciculation on dislodgement of FB if using succinylcholine.
- Literature is indecisive whether controlled ventilation is preferred over spontaneous ventilation.
- If pt is a child, consider use of inhalational induction using sevoflurane and O_2.
- Ensure availability of surgical airway kit in cases of aspiration of large supraglottic FB.
- Consider use of passive oxygenation via bronchoscope, especially during periods of inadequate ventilation or apnea when a controlled ventilation mode is chosen.

Monitoring

- Standard monitoring especially using pulse oximetry
- $ETCO_2$ waveform

Postoperative Management

- Ensure hemostasis is reached if bleeding occurs during extraction of FB.
- Ensure return of safe cognitive function, muscle strength, and ventilatory function before extubation.
- Consider the need to monitor oxygenation levels after PACU discharge.

Anticipated Problems/Concerns

- Fragmentation of FB
- Pneumonia and lung abscess
- Atelectasis
- Hemoptysis

Friedreich Ataxia

Mark Helfaer | Lee A. Fleisher

Risk

- Prevalence: 2:100,000; 80–90% have cardiac involvement.

Worry About

- Cardiac involvement, which does not correlate with neurologic involvement.
- Electrophysiologic disturbances.
- Cardiac dysfunction and failure.

Overview

- Progressive degeneration of posterior columns and corticospinal and posterior spinocerebellar tracts.
- Muscle weakness.
- General anesthesia can lead to postop respiratory disorders caused by thoracic kyphoscoliosis, which is associated with restrictive respiratory function.
- Abnormal glucose homeostasis.
- Most individuals have onset of symptoms of FA between the ages of 5–18 y.
- Proprioceptive sensory loss, areflexia, ataxia of limbs, Babinski sign.
- Pes cavus and scoliosis.
- Cardiomyopathy.

Etiology

- Inherited: Usually autosomal recessive but occasionally dominant
- Mutations or DNA changes in the *FXN* gene
- Frataxin (mitochondrial iron content protein) deficiency

Usual Treatment

- Usually untreatable and progressive
- Medical management of cardiac abnormalities
- Scoliosis repair
- Can be mistaken for metabolic disorders (hexosaminidase A deficiency, adrenomyeloneuropathy, vitamin E deficiency)
- Clinical trials of coenzyme Q10 (CoQ10)/vitamin E ongoing.

Assessment Points

System	Effect	Assessment by Hx	Test
CV	Left ventricular hypokinesia Concentric and asymmetric hypertrophy Cardiomyopathy	Severities of heart and neurologic manifestations are not proportional	ECG ECHO Endomyocardial biopsy
RESP	Severe scoliosis Neuromuscular impairment	Noncardiac dyspnea	Lung function
MS	Pes cavus Scoliosis Respiratory muscle weakness Unpredictable andvariable response to muscle relaxants	Ability to walk without assistance	

Key References: Pancaro C, Renz D: Anesthetic management in Friedreich's ataxia, *Paediatr Anaesth* 15(5):433–434, 2005; Huercio I, Guasch E, Brogly N, Gilsanz F: Anaesthesia for orphan disease: combined spinal–epidural anaesthesia in a patient with Friedreich's ataxia, *Eur J Anaesthesiol* 31(6):340–341, 2014.

Perioperative Implications

Preoperative Preparation

- Usual premedication

Monitoring

- Train of four to monitor effects of neuromuscular blocking agent with unpredictable response due to neuromuscular disease

Airway

- None

Preinduction/Induction

- Case report of sensitivity to curare (0.06 mg/kg caused 90 min of apnea)
- Possibility of hyperkalemia and cardiac arrhythmias after succinylcholine

Maintenance

- Case reports of successful spinal and epidural anesthesia
- Case reports of spotty lumbar epidural block
- Case reports of successful GA with cautious use of nondepolarizing agents
- Case report of successful use of hypotensive anesthesia with isoflurane
- Case report of marked decrease in cardiac output and supraventricular tachycardia with nitroprusside for hypotensive anesthesia
- Case report of successful use of epidural narcotic

Extubation

- If adequate strength from neuromuscular blocker and adequate pulm function, extubation is appropriate.

Adjuvants

- See Maintenance.

Galactosemia

Charles Fox III | Rachel J. Kaye | Alan David Kaye

Risk

- Rare autosomal recessive metabolic disorder that can present increased anesthesia risks.
- Inherited disease of carbohydrate metabolism affecting how the body processes the simple sugar galactose. The primary risk factor is having parents who carry the gene for galactosemia.
- Life-threatening complications in the newborn may occur shortly after introducing galactose into the diet.
- Three types of galactosemia:
  - Type I (classic galactosemia) involves a deficiency of GALT enzyme. This is the most common form of the disease, with overall incidence between 1:40,000 and 1:60,000 in USA.
  - Type II occurs in fewer than 1:100,000.
  - Type III is very rare.

Perioperative Risks

- Commonly causes renal, liver, neural, and ophthalmic imbalances.
- Abnormal liver function tests will document extent of liver damage.
- Due to liver damage, these pts may experience abnormal bleeding both intraop and postop. If undergoing a cardiac procedure requiring bypass, heparinization will compound the risk of bleeding.
- These pts are prone to *Escherichia coli* neonatal sepsis, so extra precautions should be used if placing intravascular catheters.
- Drugs that are metabolized by the liver or found to be hepatotoxic should be avoided in these pts.
- Intravascular volume may be depleted in these pts due to poor feeding, vomiting, and/or diarrhea, which commonly exists in these pts.
- Neurodevelopment problems are common and sometimes severe. Ataxia and intention tremor may occur in older children and adults.
- Renal tubular acidosis, galactosuria, and albuminuria are common with these patients.
- Hemolytic anemia due to an increase in red blood cell galactose-1-phosphate is not unusual.

Worry About

- Long term complications:
  - Stunted growth
  - Learning disabilities
  - Speech/language problems
  - Fine and gross motor skill delays
  - Ovarian failure
  - Decreased bone mineral density (lack of dairy products in diet)

Overview

- Type I is referred to as classic galactosemia and results from a deficiency of the enzyme called GALT. GALT changes galactose to glucose. It usually presents in the neonatal period with life-threatening illness.
- Type II is a less severe form due to low levels of galactose kinase.
- Type III is a form with variable severity due to low levels of galactose epimerase.

Etiology

- Lactose is broken down into glucose and galactose. In individuals with galactosemia, the ability to further break down galactose is impaired or missing. This leads to increased and/or toxic levels of galactose-1-phosphate. Without treatment, in neonates, mortality approaches 75%. Classic galactosemia is an autosomal recessive disorder, meaning a child must inherit one defective gene from each parent.
- An infant with galactosemia appears normal at birth. Within the first few days or weeks of life after the baby is introduced to breast milk or a lactose-containing formula, symptoms begin to occur, which may include:
  - Excessive bleeding.
  - Encephalopathy.
  - Cataracts.
  - Hepatomegaly.
  - Hypotonia.
  - Lethargy.
  - FTT.
  - Delayed development.
  - Feeding problems.
  - Vomiting.
  - Diarrhea.
  - Jaundice.
  - Infection.
  - Neonatal death.
- Dx: Blood tests can reveal increased levels of galactose and galactose-1-phosphate. DNA tests look for mutations in GALT gene. Newborn screening tests should check for GALT enzyme.

Usual Treatment

- Lactose and galactose-free diet, with the following precautions:
  - Milk and all dairy products should be avoided.
  - Processed and prepackaged foods should be screened for lactose.
  - Infants should consume special lactose-free formula, including soy formula, meat-based formula, or Nutramigen (a protein-based formula).
- Calcium supplements.
- Supportive care should be provided depending on severity of liver, renal, and central nervous system disease. Antibiotics, IV fluids, plasma, and vitamin K are frequently needed.
- Drug considerations: A majority of medications, particularly tablets, contain lactose—these should be avoided. Avoid drugs that may be hepatotoxic or require extensive liver metabolism.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Prolonged QT syndrome			ECG
GI	Liver dysfunction		Ascites Vomiting Diarrhea Jaundice in newborn	Unconjugated or combined hyperbilirubinemia Abnormal LFTs Abnormal clotting
RENAL	Renal tubular dysfunction			Metabolic acidosis on blood gas Urine-albumin, aminoaciduria
HEME	Anemia (hemolytic) Risk of bleeding		Easy bruising	Coombs test Increased bleeding times, increased PT and PTT Low Hct and Hgb
NEURO			Impaired mental abilities	
IMMUNE	Increased incidence of *E. coli* septicemia		Hypotension, tachycardia	Blood cultures

Key References: Bosch AM: Classic galactosemia revisited, *J Inherit Metab Dis* 29(4):516–525, 2006; Choudhury A, Das S, Kiran U: Anaesthetic management of a newborn with galactosemia for congenital heart surgery, *Indian J Anaesth* 53(2):219–222, 2009.

Perioperative Implications

Preoperative Preparation

- Pts with galactosemia have elevated bleeding times and are at risk for increased bleeding during surgery.
- Hypoalbuminuria can cause an osmotic shift by diuresis. Urine volume is a poor predictor of intravascular volume in these pts. They may need preop fluid to replace deficits.
- These pts are prone to *E. coli* sepsis.

Monitoring/Induction/Maintenance

- Standard ASA monitors, with supplementation of invasive monitoring if risk factors present.
- Precautions should be undertaken when placing vascular access. These pts are prone to *E. coli* sepsis. Pts with long-standing gout may have coexisting nephropathy. Consideration should be made to adjust the dose of renally cleared paralytics and analgesics.
- Medications that cause hepatotoxicity or are metabolized by the liver should be avoided.
- Intraop hypotension should be treated aggressively, since these pts already suffer from hepatic and renal impairment.

Postoperative Period

- Preop hypotonia could predict respiratory issues.
- Hypotension should be treated aggressively.

Gastrinoma

Ashley R. Valentine | Jeffrey R. Kirsch

Risk

- Occurs in about 0.1–3 cases per million, usually in pts aged 20–50 y; male/female predominance about equal.
- 65–80% of gastrinomas are sporadic and have high (40–85%) malignant potential.
- 20–35% of cases occur with MEN1, with low (7–12%) malignant potential.
- Less than 0.1% of all PUD is caused by gastrinomas.

Perioperative Risks

- Risks associated with PUD
- Associated abnormalities of MEN1
- Risks associated with metastatic disease (regional lymph nodes, liver, bone)

Worry About

- Large gastric fluid volume
- Esophageal reflux (common)
- Lyte imbalance and volume depletion secondary to secretory diarrhea
- Coagulopathy due to liver metastases/resection

Overview

- Gastrinoma is a gastrin-secreting neuroendocrine tumor (non-beta islet cell tumor), occurring most commonly in duodenum and/or pancreas.
- Gastrin release stimulates gastric acid hypersecretion, causing symptoms of abdominal pain (due to refractory peptic ulcer disease), diarrhea, and reflux.
- Diagnosis often delayed several years from onset of symptoms because of difficulties distinguishing gastrinoma from other causes of PUD.
- Symptom control with PPIs also may delay diagnosis.
- May occur with other functional pNETs (e.g., carcinoid, insulinoma, parathyroid hormone-related peptide secreting tumor, Cushing).
- See also Multiple Endocrine Neoplasia Type I and II, Cushing Syndrome, Carcinoid Syndrome, Insulinoma, and Hyperparathyroidism for more information.

Usual Treatment

- Control gastric acid hypersecretion with PPIs and H_2 blockers.
- Chemotherapy, mTOR or tyrosine-kinase inhibitors, and/or somatostatin analogues for metastatic disease.
- Surgical exploration and resection.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia Right-sided valvular disease* Tachyarrhythmias*	Weakness, dizziness Dyspnea, edema, ascites, palpitations	Vital signs Cardiac murmur Cardiac exam	Orthostatics ECHO ECG
RESP	Wheezing*	Dyspnea	Pulmonary exam	CXR
GI	Gastric acid hypersecretion	Abd pain, reflux, diarrhea	Abdominal exam	Fasting gastrin, secretin stim
METAB	Hypokalemia	Weakness, muscle cramps		Lytes, ECG
ENDO	Hyperparathyroidism* Hypoglycemia*	Confusion, nausea/vomiting, abdominal pain, nephrolithiasis Dizziness, confusion	Mental status exam, abdominal exam	Serum parathyroid hormone, serum calcium CBG
RENAL	Nephrolithiasis*	Flank pain, hematuria	CVA tenderness	Urinalysis
CNS	Pituitary adenoma*	Headaches, visual changes	Visual field exam	MRI, prolactin level
MS	Weakness, arthralgias*	Proximal muscle weakness	Strength, reflexes	Serum calcium
HEME	Coagulation disorder	Bleeding abnormalities		INR/PT, PTT

*If gastrinoma presents as component of MEN I or other functional pNETs.

Key References: Ito T, Igarashi H, Robert J: Zollinger-Ellison syndrome: recent advances and controversies, *Curr Opin Gastroeterol* 29(6):650–661, 2013; Perry RR, Feliberti E, Vinik A: Gastrinoma Zollinger-Ellison-syndrome. In De Groot LJ, Beck-Peccoz P, Chrousos G, et al., editors: *Endotext* [Internet], South Dartmouth, MA, 2000, MDText.com, Inc., updated 2013.

Perioperative Implications

Preoperative Preparation

- Ensure adequate treatment of gastric hypersecretion.
- Evaluate for other endocrinopathies of MEN I syndrome.
- Evaluate for other functional pNETs; plan intraop management accordingly.
- Assess volume status.
- Check lytes and coagulation tests.
- Consider epidural catheter for intraop/postop pain control if no contraindications.
- Consider preop NG tube placement.

Monitoring

- May require central venous pressure monitoring and arterial line, depending on associated symptoms and comorbidities. Measure urine output with a bladder cath.

Induction

- Treat as full stomach due to increased gastric acid volumes and increased risk for aspiration.
- Use rapid-sequence induction with cricoid pressure.

Extubation

- Ensure adequate respiratory function and neuromuscular blockade recovery before extubation.

Postoperative Period

- Decreased vital capacity and functional residual capacity due to pain and ileus.

Anticipated Problems/Concerns

- Continued symptoms may occur if surgical resection is not curative.
- There are lower cure rates after resection for pts with gastrinomas associated with MEN1 or in the presence of metastatic liver disease.

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Gastroesophageal Reflux in Children

Francine S. Yudkowitz

Risk

- Physiologic GER usually resolves by 12–15 mo of age.
- 10% of pyloric stenosis pts.
- After diaphragmatic hernia, tracheoesophageal fistula, and esophageal atresia repairs
- Neurologically impaired, developmentally delayed, trisomy syndromes, and hiatal hernia.

Perioperative Risks

- Aspiration during induction of anesthesia
- Severe bronchospasm in pts with RAD
- Decreased pulm reserve secondary to chronic aspiration and pneumonitis

Worry About

- Pulm complications from aspiration pneumonitis and RAD
- Anemia and malnutrition

Overview

- Lower esophageal sphincter function matures by 6 wk postnatal age.
- GER is defined as regurgitation without pathologic consequences. GERD is defined as regurgitation resulting in esophagitis, nutritional compromise, and/or respiratory complications.
- Presence of a hiatal hernia does not necessarily mean pt will have GER.
- Sandifer syndrome: Opisthotonos or other abnormal head movements.
- Older children may complain of heartburn, dysphagia, and chest and abdominal pain.
- Degree of reflux, duration of acid exposure in the esophagus, and ability of the esophagus to clear the

reflux material help determine extent of mucosal damage and degree of esophagitis.
- Esophagitis may lead to bleeding, which may result in hematemesis, iron-deficiency anemia, and esophageal stricture. Also, pts are predisposed to Barrett esophagus.
- GER may be a cause of neonatal apnea.
- Diagnostic procedures include upper GI series, esophagoscopy, and esophageal pH probe.

Etiology

- Immature maturation of the lower esophageal sphincter
- Discoordination of swallowing mechanism in neurologically impaired pts

Usual Treatment

- Medical:
  - Infants: Thicken feeds, elevate the head of the bed maximum of 30 degrees, or place infant in prone position (although noted to be a risk for SIDS).
  - Older children: Avoid foods and beverages that exacerbate acid reflux (e.g., citrus, tomatoes, spicy/fried foods, caffeine). Place pt in upright position; sitting position worsens reflux.
  - H_2 blockers or PPIs to decrease gastric acidity.
- Surgical:
  - Indicated when medical therapy fails or in the presence of significant comorbidities (e.g., recurrent aspiration, apnea, failure to thrive, Barrett's esophagus).
  - Open or laparoscopic Nissen fundoplication has a 95% success rate in neurologically intact pts. Pts who are neurologically impaired have a greater morbidity and mortality with surgical repair.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Chronic aspiration RAD	Cough, cyanotic episodes, apnea Dyspnea, wheezing, cough	Rales, rhonchi Wheezing Decreased breath sounds, prolonged expiration	CXR, ABG (if indicated) CXR, peak flow ABG (if indicated)
HEME	Iron deficiency		Pallor	CBC
GENERAL	Malnutrition	Weight loss	Decreased SQ tissue	Serum albumin

Key References: Suwandhi E, Ton MN, Schwarz SM: Gastroesophageal reflux in infancy and childhood, *Pediatri Annals* 35(4):259–266, 2006; Hammer G, Hall S, Davis PJ: Anesthesia for general abdominal, thoracic, urologic, and bariatric surgery. In Davis PF, Cladis FP, Motoyama EK, editors: *Smith's anesthesia for infants and children,* ed 8, Philadelphia, PA, 2011, Elsevier, pp 745–785.

Perioperative Implications

Preoperative Preparation

- Assess the severity of pulm compromise.
- Optimize respiratory status: Treat pneumonia and control bronchospasm.
- Correct anemia.
- Improve nutritional status.
- Confirm availability of blood.
- Continue acid-suppressing therapy.

Monitoring

- Consider arterial line.

Induction

- For pts at risk for aspiration, utilize rapid-sequence induction with cricoid pressure.
- For pts with RAD, ensure adequate depth of anesthesia prior to instrumenting the airway.

Maintenance

- No one anesthetic is preferred.
- Avoid N_2O in laparoscopic procedure.
- Esophageal bougie may be required.
- Watch for possible pneumothorax, trauma to viscera, hemorrhage, and vena cava compression or laceration. Air or carbon dioxide embolism may occur during laparoscopic procedures.
- During laparoscopic procedures, intra-abdominal pressures of ≤12 mm Hg should be maintained.

Extubation/Postoperative Period

- May be extubated after uncomplicated surgery.
- Pts with severe respiratory compromise preop or with neurologic impairment may require a period of postop ventilation.
- Analgesic requirements will be less after laparoscopic procedures.

Surgical Procedure

- Fundus of the stomach is wrapped around the lower part of the esophagus. May be accomplished either open or laparoscopically.
- Pyloroplasty may be performed for associated delayed gastric emptying.
- Pneumoperitoneum created during laparoscopic surgery will result in increased SVR, increased CVP, increased CO, and increased BP. Intra-abdominal pressures >20 mm Hg will decrease venous return and decrease CO, but the BP will remain unchanged due to increased SVR.
- Pneumoperitoneum will also elevate the diaphragms, which will decrease lung volumes, decrease FRC, decrease pulm compliance, increase airway resistance, and increase V/Q mismatch.
- Pneumoperitoneum should not exceed 12 mm Hg. Pts are placed in the reverse Trendelenburg position. This will help ameliorate both diaphragmatic elevation and the CVP elevation.
- Pneumoperitoneum is accomplished by the insufflation of CO_2, which may necessitate increased minute ventilation.
- Laparoscopic procedures are associated with reduced rates of postop respiratory and wound complications and analgesic requirements, and shorter hospital stays.

Anticipated Problems/Concerns

- Respiratory system may be compromised.
- Pts are unable to vomit postop and up to 3 mo after surgery. Therefore, intestinal obstruction in the postop period should be treated as a dire emergency.

Gaucher Disease

Sydney E. Rose

Risk

- General population: 1:50,000 to 1:100,000.
- Inheritance follows an autosomal recessive pattern.
- Type 1 (nonneuropathic) most common and represents 99% of cases.
  - Population with highest prevalence is Ashkenazi Jewish.
  - 1:18 carrier rate
  - 3:1000 of the Ashkenazi Jewish population have type 1 disease.
- Types 2 (infantile) and 3 (juvenile) are exceedingly rare
  - No specific populations are at elevated risk.

Perioperative Risks

- Upper airway obstruction
- Coagulopathies
- GERD
- Insulin resistance

Worry About

- Glycosphingolipid deposits in head and neck
- Chronic aspiration
- Interstitial lung disease
- Cardiovascular calcifications
- Hepatosplenomegaly
- Osteonecrosis
- Coagulopathies
- Hematologic malignancies
- Polyneuropathies
- Parkinson disease

Overview

- Inborn error of metabolism.
- Lysosomal storage disorder due to defect or deficiency of the enzyme glucocerebrosidase.
- Nondegraded glucocerebroside and other glycolipids build up in macrophage and other peripheral leucocyte lysosomes.
- Lipid-laden macrophages then deposit in the spleen, liver, bone marrow, and other visceral organs, setting off an inflammatory and hyperplastic cellular response.
- Disease severity ranges from fatal in the perinatal period to completely asymptomatic and incidentally detected.
- Presenting features are variable and may occur at any age.
- Typically, visceral organs, bone marrow, and bones are involved in all three types.
- Type 1 can be differentiated from types 2 and 3 by lack of CNS involvement.
- Types 2 and 3 are both considered neuropathic:
  - Type 2, or "infantile GD," is acute in nature with onset occurring typically within the first year.
  - Type 3, or "juvenile GD," is more subacute, and disease progression is generally slower.
- Splenomegaly is typically the initial presenting sign.

Etiology

- Autosomal recessive trait with variable penetrance.
- Caused by mutations in the GBA gene located on chromosome 1q21.
- Greater than 200 mutations have been reported.
- 80% of mutations are caused by single nucleotide substitutions.
- A parent with GD has a 100% chance of passing on the gene.
- If the other parent is heterozygous for a mutated GBA gene, the child has a 50% chance of getting the disease.
- If parents are both heterozygous carriers, there is a 25% chance a child will be born with GD.
- Disease severity prediction based on genotypes is difficult due to the range of phenotypic variability.

Usual Treatment

- Treatment depends on severity of the disease.
- ERT with recombinant glucocerebrosidase in pts with GD1.
- Substrate reduction therapy reduces glycolipid buildup by decreasing the amount of glucocerebroside synthesized in patients unable to get ERT.

Assessment Points

System	Effect	Assessment by Hx and PE	Test
NEURO*	Apnea/asphyxia Spasticity Seizures Ataxia	Progressive brainstem degeneration Hyporeflexia Jerking movements Chorea Hypertonia/myoclonus Severe developmental delay Postop delirium	Reflex hammer Age-appropriate cognitive testing MRI brain
HEENT	Glycosphingolipid accumulation in head and neck	Ophthalmoplegia Strabismusa* Hx of upper airway obstruction Difficult airway Small mouth Trismusa*arching of neck	Vision testing Airway exam ENT consult
CV	Infiltration of myocardium by Gaucher cells Increase in LV mass Septal muscular prominence Apical akinesis structural pericardial changes Aortic and mitral valve pathologies Constrictive/hemorrhagic pericarditis	Arrhythmias Decreased exercise tolerance Cardiomyopathy Calcifications in ascending aorta, mitral valve, aortic valve CHF	ECG ECHO (TEE) Cardiac cath
ENDO	Glucocerebroside accumulation in lysosomes Peripheral insulin resistance Increase basal glucose production	Hypoglycemia	glucocerebroside and Phosphatase activity assays Blood glucose/HbA_{1c} Serum insulin assay
RESP	Post-extubation laryngospasm and/or respiratory failure Pulm Htn Cor pulmonale Intrapulmonary shunting Restrictive lung disease	History of choking/aspiration, may be chronic Chronic cough Pneumonia Glycosphingolipid deposits in lungs Kyphoscoliosis	CXR ABG PFTs LFTs Bronchoscopy ECHO
GI	GERD Portal Htn Splenic infarct	Epigastric pain GERD Weight loss Malnutrition	Barium swallow EGD Serum albumin assay Serum transferrin assay
HEME	Anemia Thrombocytopenia Acquired coagulation deficiencies in factors IX, XI, and vWF	Bleeding diathesis	CBC PT/PTT/INR BMP Glucocerebrosidase assay
MS	Pathologic osseous fractures Kyphoscoliosis Avascular necrosis of femoral head	Painful bone crises Fevers of unknown origin Decreased bone density in long bones Vertebral collapse Pes cavus	Bone density scan Bone marrow biopsy X-rays CT scan when necessary
IMMUNE	Infiltration of lymph nodes and lymphoid tissue Lymphoid tumors	Enlargement of lymphoid tissue lymph nodes, thymus, and tonsils Presence of peyer patches	US neck FNA lymphoid tumor
DERM	Pigmentation changes	Yellowish brown skin discoloration on face and/or lower extremities	Skin exam

*Types 2 and 3 only.

Key References: Kita T, Kitamura S, Takeda K, Fukumitsu K, Kinouchi K: Anesthetic management involving difficult intubation in a child with Gaucher disease, *Masui* 47(1):69–73, 1998; Dell'Oste C, Vincenti F: Anaesthetic management of children with type II and III Gaucher disease, *Minerva Pediatr* 49(10):495–498, 1997.

Perioperative Implications

Preoperative Preparation

- Evaluate for signs of neurologic, pulmonary, cardiac, hepatic, and bone marrow dysfunction.
- Warm the room.
- CBC, BMP.
- ST segment analysis in pts with signs or history of CAD.
- Consider TEE +/– PA catheter in surgeries expected to have large fluid shifts or in pts with infiltration of myocardium with Gaucher cells.

Monitoring

- A-line if comorbidities dictate.
- CVP +/– PA cath if pulm Htn or cardiac comorbidities dictate.
- Routine monitors.

Airway

- Thorough airway history and examination; discuss previous airway manipulation and evaluate oropharynx for deformities, fullness, and trismus.
- Prepare for possible difficult airway; glycosphingolipid deposits can narrow the upper airway yet be difficult to identify on PE.
- Smaller ETTs readily available.
- Have multiple airway devices available for multimodal airway management (LMA, video laryngoscope).
- Consider awake fiberoptic intubation.
- If warranted, have surgeon available at bedside for possible tracheostomy.

Positioning

- Bone fragility may be present; double-check pressure points and padding are adequate.

Induction

- Pts with swallowing difficulties are at risk for aspiration; consider rapid sequence.

Intubation
- Trismus resolves with muscle relaxant.
- If cardiac involvement, avoid agents that depress cardiac contractility.

Maintenance
- Choose drugs based on hemodynamic status.
- If hepatosplenomegaly or liver disease is present, avoid muscle relaxants dependent on hepatic metabolism.
- Regional anesthetics have been used and may be beneficial in minimizing airway manipulation and aiding in postoperative pain control. Bleeding dyscrasias must be ruled out prior to having a regional anesthetic.

Emergence/Extubation
- Fully awake and supine pts are ideal.
- Check for cuff leak if airway felt "tight" on intubation.
- Potential for prolonged ventilation, especially chronic aspirators.
- Rapid emergence agents (propofol, remifentanil, desflurane) will help facilitate process especially if neurologic component.
- Avoid hypoxia and hypercarbia.

Regional Anesthesia
- Thrombocytopenia and/or factor deficiencies may preclude regional anesthesia.

Adjuvants
- Dexmedetomidine 0.5 mcg/kg can be administered for postop delirium or agitation, especially in children.
- IV acetaminophen 1 g (adults) for pain control if no hepatic involvement; children may receive up to 15 mg/kg.
- H_2 blocker or PPI IV if symptomatic GERD preop.

Anticipated Problems/Concerns
- Airway difficulty during induction and intubation, especially if Hx of dysphagia or upper airway obstruction.
- If present preop, aspiration risk may still continue postop; consider leaving an NG or OG tube.
- Postop airway obstruction due to swelling of lymphoid tissue in head and neck area.
- Postop respiratory failure.
- Postop muscle spasms.
- Postop bleeding, especially if known bleeding dyscrasia preop.

Glaucoma, Closed-Angle

Steven Gayer

Risk
- According to the WHO, glaucoma is the second most common cause of blindness worldwide.
- Risk factors include hyperopia (far-sightedness), age >60, female gender, and family Hx.

Perioperative Risks
- Postop vision loss
- Inducing acute ACG

Worry About
- Causing sustained, marked elevations in IOP
- A chronic, narrowed angle becoming acutely closed periop

Overview
- There are a number of variants of glaucoma, and terminology can be confusing. These include acquired versus congenital, high IOP versus normal pressure, acute versus chronic, and open angle versus closed angle.
- ACG is categorized as either acute or chronic. Acute ACG is an urgent condition; chronic ACG is far more common and often asymptomatic.

Etiology
- ACG occurs when the distance at the outer periphery of the globe between the iris and cornea diminishes. Some individuals are born with narrowed angles and as they age and the lens thickens, further compromising the space.
- In predisposed individuals, chronic narrow-angle glaucoma may acutely progress to full-angle closure. Acute-angle closure occurs when the iris moves into direct contact with the cornea, physically blocking the natural egress of aqueous fluid.

Usual Treatment
- Acute ACG:
  - Administer topical beta-blocker, α2-agonist, pilocarpine 2% or 4% (pilocarpine is effective in inducing miosis only when iris ischemia is relieved, i.e., when IOP falls to <50 mm Hg).
  - Administer IV/oral acetazolamide 5–10 mg/kg (alternatives include hyperosmotic agents, e.g., IV 20% mannitol 1–2 g/kg, oral 50% glycerol 1–1.5 g/kg [contraindicated in diabetics], oral isosorbide 1.5–2.0 g/kg).
  - Topical steroids.
  - Place pts in the supine position (to allow lens-iris diaphragm to move posteriorly).
  - Analgesia and antiemetics.
  - Laser iridotomy.
- Chronic ACG:
  - Reduce IOP with prostaglandins (latanoprost, bimatoprost, travoprost).
  - Other surgical options include trabeculectomy, gonioplasty, or lens extraction.
  - Trabeculectomy, the gold standard procedure, involves creating a small hole in the sclera to allow freer drainage of aqueous humor.
  - Drainage device implants involve insertion of a tube shunt into the anterior chamber.
  - Cataract surgery may relieve a narrowed drainage angle.

Assessment Points

System	Effect	Hx	PE	Test
HEENT	Acute ACG	Sudden unilateral painful eye Blurred vision Photophobia Colored halos around lights Headache N/V	Ocular injection Hazy cornea Mid-dilated pupil	Penlight Gonioscope Slit-lamp Ultrasound biomicroscopy
	Subacute ACG	Headaches (often mistaken for migraine) or asymptomatic		
	Chronic ACG	Generally asymptomatic		

Key References: Gayer S: Prone to blindness: answers to postoperative visual loss, *Anesth Analg* 112(1):11–12, 2011; Gayer S, Gedde SJ: Intraoperative management of increased intraocular pressure in a patient with glaucoma undergoing robotic prostatectomy in Trendelenburg position, *Anesth Analg Case Rep* 6(2):19–21, 2015.

Perioperative Implications

Preoperative Preparation
- Consider preop consultation with pt's ophthalmologist if planned procedure involves prolonged steep Trendelenburg or prone position.
- Avoid mydriasis, either due to stress, dim lighting, or drugs (particularly topical sympatholytic or parasympathomimetic agents).
- Consider checking lytes if pt is on a diuretic.
- Preop antisialagogues or scopolamine are microfractionally absorbed into the globe and thus are considered generally safe to administer parenterally. Antimuscarinic ophthalmic drops (atropine, scopolamine) can induce acute ACG.
- Glaucoma surgery is generally considered to be low risk for sight-threatening bleeding. The consensus of studies exploring this controversial issue suggests that surgery can be safely performed under regional anesthesia without the need to discontinue antithrombotic agents.
- Phospholine iodide (echothiophate) should be discontinued 4 to 6 wk prior to surgery. Systemic absorption can inhibit plasma cholinesterase, causing prolonged muscle paralysis after succinylcholine, as well as inhibit metabolism of ester local anesthetics, predisposing a pt to toxicity.
- Regional anesthesia:
  - Needle-based block: Intraconal (retrobulbar) or extraconal (peribulbar)
  - Cannula-based block: Sub-Tenon's

- Subconjunctival and/or intracameral injection and/or topical anesthetics

Induction

- Anesthetic goals center around minimizing interventions that may increase IOP or cause further damage to the optic nerve. Succinylcholine increases IOP by 9 mm Hg for 5–10 min; nonetheless it is acceptable. Direct laryngoscopy and endotracheal intubation causes a similar or greater increase in IOP. Bucking, coughing, and vomiting increase IOP by 30–40 and should be avoided. A supraglottic airway may be preferred.

Maintenance

- Avoid IOP elevating maneuvers, including constriction around the pt's neck, prolonged Trendelenburg or prone position, and hypercapnia, which may cause choroidal vascular congestion.
- Consider prophylactic administration of acetazolamide and/or mannitol for select pts—for example, the chronic untreated ACG pt for robotic assisted laparoscopic prostatectomy who will undergo prolonged steep Trendelenburg position coupled with potential elevated CO_2, or a similar pt having prolonged prone position spine surgery.

Extubation

- Carefully avoid IOP increasing events such as coughing, bucking, retching, and tight lid squeezing. Elevate head of bed.

Anticipated Problems/Concerns

- Acute ACG is an urgent vision-threatening condition. The challenge for the anesthesiologist is to distinguish whether a painful eye following nonophthalmic surgery is due to a corneal abrasion or acute ACG. Consult an ophthalmologist if the clinical scenario resembles acute ACG.
- Avoid use of ocular decompression devices such as the Honan balloon with regional anesthesia.
- Potentially life-threatening side effects: Systemic absorption of topical beta-blockers (especially Timolol) may exacerbate asthma, produce bradycardia or heart block, and induce CHF. Acetazolamide can cause diuresis and produce electrolyte abnormalities with chronic use. Mannitol can result in osmotic diuresis, CHF, pulmonary edema, and full bladder discomfort. For phospholine iodide (echothiophate), see the previous section.
- Controversial: Postop visual field "wipe-out" or worsening of vision. There is no obvious etiology; however, numerous surgical, anesthetic, and postop causes have been postulated. Theoretical anesthesia mechanisms include:
  - Local anesthetic mass effect: Pressure from local anesthetic, bleeding, or placement of a compression device
  - Direct trauma to the optic nerve
  - Hypoperfusion of the optic nerve head: Hypotension during general anesthesia and vasoconstrictors in local anesthetic

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Glaucoma, Open-Angle

James W. Ibinson | Laura H. Ferguson

Risk

- Open-angle glaucoma is the leading cause of blindness among African Americans and the second leading cause overall in USA.
- African American race, advanced age, elevated IOP, myopia, low diastolic perfusion pressures, and family Hx of open-angle glaucoma increase the risk for primary open-angle glaucoma.
- Incidence in US: Estimates suggest over 2.25 million Americans over age 40 have open-angle glaucoma.

Perioperative Risks

- Vision loss secondary to optic nerve damage from pressure or ischemia

Worry About

- Interactions between ophthalmologic drugs and anesthetics
- Increases in IOP
- Periop derangements in electrolytes secondary to ophthalmologic drugs

Overview

- Glaucoma is a degenerative optic neuropathy characterized by optic-nerve cupping that results in progressive vision loss and possibly blindness if not treated. Treatment does not reverse the blindness.
- Elevated IOP is often found in glaucoma but is not required for the diagnosis. Nonetheless, treatment for all forms is aimed at maintaining a low-normal IOP.
- Onset is gradual, bilateral, and often unnoticed. While juvenile forms exist, it is much more common in those >40 y.

Etiology

- Likely caused by sclerosis of the trabecular meshwork near the canal of Schlemm, which decreases aqueous humor outflow and elevates IOP.
- Normal pressure, open-angle glaucoma is thought to be caused by insufficient blood flow leading to optic nerve damage, but treatment is the same as with primary open-angle glaucoma.

Usual Treatment

- Treatment goal is to maintain a low-normal IOP. Treatment is most successful if disease is detected early.
- Medical treatment includes topical timolol, betaxolol, epinephrine, echothiophate, or dipivefrin and oral acetazolamide.
- Surgical treatment includes laser trabeculoplasty, trabeculectomy, Baerveldt and Ahmed device implantation, and cycloablation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Optic nerve damage, increased IOP	Visual changes, family Hx of glaucoma, myopia	Decreased visual acuity, increased optic cup-to-disk ratio, visual field losses	Slit lamp exam Tonometry Visual fields Visual acuity
CV	Excessive beta blockade	Fatigue, syncope or near-syncope, SOB, chest pain	Hypotension, bradycardia	

Key References : Kwon YH, Fingert JH, Kuehn MH, Alward WL: Primary open-angle glaucoma, *N Engl J Med* 360(11):1113–1124, 2009; Jaakola MI, Ali-Melkkilä T, Kanto J, Kallio A, Scheinin H, Scheinin M: Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery, *Br J Anaesth* 68(6):570–575, 1992.

Perioperative Implications

Preoperative Preparation

- Maintain miosis by continuing topical and systemic treatment medications except for echothiophate, which should be stopped 4 wk prior to elective surgery.
- Pts taking acetazolamide, a carbonic anhydrase inhibitor, should have electrolytes checked preop with specific attention to Na^+, K^+, and bicarbonate levels.
- Antisialagogue premedication with glycopyrrolate or atropine is not contraindicated; however, several texts suggest scopolamine should be avoided due to its greater mydriatic effect.

Induction

- Blunt increases in IOP during laryngoscopy and intubation with the use of IV agents, which tend to decrease IOP. Controversy surrounds ketamine's effect.
- Succinylcholine is safe for induction and intubation, provided echothiophate has been discontinued.
- Hypotension should be avoided due to optic nerve perfusion concerns.
- Use of LMA may not increase IOP as much as direct laryngoscopy and intubation.

General Anesthesia

- All inhalational agents decrease IOP. This should be taken into account when providing anesthesia for eye exams.
- Hypercarbia should be avoided, since it increases IOP. Hypothermia, on the other hand, lowers IOP.
- Timolol is systemically absorbed and can cause asthmatic crises and severe sinus bradycardia, especially when other beta-blockers are administered. Betaxolol is more oculospecific, but additional beta blockade during anesthesia should be done with extreme caution. Effects of calcium channel blockers like verapamil are addictive and should be administered with care.
- Pneumoperitoneum and head-down positioning can increase IOP, but maintaining adequate anesthetic depth likely eliminates any measurable pressure increase.

Regional Anesthesia
- Ester local anesthetics should be avoided in pts taking echothiophate due to reduced plasma cholinesterase activity and altered metabolism.

Extubation
- Avoid coughing and bucking, which can cause acute increases in IOP.
- Neuromuscular blockade reversal agents and antimuscarinics in usual dosages are considered safe.

Postoperative Period
- If emergency surgery is required in pts currently taking echothiophate, expect the need for prolonged postop ventilation.

Anticipated Problems/Concerns
- Avoid increases in IOP.
- Echothiophate therapy produces decreased plasma cholinesterase activity and should be stopped 4 wk prior to surgery to avoid a prolonged paralysis with the use of succinylcholine.
- Be aware that topical beta-blockers are systemically absorbed and can have systemic effects.

Glomus Jugulare Tumors

Ghaleb A. Ghani

Risk
- Account for 0.6% of head and neck tumors worldwide
- Male-to-female prevalence ratio: 1:2.5
- Slow-growing
- Can coexist with other paragangliomas
- Histologically benign but can be malignant with metastases
- Can be familial

Perioperative Risks
- Hypothermia
- Massive blood loss
- Venous air embolism
- Htn
- Bradycardia
- Hypotension
- Bronchospasm
- Tumor-parts embolization

Worry About
- Glomus jugulare tumors can appear in multiple locations; symptoms can persist after resection of the tumor.

Overview
- Tumors of neural crest at base of skull in jugular bulb area
- Highly vascular
- May extend into the posterior fossa
- May cause hydrocephalus
- May damage the lower cranial nerves (IX–XII)
- May involve internal carotid artery
- May grow into lumen of the jugular vein, as far as the RA
- May cause Horner syndrome
- May secrete catecholamines: 5%
- May secrete serotonin, histamine

Etiology
- Congenital (usually benign) hypertrophied arteriovenous anastomosis
- Epithelial cells with abundant capillary network

Usual Treatment
- Resection
- Embolization, alone or pre-resection
- Radiation
- Radiosurgery

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Cranial nerve injury	Hoarseness Dysphagia Tinnitus Vertigo	Tongue movement Soft palate motion Gag reflex Hearing test	Video laryngoscopy
CV	Htn Intravascular growth	Headache Palpitations	BP	Catecholamines level MRI/CT scans Angio (if indicated)
RESP	Aspiration	Cough Fever SOB	Rhonchi, wheezing	CXR
GI	Delayed gastric emptying	Heartburn Regurgitation		
GU		No different from normal		
CNS	Intracranial extension	Hearing loss Headache Dizziness Ataxia		CT scan MRI Paragangliomas in other locations

Key References: Jensen NF: Glomus tumors of the head and neck: anesthetic considerations, *Anesth Analg* 78(1):112–119, 1994; Heth J: The basic science of glomus jugulare tumors, *Neurosurg Focus* 17(2):E2, 2004.

Perioperative Implications

Preoperative Preparation
- Control Htn (in cathecholamine-secreting tumors). Preparation is similar to pheochromocytoma (see also Pheochromocytoma).
- Trial balloon occlusion of the internal carotid artery if there is a chance of ligating it intraop.
- Treat pneumonia.
- Metoclopramide for delayed gastric emptying.
- Adequate venous access for rapid fluid infusion.

Monitoring
- Consider arterial line and CVP.
- Monitor for venous air embolism (frequent ABG, $ETCO_2$, N_2; precordial Doppler).
- Cerebral oximetry.
- Facial nerve.
- Tenth nerve by using the NIM-EMG-ETT.

Maintenance
- Watch out for massive blood loss, Htn, hypotension, bradycardia, bronchospasm, venous air embolism, and tumor-parts embolization.
- Provide controlled hypotension if needed.
- Measure to decrease the ICP for intracranial extension:
  - Administer mannitol.
  - Assess for hyperventilation.
  - Optimize venous return from brain.
  - Assess CSF drainage.

Extubation
- Evaluate for airway swelling and neck hematoma.
- Evaluate for sequelae of pulm embolism.
- Evaluate for cranial nerves (IX–XII) injury.
- Evaluate for brain stem injury.

Adjuvants
- Controlled ventilation
- Muscle relaxants to prevent spontaneous ventilation intraop
- Controlled hypotension

Anticipated Problems/Concerns
- Loss of upper airway reflexes
- Airway obstruction
- Aspiration
- Delayed gastric emptying
- Ileus
- CNS insult
- CSF leak

Glossopharyngeal Neuralgia

R. David Todd

Risk

- Majority of cases of GPN are idiopathic.
- Increased prevalence with extracranial neoplasms, trauma/infection/inflammation to tonsils, and pharynx, arachnoiditis.
- More common in pts older than 50 y and middle-aged females.

Perioperative Risks

- Vagoglossopharyngeal neuralgia occurs in 10% of pts with GPN. Attacks of pain can trigger bradycardia/asystole, arterial hypotension, syncope, ECG changes (arrhythmias), or even cardiac arrest.
- Tonic-clonic limb jerking and facial movements that resemble seizure activity can accompany attacks of pain.

Worry About

- Bradycardia, asystole, arterial hypotension, syncope, arrhythmias, and cardiac arrest during pain attacks
- Drug interactions with anticonvulsants: Carbamazepine, phenytoin, and oxcarbazepine
- Chronic narcotic use

Overview

- Rare: Represents ~1% of facial pain cases.
- Sudden, sharp, and excruciating pain shooting to the pharynx, tonsil, base of tongue, with possible radiation to eustachian tube and inner ear structures and/or mandible angle.
- Attacks may be triggered by swallowing (most common), chewing, talking, coughing, or yawning.
- Paroxysms of pain are usually <1 min and can recur after brief periods.
- Clusters of attacks last from weeks to months.
- Trigger zones can be located when application of topical anesthetic solution relieves pain.
- Pain typically stays on same side, and left side symptoms are more common (3:2).
- Attacks can precipitate bradycardia, syncope, tachycardia, and arterial hypotension.
- Cranial nerve (IX) receives afferent input from chemoreceptor and stretch baroreceptor of carotid body and carotid sinus, which may be responsible for CV reflex symptoms.
- Differential Dx can include trigeminal neuralgia, superior laryngeal neuralgia, cluster headache, or sick sinus syndrome.

Etiology

- Usually idiopathic
- Secondary causes:
  - Vascular compression of the glossopharyngeal nerve (most common)
  - Neoplasms (cerebellopontine, skull base, pharynx, tongue, laryngeal carcinomas)
  - Infection (tonsillitis, pharyngeal abscess, arachnoiditis)
  - Trauma (skull base fractures, tonsillectomy, dental extraction, neck dissection)
  - Other (Chiari I malformation, MS, elongated styloid process [Eagle's syndrome])

Usual Treatment

- Pharmacologic treatment involves anticonvulsants: Carbamazepine, gabapentin, phenytoin, oxcarbazepine, pregabalin.
- Nerve block and possible neurolysis.
- Microvascular decompression is the best surgical treatment, with >70% success rate.
- Rhizotomy of the glossopharyngeal (IX) nerve is surgical alternative for MVD.
- Evolving care includes gamma knife surgery and stereotactic radiosurgery.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Bradycardia, tachycardia, syncope, hypotension	Syncope, palpitations	BP HR/rhythm	ECG or biotelemetry to capture pain attacks
CNS	Pain in IX/X distribution	Paroxysmal pain attacks in IX/X distribution with various triggers	Attempt to trigger pain and find distribution	MRI/MRA to ID etiology and vascular compression

Key References: Blumenfeld A, Nikosskaya G: Glossopharyngeal neuralgia, *Curr Pain Headache Rep* 17(7):343, 2013; Kandan SR, Khan S, Jeyaretna DS, Lhatoo S, Patel NK, Coakham HB: Neuralgia of the glossopharyngeal and vagal nerves: long-term outcome following surgical treatment and literature review, *Br J Neurosurg* 24(4):441–446, 2010.

Perioperative Implications

Preoperative Evaluation

- Assess triggers and subsequent pain with emphasis on Hx of bradycardia, palpitations, syncope, and seizures.
- Check medications, dosing, and efficacy, and review potential side effects along with drug interactions. Maintain preop regimen.

Monitoring

- Monitor preinduction arterial line in pts with significant CV symptoms and central venous catheter when temporary pacemaker might be indicated (vagoglossopharyngeal neuralgia).

Airway

- Direct laryngoscopy can trigger an attack.
- Topical anesthesia to oropharynx prior to laryngoscopy can blunt CV symptoms.
- Glossopharyngeal nerve block is an alternative to topical anesthesia for prophylaxis.

Maintenance

- Remain vigilant and promptly treat cardiac symptoms and labile BP.
- Watch for sudden arterial hypotension, bradycardia, and cardiac arrhythmias.

Extubation

- Look for possible IX/X nerve palsy and subsequent vocal cord paralysis following microvascular decompression surgery.

Anticipated Problems/Concerns

- Direct laryngoscopy triggering a pain attack with hypotension, bradycardia, and cardiac arrhythmias
- Periop pain attack with severe uncontrolled pain
- Chronic narcotic use and tolerance

Glucose-6-Phosphate Dehydrogenase Deficiency

Stephanie Huang | Lee A. Fleisher

Risk

- Most common enzyme deficiency in the world.
- Due to X-linked recessive inheritance.
- Worldwide incidence: 400 million.
- Regions with highest prevalence include Africa, Southeast Asia, the Mediterranean, and the Middle East.
- In USA, G6PD deficiency is prevalent among black males and immigrant populations from the previously listed regions. Approx 10% of African-American males have G6PD deficiency.

Perioperative Risks

- Increased risk of acute hemolysis of RBCs with exposure to oxidative stressors.
- Infection and surgical stress can lead to hemolysis.
- Severe hemolysis may require transfusion and acute renal failure requiring hemodialysis.

Worry About

- General anesthesia masks early signs and symptoms of hemolytic crisis. Hypotension with hemolysis can be attributed to other causes, delaying diagnosis of acute hemolytic crisis.
- Early recognition and treatment of hemolytic anemia is required to prevent permanent neurologic damage, renal failure, or death.

Overview

- Enzyme deficiency is associated with chronic and/or acute hemolysis of RBCs.
- Most pts with G6PD deficiency are clinically asymptomatic unless exposed to triggers.
- Hemolysis occurs when pts are exposed to an oxidative stressor: infection, oxidative drug, fava beans, metabolic derangements.
- Hemolysis is usually seen 1–3 d after exposure.
- Clinical manifestations include fatigue, lumbar pain, abdominal pain, jaundice, splenomegaly, hemoglobinuria, scleral icterus, hypotension, tachycardia, dyspnea, headache, and pallor.
- Acute hemolysis is self-limited; resolution occurs within 4–7 d.
- Chronic nonspherocytic hemolytic anemia with severe deficiency may occur (<10% of normal enzyme levels).
- Associated with neonatal jaundice.

Etiology

- G6PD is an enzyme that catalyzes NADP into NADPH in the pentose phosphate pathway. NADPH then generates antioxidants that protect cells against oxidative damage.
- RBCs' only source of NADPH is through the pentose phosphate pathway. G6PD deficiency results in

RBCs being unable to protect themselves from oxidative stress. This leads to eventual cell death.
- There are over 180 different known mutations to the G6PD gene that lead to deficiency.
- Frequency, risk, and severity of hemolysis varies depending on severity of deficiency.
- Drugs to avoid include sulfonamides, dapsone, methylene blue, nitrofurantoin, phenazopyridine, primaquine, rasburicase, and toluidine blue.

Usual Treatment

- The main treatment for G6PD deficiency is preventative; avoid oxidative stressors.
- If hemolysis were to occur, discontinue the offending agent and maintain urine output with IVF and diuretics.
- Hemodialysis may be indicated in severe acute renal failure.
- PRBC transfusion can be necessary in cases of severe anemia or hemodynamic compromise.
- Folic acid and iron are beneficial.
- Splenectomy and antioxidants are not indicated.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Excess bilirubin buildup		Scleral icterus	
CV	Anemia leading to decreased oxygen delivery, compensatory increased CO, tissue hypoxemia	Substernal pain, fatigue	Tachycardia,Hypotension, flow murmur	ECG, ECHO in severe refractory hypotension
RESP	Hypoxemic hypoxia if severe	Dyspnea	Tachypnea, possibly decreased SpO_2	ABG
GI	Destruction of RBCs in spleen, cholelithiasis	Abdominal pain	Splenomegaly, jaundice, RUQ tenderness	LFTs (increased indirect bilirubin), increased LDH, RUQ ultrasound
RENAL	Excretion of excess hemoglobin leads to nephropathy	Dark brown urine	Hemoglobinuria	BUN/ Cr, UA (+RBC)
HEME	Hemolytic anemia		Pallor	CBC (decreased Hgb/Hct), decreased haptoglobin, peripheral blood smear with Heinz bodies and RBC fragments
CNS	Kernicterus (bilirubin encephalopathy) in neonates with severe disease	Lethargy, eventual mental retardation	Early hypotonia leads to late hypertonia, gaze abnormalities, hearing loss, movement disorders	Brain MRI with high signal in globus pallidus on T-2 weighted images
MS	Increased erythropoietic response of the bone marrow	Lumbar pain		Increased reticulocyte count

Key References: Luzzatto L: Hemolytic anemias and anemia due to acute blood loss. In Kasper D, Fauci AS, Hauser SL, Longo D, Jameson JL, Loscalzo J editors: *Harrison's principles of internal medicine, ed 19,* New York, NY, 2015, McGraw-Hill; Elyassi AR, Rowshan HH: Perioperative management of the glucose-6-phosphate dehydrogenase deficient patient: a review of literature, *Anesth Prog* 56(3):86–91, 2009.

Perioperative Implications

Preoperative Preparation

- Consider anxiolytic premedication.
- Clarify severity of disease if possible. If Hgb/Hct is stable and no other clinical signs of hemolytic anemia are present, no further testing is typically needed.
- Adequately treat any infections prior to surgery.

Monitoring

- Monitor urine output and color.
- Consider A-line for frequent labs.

Induction

- Maintain baseline HR/BP; blunt response to airway manipulation to minimize physiologic stress.

Maintenance

- Reduce surgical stress with adequate anesthesia and analgesia.
- Hypotension, decreased urine output, and tachycardia may be early signs of hemolysis.
- Maintain diligent use of hand hygiene and infection prevention methods.
- Monitor temperature; hypothermia can lead to hemolysis.
- Aggressively treat acidemia and hyperglycemia; both can lead to hemolysis.

Extubation

- Avoid hypercarbia.

Postoperative Period

- Watch for signs/symptoms of hemolytic crises. At minimum, monitor daily CBC.
- Adequate multimodal pain control.

Anticipated Problems/Concerns

- While in vitro studies have shown isoflurane, sevoflurane, diazepam, and midazolam to inhibit G6PD activity, there have been no in vivo cases or studies showing these and other common anesthetic agents causing hemolytic crisis in the G6PD deficient pt.
- Avoid medications that can induce methemoglobinemia, such as benzocaine, nitrates, and metoclopramide. The treatment for methemoglobinemia, methylene blue, is a known oxidative drug that can lead to acute hemolysis.
- If possible, minimize use of cardiopulmonary bypass, a known cause of oxidative stress.

Glycogen Storage Diseases

Jeffrey D. Roizen

Risk

- There are a total of 11 GSDs (0–7, 9, 11, and 12; there is no GSD 8 or 10); the most common are GSD I (Von-Gierke), GSD II (Pompe [3 types]) and GSD III (Cori or Forbe), which may each be as common as 1:50,000 individuals. The least common may occur as rarely as 1:1,000,000 or even less.
- GSDs I and III each account for roughly 25% of GSDs in US.
- All of the described diseases are inherited in an autosomal recessive fashion and molecular diagnosis is available for all aside from GSD 0 (what was once type 8 is now a subtype of type 6 and is x-linked recessive; what was once type 10 is now a subtype of type 6).
- No racial predilection for most types of GSD. Non-Ashkenazi Jews in northern Africa have an increased prevalence of GSD 3 (1:5000), and there may also be an increased incidence of GSD 7.

Perioperative Risks

- These diseases have heterogeneous risks.
  - Several are associated with a risk for hypoglycemia (0, 1, 3, 6), with 1 and 3 requiring careful glucose monitoring.
  - Hepatomegaly and liver failure in 1, 3, and 4.
  - Lactic acidosis in several (most extremely in 1) when too much glucose is given. This is not usually a clinically relevant problem, but when supplementing with glucose-containing fluids, it is ideal to keep glucose above 80 and below 160.
  - Myopathies (and specifically cardiac failure) in several. For cardiac failure, 2, 3, 4, and 7; for 5 (McArdle) tourniqueting can cause muscle damage.
  - The adult form of GSD 2 (Pompe disease) can be associated with sleep apnea later in life (all forms can be associated with limited respiratory reserve. The infantile form has a lethal outcome caused by progressive cardiorespiratory insufficiency, which usually starts by the end of the first year of life. The juvenile form has a slower course with some individuals living into their 20s or 30s).
  - In GSD type 5 and 7, rhabdomyolysis can cause renal failure.
  - In GSD II, macroglossia can be present.

Worry About

- Hypoglycemia in 0, 1, 3, and 6
- Cardiac function in 2, 3, 4, and 7
- Rhabdomyolysis leading to renal failure in 5 and 7
- Coagulopathy and cirrhosis in 4
- Renal function and platelet function in 1

Overview

- Glucose is the primary energy substrate for the majority of the tissues in the body (heart and brain can function well on ketones, but most other organs cannot). When a person is fasting or between meals, serum glucose (and thus intracellular glucose) is maintained primarily by the breakdown of glycogen in the liver.
- The GSDs result from mutations in genes involved in glycogen synthesis and breakdown, leading to the inability to use glycogen (in one way or another—usually tissue-limited).
- Ideally the NPO time should be limited, and for those associated with hypoglycemia, glucose should be monitored and periop glucose-containing fluids administered.
- The consequences of these mutations depend on (1) the tissue where the enzyme is expressed and (2) the effect of the mutation on the pathway. Whether it prevents the synthesis of glycogen, debranching of glycogen, phosphorylation/dephosphorylation of glucose, or other steps in glycogen breakdown.

Etiology

- Caused by homozygous mutations in enzymes involved in the synthesis or breakdown of glycogen.
- Autosomal recessive trait with a few case reports of compound heterozygotes who have mutations in two different enzymes in the pathway.
- Each heterozygous parent has a 50% chance of passing on the gene.
- Long-term prognosis depends on the enzyme affected (type of GSD): 0, Muscle cramping and occasional growth failure; 1, growth failure; 2, infantile—death by 2, juvenile—death by 30, adult—sometimes heart failure or sudden death in adulthood; 3, myopathy; 4, FTT and death by 10; 5, exercise-induced cramps; 6, growth retardation; 7, growth retardation; 9, delayed motor development and growth retardation; 11, pretty normal; 12, exercise intolerance; 13, exercise intolerance and muscle pain with aging.

Usual Treatment

- Several GSDs can be treated with liver transplant with excellent outcomes (1, 3, and 4).
- Several are managed with enteral cornstarch supplementation (1, 3, and 6).
- 2 (Pompe) may be treated with recombinant human α-glucosidase enzyme replacement therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	In 2 (Pompe) macroglossia can occur		Limited ability to visualize glottic opening	
CV	Cardiomyopathy	Determine GSD type		ECG, ECHO
RESP	Decreased resp reserve (in 2)	Sleep apnea	Assess for sleep apnea	Sleep study
GI	Coagulopathy/liver failure in 1		Jaundice and hepatomegaly with a very firm liver raising concern for cirrhosis	LFTs and coagulation studies (PT/PTT/INR)
HEME	Platelet dysfunction (leading to decreased platelets) in 1	Easy bleeding and bruising	Ecchymosis	CBC with plts and plt function tests if possible
RENAL	Renal dysfunction in 1			Comprehensive metabolic panel (CMP) with calculated GFR
MS	Truncal obesity in 1 and 3		BMI	

Key References: Stuart G, Ahmad N: Perioperative care of children with inherited metabolic disorders, *Contin Educ Anaesth Crit Care Pain* 11(2):62–68, 2010; Fleisher L: *Anesthesia and Uncommon Diseases,* ed 5, Philadelphia, PA, 2006, Elsevier, pp 177.

Perioperative Implications

Preoperative Preparation

- Fasting should be minimized to the extent possible.
- Blood glucose should be monitored and periop glucose-containing fluids administered.
- The appropriate tests for GSD type should be performed; where risks are present, they should be managed appropriately (e.g., for decreased platelets or platelet function, the administration of platelets).
- For altered liver function, be aware that some medications may have altered metabolism.
- Conscious sedation is also possible; concern for sleep apnea syndrome.
- Assess individual pt based on systems approach and review relevant studies.
- For pts with decreased cardiac function, avoid myocardial depressants when possible.
- Avoid tourniqueting with type V; some evidence points to an association of MH with type V, so it is recommended to avoid MH-triggering medications (or to do an IVCT test).
- Similarly, there are case reports suggesting avoidance of propofol and sevofluorane in 2.
- There are theoretical preferences for some approaches, but the key factors of a successful outcome are attention to anesthetic technique and close monitoring.

Monitoring

- Standard ASA monitors
- For cases associated with hypoglycemia, glucose monitoring every 30 min (can use CGM)
- For cases associated with rhabdomyolysis leading to renal failure, consider intraop CKs.
- Bispectral index may be misleading in GSD 1.

Airway

- Anticipate difficulty intubating in 2 if macroglossia is present.
- Other diseases with skeletal muscle involvement can predispose pts to upper airway obstruction.

Induction

- As above in preparation

Maintenance

- Careful positioning in types 5 and 7 to avoid rhabdomyolysis

Postoperative Period

- Continuous pulse oximetry due to high incidence of sleep apnea in 2
- Continued glucose-containing fluids and monitoring for 0, 1, 3, 6

Anticipated Problems/Concerns

- Hypoglycemia in 0, 1, 3, and 6
- Cardiac dysfunction in 2, 3, 4, and 7
- Rhabdomyolysis leading to renal failure in 5 and 7
- Coagulopathy and cirrhosis in 4
- Renal function and platelet function in 1

Goldenhar Syndrome

Zulfiqar Ahmed

Risk

- Incidence: 1:5500 live births.
- Second most common facial birth defect after cleft lip and palate.
- Extracraniofacial anomalies can range from one anomaly (13%) to multiple affected organ systems (42%). No gender or side predominance was detected. Central nervous system, cardiac, and skeletal anomalies each occurred in more than 10% of cases. Surgical correction usually takes place in severe cases.
- Cleft palate occurs in 25% of pts

Perioperative Risks

- Difficulties with airway management
- Possible need for tracheostomy
- High risk of anesthesia overdose in premature and low-weight pts

Worry About

- Stabilizing the heart rate.
- Difficulty with airway management.
- Ensuring good mask fit. There are many sizes to choose from, and the mask must fit prior to induction. Mask may have to be changed after induction for better fit. The degree of inflation of the facemask cuff may be adjusted in order to ensure an appropriate seal.
- IV access.
- Associated anomalies, such as cardiac and or cervical spine malformation that may influence decisions.
- Cancelation of procedure owing to inability to intubate.
- Increased severity of microsomia. Pruzansky classification type III is associated with increased intubation difficulties.

Overview

- Craniofacial microsomia, also known as HFM or oculoauriculovertebral spectrum.
- Bilateral microsomia can occur.
- CNS, cardiac, and skeletal anomalies (expanded HFM spectrum) may occur
- Pulmonary, gastrointestinal, and renal deformities are less common.
- The majority of associated heart defects involve the outflow tract or septum. The increased frequency of cardiac anomalies with this condition suggests that abnormal development of the neural crest may result in both HFM and conotruncal heart defects.
- Children with HFM may have fused or hemivertebrae, resulting in limitation of neck flexion and extension and increasing the difficulty of intubation.
- There are positive correlations between the number of involved abnormal components and the degree of difficulty in visualizing the larynx in pts with both bilateral and unilateral microtia.
- Bilateral mandibular and auricular malformations increase the risk of difficult intubation.

Etiology

- Rare congenital abnormality
- May result from chromosomal abnormality or disrupted blood flow to the head in utero

Usual Treatment

- Removal of preauricular skin tags
- Remodeling, especially in the presence of orbital dystopia
- Orthodontic treatment
- Ear reconstruction
- Maxillary repositioning (Le Fort 1), mandibular advancement and soft tissue augmentation
- Mandibular distraction osteogenesis as required to facilitate subsequent intubations
- Rib grafting as required

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mandibular hypoplasia	Facial asymmetry	Micrognathia, ear tags, OMENS	CT/MRI
CV	Conotruncal malformation	Dyspnea/poor feeding/delayed growth	Murmur	ECHO
MS	Fused or hem vertebrae	Neuromuscular changes	Limited neck flexion/extension	CT/MRI

Key References: Nargozian C, Ririe DG, Bennun RD, et al.: Hemifacial microsomia: anatomical prediction of difficult intubation, *Paediatr Anaesth* 9(5):393–398, 1999; Walker RM, Ellswood J: The management of difficult intubation in children, *Paediatr Anaesth* 19(Suppl 1):77–87, 2009.

Perioperative Implications

Preoperative Preparation

- Conduct craniofacial assessment OMENS:
  - Orbit: Orbital distortion.
  - Mandible: Mandibular hypoplasia.
  - Ear: Microtia, periauricular tags.
  - Facial nerve: Facial muscle hypoplasia.
  - Soft tissue: Hypoplasia or absence of the parotid gland and masticatory muscles (temporalis, masseter).
- Review detailed history with surgeon, radiologist, and parents/guardians.
- Be prepared to call for help early.
- Assemble ear/nose/throat team in case rigid bronchoscopy or tracheostomy is required.
- Determine correct ET tube size and depth, as changing the tube or having too short a tube can lead to complications.
- Discuss and plan all approaches and backup plans.
- Check and prepare all the instruments before bringing the pt to the OR.
- Determine severity of mandibular hypoplasia in radiologic reports to estimate the degree of difficulty of intubation.
- Plan for difficult IV access. Presence of preexisting IV may facilitate concurrent IV and inhalational induction.

Monitoring

- Arterial line may be required in the presence of cardiac or pulmonary morbidity.

Airway

- Make your first attempt the best attempt.
- Assess and plan mask ventilation.
- For pts who are difficult to ventilate, oral, nasopharyngeal, or LMA insertion can improve ventilation.
- Avoid higher peak pressure as much as possible.
- If direct laryngoscopy fails, quickly go to video-assisted technique.
- Conventional laryngoscopy with a flat curved blade, such as a Macintosh, will be less helpful in a pt with micrognathia, as even the normal-sized tongue cannot be compressed adequately into the mandibular space to reveal the laryngeal structures.
- Paraglossal approach: Use a narrow, low-profile, straight-bladed laryngoscope in a paraglossal manner. Advance the blade in the space between the tongue and the lateral pharyngeal wall or tonsillar fossa.
- Lateral approach: The straight axis is shorter and insertion of the ET may be aided by a stylet or use of a gum elastic bougie. This approach is also called the retromolar approach, far lateral approach, and right molar approach.
- LMA can be used as a conduit for fiberoptic insertion of an ET tube.
- Confirm LMA placement with a fiberoptic examination.
- Use an antisialagogue to decrease airway secretions.
- It may be appropriate to leave the LMA in situ so as to minimize manipulation. Have a clear plan to remove it if necessary. Can load up two ET tubes back to back on the fiberoptic scope to facilitate removal of the LMA.
- Use humidified oxygen and steroid prophylactically after difficult intubation to minimize edema.
- Multiple approaches for laryngoscopy may be required.
- Direct laryngoscope with various blade sizes; McCoy and Sward laryngoscope blades.
- Video-assisted airway devices: Fiberoptic scope, Glidescope, Truview, etc.
- Supraglottic airways; LMA classic, Proseal LMA, iGel and COPA, etc.
- Hopkins rod rigid bronchoscope.
- Use Tegaderm/Vaseline gauze or hold the mask with both hands to improve seal.

Postoperative Period

- Prolonged monitoring is recommended, especially when opioids are used to manage pain.
- Monitor pts for hemorrhage, regurgitation of gastric contents, hypoxic events.

Anticipated Problems/Concerns

- Temporomandibular joint malformation may make jaw thrust difficult.

Gonorrhea

Seth Eisdorfer

Risk

- The prevalence of gonorrhea is decreasing, with 106.1:100,000 as of 2013.
- Most common in people ages 15–24 y, in large urban areas, and among people with low socioeconomic status and/or low levels of education.
- Incidence higher in men; prevalence higher in women.

Overview

- Sexually transmitted disease.
- High incidence of coexisting chlamydial infection.
- Local infection: Purulent, profuse urethral discharge and possible epididymitis, prostatitis, or proctitis in men. It is often asymptomatic in women, but may have cervical discharge, vaginitis, salpingitis, or proctitis. Ascending infection may lead to PID.
- Disseminated infection: Fever/rash, tenosynovitis/arthritis (common), conjunctivitis (usually from autoinoculation), possible myopericarditis, and toxic hepatitis or perihepatitis (Fitz-Hugh-Curtis syndrome), rarely with endocarditis or meningitis.

Etiology

- *Neisseria gonorrhoeae*: Gram-negative intracellular diplococcus, usually found inside polymorphonucleocytes.
- Humans only natural hosts for *N. gonorrhoeae*.

Usual Treatment

- Dx gold standard involves the isolation of the organism by culture, testing for antimicrobial resistance.
- Test for other STDs, including syphilis and HIV; test partners as well.

- Penicillins and tetracyclines not recommended as first-line agents due to resistance.
- Fluoroquinolones no longer recommended as first-line therapy due to increasing resistance, especially in men who have sex with men.
- For uncomplicated cervicitis/urethritis, ceftriaxone is drug of choice; other third-generation cephalosporins (cefixime, cefpodoxime) are also commonly used. Spectinomycin can be used in penicillin allergic pts.
- Add doxycycline or azithromycin for coexisting chlamydial infections.
- Symptoms may subside without treatment, leaving a chronic asymptomatic carrier state.
- Pharyngeal infection is frequently asymptomatic; it may clear spontaneously over several wk, even without therapy. Ceftriaxone and trimethoprim-sulfamethoxazole can be used for treatment.
- Complicated infections can be treated via penicillin G IV × 5 d or ceftriaxone × 5 d. Oral fluoroquinolones may be used provided susceptibility.
- PID requires second-generation cephalosporin such as cefotetan or cefoxitin or a combination of clindamycin and gentamicin. Treat for chlamydial coinfection.
- Resolution of symptoms after treatment suggests cure; follow-up cultures are recommended.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Conjunctivitis, ophthalmia neonatorum, adult gonococcal conjunctivitis			
	Pharyngeal infection		Exudative tonsillitis	Cultures
GI	Anorectal infectionsProctitis	Pain, pruritus	Purulent discharge, bloody diarrhea	Cultures
GU	*Women*			
	Urogenital tract disease	Abnormal vaginal discharge, dysuria, urinary frequency, lower abdominal pain, labial pain, abnormal menstruation	Mucopurulent cervicitis	Cultures from urethra and vagina
	Men			
	Acute epididymitisProstatitis	Pain		
CV	Gonococcal endocarditis		Possible murmur	ECHO
GI	Perihepatitis (Fitz-Hugh–Curtis syndrome)		RUQ tenderness	Liver enzyme elevation
GU	*Women*			
	PID	Lower abdominal pain, vaginal discharge, fever, palpable adnexal mass	Severe pain to palpation	Endocervix cultures
	Men			
	Urethritis	Dysuria	Purulent urethral discharge	Cultures from urethra
CNS	Gonococcal meningitis		Meningeal signs	
MS	Septic arthritis	Most common cause of septic arthritis in young adults, tends to involve single joints	Warmth, tenderness of affected joint(s)	
DERM	Disseminated lesions			Ranging from maculopapular to pustular or hemorrhagic, usually peripheral

Key References: Tapsall JW: *Neisseria gonorrhoeae* and emerging resistance to extended spectrum cephalosporins, *Curr Opin Infect Dis* 22(1):87–91, 2009; Centers for Disease Control and Prevention: Sexually transmitted disease surveillance, 2014. Atlanta, GA, 2015, US Department of Health and Human Services. <http://www.cdc.gov/std/stats>.

Perioperative Implications

- Universal blood and body fluid precautions and/or barrier precautions

Monitoring

- Awareness of Foley catheter/temp probe placement

Airway

- Awareness if pharyngitis exists

Positioning

- Awareness of joint involvement

Maintenance

- Awareness of extent of disease

Adjuvants

- Vary with hepatic involvement.

Anticipated Problems/Concerns

- No vaccine available
- Follow-up cultures
- Effective antibiotics
- Testing isolates for antibiotic susceptibility
- Routine culturing of high-risk populations
- Diligent contact tracing and prompt referral; treatment of sexual partners
- Education targeted at high-risk groups
- Use of condoms or other barrier methods

Goodpasture Syndrome

Michael A. Hall | Lee A. Fleisher

Risk

- Incidence of 1 case per million people per y.
- Accounts for 20% of cases of RPGN or crescentic glomerulonephritis.
- In terms of bimodal age distribution, more common in males 20–30 y of age and females 60–70 y of age.

Perioperative Risks

- Anemia from recurrent or persistent intrapulmonary hemorrhage
- Hypoxia or hypoxic respiratory failure in cases of massive intrapulmonary hemorrhage
- Rapidly progressive renal failure or uremia
- Significant third-space fluid loss secondary to proteinuria

Worry About

- Pts with active pulmonary hemorrhage may require mechanical ventilation in the postop period for hypoxic respiratory failure.
- Renal failure will alter drug pharmacokinetics and require adjustment of dosing or choice of anesthetic drugs.
- Anemia secondary to iron deficiency from repeated pulmonary hemorrhage, as well as anemia related to chronic kidney disease.
- Opportunistic infections such as pneumocystitis pneumonia in pts receiving immunosuppressive therapy.
- Volume overload in pts with severe renal insufficiency.

Overview

- Rare, autoimmune, renal-pulmonary syndrome caused by autoantibodies directed against the glomerular basement membrane (anti-GBM antibodies).
- Major cause of RPGN, defined as a ≥50% loss of renal function (as quantified by glomerular filtration rate) over a 3-mo period.
- Usually presents with constitutional symptoms (night sweats, malaise), chronic cough progressing

to hemoptysis, and hematuria or foamy urine (from proteinuria).
- Pulmonary symptoms may be episodic in nature, related to discreet episodes of pulmonary hemorrhage. Each episode may be severe and can lead to life-threatening respiratory failure requiring mechanical ventilation.
- Pts may present for elective surgery, such as placement of dialysis access, or require kidney transplantation related to loss of renal function caused by progression of Goodpasture syndrome.

Etiology

- Autoimmune disease caused by anti-GBM antibodies. These antibodies also have affinity for the alveolar basement membrane, causing the renal-pulmonary syndrome.
- In most pts, the anti-GBM antibodies are directed against a specific subunit within the alpha 3 chain of type IV collagen.
- In a classic type II hypersensitivity reaction, anti-GBM antibodies bind to target epitopes and activate the complement system, leading to cellular damage.
- Cellular damage within the glomeruli leads to glomerulonephritis with proteinuria and hematuria. In RPGN, crescentic scarring of the glomeruli can be seen on kidney biopsy.
- Within the alveoli, cellular damage leads to a breakdown in the barrier between airspaces and blood vessels, leading to diffuse alveolar hemorrhage.
- Evidence of a genetic predisposition. A positive association among Goodpasture syndrome, pernicious anemia, systemic lupus erythematosus, and Sjogren syndrome and HLA-DR15 has been demonstrated.
- All other known risk factors are pulmonary insults, such as exposure to hydrocarbon fumes, exposure to metal dusts, inhalation of smoke or cocaine, or viral infections. These insults may lead to damage of the alveolar basement membrane and exposure of type IV collagen to the immune system, leading to the development of autoantibodies.

Usual Treatment

- There are no large trials to guide treatment; however, the basis for treatment of other autoantibody-mediated diseases can be adapted.
- Suppression of antibody production is achieved with immunosuppressant medications such as cyclophosphamide and steroids. Pulse-dose steroids can be used in cases of acute, severe alveolar hemorrhage, followed by a prolonged taper to a low, standing dose.
- Rituximab, which depletes CD20-positive B cells (antibody producing), has also been reported to control anti-GBM antibody levels in pts intolerant of cyclophosphamide.
- Plasmapheresis has been shown to effectively remove anti-GBM antibodies, and can be used in the acute setting or upon initial diagnosis. The pt will undergo plasmapheresis for 2–3 wk, or until clinical status improves, and then be maintained on immunosuppressant medication.
- Treatment for alveolar hemorrhage is usually supportive, and rarely may require mechanical ventilation, while therapy to clear anti-GBM antibodies is instituted.
- Renal dysfunction, especially when present as RPGN, may require renal replacement therapy or kidney transplant, although if anti-GBM antibody levels are not controlled, disease can recur in the allograft.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Volume overloadHypertension	Dyspnea	Vital signs Peripheral edema Rales	Monitor BP and HR
RESP	Alveolar hemorrhage	Cough Hemoptysis Dyspnea	Vital signs (low SpO_2) Tachypnea Rales	Monitor SpO_2 PaO_2 on ABG Increased A-a gradient
RENAL	Acute or chronic renal failure	Oliguria Hematuria Peripheral edema Nondependent edema	Peripheral or nondependent edema	Lytes Serum Cr UA for blood or protein
HEME	Anemia	Dyspnea Recurrent hemoptysis	Conjunctival pallor	CBC Iron studies

Key References: Greco A, Rizzo MI, De Virgilio A, et al.: Goodpasture's syndrome: a clinical update, *Autoimmun Rev* 14(3):246–253, 2015; Copponex K, Kaye AD: Perioperative management of the patient with Goodpasture's syndrome, *Middle East J Anesth* 20(6):779–783, 2010.

Perioperative Implications

Preoperative Preparation

- Elective surgery, such as the placement of permanent dialysis access, should be delayed until the disease is in an inactive state, as evidenced by controlled anti-GBM antibody levels and resolution of any respiratory symptoms.
- Blood count, given risk of significant anemia.
- In pts with renal dysfunction, volume status should be optimized prior to surgery to decrease risk of compounding kidney injury with hypovolemia or hypotension.
- Preop respiratory status and supplemental oxygen requirements should be evaluated, as this may indicate need for postop mechanical ventilation.
- If pt is dialysis-dependent, close attention to electrolyte and volume status should be paid, and consideration given to supplemental preop hemodialysis if significant disturbance is present.
- Pts on immunosuppressant medications should be evaluated for signs of occult infection.

Monitoring

- Standard monitors.
- Urinary cath for UOP monitoring, especially in pts with moderate to severe renal dysfunction.
- Advanced monitors of volume status may be helpful in order to optimize renal perfusion.
- Arterial line, if otherwise indicated by the procedure or the pt's clinical status, would allow for monitoring of stroke volume variation as an indicator of volume status.

Airway

- If a pt has active alveolar hemorrhage, an endotracheal tube of sufficient diameter to allow for pulm suctioning should be used.

Induction

- May need to adjust choice and dosage of anesthetic drugs to account for renal dysfunction.

Maintenance

- Remain cognizant of dosing adjustment for renal and hepatic dysfunction.
- In pts with recent or active alveolar hemorrhage, frequent suctioning and recruitment maneuvers should be performed.
- Close attention to volume status is required in pts with renal failure, as hypovolemia may worsen kidney injury and volume overload may not be correctable until the pt is dialyzed postop.

Extubation

- Requires full reversal of neuromuscular blockade, as duration of action of neuromuscular blockers may be altered by renal dysfunction.
- Ensure that pt will be able to maintain adequate oxygenation after extubation.

Postoperative Period

- Pts require close attention to volume status and electrolytes, with the possibility of supplemental dialysis therapy if necessary in the periop period.
- Choice of analgesic medications must be made with consideration to altered metabolism in renal failure, particularly in avoidance of NSAIDs, morphine, and meperidine.

Anticipated Problems/Concerns

- Hypoxic respiratory failure in the event of massive alveolar hemorrhage.
- Anemia caused by chronic alveolar hemorrhage as well as by renal dysfunction.
- Renal failure can quickly progress to end stage with dialysis dependence.
- Pts susceptible to infection when appropriately treated with immunosuppressant medications.

Gout

Christopher J. Cullom | Amit Prabhakar | Alan David Kaye

Risk

- Overall incidence: 0.05% in the USA population
- Most common inflammatory joint disease among men
- Associated with nephropathy, most commonly nephrolithiasis (10–40% of pts)
- Also associated with CV disease, specifically an increased risk of myocardial infarction, but also including heart failure, cerebrovascular accident, transient ischemic attack, and peripheral vascular disease
- Metabolic syndrome
- Hypertension
- Chronic renal dysfunction

Perioperative Risk

- Medication toxicity and side effects
- Comorbid conditions associated with chronic hyperuricemia
- Tophi or gouty joint location considerations

Overview

- Disorder of purine metabolism resulting in urate crystal deposition in and around the joints due to long-standing hyperuricemia
- Largely due to inefficient renal urate excretion

Etiology

- Uric acid is the final metabolite of purine metabolism.
- Urate is largely present as monosodium urate due to high Na content of the extracellular compartment.
- When urate concentrations exceed 380 umol/L, risk of monosodium nitrate crystal formation and precipitation increases.
- Urate production depends on balance between de-novo synthesis in cells, recycling, purine ingestion, and degradation function of xanthine oxidase.
- Diseases such as lymphoproliferative disorders, psoriasis, and hemolytic anemia are associated with high nucleic acid turnover and hyperuricemia.
- Acute gouty arthritis begins with a single joint in lower limbs, usually the first metatarsophalangeal joint. The next most frequent initial joints are midtarsal, ankles, knees, and arms.
- The affected joint becomes warm, swollen, erythematous, and tender.
- Differential diagnosis includes a septic joint.
- Subsequent attacks last longer, affect multiple joints, and spread to upper limbs.
- Gouty attack triggers include alcohol, meat and seafood, fasting, trauma, surgery, and drugs, including diuretics, low-dose aspirin, and organ transplant immune suppressants.
- Chronic gout is characterized by chronic destructive polyarticular involvement with low-grade joint inflammation, joint deformity, and tophi, which are monosodium urate crystals surrounded by mononuclear and giant cell reactions.
- Tophi can occur anywhere in the body, commonly in helix of ear or over the olecranon process, but rarely found in the spinal cord, flexor tendons of hand, vocal cords, heart, and colon.
- Analysis of the synovial fluid or tophus for identification of monosodium urate crystals is the gold standard diagnostic method.

Usual Treatment

- For acute attack, indicate ice, rest, colchicines, or NSAIDs for 1–2 wk.
- Oral prednisone and indomethacin may also be used for acute attacks.
- Urate lowering therapy is then used to maintain urate levels below saturation point. Therapy dissolves crystals and cures gout.
- Urate lowering therapy is indicated for pts with recurrent attacks, chronic arthropathy, tophi, and kidney stones.
- Allopurinol is the initial drug of choice, which lowers uricemia through inhibition of xanthine oxidase.
- Probenecid, sulfinpyrazone, and benzbromarone are second line agents and function by increasing urinary urate excretion.
- Drug considerations:
  - Chronic NSAID use is associated with chronic renal impairment, GI bleeding, and CV adverse events.
  - Colchicine has a narrow therapeutic index, and dose dependent GI toxicity is common.
  - Colchicine toxicity may result from interactions with diltiazem, verapamil, clarithromycin, and ketoconazole.
  - Allopurinol adverse events include rash, GI, and allopurinol hypersensitivity syndrome (characterized by toxic epidermal necrolysis, exfoliative dermatitis, fever, and renal failure).
  - Adjust allopurinol dose for chronic renal failure pts.
  - Febuxostat adverse events include liver function test abnormalities, diarrhea, headache, musculoskeletal signs, and rare CV events.
  - Pegloticase adverse events include infusion related reactions, headache, nausea, and rare CV events.
  - Probenecid adverse events include rash, headache, GI symptoms, and rarely nephrotic syndrome.

Assessment Points

System	Effect	Assessment by Hx	PE/Clinical Sequelae	Test
CV	Increased risk of MI, TIA, CVA, CHF, PVD Febuxostat: Increased risk of CV events NSAID: Fluid overload in CHF	Symptoms of angina or CHF Hx of ischemic or congestive heart disease Hx CHF	S3, rales, JVD S3, rales, JVD	ECG, ECHO, stress ECG ECHO
GI	NSAID: Increased risk of GI bleeding Colchicine: Nausea, vomiting Febuxostat: Diarrhea Benzbromarone: Hepatotoxicity	Chronic NSAID use		
RENAL	Risk of nephrolithiasis and chronic renal impairment NSAID: Chronic renal impairment Colchicine: Nephropathy			Cr, BUN, GFR
HEME	NSAID: Risk of bleeding	Anticoagulant use (e.g., warfarin)		
MS	Tophus	Painful joint	Warm/painful joint or nodular soft tissue structure	Joint fluid aspiration and analysis
IMMUNE	Allopurinol: Hypersensitivity syndrome			HLA-B5801 genotype testing

Key References: Stamp L: Safety profile of anti-gout agents: an update, *Curr Opin Rheumatol* 26(2):162–168, 2014; Nunes EA, Rosseti AG Jr, Ribeiro DS, Santiago M: Gout initially mimicking rheumatoid arthritis and later cervical spine involvement, *Case Rep Rheumatol* 2014:357826, 2014.

Perioperative Implications

Preoperative Preparation

- Pts with long-standing gout are at higher risk for CV events and metabolic abnormalities, including diabetes, and appropriate preop workup should be performed.
- Airway considerations: Pts with chronic gout may have tophi located anywhere in the body, rarely located on the spinal cord, spine, vocal cords, and heart; thus consideration must be taken prior to any procedure.
- GI prophylaxis should be considered for pts on chronic NSAIDs or corticosteroid therapy, due to a high likelihood of developing stomach ulcers from the stress of surgical procedures. H_2 blockers or PPIs can be given for prophylaxis.

Monitoring/Induction/Maintenance

- Standard ASA monitors with supplementation of invasive monitoring if risk factors are present.
- Pts with long-standing gout may have coexisting nephropathy. Consideration should be made to adjust the dose of renally cleared paralytics and analgesics.
- Medications should be considered for not only drug interactions (colchicine with diltiazem, verapamil), but triggers for acute gout attack (diuretics, aspirin, and organ transplant immune suppressants).
- Careful consideration should be taken during positioning where active gout is present, and care should be taken to protect these joints.

Extubation

- Routine unless pt has a known difficult airway.

Postoperative Period

- Clinician should be aware that surgery or trauma can trigger an acute gouty attack.
- Adequate pain control.

Graves Disease

Sankalp Sehgal | Henry Liu

Risk

- Incidence: Approximately 5:10,000; prevalence: 1.12%, with 1.3 million pts in USA.
- Female-to-male ratio: 7:1; more common in women age 30–60 y.
- Family history indicating genetic factor(s) can be involved.

Perioperative Risks

- "Thyroid storm" due to surge of plasma thyroid hormones
- Airway compromise due to hematoma compressing airway or nerve injury
- Hypocalcemia
- Cardiovascular complications: dysrhythmia, hemodynamic alterations

Worry About

- Signs of airway obstruction, nerve injury
- Signs of metabolism and electrolyte abnormalities
- Dysrhythmias

Overview

- Most common cause of hyperthyroidism.
- Clinical manifestations are generally nonspecific initially: Fatigue, weight loss, muscle weakness, heat intolerance, diarrhea, nervousness, diffuse glandular enlargement in neck, anemia, and thrombocytopenia.
- Extrathyroid involvement includes ophthalmopathy (25%), dermopathy (1%), and clubbing (0.1%).
- Dx involves normal/low TSH with high T_3, T_4 positive TSH-receptor antibody, RAI uptake, and ultrasound with Doppler.
- Life-threatening "thyroid storm" can be induced by stress or illness. Symptoms include tachycardia, dysrhythmias, MI, worsened CHF, hyperthermia, anxiety, agitation, confusion, hyperpyrexia, and anorexia. Rx includes fluids, propranolol (1–5 mg IV), hydrocortisone (replacing the exhausted adrenocortical hormone), potassium iodide (KI 60 mg or NaI 1–2.5 g), and PTU (initiate therapy as soon as possible).

Etiology

- Autoimmune disease.
- An autoantibody binds to a TSH receptor-stimulating thyroid to enlarge and produce more thyroid hormones.

Usual Treatment

- Beta-blockers:
  - Block sympathetic overactivity, decreased palpitations, anxiety, tremor.
  - Inhibit peripheral conversion of $T_4 \rightarrow T_3$ at high doses (e.g., >160 mg/d of propranolol).
- Thionamide antithyroid drug therapy:
  - PTU and methimazole decreased $T_4 \rightarrow T_3$ conversion.
  - Hormone synthesis interferes with TPO.
  - They are given for several mo (12–18 mo) and take several wk for effect.
  - PTU has hepatotoxicity but is used in pts with intolerance to methimazole, first trimester pregnancy, thyroid storm.
  - Other adverse effects include agranulocytosis (1:500 with methimazole), antineutrophil cytoplasmic antibody-positive vasculitis, pruritic rash, and arthralgias.
- RAI therapy:
  - Decreased hormone secretion and synthesis by integrating within the thyroid hormone and causing ionizing damage to thyroid follicular cells.
  - Takes 6–10 wk for clinical effect.
  - Most pts become hypothyroid after a single dose.
  - Destruction of thyroid tissue occasionally results in worsening of thyrotoxicosis, so pretreatment with PTU is considered in high-risk pts (e.g., CAD).
  - Contraindicated in pregnancy and breastfeeding.
- Dexamethasone:
  - Inhibit peripheral conversion of $T_4 \rightarrow T_3$.
- Thyroidectomy:
  - Indications include very large goiters with compressive symptoms, concomitant suspicious thyroid nodules, vital organ dysfunction, and concurrent hyperparathyroidism requiring surgery.
  - For preparation of surgery, pts should be rendered euthyroid, and 1–3 mo of antithyroid drug therapy is indicated.
  - For urgent surgery, preparation with beta-blockers dexamethasone and cholestyramine has been recommended.
  - Pts not euthyroid at surgery are at greater risk for thyroid storm.
- Potassium iodide therapy:
  - For use with pts allergic to antithyroid drugs or as primary therapy in mild disease.
  - Iodide reduces vascularity and has acute inhibitory effects on new thyroid hormone synthesis referred to as Wolff-Chaikoff effect.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	T_3, T_4 increase HR, contractility	Palpitation, angina	Increased HR, Htn	ECG, CXR, ECHO
HEME	Anemia, agranulocytosis (secondary to PTU)	Decreased menstrual flow	Diffusely enlarged thyroid	CBC, nuclear scan
GI	T_3, T_4 affect GI motility	Diarrhea, increased appetite	Weight loss	
RESP	Airway compression	Breathlessness, tracheomalacia	Trachea deviation	CXR, CT
NEURO	Myopathy	Anxiety, insomnia, irritability	Shaking hands, tremors	
DERM	Autoimmune attack on eye muscles and fat tissue Carbohydrate buildup leading to Graves dermopathy	Sweating, fatigue, heat sensitivity, weight loss, pretibial myxoedema	Exophthalmos, light sensitivity, double vision, warm, wet skin	Eye exam Skin exam

Key References: Chan GW, Mandel SJ: Therapy insight: management of Graves' disease during pregnancy, *Nat Clin Pract Endocrinol Metab* 3(6):470–478, 2007; Burch HB, Cooper DS: Management of Graves disease review, *JAMA* 314(23):2544–2554, 2015.

Perioperative Implications

Preoperative Preparation/Induction/Maintenance

- Preop, all pts should be clinically euthyroid, by beta-blockade with iodide for 7–14 d.
- Airway obstruction by neck mass may be intrathoracic. Consider CXR, CT, and flow-volume loops. Potential difficult airway may arise. Use awake-fiberoptic intubation for severe obstruction and place ET tube beyond compression point.
- Goiter may make emergency tracheostomy difficult.
- Obstructive manifestations include SVC obstruction, decreased venous return, hemodynamic instability.
- Continue all thyroid medications until the day of surgery.
- Increased cardiac output may slow the rise of alveolar concentration of inhaled anesthetics.
- Catecholamines: Avoid sympathomimetic drugs ketamine, epinephrine, pancuronium, vasoactive drugs.
- Risk of "thyroid storm" periop.

Monitoring

- Routine ASA monitoring.
- Consider arterial line.
- Monitor thyroid hormone levels.

General Anesthesia

- GA is preferable, maintained with volatile or IV agents.

Extubation

- Airway edema, surgical site hematoma, or recurrent laryngeal nerve injury may cause airway compromise.
- Rule out tracheomalacia.

Anticipated Problems/Concerns

- Hematoma or airway obstruction. Administer O_2, CPAP. May require wound opening and reintubation.
- Hypocalcemia, usually 24–72 h postop. Look for Chvostek sign (facial muscle spasm) and Trousseau sign (carpopedal spasm). Monitor serum Ca^{++} and Mg^{++}. Hypoparathyroidism may present as laryngospasm. Administer Ca^{++} and Mg^{++} (promotes PTH release).
- Recurrent laryngeal nerve palsy, usually unilaterally. This results in voice change and slight stridor. Bilateral is rare and may cause complete obstruction requiring reintubation or surgical airway.
- Damage to external branch of superior laryngeal nerve.
- Dysphagia.
- Tracheomalacia.
- Hypothyroidism.
- Persistent hyperthyroidism.

Guillain-Barré Syndrome

Gordon N. Finlayson

Risk

- Occurs in both sexes, all races, all ages, but mostly affects young and middle-aged adults.
- Worldwide illness and occurs at all times of the year.
- Mortality rate is 3–7%; most pts eventually fully recover and 20% have significant residual weakness.

Perioperative Risks

- Resp failure secondary to polyneuropathy
- Autonomic dysfunction with profound CV instability

Worry About

- Rapidity of symptoms; respiratory paralysis may occur within 24 h of onset
- Pulm complications

Overview

- Polyneuropathy often encountered in critical care practice.
- Pts present initially with lower limb weakness that ascends.
- Widespread, patchy, inflammatory demyelination of peripheral and autonomic nervous systems.
- Dysautonomia occurs from chromatolysis of anteromediolateral cell column and autonomic ganglia: Fluctuating BP, Htn, hypotension, postural hypotension, tachycardia, and arrhythmias.
- CSF protein is usually normal during first few days of illness and steadily rises and remains elevated for several months, even after recovery.

Etiology

- Evidence points to infection-induced autoimmune response.
- Typically antecedent illness occurs within 4 wk of onset, with respiratory or GI infection (*Campylobacter jejuni*) in 60–70% of cases.
- Other predisposing factors incl surgery, pregnancy, malignancy, and acute seroconversion to HIV.
- Epidural or spinal anesthesia may be antecedent to the event or associated with recurrence.

Usual Treatment

- Basis of treatment is symptomatic care and plasma exchange or IVIG.
- Maintain daily bedside evaluation of vital capacity and respiratory muscle strength; pts with decreased respiratory reserve should be moved to ICU.
- Utilize elective tracheal intubation and mechanical ventilatory support when signs of respiratory distress are present before $Paco_2$ rises or vital capacity falls.
- Anticipating requirements for ventilatory support include:
  - Vital capacity <20 mL/kg or reduction of 30% from baseline.
  - Maximum inspiratory pressure <30 cm H_2O.
  - Maximum expiratory pressure <40 cm H_2O.
  - Facial and/or bulbar weakness, autonomic dysfunction, rapid disease progression.
  - Lack of foot flexion at ICU admission/end of immunotherapy, which predicts need for prolonged mechanical ventilation.
- Plasmapheresis or IVIG reduces hospital stay and time spent on ventilator if given to pts who do not improve or who worsen within first 2 wk of symptom onset.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Inability to close eyes	Dry eyes	Dry eyes	
CV	Fluctuating hypotension and Htn, postural hypotension, sinus tachycardia, arrhythmias DVT risk	Orthostatic Sx Palpitations Asymmetric limb swelling	BP/pulse Asymmetric limb swelling	ECG Doppler US
RESP	Respiratory failure secondary to weakness Aspiration risk with bulbar dysfunction	Stamina—for breathing	Decreased strength on repeated ventilation Inability to sustain head lift	VC Maximum inspiratory pressure Maximum expiratory pressure
GI	Bowel obstruction	Constipation	Abdominal exam	Abdominal x-ray
CNS	Autonomic dysfunction Pain: Acute nociceptive and chronic neuropathic	Early satiety Orthostatic hypotension Lack of sweating Pain	BP lying and standing	ECG with R-R interval on deep breathing
MS	Weakness, joint fixation	Lack of stamina		

Key References: Liu J, Wang LN, McNicol ED: Pharmacological treatment for pain in Guillain-Barré syndrome, *Cochrane Database Syst Rev* 4:CD009950, 2015; McSwain JR, Doty JW, Wilson SH: Regional anesthesia in patients with pre-existing neurologic disease, *Curr Opin Anesth* 27(5):538–543, 2014.

Perioperative Implications

Preoperative Preparation

- Avoid rapid turning of pt; autonomic instability and postural hypotension may result.
- Avoid head-up (reverse Trendelenburg) position; pt will be unable to maintain CV stability with tilt.
- Treat increased gastric acidity; use antacid and metoclopramide, 10 mg/70 kg.
- Maintain appropriate environmental temp.
- Coagulopathy and hypocalcemia may complicate plasma exchange therapy.

Monitoring

- Arterial line for continuous pressure monitoring started prior to anesthetic induction.
- Monitor for potential fluid shifts that result from positional changes and cardiac dysrhythmias.
- Temperature; pts may become poikilothermic.
- Neuromuscular monitoring; pt may be sensitive to relaxants.

Airway

- Most pts have early tracheostomy; airway access should not be a problem; previous tracheostomized pts may have tracheal stenosis.
- Endotracheal suction may provoke bradydysrhythmias and asystole.

Induction

- Avoid barbiturates and phenothiazines, which may produce profound CV depression.

Maintenance

- Local anesthesia is preferred.
- GA: Nonsympatholytic technique.
- Pt may be sensitive to positive pressure ventilation, which may result in autonomic instability.

Extubation

- Continue to ventilate postop if pt required ventilatory support preop.
- Residual weakness from anesthetic agents and muscle relaxants may necessitate postop ventilation in pts not ventilated preop.

Adjuvants

- Muscle relaxants:
  - Avoid succinylcholine; can cause hyperkalemia with cardiac arrest.
  - Pts have increased sensitivity to nondepolarizing muscle relaxants.
  - May have residual muscle weakness after apparent full recovery from GA.
- Anticonvulsants:
  - Low-quality evidence demonstrates gabapentin and carbamazepine to reduce pain in short term.

Anticipated Problems/Concerns

- Autonomic instability
- Respiratory failure
- Parturient: Third trimester and postpartum, risk of exacerbation; for labor, a regional anesthetic indicated to avoid exaggerated hemodynamic response to pain from autonomic dysfunction. Aspiration pneumonitis and respiratory failure may result in premature labor and maternal mortality. For C-section, implement a regional anesthetic relatively contraindicated even for pt with mild respiratory involvement. Some cases have reported newborns with GBS features following delivery by affected mother.
- Fecal impaction
- Stress ulcers

Hashimoto Thyroiditis

Lee A. Fleisher

Risk

- Hashimoto thyroiditis is the most common cause of hypothyroidism in iodine-sufficient countries and primary hypothyroidism in adults.
- Incidence in USA: Approximately 100,000–400,000 new cases diagnosed each year.
- Causes thyroid failure in 10% of pts.
- Prevalence increases with age but it is also the most common cause of hypothyroidism in children as young as 1–2 y of age. Individuals between the ages of 30–50 y are most commonly affected.
- No documented ethnic predominance.
- Gender predominance: F:M ratio 7:4; age 30–50 y.

Perioperative Risks

- Increased risk of thyroid storm even if pt is euthyroid preop, as the progressive inflammatory process may cause significant apoptosis of thyroid follicles, leading to the release of thyroid hormone. Life-threatening illness can ensue if hyperthyroidism is severely exacerbated by the stress of operation, typically manifested by hyperpyrexia, tachycardia, and alterations in consciousness.
- Risk of respiratory failure or insufficiency and increased bleeding periop.
- Chronic hyperthyroidism and its concomitants.
- Coexisting autoimmune disease and adrenal failure.

Overview

- Hashimoto thyroiditis, or chronic autoimmune thyroiditis, involves progressive thyroid dysfunction due to autoimmune-mediated destruction of the thyroid gland through the apoptosis of thyroid epithelial cells. Typical manifestations of the disease may encompass high serum concentrations of antibodies against one or more thyroid antigens, diffuse lymphocytic infiltration of the thyroid, and destruction of the thyroid gland, resulting in thyroid failure.
- Chronic inflammation of the thyroid (painful or painless) with lymphocytic infiltration due to autoimmune factors.
- Acute inflammation results in increased release of preformed hormone with hyperthyroidism.
- Chronic inflammation results in decreased thyroid gland function with resistant hypothyroidism.

Etiology

- Autoantibodies against thyroid peroxidase, thyroglobulin, or TSH receptors causing immune-mediated destruction of thyroid epithelial cells, although a small percentage of pts do not have such antibodies
- Associated with other autoimmune diseases, including Sjögren syndrome, SLE, RA, pernicious anemia, autoimmune endocrinopathies, Addison disease, hypoparathyroidism, diabetes mellitus, and gonadal failure
- Increased incidence in pts with a family Hx and with chromosomal disorders such as Turner, Down, or Klinefelter syndrome
- Also linked to several polymorphisms in genes for HLA and T-cell antigen receptors
- Precipitating causes: Thyroid injury (infection, radiation, drugs), stress, steroids, pregnancy, and excessive iodine intake

Standard Treatment

- Chronic thyroid hormone replacement in hypothyroidism
- NSAIDs in acute thyroiditis for pain and propranolol to control symptoms of hyperthyroidism

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Swollen, tender neck Enlarged tongue Tracheal compression	Neck pain, hoarseness	Examine airway and neck	Lateral neck x-rays or CT of the neck
CV	Dehydration, tachydysrhythmias or bradydysrhythmias	Orthostatic symptoms		Tilt-table test, ECG
RESP	Decreased respiratory muscle strength	Shortness of breath Dyspnea on exertion		
GI	Ileus Constipation			
ENDO	Acute hyperthyroidism Chronic hypothyroidism	Shaking, anxiety, emotional lability	Reflex speed, HR Tremor, nervousness Mental status	Free T_4 estimate
HEME	Anemia			Hgb, Hct
CNS	Cold intolerance Slow or fast movement, depending on stage	Cold intolerance	Reflexes, mental status exam	
DERM		Rough pale skin Coarse dry hair	Careful inspection of hair and skin	
MS		Arthralgias and myalgias		
GENERAL	Other autoimmune dysfunction	Weakness	Inability to arise from chair without using hands	Serum K^+/Na^+

Key References: Bennett-Guerrero E, Kramer DC, Schwinn DA: Effect of chronic and acute thyroid hormone reduction on perioperative outcome, *Anesth Analg* 85:30–36, 1997; Wiersinga WM: Clinical relevance of environmental factors in the pathogenesis of autoimmune thyroid disease, *Endocrinol Metab (Seoul)* 31(2):213–22, 2016.

Perioperative Implications

Preoperative Preparation

- Assess NPO status (may have poor gastric emptying).
- Use preop drugs cautiously (increased sensitivity of central nervous and respiratory systems to depressants).
- Make sure that pt is euthyroid so as to avoid thyroid storm.
- Assess fluid status.
- Assess for comorbidities (autoimmune/adrenal/pancreatic dysfunction),

Monitoring

- Temp (consider placing cooling blanket on OR table as treatment for thyroid storm)
- Consider invasive monitoring if there is CV or resp compromise.

Airway

- If normal preop, consider routine management.
- If displaced or distorted, consider awake fiberoptic and armored tube intubation.

Induction/Maintenance

- No data indicate that one technique is preferred over another.

Extubation

- Consider extubation in an optimal situation for reintubation.

Postoperative Concerns

- Routine monitoring and treatment of comorbidities if there is coexisting autoimmune disease

Adjuvants

- Beta-blockade for acute hyperthyroidism.
- Steroids are sometimes necessary to treat for adrenal dysfunction.
- Oral hypoglycemics (chronic use) can cause hypoglycemia for longer duration and of greater severity in a periop pt.

Headache, Migraine

Alan David Kaye | Diana Mekler | Adam Shomstein

Risk

- Incidence in USA: >28 million; maximum prevalence is in 25–55 y of age.
- Can start as early as 1 y of age; 10–20% of instances occur in children by 20 y of age, with males and females being equally affected.
- More frequent in women after age 11 y; ratio is approx 3:1 for female: male; prevalence declines after age 40 y.
- Familial aggregation: CACNA1A (P/Q voltage-gated calcium channel), ATP1A2 (Na^+-K^+ ATPase), and SCN1A (Na_v 1.1 voltage-gated sodium channel) genes are implicated in genetic predisposition for variations of familial hemiplegic migraine.
- Can be associated with sinusitis; AVM; stroke; patent foramen ovale; epilepsy; ischemic myocardial infarction; depression; anxiety disorder; sensitivity to foods rich in tyramine, phenylethylamine, or octopamine (chocolate, wine, dairy products); and electroencephalographic abnormality.
- Socioeconomic status: Migraines are inversely related to household income and education.

Perioperative Risks

- Increased incidence of Htn, stroke, CAD
- Gastric stasis
- Drug toxicity and side effects

Worry About

- Toxic and side effects of antimigrainous preparations, adverse interaction with anesthetic drugs
- Associated intracranial disorders
- Increased aggregation of platelets with increased risk of stroke and CAD

Overview

- Recurrent, frequently unilateral, throbbing head pain with strong family Hx
- Often associated with increased sensitivity to touch, N/V, phonophobia, and/or photophobia.
- May be preceded by a visual, sensory, or motor aura; headache and aura may present independently.
- Dx is Hx dependent in the absence of secondary causes.
- Migrainous infarction with permanent neurologic damage is rare.

Etiology

- Central or peripheral mechanisms can be incited by internal or external stimuli.
- Lowering Mg^{2+} levels increase the affinity and release of serotonin at cerebrovascular and neuronal sites as well as NO production and activation of NMDA receptors.
- Can be precipitated by trigger factors.
- Cerebral and extracerebral arteries are the most likely sources of pain.
- Pain results from exaggerated pulsations in association with trigeminal release of sP, CGRP, and VIP and sensitization of nociceptors around blood vessels.

Usual Treatment

- There is no permanent cure for migraines.
- Elimination of trigger factors when possible can reduce incidence, including regular sleep, meals, and hydration, along with decrease in stress.
- Abortive therapy includes NSAIDs, barbiturates, ergotamines, triptans, phenothiazines, dihydroergotamine, sphenopalatine ganglion block, nonopioid and opioid analgesics, single-pulse transcranial magnetic stimulation, and vagal nerve stimulation.
- Prophylactic therapy:
  - Effective: β-blocking agents (metoprolol, propranolol, timolol), TCA (amitriptyline), antiepileptic drugs (AED; topiramate, divalproex sodium), and serotonin agonists.
  - Ineffective: ACE inhibitors (lisinopril, candesartan), AED (gabapentin), β-blocking agents (atenolol, nadolol), antidepressants (fluoxetine, venlafaxine), serotonin agonists (naratriptan, zolmitriptan; short-term prevention in menstrual migraine), histamine, cyproheptadine, MIG-99 (feverfew), and vitamins (riboflavin, CO-Q10, Mg^{2+}).
  - Possibly effective: α-agonists (clonidine, guanfacine), Ca^{2+}-channel blockers (verapamil, nicardipine, nifedipine, nimodipine), AED (carbamazepine). Conflicting evidence exists for the efficacy of MAOIs. Botulinum toxin is probably not effective. CGRP antagonist and antibodies are in the experimental stages.
- Behavioral treatment involves biofeedback, self-hypnosis, relief by dark surroundings, and sleep.

Assessment Points (Mainly Side Effects and Toxicity of Antimigrainous Therapy)

System	Effect	Assessment by Hx	PE	Test
CV	Ergotamine, sumatriptan: Worsening of Htn, ischemic heart disease, PVD, serotonin syndrome	Symptoms of angina and peripheral vascular insufficiency		ECG Stress ECG
	β-adrenergic receptor blocking agents and Ca^{2+}-channel blockers: Excessive depression of myocardial function	Symptoms of CHF	S_3 Rales Decreased heart sounds	CXR CXR, ECHO
	Methysergide (no longer available): Pericardial fibrosis, cardiac valvular fibrosis	Syncope		ECG
	TCAs and Ca^{2+}-channel blockers: Cardiac conduction abnormalities		Q-T prolongation	
RESP	β-blockers: Worsening of COPD	Dyspnea	Expiratory wheezing	CXR ABGs
	Methysergide (no longer available): Pleuropulmonary fibrosis	Dyspnea	Rapid shallow breathing	PFTs
GI	Gastroparesis	Early satiety		
CNS	Intracranial disorders TCAs Anticonvulsants MAOIs: Anticholinergic and CNS stimulation	Tachycardia, dry mouth Blurred vision, urinary Somnolence, diplopia, ataxia, cognitive impairment Retention, delayed gastric emptying	Focal deficit	NeuroimagingECG

Key References: Weatherall MW: The diagnosis and treatment of chronic migraine, *Ther Adv Chronic Dis* 6(3):115–123, 2015; Chatterjee S, Rudra A, Sengupta S: Current concepts in the management of postoperative nausea and vomiting, *Anesthesiol Res Pract* 2011:748031, 2011.

Perioperative Implications

Preoperative Preparation

- Detailed pharmacotherapy Hx
- D/C MAOIs 14–21 d in advance if possible (see Monoamine Oxidase Inhibitors)
- Gastroparesis: Metoclopramide (10 mg/70 kg pt)

Monitoring

- Routine, unless signs of ischemic heart disease

Airway

- None

Preinduction/Induction

- Pts receiving β-blockers and Ca^{2+}-channel blockers may develop reduced CO and hypotension.

Maintenance

- Exaggerated response to indirect-acting vasopressors may occur with pts on ergotamine, sumatriptan, TCAs, and MAOIs.
- Hyperpyrexic coma reported after administration of narcotic to pts receiving MAOIs.

Extubation

- Increased risk of CNS stimulation with sumatriptan, ergotamine, TCAs, and MAOIs

Postoperative Period

- Pain management may be critical.
- Avoid withdrawal syndromes.
- Increased risk of postop N/V.

Anticipated Problems/Concerns

- Possible adverse interactions of anesthetic drugs and antimigrainous preparations
- No unique hazards of anesthesia administered to pts with migraines

Heart Disease, Congenital

Anila B. Elliott | Evan Serfass

Risk

- CHD is the most common birth defect.
- Incidence: 1:25 live births.
- 85–90% of pts with CHD survive to adulthood in USA due to advances in medical care.

Perioperative Risks

- The highest risk factors of this complex disease include HLHS; poorly compensated physiology; presence of long-term complications (arrhythmia, pulm Htn, CHF); and emergency surgery.
- Intermediate risk factors include major surgery, age less than 2 y, preop hospital stay >10 d, ASA physical status IV or V.
- Cardiac failure.
- Pulm Htn defined as PAP >25 mm Hg at rest and >30 mm Hg during exercise.
- Arrhythmias.
- Cyanosis.
- Mortality: there is a twofold increase in mortality in children with congenital cardiac lesions compared to those without CHD who present for noncardiac surgery.
- POCA registry.
- Majority of cardiac arrests occurred in general OR (54%) in children undergoing noncardiac surgery.
- Out of all the children with heart disease that arrested, 75% of them were <2 y, often with unrepaired lesions.

Worry About

- Resource availability: Is this child's cardiac history too complex for this institution/periop team?
  - Send the following children to a specialist center: Cyanosis, neonate with CHD, Eisenmenger syndrome, pulm Htn, aortic stenosis, HLHS, single ventricle physiology (BT shunt/Sano, Glenn, Fontan).
  - If true emergency and cannot be transferred, then understanding anatomy, physiology, and shunting is key to management.
  - Use PICU for postop management, especially complex lesions.
- Maintain forward flow/cardiac output.
- Balance pulmonary and systemic blood flow.
- Maintain adequate tissue oxygen delivery.
- Prevent arrhythmia.
- Optimize fluid balance.

Overview

- How to group these children: There are multiple ways, but the most useful is by physiology.
- Normal "series" circulation: Most repaired pts; there can be a small amount of mixing.
  - ASD/VSD
    - L-to-R shunting: This increases pulmonary blood flow and potentially decreases systemic blood flow.
    - R-to-L shunting: Deoxygenated blood flows into systemic circulation and causes reduced pulmonary blood flow and increased cyanosis.
    - Changes in SVR and PVR during anesthesia have the greatest effect in pts with large, unrestrictive defects.
- Parallel "balanced" circulation:
  - Pts with large AV septal defect or VSD, BT or Sano shunt, Truncus arteriosus.
  - Mixing of systemic venous and pulmonary venous blood; potential for cyanosis.
  - Balance between SVR and PVR.
- Single-ventricle circulation:
  - Blood flows passively to the lungs down a pressure gradient from the pulmonary artery to left atrium in pts who have a Glenn shunt or Fontan circulation.
  - Changes in intrathoracic pressure or in PVR affect pulmonary blood flow, which then affects systemic blood flow.
  - BT or Sano shunts are usually the first stage of creating Fontan circulation (palliative, to supply blood flow to the lungs).
    - Graft is connected between the subclavian artery (BT) or right ventricle (Sano) and the pulmonary artery.
    - Complete mixing of systemic venous and pulmonary venous blood (normal SpO_2 75–85%).
    - Flow is determined by SVR and PVR ratio: These pts are sensitive to changes in PVR or SVR, which can be caused by increased FIO_2, changes in $PaCO_2$, and volatile anesthetics or other vasodilators.
  - Glenn shunt is second stage of Fontan repair:
    - Bidirectional superior cavopulmonary shunt.
    - Connects SVC to the right pulmonary artery.
    - IVC drains to right atrium.
    - Pulmonary venous and systemic venous blood mix, yielding SpO_2 75–85%; pt will have cyanosis after procedure.
    - Can tolerate FIO_2 100% usually without issues.
  - Fontan circulation:
    - Inferior vena cava connected to the right pulmonary artery.
    - Separates the pulmonary and systemic circulation.
    - Passive flow to pulmonary circulation.
    - Normalizes oxygenation (children are sensitive to increases in PVR; decreases blood return to the heart, leading to a reduction in cardiac output).
    - Pressure gradient from the pulmonary artery to LA is the force driving pulmonary blood flow.

Etiology

- Genetics/syndromes:
  - Chromosomal abnormalities: Down syndrome (up to 30% can have heart defect), trisomy 18 and 13, Turner syndrome, Cri-du-chat syndrome, Wolf-Hirschhorn syndrome, DiGeorge syndrome
  - Associations: VACTERL
  - Syndromes: William syndrome, Goldenhar syndrome, Marfan syndrome, Noonan syndrome, Smith-Lemli-Opitz syndrome
- Family history of congenital cardiac disease
- Maternal factors/medications:
  - Untreated maternal PKU has a sixfold increased risk.
  - Preexisting maternal diabetes has a fivefold increased risk.
  - Medications: Lithium, thalidomide, isotretinoin, and bactrim.
  - Rubella.
  - Febrile infection, especially in the first trimester.

Usual Management

- Management is dependent on specific anatomy and physiology.
- Attempt to maintain same SpO_2 and other vital signs, as when the pt is at their baseline.
- L-to-R shunts:
  - Avoid increases in SVR, which will increase shunt.
  - Avoid decreases in PVR, which will increase shunt.
  - Avoid negative inotropes.
  - Avoid hypervolemia, which can lead to congestion.
  - In the event of desaturation, consider whether cause could be reversal of shunt.
- R-to-L shunts:
  - Maintain high SVR, to decrease shunt: Ketamine, phenylephrine.
  - Avoid increases in PVR.
  - Minimize intrathoracic pressure.
  - Avoid air bubbles in IV.
- Single ventricle physiology:
  - Common outpatient medications: Diuretics, antiarrhythmics, anticoagulants, antihypertensives
  - Corrective/palliative procedures (see overview for more detailed anatomy/pathophysiology of the following):
    - BT or Sano shunt: Systemic and pulmonary blood flow is determined by SVR and PVR ratio; avoid changes to PVR, as this leads to changes in systemic flow; use caution with volatile agents and vasodilators.
    - Glenn shunt: This can typically tolerate FIO_2 100%.
    - Fontan circulation: Avoid increases in PVR; maintain normal SpO_2.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pulm edema Cyanosis Pulm Htn Decreased lung compliance	Baseline SpO_2 when healthy Dyspnea TET spells Previous surgeries: rib resection, RLN injury	Crackles Blue/gray skin Clubbing in extremities	CXR SpO_2 ABG
CV	New murmur Heart failure Arrhythmia ASD/VSD Shunting Mixing	Dyspnea Lethargy Syncope Low functional capacity Poor feeding Sweating while eating	Tachycardia Tachypnea Hypotension Cool extremities Hepatomegaly Peripheral edema S_3 gallop Diaphoresis Elevated JVP	ECG ECHO (TTE) CXR Cardiac cath BP in upper and lower extremities
GI	Poor weight gain Protein losing enteropathy in post-Fontan patients (particularly in adolescence)	Poor feeding Poor weight gain Nausea Ascites	Hepatomegaly	LFTs Synthetic function of liver (coagulation panel)
CNS	CVA Syncope	Syncope Fatigue Headache Seizures	Neurologic deficits Blurred vision	ECHO (TTE) CBC (hyperviscosity)
HEME	Polycythemia	Low SpO_2 CVA	Neurologic deficits Blurred vision	CBC, peripheral smear Coagulation studies
METAB	Lyte abnormalities	Medication history Diuretics	Peripheral edema	Lytes Ca^{2+}, Mg^{2+}, phosphate

Key References: Thomas J: Anaesthesia for the child with congenital heart disease: pointers and pitfalls, *CME* 29(11):463–466, 2011; Cannesson M, Earing M, Collange V, Kersten JR: Anesthesia for noncardiac surgery in adults with congenital heart disease, *Anesthesiology* 111(2):432–440, 2009.

Perioperative Implications

Preoperative Preparation

- Hx can include poor feeding and failure to gain weight.
- Physical examination:
  - New onset murmur: Examine heart first; ignore the murmur, define the nature of the first and second heart sounds; most systolic murmurs are benign; all pansystolic and diastolic murmurs are pathologic and should be worked up prior to elective procedures; all murmurs that radiate are pathologic (PDAs, aortic valve); if child has a murmur, have BP taken in upper and lower extremities (coarctation).
  - Pathologic murmurs: Obtain TTE prior to proceeding.
  - Pt color:
    - Pink: Normal or L-to-R shunt; pathology—ASD, VSD, PDA
    - Blue: R-to-L shunt or mixing lesions; pathology—TOF, TGA, single ventricle
    - Gray: Sick children, usually critically ill; decreased CO; pathology—severe coarctation, interrupted aortic arch
  - Examine for cyanosis/clubbing.
  - Labs/studies: Hematocrit—could have polycythemia -> compensating for hypoxemia; ECG; recent TTE or cardiac catheterization; CXR.

Monitoring

- Dependent on the surgical procedure.
- Arterial line.
- Consider CVP.
- TEE if indicated.
- If PDA is present, have pulse ox on right upper extremity (preductal oxygenation) and any other extremity (postductal oxygenation).

Airway

- Consideration for syndromes that include CHD that could lead to difficult airway: Down syndrome, Pierre Robin (10% have cardiac anomalies), Beckwith-Wiedemann, Goldenhar syndrome, mucopolysaccharidoses

Preinduction/Induction

- Consider IV preinduction.
- Premedication is acceptable (and often indicated): Consider monitoring premedicated pts.
- Propofol: Reduces SVR and MAP; no change in heart rate, PVR, and PAP; left-to-right shunting decreases; right-to-left shunting increases; propofol may cause reduction in oxygenation and PBF by increasing shunting.
- Ketamine: Well tolerated in children with CHD; increases MAP; minimal effect on SVR, PVR, and PAP.
- Inhalational induction: Induction may take longer than in children without CHD; volatile agents decrease SVR and myocardial contractility; use caution with higher levels of inhalational agent, as these children may not tolerate high concentrations as well as children without CHD.

Maintenance

- Inhalational agents usually can be used with minimal effects on myocardial contractility and shunting. Caution with sicker/younger children who have lesions sensitive to PVR: SVR. Studies are limited on use of desflurane in this population.
- Can use opioids to minimize activation of SNS.
- Remember endocarditis prophylaxis if appropriate.

Extubation

- Period with the highest oxygen demand

Postoperative Period

- Acute care or ICU level of care, unless child has fully repaired ASD, PDA, VSD, or other two-ventricle repairs without significant sequelae.
- Good pain control.
- Maintenance of normothermia.
- Avoid hypovolemia.
- Maintain normal acid/base balance.
- Continue to minimize physiologic changes that could affect shunt fraction.

Anticipated Problems/Concerns

- If at all possible, consider transferring pt to center equipped to handle complexity of anatomy and physiology; if unable to transfer, contact pediatric cardiac anesthesia specialists for advice if pt presents in an emergency and transfer is not an option.
- Who to transfer:
  - Children with complex lesions, such as single ventricles, Fontan circulation, BT shunts, bidirectional cavopulmonary shunt, and cyanosis, should be transferred if possible.
  - Repaired ASD, VSDs can typically be cared for safely in most institutions.
  - For adults presenting with CHD with complete anatomic repair, manage with conventional strategies.
  - For adults presenting with CHD with complex anatomy and physiology, transfer to a center that has subspecialty consultants and cardiac anesthesiologists experienced in caring for complex physiology. These pts should transfer when able: Fontan circulation, repaired TOF with pulmonic valve stenosis or right ventricular failure, cyanotic lesions.

HELLP Syndrome

David J. Birnbach

Risk

- Occurs in 0.1–0.9% of all pregnancies.
- Previous history of preeclampsia or HELLP syndrome is a risk factor for HELLP.
- Occurs in 10–20% of women suffering from preeclampsia with severe features.
- May be a form of preeclampsia. Preeclampsia occurs in 2–10% of pregnancies; it is more prevalent in women with diabetes, women who are obese, and older women.

Perioperative Risks

- High maternal and fetal morbidity and mortality
- Increased cesarean delivery rate, increased intraop hemorrhage

Worry About

- Can be confused with hepatitis, thrombotic thrombocytopenic purpura, gallbladder disease, viral illnesses, antiphospholipid syndrome, and acute fatty liver of pregnancy.
- Thrombocytopenia and coagulopathy increase risk of hematoma associated with neuraxial anesthetic.
- High risk of hemorrhagic complications; associated with placental abruption.
- Upper airway and laryngeal edema can lead to airway obstruction and difficult or failed intubation. Fluid management can be difficult; pulm edema may ensue.

Overview

- HELLP is an acronym for the findings that suggest hepatic involvement in preeclamptic pts: **H**emolysis, **E**levated **L**iver enzymes, **L**ow **P**latelets. It typically presents between 28–36 wk gestation but has been reported to occur postpartum.
- Diagnostic criteria include hemolysis, defined by abnormal peripheral smear/microangiopathic hemolytic anemia and increased bilirubin levels; elevated liver enzymes; and thrombocytopenia.
- Failure to treat may lead to eclampsia or death due to hepatic hematoma or rupture.
- Up to 20% of pts with HELLP syndrome do not have antecedent Htn.

Etiology

- Poorly understood; may be severe form of preeclampsia resulting from abnormal prostaglandin control, intravascular platelet activation, and microvascular endothelial damage

Usual Treatment

- Definitive treatment is delivery as quickly as possible.
- After delivery, many experience full recovery and plt counts returning to normal within 1 wk.
- Recent evidence challenges the role of glucocorticoid therapy.
- Platelets, FFP, and cryoprecipitate administered as needed.
- Magnesium sulfate for CNS irritability and antihypertensives for Htn.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Upper airway edema	Dyspnea, voice change	Poor visualization on airway exam	Mallampati assessment
CV	LV failure	Dyspnea, desaturation	Adventitious sounds, desat	CVP and/or LVEDP
RESP	Resp depression	Magnesium administration	Decreased reflexes	$MgSO_4$ level
GI	Liver swelling Subcapsular hematoma	Epigastric pain N/V		Elevated AST, ALT, LDH >600 IU/L
HEME	Thrombocytopenia Hemolytic anemia	Bruising Pallor, jaundice	Bleeding (IV site oozing)	Platelet count <100,000 Bilirubin >1.2 mg/dL Peripheral smear
RENAL	Acute renal failure	Oliguria		Elevated uric acid, BUN, serum Cr
CNS	Eclampsia, cerebral edema	Seizures		

Key References: American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy: Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy, *Obstet Gynecol* 122(5):1122–1131, 2013; Fitzpatrick KE, Hinshaw K, Kurinczuk JJ, Knight M: Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liver enzymes, low platelets syndrome, *Obstet Gynecol* 123(3):618–627, 2014.

Perioperative Implications

Preoperative Preparation

- Obtain CBC, PT, PTT, fibrinogen, ALT, AST, LDH, BUN, and Cr.

Monitoring

- Consider arterial line and baseline ABG.
- Consider CVP if oliguria persists despite fluid administration or CHF.

Airway

- Assess airway early and repeat airway exam periodically.
- Laryngeal edema may preclude normal tracheal intubation in the event of emergency C-section. Videolaryngoscopy should be considered for intubation.
- Difficult intubation equipment should be immediately available.
- Consider preemptive epidural or continuous spinal cath before platelet count drops.

Induction

- Control neuraxial anesthesia with incremental dosing of catheter, if not contraindicated. Spinal techniques can be safely used in severe preeclampsia without coagulopathy.
- If GA is required, the hypertensive surge associated with ET intubation can be reduced by pretreatment with magnesium, antihypertensives, and/or opioids.

Adjuvants

- If significant Htn, antihypertensive therapy prior to laryngeal intubation.
- If receiving magnesium sulfate and needs GA, small doses of neuromuscular blocking agents with close neuromuscular blockade monitoring.

Hemochromatosis

Megan K. Werntz | Brandon M. Togioka

Risk

- Incidence of primary (hereditary) hemochromatosis: In some Caucasian populations, 10% are heterozygous carriers and 0.25–1% homozygous.
- Age: Clinical manifestations typically occur after age 40 in men and later in women due to the protective effect of menses.

Perioperative Risks

- Infection due to accumulation of iron in immune cells
- Glycemic disturbances
- Bleeding risk from low levels of clotting factors or platelet dysfunction
- Decompensated heart failure and/or arrhythmias

Worry About

- Iron deposition in the liver, heart, and endocrine glands leading to dysfunction

Overview

- Primary (hereditary) hemochromatosis is transmitted by genes, and secondary hemochromatosis is acquired.
- HH is an autosomal recessive disorder (HFE gene) that results in excess iron absorption.
- Once excess iron is absorbed, humans have no way to increase excretion. Iron accumulates in organs and results in cell damage. Because 90% of excess iron is deposited in the liver, it is often most affected.
- HCC is one of the most serious complications from untreated HH, responsible for 45% of deaths in pts with HH. Presence of cirrhosis is the greatest prognostic indicator for increased mortality.

Diagnosis

- Diagnosis is made by looking for elevated serum ferritin (>200 ng/mL in women and >300 ng/mL in

men) and high fasting transferrin saturations (>50% in women and >60% in men).
- Genetic testing may reveal mutations in the HFE gene on chromosome 6.

Usual Treatment

- Dietary changes to avoid red meat, vitamin C, and alcohol.
- Weekly or biweekly phlebotomy is initiated in symptomatic pts.
- Iron chelation therapy if phlebotomy is not tolerated (i.e., anemic pts).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Hepatic encephalopathy	Confusion, lethargy		MMSE
ENDO	Diabetes mellitus Hypoparathyroidism Impotence/infertility	Hypoglycemia Hypocalcemia Amenorrhea	Foot examination Chvostek and Trousseau signs	Glucose Calcium FSH/ LH, TSH
CV	Cardiomyopathy Arrhythmias Heart failure	Poor functional status (Pre) syncope Orthopnea	Displaced PMI Peripheral edema Elevated JVD	ECG, Holter monitor ECHO, CXR
RESP	Hepatopulmonary syndrome	Dyspnea	Pleural effusions	CXR
GI	Cirrhosis/hepatocellular carcinoma	Malaise Weight loss Indigestion	Hepatomegaly Splenomegaly Spider nevus	Serum ferritin LFTs, INR, CBC, albumin
MS	Arthralgia	Pain with activity	Swollen joints	
DERM	Bronzed pigmentation (late manifestation)		Bronze/gray skin	

Key References: Shander A, Berth U, Betta J, Javidroozi: Iron overload and toxicity: implications for anesthesiologists, *J Clin Anesth* 24(5):419–425, 2012; Ajloka RS, Kushner JP: Clinical consequences of iron overload in hemochromatosis homozygotes, *Blood* 101(9):3351–3354, 2003.

Perioperative Implications

Preoperative Preparation

- Consider risk for potentiation or precipitation of hepatic encephalopathy and plan to mitigate risk through careful selection of drugs, maintaining normal acid-base status, normalizing electrolytes, and avoiding hypoglycemia and hypotension.
- ECG, low threshold, to obtain ECHO.
- Assess bleeding risk by checking INR, PTT, and platelets, especially if considering RA.

Monitoring

- Decision on invasive lines should be based upon degree of cardiac and liver dysfunction as well as surgical risk.
- Avoid instrumentation of the esophagus (TEE, esophageal stethoscope, temperature probe) in advanced liver disease.

Airway

- Pts may require preoxygenation in the sitting position when orthopnea is present.
- Expect poor preoxygenation and quick desaturation with advanced liver or heart disease.
- If there is evidence of coagulopathy, employ gentle airway manipulation.

Preinduction/Induction

- Consider RSI (with H_2 antagonist and cricoid pressure) if evidence of ascites or gastroparesis associated with diabetes mellitus.
- In pts with severe liver disease, sensitivity to induction agents and anxiolytics may be increased and metabolism of succinylcholine may be slowed.
- Pts with a diseased liver may require a larger initial dose of nondepolarizing neuromuscular blocking agent due to altered protein binding and a larger volume of distribution.

Maintenance

- Consider blood-sparing strategies such as acute normovolemic hemodilution or using colloids, as blood transfusions are especially bad in this population.
- Intraop hourly glucose checks; consider background infusion of dextrose containing crystalloid.
- All volatile agents decrease hepatic blood flow and have minimal hepatic metabolism. All are likely safe.
- Consider cisatracurium as it does not rely on hepatic metabolism.
- Consider the potentiation of morphine, meperidine, alfentanil, benzodiazepines, and dexmedetomidine in pts with advanced liver disease.

Extubation

- Gentle oropharyngeal suctioning due to risk of coagulopathy and bleeding.
- Consider taking the pt intubated to the ICU for chelation therapy in pts that receive large volumes of blood.

Postoperative Period

- Careful glycemic management.
- Surgery and/or anesthetic may result in worse liver function. Remain vigilant for postop coagulopathy, renal impairment, or cognitive dysfunction.
- Pts with cardiac disease should have 24-h telemetry.
- Generally avoid NSAIDs and acetaminophen for pain control.

Hemophilia

Vincent S. Cowell

Risk

- Incidence of hemophilia A, factor VIII (FVIII) deficiency is 1:5000 male births; for hemophilia B, factor IX (FIX, Christmas disease) deficiency, it is 1:25,000 male births.
- Number of people affected with hemophilia in USA is estimated at approximately 20,000.
- Von Willebrand disease is the most common hereditary bleeding disorder, with a prevalence of about 1%.
- Hemophilia A, FVIII deficiency, affects 80–85% of hemophiliacs; the remainder has hemophilia B because of factor IX deficiency.
- Hemophilia A and B are X-linked recessive hereditary disorders, which occur in males and are transmitted by females who may be heterozygous for the gene mutation.
- Females may be asymptomatic carriers of the hemophilia gene and may have partial deficiency of FVIII of FIX, resulting in increased bleeding tendency.
- Hemophilia is without ethnic or geographic predilection.

Perioperative Risks

- Prolonged and potentially fatal hemorrhage may occur both during and after surgery.
- Closed-space bleeding can lead to nerve injury and vascular or airway obstruction.
- Surgery should not proceed without adequate supply of coagulation factor replacement to support the procedure and postop course.

Worry About

- Venous access issues may lead to central venous access.
- Spontaneous bleeding and intraop and postop hemorrhage despite optimal replacement therapy of deficient coagulation factor.
- FVIII and FIX inhibitor antibodies (up to 33% for FVIII and 3% for FIX).

Overview

- Hemophiliacs can have severe deficiency (<1% nml levels) approximately 40%, moderate deficiency (1–5% of nml levels) approximately 10%, or mild deficiency (5–40% of nml levels) approximately 50%.
- This congenital disorder is inherited as an X-linked recessive trait, affecting males almost exclusively.
- Acute and chronic complications often are due to recurrent spontaneous bleeding, the hallmark of which is bleeding into the joints (e.g., cycle of joint hemorrhage, inflammation, synovial proliferation, and erosion of cartilage, causing pain and disability).
- Hemophilia pts generally have normal PT, normal bleeding times, and a prolonged aPTT. Specific laboratory factor assays make the distinction, and plasma concentrations of FVIII or FIX determine the severity.
- Early prophylaxis is now the standard of care for pts with severe hemophilia.
- Plasma and recombinant factor products are now considered safe and equally effective.

Etiology

- Hereditary disorder that is X-linked recessive.
- Acquired hemophilia is the development of FVIII inhibitors (autoantibodies) in persons without a Hx of FVIII deficiency.

Usual Treatment

- Desmopressin (DDAVP injection or Stimate nasal spray) whenever possible for mild hemophilia A.
- Treatment includes clotting factor replacement therapy and recombinant FVIII and FIX products; plasma and recombinant factor products are now considered safe and equally effective; and there is no reported seroconversion to HIV, HVB, or HVC.
- Plasma concentrations of deficient factors are maintained at a minimum of 40–70% throughout the periop period; for major procedures, 100% is recommended before surgery and is maintained for 24–48 h.
- Cryoprecipitate is no longer recommended as a treatment alternative.
- Thrombin is produced via alternative pathways; prothrombin complex concentrate and recombinant factor VIIa (NovoSeven) is used in pts with inhibitors to FVIII of FIX.
- Gene insertion therapy shows a promising future.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Pharyngeal bleeding	Often seen in children	Tongue and mouth lacerations	Exam
GI	GI bleeding not common	When it occurs, bleeding can be excessive	Stool exam and endoscopy	Hemoccult, angio
HEME	Anemia, hematoma formation, and bruising	Lethargy, SOB, and skin discoloration	Hematomas	PT/PTT, plt count, bleeding FVIII and FIX assay, gene analysis
GU	Hematuria	Blood in urine		UA, cysto, IVP
CNS	Intracranial hemorrhage	Head trauma, headache, and change in mental status	Any sign or symptom of head injury or trauma	Head CT
MS	Joint hemorrhage Joint deformities Muscle hemorrhage Compartment syndrome Chronic pain	Painful distention of the joint Bruising Restricted movement Narcotic dependence	Hemarthroses Limited ROM Tenderness	Physical exam X-ray

Key References: Franchini M, Mannucci PM: Past, present and future of hemophilia: a narrative review, *Orphanet J Rare Dis* 7:24, 2012; Cabani LM, Ramsey G: Hemostasis and transfusion medicine. In Barash PG, Cullen BF, Stoelting RK, et al, editors: *Clinical anesthesia*, ed 7, Philadelphia, PA, 2013, Lippincott Williams & Wilkins, pp 433–434.

Perioperative Implications

Preoperative Preparation

- Preparation for the care of a pt with hemophilia should include consultation with a hematologist and when available, a hemophilia treatment center.
- Ideally, the anesthesiologist should have experience treating pts with bleeding disorders.
- A comprehensive detailed plan should be in place that outlines the type of hemophilia, factor levels, and dosing strategy for replacement of coagulation factor deficiencies.
- In elective surgery, levels of deficient coagulation factor should be restored to 40–70% of normal before surgery.
- Inhibitor screening and inhibitor assay assessments are essential to preop preparation.
- Adequate quantities of clotting factor concentrates should be available for surgery and the postop course.
- One unit of factor concentrate per kilogram of body weight normally increases the factor concentration by 2%. For factor VIII the half-life is 6 to 10 h, and for factor IX the half-life is 8–16 h, and thus approximately 1.5 U/h per kg of factor VIII or 1.5 U/2 h per kg of factor IX should be given.

Airway

- Care with laryngoscopy to avoid any trauma and thus bleeding to the airway is essential.
- Avoid nasal cannulations (i.e., endotracheal and nasogastric tubes).

Maintenance

- Noninvasive monitoring is optimal; risk/benefit ratio of invasive monitoring vs. site bleeding risk deserves significant consideration.
- Incorporate techniques to minimizing blood loss relative to the procedure.
- Antifibrinolytic drugs such as tranexamic acid are effective as adjunctive treatments for mucosal bleeds and dental extractions.

Adjuvants

- Risk of uncontrolled bleeding detracts from the selection of regional anesthetic technique. However, brachial plexus blocks performed at the axilla without complications have been reported.

Anticipated Problems/Concerns

- Blood bank support for plasma components, if needed, should be included in plans.
- Minimal risk of transmitting hepatitis and AIDS accompanies transfusion of blood components.

Hemosiderosis, Pulmonary

Fredrick Ntumy | Roy G. Soto

Risk

- Classically affects infants and children (80% manifest before 10 y old), but can affect any age group.
- No predilection for males or females.

Worry About

- Restrictive lung disease
- Pulm Htn
- Cor pulmonale
- Alveolar hemorrhage
- Increased need for transfusion secondary to acute and chronic anemia
- Adrenal insufficiency secondary to chronic steroid use

Overview

- Rare disorder of unknown etiology characterized by repeated episodes of intraalveolar hemorrhage and deposition of hemosiderin in alveolar macrophages. The cycle of recurrent hemorrhage frequently leads to the development of pulm fibrosis, pulm Htn, and cor pulmonale. Disease course is variable and can be marked by multiple spontaneous remissions, and the extent of pulm hemorrhage can be massive, leading to early death, or can be clinically insignificant.
- Presents with classically with the triad of hemoptysis, anemia, and pulm infiltrates on CXR.

Etiology

- Unknown; thought to be immune-mediated due to its responsiveness to immunosuppressive therapy
- Associated with immune-mediated disorders such as Goodpasture syndrome, SLE, Heiner syndrome, and Wegener granulomatosis, which can cause diffuse alveolar hemorrhage via immune-mediated mechanisms

Usual Treatment

- Immunosuppression with steroids (IV and PO) and supportive care. Other immunosuppressive agents such as azathioprine, chloroquine, and cyclophosphamide may be tried in steroid-unresponsive pts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pulm hemorrhage, restrictive lung disease, pulm Htn	Fatigue, weakness, cough, dyspnea, hemoptysis	Tachypnea, pallor, tachycardia, crackles, wheezing, clubbing, growth failure	CXR, PFTs, TTE
CV	Cor pulmonale, ischemia (secondary to anemia and CAD)	Fatigue, tachypnea, exertional dyspnea, cough, angina	Cardiac exam with emphasis on right heart failure	ECG, TTE
ENDO	Adrenal suppression secondary to chronic steroid use; pts may need stress dose steroids			
HEME	Acute and chronic iron deficiency anemia	Fatigue, exertional dyspnea, angina (if CAD)	Pallor of mucous membranes, tachycardia	CBC, iron studies

Key References: Bakalli I, Kota L, Sala D, et al: Idiopathic pulmonary hemosiderosis—a diagnostic challenge, *Ital J Pediatr* 40:35, 2014; Soto RG, Soares MM: Idiopathic pulmonary hemosiderosis in pregnancy: anesthetic implications, *J Clin Anesth* 17(6):482–484, 2005.

Perioperative Implications

Preoperative Preparation

- Evaluate for ongoing alveolar hemorrhage (look for classic signs and symptoms); delay elective surgery in pts with acute disease.
- Assess extent of restrictive lung disease; pt may need PFTs, ABG, and pulm optimization depending on procedure and severity of pt's disease.
- A decrease in vital capacity below 15 mL/kg or the presence of hypercapnia suggest that the pt is a high-risk candidate for pulm compromise.
- Assess degree of anemia and correct as needed to maximize oxygen carrying capacity.
- Evaluate pt for coagulopathy.
- Pts may require stress dose steroids if on chronic immunosuppressive therapy.
- Treat infections.
- Consider postponing elective procedures in setting of alveolar hemorrhage.

Monitoring

- Blood loss (pt may need transfusion)
- Emphasis on ventilation and oxygenation
- Airway pressures

Airway

- Use largest possible ETT for pt to allow for bronchoscopy and pulm toilet in the event of acutealveolar hemorrhage.

Induction

- Be wary of hypotension and the potential for cardiac ischemia in pt with decreased oxygen-carrying capacity and CAD.

Maintenance

- Check Hb/monitor blood loss.
- Avoid high airway pressures (use smaller TVs and/or increase inspiratory time) to avoid barotrauma or pneumothorax.
- Use PEEP.

Extubation

- Use standard extubation criteria.

Adjuvants

- Transfuse blood as needed.

Postoperative Period

- Maintain adequate oxygenation and ventilation.

Anticipated Problems/Concerns

- Acute alveolar hemorrhage

Henoch-Schönlein Purpura

Madhuri S. Kurdi

Risk

- Most common childhood systemic vasculitis; rare in adults.
- Reported annual incidence varies between 10-30 cases per 100,000 in children younger than 17 y and 3.4–14.3 cases per million in adults.
- Mean age of presentation is 6 y; mainly affects children between 4-11 y of age in up to 90% of cases.
- Occurs most commonly in spring; associated with recent URTIs in 90% of cases.
- Cases are reported all over the world; highest incidence is found in Caucasians and lowest in African Americans in North America.

Perioperative Risks

- Morbidity/periop complications increase with abnormal renal function and neurologic/pulm/cardiovascular involvement/emergency surgery.

Worry About

- Problems of concurrent supportive medications (NSAIDs, immunosuppressants, steroids, ACE inhibitors) that the pt may be taking
- Hypoproteinemia due to proteinuria if renal involvement
- Anemia due to hematuria if renal involvement and GI bleeding
- Fluid and lyte imbalance due to N/V and renal involvement

Overview

- HSP is an acute, self-limiting, autoimmune, small vessel childhood vasculitis commonly affecting those of the dermis, bowel wall, and rarely the ureter, myocardium, adrenals, brain, and lungs. Glomerular mesangial hypercellularity with endocapillary proliferation occurs commonly.
- It begins commonly with a nonthrombocytopenic purpuric rash. Arthritis or arthralgia is present in three-quarters of children and approximately 61% adults. GI symptoms occur in up to 85% of children and 48% of adults. Renal involvement is seen in 20–55% of children and approximately 32% of adults. GN is seen in a third of cases and may manifest as isolated hematuria, hypertension, or nephritic/nephrotic syndrome. 1–5% of children and 50% of adults with renal involvement progress to ESRD. Renal failure is the most common cause of death. The disease usually runs its entire course in 4 wk, and many children have no permanent sequelae. Renal symptoms can develop up to 3 mo after initial presentation. The course is complicated in adults.
- HSP is a clinical Dx, and none of the laboratory features are pathognomonic. Palpable purpura plus at least one feature like diffuse abdominal pain/IgA deposition in any biopsy/arthritis/renal involvement suggests the Dx.

Etiology

- Unknown; often triggered by URTI due to respiratory pathogens like group A Streptococcus, methicillin resistant *Staphylococcus aureus*, *Helicobacter pylori*, hepatitis HIV, parvovirus B19, multiple vaccines including H1N1 vaccine, insect bites, drugs like penicillin, quinine, chlorothiazide, food allergies, and malignancy-associated tumor antigens.
- Involves IgA-mediated autoimmune hypersensitivity; the large immune complexes formed face the problem of impaired clearance, settle in the small vessel walls of the affected organs, and trigger an inflammatory response.

Usual Treatment

- Mainly supportive and symptomatic; includes maintenance of adequate hydration, symptomatic pain relief with opioids/NSAIDs, and monitoring for the development of complications
- Short course of low dose oral steroids for those with severe abdominal pain
- High-dose IV corticosteroids, azathioprine, cyclophosphamide, cyclosporine, plasmapheresis, IV immunoglobulins for massive GI hemorrhage/severe proteinuria
- ACE inhibitors for severe nephritis, dapsone for vasculitis, colchicine for skin lesions sometimes
- Renal transplant in ESRD; emergency surgery for acute abdomen due to intussusception/bowel ischemia or perforation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Cutaneous vasculitis: Petechiae, purpura (common)	Rash	Symmetric palpable nonblanching nontender purpura over extensor surfaces of lower limbs, predominantly buttocks, forearms; trunk and face sometimes Lesions appear in crops Erythematous macular rash sometimes Subcutaneous edema over scalp, hands, feet Blisters and ulcers in adults sometimes	CBC with plt count PBS PT aPTT
GI	Edema and focal hemorrhage of bowel wall and mesentery: Acute abdomen, GI bleed, intussusceptions with an intestinal wall hematoma as the lead point	Colicky, poorly localized abdominal pain (most common) Nausea, vomiting are common, bloody diarrhea, melena, obstipation (less common)	On abdominal palpation—rigidity/distension/guarding/mass	Stool guaiac test for occult blood Abdominal US CT, MRI of abdomen GI endoscopy
GU	Microscopic hematuria, variable grade proteinuria, acute GN, nephrotic syndrome, distal ureteric stenosis, rapidly progressive GN ESRD	Renal colic, pink urine (hematuria), foamy urine (proteinuria), fatigue, swelling around face and eyes, weight gain	Facial/scrotal/penile edema Check BP for Htn	Urine microscopy for RBCs, RBC casts Urine dipstick test for blood and protein BUN Serum Cr, protein; lytes, especially potassium Abdominal US for kidneys, ureter Percentage of cellular crescents on renal biopsy for prognosis indication
MS	Symmetric arthritis/arthralgia of ankle, knee, hip, elbow Cervical joint arthritis rarely	Joint pains/swelling, neck pain	Periarticular swelling, tenderness, erythema, Decreased range of joint movements Restricted neck movements	X-ray/MRI of involved joints X-ray/MRI of cervical spine
CNS	Cerebral vasculitis, myelopathy, subarachnoid hemorrhage, PRES (rarely)	Headache, drowsiness, altered mental status, seizures, stroke	LOC Detailed neurologic examination for paresis, focal deficits, neuropathies	Contrast CT/MRI/MRI angiography brain, spine
CV	Vasculitis: Myocarditis, AV block (rarely), Htn if renal dysfunction	Palpitations Dizziness, syncope, chest pain	Look for bradycardia, ventricular arrhythmias, signs of heart failure	ECG, 2D ECHO, CXR, CT chest
RESP	Interstitial pulm hemorrhage/pneumonia/fibrosis (rarely)	Breathlessness, cough	Signs of respiratory distress, hypoxemia	CXR, CT chest
ENDO	Adrenal insufficiency due to chronic steroid therapy, adrenal hematomas (rare) Acute pancreatitis (rare)	Pain in abdomen radiating to the back	Look for obesity, BMI, fat deposits in the neck and decreased range of neck movement Measure thyromental distance	US/contrast CT abdomen Serum amylase, lipase
HEME	Anemia	Fatigue, breathlessness	Pallor	Hgb level, ESR, CRP, serum total IgA, galactose deficient IgA, PT, APTT

Key References: Trnka P: Henoch-Schönlein purpura in children, *J Paediatr Child Health* 49(12):995–1003, 2013; Kurdi MS, Deva RS, Theerth KA: An interesting perioperative rendezvous with a case of Henoch-Schönlein purpura, *Anesth Essays Res* 8(3):404–406, 2014.

Perioperative Implications

Preoperative Preparation

- Assess and improve volume status if vomiting/GI bleed/renal dysfunction present.
- Correct anemia if severe GI bleed/renal failure.
- Steroid supplementation if on steroids.
- If on ACE inhibitors, skip dose 24–48 h before surgery.
- IV access may be difficult because of deep-seated veins due to steroids and purpuric rash.

Monitoring

- Routine monitoring.
- Kidney and cardiac function monitoring are important. Look for bradycardia and arrhythmias.

Airway

- Cervical joint arthritis (rarely) and obesity with fat deposition on the neck and chin due to steroid therapy can lead to limited neck extension, so a difficult airway is a possibility. Keep difficult airway cart ready.
- Avoid invasive airway access.

Technique/Induction

- No preference for any technique in general exists; go for rapid sequence induction if administering general anesthesia for emergency abdominal surgery.
- Opt for regional if neck and cervical joint movements are restricted.
- Choose anesthetic drugs depending on renal, CNS, CV status, endocrine status, and presence of hypertension.

Maintenance

- Take care of joints and pressure points. Presence of arthritis, joint effusions, skin blisters, and ulcers should be kept in mind during positioning.
- Ensure sufficient IV fluid administration.
- Choose drugs like isoflurane/sevoflurane for maintenance and atracurium for neuromuscular blockade, keeping in mind renal involvement.

Postoperative Period

- The disease can worsen. Monitor and maintain renal function. Watch for cardiac arrhythmias.
- Avoid NSAIDs for pain relief if GI hemorrhage/renal involvement are present.
- Continue ACE inhibitors that were skipped preop.

Anticipated Problems/Concerns

- Risk of tissue compression and necrosis over pressure points due to positioning, BP cuff, and endotracheal intubation.
- Varying degrees of hypoxemia due to IgA deposits and periop alveolar hemorrhages; may require postop ventilator support.
- Anemia, hypoproteinemia, fluid, and lyte imbalance may increase morbidity.
- Insufficient supplementation of steroids may lead to precipitous hypotension due to acute adrenergic crisis.
- AV block, bradycardia, and cardiac arrhythmias with need for ventricular pacing and death can occur; nevertheless cardiac involvement is extremely rare.

Hepatic Encephalopathy

Man Piu Wong | Vivek K. Moitra

Risk

- Incidence in pts with hepatic cirrhosis (about 0.1% of the population) is 50–70%. It is frequently subclinical, but can be exacerbated in the postop period by the surgical stress response, dehydration, and postop infection.
- HE is acutely worsened, in about 20% of pts, following surgical portacaval shunts, minimally invasive TIPS, and hepatic resections.

Perioperative Risks

- Precipitation of encephalopathy from benzodiazepines, surgical procedure (portacaval shunt), postop infection, GI hemorrhage, or erosive gastritis
- In pts with severe underlying liver disease, Childs Class B and C, or high MELD score (>15)

Worry About

- Preop respiratory depression from benzodiazepine premedication.
- Hemorrhage from underlying hepatic dysfunction (e.g., decreased coagulation factors, thrombocytopenia).
- Underlying precipitating factor (infection, bleed) may create hemodynamic instability. HE in absence of precipitating factor, or when accompanied by seizure or focal neurologic deficit, should prompt brain imaging to rule out intracerebral bleed.
- Undiagnosed cerebral edema with a risk of cerebral ischemia in fulminant hepatic failure presenting for liver transplantation.

Overview

- A syndrome of alteration in mental status, from impaired concentration to coma, caused by portosystemic shunting, usually in the presence of liver failure. Hyperammonemia from protein breakdown is usually present, and the degree of hyperammonemia generally correlates with the degree of encephalopathy.
- Multifactorial in origin, but altered neurotransmission and elevated levels of endogenous benzodiazepines and opioids appear important contributors. Although not effective in improving outcome, administration of flumazenil and naloxone temporarily improves mental status in about 50% subjects with HE.
- Underlying hepatocellular injury may arise from multiple etiologies, but the most common are chronic alcohol abuse, chronic viral hepatitis, and NASH.
- HE usually reflects advanced hepatic dysfunction and is frequently seen in pts awaiting liver transplantation.

Etiology

- Underlying liver disease with identifiable hyperammonemic precipitating cause in >90% of cases: GI hemorrhage, infection, azotemia, hypoglycemia, electrolyte derangements, diuresis/hypovolemia, constipation, sedatives, especially benzodiazepines
- Elevated levels of endogenous benzodiazepines, γ-aminobutyric acid agonists and opioids
- Direct ammonia neurotoxicity

Usual Treatment

- Identify and treat precipitating cause.
- Reduce plasma ammonia with lactulose: 20 g q6–12 h orally or by NG tube until softening of stool; reduce dose if diarrhea. Alternately, 300 mL lactulose mixed with 700 mL tap water given as retention enema in pts with severe HE that cannot protect their airway.

Certain Antibiotics Can Be Used in Conjunction With Lactulose

- Neomycin (risk of ototoxicity and nephrotoxicity)
- Metronidazole (GI and systemic side effects)
- Rifaximin (combined with lactulose shown to decrease risk of hepatic encephalopathy versus lactulose alone)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Impaired concentration, lethargy, coma	Amnesia/memory deficits Fatigue	Transition of reflexes from hyperactive to hypoactive, and disappearance of asterixis, signify onset of severe HE	Plasma ammonia, CT
CV	Hypotension	Liver failure	Systolic BP 90 may be acceptable in liver failure	BP
RESP	Hyperventilation, hypoxemia	Dyspnea	Ascites, pleural effusions	CXR, ABG, US Abdominal CT
METAB	Hyponatremia, hypokalemia	Correction of hyponatremia or worsening of hypokalemia can further impair mental status	Free water excess exacerbates ascites and anasarca	BMP
HEME	Anemia, coagulopathy	GI bleeding	Pallor, splenomegaly	Hgb, plt count, prothrombin time

Key References: Poh Z, Chang PE: A current review of the diagnostic and treatment strategies of hepatic encephalopathy, *Int J Hepatol* 2012:480309, 2012; Kiamanesh D, Rumley J, Moitra VK: Monitoring and managing hepatic disease in anesthesia, *Br J Anesth* 111(Suppl 1):i50–i61, 2013.

Perioperative Implications

Liver Transplantation

- Recurrent or persistent HE predicts poor survival in cirrhosis and indicates decompensated liver disease which is best treated by liver transplantation.
- When severe, particularly in association with fulminant hepatic failure, HE is frequently associated with cerebral edema. The resulting intracranial Htn may be underestimated by CT scan, and ICP monitoring is indicated to ensure adequate cerebral perfusion pressure periop.
- ICP can be reduced via hyperventilation, hypertonic saline, mannitol, propofol, and elevation of head of bed. Recent evidence of hypothermia has been shown to reduce cerebral edema and intracerebral Htn.

Other Surgeries

- Mental capacity may be impaired to the degree that consent is problematic.
- Pt may be hypovolemic from impaired ability to maintain PO intake, lactulose therapy causing diarrhea, diuretic therapy for associated ascites, or recent GI bleed. Maintenance of hydration is important to prevent acute tubular necrosis the incidence of which is increased in liver failure.
- Placement of TIPS or surgically fashioned portosystemic shunt are performed for refractory esophagogastric variceal bleeding. HE may be precipitated or exacerbated postop, particularly if a significant degree of encephalopathy is present preop, or if the pt is elderly.
- Reversal of benzodiazepine precipitated hepatic encephalopathy can be performed with flumazenil. However, pts with history of alcohol use may tolerate higher doses of benzodiazepines.

Hepatitis, Alcoholic

Anthony K. Woodall | Melville Q. Wyche III | Amir Elhassan | Alan David Kaye

Risk

- In USA, 8.5% of adults met DSM-IV criteria for current alcohol use disorder; 30.3% of adults met DSM-IV criteria for lifetime alcohol use disorder. Approximately 10–15% of alcoholics will develop alcoholic hepatitis and cirrhosis.

Perioperative Risks

- Mortality rate of 60–100% of pts undergoing surgery during acute alcoholic hepatitis.
- Poorer prognosis when accompanied by increased bilirubin, increased Cr, PT >1.5× control, ascites, or encephalopathy.
- >10% of pts develop DTs without prophylaxis.
- Abdominal surgeries are associated with higher risk due to reduced hepatic blood flow.

Worry About

- Anemia and coagulopathy
- Pulmonary shunting leading to arterial hypoxemia
- Altered mental status and/or hepatic encephalopathy
- Cerebral edema and increased ICP with hepatic encephalopathy, which may progress to coma
- Hemodynamic instability secondary to DTs
- Hypoglycemia due to poor gluconeogenesis
- Insulin resistance
- Electrolyte abnormalities
- Renal insufficiency, which means hypotension and nephrotoxic drugs should be avoided
- Citrate toxicity with blood transfusion due to decreased citrate metabolism

Overview

- Most common form of liver disease in USA.
- Usually preceded by period of heavy alcohol consumption.
- An intermediate stage between fatty liver and alcoholic cirrhosis.
- Can vary from mild (with only elevated liver function tests) to severe liver inflammation (prolonged prothrombin time and liver failure).
- Can be chronic (less severe) or acute (more severe).
- Characteristic clinical features include fever, hepatomegaly, jaundice, anorexia, and abdominal bruit over liver (indicated in >50% pts).
- 10–20% mortality risk with each episode of acute alcoholic hepatitis.
- Mortality is 50% within 30 d of onset, with pts having hepatic encephalopathy, derangement in renal function, hyperbilirubinemia, and prolonged PT.

Etiology

- A daily intake of >40 g of alcohol, (e.g., roughly 4 beers or 3.5 oz of 80-proof liquor) in men and >20 g (e.g., 2 beers or approximately 2 oz of 80-proof liquor) in women significantly increases the risk of alcoholic hepatitis.
- Inflammatory process via leukocytic infiltration that leads to hepatocellular necrosis with intracellular deposition of Mallory Bodies (characteristic, not specific).
- Repeated episodes are a precursor to cirrhosis after healing and scar tissue formation.

Treatment

- Abstinence with counseling
- Nutritional support: Diet, multivitamin, and mineral supplementation
- Medications: Pentoxifylline, steroids (which may reduce mortality in pts with severe alcoholic hepatitis or encephalopathy)
- Supportive care including diet adjustment, multivitamin supplementation, lactulose, and neomycin if needed

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	High CO Low SVR Low CO (in advanced disease)	Exercise tolerance	Hyperdynamic cardiac exam	ECG ECHO
RESP	Pulm shunts Restrictive disease Pulm effusions Central hyperventilation	Orthodeoxia Ascites	Effusions on CXR, ascites on abdominal exams	Resp alkalosis on ABG
GI/HEPAT	Disrupted synthetic and metabolic function	Anorexia, N/V, malaise, weight loss, fever	Jaundice, ascites, tender hepatomegaly, splenomegaly	Elevated transaminases (AST/ ALT>2), PT, ALP, bilirubin Decreased albumin
RENAL	Mg^{2+} and PO_4^{2-} wasting Free water retention		Ascites	Serum Mg^{2+} and PO_4^{2-} Hyponatremia
ENDO	Insulin resistance			Glucose
HEME	Anemia and thrombocytopenia GI blood loss Hypersplenism	Bruising/bleeding	Splenomegaly	Hgb/ Hct, plts
CNS	Decreased clearance of amines	Altered mental status	Neurologic exam	NH_3 levels

Key References: Muilenburg DJ, Singh A, Torzilli G, Khatri VP: Surgery in the patient with liver disease, *Anesthesiol Clin* 27(4):721–737, 2009; Steadman RH, Braunfeld M, Park H: Liver and gastrointestinal physiology. In Hemmings HC, Egan TD, editors: *Pharmacology and physiology for anesthesia: foundations and clinical application*, Philadelphia, PA, 2013, Elsevier, pp 475–486.

Perioperative Implications

Preoperative Preparation

- Pt should be assessed via Child-Pugh or MELD score. Elective procedures should be postponed for Child-Pugh score >7 or MELD >8.
- Increased sensitivity to sedative medications (increased cerebral uptake of benzodiazepines).
- Ascites may be treated by diuretics (spironolactone) or percutaneous drainage. Contains <3 g/dL protein and the same concentration as blood for solutes.
- Hypokalemia and hyponatremia should be corrected slowly (over 24–36 h).
- Correct coagulopathy with vitamin K, FFP, and platelets (if needed).

Monitoring

- Consider CVP or PA cath: Following the removal of large amounts of ascitic fluid, IV colloid fluid replacement is often necessary to prevent profound hypotension and renal shutdown.
- Monitor blood glucose closely due to deranged insulin production secondary to liver pathology.
- Arterial cath for hemodynamic lability, frequent blood gas sampling, and large fluid shifts.

Airway

- Rapid sequence intubation: Some pts are at risk for aspiration due to ascites (increased abdominal pressure, and slowed gastric emptying).
- Inadvertent esophageal intubation can cause enough trauma to damage the esophageal varices and cause significant bleeding.
- Beware of airway edema with reduced liver function.

Induction

- Hypoalbuminemia may decrease V_d and therefore increase pharmacologic response to standard drug dosages.
- Water-soluble drugs may have increased V_d, owing to ascites.
- RA is well tolerated (if coagulation status permits).

Maintenance

- Impaired drug metabolism, detoxification, and excretion by the liver can prolong drug half-lives. (Volatile agents, muscle relaxants, analgesics, and sedatives may be affected.)
  - Remifentanil has organ independent metabolism, a benefit for severe liver disease.
  - Fentanyl is a very common opioid choice.
  - Cis/Atracurium are neuromuscular blockers of choice due to organ independent metabolism.
  - Increase initial dose of neuromuscular blockers due to increased volume of distribution, reduce subsequent doses due to decreased metabolism.
  - Decrease dose 50% for morphine, meperidine, barbiturates, and benzodiazepines.
- Desflurane is the most minimally metabolized inhalational agent; however, sevoflurane and isoflurane are also shown to be safe in pts with impaired liver function. Factors known to reduce hepatic blood flow, such as hypotension, excessive sympathetic activation, and high mean airway pressures during controlled ventilation, should be avoided.

Extubation

- Extubate when pt fully awake to ensure highest degree of airway protection.

Adjuvants

- Multivitamins, minerals, and vitamin K 10 mg SQ or IM

Postoperative Period

- Regional pain control is ideal so as to avoid pharmacokinetic disturbances of systemic agents.
- Maintain low threshold for transfer of pt to ICU environment, particularly in unstable pts.
- Vigilant observation for signs of acute hepatic decompensation (jaundice, encephalopathy, and ascites), delirium tremens, and sepsis (with secondary DIC).
- Liver failure is the most common cause of postop death in cirrhotic pts.

Anticipated Problems/Concerns

- Increased risk of postop complications, including acute hepatic failure, sepsis, bleeding, and renal dysfunction
- Need for prolonged airway protection because of altered mental status and pulm dysfunction
- Acute withdrawal from alcohol
- Multiple coagulation abnormalities due to synthetic dysfunction and hypersplenism

Hepatitis, Halothane

Mark G. Mandabach | Jeffrey B. Dobyns

Risk

- Multiple exposures to halothane is the most important risk factor.
- Prior Hx of jaundice or fever after anesthesia.
- Females more susceptible.
- Obesity an important factor.
- Age:
  - Halothane hepatitis is rare in pts <10 y old (3% of all cases).
  - Pts <30 y of age make up about 10% of all cases.
  - Most cases occur in pts >40 y.
  - In older pts, the disease is more devastating.
- Genetics: There is a strong family linkage associated with halothane hepatitis.

Perioperative Risks

- Type or duration or extent of surgery is not a risk factor.
- Hx of non-halothane-related liver disease is also not a risk factor.

Worry About

- Concerns arise with the induction of cytochrome P450 2E1 enzyme by alcohol, barbiturates, or isoniazid. Hepatitis is more severe if CYP450 2E1 was previously induced by other medications/substances.

Overview

- Estimated incidence:
  - First exposure: 0.3 -1.5:10,000
  - With multiple exposures: 10-15:10,000
  - F:M ratio: 2:1
  - Latency period before clinical symptoms
  - After first exposure: ~6 d, with overt jaundice in ~11 d
  - After multiple exposures: ~3 d, with overt jaundice in ~6 d
- Presenting symptoms:
  - Fever: 75%
  - Leukocytosis, eosinophilia: 20–60%
  - Myalgias: 20%
  - Rash: 10%
  - Jaundice: 25%
  - Ascites, coagulopathy, GI hemorrhage: 20–30%
- Liver enzyme markers:
  - Alanine aminotransferase: 25–250× upper limit of normal
  - Aspartate aminotransferase: 25–250× upper limit of normal
  - Alkaline phosphatase: 1–3× upper limit of normal
- Histologic liver findings:
  - Zone 3 necrosis (massive in 30% of cases, submissive in 70% of cases)
  - Inflammation, granulomas, eosinophilic infiltrates
- Clinical course:
  - Mortality rate in preliver transplant era is as high as 80% if encephalopathy is present.
  - Recovery becomes evident as symptoms resolve over 5–14 d, with full recovery taking weeks to months.

Etiology

- Two distinct types of hepatitis are associated with halothane exposure:
  - Halothane hepatotoxicity (type I):
    - Subclinical disease with mild elevation of liver enzymes, no jaundice
    - Mild pattern of injury characterized by nausea, lethargy, and fever
    - Caused by the anaerobic, reductive metabolism of halothane
    - May occur in up to 20–30% of pts receiving halothane
    - Transaminases remain elevated for 1–2 wk postexposure, then resolve spontaneously.
    - Nonimmune reaction
    - Hepatic hypoxia may play a role.
  - Halothane hepatitis (type II):
    - Fulminant liver failure with massive zone 3 liver necrosis
    - Caused by oxidative metabolism of halothane
    - TFA intermediates conjugate liver proteins.
    - Strong evidence for immune reaction:
    - In susceptible individuals, antibodies to the metabolite-liver protein complex are formed causing an immune response.
    - Incidence is 10 times higher in second exposure cases, and severity of illness greater if second exposure follows soon after first exposure.

Drug Class/Metabolism

- Halothane: A nonvolatile anesthetic; a halogenated hydrocarbon
  - Molecular formula C2HBrClF3
  - Systematic (IUPAC) name: 1-bromo-1-chloro-1,1,1-trifluoroethane
  - Metabolized in the liver through both oxidative and reductive pathways
- Comparison of oxidative metabolism of volatile anesthetics:
  - Halothane: 20%
  - Enflurane: 2%
  - Isoflurane: 0.2%
  - Desflurane: 0.02%
- There are a few case reports of type II hepatitis associated with isoflurane and desflurane in the world literature.

Assessment Points

System	Assessment by Hx	PE	Test
GI	N/V, malaise	Jaundice (about 6 d after second exposure, longer if first exposure)	Eosinophilia, leukocytosis Elevated liver enzymes: 1. AST 2. ALT (25–250× upper limit of normal) 3. Alk phos (1–3× upper limit of normal)Liver biopsy: Zone 3 centrilobular necrosis

Key References: Habibollahi P, Mahboobi N, Esmaeili S, et al.: Halothane-induced hepatitis: a forgotten issue in developing countries, *Hepat Mon* 11(1):3–6, 2011; Lewis JH: Liver disease caused by anesthetics, toxins, and herbal preparations. In Feldman M, Friedman LS, Brandt LJ, editors: *Sleisenger & Fordtran's gastrointestinal and liver disease,* ed 9, Philadelphia, PA, 2010, Elsevier, pp 1447–1460.

Perioperative Implications

Preoperative Preparation

- Prior records should be reviewed and prior exposure documented.
- Avoid volatile anesthetics in a pt with a confirmed Hx of postop liver dysfunction from halogenated agents.
- Total IV anesthesia is one approach if general anesthesia is planned.
- RA not contraindicated.

Anticipated Problems/Concerns

- How to evaluate postop liver dysfunction:
  - Incidence: 25–75% of surgical pts may have some form of hepatic dysfunction, from mild elevation in liver enzymes to global liver failure.
  - Up to 50% of pts with cirrhosis may have postop jaundice.

Categories of Postoperative Liver Dysfunction

- Hepatocellular injury (elevated alanine amino-transferase, +/– hyperbilirubinemia)
  - Etiologies: Inhalational anesthetics and other drugs, hypotensive shock, transfusion reactions, unrecognized preop liver dysfunction
- Cholestatic jaundice (elevated alkaline phosphatase, +/– elevated ALT; direct hyperbilirubinemia)
  - Etiologies: Benign postop cholestasis, prolonged cardiac bypass, sepsis, prolonged administration of total parenteral nutrition, cholecystitis, cholangitis, microlithiasis, drugs (especially antibiotics)
- Indirect hyperbilirubinemia (other liver enzyme markers often normal)
  - Etiologies: Multiple transfusions, hemolysis, glucose-6-phosphate dehydrogenase deficiency, Gilbert's syndrome
- Diagnosis: Liver biopsy usually not necessary; histologic appearance often identical to viral hepatitis.

Differential Diagnosis for Inhalational Anesthetic Induced Hepatitis

- First rule: AIH is a diagnosis of exclusion
- Preexisting liver disease:
  - Viral hepatitis
  - Steatohepatitis: Alcoholic or nonalcoholic (NASH)
  - Autoimmune hepatitis
  - Wilson disease
- Periop disorders:
  - Drug reactions
  - Hypotensive shock and other causes of liver ischemia
- Second rule: In pts with drug-induced liver injury, jaundice may herald impending global liver failure and should be considered life threatening.
- Third rule: Treatment is supportive in nature, and orthotopic liver transplant may be life saving.
- Fourth rule: In a pt with documented or suspected AIH, avoiding all volatile anesthetics is the safest course for future anesthetics, due to immune cross reactivity, the possibility of trace amounts of volatile anesthetics in the anesthesia circuit, as well as the many unanswered issues regarding this disorder.

Hepatitis, Viral

Lee A. Fleisher

Risk

- Viral hepatitis accounts for more than 50% of cases of acute hepatitis in USA.
- Caused by infection with any of at least five distinct viruses: HAV, HBV, HCV, HDV, and HEV.
- Most commonly caused by HAV, HBV, or HCV.
- With more widespread use of the HAV and HBV vaccine, the rate of infection has decreased.
- Hepatitis is a very common infection in economically developing countries of Africa, Asia, and Latin America; children are frequently sources of outbreaks in crowded households, day care centers, and institutions; increased risk of disease is associated with travel to developing countries, men who have sex with men, users of injected and noninjected drugs, and persons with clotting-factor disorders.
- Healthcare workers do not appear to be at increased risk for occupationally acquired infection.

Perioperative Risks

- Elective surgery should not be performed on pts with acute HAV infection.
- Surgery in HBV infection depends on activity and stage of infection.
- Worsening liver function, hepatic encephalopathy, and coagulopathy are risks in all cases of acute infection.
- Risk of transmission of HCV from carrier to anesthesia personnel is ~2% after percutaneous exposure.

Worry About

- With acute hepatic failure or end-stage liver disease: Coagulation abnormalities, decreased hepatic metabolism of drugs, decreased levels of plasma cholinesterase, hypoxemia from pulm shunting and edema, ascites and Na^+ overload, hypokalemia, hepatic encephalopathy and cerebral edema, impaired glucose metabolism and hypoglycemia, portal Htn and GI bleeding, acute renal failure and hepatorenal syndrome, infection and sepsis, malnutrition.
- Maintenance of liver blood flow and O_2 delivery; metabolism of drugs with hepatic clearance; hypoglycemia; prolonged effect of sedatives.
- In addition to the use of universal precautions by anesthesia personnel, use of sharp devices for invasive procedures should be minimized and/or safety devices should replace standard sharps.

Overview

- HAV replicates in the liver and is shed in the stool; the concentration in the stool is highest during the 2-wk period before to 1 wk after the onset of clinical symptoms; the risk of transmission of infection via the fecal-oral route is greatest during this time.
  - Symptoms do not occur until the viral load in the stool begins to decrease; most pts with hepatitis A do not require hospitalization for treatment.
  - In children <6 y of age, most HAV infections are asymptomatic; among older children and adults, most infections are symptomatic, with jaundice occurring in over 80%.
  - The two most common physical findings are jaundice and hepatomegaly. In symptomatic pts, the most common lab findings are elevated levels of serum ALT and bilirubin.
  - Chronic HAV infection does not occur; most acute infections resolve within 2 mo; 10–15% of symptomatic pts may have a relapse of illness for up to 6 mo.
  - Fulminant hepatitis with acute liver failure occurs in about 0.5% of all pts with HAV infection; the rate is 1.8% among adults >50 y of age; pts with chronic liver disease are at increased risk for fulminant hepatitis when infected with HAV.
- Hepatotropic viral infection: 90% of pts have self-limiting acute hepatitis; 10% become chronic HBV carriers, with about half of those progressing to chronic active hepatitis, cirrhosis, or hepatocellular carcinoma; 0.5% of pts with acute infection develop fulminant hepatitic failure.
  - 70% with acute infection have subclinical hepatitis; symptomatic infection may produce jaundice, malaise, nausea, and abdominal pain.
- Hepatotropic insidious viral infection; fulminant acute hepatitis C is rare.
  - 60–70% of individuals with acute HCV infection are asymptomatic or have only a mild clinical illness.
  - 70–85% of pts infected with HCV develop chronic infection; cirrhosis develops in up to 50% of individuals with chronic hepatitis C and hepatocellular carcinoma in 1–5%.
  - Pts >50 y may have a more rapid progression of liver injury; alcohol use increases the risk of liver injury.

Etiology

- HAV is a 27-nm RNA nonenveloped virus transmitted by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water; rarely, HAV has been transmitted by transfusion of blood or blood products collected from donors in the viremic phase of infection.
- HBV is a 42-nm DNA virus with eight genotypes that is carried in and spread by blood and body fluid contact. It is transmitted to nonimmune individuals via parenteral or mucocutaneous exposure to HBV-infected blood or body fluids.
- HCV is a 30- to 60-nm RNA virus with at least six genotypes that is carried in and transmitted by exposure to blood and body fluids.

Usual Treatment

- Ig provides protection through passive transfer of antibodies to exposed individuals; a single dose of Ig should be administered as soon as possible after exposure to HAV or HBV.
- Pts with acute liver failure require intensive support and may require liver transplantation.
- Hepatitis A vaccine provides preexposure protection from HAV infection and is recommended by the CDC Advisory Committee on Immunization Practices for all children at age 1 y and adults in high-risk categories (men who have sex with men, users of illicit drugs, travelers to areas of the world where HAV is endemic, and people with chronic liver disease or who receive clotting factor concentrates).
- Prevention with hepatitis B vaccine.
- Medications for chronic hepatitis C infection include injectable alpha interferons (Pegasys), ribavirin (Rebetol, Copegus), boceprevir (Victrelis), simeprevir (Olysio), sofosbuvir (Sovaldi), simeprevir (Olysio), daclatasvir (Daklinza), ledipasvir/sofosbuvir (Harvoni), ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak).
- Medications for chronic hepatitis B infection include injectable alpha interferons, lamivudine (Epivir), adefovir (Hepsera), entecavir (Baraclude), telbivudine (Tyzeka), and tenofovir (Viread).

Assessment Points

For Patients With Acute Hepatitis A or Fulminant Hepatitis A

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	N/V, GI bleed	Tachycardia, hypotension	Orthostatic BP changes; measure CO, SVR
RESP	Hypoxemia	Tachypnea	O_2 saturation, ABG	
GI	Bleeding, jaundice, N/V, hypoalbuminemia, hepatitis	Hx of bleeding, dark urine, N/V	Stool guaiac test + material, icteric sclera, edema, ascites, abdominal pain	Hct, endoscopy, bilirubin, serum albumin, ALT, AST
ENDO	Hypoglycemia	Altered consciousness	Blood glucose	
HEME	Anemia, thrombocytopenia, immunosuppression, coagulopathy	Tachycardia, easy bruising, infections, abnormal bleeding	Bruises, bleeding in wounds	Hct, plt count, PT (low factor V, VII, IX, X, fibrinogen)
RENAL	Hepatorenal syndrome, hyponatremia	Oliguria, altered consciousness, seizures	Urinary Na^+ low, serum Na^+	
CNS	Encephalopathy, cerebral edema	Mental status exam	LOC	Serum ammonia level, measure ICP

Key References: Lentschener C, Ozier Y: What anaesthetists need to know about viral hepatitis, *Acta Anaesthesiol Scand* 47(7):794–803, 2003; Mcclain RL, Ramakrishna H, Iii SA, et al: Anesthetic pharmacology and perioperative considerations for the end stage liver disease patient, *Curr Clin Pharmacol* 10(1):35–46, 2015.

Perioperative Implications (Acute Hepatitis)

Preoperative Preparation

- Elective surgery should be postponed in pts with acute hepatitis.
- Correction of clotting abnormalities with FFP, platelets, or cryoprecipitate as needed.
- Administration of vitamin K to facilitate production of coagulation factors (prolonged PT), if time permits.
- Premedication with depressive or sedative drugs should be avoided.

Monitoring

- Arterial line for ABG, lytes, glucose, and BP.
- Consider central venous or pulm artery cath.

Airway

- Consider rapid sequence induction if there is N/V or upper GI bleeding.

Preinduction/ Induction

- Consider ketamine or etomidate in hypovolemic pts.

- Acute liver failure is not likely to reduce plasma cholinesterase levels, so succinylcholine may be used if indicated.
- Increased bioavailability of IV drugs if serum albumin concentration is decreased.
- Limit sedative drugs.

Maintenance

- Inhalational agent with high inspired O_2 concentration is useful for maintaining hepatic blood flow and O_2 supply; halothane should probably be avoided.
- Effect of muscle relaxants with hepatic clearance may be prolonged.
- Increased blood loss with coagulopathy.

Extubation

- Postop mechanical ventilation to ensure time for adequate metabolism of depressant drugs

Adjuvants

- Hypocalcemia can occur with citrate administration.

Anticipated Problems/Concerns

- Worsening of hepatic or renal function
- Delayed awakening from prolonged drug metabolism or encephalopathy
- Need to protect airway with reduced consciousness
- Hypoglycemia

Hepatopulmonary Syndrome

Gregory Hertel | Gaurav Malhotra

Risk

- Occurs in up to 10–32% of pts with cirrhosis.
- Dyspnea is present in up to 70% of cirrhotic pts for varying reasons (ascites, ILD, volume overload, anemia).

Perioperative Risks

- Hypoxemia, often worsened on induction and post LT
- Aspiration
- Hemodynamic instability and CV collapse
- Acute/chronic renal insufficiency
- Myocardial infarction

Worry About

- Full stomach and aspiration risk in presence of ascites and increased intraabdominal pressures
- Hypoxemia (exacerbated in immediate post LT period)
- Severe post LT hypoxemia and possible RV failure related to pulm vasoconstriction from an abrupt change in vascular mediators from the new liver
- Hemodynamic instability, especially related to reperfusion during LT

Overview

- Pulm complication of cirrhosis resulting in arterial hypoxemia.
- Defined as triad of liver disease, intravascular pulm vasodilatation, and abnormal gas exchange.
- Cirrhosis pts with hepatopulmonary syndrome have a higher mortality than those without it.
- Liver transplant is the only definitive treatment.

Etiology

- Involves a widespread vasodilatation of the precapillary pulm arterioles up to 100 μm.
- Overall understanding of the pathogenesis of HPS is limited.
- Animal models suggest increased endothelin (and subsequently increased NO), pulm monocytes, and VEGF all contribute to pulm vasodilatation and angiogenesis, which in turn contribute to oxygen impairment.
- Increased vessel diameter in addition to impaired hypoxic pulm vasoconstriction results in increased flow across the capillary bed without an increase in alveolar ventilation, causing a V/Q mismatch.
- Hypoxemia is exacerbated by inability of oxygen at room air concentration to diffuse to blood at the center of the dilated vessels.

Usual Treatment

- Liver transplantation remains the only effective treatment for HPS.
- Angiogenesis hypothesis is supported by the observation that correction of hypoxemia is not immediate post LT and may take up to a year; NO returns to normal post LT.
- TIPS has not been shown to be consistently beneficial in HPS.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Volume overload Hypotension Cirrhotic cardiomyopathy (increased CO, decreased ventricular response to stress) Postreperfusion syndrome (LT) CAD LVOT obstruction	Poor exercise tolerance CAD/MI	Vital signs Pitting edema	Monitor BP and HR ECG and ECHO
RESP	V/Q mismatch Hypoxemia Hepatic hydrothorax Portopulmonary Htn	Dyspnea, tachypnea	Orthodeoxia- worsened hypoxia with standing as flow increases to larger vessels in lung bases	Monitor pulse oximetry and RR, increased A-a gradient (>15 mm Hg) ABG Contrast-enhanced TTE
GI	Ascites Portal Htn Esophageal varices SBP	Abdominal distension Hematemesis, melena	Fluid wave Guarding and rebound (SBP)	Abdominal x-ray, CT scan, US WBC count, peritoneal fluid analysis
RENAL	Hepatorenal syndrome Hypervolemia Hyponatremia	Oliguria Peripheral edema	Vitals signs	UA, serum lytes, BUN and Cr
HEME	Coagulopathy (decreased clotting factors and thrombocytopenia)	Easy bruising/bleeding	Purpura	INR/PT, PTT, fibrinogen, CBC Thromboelastogram
CNS	Hepatic encephalopathy Intracranial Htn Cerebral edema	Confusion Coma	GCS Asterixis	Head CT Serum ammonia

Key References: Dalal A: Anesthesia for liver transplantation, *Transplant Rev (Orlando)* 30(1):51–60, 2016; Koch DG, Fallon MB: Hepatopulmonary syndrome, *Clin Liver Dis* 18(2):407–420, 2014.

Perioperative Implications

Preoperative Preparation

- Baseline ABG to evaluate severity of hypoxemia
- ECHO to evaluate cardiac function
- Thorough H+P and consent, including risks of anesthesia and full anticipated lineup

Monitoring

- Standard monitors
- Urinary cath
- Arterial line for frequent ABGs to assess hypoxemia and hemodynamic monitoring
- Consider central line with pulm arterial cath and SvO_2.
- Consider possible VV bypass for LT.
- Consider intraop TEE.

Airway

- Ensure adequate preoxygenation.
- Ideally utilize tools for rapid intubation (video laryngoscopy).
- Full stomach precautions.

Induction
- Rapid sequence induction with cuffed ETT in setting of ascites or full stomach.
- Induction alone may worsen hypoxemia.
- Anticipate hypoxemia and hemodynamic instability in setting of decompensated cirrhosis and HPS.
- Ketamine decreases hepatic blood flow; propofol increases it.

Maintenance
- Higher FIO_2 and PEEP throughout case augment oxygenation.
- Standard maintenance with adequate muscle relaxation.
- Trendelenburg positioning if tolerated by surgical needs.
- All inhaled anesthetics decrease MAP and portal blood flow.
- Allow adequate preparation for transfusion, adequate access, and readily available products (RBCs, FFP, plts, cryoprecipitate).

Extubation
- Extubate only if conditions optimized with pt awake, strong, and with assuring ABG, with caution given to potential for severe postop hypoxemia
- Low threshold to remain intubated with plan for SICU postop
- Postop period
- Supplemental oxygen therapy
- May require PEEP to improve oxygenation
- In case of severe postop hypoxemia:
  - Trendelenburg positioning
  - Inhaled vasodilators (epoprostenol and NO, selectively targeting constricted normal vessels in the more ventilated middle and upper lobes);
  - IV methylene blue (vasoconstrictor preferentially targeting dilated vessels in the bases);
  - Embolization of lower lobar pulm vessels;
  - ECMO.

Anticipated Problems/Concerns
- Hypoxemia
- CV instability
- Coagulopathy

Hereditary Hemorrhagic Telangiectasia

(Osler-Weber-Rendu Disease)

Rishi Chokshi | Lee A. Fleisher

Risk
- Effects vary in racial and ethnic groups, with a wide geographic distribution.
- Men and women affected equally.
- In Vermont, frequency is 1:16,500.
- In Europe and Japan, frequency is 1:5000–8000.

Perioperative Risks
- Excessive bleeding
- Paradoxical air, bland, or septic embolism to brain

Worry About
- Chronic anemia due to hemorrhage, especially recurrent epistaxis.
- Due to danger of intrapartum or postpartum pulm hemorrhage, a pregnant woman with HHT who has not had a recent pulm evaluation should be evaluated as soon as pregnancy is recognized.

Overview
- Mucocutaneous and visceral vascular dysplasia can occur.
- Combination of defective perivascular connective tissue, insufficient smooth muscle contractile element, endothelial cell junction defects, and increased endothelial tissue plasminogen activator impairing thrombus formation in case of vascular damage.
- International consensus diagnostic criteria (Curacao criteria) indicates HHT diagnosis classified as definite if three criteria present, possible or suspected if two criteria present, and unlikely if one criterion present. The criteria are:
  - Epistaxis: Spontaneous recurrent nosebleeds.
  - Mucocutaneous telangiectasia.
  - Visceral involvement (i.e., GI telangiectasia, pulm AVM, hepatic AVM, cerebral AVM, spinal AVM).
  - Affected primary relative.
- Manifestations of HHT are not present generally at birth but develop with increasing age, with epistaxis usually being the earliest sign that may lead to chronic anemia. About 90% of pts have signs and symptoms by age 40.

Etiology
- Autosomal dominant trait with varying penetrance and expressivity

Usual Treatment
- Epistaxis is medically treated with Fe supplementation, estrogen therapy, and humidification. With intractable epistaxis ablative therapy with Nd:YAG laser is effective, although multiple treatments are required.
- Multiple transfusions.
- Pulm AVMs with feeding artery diameter ≥3 mm require treatment with transcatheter embolotherapy with coils.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Telangiectasia of nasal mucosa, conjunctival telangiectasias, retinal vascular malformations	Recurrent frequent epistaxis		
CV	High-output heart failure, thromboembolism	Fatigue, SOB	Rales, neurologic deficits	CXR
RESP	AVMs with R-to-L shunt leading to hypoxemia, absence of filtering capillary bed allowing particulate matter to reach systemic circulation, fragile vessels may hemorrhage into bronchus or pleural cavity	Fatigue, dyspnea on exertion, hemoptysis, embolic cerebral events	Cyanosis, clubbing, neurologic deficits	CXR, CT, detection of R-to-L shunt via radionuclide perfusion scans or contrast ECHO
HEME	Anemia, coagulopathy, associated with von Willebrand disease	Recurrent epistaxis	Pallor	CBC, PT/INR, PTT
CNS	Cerebral AVM, aneurysms, cavernous angiomas paradoxical embolism, spinal AVM, migraines	CVA, brain abscess	Headache, seizure, hemorrhage, ischemia of the surrounding tissues due to a steal effect	MRI
HEPAT	Hepatomegaly, high output heart failure, portal Htn, encephalopathy, biliary disease	Hemorrhage, sepsis	Jaundice	LFTs, PT/INR, PTT

Key References: Lomax S, Edgcombe H: Anesthetic implications for the parturient with hereditary hemorrhagic telengiectasia, *Can J Anaesth* 56(5):374–384, 2009; Weingarten TN, Hanson JW, Anusionwu KO, et al.: Management of patients with hereditary hemorrhagic telengiectasia undergoing general anesthesia: a cohort from a single academic center's experience, *J Anesth* 27(5):705–711, 2013.

Perioperative Implications

Preoperative Preparation
- Preop cardiac and pulm evaluation to exclude high-output cardiac failure and pulm AV malformations, which are often asymptomatic.
- CBC for anemia from bleeding or polycythemia from pulm shunt.
- Check liver and renal function.
- Perform neurologic assessment to exclude previous paradoxical emboli and severe brain AVM.
- Debubble IV lines and add air filters to prevent paradoxical air emboli.
- Use meticulous aseptic technique.

- For regional technique, assess any possibility of AVMs in the neuraxial region prior to performing the technique.

Monitoring

- Avoid or use with great caution TEE, gastric suctioning or esophageal stethoscope if esophageal varices or AVMs are present, and avoid nasal temperature probes.

Airway

- If oropharyngeal AVMs are present, there is a high risk of airway bleeding.
- Nasal intubation contraindicated if nasal telangiectasias are present.
- Well-lubricated smaller size ETT to prevent any tissue trauma.

Maintenance

- When there is a risk of high-output heart failure and liver failure, modify anesthetic management.
- Pulm AVMs could be large enough to lead to heart failure and polycythemia.
- Key aspects of anesthetic management are interventions to maintain nml hemodynamic parameters and to prevent bleeding and the formation of emboli.

Postoperative Period

- Avoid immobilization for prolonged periods of time to avoid thromboembolism to CNS.

Adjuvants

- Watch for incompatible drugs in IVs or peripheral veins to avoid particulate matter precipitation and embolization to the brain.
- Broad-spectrum antibiotic prophylaxis to decrease risk of CNS infections.
- NSAIDs may precipitate GI or mucosal bleeding and impair renal function.

Anticipated Problems/Concerns

- Anemia due to recurrent bleeding; most commonly epistaxis.
- Transfusion is complicated: Low Hct may increase the risk of high-output CHF by increasing extent of arteriovenous shunting (decreasing viscosity effect), but a high Hct may increase risk of thromboembolism.
- Coagulopathy: Multiple hemostatic defects, including low-grade DIC, reduced plt aggregation, and factor XI deficiency, may aggravate bleeding caused by local vessel wall pathology.
- Paradoxical embolism: Owing to pulm AVMs, peripheral microemboli (air, bland, or septic) bypass nml pulm capillary filtering and embolize, causing transient or permanent neurologic defects or brain abscess.
- Special attention should be paid to pregnant women with the diagnosis of HHT. In the rare instances, deterioration of preconception AVMs and the development of new AVMs will present with clinically silent but potentially life threatening complications of the disorder. These are most commonly located in the pulm vasculature, followed in frequency by the cerebral, GI, and spinal circulation. With CV and hormonally induced enlargement of certain AVMs, there is concurrent risk of rupture, as well as shunt-induced high cardiac output failure and systemic embolism.

Herniated Nucleus Pulposus

Christine Peeters-Asdourian | Efrain I. Cubillo

Risk

- Incidence of symptomatic disc herniation is 1–2% in the general population.
- Most common age of presentation is during third and fourth decades of life.
- Smoking leads to reduced O_2 tension secondary to vasoconstriction, significant inhibition of cell proliferation and extracellular matrix synthesis, and increased abnormal type I collagen versus type II collagen overall, leading to disc degeneration.
- Chronic stress (e.g., chronic coughing, sitting without lumbar support, heavy lifting) increases strain on disc.
- Poor posture combined with poor body mechanics places stress on the lumbar spine and affects the distribution of body weight.
- Obesity and largely sedentary lifestyle.

Overview

- Structurally the lumbar disc has three components: the annulus fibrosus, forming the circumferential rim of the disc; the nucleus pulposus, composing its central core; and the cartilaginous end plates on the adjacent vertebral bodies.
- The intervertebral disc is the largest avascular structure in the body.
- The nucleus pulposus is composed of H_2O, collagen, and PGs. PG molecules are important because they attract and retain H_2O, constituting a hydrated gel-like matter that resists compression. The amount of H_2O in the nucleus varies throughout the day, depending on activity. It decreases with age, leading to degenerative disc disease.
- The annulus fibrosus is an annular structure composed of concentric sheets of collagen fibers connected to the vertebral end plates. The sheets are oriented at various angles and enclose the nucleus pulposus.
- Disc herniation occurs when the annulus fibrosus breaks open or cracks, allowing the nucleus pulposus to escape. This is called a HNP or herniated disc. Escaping material initiates an inflammatory reaction.
- Disc herniation typically gives rise to radicular pain, which is pain in the distribution of the nerve root affected by the herniation. This pain has strong inflammatory and neuropathic components with or without neurologic change. If radicular changes take place, the presentation is that of a radiculopathy.
- Lumbar region L4–L5 is most common site (59%), followed by L5–S1 (30%) and L3–L4 (9%).
- Natural history of disease is favorable.
- Most pts have substantial improvement of symptoms within a few mo.

Etiology

- Ability of the nucleus pulposus to retain H_2O declines progressively with age.
- Displacement of nuclear material initiates a robust inflammatory response, eliciting known inflammatory mediators such as IL-1, IL-8, IL-17 and TNF α in addition to several recently identified contributing mediators including NGF, IFNγ, and Th1 lymphocyte activation.
- The inflammatory response results in migration and activation of macrophages, leading to scar production and an increase in substance P.
- Symptoms do not always correlate with herniation size (asymptomatic herniation is frequent).

Disease Presentation

- May begin either suddenly, with physical activity, or slowly.
- Frequently presents with a combination of back pain and radicular symptoms; neurologic signs such as weakness or sensory deficits are possible. Isolated low back pain may also be the sole presentation.
- Pts often describe a popping sensation prior to onset of radicular symptom.
- Neural impingement is responsible for dysfunction. Compression of a motor nerve results in weakness in less than 50% of pts; compression of a sensory nerve results in numbness.
- Radicular pain is caused by inflammation of the nerve (which can explain the lack of correlation between the size of a herniation and symptoms of pain).
- Ideal imaging modality is MRI, although CT may also be helpful, EMG/NCS can help to identify the nerve root involved. However, there is not always a correlation between findings on imaging studies and clinical presentation.
- Maneuvers that increase intrathecal pressure (coughing, sneezing, prolonged sitting) can aggravate pain.

Usual Treatment

- Conservative therapies:
  - NSAIDs are supported by the literature.
  - Systemic corticosteroids have not been shown to be superior to placebo.
  - Opioids, muscle relaxants, neuropathic agents (empirical data, limited EBM data)
  - Contrary to prior belief, activity is now preferred over bed rest.
  - Physical therapy.
  - Several other modalities, poorly supported by the literature, include bracing, traction, acupuncture, chiropractic manipulation, behavioral therapy, and biofeedback.
  - Favorable outcomes are more common among better-educated pts and those who are self-motivated. A second neurologic examination within 12 wk is suggested. nml psychological profile, and absence of a workers compensation claim or litigation
- Injection therapy:
  - Epidural injections utilizing fluoroscopy are the standard of care as fluoroscopy is one modality that may reduce catastrophic neurologic injuries, including stroke and spinal cord injury
  - Interlaminar epidural steroid injections are commonly performed.
  - Transforaminal epidural steroid injections target a given area more precisely (commonly performed in the lumbar region but controversial in the cervical region).
  - Investigational studies have shown evidence for lumbar intradiscal PRP.
- Percutaneous discectomy:
  - Does not directly remove the herniated portion but rather removes only the nucleus pulposus in the hope that the herniation portion will regress (limited studies showed a success rate of about 30%).
  - Nucleoplasty.
  - Laser disc decompression.
  - Endoscopic discectomy.

- These techniques may be performed in ambulatory surgery or even office settings with moderate sedation or monitored anesthesia.
- Surgical intervention:
  - Most common procedure for a herniated or ruptured intervertebral disc is a microdiscectomy.
  - Lumbar discectomy is the most commonly performed spinal surgery in USA, with over 300,000 discectomies performed annually.
  - Cauda equina syndrome or a high degree of motor dysfunction is a surgical emergency.
  - Most recently a randomized controlled trial comparing surgery with prolonged conservative treatment at 5 y demonstrated no significant differences in either disability scores and VAS for leg and back pain.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS	Decreased ROM, pain	Lumbar sprain: Stiffness, decreased ROM	Muscle tenderness	MRI MRI/CT
		Annular tear: Axial pain, difficulties sitting	Decreased ROM referred dermatomal pain	MRI/CT EMG/NCS
		HNP: Numbness, weakness or simply pain Cauda equina	Decreased reflexes, sensory loss "Saddle anesthesia"	Surgical emergency
NEURO	Decreased reflexes or increased reflexes with severe spinal stenosis			
PSYCH	Anxiety, chronic opioid intake, litigation issues	Medications preop	If opioid abruptly stopped, may present with withdrawal	Need for multimodal analgesia

Key References: Ropper AH, Zafonte RD: Sciatica, *N Engl J Med* 372(13):1240-1248, 2015; Dunn LK, Durieux ME, Nemergut EC: Non-opioid analgesics: novel approaches to perioperative analgesia for major spine surgery, *Best Pract Res Clin Anaesthesiol* 30(1):79-89, 2016.

Perioperative Implications

- Pts may present on high-dose opioids, which may present a challenge intraop and postop.
- Nonopioid therapies have been increasingly used as part of a multimodal analgesic regimen to provide improved pain control while minimizing opioid-related side effects.
  - A single dose of preoperative gabapentin at 1200 mg versus placebo in pts undergoing elective lumbar surgery was associated with a significant reduction in pain up to 4 h after the procedure (P <0.01).
  - Periop pregabalin (300 mg before surgery as well as 150 mg for two postop doses 12 h apart) was associated with decreased VAS scores in addition to improved functional outcome at 3 mo postop.
  - IV acetaminophen administered at 1 g intraop followed by another dose of 1 g every 6 h throughout the first postop day resulted in significantly improved pain scores at 24 h in the treatment group versus the placebo group.
  - Dexamethasone versus placebo given intraop in a randomized controlled study involving pts undergoing lumbar discectomy led to a significant improvement in mean pain scores on postop day 1.
  - Ketamine administered IV before surgery resulted in reduced postop opioid demands and 24-h postop pain scores. Studies examining continuous IV infusion of ketamine demonstrated decreased opioid demands in 9 of 13 trials, with pts in 2 trials maintaining reduced pain scores for 48 h postop.
  - There have been some reports of epidural catheter placement by the surgeon intraop (at the end of the procedure but prior to wound closure) leading to reduced VAS pain scores and morphine PCA consumptions after lumbar microdiscectomy.

Herpes, Type I

Daniel C. Sizemore | Travis W. Hammond | Manuel C. Vallejo

Risk

- 500,000 new cases of HSV-1 each year in USA (prevalence approximately 68%); 58% of people worldwide are seropositive.
- Symptoms are typically minor (malaise, myalgias, and painful vesicular oral lesions) or absent, except in immunocompromised pts.

Perioperative Risks

- Theoretical risk that spinal anesthesia can spread HSV-1 infection to new dermatomes.
- Association of intrathecal morphine and reactivation of HSV-1 infections in obstetric population.

Worry About

- Transmission of infection to healthcare workers or other pts
- Reactivation after organ transplantation and initiation of immunosuppression
- Secondary infection of herpetic lesions with bacteria or fungi

Overview

- Transmission occurs after contact with secretions or mucus.
- Primary infection associated with fever/malaise, with a mean duration of 19 d. Recurrences are milder, with a mean duration of 10 d.
- Lesions recur about once per y (in contrast with four times per y for HSV-2) in immunocompetent pts.
- 27% of the population is seropositive by age 4.
- Oral symptoms include gingivostomatitis/oral ulcers. Genital, ocular, pneumonitis, and additional dermatologic infections may occur.
- Symptoms may last 1–4 wk.
- Can be diagnosed via a viral culture (titer 1000 times nml while active lesions exist) or HSV antibodies.

Etiology

- Transmission occurs after contact with lesions or body fluids such as saliva or genital secretions. Fifty-eight percent of the world population is seropositive. Transmission can be vertical (transmission to infant via vaginal tract), which is a TORCH pathogen associated with greater risk of infant death or blindness. Vertical transmission (8-60:100,000 live births) and postpartum transmission is exceedingly rare.
- No animal/insect reservoir or vectors exist for HSV-1.
- Infection is usually mild in pts with an intact immune system.
- Dx is by viral culture, PCR, fluorescent antibody testing, or serology.

Usual Treatment

- Acyclovir, valacyclovir, and famciclovir are effective as episodic therapy when initiated within 72 h of appearance of symptoms reducing viral shedding, lesion healing time, and symptoms.
- Suppressive therapy (lower dose initiated while asymptomatic) is effective in reducing frequency and severity of recurrences, as well as transmission to an uninfected partner.
- Foscarnet or vidarabine may be used in acyclovir-resistant herpes infections.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pneumonitis	Aspiration of oral secretions; previous HSV esophagitis	Bilateral crackles	CXR (bilateral interstitial infiltrates)
GI	Esophagitis	Odynophagia, dysphagia, substernal pain	Multiple shallow mucosal ulcers	
GU	Cystitis			
CNS	Encephalitis, meningitis	Headache, confusion, lethargy	Anosmia, memory loss, expressive aphasia, focal seizures	Brain biopsy
DERM	Cutaneous ulcers	Recurrent painful skin or mucosal ulcers	Multiple vesicular lesions on an erythematous base with subsequent ulceration	
	Stevens-Johnson syndrome	Extensive painful skin lesions	Deep bullous erosive lesions	

Key References: Chayavichitsilp P, Buckwalter JV, Krakowski AC, et al.: Herpes simplex, *Pediatr Rev* 30(4):119–129, 2009; Davies PW, Vallejo MC, Shannon KT, et al.: Oral herpes simplex reactivation after intrathecal morphine: a prospective randomized trial in an obstetric population, *Anesth Analg* 100(5):1472–1476, 2005.

Perioperative Implications

Preoperative Preparation

- Cover exposed herpetic lesions.
- Strict adherence to universal precautions.

Monitoring

- Avoid disturbing active lesions.

Regional Anesthesia

- Needle should not be inserted through lesion. There is a theoretical risk of spreading herpes from one infected ganglion to another, but regional anesthesia is not contraindicated.
- Neuraxial morphine remains a common practice, as rare occurrence of vertical transmission from mother to neonate does not support withholding this technique.

Postoperative Period

- Thoroughly disinfect any surface area that might have been in contact with oral secretions or herpetic lesions. Most disinfectants are effective, including chlorine and alcohol.

Anticipated Problems/Concerns

- No effective preexposure or postexposure prophylaxis.
- Acyclovir may reduce effectiveness of phenytoin.
- C-section should be offered for pregnant women with active HSV.
- Vaginal delivery is acceptable for women in remission; acyclovir is often used.

Herpes, Type II

Jonathan G. Ma | Alan David Kaye | Amit Prabhakar

Risk

- Incidence within USA of HSV-2 is estimated at 40–60 million (20% of sexually active adults).
- Approximately 536 million people (16% of population) infected worldwide, most unaware of the disease.
- Highest prevalence in women, African Americans, and lower socioeconomic groups.
- Frequency and severity of infection increases in immunocompromised pts, including HSV encephalitis.
- Incidence of neonatal HSV infection is estimated at 1:2000-5000 deliveries.

Perioperative Risks

- Vertical transmission from infected mother to fetus during vaginal birth
- Intrauterine fetal infection after rupture of membranes

Worry About

- Transmission of infection to health care personnel resulting in herpetic whitlow via inoculation of virus into digits is very well described and completely preventable with universal precautions (e.g., gloves at all times).
- Neonatal herpetic infection during vaginal births.
- Viremia secondary to needle placement within infected area during regional anesthesia with possible extension of infection to adjacent areas.
- Secondary bacterial or fungal infection of herpetic lesions.

Overview

- Primarily caused by infections below the waist transmitted by sexual contact.
- Maternal primary HSV-2 infection is associated with spontaneous abortion.
- Newborns can be infected with HSV-2 during vaginal delivery from the mother's genital infection (high neonatal mortality).
- Primary genital HSV-2 infection has the highest incidence of systemic symptoms (malaise, fever, headache, myalgias).
- Latent infection remains dormant in sensory ganglia, innervating the infected area until reactivation.
- Recurrent infection involves clusters of genital sores (papules and vesicles) on outer surface of genitals, usually appearing 4–7 d post HSV exposure.
- No increased risk of reactivation of HSV-2 is associated with neuraxial anesthesia.
- Chronic recurrent HSV-2 infection is associated with development of cervical and vulvar cancer.
- Reactivation is known to occur with exposure to UV light, immunosuppression, trauma, and fever.
- Dx by viral culture (gold standard) is the most sensitive and specific (rapid Dx by Tzanck smear).
- Genital herpes increases the risk of transmission and acquisition of HIV-1 infection threefold to fourfold.

Etiology

- Double-stranded DNA virus in the family of Herpesviridae.
- Acquired via genital infection primarily by sexual transmission of HSV-2.
- Immunosuppression and increased number of sexual partners are risk factors for acquisition.
- Diagnosed by multinucleated giant epithelial cells (polykaryocytes) with intranuclear (Cowdry type A) inclusion bodies on Giemsa stain smears (Tzanck preparation) taken from vesicle or tissue biopsy.

Usual Treatment

- Administer IV acyclovir for neonatal HSV-2 infection.
- Oral acyclovir and topical cream shorten duration of lesions for recurrent infections.
- Most recommend that full-term parturients with visible genital lesions (especially primary infection) undergo cesarean delivery to decrease incidence of neonatal HSV infection. Neonates exposed to asymptomatic shedding of HSV during parturition (fourfold increase in HIV seropositive women) may also rarely acquire neonatal HSV.
- Active genital herpes lesions are indications for cesarean delivery for prevention of neonatal herpes infection. This significantly reduces risk of transmission. Use of third trimester oral suppression for outbreak prophylaxis is effective at reducing risk of needing cesarean delivery.

Novel Therapies

- Pericoital application of tenofovir gel showed reduction in HSV-2 acquisition, decreased shedding, decreased lesion rate, and decreased quantity of viral shedding.
- Administer imiquimod for acyclovir-resistant HSV-2.
- The combination of imiquimod immunomodulator, imiquimod, and acyclovir appears to provide effective therapy for acute genital HSV-2 infection, even when begun after lesion development.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Pharyngitis (primary)		Cervical adenopathy Mucosal ulceration	
GU (mucous membranes)	Cystitis (primary) Genital ulcers (recurrent)	Dysuria	Vaginal or urethral discharge Ulcerated lesions of penis or labia or cervix	Viral culture (gold standard) Tzanck smear; direct immunofluorescent assay Biopsy; intranuclear inclusion bodies
LYMPH		Lymphadenopathy	Tender inguinal nodes	
DERM	Herpetic whitlow (recurrent)	Painful vesicular or papular lesion	Pain	Tzanck smear
CNS	Aseptic meningitis (primary)	Headache	Cauda equina syndrome	
RECTAL	Herpes proctitis (primary)	Constipation Tenesmus Discharge		Proctosigmoidoscopy

Key References: Armitage KB, Salata RA: Sexually transmitted diseases. In Andreoli TE, Carpenter C, Griggs RC, editors: *Andreoli and Carpenter's Cecil essentials of medicine,* ed 7, Philadelphia, PA, 2007, Saunders, pp 980–988; Augenbraun M, Feldman J, Chirgwin K, et al.: Increased genital shedding of HSV-2 in HIV-seropositive women, *Ann Intern Med* 123(11):845–847, 1995.

Perioperative Implications

Preoperative Preparation
- Universal precautions

Monitoring
- Routine

Regional Anesthesia
- Needle placement in infected area contraindicated secondary to risk of viremia and local extension into deep tissues
- Preferred in pregnant women with recurrent infection, no systemic symptoms, and no infection in area of block placement

Postoperative Period
- Universal precautions

Anticipated Problems/Concerns
- Difficulty identifying asymptomatic carriers of HSV-2 with viral shedding
- No effective prophylaxis for newborns

Hirschsprung Disease

Franklyn P. Cladis | Annie Lynn Penaco

Risk
- Incidence of 1:5000 live births; varies among different ethnic groups.
- Male to female ratio is 4:1, although bias is lost in longer segment disease.
- Occurs as an isolated phenotype but may be associated with congenital abnormalities and associated syndromes.
- Up to 30% of affected individuals have at least one coexisting congenital anomaly, which may include congenital heart defects, gastrointestinal malformations, central nervous system, genitourinary, and craniofacial abnormalities, and spina bifida.
- Between 2-15% of affected individuals have trisomy 21. Other associated syndromes include Waardenburg syndrome type IV, congenital central hypoventilation syndrome (Ondine's Curse), multiple endocrine neoplasia type 2, and neurofibromatosis.

Perioperative Risks
- Intestinal obstruction.
- HAEC, characterized by explosive foul-smelling diarrhea, abdominal distension, and fever, may progress to potentially fatal toxic megacolon.
- Septic shock.
- Hypovolemia.
- Lyte abnormalities.

Worry About
- Intestinal obstruction increases the risk of regurgitation and pulmonary aspiration.
- Vomiting and possible diarrhea leads to hypovolemia and lyte abnormalities, necessitating adequate resuscitation.
- Pts presenting with HAEC may have septicemia requiring preop antibiotic administration.

Overview
- HSCR is a multigenic disorder with variable penetrance. In over 80%, aganglionosis is restricted to the rectosigmoid colon (short segment HSCR), but may affect significant lengths of colon and even extend into the small intestine (long segment HSCR) or rarely in 3–8% affects the entire small and large intestines (total intestinal aganglionosis).
- Most often, pts are diagnosed in the neonatal period with distended abdomen, delayed passage of meconium (>24–48 h), and vomiting.
- Pts diagnosed later in childhood present with chronic constipation and failure to thrive.
- Diagnosis can be made with plain radiography (with marked gaseous distension of colon and an undilated rectum), contrast enema (which defines the transition zone between dilated normal bowel and narrow aganglionic bowel), and anorectal manometry.
- Gold standard for diagnosis is a rectal biopsy (submucosal suction or full thickness), demonstrating absence of ganglion cells and presence of acetylcholinesterase-positive hypertrophic nerve fibers.

Etiology
- Initial symptoms are caused by failure of neural crest cells to caudally migrate and colonize variable lengths of the intestinal tract.
- Complete absence of enteric neuronal ganglion cells in the affected bowel results in tonic contraction, leading to obstructive symptoms.
- Several key genes regulating neural crest cell development, including *RET*, *GDNF*, and *EDNRB*, are associated with HSCR but only account for about 50% of known cases.
- Combinations of genetic mutations and modifiers likely contribute to etiology and pathogenesis.

Usual Treatment
- If neonate presents with enterocolitis, aggressive resuscitation, rectal irrigation, and antibiotics are utilized for initial management.
- Surgery, the only definitive treatment for HSCR, aims to remove aganglionic bowel and anastomose normal bowel to the anus while preserving sphincter function.
- Transition zone identified by intraop frozen sections sent to pathology may determine operative time.
- Traditionally, operative repair was performed in two or three stages. First stage required a diverting ostomy, second stage (usually at 3 mo-1 y of age) involved resection of aganglionic bowel and coloanal anastomosis, and third stage entailed closure of preexisting stoma.
- Classical operations (Swenson, Soave, Duhamel) are now reduced to one or two stages. Standard approach in otherwise healthy, nondistended neonatally diagnosed HSCR is a one-stage repair.
- TERPT or LATEP is associated with faster recovery, shorter hospital stay, and fewer postop complications.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Congenital hypoventilation ("Ondine's curse")	Apnea		
CV	Hypovolemia, septic shock, 2-5% cardiac anomalies (tetralogy of Fallot)	IV replacement Extent of vomiting Cyanosis	Mucous membranes Vital signs/UO Murmur, cyanosis Capillary refill	BUN, Cr BUN/Cr ratio ECHO
GI	Intestinal obstruction	Presence of meconium Constipation Diarrhea Vomiting	No feces in rectum, Abdominal distention Malnutrition	Lyte panel Abdominal films Barium enema

Key References: Butler Tjaden NE, Trainor PA: The developmental etiology and pathogenesis of Hirschsprung disease, *Transl Res* 162(1):1–15, 2013; McKeown SJ, Stamp L, Hao MM, et al.: Hirschsprung disease: a developmental disorder of the enteric nervous system, *Wiley Interdiscip Rev Dev Biol* 2(1):113–129, 2013.

Perioperative Implications

Preoperative Preparation

- Consider associated congenital anomalies or syndromes and the possible need for further cardiac evaluation and genetic testing.
- Thoroughly assess volume status. Assess for bowel preparation, diarrhea, and vomiting and ensure adequate preop fluid resuscitation.
- Review preop labs to assess for lyte abnormalities.
- Consider cardiac evaluation with associated cardiac anomalies.

Monitoring

- Standard ASA monitors
- Urinary cath

Airway

- Consider associated syndromes affecting airway anatomy.

Induction

- Rapid sequence induction necessary in the presence of bowel obstruction to avoid pulmonary aspiration.
- In the setting of hypovolemia or sepsis (HAEC), IV and volatile anesthetics may be poorly tolerated.

Maintenance

- Use neuromuscular blocking drugs for maintenance of muscle relaxation.
- Maintenance IV fluids with balanced, isotonic solution.
- Consider checking intraop blood glucose level.
- Monitor urine output.
- Avoid nitrous oxide.
- Maintain normothermia with warming devices (full access warming blankets and radiant warmers), as radiant heat loss may be excessive. Keep forced warm air blankets dry. They cool the pt if they become wet.
- Carefully position pt; use added care with lithotomy position.

Extubation

- Reverse neuromuscular blockade.
- Routinely extubate when pt is awake and meets extubation criteria.

Postoperative Period

- Consider regional technique with epidural/caudal anesthesia for postop pain management (which may need to be performed postop if lower body antibacterial preparation performed).
- Postop apnea in newborns more likely following narcotic administration.

Anticipated Problems/Concerns

- Early postop complications include prolonged ileus, anastomotic leak, and wound infection/dehiscence.
- Late complications include anastomotic strictures, constipation, fecal incontinence, bowel obstruction, and enterocolitis.
- Postop HAEC, with an incidence between 5-42%, is a major cause of increased morbidity and mortality after definitive pull-through procedure. This is hypothesized to involve intestinal stasis and immature mucosal immunity, allowing for proliferation and mucosal invasion by luminal pathogens.
- Mild obstructive symptoms are treated with dietary changes, laxatives, enemas, or repeated botulinum toxin injections. Myectomy procedure may be required.
- For residual aganglionosis, strictures, or dysfunctional proximal bowel, repeat pull-through procedure can be done, although this is challenging due to scarring.
- In individuals with extensive intestinal aganglionosis and irreversible intestinal failure, intestinal transplantation may be considered.

Histiocytosis

Tyler J. Paradis | Jeffrey R. Kirsch

Risk

- LCH is the most commonly known form.
- Incidence: 1:250,000 in children, with about a third of this incidence in adults.
- Seen in all ages, but peak incidence is at 0–3 y of age.
- Male:female ratio: 1.5:1.
- Sporadic development with no established genetic predisposition.

Perioperative Risks

- Dependent on organ systems involved and extent of dysfunction

Worry About

- Specific organ dysfunction caused by infiltration with histiocytes, including liver, lungs, hematopoietic system, pituitary, spleen, and bone
- Can involve single or multiple sites and organs
- Treated with steroids and chemotherapy, which may cause adrenal insufficiency and result in the pt requiring stress steroids in the periop period
- Central diabetes insipidus due to posterior pituitary involvement
- Cervical instability if lesions present in cervical vertebrae
- Severe pulm dysfunction possible; pulm Htn without overt right heart failure

Overview

- A broad group of disorders involving infiltration of affected organs with monocytes, macrophages, and dendritic cells.
- The most commonly discussed disorder is LCH, previously known separately as eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease.
- Severity of clinical symptoms varies markedly and can involve primarily skin and/or bone or liver, lung, or brain.
- Can be limited or progressive and fatal. Younger children with multiple or severe organ involvement of "risk organs" (liver, lungs, spleen, hematopoietic system) have a high mortality.
- Usual clinical presentation is in the first decade of life.
- Pathophysiology is unclear and treatment is nonspecific.

Etiology

- Unknown; suggested factors include immune dysfunction, viral infections, neoplastic processes, and genetic predisposition.
- Isolated pulm LCH is strongly associated with cigarette smoking.

Usual Treatment

- 10–20% spontaneous regression rate, almost exclusively in pts with single system disease.
- Chemotherapy with steroids for multisystem disease with local or constitutional symptoms (vinblastine, etoposide, mercaptopurine, doxorubicin, cyclophosphamide, methotrexate, others).
- Surgery is required for biopsy and Dx, isolated bone lesions, and occasionally splenectomy.
- Orthotopic liver or lung transplantation has been performed for end-stage disease.
- Radiation therapy (bone lesions, pituitary disease).
- Bone marrow or stem cell transplant.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Soft tissue distortion of airway, loose teeth, mucosal ulceration	Stridor	Airway and dental evaluation	
RESP	Spontaneous pneumothorax, reactive airways, infiltrates, fibrosis, pulm Htn	Tachypnea, dyspnea, cough, smoking history		CXR, ABG, PFTs, CT with cysts or nodular infiltrate
GI	Ulceration, obstruction, hepatic dysfunction		Jaundice Hepatomegaly	Bilirubin, albumin AST, ALT, INR
CNS	Diabetes insipidus, neuropathy, exophthalmos	Polyuria, polydipsia	Neuro exam	Urine and serum Osm, lytes
HEME	Thrombocytopenia, anemia, leukopenia	Bruising or bleeding	Splenomegaly	CBC

Key References: Morimoto A, Oh Y, Shioda Y, et al.: Recent advances in Langerhans cell histiocytosis, *Pediatr Int* 56(4):451–461, 2014; Broscheit J, Eichelbroenner O, Greim C, et al.: Anesthetic management of a patient with histiocytosis X and pulmonary complications during Caesarean section, *Eur J Anaesthesiol* 21(11):919–921, 2004.

Perioperative Implications

Monitoring

- Routine
- Foley in pt with DI
- Arterial cath for ABG in those with pulm involvement, frequent Na checks in those with DI, as well as pulse pressure variation as a marker of volume status in those with DI

Preinduction/Induction

- Airway soft tissue or mandibular involvement may distort anatomy.
- Cervical vertebrae lesions may cause cervical instability.
- Ensure adequate preoxygenation, especially if there is significant pulm involvement.
- Usual precautions, depending on severity of organ involvement.

Maintenance

- For pts with DI, consider aqueous ADH infusion and isotonic crystalloid fluids.
- Stress dose steroids if pt has had steroid therapy.
- Usual precautions, depending on severity of organ involvement.

Extubation

- Awake extubation if anatomy is distorted and airway was difficult for mask ventilation or intubation.
- Severe pulm involvement may delay extubation.

Regional Anesthesia

- Follow ASRA precautions if thrombocytopenic or elevated INR.
- Use caution with interscalene and supraclavicular blocks in pts with pulm disease.

Postoperative Period

- May need continued stress dose steroid coverage for several days postop.
- Closely monitor oxygenation and ventilation when pulm disease present, and evaluate for pneumothorax.

Anticipated Problems/Concerns

- Organ dysfunction (hepatic, pulm, hematologic, hypothalamic, or bone).
- DI.
- Adrenal suppression due to chronic steroid therapy; may experience intraop hypotension without stress steroids.
- Severe pulm involvement may increase risk of pneumothorax and complicate extubation.

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Huntington Disease

David A. Wyler

Risk

- General prevalence: 5-7:100,000
- Highest prevalence in Caucasians of western European descent

Perioperative Risks

- Increased risk of respiratory complications secondary to bulbar muscle incoordination
- Autonomic dysfunction

Worry About

- Microaspiration, bronchospasm, chemical pneumonitis, and aspiration pneumonia
- Drug-drug interactions with anesthetic drugs and psychotropic medications
- Prolonged effects with succinylcholine
- Dysautonomia, gastroparesis, and fluctuating HR and BP

Overview

- Inherited progressive neurodegenerative disease of the CNS, primarily the basal ganglia.
- More common adult-onset variant begins in the fifth decade and leads to complete disability and death within 20 y.
- Heterogeneous presentation of dysregulation of motor coordination, cognitive decline, and psychiatric manifestations.
- Classically known for choreiform (repetitive, rapid, jerky, involuntary) movements from degeneration of GABAergic neurons of the basal ganglia specifically of the striatum (caudate and putamen).
- Chorea, early motor sign along spectrum; progresses to parkinsonian-like movements (bradykinesia, rigidity, and postural instability) late in the adult-onset disease.
- Worsening subcortical dementia (declining executive function and cognition without amnesia) and severe depression accompany disease progression.
- Juvenile variant presents with parkinsonian signs at onset, lacks choreiform movements, and has least favorable prognosis along spectrum.
- Skeletal muscle incoordination of the laryngeal and pharyngeal muscles leads to devastating respiratory sequelae and death.
- See also Parkinson Disease.

Etiology

- Autosomal dominant inheritance.
- Trinucleotide repeat expansion of CAG codon on the IT15 gene on chromosome 4 results in the overproduction and aggregation of the protein Huntingtin.
- Length of repeat correlates well with extent of Huntingtin production, disease severity, and age of onset.
- Huntingtin accumulates in the nuclei and cytoplasm of all CNS neurons; degeneration occurs most notably in vulnerable neurons of the caudate and putamen.
- Striatal cell death occurs by glutamate- and dopamine-induced excitotoxicity, oxidative stress, impaired energy metabolism, and apoptosis.

Usual Treatment

- No definitive cure; treatment is supportive, focusing on alleviation of symptoms.
- Early symptoms of chorea are treated with neuroleptics, dopamine-depleting medication. Surgical implantation of deep brain stimulators may be helpful.
- Gene-modifying therapy is currently under investigation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Extraocular eye movements smooth on pursuit and jerky saccade; excessive drooling, dysarthria		Test muscles controlling extraocular movements and word/sentence formation	Swallow evaluation
CV	Fluctuating HR and BP	Review med list for CNS active meds and possible drug-drug interactions with anesthetic drugs	Compare HR/BP from supine to seated and standing	ECG
RESP	Aspiration pneumonia	Complaints of fever and chills	Chest auscultation and percussion	CXR, CBC
GI	Gastroparesis secondary to skeletal muscle incoordination and autonomic dysregulation	Dysphagia and early satiety		Swallow evaluation
RENAL	Possibly dehydrated	Recent poor PO intake	Dry mucous membranes	BUN/CR ratio ≥20; FNa <1
ENDO	Poor nutrition status	Poor PO intake frequently requiring feeding tube	Cachexia	Albumin, prealbumin
CNS	Choreiform motor movements, depression, and dementia	Erratic behavior; decreased independence with ADL; gait disturbance	Cognitive impairment and poor executive function on MMSE; erratic movements on extremity motor exam	CT or MRI to grade severity by extent of caudate atrophy
PNS	Dysautonomia	Symptoms of orthostatic hypotension or sexual dysfunction		
MS	Skeletal muscle incoordination primarily limbs and bulbar secondary to to striatal dysregulation			

Key References: Kivela JE, Sprung J, Southorn PA, et al.: Anesthetic management of patients with Huntington disease, *Anesth Analg* 110(2):515–523, 2010; Roos RA: Huntington's disease: a clinical review, *Orphanet J Rare Dis* 5:40, 2010.

Perioperative Implications

Preoperative Preparation

- Glycopyrrolate (0.2 mg/70 kg) in pts with excessive drooling
- Metoclopramide (10 mg/70 kg) with caution in pts with gastroparesis and dysphagia as this may worsen EPS

Monitoring

- Fluctuating HR; the pt can have bradyarrhythmias and tachyarrhythmias.
- End-tidal CO_2 waveform to be watched for steep upstroke, signifying bronchospasm and microaspiration.
- Pulse oximetry to evaluate for hypoxemia due to bronchospasm or V/Q mismatch (pneumonia or pneumonitis).
- Monitoring may be technically difficult owing to pt's erratic movement.

Airway

- Avoid awake procedures if airway is assessed as difficult; also avoid in advanced disease if ideal surgical field conditions are required.
- Pt may have sialorrhea.

Induction

- Consider RSI for aspiration risk; rocuronium 1 mg/kg is preferred over succinylcholine, which multiple studies link with a fluoride-resistant variant of pseudocholinesterase deficiency.

Maintenance

- Drug-drug interactions can occur between anesthetics and psychotropic drugs, such as hypotension with parkinsonian drugs (L-dopa and bromocriptine). Avoid sympathomimetics with MAO inhibitors. Dysrhythmias and orthostatic hypotension can occur with TCAs.

Extubation

- Corticobulbar dysfunction theoretically increases aspiration risk while anesthetics are lingering.

Adjuvants

- Sedative hypnotics (e.g., BZDs) help reduce EPS but increase drug-drug interactions with home psychotropic medications. They can also potentiate hypotension and may prolong emergence.

Postoperative Period

- Monitor for respiratory complications, fluctuations of HR and BP; expect behavioral challenges in advanced disease.

Anticipated Problems/Concerns

- Poor bulbar muscle coordination may increase risk for aspiration events and a subsequent respiratory complication, namely pneumonia.
- Drug-drug interactions between anesthetics and home psychotropic prescriptions may lead to hypotension, dysrhythmias, neuroleptic malignant syndrome, or worsening EPS.
- Succinylcholine should be avoided, as cases of pseudocholinesterase deficiency and prolonged muscle paralysis are reported.

Hydrocephalus

Joseph R. Tobin | Timothy E. Smith

Risk

- Found in newborns and children with anatomic CNS abnormalities (including myelomeningocele)
- Head trauma and intracranial hemorrhage (prematurity, SAH, other causes)
- CNS tumors
- Meningitis
- Recurrent VP shunt malfunction

Perioperative Risks

- Cerebral ischemia and neurologic sequelae
- Impaired airway reflexes,LOC, gastric emptying
- Cardiorespiratory arrest

Worry About

- Intracranial Htn
- Persistent N/V
- Bradycardia
- Decreased LOC

Overview

- Excess accumulation of CSF due to obstruction in normal CSF flow pattern from ventricular system to cortical surface (obstructive hydrocephalus), or from impaired reabsorption of CSF at arachnoid villi (communicating hydrocephalus).
- Slow progressive hydrocephalus can be well tolerated for weeks, with slowly worsening symptoms (headache, nausea, papilledema).
- Acute hydrocephalus results in acute symptoms and may be life-threatening, owing to herniation of brain with catastrophic ischemic injury (bradycardia, Htn, depressed LOC, depressed airway reflexes and resp drive, and gastric atony).

Etiology

- Congenital: Anatomic abnormalities, including aqueductal stenosis, Arnold-Chiari malformation, Dandy-Walker syndrome
- Posthemorrhagic/posttraumatic: Intraventricular hemorrhage (newborns or adults) with blood clot in ventricular system
- Neoplastic: Brain tumor obstructing normal CSF flow
- Postinflammatory: Meningitis, abscess, meningoencephalitis, intracranial hemorrhage

Usual Treatment

- Surgical correction of underlying cause or CSF diversion procedures (ventriculoperitoneal, ventriculoatrial, or lumboperitoneal shunts).

- Glucocorticoids are used acutely to diminish edema associated with neoplasm or abscess and may diminish associated intracranial Htn.
- Acetazolamide to diminish CSF production and reduce intracranial Htn.
- Furosemide to acutely decrease cerebrovascular volume.
- Mannitol to decrease ICP.

Assessment Points

System	Effect	Assessment by Hx	Physical Examination	Test
CV	Bradycardia, Htn	Late signs	Pulse, BP	
RESP	Impaired respiratory drive and airway reflexes		Cranial nerve exam, stridor, swallowing abnormality	Pulse oximetry
GI	N/V, aspiration, abnormal feeding	Hx of progression of N/V		
CNS	Depressed LOC, increased ICP, headache	Timing of onset	Arousability and neurologic exam, tense fontanel, inferior eye deviation	CT scan

Key References: Bober J, Rochlin J, Marneni S: Ventriculoperitoneal shunt complications in children: an evidence-based approach to emergency department management, *Pediatr Emerg Med Pract* 13(2):1–22, 2016; Christian EA, Melamed EF, Peck E, Krieger MD, McComb JG: Surgical management of hydrocephalus secondary to intraventricular hemorrhage in the preterm infant, *J Neurosurg Pediatr* 17(3):278–284, 2016.

Perioperative Implications

Preoperative Preparation

- Assess urgency of presentation. Catastrophic increased ICP requires emergent intubation and hyperventilation. In young infants, direct neurosurgical needle puncture of a proximal lateral ventricle or previously inserted shunt may diminish ICP sufficiently to avoid a catastrophe.
- Secure IV access if possible, and consider acetazolamide 10 mg/kg IV or furosemide 1 mg/kg IV.

Monitoring

- LOC
- Routine

Airway

- Head up 10-20 degrees and midline may diminish ICP
- Aspiration risk due to gastric atony

Preinduction/Induction

- Sedatives usually are not indicated so that resp compromise or sedation does not increase ICP. Minimal sedation or use of local anesthetic can secure IV access without causing increased ICP due to pain, crying, or struggling.
- Rapid-sequence IV induction is preferred (because of aspiration risk), unless in doubt of airway anatomy.
- Debate over use of succinylcholine versus rapid-onset nondepolarizing muscle relaxant (rocuronium). Thiopental, propofol, or etomidate IV agents preferred; avoid ketamine.
- Mask induction may increase ICP by increasing cerebral blood volume. Once fontanelles are closed, the brain is limited to a closed space within the cranium; prior to that time (<18 mo), the brain has some room to expand. Sevoflurane may be the preferable agent for inhalation induction (well tolerated and minimal effects on cerebrovascular tone). Isoflurane and desflurane are associated with coughing and are not recommended for induction.
- Lidocaine 1–1.5 mg/kg IV may be useful adjunct to minimize increase in ICP due to laryngoscopy and endotracheal intubation.

Maintenance

- Volatile anesthetic (most commonly sevoflurane or isoflurane) <1 MAC, N_2O 0–70% (debatable) and opioid (i.e., fentanyl 2–5 μg/kg or equivalent).
- Maintain normothermia, cardiac output. Hyperventilation may be acutely helpful until CSF is diverted and ICP reduced.
- Normal saline at restricted or maintenance rate. Glucose support should only be administered for infants; avoid hyperglycemia.

Extubation

- Ensure return of airway reflexes, LOC, and resp drive.
- Failure of achieving above criteria may require CT scan and/or ICU monitoring.

Postoperative Period

- Usually unremarkable; depressed LOC is concern for periop ischemic insult or hemorrhage.
- EBL should be minimal.

Adjuvants

- Lidocaine, mannitol, furosemide, and spontaneous hyperventilation by pt

Anticipated Problems/Concerns

- Immediate postop neurologic exam should demonstrate improvement. If not improved, urgent CT scan and secure airway must be maintained. Postop ICU admission not required unless impaired neurologic status continues.

Hyperaldosteronism, Primary

Marc Chikhani | Jonathan G. Hardman

Risk

- Responsible for up to 20% of moderate to severe systemic arterial Htn.
- End organ damage from long-standing Htn (e.g., chronic kidney disease, cardiomyopathy).
- Abnormal glucose tolerance in up to 50% of pts with hyperaldosteronism.

Perioperative Risks

- Hypernatremia and hypervolemia with high total body sodium.
- Htn may be refractory to treatment, with increased risk of cardiovascular complications, including malignant hypertensive crisis.
- Hypokalemia and hypomagnesaemia with low intracellular potassium and magnesium may cause cardiac arrhythmia and general muscle weakness.

Worry About

- Hypertensive response to intubation or surgical incision
- Hypokalemia and associated muscle weakness or potential for arrhythmia
- Metabolic alkalosis

Overview

- Also known as Conn syndrome; described by Jerome W. Conn, University of Michigan, in 1955.
- Characterized by Htn, hypernatremia, hypokalemia, metabolic alkalosis, and low plasma renin level.
- Classically caused by a unilateral aldosterone producing adrenal adenoma.
- Primary hyperaldosteronism is a renin-independent and incompletely suppressible over secretion of the mineralocorticoid aldosterone secreted from the zona glomerulosa of the adrenal cortex.
- Aldosterone acts on the mineralocorticoid receptor in the distal convoluted tubule of the nephron and the collecting ducts to enhance sodium and water reabsorption, at the expense of potassium. Excess loss of potassium leads to loss of hydrogen ions to maintain electroneutrality.
- Usually aldosterone secretion is controlled by the renin-angiotensin feedback system in response to thirst, hypovolemia, reduced renal juxtaglomerular apparatus perfusion pressure, and reduced tubular sodium concentration.
- Aldosterone promotes restoration of circulating volume by correcting water and sodium depletion.
- Dx is by combination of clinical suspicion of persistent Htn, hypernatremia and spontaneous hypokalemia, and metabolic alkalosis in the absence of diuretics. Dx is confirmed by measuring the plasma aldosterone to renin ratio—a value over 35 ng/dL per ng/mL/h has sensitivity of 100% and specificity of 92%. Post test specificity can be improved by measuring post-sodium infusion aldosterone. Values above 7 ng/dL showed specificity of 100%.

Etiology

- 60–70% idiopathic hyperaldosteronism or bilateral idiopathic adrenal hyperplasia
- 30–40% unilateral aldosterone-producing adrenal adenoma (first described by Conn in 1955)
- Uncommon causes:
  - Unilateral adrenal hyperplasia
  - Familial hyperaldosteronism
  - Aldosterone producing adrenocortical carcinoma and ectopic aldosterone secreting tumors

Usual Treatment

- Aldosterone antagonists such as spironolactone (up to 300 mg/d) or the newer drug eplerenone (up to 100 mg/d).
- Both spironolactone and eplerenone are mineralocorticoid receptor antagonists and therefore have a potassium-sparing diuretic effect. Eplerenone is more selective for the mineralocorticoid receptor than spironolactone and has fewer glucocorticoid or androgen receptor antagonist side effects.
- Htn may be refractory to treatment with aldosterone antagonist alone and may require formal

antihypertensive therapy with ACE inhibitor or beta-blocker.
- Treatment of Htn may be needed for several wk before any benefit to periop morbidity.
- Hypervolemia should be treated with a potassium-sparing diuretic, such as amiloride, to avoid exacerbating potassium loss.
- Potassium deficit is likely to be severe and larger than apparent from serum levels.
- Unilateral primary hyperaldosteronism (from either aldosterone producing adenoma or unilateral adrenal hyperplasia) should be treated with surgical adrenalectomy.
- Bilateral primary hyperaldosteronism should be treated medically with long-term mineralocorticoid receptor antagonist therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, often resistant to therapy; increased sympathetic activity, cardiac output often increased except where there is hypertensive cardiomyopathy	Exercise tolerance, dyspnea, orthopnea, Htn—headache, visual disturbance	BP (compare R to L or arms with legs with coarctation) Third heart sound Fine inspiratory crackle	BP, ECG, ABG, CXR, ECHO
HEME	Hypervolemia results in Htn, hypokalemia, metabolic alkalosis, and congestive cardiac failure	Weakness, fatigue, headache	JVP, motor power	Hematocrit, serum lytes, biocarbonate, ABG
RENAL	Hypokalemia, alkalosis	Weakness, palpitations	Motor power, arrhythmia	ECG, serum and urine lytes, ABG

Key References: Jano A, Domi R, Derdica H, et al.: Anesthetic considerations of Conn syndrome, *Clin Med Res* 3(5):123–135, 2014; Reilly CS: Adrenal disease: cortex and medulla. In Hall GM, Hunter JM, Cooper MS, editors: *Core topics in endocrinology in anaesthesia and critical care*, Cambridge, 2010, Cambridge University Press, pp 45–56.

Perioperative Implications

Preinduction/Induction/Maintenance
- Correct hypokalemia and associated electrolyte disturbance (e.g., magnesium); this may require IV supplementation preop and intraop.
- Htn may be refractory; require treatment with several classes of drugs with the potential for extreme cardiovascular instability, and there may be a disproportionate hypertensive response to laryngoscopy or surgical stimulation.
- Avoid hyperventilation and hypocapnia to prevent worsening metabolic alkalemia and subsequent intracellular potassium shift.
- Anticipate increased sensitivity to nondepolarizing neuromuscular antagonists due to hypokalemia. Consider using drugs with spontaneous organ independent metabolism (e.g., atracurium or cisatracurium, or rocuronium and sugammadex combination).

Monitoring
- Consider arterial pressure monitoring.
- Consider central venous cath insertion for access and administration of concentrated potassium and magnesium in the face of hypervolemia, or for monitoring filling pressure where there is cardiomyopathy and heart failure.
- Urinary cath.
- Peripheral nerve stimulation for neuromuscular function.

General Anesthesia
- Hypokalemia may potentiate muscle relaxants and arrhythmia.
- Surgical manipulation of the aldosterone producing structure may cause severe Htn.
- High pH decreases availability of intracellular calcium.

Regional Anesthesia
- Local anesthetic mixtures with sympathomimetic may exacerbate preexisting Htn.
- Altered pharmacokinetics resulting from hypervolemia and end organ damage such as renal dysfunction may need dose adjustments.

Postoperative Period
- Appropriate care predicated on surgical procedure, co-morbidities, and hemodynamic stability.
- Monitor and correct ongoing electrolyte abnormalities.
- Consider glucocorticoid supplementation, though it should not be required if there is at least one intact adrenal gland.

Anticipated Problems/Concerns
- Labile blood pressure.
- Increased sympathetic activity leads to activation of the renin-angiotensin system.
- Arrhythmia from severe hypokalemia.
- Generalized muscle weakness from hypokalemia.

Hyperaldosteronism, Secondary

Marc Chikhani | Jonathan G. Hardman

Risk
- High renin states, and greater risks may be associated with the primary problem, leading to hyperreninemia.
- End organ damage from long-standing Htn (e.g., chronic kidney disease, cardiomyopathy).
- Abnormal glucose tolerance in up to 50% of pts with hyperaldosteronism.

Perioperative Risks
- Risks include hypernatremia and hypervolemia with high total body sodium.
- Htn may be refractory to treatment, with increased risk of cardiovascular complications, including malignant hypertensive crisis.
- Hypokalemia and hypomagnesaemia with low intracellular potassium and magnesium may cause cardiac arrhythmia and general muscle weakness.

Worry About
- The underlying primary medical disorder that leads to increased renin and, hence, increased aldosterone secretion.
- Hypertensive response to intubation or surgical incision.
- Hypokalemia and associated muscle weakness or potential for arrhythmia.
- Metabolic alkalosis.

Overview
- Secondary hyperaldosteronism is a renin-dependent oversecretion of the mineralocorticoid aldosterone secreted from the zona glomerulosa of the adrenal cortex.
- Renin is released from the JGA as a response to decreased renal perfusion pressure. Osmoreceptors in the macula densa will also stimulate renin release in the presence of decreased sodium concentration in the distal tubule.
- Renin enzymatically alters angiotensinogen to angiotensin I. ACE (found in the pulmonary and renal vascular endothelium) then converts angiotensin I to angiotensin II. Angiotensin II, a potent vasoconstrictor, then stimulates release of aldosterone from the zona glomerulosa of the adrenal medulla.
- Aldosterone promotes restoration of circulating volume by correcting water and sodium depletion.
- Diagnosis is suggested by increases in both plasma renin (>2 ng/mL) and aldosterone, but the ratio of plasma aldosterone concentration to renin activity is <10 ng/dL per ng/mL/h (ratio >35 strongly suggests primary hyperaldosteronism).
- In some situations, such as pregnancy and chronic renal disease, increased aldosterone is an adaptive response and is not necessarily deleterious.

Etiology
- Any pathophysiologic process that causes a chronic and relative decrease of perfusion pressure in the juxtaglomerular apparatus has the potential to cause secondary hyperaldosteronism. Examples include:
  - Increased central venous pressure and therefore increased capillary hydrostatic pressure.
  - Decreased cardiac output.
  - Vasodilation.
  - Impaired plasma protein synthesis and excess loss.
- Common causes:
  - Heart failure (increased venous pressure and reduced cardiac output).
  - Liver disease with cirrhosis (peripheral and splanchnic vasodilation and reduced albumin synthesis).
  - Nephrotic disease (protein loss).
- Renovascular (hyper-reninemic) Htn: Related to atherosclerosis (renal artery stenosis) or fibromuscular dysplasia.
- Renovascular disease causing decreased renal perfusion pressure independent of systemic pressure: Renal artery stenosis, aortic coarctation.
- Renin-secreting tumors (e.g., tumor of the juxtaglomerular apparatus or renal cell carcinoma).
- Pregnancy.

Usual Treatment

- Aldosterone antagonists, such as spironolactone (up to 300 mg/d) or the newer drug eplerenone (up to 100 mg/d).
- Both spironolactone and eplerenone are mineralocorticoid receptor antagonists and therefore have a potassium-sparing diuretic effect. Eplerenone is more selective for the mineralocorticoid receptor than spironolactone and has fewer glucocorticoid or androgen receptor antagonist side effects.
- Htn may be refractory to treatment with aldosterone antagonist alone and may require formal antihypertensive therapy with ACE inhibitor or beta-blocker.
- Treatment of Htn may be needed for several wk before any benefit to periop morbidity.
- Assess volume status thoroughly; there may be occult hypovolemia if diuretic treatment has been started.
- Hypervolemia should be treated with a potassium-sparing diuretic such as amiloride to avoid exacerbating potassium loss.
- Potassium deficit is likely to be severe and larger than apparent from serum levels.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, often resistant to therapy; increased sympathetic activity, cardiac output often decreased even in absence of Htn. May have unexplained congestive failure	Exercise tolerance, dyspnea, orthopnea, Htn-headache, visual disturbance	BP (compare R to L or arms with legs with coarctation) Third heart sound Fine inspiratory crackle Oedema	BP, ECG, ABG, CXR, ECHO
HEME	Hypervolemia or hypovolemia (or decreased plasma volume in edematous states) may result in Htn or hypotension, hypokalemia, metabolic acidosis	Syncope, weakness, fatigue	JVP, postural BP, motor power	Serum electrolytes, bicarbonate, ABG
RENAL	Increased renal tubular sodium absorption Azotemia may be caused by decreased renal perfusion or ineffective plasma volume. In setting of renal artery stenosis, ACE inhibitors may exacerbate renal failure; hypokalemia, alkalosis	Htn, decreased urine output, chronic renal disease, weakness	Abdominal bruit suggests renal artery stenosis Edema	ECG, serum and urine lytes, ABG, abdominal ultrasound with renal artery Doppler or contrast CT imaging, renal biopsy.
HEPAT	Cirrhosis is an edematous state and may be associated with occult hypovolemia, altered pharmacokinetics, hypoalbuminemia, coagulopathy, encephalopathy, variceal bleeding risk	Alcohol excess, hepatitis, other liver disease, bruising after minor injury.	Pallor, jaundice, ascites, asterixis ephalopathy, porto-systemic anastomoses, bruising, hepatomegaly	Full blood count including coagulation studies and platelets, serum lytes, hepatic enzymes, bilirubin, ammonia, abdominal ultrasound, liver biopsy

Key References: Davies M, Hardman JG: Anaesthesia and adrenocortical disease, *Contin Educ Anaesth Crit Care Pain* 5(4):122–126, 2005; Reilly CS: Adrenal disease: cortex and medulla. In Hall GM, Hunter JM, Cooper MS, editors: *Core topics in endocrinology in anaesthesia and critical care*, Cambridge, 2010, Cambridge University Press, pp 45–56.

Perioperative Implications

Preinduction/Induction/Maintenance

- Dependent on primary underlying medical problem causing increased renin secretion.
- Assess cardiac function and circulating volume status to guide choice of induction agent; beware of altered pharmacokinetics; anticipate severe cardiovascular instability.
- Correct hypokalemia and associated electrolyte disturbance (e.g., magnesium); this may require IV supplementation preop and intraop.
- Htn may be refractory; require treatment with several classes of drugs with the potential for extreme cardiovascular instability. There may be a disproportionate hypertensive response to laryngoscopy or surgical stimulation.
- Avoid hyperventilation and hypocapnia to prevent worsening metabolic alkalemia and subsequent intracellular potassium shift.
- Anticipate increased sensitivity to nondepolarizing neuromuscular antagonists due to hypokalemia. Consider using drugs with spontaneous organ independent metabolism (e.g., atracurium or cisatracurium, or rocuronium and sugammadex combination).

Monitoring

- Consider arterial pressure monitoring.
- Consider central venous cath insertion for access and administration of concentrated potassium and magnesium in the face of hypervolemia, or for monitoring filling pressure where there is cardiomyopathy and heart failure.
- Urinary cath.
- Peripheral nerve stimulation for neuromuscular function.

General Anesthesia

- Consider underlying and associated underlying medical comorbidities.
- Hypokalemia may potentiate muscle relaxants and arrhythmia.
- High pH decreases availability of intracellular calcium.

Regional Anesthesia

- Pt with severe edema may be unable to tolerate supine operating positions while awake.
- Local anesthetic mixtures with sympathomimetic may exacerbate preexisting Htn.
- Altered pharmacokinetics resulting from hypervolemia, edema, and end organ damage such as hepatic and renal dysfunction may need dose adjustments.

Postoperative Period

- Appropriate care predicated on surgical procedure, comorbidities, and hemodynamic stability.
- Monitor and correct ongoing electrolyte abnormalities.
- Altered pharmacokinetics may be associated with prolonged recovery times from anesthetic agents and exaggerated response to opioid analgesia.

Anticipated Problems/Concerns

- Labile BP
- Pts with preexisting Htn, left ventricular hypertrophy, and cardiac failure are at increased risk of morbidity and mortality from stroke and MI.
- Increased sympathetic activity leads to further activation of the renin-angiotensin system.
- Arrhythmia from severe hypokalemia.
- Generalized muscle weakness from hypokalemia.

Hypercalcemia

John A. Helmstetter | Alan David Kaye

Perioperative Risks

- Pts with normal renal and CV function who have moderate hypercalcemia (11.5–13 mg/dL) have no special preop problems but may exhibit lethargy, anorexia, nausea, and polyuria.
- Lithium and thiazide diuretics should be held.
- Severe hypercalcemia (>13 mg/dL) carries risk for hypovolemia and acid-base abnormalities; therefore, normal intravascular volume and electrolyte status should be restored prior to surgery.
  - Neuromuscular symptoms may occur with associated muscle weakness.
  - Neurologic disturbances ranging from poor concentration to coma can develop.
  - CV effects include Htn, dysrhythmias, heart block, ST segment elevation mimicking MI, cardiac arrest, and digitalis sensitivity.
- Total serum Ca^{2+} >14 mg/dL is a medical emergency and requires immediate treatment and delay of elective surgical procedures.

Worry About

- Volume status (hypovolemia secondary to polyuria, fluid overload secondary to treatment).
- Electrolyte disturbances.
- Dysrhythmias and/or ECG changes.
- Organ system manifestations of hypercalcemia and underlying disease.
- Longstanding hypercalcemia can lead to calcification in the myocardium, blood vessels, brain, and kidneys. Beware of seizures from cerebral calcifications. Polyuria that is unresponsive to vasopressin may result from renal calcifications.

Overview

- Total body Ca^{2+} is stored in bone (99%) and serum (1%).
- Total serum Ca^{2+} exists in three fractions: 50% protein-bound (mainly to albumin), 40–50% free or ionized (the physiologically active fraction), and 5–10% anion-bound (to phosphate or citrate).
- The normal range for total serum calcium is 8.6–10.4 mg/dL; the normal range for ionized calcium is 4.7–5.3 mg/dL. Hypercalcemia is defined as total serum Ca^{2+} >10.4 mg/dL.
- The total serum Ca^{2+} level should be corrected for serum albumin level; for every 1 mg/dL decrease in serum albumin, there is a 0.8 mg/dL increase in Ca^{2+}.
- Normal serum Ca^{2+} is regulated by several factors:
  - PTH, which increases bone resorption and renal tubular resorption of calcium.
  - Calcitonin, which inhibits bone resorption.
  - Vitamin D, which augments intestinal absorption of Ca^{2+}.

Etiology

- Increased resorption of calcium from bone (primary/secondary hyperparathyroidism, malignancy, hyperthyroidism, administration of estrogen or antiestrogens to breast cancer pts), with breast cancer accounting for 25–50% of malignancy-related hypercalcemia
- Increased absorption from GI tract (granulomatous diseases such as sarcoidosis, vitamin D intoxication, milk-alkali syndrome)
- Decreased renal excretion of calcium (thiazide diuretics, lithium therapy, familial hypocalciuric hypercalcemia, and renal insufficiency)

Usual Treatment

- Initiated in pts with total serum Ca^{2+} >14 mg/dL or symptomatic pts with total serum Ca^{2+} <14 mg/dL.
- Volume expansion with saline to correct fluid deficit (from polyuria) and increase urinary excretion of Ca^{2+}.
- Loop diuretics increase urinary excretion of sodium and Ca^{2+} with avoidance of thiazide diuretics.
- Discontinue offending drugs, implement dietary Ca^{2+} restriction, and encourage increased physical activity.
- Calcitonin, bisphosphonates, or mithramycin may be required in disorders associated with osteoclastic bone resorption.
- Hydrocortisone may be used to reduce GI absorption of Ca^{2+} in granulomatous disease, vitamin D intoxication, lymphoma, and myeloma. Hydrocortisone is not helpful in pts with hypercalcemia due to hyperparathyroidism or other malignancies.
- Dialysis may be required for life-threatening hypercalcemia.
- Surgical removal of the parathyroid glands can treat primary or secondary hyperparathyroidism.
- Treat underlying cause.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia Shortening of the Q-T interval, prolonged P-R intervals, wide QRS complexes, bradycardia Htn	Postural symptoms Palpitations, fatigue, poor exercise tolerance, dizziness, syncope Headache	Orthostatic vital signs, narrowed pulse pressure, tachycardia Auscultation, variable or slow heart rate Elevated BP	ECG
NEURO	Decreased concentration, confusion, fatigue, stupor and/or coma, seizure (rare)	Confusion Obtundation and/or coma	Mini-mental exam	EEG
RENAL	Polyuria; polydipsia; renal tubular acidosis; nephrogenic diabetes insipidus Nephrolithiasis; nephrocalcinosis Acute and chronic renal insufficiency	Increased frequency of urination, excessive thirst, lithium use, abd pain Low urine output	Signs of dehydration (dry mucous membranes, poor capillary refill, decreased skin turgor) Flank pain	Lytes, BUN, Cr, UA urinalysis Abdominal x-ray or CT
MS	Muscle weakness Lytic bone lesions Osteopenia and/or osteoporosis	Muscle weakness Bone pain	Decreased muscle strength and tone, depressed deep tendon reflexes Pain on palpation or limited ROM	X-ray (lytic lesions or pathologic fracture) DXA
ENDO	Excess PTH or production of PTH-related hormone			Radioimmunoassay of PTH or PTH-related peptides
GI	Anorexia, nausea and/or vomiting, bowel hypomotility and constipation, pancreatitis PUD	Poor appetite, nausea and/or vomiting, constipation, abd pain GI bleeding	Abdominal pain	Abdominal x-ray or CT scan, colonoscopy, LFTs (amylase and lipase) EGD

Key References: Shane E, Dinaz I: Hypercalcemia: pathogenesis, clinical manifestations, differential diagnosis, and management. In Favus MJ, editor: *Primer on the metabolic bone diseases and disorders of mineral metabolism*, ed 6, Philadelphia, PA, 2006, Lippincott Williams and Wilkins; Nishi SP, Barbagelata NA, Atar S, Birnbaum Y, Tuero E: Hypercalcemia-induced ST-segment elevation mimicking acute myocardial infarction, *J Electrocardiol* 39(3):298–300, 2006.

Perioperative Implications

Preinduction

- Acquire knowledge of and treat the underlying cause.
- Determine if the hypercalcemia is acute or chronic.
- Assess volume status: Hydrate to attain normal intravascular volume and to promote renal excretion of Ca^{2+}.
- Administer diuretics (loop diuretics, as thiazides increase reabsorption of calcium) to increase urinary Ca^{2+} excretion if serum Ca^{2+} >14 mg/dL.
- Correct other electrolyte imbalances, including hypophosphatemia, hypokalemia, and hypomagnesemia.

Induction

- No specific anesthetic drug or technique has advantages in a pt with hypercalcemia; however, hemodynamic instability may occur if standard dosing is used in a hypovolemic pt.

Monitoring

- Standard ASA monitors +/– CVP monitoring.
- Volume status (urine output and fluid administration); depending on the severity of hypercalcemia, underlying cause, the pt's CV status, and type of surgery, additional monitors of volume status (CVP or TEE) should be considered.
- Lytes (venous or arterial).
- 5-lead ECG to monitor for shortened Q-T interval, S-T changes, decreased T wave amplitude, or T wave inversion.
- BP to monitor for Htn; approximately one-third of hypercalcemic pts have Htn that usually resolves with treatment of the primary disease.

General Anesthesia/Maintenance

- Routine maintenance tailored to the comorbidities of the pt and the surgical needs.
- Continued hydration and electrolyte replenishment to attain normal intravascular and acid-base status.
- Hypercalcemia may be associated with decreased sensitivity to muscle relaxants and thus a shortened time course of neuromuscular blockade; however, associated electrolyte disturbances or renal insufficiency may prolong neuromuscular blockade.
- Careful positioning of the anesthetized pt is important because osteopenia/lytic bone lesions predispose these pts to pathologic bone fractures.
- If the pt is mechanically ventilated, avoid resp alkalosis because alkalosis lowers plasma K^+, which would leave hypercalcemia unopposed.

Regional Anesthesia

- General anesthesia is most commonly used for parathyroid surgery; however, a cervical plexus block or local anesthesia with hypnosis has also been used.

Postoperative Period

- Continue to monitor the same intraop parameters, with continued close attention to volume status.
- Hypercalcemia, hypermagnesemia, and hyponatremia are rare causes of delayed emergence.
- After parathyroid surgery, monitor for bleeding, recurrent laryngeal nerve injury or hypocalcemia (secondary to profound decrease in PTH).

Anticipated Problems/Concerns

- Fluid and electrolyte disturbances: Correct Mg^{2+}, phosphate, and K^+ levels in the periop period, as they may be altered with the treatment of hypercalcemia.
- Acute ECG changes and arrhythmias.
- Neurologic impairment: As Ca^{2+} increases, the worsening mental status may lead to impaired airway protection.
- When hypercalcemia is severe and/or the pt is symptomatic, do not hesitate to consult a specialist (endocrinologist, nephrologist, or cardiologist) and postpone surgery if possible.

Hypercholesterolemia

Dilipkumar K. Patel | William L. Runcie

Risk

- Incidence in USA: 71 million American adults have high LDL-C levels. Nearly 31 million adult Americans have a total cholesterol level >240 mg/dL.
- Risk factors for ASCVD include being a male age >45 y, being a woman age >55 y, family Hx of premature CAD, current cigarette smoking, DM, obesity, obstructive sleep apnea, Htn, CAD, high stress, high LDL-C, and low HDL-C.
- The LDL-C level of ≥190 mg/dL and HDL-C <40 increases the risk for CHD.
- A high triglyceride level combined with low HDL-C level in adults increases the risk of CHD and stroke.
- Familial hypercholesterolemia, an autosomal dominant trait (LDL >260 mg/dL), increases risk for premature CHD.
- Perioperative risks:
  - Acute coronary syndrome, myocardial ischemia, infarction, and ventricular tachyarrhythmia.
  - Cardiac events and worsened CHF.
  - Stroke or death.
  - Knowledge gap exists on whether statin therapy causes periop cognitive dysfunction or delirium in some circumstances.

Worry About

- New-onset angina or increasing frequency or severity of angina, stent thrombosis, bleeding, periop myocardial ischemia, and infarction
- Hypotension, Htn, ventricular arrhythmia, worsening, or new-onset CHF
- TIAs or stroke of the CNS
- Peripheral atherosclerosis, acute pancreatitis

Overview

- Association between high level of LDL-C and an increased risk of ASCVD, including coronary heart disease, stroke, and peripheral arterial disease.
- Desirable or target cholesterol levels are variable and based on existing CV disease and risk of developing CV disease in future and statin therapy.
- The ASCVD risk assessment for 10 y and lifetime can be estimated using various web-based ASCVD risk estimator tools.
- Preop treatment with statins is associated with significant improvement in postop mortality and early clinical outcome in pts undergoing cardiac, vascular, and noncardiac surgery.

Etiology

- Can be primary or secondary to systemic illness such as diabetes, nephrotic syndrome, chronic renal failure, hypothyroidism, or drugs that increase LDL such as anabolic steroids.
- Obesity, sedentary lifestyles, and diets high in saturated fats, trans fat, and cholesterol increase the risk of high LDL-C.

Usual Treatment

- Lifestyle modification, including dietary, physical exercise, and weight control are critical components of reducing cholesterol and ASCVD risk reduction.
- 2013 ACC/AHA updated guideline on treatment of blood cholesterol to reduce ASCVD risk in adults emphasizes lifestyle modification and use of high-, moderate-, and low-intensity statin therapy to four groups of pts, including history of clinical ASCVD, history of diabetes, LDL-C level, and estimated ASCVD risk.
- HMG CoA reductase inhibitors or statins like rosuvastatin (Crestor), lovastatin (Mevacor), pravastatin (Pravachol), simvastatin (Zocor), atorvastatin (Lipitor), and fluvastatin (Lescol) are drugs of choice in most pts with hypercholesterolemia, as they reduce LDL levels effectively.
- In high-risk pts with high triglyceride or low HDL levels, consideration can be given to combine a fibrate or nicotinic acid with an LDL-lowering drug.
- The combination treatment with HMG reductase inhibitor and cholesterol absorption inhibitor (ezetimibe) is highly synergistic in treating high-risk pts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia and infarction Left ventricular dysfunction	Angina or its equivalents Dyspnea, edema, exercise intolerance, coronary stent location and type	Displaced PMI, S_3	ECG, CXR, stress test, ECHO, cardiac MRI, coronary angio
RESP	CHF	Dyspnea, orthopnea, cough	Rales and rhonchi	CXR
RENAL	Impaired renal perfusion	Nighttime urinary frequency		Cr
CNS	Cerebrovascular atherosclerosis Peripheral vascular atherosclerosis	TIAs Poor leg circulation Cramping, pain, heaviness	Carotid bruit ABI	Carotid US and angio Doppler/duplex US, MRA, CT Angiogram

Key References: Stone NJ, Robinson JG, Lichtenstein AH, et al.: 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *J Am Coll Cardiol* 63(25 Pt B):2889–2934, 2014; Turan A, Mendoza ML, Gupta S, et al.: Consequences of succinylcholine administration to patients using statins, *Anesthesiology* 115(1):28–35, 2011.

Perioperative Implications

Preoperative Preparation

- Assess for CAD, DM, valvular disease, and PVD.
- Assess and screen for obesity, related OSA, and metabolic syndrome.
- Routine preop liver function testing is not necessary for pts on statins.
- For pts currently on statins and undergoing noncardiac surgery, statins should be continued.
- For pts undergoing vascular surgery with or without clinical risk factors, initiation of statins should be considered.
- Periop statins have a protective effect on cardiac complications during noncardiac surgeries. Initiation of a statin prior to cardiac surgery may reduce risk of postsurgical AKI.
- Pts with hypercholesterolemia and another risk factor (smoking, diabetes, hypertension or age >60) should be started on a beta-blocker 2 to 7 d prior to surgery. Starting a beta-blocker 1 d prior to surgery shows no benefit and may be harmful.
- Assess for myopathy, liver damage, cognitive impairment, and new onset DM in moderate or high intensity statin therapy and older pt groups.

Monitoring

- Consider appropriate invasive monitoring in presence of large fluid shifts, ischemic Hx, and high-risk surgery.
- Implement ST-T measurement or mapping in pts with CHD or risk factor for CHD.

Airway

- May be overweight and difficult to intubate or ventilate

Induction

- Succinylcholine induced fasciculations and mild elevation of plasma myoglobin are clinically not significant to cause rhabdomyolysis or renal injury in pts on statin therapy in absence of myopathy. Succinylcholine should be avoided in pts with myopathy, muscle pain, injury, breakdown, prolonged muscle compression after being intoxicated, or surgery involving elevated risk for developing rhabdomyolysis, whether they are on statins or not.
- Implement aggressive treatment for tachycardia, Htn, or hypotension during induction.

Maintenance

- Maintain hemodynamic stability without hypothermia or anemia; ideal Hct may be >27%.
- No anesthetic agent or technique has proven superior.
- Monitor for ischemia and CHF.
- Rhabdomyolysis is a rare complication of statins. Monitor for darker urine myoglobinuria, increase in serum CK, and acute renal failure.

Extubation

- For noncardiac surgery, this is the period of greatest risk for ischemia.

Postoperative Period

- High incidence of tachycardia, ischemia, and MI for several d after noncardiac surgery.
- Treat pain, unstable hemodynamic, and biochemical abnormality aggressively.
- Statin therapy initiated prior to surgery should continue postop.

Adjuvants

- Depends on end-organ disease

Anticipated Problems/Concerns

- Problems are related to atherosclerosis in multiple organs, including heart, kidneys, and brain.
- Risk factors for rhabdomyolysis involving skeletal muscle breakdown are young age, obesity, diabetes, CKD, periop bleeding, exaggerated position such as flank, lithotomy, and prone position with prolong muscle compression.
- Pts with intense physical activity while on statins may have increased the risk of developing rhabdomyolysis.

Hyperglycemia

William L. Lanier

Risk

- Incidence in USA: Can occur in virtually any anesthetized or critically ill pt
- Race with the highest prevalence: None

Perioperative Risks

- Dehydration resulting from osmotic diuresis
- Increased likelihood of neurologic injury following brain ischemia and perhaps traumatic brain injury and spinal cord injury
- Increased infection rate
- Diminished wound healing

Worry About

- Lyte abnormalities, particularly hypokalemia, while treating hyperglycemia.
- Hypoglycemia following insulin, resulting in insult to the CV system and CNS.
- Polyuria complicates assessment of fluid balance.

Overview

- Is not a disease.
- Typically produces adverse effects by three mechanisms: Increases in plasma osmolality, increases in postischemic tissue lactic acidosis, and inhibition of white blood cell function.
- In acute setting, blood glucose concentration can be estimated using indicator-impregnated strips or other point-of-care methodologies; confirmation can be made by mechanized techniques in a reference laboratory.

Etiology

- Results from DM (both insulin-requiring and non-insulin–requiring), other endocrinopathies (Cushing syndrome, acromegaly, obesity, pheochromocytoma), physiologic stress, drug administration (particularly corticosteroids), and glucose-containing fluid infusions

Usual Treatment

- Insulin.
- Isotonic IV crystalloid solutions to treat hypovolemia and dilute existing blood glucose.
- If possible, treat underlying cause (e.g., discontinue infusion of glucose-containing solutions, discontinue corticosteroids, reduce physiologic stress to pts).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dehydration in extreme cases		Dry mucosa in extreme cases	
CV	Mild positive inotropic effect with mild hyperglycemia Dehydration		Tachycardia, orthostatic hypotension	
GI		Polydipsia in extreme cases		
RENAL	Osmotically induced diuresis	Polyuria, urinary frequency		Elevated urine glucose
ENDO		See Etiology		Elevated blood glucose
HEME	Diminished WBC activity; changes in serum sodium concentrations			Serum sodium concentration decreases 1.6 mEq/L for each 100 mg/dL increase in glucose concentration
CNS			Altered consciousness, neurologic deficits	Plasma osmolality

Key References: Akhtar S, Barash PG, Inzucchi SE: Scientific principles of perioperative glucose regulation and control, *Anesth Analg* 110(2):478–497, 2010; Pasternak JJ, McGregor DG, Schroeder DR, et al: Hyperglycemia in patients undergoing cerebral aneurysm surgery: its association with long-term gross neurologic and neuropsychological function, *Mayo Clin Proc* 83(4):406–417, 2008.

Perioperative Implications

Preoperative Preparation

- Glucose reduction with insulin
- Hydration
- Normalization of lytes

Monitoring

- Blood glucose concentrations in all cases
- In severe cases, blood lytes, blood osmolality, and urine output

Airway

- Abnormality typically related to DM (reduced range of motion and abnormal atlanto-occipital contractions), acromegaly (distorted anatomy), or chronic corticosteroid use or Cushing syndrome (Cushingoid signs and symptoms, friable tissues)

Maintenance

- Maintain hydration.
- Insulin therapy.
- K+ replacement.

Extubation

- No special considerations, other than those related to underlying disease

Adjuvants

- Limit attempted reduction of blood glucose concentration to approximately 75 mg/dL/h to avoid problems with osmotic injury to brain and lyte disturbances.
- Monitor ECG during correction of profound hyperglycemia.

Postoperative Period

- Variations in physiologic stress, fluid administration, and drug usage make postop blood glucose concentrations difficult to predict and control.

Anticipated Problems/Concerns

- Increases in blood glucose concentrations by a mere 40 mg/dL may worsen outcome following cerebral ischemic insult. Hyperglycemia may also harm wound healing, increase infection rates, and worsen outcomes after myocardial infarction. In contrast, hypoglycemia resulting from excessive use of insulin may result in pt morbidity and mortality from neurologic and other causes, independent of ischemic events.
- Limb hypothermia or hypoperfusion will harm the accuracy of glucose measurements from skin-prick blood samples.
- Target blood glucose should be <180 mg/dL in most pts.

Hyperglycemic Hyperosmolar State

Jesse M. Raiten

Risk

- Elderly pts with DM, usually type II
- Debilitated pts who cannot care for themselves
- Chronically ill diabetic pts who experience exacerbation of an underlying comorbidity
- Incidence increased in African Americans, Hispanics, and Native Americans

Perioperative Risks

- Severe hypovolemia and hemodynamic instability
- Presence of diffuse organ system damage from poor glycemic control
- Altered mental status and increased risk of pulmon aspiration
- Periop stress causing further elevations in serum glucose

Worry About

- Cause of hyperglycemic hyperosmolar state.
- Volume status and potential hemodynamic instability.
- Electrolyte and acid-base abnormalities increase the risk of cardiac arrhythmias.

Overview

- Serious metabolic condition characterized by hyperglycemia, hyperosmolarity, and dehydration
- Is one of several potentially fatal states associated with poorly controlled DM
- Requires aggressive treatment and close electrolyte and hemodynamic monitoring

Etiology

- Inadequate insulin production and increased counter-regulatory hormone production (catecholamines, glucagon, cortisol) in the setting of an acute insult leads to severe hyperglycemia, dehydration, and electrolyte abnormalities.
- Triggering event may be infection, dehydration, CVA, inadequate dosing of insulin, silent myocardial

infarction, pancreatitis, or drug ingestion (drugs that affect carbohydrate metabolism).

Usual Treatment

- Aggressive volume resuscitation with isotonic fluids to re-establish end-organ perfusion
- Insulin replacement and correction of electrolyte abnormality (start dextrose-containing fluids when serum glucose approaches 250 mg/dL to help to prevent hypoglycemia and cerebral edema)
- Identify and treat underlying cause of hyperglycemic state
- Frequent evaluation of volume resuscitation and metabolic status in an ICU setting

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Altered mental status, obtundation, coma, seizures	Progression of mental status changes over days	Mental status exam, airway reflexes	Head CT, CSF culture
CV	Hypovolemia and shock	Polyuria progressing to anuria, sense of thirst, headaches, dry mouth	Orthostatic hypotension, tachycardia, dry mucous membranes	CVP, PAP, ECHO
PULM	Hyperventilation if severe metabolic acidosis, hypoventilation if brainstem malperfusion		Resp rate and pattern of ventilation	ABG
ENDO	Insulinopenia, hyperglycemia, hyperosmolarity	DM, recent infection or stress		Serum glucose and osmolarity
RENAL	Polyuria progressing to anuria, metabolic acidosis, electrolyte abnormalities			BUN and Cr, FEN_a, UO, ABG, lytes

Key References: Maletkovic J, Drexler A: Diabetic ketoacidosis and hyperglycemic hyperosmolar state, *Endocrinol Metab Clin North Am* 42(4):677–695, 2013; Pichardo-Lowden A, Gabbay RA: Management of hyperglycemia during the perioperative period, *Curr Diab Rep* 12(1):108–118, 2012.

Perioperative Implications

Monitoring and Intravenous Access

- Large-bore IV access for volume resuscitation, particularly before induction.
- Invasive monitoring including arterial line and CVP may be useful to guide volume replacement and allow for frequent glucose and electrolyte sampling.

Induction

- Aggressive volume resuscitation before induction.
- Rapid sequence induction if altered mental status and concern for aspiration.
- Limited use of succinylcholine if metabolic acidosis and hyperkalemia are present.
- Be prepared for exaggerated hemodynamic changes with induction despite adequate volume resuscitation.
- Smaller doses than usual of induction agent if pt is obtunded.

Maintenance

- Closely follow serum glucose, lytes, and acid-base status.
- Continue volume resuscitation until UO is adequate and hemodynamics have stabilized.

Emergence

- Assessment of airway reflexes and ability to protect airway before tracheal extubation.
- Ensure metabolic and lyte status is corrected and pt meets the usual criteria for extubation

Postoperative Period

- Continued insulin therapy and observation for worsening hyperglycemia due to surgical stress response

Anticipated Problems/Concerns

- Comorbidities and diffuse end-organ damage increase morbidity and mortality of pts with HHS, particularly periop.

Hyperkalemia

Alan David Kaye | Mark R. Jones | Rachel J. Kaye

Risk

- Any pt with plasma K^+ concentration <5.5 mEq/L

Perioperative Risks

- Muscle weakness and paralysis
- Cardiac conduction system abnormalities
- CV collapse:
  - Peaked T waves (6–7 mEq/L)
  - ST depression
  - Prolonged P-R interval and widened QRS (10–12 mEq/L)
  - Ventricular fibrillation or asystole

Worry About

- Adverse effects are likely to accompany acute increases in K^+; chronic increases are better tolerated.
- Depolarizing muscle relaxants, especially if given to pts with burns, spinal cord transection, catatonia with immobility, or muscle trauma.
- Digitalis toxicity.
- Acidosis.

Overview

- Condition that can be due to increased total body K^+ content or alterations in distribution between intracellular and extracellular sites

Etiology

- Diminished renal excretion
- Acute oliguric renal failure
- Chronic renal failure
- Addison disease
- Hyporeninemic hypoaldosteronism
- Medications: Potassium-sparing diuretics, NSAIDs, heparin, K^+-containing antibiotics
- RAASi: Incidence of hyperkalemia <2% with RAASi monotherapy: Increased to 5% in pts receiving dual-agent RAASi therapy, and to 5%–10% when dual therapy was administered to pts with CKD
- Ingestion of K^+-rich foods, salt substitutes in pts with renal insufficiency
- Transcellular shifts
- Acidosis: Respiratory or metabolic
- Cell destruction: Trauma, burns, rhabdomyolysis, hemolysis, tumor lysis, or reperfusion of ischemic limb or organ
- Hyperkalemic periodic paralysis
- Diabetic hyperglycemia
- Depolarizing muscle relaxant causing K^+ release, especially in pts with burns, spinal cord transection, catatonia with immobility, muscle trauma, or denervating muscle
- Massive transfusion, particularly with irradiated blood
- Factitious hyperkalemia
- Tourniquet method of drawing blood
- Hemolysis of drawn blood due to delay in chemical determination

Usual Treatment

- Promote transfer of K^+ from ECF to ICF.
- Glucose and insulin: 25–50 g glucose with 10–20 units regular insulin/70 kg.
- Sodium bicarbonate: 50–100 mEq/70 kg.
- Hyperventilation: with each pH change of 0.1, there is an inverse change in K^+ of 0.5 mEq/L (goal $PaCO_2$ 25–30 mm Hg).
- Enhance K^+ elimination: Diuretics, exchange resins (Kayexalate), dialysis.
- Antagonism of cardiac effects: Ca^{++} gluconate—10–30 mL of a 10% solution over 10–20 min/70 kg counteracts cardiac effects.
- 50–250 mL hypertonic saline (3%–5%): Stabilizes membrane potential; effective only in hyponatremic pts.
- β_2-receptor agonists: 10–20 mg aerosol (nebulized) or 0.5 mg in 100 mL of 5% dextrose in water (IV) redistributes K^+ from ECF to ICF; use with caution in pts with CAD.
- New treatments: K^+ binders (patiromer and sodium zirconium cyclosilicate [ZS-9]) increase fecal potassium excretion; may offer better predictability, tolerability, and safety for pts with hyperkalemia; importantly, these new K^+ binders may allow the continued use of such medications as RAASis

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tall peak T waves Decreased amplitude R wave Widened QRS complex Decreased and eventual disappearance of P wave QRS blends into T wave—"sine wave of hyperkalemia" Ventricular arrhythmia Cardiac arrest	 Possible hemodynamic instability CV collapse		ECG ECG ECG
MS	Weakness Paralysis			
ENDO	Increased aldosterone Insulin release Increased glucagon Epinephrine release		Increased BP, HR	K^+, renin, aldosterone, glucose

Key References: Kovesdy CP: Management of hyperkalaemia in chronic kidney disease, *Nat Rev Nephrol* 10(11):653–662, 2014; Seferovic PM, Pelliccia F, Zivkovic I, et al: Mineralocorticoid receptor antagonists, a class beyond spironolactone—focus on the special pharmacologic properties of eplerenone, *Int J Cardiol* 200:3–7, 2015.

Perioperative Implications

Preoperative Preparation

- Normal K^+ levels before elective surgery
- Avoid sedatives (decreased ventilation) prior to K^+ normalization

Monitoring

- ECG
- Plasma K^+ levels
- ABG concentration
- Peripheral nerve stimulator

Maintenance

- Adequate ventilation to avoid respiratory acidosis.
- Avoid metabolic acidosis: Arterial hypoxemia or excessive depths of anesthesia.
- IV fluids: Avoid lactated Ringer or others containing K^+.

Adjuvants

- Muscle relaxants: avoid depolarizing agents; increase K^+ 0.3–0.5 mEq/L with succinylcholine.
- Dose of nondepolarizing relaxants required is unclear; may need diminished dose.

Anticipated Problems/Concerns

- Acute increases in K^+ leading to acute ECG changes or adverse cardiac effects. Rx (see Usual Treatment).
- Avoid use of depolarizing muscle relaxants in pts with burns, neuropathies, paraplegia or quadriplegia, muscle trauma, or catatonia with immobility.

Hypermagnesemia

Alan David Kaye | Lien Tran | Erik M. Helander

Risk

- Pts with renal insufficiency, especially those receiving Mg^{2+}-containing cathartics or antacids.
- Parturients on $MgSO_4$ therapy.
- "Runaway" infusion of Mg^{2+} during transportation to the OR can cause acute, life-threatening hypermagnesemia. Risk of developing very high serum Mg^{2+} levels in such cases can be reduced by always using a small-volume buretrol device in pts receiving IV Mg^{2+} therapy.

Therapeutic Uses

- Treatment of preeclampsia, eclampsia, and preterm labor.
- Evidence indicates that Mg^{2+} therapy reduces the risk of cerebral palsy in women at risk of preterm delivery.
- Treatment of ventricular dysrhythmias, especially torsades de pointes.
- Treatment of severe asthma in pts who have not responded to initial therapy.
- Treatment of migraine.
- Lowers risk of metabolic syndrome.

Perioperative Risks

- Potentiates nondepolarizing neuromuscular blocking agents.
- May increase risk of modest hypotension during administration of regional anesthesia.
- Potentiates hypotension associated with use of volatile anesthetics, CCBs, and butyrophenones.
- Can exacerbate local anesthetic toxicity.
- Hypermagnesemia may be associated with increased in bleeding time and TEG changes, although no clinically significant coagulopathies have been attributed to Mg^{2+}.

Worry About

- Intraop hypotension
- Muscle weakness (especially respiratory)
- Excessive sedation
- Myocardial depression and cardiorespiratory arrest with very high levels

Overview

- Defined as an elevated Mg^{2+} concentration in plasma, in excess of 1.1 mmol/L.
- Equivalent Mg^{2+} concentrations in the three unit systems in common use: mg/dL, mEq/L, mmol/L.
  - Normal serum level 1.8–2.4 mg/dL, 1.5–2.0 mEq/L, 0.75–1.0 mmol/L.
  - Therapeutic level 4.8–8.4 mg/dL, 4–7 mEq/L, 2–3.5 mmol/L.
  - Neuromuscular toxic level greater than 12 mg/dL, greater than 10 mEq/L, greater than 5 mmol/L.
- Mg^{2+} elimination is dependent on GFR; with GFR less than 30 mL/min, pts are at significant risk.
- Signs and symptoms vary with plasma concentration and become more serious as the plasma concentration increases greater than 4 mmol/L.
- CV, respiratory, and MS systems are predominantly affected.
  - Pts with chronic renal failure frequently have Mg^{2+} levels up to 3 mmol/L but are seldom symptomatic.
  - Acidemia will decrease serum level at which side effects occur; e.g., in presence of acidemia, cardiac arrest can occur at a serum level of 8–10 mmol/L.

Etiology

- Pts with chronic renal failure who are receiving Mg^{2+}-containing antacids or laxatives
- Often iatrogenic; for example, excessive administration of $MgSO_4$ infusion to parturient pts with preterm labor or pregnancy-induced Htn
- Less common causes: Addison disease, myxedema, excessive tissue breakdown, or lithium therapy

Usual Treatment

- Discontinue Mg^{2+} therapy and delay nonessential surgery.
- Fluid load and diuretic therapy in pts with normal renal function.
- Adults: IV calcium gluconate 1 g (temporary but effective).
- Neonates: IV calcium gluconate 100–200 mg/kg over 5 min and continuous infusion 100–300 mg/kg per d.
- Peritoneal dialysis or hemodialysis for persistent or life-threatening hypermagnesemia.
- Assist ventilation/protect airway if necessary.

Assessment Points

The side effects of hypermagnesemia are more serious as the serum level of magnesium increases.

System	Signs and Symptoms	Serum Mg^{2+} Concentration (mmol/L)
GENERAL	Normal	0.7–1.1 (normal range)
CV	Warmth, flushing, headache, nausea, dizziness	2.5–4.0
	Decreased AV and intraventricular conduction	3.7–4.9
	ECG: Prolonged PR and widening of QRS	
	Hypotension	
	Cardiopulmonary arrest*	>8.9
CNS	Confusion or sedation	3.7–4.9
MS	Absent deep tendon reflexes	3.7–4.9
	Profound muscle weakness	5–6.95

*The ability of this degree of hypermagnesemia to cause cardiac arrest is uncertain if ventilatory support and normal acid-base balance are maintained.

Key References: Jahnen-Dechent W, Ketteler M: Magnesium basics, *Clin Kindey J* 5(Suppl 1):i3–i14, 2012; Herroeder S, Schönherr ME, De Hert SG, et al.: Magnesium–essentials for anesthesiologists, *Anesthesiology* 114(4):971–993, 2011.

Perioperative Implications

Preoperative Preparation

- Discontinue $MgSO_4$ unless being used to treat seizures or ventricular dysrhythmias.
- Check serum level.
- ECG, Cr, and lytes.

Monitoring

- Routine

Airway

- Does not affect onset or duration of succinylcholine; fasciculations may not be observed.
- Reduce dose of nondepolarizing NMBs by one-third to one-half.

Preinduction/Induction

- Avoid sedative premedications.
- Ensure full denitrogenation of lungs.
- Avoid precurarization or priming dose of NMB.

Maintenance

- May decrease requirement for anesthetics owing to decreased neurotransmitter release.

Extubation

- Ensure full return of train-of-four, ability to sustain head lift, and vital capacity lesser than 10 mL/kg.
- Ensure pt responsiveness.

Adjuvants

- Hypermagnesemia may exacerbate hypotension associated with hypovolemia, CCBs, volatile inhalation anesthetics, butyrophenones, lumbar epidural, or subarachnoid anesthesia.
- Treat with IV calcium gluconate 1 g, IV fluids, and diuretics.

Postoperative Period

- Beware of excessive sedation, weakness, hypoventilation, and cardiac arrest.
- May cause or aggravate neonatal hypotonia and hypotension.
- May reduce postop analgesic requirements by antagonism of *N*-methyl-D-aspartate.

Anticipated Problems/Concerns

- Hypermagnesemia potentiates action of nondepolarizing NMBs by inhibiting release of acetylcholine from motor nerve terminal, decreasing sensitivity of postjunctional membrane, and reducing excitability of muscle fibers.
- Many common anesthetic drugs exacerbate weakness and sedation associated with hypermagnesemia.
- Potentiates local anesthetic toxicity.
- Excessively high plasma Mg^{2+} concentrations can cause cardiorespiratory arrest.

Hypernatremia

Amit Prabhakar | Alan David Kaye | Jonathan G. Ma

Risk

- Older age, infants, prior brain injury, DM, surgery, diuretic therapy, altered mental status, insufficient water intake, DI, hypertonic sodium solution (including sodium bicarbonate), hyperalimentation, hyperaldosteronism, Cushing syndrome, and hypothalamic injury

Perioperative Risks

- Increased incidence of morbidity and mortality, seizures, coma, cerebral bleeding, and subarachnoid hemorrhage

Worry About

- Increased risk of hospital death, residual and/or permanent neurologic disability
- If Na^+ corrected too rapidly, cerebral edema, seizures, and death

Overview

- Hypernatremia is a relative deficit of body H_2O in relation to body sodium content.
- Serum Na^+ is preserved within a fine physiologic range (138–142 mEq/L).
- Sodium metabolism is regulated by the kidney through the interaction of the RAAS, sympathetic nervous system, atrial natriuretic peptide, brain natriuretic peptide, effective circulating volume, and serum H_2O content. H_2O metabolism is tightly regulated by arginine vasopressin.
- Most commonly found in pts with impaired sense of thirst (brain injury, altered mental status), lack of access to H_2O, diuretic therapy, and severe GI losses of H_2O.

Etiology

- Lack of access to H_2O
- Impaired thirst mechanism
- DI (central and nephrogenic)
- Osmotic diuresis (mannitol, glucose); diuretics (furosemide, thiazides)
- Insensible losses from the dermal or respiratory systems
- GI losses from diarrhea or osmotic cathartics (lactulose, sorbitol), vomiting, or nasogastric suctioning
- Seizures or severe exercise (transient intracellular shift of H_2O)
- Excess sodium administration; hyperalimentation
- Hyperaldosteronism and Cushing syndrome

Usual Treatment

- H_2O replacement (see later); central DI can be treated with desmopressin (5–20 µg intranasal once or twice per day), nephrogenic DI can be treated with thiazide diuretics.
- Free H_2O deficit = 0.6 × weight (kg) × ([current Na^+/140]–1).
- Total body water is approximately 0.6 and 0.5 times the lean body weight for men and women, respectively. Replace ½ of the free H_2O deficit over the first 24 h as an initial starting point. Note that the free H_2O deficit does not take into account ongoing losses, so ultimately the rate of H_2O replacement must be guided by serial measurements of serum Na^+.
- Rate of correction of Na^+ to level of 145 mmol/L:
  - If hypernatremia developed acutely, Na^+ can be corrected rapidly (1 mmol/L per h with a limit of 12 mmol/L per 24 h).
  - If hypernatremia developed slowly, Na^+ can be corrected at a maximum rate of 0.5 mmol/L per h (or in the case of life-threatening complications, at 1 mmol/L per h with a limit of 12 mmol/L per 24 h).
  - Measurement of Na^+ at least every 4–6 h, and adjustment of the rate of H_2O replacement is important to ensure safe and expeditious correction of Na^+.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dry mouth/mucous membranes		Mouth exam	
CV	Tachycardia/hypotension	Orthostatic changes	HR/BP	ECG
CNS	Restlessness, irritability, lethargy, seizures, coma		CNS exam	EEG
GI	N/V, diarrhea			
RENAL	Polyuria	Urinary frequency and color		Serum and urine Na^+, K^+, osmolarity

Key References: Sterns RH: Disorders of plasma sodium-causes, consequences, and correction, *N Engl J Med* 372(1):55–65, 2015; Bagshaw SM, Townsend DR, McDermid RC: Disorders of sodium and water balance in hospitalized patients, *Can J Anaesth* 56(2):151–167, 2009.

Perioperative Implications

Preoperative Preparation
- Correct lytes, replace H_2O deficit in controlled and calculated manner, assess neurologic status.
- Consider delaying elective surgery until serum Na^+ is normal. If surgery cannot be delayed, care must be taken to avoid rapid correction of Na^+.

Monitoring
- Electrolytes

Airway
- None

Maintenance
- Restore circulatory volume.
- Maintain urine output.
- Correct lytes.

Extubation
- Assess neurologic status to determine whether the pt is a candidate for extubation.
- Possible muscular weakness.

Adjuvants
- In central DI, vasopressin 5 U IVP will dramatically reduce UOP for 1–2 h, making it possible to catch up on IV fluids.
- Caution must be used to avoid too-rapid correction of Na^+.

Postoperative Period
- Assess for lethargy, irritability, muscular weakness, and confusion.
- Monitor serum Na^+.

Anticipated Problems/Concerns
- Too rapid correction and resultant neurologic effects

Hyperparathyroidism

Geoffrey L. Liu | Henry Liu

Risk
- Incidence in USA: 100,000 pts/y; increases with age
- Male:female ratio: 1:2; 0.8% in pregnancy
- Prevalence: 0.7% in general population; up to 3% in postmenopausal women
- Due to malignancy, vitamin D deficiency, sarcoidosis

Perioperative Risks
- Hypovolemia and electrolyte disturbances
- Increased risk of cardiac dysrhythmias secondary to hypercalcemia
- Aspiration from full stomach and/or mental change
- Postop hypocalcemia
- Airway compromise due to hematoma or recurrent laryngeal nerve injury

Worry About
- Signs of hypercalcemia and other electrolyte irregularities
- Intravascular volume changes
- Fluid overload and Na^+ retention in CV fragile pts
- Renal, cardiac, skeletal, and CNS abnormalities
- Pancreatitis due to hypercalcemia

Overview
- Endocrinopathy associated with elevation in PTH levels.
- Primary problem is hypercalcemia, leading to "moans, groans, and stones."
- Diagnosis supported by increased PTH level with hypercalcemia.
- Most pts with primary hyperparathyroidism are hypercalcemic but asymptomatic.
- Hyperparathyroidism in pregnancy, leading to high maternal and fetal morbidity (50%) and neonatal hypocalcemia and tetany.

Etiology
- Primary hyperparathyroidism usually due to benign parathyroid adenoma (80–90%), hyperplasia (15%), or parathyroid carcinoma (uncommon).
- May be manifestation of multiple endocrine neoplasia type I or IIa.
- Secondary hyperparathyroidism may be seen in pts with chronic renal disease.

Usual Treatment
- Parathyroidectomy shifting from standard four glands to only pathologic gland(s) removal.
- Advances in nuclear imaging to accurately localize parathyroid tumor(s), quick hormone assays, and radio-guided or video-assisted techniques facilitate minimally invasive parathyroidectomy, possibly under local/regional anesthesia.
- Medical treatment: Saline hydration, furosemide, and phosphate repletion in emergency situations to restore serum Ca^{2+} to a safe level (<14 mg/dL).
- Other Ca^{2+}-lowering modalities: calcitonin, cinacalcet, bisphosphonates (inhibit bone resorption), mithramycin (for more resistant hypercalcemia; toxic effects limit use), glucocorticoids, or hemodialysis.
- Pregnant women with primary hyperparathyroidism should be treated with parathyroidectomy, ideally in the second trimester.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, dysrhythmias	Palpitation, headache	Abnormal HR, rhythm, increased BP	ECG, lytes, total and ionized Ca^{2+}, QT_c* interval
RESP	Decreased bronchial clearance of secretions	Cough	Adventitious sounds	
GI	Peptic ulcers, pancreatitis	Constipation, anorexia, N/V, epigastric pain		
RENAL	Nephrocalcinosis, nephrolithiasis, leading to renal abnormalities	Polyuria, polydipsia, hematuria		BUN, Cr
CNS	EEG abnormalities, seizures Lethargy	Depression, personality change, psychomotor retardation, memory impairment	Psychosis, disorientation Obtundation, coma	
MS	Hyporeflexia, osteopenia, osteitis fibrosa cystica	Weakness, bone pain	Muscular atrophy, arthritis Pathologic fractures	Bone density

* $QT_c = \frac{QT}{\sqrt{R-R}}$; *R-R,* R-R interval.

Key References: Kelz RR, Fraker DL: Hyperparathyroidism: what preoperative imaging is necessary? *Adv Surg* 49:247–262, 2015; Nahrwold ML, Nahrwold DA: Hyperparathyroidism. In Fleisher LA, Roizen MF, editors: *Essence of anesthesia practice,* ed 3, Philadelphia, PA, 2011, Elsevier.

Perioperative Implications

Preoperative Preparation

- Assess total and ionized Ca^{2+} levels. No intervention for Ca^{2+} level <12 mg/dL.
- Reduce serum total calcium to <14 mg/dL.
- For higher Ca^{2+} levels use saline hydration, furosemide (rapid action), phosphate repletion, and consider calcitonin (acts in 1–2 h), mithramycin (acts in 6–12 h), cinacalcet, bisphosphonates, glucocorticoids, or hemodialysis.
- Consider H_2-receptor antagonists, nonparticulate antacids, and metoclopramide.

Monitoring

- Routine; pay attention to changes in QT_c interval (QT_c by itself poorly correlated with ionized Ca^{2+}, but changes correlate).
- Intraop calcium and PTH level.

Airway

- Possibility of pathologic fractures requires careful positioning for laryngoscopy.

Preinduction/Induction

- No preferred agents or techniques.
- Avoid ketamine in pts with psychosis due to hypercalcemia.
- Hypovolemia can lead to hemodynamic instability if usual dose of induction agents is given.
- Minimally invasive procedures can be performed using local or regional anesthesia.

Maintenance

- No preferred agents or techniques. Possibility of pathologic fractures requires careful positioning and padding of pressure points.
- Weakness may warrant smaller dose of nondepolarizers.

Extubation

- Airway edema, surgical site hematoma, or recurrent laryngeal nerve injury may cause airway compromise.

Adjuvants

- Response to NM blockers may be unpredictable if Ca^{2+} level elevated.

Anticipated Problems/Concerns

- Cardiac arrhythmias due to hypercalcemia
- Postop airway compromise secondary to bleeding or recurrent laryngeal nerve injury
- Pneumothorax secondary to surgical procedure
- Fluid overload and lyte abnormalities from too aggressive hydration

Hypertension

Lee A. Fleisher

Risk

- In USA about 77.9 million (1:3) adults have high BP.
- Incidence of Htn increases with advancing age. Half of people 60–69 y and three-quarters of people >70 y are affected.
- There is a continuous relationship between BP and the risk of CVD, including MI, heart failure, stroke, and kidney disease. For people 40–70 y, an increase of 20 mm Hg in systolic pressure or of 10 mm Hg in diastolic pressure doubles the risk of CVD across the entire range of BPs.

Perioperative Risks

- BPs of up to 180/100 mm Hg are not independently associated with an increased risk of periop complications. Limited data suggest that BPs greater than this may be associated with an increased risk of such complications.
- In cardiac surgery, high preop pulse pressures have been associated with a threefold increase in periop mortality, an increased incidence of renal impairment, and reduced long-term survival.
- Isolated systolic Htn (>180 mm Hg, or marked increase to >200 mm Hg) has been associated with increased risk in noncardiac surgery in some studies.
- Intraop CV lability, especially hypotension, poses risks that may precipitate myocardial ischemia or predispose a pt to stroke.

Worry About

- Markedly elevated BP (>180/110 mm Hg)
- Possible second-degree Htn
- Myocardial ischemia and MI
- CVA

Overview

- Approx 95% of people with elevated BP have essential Htn: in 5% of people, an underlying cause for Htn can be identified.
- The aim of the long-term medical management of Htn is to reduce the burden of CV morbidity and mortality associated with chronically raised BP.
- The primary concern of the anesthetist in managing a hypertensive pt through the periop period is to prevent or curtail myocardial ischemia and labile BP that have been associated with anesthesia and surgery in Htn pts.
- Target-organ damage associated with Htn may of itself increase periop risk.
  - Ischemic heart disease
  - Heart failure
  - Cerebrovascular disease
  - Renal impairment
  - Peripheral vascular and aortic disease
- Recent JNC 8 recommendations for blood pressure treatment advocate lower blood pressure goals than previously

Etiology

- Essential Htn appears to be a complex, mulitfactorial condition; a single cause has not been identified. Factors that play a role in the development of essential Htn include genetics, race (increased prevalence and severity in African Americans), age, sedentary lifestyle, obesity (in particular visceral obesity), sodium intake, alcohol intake, childhood influences (birth weight, BP tracking). Htn is part of the constellation of disorders that constitute the metabolic syndrome.
- Secondary Htn is found in approx 5% of people with raised BP. Identifiable causes of Htn incl sleep apnea, drug-induced Htn, chronic renal disease, renovascular disease, primary aldosteronism, Cushing syndrome, chronic steroid treatment, pheochromocytoma, and thyroid/parathyroid disease.
- Many pts who are found to have elevated BP at presentation for surgery will be found to not to be hypertensive when the BP is rechecked in a less stressful setting.

Usual Treatment

- Lifestyle modification should be encouraged in all pts with elevated BP.
- In the general population above age 60, the current goal of pharmacologic treatment is to establish a goal of <150 mm Hg for systolic BP and <90 mm Hg for diastolic BP.
- BP reduction is more important than the choice of drug in the primary prevention of CV complications. There is evidence to support ACEIs, ARBs, calcium channel blockers, and thiazide diuretics as first-line therapy. Combination therapy is frequently required to achieve and sustain long-term BP control.
- Specific classes of antihypertensive drugs may provide better secondary prevention in pts with compelling indications for BP control based upon race.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CAD	MI, angina, previous CABG or PCI		ECG
	LVH/LVF	Dyspnea, orthopnea	Displaced apex beat S_3, basal crepitations	CXR, ECHO
	Peripheral vascular/aortic disease	Claudication/rest pain	Rales Pulses Ankle brachial pressure index	Doppler Angiography/CT angiography/MR angiography
METAB	Metabolic syndrome		Central obesity	Fasting blood glucose Triglycerides HDL cholesterol
RENAL	Renal impairment			Creatinine Estimated creatinine clearance Microalbumin urine test
CNS	TIA/CVA	Hx of TIA/CVA	Neurologic signs Carotid bruit	Doppler CT/MRI Angiography/CT angiography/MR angiography

Key References: Lapage KG, Wouters PF: The patient with hypertension undergoing surgery, *Curr Opin Anaesthesiol* 29(3):397–402, 2016; James PA, Oparil S, Carter BL, et al.: 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8), *J Am Med Assoc* 311(5):507–520, 2014.

Perioperative Implications

Preinduction/Induction/Maintenance

- There is no clear evidence to support deferring surgery or for acute management of BP in pts presenting with moderate Htn in the absence of CAD.
- Severe Htn (>180/110 mm Hg) confirmed on multiple readings should be controlled prior to surgery if the delay necessary to achieve this will not compromise the pt (especially if the pt has evidence of target-organ damage).
- Consider withholding ACEIs and ARBs for 12 h before surgery, as they may be associated with an increased incidence of intraop hypotension. If they are held, it is critical to restart them as soon as possible.
- Maintain treatment with other antihypertensive medications (in particular beta-blockers) unless the pt is hypotensive or has evidence of postural hypotension.
- Maintain euvolemia, especially in pts taking vasodilating drugs such as ACEIs or ARBs.

Monitoring

- Standard monitoring.
- Frequent BP readings should be taken at times of potential CV instability, such as induction, in order to detect sudden changes in BP.
- Consider direct arterial pressure monitoring if surgery is proceeding in the face of severe Htn or a large fluid shift.
- Consider dynamic (e.g., pulse pressure variation) or static (CVP) monitoring if significant hypovolemia is suspected.

General Anesthesia

- Pts may develop profound hypotension at induction and Htn at intubation.
- Consider a fluid preload prior to induction if relative hypovolemia is suspected.
- Consider preparing a short-acting vasopressor prior to induction.
- Consider the use of opiates or short-acting vasoactive drugs to control the response to intubation in pts with significant CVD.
- Aim to keep intraop BP within 20% of best estimate of preop BP with appropriate use of fluids and vasoactive drugs.
- No anesthetic maintenance technique has been demonstrated to be superior in this setting.

Regional Anesthesia

- Risk of hypotension with neuroaxial blockade.
- Consider a fluid preload prior to neuroaxial blockade.
- Take BP readings every 1–2 min immediately after neuroaxial blockade if using noninvasive monitoring.
- As with general anesthesia, aim to keep intraop BP within 20% of best estimate of preop BP.

Postoperative Period

- Resume normal antihypertensive treatment as soon as possible.
- If the pt is not on appropriate CVD prevention, make appropriate medical referrals to rectify this if possible.
- In some cases, parenteral treatment of BP may be required if the pt cannot take oral medications.
- Consider parenteral beta blockade if a pt who is chronically treated with a beta-blocker is unable to resume this treatment.

Anticipated Problems/Concerns

- In pts with preexisting CVD, poorly controlled BP in the postop period may precipitate myocardial ischemia and cardiac complications.

Hypertension, Uncontrolled With Cardiomyopathy

Jonathan G. Ma | Alan David Kaye | Julie Gayle | Ryan E. Rubin

Risk

- 1.5 billion worldwide in 2014
- 70 million people in USA; approximately 1:3 people
- USA highest prevalence: African American
- Male = female

Perioperative Risks

- Increased risk of MI and stroke
- Increased risk of CHF, ventricular hypertrophy, coronary artery disease, and atrial fibrillation
- Increased risk of cerebral hypoperfusion due to right shift of the cerebral blood flow autoregulation curve
- Increased risk of renal failure
- Increased blood loss
- Prolonged hospitalizations

Overview

- Eighth Joint National Commission Hypertension Guidelines:
  - BP goal <150/90 mm Hg—anyone >60 y who does not have DM or CKD.
  - BP goal <140/90 mm Hg—anyone <60 y without major comorbidities and in pts >60 y with DM, CKD, or both.
  - Possibility of masked hypovolemia.
  - Silent myocardial ischemia may occur from supply-demand mismatches, even in absence of CAD.
  - May be forerunner of renal failure and/or stroke.
  - CHF may be presenting sign.
  - May develop LVH ± strain pattern on ECG.
  - May require >6 wk of treatment for regression of LVH.

Etiology

- Idiopathic with genetic predisposition (>90%) and with up to 50% of global population
- Secondary hypertension due to thyroid, renal, and adrenal abnormalities
- Substance abuse (alcohol, cocaine, amphetamines)
- Valvular heart pathology (e.g., aortic insufficiency)
- High peripheral resistance is accelerated with time

Usual Treatment

- Preload optimization (diuretics, venodilators)
- Afterload optimization (ACE inhibitors, angiotensin receptor blockers, CCBs, $alpha_1$-blockers, beta-blockers with $alpha_1$ activity, $alpha_2$ adrenomimetics, direct vasodilators, and sodium nitroprusside for emergencies)
- Drugs with negative inotropic effect (beta-blockers, calcium channel blockers)
- Atherosclerosis prophylaxis (statins)
- Surgical correction of secondary forms of hypertension

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	LV function LVH	Exercise tolerance	Two-flight walk	ECG, CXR ECHO, MUGA Stress thallium
RESP	Pulm edema	Orthopnea Dyspnea	Rales	CXR
CNS	Stroke	Blackouts	Carotid bruit	Carotid study
RENAL	Nephropathy	Edema		BUN/Cr

Key References: James PA, Oparil S, Carter BL, et al.: 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8), *J Am Med Assoc* 311(5):507–520, 2014; Mauck KF, Sundsted KK: *Update in perioperative medicine: evidence published in 2014, Ann Intern Med* 162(9):W111–W116, 2015.

Perioperative Implications

Preoperative Risks

- Continue and/or increase antihypertensive medicine.
- Short-acting vasodilators prepared, including nitroglycerin.
- Assess myocardial and volume status.
- Anxiolytics on the day before surgery.
- Correction of electrolyte imbalances if present.

Monitoring

- Arterial monitoring
- Foley catheter to monitor urine output for traumatic or long procedures or for the procedures with expected significant blood loss
- Volume status monitoring depending on LV function (e.g., CVP, possibly PA cath, TEE)

Induction

- Preintubation opiates to blunt hypertensive response to laryngoscopy and ETT placement.
- Consider administration of the high end of the dose range of the IV induction agent with uncontrolled Htn. However, with significant cardiomyopathy consider etomidate to maintain cardiac hemodynamics.
- Use of defasciculating dose of nondepolarizing neuromuscular blocker to prevent mesenteric blood mobilization during abdominal muscle contractions during acetylcholine-induced muscular fasciculations.
- Avoiding significant fluctuations in blood pressure during induction and intubation by using lidocaine, fentanyl, and esmolol.
- Rapid correction of hypotension with ephedrine or phenylephrine.
- If severely hypertensive, consider vasodilators (e.g., nitroglycerin or nitroprusside prior to induction).

Maintenance

- Careful monitoring of the depth of anesthesia to avoid light anesthesia masking intravascular volume deficit.
- Maintain euvolemia.
- Preemptive analgesia to prevent primary sensitization phenomenon.
- Consider high-dose opioids if high hemodynamic stability is needed and prolonged postop ventilation is not an issue.

Extubation

- Adequate analgesia prior to termination of anesthesia
- Short-acting vasodilator and/or beta-blockers to prevent hypertension and tachycardia

Adjuvants

- Regional: May prevent severe increases in BP. Hypotension may occur due to vasodilation.
- Continuous infusions of nitroglycerin, nitroprusside, or esmolol.
- If treated with antihypertensives preop, severe hypotension may not respond to usual doses of vasoconstrictors.
- Consider use of alpha-$_2$ adrenomimetics.
- Inhalational agents, in particular, above 1 MAC can cause dose-dependent increase in heart rate and have different hemodynamic effects.

Postoperative Period

- Restart antihypertensive medication as soon as possible in postop period.
- Patch therapy for some drugs (e.g., clonidine and fentanyl) must be started 12 h prior to allow absorption from skin.
- Effective pain control using opioids and/or NSAIDs or continuous blockade.

Anticipated Problems/Concerns

- Watch for symptoms of CNS, renal, or myocardial dysfunction.
- Preop period affords opportunity to educate pts about importance of complying with antihypertensive therapy.
- Rebound hypertension if certain medications are discontinued (e.g., clonidine).
- Discontinue ACEIs and ARBs >10 h prior to surgery. Continuation of ACEIs and ARBs has increased risk of intraop hypotension. Discontinuation not associated with increased prevalence of postop Htn.
- Periop BP lability has been reported to increase the risk for stroke, acute kidney injury, and 30-day mortality in pts undergoing cardiac surgery.
- It is generally recommended that elective surgery be delayed for severe hypertension (diastolic BP >115 mm Hg, systolic >200 mm Hg) until BP <180/110.
- Expect with anesthetics, such as propofol or any inhalational agents, to have clinically apparent vasorelaxation of excessively constricted arterioles in long-standing hypertension, resulting in hypotension post induction.
- Human physiology and the Frank-Starling Law explain the rationale for treatments, such as diuretics in congestive heart failure and cardiomyopathies.

Hyperthyroidism

Michael F. Roizen

Risk

- Incidence in USA: 300,000-500,000 individuals/y develop hyperthyroidism. In addition, 7.5% of pregnant women become hyperthyroid (highest prevalence in second trimester).
- 1:1000 females; 1:3000 males.
- Race with highest prevalence: Unknown.

Perioperative Risks

- Risk related to occurrence of thyroid storm; increased risk of storm even if pt is made euthyroid prior to surgery.
- Some increased risk of resp insufficiency.
- Progressive increased risk of hypothyroidism after surgery on thyroid, radioactive Rx of hyperthyroidism, and thyroiditis.

Worry About

- Assessing that pt is euthyroid.
- Securing airway in pt with large goiter or displaced trachea.
- Postop risks of nerve injury (immediate stridor requires immediate reintubation), surreptitious bleeding (examine wound, which can drain externally, prior to PACU discharge), and thyroid storm (uncommon without another acute illness or >3 d postop).

Overview

- Endocrinopathy with CVD: Tachycardia (commonly idiopathic if no prior Dx of hyperthyroidism has been made), CHF, dysrhythmias AFIB as major manifestations.
- Other targets: Resp and CNS (decreases drive to breathe; worsens anxiety, psychoses) and metabolic (hypermetabolism and increased protein turnover, resulting in weakened muscles and malnourishment); can present as unintentional weight loss.
- If pt is euthyroid prior to operation, risk of storm and of periop CV problems is diminished by >90%.
- If pt is not euthyroid, delay operation if possible until he or she is euthyroid.
- If emergency (life-threatening trauma, ruptured viscus), use beta-blocking agents and iodides to decrease periop effects as well as further synthesis and release of thyroid hormones; keep pt in ICU until risk of storm has passed.

Etiology

- Multinodular diffuse enlargement (Graves disease); almost never malignant; soft large gland; thought to be autoimmune (thyroid-stimulating IgGs that bind to TSH receptors on thyroid associated with goiter and ophthalmopathy)
- Pregnancy (ectopic TSH-like substance)
- Thyroiditis (autoimmune) in acute phase, often with sore neck and hoarseness
- Thyroid adenoma: Toxic multinodular goiter (firm gland) later in life and rarely (almost never) malignant; unilateral solitary nodule with autonomous function earlier in life, also almost always benign
- Choriocarcinoma
- TSH-secreting pituitary adenoma
- Surreptitious ingestion of T_4 or T_3

Usual Treatment

- Antithyroid drugs for 2–6 mo; if hyperthyroidism recurs, retreat; if recurs again, consider surgery or radioiodine Rx.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Weakened tracheal rings, distorted/displaced trachea Ophthalmopathy	Snoring, hoarseness, neck pain	Ask pt to vocalize "e," examine airway and neck, look at the eyes, test for diplopia, note change over time in measure of eye protrusion	Check CXR (PA and lateral), lateral neck films; CT scan or US of neck
CV	Dysrhythmias, AFIB, sinus tachycardia, mitral valve prolapse CHF, cardiomyopathies	Palpitations; increased HR during sleep, DOE, orthostatic SOB	Standard exam	Rhythm strip or full ECG CV system is involved in either Hx or PE
GI	Weight loss, diarrhea, dehydration Hepatic enzyme abnormality due to medications	Dizziness on arising; Hx of diarrhea, constipation	Skin turgor; other measures of volume status such as orthostatic vital signs	Increased serum alkaline phosphatase
HEME	Mild anemia, thrombocytopenia; agranulocytosis secondary to propylthiouracil or methimazole		Skin/mucous membranes for infection/petechiae	CBC with platelet count and differential
CNS		Shaking, anxiety, emotional lability	Reflex speed, tremor, nervousness, mental status	
METAB	Need to assess if euthyroid and/or malnourished	Refer to all other systems, especially reflex speed, tremor, heat intolerance, fatigue, weakness, weight loss, anorexia, increased appetite	Reflex speed; HR	Free T_4

Key Reference: Roizen MF, Fleisher L: Anesthetic implications of concurrent diseases. In Miller RD et al, editors: *Anesthesia,* ed 7, New York, 2010, Elsevier, pp 1077–1080.

Perioperative Implications

- See Thyroidectomy, Subtotal.

Preoperative Preparation
- Assess if euthyroid.
- Assess for associated autoimmune diseases.

Preinduction/Induction
- Prehydrate liberally if CV status will tolerate it.
- Check and protect eyes.

Anesthetic Technique
- No one technique has proved superior.
- Hyperthyroidism is an associated risk factor for halothane hepatitis.

Monitoring
- Temperature. (Also place cooling blanket on OR table for possible treatment of thyroid storm.)
- Consider invasive monitoring if pt has dilated cardiomyopathy/thyroid storm/severe dysrhythmia.
- If head-up position is utilized, consider air embolus monitoring and therapy.

Airway
- Consider awake fiberoptic intubation if there are questions regarding adequacy of airway or distortion/involvement of the trachea.
- Consider armored tube or equivalent if tracheal rings are affected.

Induction/Maintenance
- Routine

Adjuvants
- Usually no requirement for muscle relaxants

Anticipated Problems/Concerns

- Thyroid storm is a life-threatening condition if hyperthyroidism has been severely exacerbated by illness or operation. Manifested by hyperpyrexia, tachycardia, and striking alterations in consciousness. Early signs include delirium, confusion, mania, excitement. Differential Dx: Malignant hyperthermia, pheochromocytoma crisis, NMS.
- Rx includes supportive care, methimazole or propylthiouracil followed in 1 h by iodides and propranolol or atenolol; these decrease conversion of the less active T_3 to the more active T_4.
- Surreptitious bleeding behind neck bandages or into chest if minimally invasive technique is used from axilla, can suddenly compromise airway function or result in CV collapse.
- Injuries to the recurrent laryngeal nerve after thyroidectomy usually result in damage to abductor fibers, resulting in hoarseness.
- Bullous glottic edema can require immediate reintubation.
- Occasionally late tetany (usually 2–3 d after thyroidectomy) can occur from accidental removal of or damage to parathyroid glands.

Hypertriglyceridemia

Andrew Bowdle

Risk

- Prolonged propofol infusion due to lipid vehicle
- Genetic defects in triglyceride metabolism
- Component of the metabolic syndrome (obesity, hypertriglyceridemia, low HDL, Htn, diabetes)

Perioperative Risks

- Associated with atherosclerosis, coronary, and cerebrovascular disease.
- Hyperglycemia (metabolic syndrome) increases risk of surgical wound infection.
- Severe hypertriglyceridemia may cause acute pancreatitis.

Worry About

- Coronary and cerebrovascular disease
- Pancreatitis
- Blood sugar control in metabolic syndrome
- Propofol infusion syndrome if hypertriglyceridemia is due to prolonged propofol infusion (hypertriglyceridemia due to propofol may occur with or without other features of propofol infusion syndrome, including rapidly progressive myocardial failure, bradycardia, ECG changes resembling Brugada syndrome, lactic acidosis, rhabdomyolysis, elevated serum creatine kinase, urea and potassium, elevated liver enzymes, hepatomegaly, and lipemic blood)

Overview

- High triglycerides are strongly associated with coronary artery atherosclerosis.
- Normal <150 mg/dL, borderline high 150–199 mg/dL, high 200–499 mg/dL, very high >500.
- >1000 mg/dL: Severe hypertriglyceridemia may cause acute pancreatitis.
- Prolonged and/or high-dose propofol infusion may produce hypertriglyceridemia.

Etiology

- Primary hypertriglyceridemia is caused by a variety of disorders of triglyceride metabolism.
- Secondary hypertriglyceridemia is caused primarily by obesity, diabetes, nephrotic syndrome, hypothyroidism, pregnancy, restrogen replacement, tamoxifen, beta-blockers, immunosuppressive medications, HIV antiretroviral agents, and retinoids.

Usual Treatment

- Diet and weight loss if due to obesity
- Lipid-lowering drugs: Statins for triglycerides <500 mg/dL (mainly to reduce risk of coronary artery atherosclerosis), fibrates for triglycerides >500 mg/dL
- If due to propofol infusion, discontinue or reduce infusion

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Atherosclerosis	Hx of coronary disease or heart failure	JVD, peripheral edema, S_3, S_4	ECG, CXR, coronary CT, ECHO, stress test, coronary angiography
ENDO	Associated with altered glucose metabolism	Hx of diabetes, ketoacidosis; hypothyroidism		Blood glucose, HgbA1C; thyroid function tests when applicable
RENAL	Caused by nephrotic syndrome, renal failure	Urinary frequency		BUN, Cr, lytes
CNS	Atherosclerosis, cerebrovascular disease	TIA or stroke	Neurologic exam	CT angiography, head CT
GI	Fat accumulation in liver and spleen; acute pancreatitis	Abd discomfort, pain	Hepatosplenomegaly, obesity	Amylase, lipase
DERM			Cutaneous xanthoma	

Key References: Bowdle A, Richebe P, Lee L, et al.: Hypertriglyceridemia, lipemia and elevated liver enzymes associated with prolonged propofol anesthesia for craniotomy, *Ther Drug Monit* 36(5):556–559, 2014; Brinton EA: Management of hypertriglyceridemia for prevention of atherosclerotic cardiovascular disease, *Cardiol Clin* 33(2):309–323, 2015.

Perioperative Implications

Preoperative Preparation

- Blood glucose.
- Severe hypertriglyceridemia should be controlled prior to elective surgery due to risk of pancreatitis.

Monitoring

- Determined based on coexisting coronary or cerebrovascular disease
- Blood glucose

Airway

- If obese, increased risk of difficult intubation.
- If obese, rapid sequence intubation may be advisable due to aspiration risk. Diabetes may cause gastroparesis.

Induction

- Determine based on coexisting coronary or cerebrovascular disease.
- Avoid propofol if history of propofol infusion syndrome (rare).

Maintenance

- Propofol infusion may cause hypertriglyceridemia if prolonged and/or high dose. Consider avoiding propofol infusion if preexisiting very high or severe hypertriglyceridemia.

Extubation

- Consider aspiration risk, such as obesity and diabetic gastroparesis (same as for induction). Extubate awake if at risk.

Postoperative Period

- Blood sugar control.
- Monitoring as dictated by coronary and cerebrovascular disease.
- Consider risk of obstructive sleep apnea if obese.
- If intubated and sedated postop, consider avoiding propofol infusion if preexisting very high or severe hypertriglyceridemia.

Anticipated Problems/Concerns

- Complications due to comorbidities: Obesity, diabetes, coronary artery disease, cerebrovascular disease, obstructive sleep apnea.
- Severe hypertriglyceridemia may cause acute pancreatitis.

Hypokalemia

Bryce C. Bernard | Daniel Cormican | Shawn T. Beaman

Risk

- Defined as plasma K^+ <3.5 mEq/L.
- Common conditions and/or treatments place pts at increased risk, including
  - Those on diuretics (especially loop and thiazide diuretics) to treat Htn, CHF, and so forth.
  - Those experiencing significant GI fluid loss (e.g., vomiting, diarrhea, or gastric suction).
  - Those with increased serum pH (metabolic or respiratory alkalosis).

Perioperative Risks

- Increased risk of cardiac dysrhythmias (with greater concern in those with preexisting heart disease and in setting of acute onset hypokalemia)
- Increased risk of muscle weakness (which includes possible respiratory muscle weakness and prolonged neuromuscular blockade)
- Increased risk of GI hypomotility

Worry About

- Cardiac dysrhythmias are the most worrisome complication of hypokalemia.
- Many medications regularly used in periop treatment can cause or worsen hypokalemia (e.g., diuretics, antibiotics, β_2-agonists, epinephrine).
- Pts requiring significant/urgent K^+ replacement may require central line placement.
- Over-replacement: Any pt requiring K^+ replacement may be at risk for hyperkalemia and thus the malignant dysrhythmias associated with hyperkalemia.

Overview

- K^+ ions have essential role in maintaining cellular resting membrane potentials and in generating functional activity in muscle cells, neurons, and cardiac tissue.
- Overall, intracellular K^+ concentration is approximately 30 times greater than extracellular K^+ concentration; this ratio is maintained by cell membrane Na^+/K^+ ATPase.
- Decreases in extracellular K^+ impairs nml gradients required for membrane potential/action potential transmission.
- Acute/rapid decreases in serum K^+ concentration create more concerning derangements in cellular membrane potential physiology than chronic or slowly developing decreases in K^+.

Etiology

- Inadequate K^+ intake: Seen in eating disorders, inability to eat, "tea and toast" diet, alcoholism, and those receiving K^+-poor TPN
- Increased K^+ excretion:
  - Renal losses: Mineralocorticoid excess (primary or secondary hyperaldosteronism, Cushing disease, congenital adrenal hyperplasia), hyperreninism, congenital renal disorders (Bartter/Gitelman/Liddle syndromes), medication-induced (loop and thiazide diuretics, carbonic anhydrase inhibitors, amphotericin B, some penicillins, gentamicin)
  - GI losses: Vomiting, diarrhea, NGT/OGT suction, villous adenoma, ureterosigmoidostomy
- Intracellular K^+ shifts: alkalosis (metabolic or respiratory), medication induced (insulin administration, β_2-agonists, epinephrine, terbutaline, ritodrine), refeeding syndrome, periodic paralysis, barium toxicity

Usual Treatment

- Identify and attempt to correct the underlying factors causing the hypokalemia (e.g., adjust diet intake, review medications, lower pH of pts with alkalosis by treating primary disorder).
- K^+ repletion: It is reported that each 10 mEq of K^+ given will raise serum K^+ by 0.1 mEq/L.
  - Oral K^+: Can use K^+ paired with gluconate, phosphate, chloride, or citrate, with delivery via tablet or solution.
  - IV K^+: Most commonly as K^+ chloride. Careful repletion required via programmable infusion pump to avoid hyperkalemic complications; patients receiving >10–20 mEq/h should have cardiac monitoring in place. Peripheral IV administration can cause burning sensation and vascular epithelium damage; consider placement of central line.
- Coexisting hypomagnesemia: requires correction before repletion of potassium will be successful.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Muscle weakness Cramping/myalgia	Decreased mobility, falls, decreased ADL Complaints of muscle pain	Decreased muscle strength	TOF intraoperative
RESP	Resp muscle failure	SOB, hypoventilation, ventilator dependence	Poor inspiratory effort, low TV	ABG, NIF
CV	Dysrhythmias Vasomotor instability	Complaints of palpitations, syncope, cardiac arrest Syncope, falls, disorientation	 Refractory shock, hypotension	ECG
GI	Decreased GI motility	Constipation, abdominal pain	Loss of bowel sounds, abd tenderness and distention	KUB
RENAL	Polyuria Polydipsia Increased renal ammonia Edema and sodium retention	Frequent urination Frequent drinking		 Urine ammonia Urine sodium

Key References: Gennari FJ: Hypokalemia, *N Engl J Med* 339(7):451–458, 1998; Wong KC, Schafer PG, Schultz JR: Hypokalemia and anesthetic implications, *Anesth Analg* 77(6):1238–1260, 1993.

Perioperative Implications

Preoperative Preparation

- Obtain serum K^+ concentration preop if pt presents with risk factors for hypokalemia.
- Attempt to identify and/or address the etiology of hypokalemia.
- For elective cases, replete serum K^+ concentration to >2.6 before going to OR. Discuss concerns and implications with pt/family, and surgical team.
- Have ACLS medications on hand and transport with cardiac monitoring.

Monitoring

- ECG/continuous cardiac monitoring (watch for T wave flattening, U waves, PVC, VT/VF).
- BP cuff or arterial line (watch for hypotension related to vasomotor insufficiency).
- Periodic ABG and lyte panels as needed (watch for pH and K^+ trend).
- Twitch monitor (watch for prolonged neuromuscular blockade).

Maintenance

- Judicious use of medications associated with causing or exacerbating hypokalemia.
- Control glucose and fluid volume.
- Avoid hyperventilation and respiratory alkalosis.

Anticipated Problems/Concerns

- Pts with symptomatic hypokalemia (especially with cardiac symptoms) that are not well controlled after initial treatments may need elective surgical procedures delayed.
- Cardiac dysrhythmias are of greatest concern in hypokalemia because these can be lethal. Risk is greatest when hypokalemia is acute and serum K^+ <3.0.
- Preop problems: ECG changes and volume status (related to diuretics or polydipsia).
- Intraop problems: Persistent hypotension after induction (related to refractory vasomotor response to catecholamines), prolonged neuromuscular blockade, respiratory muscle weakness.

Hypomagnesemia

Sara M. Skrlin

Risk

- 12% of all hospitalized pts as well as 44–60% of all pts admitted to medical/surgical and pediatric ICUs, are hypomagnesemic.
- Associated with
  - Poor nutrition.
  - GI losses: Diarrhea and severe vomiting; malabsorption (steatorrhea, bowel resection, intestinal fistulas, celiac disease); acute pancreatitis; medications (proton pump inhibitors, laxatives).
  - Renal losses: Medications (loop/thiazide diuretics, aminoglycosides, amphotericin B, cisplatin, foscarnet, cyclosporine); familial renal Mg^{2+} wasting syndromes; uncontrolled diabetes mellitus; metabolic acidosis; alcohol abuse.
  - Miscellaneous: Prolonged IV therapy; massive blood transfusions; digitalis.

Perioperative Risks

- Arrhythmias (atrial, ventricular, prolonged QT, and torsades de pointes). Hypomagnesemia should be corrected prior to elective procedures due to the potential for malignant arrhythmias.
- Worsening cardiac ischemia and CHF.
- Increased susceptibility to seizures, bronchoconstriction, and vasospasm.
- Refractory hypokalemia and hypocalcemia.
- Resistance to vasodilators.
- Aggravates insulin resistance in the diabetic pt.

Worry About

- Weakness, lethargy, paresthesias, muscle spasms.
- Seizures (especially in preeclampsia).
- Arrhythmias (especially torsades de pointes).
- During treatment of hypomagnesemia: Burning at IV site, overall sense of warmth and flushing. Transient and mild hypotension may occur if $MgSO_4$ is given too fast. Administration of Mg^{2+} will also potentiate the neuromuscular blockade with all nondepolarizing drugs.

Overview

- Normal range of plasma Mg^{2+} is 1.7–2.4 mg/dL. Most symptomatic pts have levels <1 mg/dL.
- Mg^{2+} levels are not routinely checked in screening tests. Hypomagnesemia should be suspected, especially in chronic diarrhea, alcoholism, malnutrition, long-term hospitalization, and hypoalbuminemia.
- Mg^{2+} is primarily an intracellular ion. Plasma levels may not reflect the true magnitude of deficit. Intracellular shift may occur with the administration of insulin and thyroid hormone.
- Normomagnesemic Mg^{2+} depletion has been described; if clinical suspicion of hypomagnesemia is present, Mg^{2+} should be administered, even with normal plasma levels.
- If it is unclear from the pt's history, a 24-h urine sample may help to differentiate renal from nonrenal causes. Mg^{2+} loss of less than 3–4 mEq/d supports a renal etiology.
- Alternatively, a fractional excretion of Mg^{2+} can be calculated in a spot urine sample.
  - $FE_{Mg} = [(U_{Mg} \times P_{Cr})/(0.7 \times P_{Mg}) \times U_{Cr}] \times 100$, where U_{Mg}/U_{Cr} and P_{Mg}/U_{Cr} denotes urinary and plasma concentrations of Mg^{2+} and Cr.
  - Usually, FE_{Mg} greater than 2% indicates renal Mg^{2+} wasting.

Usual Treatment

- Chronic hypomagnesemia may be treated with oral magnesium.
- Acute administration of 1-2 g $MgSO_4$ IV over 20-30 min for pts with symptoms. Significantly decreased Mg^{2+} levels may require 4-8 g $MgSO_4$ IV over the next 24 h.
- If Mg^{2+} replacement is needed, give at the beginning of an anesthetic because $MgSO_4$ may interfere with neuromuscular blockade reversal.
- Torsades de pointes can be treated with 1–2 g $MgSO_4$ IV push over 5–20 min.
- Usual doses for preeclampsia are 4–6 g bolus over 15-20 min followed by 1–2 g/h, targeting a plasma level around 6 mg/dL.
- Each g of $MgSO_4$ has 98 mg of elemental Mg^{2+} (equivalent to 4 mmol or 8 mEq).
- As long as renal function is intact, excessive Mg^{2+} levels will be cleared over several h. In pts with kidney disease, Mg^{2+} replacement should be done cautiously.

Therapeutic Uses

- Mg^{2+} has multiple functions including, but not limited to, decreasing acetylcholine in motor nerve terminals,

acting as a vasodilator, a Ca^{2+} antagonist, and acting on the myocardium to slow the rate of conduction through the SA node. In addition to correction of hypomagnesemia, Mg^{2+} replacement can be used for the following:

- CV: Myocardial protection, decreases CHF, improves contractility, diastolic relaxation, attenuates or prevents tachycardic arrhythmias, minimizes changes in heart rate and BP during intubation, decreases the risk of postop atrial fibrillation in cardiac surgery.
- Neurologic: Has neuroprotective effects, but the degree to which it is clinically useful is uncertain.
- Endocrine: Attenuates insulin resistance; helps in hemodynamic control in pheochromocytomas by causing arteriolar vasodilation and decreasing the hypertensive response to catecholamines.
- Obstetric: Widespread use in treatment of preeclampsia/eclampsia and decreases risk of cerebral palsy in preterm infants.
- Pulm: Bronchodilation in severe asthmatic.
- Anesthesia: May decrease need for inhalation agent to maintain same BIS level.
- Pain: May decrease the need for postop opiates through its blockade of NMDA receptors.
- MS: Relaxes muscle rigidity and decreases autonomic dysfunction in tetanus.
- Intoxication and recreational drugs: Helpful to treat catecholamine excess and hypertension associated with cocaine and methamphetamines.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Seizures, cerebral vasospasm (after SAH)	Lethargy, SAH (vasospasm)	Altered mental status	Plasma Mg^{2+}, TCD, cerebral angiogram
CV	Arrhythmias, torsades, wide QRS, CHF (impaired diastolic relaxation)	Tachyarrhythmia, Htn, dyspnea		ECG, plasma Mg^{2+}, BNP, ECHO
MS	Hypocalcemia (decreased secretion and resistance to PTH)	Weakness, tetany	Chvostek and Trousseau signs	Plasma Ca^{+2}, Mg^{2+}
ENDO	Insulin resistance, may affect lipid profile	Diabetes (types 1 and 2) Hyperlipidemia		Glucose, plasma Mg^{2+}, HDL, triglycerides
RESP	Bronchospasm	Asthma	Wheezing	Plasma Mg^{2+}
RENAL	Hypokalemia (K^+ loss from loop of Henle)	Alcohol abuse, nephrotoxins (antibiotics, chemo), diuretics		Cr, BUN Plasma K^+, Mg^{2+}

Key References: Herroeder S, Schönherr ME, De Hert SG, et al.: Magnesium—essentials for anesthesiologists, *Anesthesiology* 114(4):971–993, 2011; Ayuk J, Gittoes NJ: Treatment of hypomagnesemia, *Am J Kidney Dis* 63(4):691–695, 2014.

Perioperative Implications

Preoperative Preparation

- Check serum Mg^{2+} level (<1.7 mg/dL is hypomagnesemia).
- Obtain 12-lead ECG.
- Start replacing Mg^{2+} (e.g., 2 g IV over 20 min; faster replacement safe but may cause burning at the IV site).

Monitoring

- Standard ASA monitors.
- Plasma Mg^{2+} levels (normal range 1.7–2.5 mg/dL).
- TOF monitoring (replacing Mg^{+2} potentiates NMB agents).
- Consider BIS (or other depth of anesthesia) monitoring because replacing Mg^{2+} may alter anesthetic requirement.

Induction

- Mg^{2+} IV bolus during induction is safe (e.g., 2–4 g IV bolus).
- May cause mild and transient drop in BP.
- Replacing Mg^{2+} minimizes changes in heart rate and BP during intubation.
- Hypomagnesemia may cause or exacerbate bronchospasm.

Maintenance

- Replacing Mg^{2+} attenuates or prevents tachyarrhythmias and may convert some types of malignant arrhythmias.
- Insulin resistance may occur in the hypomagnesemic pt.

Emergence

- Replacing Mg^{2+} attenuates shivering.
- Replacing Mg^{2+} maintains hemodynamic stability.
- Titrate NMB agents and reverse residual NMB, especially if Mg^{2+} was replaced intraop.
- Hypomagnesemia may worsen bronchospasm in asthmatic pts.

Postoperative Period

- Actual efficacy of Mg^{2+} as an analgesic adjuvant is currently unclear, but Mg^{2+} replacement may lead to decreased opioid consumption.
- Increased catecholamine levels may exacerbate arrhythmias in the hypomagnesemic pt.

Anticipated Problems/Concerns

- Although Mg^{2+} replacement is usually well tolerated, potential problems with overdose include
  - Levels above 8–10 mg/dL may cause diaphragmatic weakness, and above 10–12 mg/dL may cause widening of QRS and conduction blocks. These levels are rarely reached with recommended doses and in the absence of decreased GFR.
  - Potentiation of neuromuscular blockade.

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Hyponatremia

Alan David Kaye | Burton D. Beakley | Ethan Phan

Risk

- Preop hyponatremia is a prognostic marker for increased 30-d mortality, major cardiac events, wound infection, and pneumonia.
- Premenopausal women, especially those undergoing procedures associated with rapid irrigant absorption, are at particularly high risk of both symptomatic hyponatremia and osmotic demyelination with Na^+ correction.
- Conditions associated with SIADH or adrenocortical insufficiency (Addison disease).
- Elderly taking diuretics.
- Pts with liver, heart, or renal failure.
- Hyponatremia especially common in elderly pts and associated with increased morbidity and mortality.
- Up to 10–15% of men undergoing TURP.
- Infants and/or children receiving multiple tap H_2O enemas.

Perioperative Risks

- Risk of CV collapse with adrenocortical insufficiency and inability to cope with stress of surgery.
- Iatrogenic dilution in TURP and endoscopic gynecologic procedures associated with CNS, cardiopulmonary, and skeletal muscle abnormality.
- Increased ADH secretion extremely common periop and may cause further decrease in serum Na^+.
- Isotonic saline (0.9%) will result in free H_2O gain and decrease in serum Na^+ in presence of SIADH.

Overview

- Normal serum sodium levels are 135 to 145 mEq/L. Hyponatremia defined as serum Na^+ >135 mEq/L; most common cause is an excess of total body H_2O, usually associated with low serum osmolality (<275 mOsmol/kg).
- Hyponatremia can be associated with low, normal, or high tonicity (tonicity defined as the contribution to osmolality of solutes that cannot freely cross cell membranes).
- There are at least two systems of classification for hyponatremia with low serum osmolality: one according to the level of inappropriately elevated or suppressed ADH and the other according to the volume status (hypovolemia, normovolemia, or hypervolemia).
- Sodium and water balance in the body regulated by the kidney affects the plasma tonicity (ADH mechanism) and effective arterial blood volume (renin-angiotensin-aldosterone system).

- Change in tonicity causes free H_2O shift leading most importantly to cerebral intracellular volume changes (edema in hypotonic hyponatremia). Extracellular volume may be decreased, normal, or increased.

Etiology

- Most common causes of severe hyponatremia in adults: Postop state, thiazide diuretics, clinical scenarios associated with SIADH, polydipsia in psychiatric pts, TURP.
- Multiple tap H_2O enemas most common cause in infants and children.
- Hypervolemic hyponatremia:
  - Cirrhosis, nephrotic syndrome.
  - Cardiac failure.
  - Renal failure postop.
  - TURP.
- Normovolemic hyponatremia:
  - SIADH (associated with CNS, pulm diseases/malignancy, pain, drugs, stress).
  - Endocrine: Glucocorticoid deficiency, hypothyroidism.
  - Pseudohyponatremia syndrome, for example, factitious hyponatremia (normotonic hyponatremia): Hyperlipidemia states (e.g., chylomicronemia) or hyperproteinemia.
- Hypovolemic hyponatremia:
  - Renal loss (diuretics, mineralocorticoid deficiency, osmotic diuresis, cerebral salt wasting, ketonuria, renal tubule acidosis/metabolic acidosis).
  - Extrarenal loss (trauma, vomiting/diarrhea, burns, pancreatitis).
- Diagnosis:
  - Laboratory: Urine osmolarity, serum osmolarity, urine sodium concentration.
  - Imaging: Consider head CT and CXR.
- Approach to treatment:
  - Based on overall risk stratification.
  - Duration: Acute = hyponatremia developing within last 24 h; subacute = hyponatremia present for 24–48 h; chronic = hyponatremia present for greater than 48 h.
  - Severity: Mild (130–135 mEq/L); moderate (125–129 mEq/L); profound (125 mEq/L or less).
  - Symptoms: Absent or present.

Usual Treatment

- Sodium levels are corrected by treating the underlying disorder, fluid restrictions, administering oral or IV sodium chloride, or vasopressin receptor antagonist therapy, depending on the etiology and severity of hyponatremia.
- Goal of sodium correction: increase plasma sodium concentration 6 mEq/L (not to exceed 12 mEq/L) in first 24 h, followed by goal increase of 8 mEq/L every 24 h after to serum sodium 130 mEq/L.
- Severe symptomatic hyponatremia: immediate treatment with IV infusion of hypertonic 3% saline with goal of 6 mEq/L increase in serum sodium over several h (not to exceed 12 mEq/L in 24 h).
- Asymptomatic or moderate hyponatremia with mild-to-moderate symptoms:
  - Hypovolemic hyponatremia: nonemergent therapy with IV infusion of isotonic saline with goal of 6 mEq/L (not to exceed 12 mEq/L) slowly over 24 h.
  - Hypervolemic hyponatremia: salt and fluid restrictions, ± loop diuretics with goal of 6 mEq/L (not to exceed 12 mEq/L) slowly over 24 h. Vasopressin (V2) receptor antagonist can also be considered.
  - Close monitoring of serum electrolytes and fluid intake/output during correction therapy is critical (every 2–4 h). Also pt's mental status should also be reassessed regularly.
  - Dose of sodium required to correct a deficit may be calculated using the following formula:

$$\text{Dose (mEq)} = (\text{Weight [kg]} \times (140 - [\text{Na}]) [\text{mEq/L}]) \times 0.6.$$

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dysrhythmias	Palpitations		Oscillation, ECG (wide QRS, increased ST, VT/VF)
	CHF, hypervolemia	DOE, orthopnea	S_3, rales	CXR
	Hypovolemia	Lightheadedness, weakness	Orthostatic hypotension, CVP, tachycardia	BP, CVP
RESP	Pulm edema	DOE	S_3, rales	CXR
CNS	Confusion, restlessness, gait disturbance, lethargy, seizures, visual disturbances, obtundation, coma			Serum Na^+ <115–120 mEq/L associated with profound symptoms
MS	Weakness, cramps	Weakness, cramps	Weakness, hyporeflexia	Reflexes
RENAL	Free H_2O retention Salt wasting			Urine Na^+, serum, and urine osmolality

Key References: Spasovski G, Vanholder R, Allolio B, et al.: Clinical practice guideline on diagnosis and treatment of hyponatraemia, *Nephrol Dial Transplant* 29(Suppl 2):i1–i39, 2014; Leung AA, McAlister FA, Rogers SO Jr, et al.: Preoperative hyponatremia and perioperative complications, *Arch Intern Med* 172(19):1474–1481, 2012.

Perioperative Implications

Preinduction

- Ensure medical optimization of comorbid diseases (hyponatremia greater risk with increasing severity of disease: ASA III and IV).
- Caution with sedatives.
- Preop lytes in high-risk procedures.
- Consider regional in TURP to facilitate monitoring of mental status.
- Increased ADH and volume changes associated with surgical trauma likely to decrease Na^+ further.
- Identify irrigating solution and prepare for irrigant-specific side effects.

Monitoring

- TURP:
  - Metal status with regional technique.
  - Automatic versus manual fluid monitoring system for fluid absorption.
  - TURP procedures of long duration and with significant bleeding or increased hydrostatic pressure of irrigant predictive for large amounts of irrigation fluid absorption (increased vigilance required).
  - Consider EEG with GA.
  - Consider invasive monitoring (CVP/PA cath/TEE) with development of TURP syndrome and CHF in elderly pts.
- Hyponatremic pts undergoing therapy to correct serum Na^+:
  - Serum Na^+.
  - Urine output.
  - Mental status.
  - ECG.

General Anesthesia

- Sodium concentration >130 mEq/L usually considered safe for pts undergoing general anesthesia, whereas moderate-to-severe hyponatremia should be postponed.
- For general anesthesia serum sodium levels should be corrected to greater than 130 mEq/L, even when no neurologic symptoms are present.
- Isotonic fluids for volume resuscitation.
- Ensure adequate depth of anesthesia as pain and/or stress associated with ADH release.

Regional Anesthesia

- Spinal or epidural with T10 block for TURP.
- Prepare for emergency airway protection if respiratory distress, seizures, obtundation.

Postoperative Period

- Monitor mental status for agitation, confusion, somnolence.
- Adequate pain management to reduce sympathetic-related Na^+ and water retention.
- Close monitoring for administration of hypotonic solutions.
- Monitor daily serum Na^+ (strict monitoring in high-risk pts).
- Initiate appropriate therapy in symptomatic or severely hyponatremic pts.
- Avoid too rapid correction and associated demyelination syndrome.
- Restore blood and/or volume loss if necessary.

Hypoparathyroidism

David N. Flynn | Jason D. Walls

Risk

- Most common cause of both acute and chronic hypoparathyroidism is surgery of the neck, including thyroidectomy, parathyroidectomy, and radical neck dissection.
- Nonsurgical hypoparathyroidism is rare. Etiologies include autoimmune disease, infiltrative diseases (e.g., hemochromatosis, Wilson disease), hypomagnesemia or hypermagnesemia, and genetic disorders involving PTH biosynthesis or parathyroid development (e.g., DiGeorge syndrome).

Perioperative Risks

- Severe hypocalcemia leading to heart failure, hypotension, arrhythmias, laryngospasm, bronchospasm, seizure, or altered mental status

Worry About

- Hypocalcemia and other lyte abnormalities.
- Pts on oral calcium maintenance therapy may require IV supplementation during long surgical procedures.
- Watch for periop causes of hypocalcemia, including both respiratory or metabolic alkalosis and citrate toxicity from large volume RBC transfusions.

Overview

- PTH is normally secreted by the parathyroid glands to maintain calcium and phosphorous homeostasis.
- PTH impacts calcium and phosphorous by increasing (1) bone resorption to release calcium and phosphorous, (2) calcium reabsorption and phosphorous excretion in the kidney, and (3) vitamin D activation, indirectly resulting in an increased absorption of calcium and phosphorous by the intestines.
- Hypoparathyroidism is characterized by hypocalcemia with an inappropriately low PTH level. It is usually accompanied by an elevated serum phosphorous level.
- Symptoms of hypoparathyroidism are due to hypocalcemia, with the severity of symptoms dictated by disease chronicity, rapidity of calcium concentration change, and the overall severity of hypocalcemia.
- Symptoms may range from mild (paresthesias, cramping, tetany) to severe (seizure, laryngospasm, altered mental status, heart failure, hypotension, cardiac arrhythmias).

Etiology

- Most common etiology of acute and chronic hypoparathyroidism is postsurgical, specifically following surgery on the neck.
- Incidence of hypoparathyroidism after total thyroidectomy is 0.5–10%, but it is usually transient. Permanent hypoparathyroidism persisting 6 mo after surgery occurs in only 4.4% of pts.
- Postsurgical hypoparathyroidism is usually evident within several h of surgery and is caused by hypoparathyroid gland damage, removal, or devascularization.
- Acquired hypoparathyroidism can also be caused by isolated autoimmune destruction of parathyroid tissue or as part of an autoimmune polyendocrine syndrome, antibodies to the calcium-sensing receptor, neck radiation, ^{131}I therapy, and infiltrative diseases, including hemochromatosis, thalassemias, and granulomatosis diseases.
- Reversible hypoparathyroidism can be caused by severe hypomagnesemia (e.g., from chronic malnutrition or alcoholism) or hypermagnesemia (e.g., from tocolytic therapy).
- Congenital hypoparathyroidism is seen in genetic disorders involving parathyroid development (e.g., DiGeorge syndrome) or PTH biosynthesis.

Usual Treatment

- Chronic hypoparathyroidism is managed with oral calcium and vitamin D supplementation.
- Pts with chronic hypoparathyroidism presenting for surgery should be maintained on supplemental therapy or given IV calcium when unable to tolerate oral medications.
- Acute severe postsurgical hypoparathyroidism causing ECG abnormalities, cardiovascular instability, seizure, or airway compromise must be treated as a medical emergency with IV calcium. Calcitriol should be given as soon as reasonably possible, although it takes several h to have an effect.
- Mild symptoms (paresthesias, muscle aches) or asymptomatic hypocalcemia can often be treated with oral calcium and calcitriol.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT			Examine for previous neck surgery; craniofacial abnormalities	
RESP	Laryngospasm Bronchospasm Respiratory muscle weakness	Dyspnea Poor cough	Tachypnea, respiratory distress Wheeze/stridor	
CV	Heart failure QTc prolongation Arrhythmia	Exercise intolerance	Displaced PMI Peripheral edema	TTE (if heart failure suspected) ECG (QT/QTc)
CNS	Paresthesias Altered mental status Seizure Muscle cramping/tetany	Hx of seizure, confusion, numbness/tingling, muscle pain	Chvostek sign Trousseau sign, disorientation, obtundation	Lytes (including total and ionized calcium, magnesium, and phosphorous) Serum PTH, serum albumin
MS	Muscle cramping/tetany Myopathy	Muscle pain, weakness	Examine strength	Lytes, CK

Key References: Shoback D: Clinical practice. Hypoparathyroidism, *N Engl J Med* 359(4):391–403, 2008; Khan MI, Waguespack SG, Hu MI: Medical management of postsurgical hypoparathyroidism, *Endocr Pract* 17(Suppl 1):18–25, 2011.

Perioperative Implications

Preoperative Preparation

- Perform a history and physical exam focusing on previous neck surgery, family history of hypocalcemia, autoimmune endocrinopathies, and congenital defects.
- Assess for signs and symptoms of hypocalcemia, including cardiac and respiratory compromise.
- Check serum lytes, including total and ionized serum calcium, magnesium, and phosphorous. Correct lytes if necessary.
- Continue oral calcium and vitamin D supplemental therapy. Consider IV calcium replacement if symptomatic or serum calcium markedly reduced.
- Consider further laboratory tests if unclear etiology including creatine, albumin, intact PTH, and 25-hydroxyvitamin D.
- Check ECG for baseline QTc.

Monitoring

- Standard ASA monitors.
- Monitor ECG trend. (QTc changes often correlate inversely with calcium concentration.)
- Consider invasive monitoring and access with severe hypocalcemia requiring IV calcium replacement, need for frequent blood sampling, or heart failure monitoring.

Airway

- Assess for potential difficult airway in pts with previous neck surgery or radiation.

Preinduction/Induction

- Choice of induction agent and technique dictated by pt's cardiopulmonary health.
- Untreated hypocalcemia may increase risk of hypotension.

Maintenance

- Continue to monitor serum lytes. Specifically recheck ionized calcium every 1–2 h if ongoing IV therapy.
- Avoid respiratory and metabolic alkalosis.
- Maintain euvolemia. Pts with congestive heart failure may benefit from diuresis.

Extubation

- Greatest risk is development of acute hypoparathyroidism leading to hypocalcemia and respiratory distress, laryngospasm, or bronchospasm following difficult thyroid/parathyroidectomy.
- For pts with preexisting hypoparathyroidism, ensure lytes are repleted prior to extubation and ensure adequate reversal of neuromuscular blockade.

Postoperative Period

- Calcium levels reach the nadir 3 d after surgery, but pts with severe, acute hypoparathyroidism may become symptomatic shortly after surgery.

Anticipated Problems/Concerns

- Severe postop hypocalcemia and potential life-threatening symptoms, including laryngospasm
- Maintenance of serum calcium level throughout periop period for pts with chronic hypoparathyroidism

Hypophosphatemia

William H. Daily | Lee A. Fleisher

Risk

- Incidence: 1% of population, 5–20% of hospitalized pts

Perioperative Risks

- Acute respiratory or cardiac failure, generalized weakness, confusion, seizures

Worry About

- Periop respiratory or cardiac failure.
- Too rapid correction can cause hypocalcemia or Ca^{2+} deposition in tissues.

Overview

- Of total body phosphorus, 90% is distributed in bone, 10% intracellularly, and <1% in extracellular fluid.
- Normal ionized phosphorus (Pi) is 2.7–4.5 mg/dL. It may fall by 30% after administration of carbohydrates/insulin. Higher in childhood and in postmenopausal women.
- Serum concentration does not correlate closely with body stores.
- Normal requirement is 1 mmol/kg/d.
- Primary absorption of Pi is in the duodenum and jejunum, stimulated by vitamin D.
- Kidney: Primary filtration in the kidney and primary reabsorption in the proximal tubules, with only 10% reabsorption in the distal tubules. Regulated by PTH, cortisol, high dietary intake, and calcitonin. Increased Pi excretion with volume expansion.
- Functions: Phosphates provide the primary energy bond in ATP and creatine phosphate. Severe Pi depletion can cause cellular energy depletion, lack of cAMP; Pi is also important for cellular structures as phospholipids, nucleic acids, and cellular membranes. As part of 2,3-DPG, phosphates promote release of O_2 from Hgb.

Etiology

- Decreased intake, increased loss, redistribution, occasionally genetic
- Decreased absorption and/or intake: Malnutrition, malabsorption syndromes, Crohn disease, celiac disease, inadequate replacement in TPN, hemodialysis, Mg^{2+} and aluminum antacids, sucralfate, vitamin E deficiency
- Increased losses: Rapid volume resuscitation, steroids, pancreatitis, burns, alcoholism, dialysis, hyperparathyroidism, diuretics
- Redistribution: Shift from serum into cells (hyperglycemia, glucose infusion, hormonal effects), catecholamines, insulin, glucagon, calcitonin
- Respiratory alkalosis, leukemic blast cell crisis

Usual Treatment

- Prefer oral over parenteral because of risk of resultant hypocalcemia or calcification of tissues. Suggested dose of K-PHOS is 2–5 mg/kg per d.
- If parenteral therapy is required, administer 10–45 mmol of IV Na^+ or K^+ phosphate over 6–12 h. Important to monitor Ca^{2+}, K^+, and Mg^{2+} levels.

Assessment Points

System	Effect	Result
CV	Depressed ATP, impaired response to norepinephrine/angiotensin	Heart failure
HEME (WBC)	Impaired phagocytic, migratory, and bactericidal activity	Sepsis
(Platelets)		Thrombocytopenia, impaired clot retraction
(RBC)	Reduced RBC 2,3-DPG	Increased Hgb-O_2 affinity
CNS	Neurologic dysfunction	Seizures, coma, hyperreflexia, paresthesia, dysarthria
MS	Respiratory failure, motor weakness	Proximal > distal, rhabdomyolysis, myoglobinuria

Key References: Bugg NC, Jones JA: Hypophosphatemia. Pathophysiology, effects and management on the intensive care unit, *Anaesthesia* 53(9):895–902, 1998; Ianov I, Wilkerson DL: Hypophosphatemia and acute postoperative respiratory distress, *J Ark Med Soc* 106(11):265–266, 2010.

Perioperative Implications

- Potential need for postop ventilation in pts with hypophosphatemia.
- Correction of severe hypophosphatemia should be done slowly over several hours to days to prevent severe hypocalcemia and vascular and interstitial Ca^{2+} precipitation.
- Consider hypophosphatemia in the pt who is difficult to wean off the ventilator, as this might be the cause.

Hypopituitarism

Amit Prabhakar | Richard C. Clarke | Jonathan G. Ma | Alan David Kaye

Risk

- Incidence: 45.5:100,000.
- 30% of pituitary macroadenomas (>10 mm) cause one or more hormone deficiencies.
- About 4.2 years after pituitary radiation therapy, some 50% of pts have hypopituitarism.
- Less common causes include empty sella syndrome, head trauma, infiltrative disease, and expansive internal carotid artery aneurysm.

Perioperative Risks

- If hormone replacement is adequate, surgery presents no increased risk.
- If due to secreting tumor, there is an increased risk of Cushing disease, acromegaly, SIADH, or hyperthyroidism.

Worry About

- Concerns regarding manifestations of disease process: Cushing disease (hypercortisolism secondary to an adrenocorticotropic hormone–secreting adenoma), acromegaly (secondary to a growth hormone–secreting adenoma), and hyperthyroidism in the setting of thyrotropic adenomas.
- Operative risks: Bleeding, DI, and SIADH.
- GH-secreting adenoma predisposing to acromegaly and subsequent airway abnormality and OSA.
- Hypoglycemia.
- Altered volume status due to increased urinary losses.
- Adequacy of adrenal function.
- Increased risk of CV disease.
- Possible increase in ICP.

Overview

- Partial or complete disruption of pituitary gland secretion. Symptoms result from end-organ hypofunction or dysfunction. Organs affected include adrenal and thyroid glands, reproductive system, and liver (glucose production) and kidneys.
- Pt may manifest cortisol deficiency, hypothyroidism, amenorrhea, infertility, insulin-induced hypoglycemia, and/or DI.
- Pituitary apoplexy is the abrupt destruction of pituitary tissue resulting from infarction or hemorrhage. Symptoms include sudden loss of pituitary function with hypotension, eye pain, blindness, and ophthalmoplegia.

Etiology

- 61% secondary to tumors of the pituitary gland
- 9% due to other types of lesions
- 19% due to other causes (radiation, hemorrhage, infarct, head trauma, infiltrative diseases)
- No cause identified in 11%

Usual Treatment

- Surgical resection of adenoma with appropriate hormonal replacement therapy for ACTH: Prednisone or cortisone PO; for TSH: thyroxine PO; for LH and FSH: estrogen and progesterone PO for women, testosterone esters IM for men; for ADH: intranasal desmopressin.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mandibular and oral soft tissue hyperplasia in acromegalics		Airway exam Check ring size	
CV	Hypovolemia Catecholamine resistance		Orthostatic hypotension	Give steroid replacement and observe effect on BP
GI	Hypoaldosteronism	Anorexia, N/V, weight loss, abdominal pain		Hyperkalemia, hyponatremia, hypocalcemia, hypovolemia
ENDO	Decreased ACTH	Fatigue, fever, stress-induced hypotension, and hyponatremia	Fever, hypotension, wt loss, mental status	Morning cortisol level, rapid ACTH stimulation test, insulin tolerance test
	Decreased LH, FSH	Decreased libido and sexual function, amenorrhea	Regression of secondary sexual characteristics	FSH, LH serum levels, serum estradiol and testosterone
	Decreased GH	Fatigue		Insulin-induced hypoglycemia, serum IGF-I
	Decreased TSH	Wt gain, cold intolerance, depression, constipation, hair loss	Myxedema, hyporeflexia	TSH, T_4
	Increased prolactin	Lactation, amenorrhea	Galactorrhea	Serum prolactin
MS	Increased GH in acromegalics		Large hands, feet, mandible, tongue	
RENAL	Increased vasopressin Decreased vasopressin	Excessive thirst Increased UO and thirst	 Hypovolemia Hypotension	Hyponatremia Hypernatremia Dilute urine

Key References: Nemergut EC, Dumont AS, Barry UT, et al.: Perioperative management of patients undergoing transsphenoidal pituitary surgery, *Anesth Analg.* 2005;101(4):1170–1181; Bajwa SJ, Kaur G: Endocrinopathies: the current and changing perspectives in anesthesia practice, *Indian J Endocr Metab.* 2015;19(4):462–469.

Perioperative Implications

Preoperative Preparation

- Ensure adequacy of hormone replacement therapy.
- Check serum Na^+, Ca^{2+}, and K^+ and correct if necessary.
- Determine volume status and adequacy of fluid replacement.
- In acromegalics, careful airway assessment and cardiac workup for possible cardiomyopathy.
- Consider steroid supplementation (hydrocortisone 100 mg/70 kg tid).
- Clinically assess for signs of increased ICP (N/V, papilledema, headache, blurry vision).

Monitoring

- Consider arterial line if severe CV compromise, central venous pressures if indicated by inadequate preop correction of fluid status
- Monitor lytes frequently if hyponatremia or hypernatremia is not corrected preop.
- Consider glucose monitoring.

Airway

- Acromegalic pts with normal airway exams may be difficult to intubate. Have LMA, fiberoptic, or glidescope available.
- Difficult airways in acromegalic pts due to macroglossia, hypertrophy of soft tissues of oropharynx, enlargement of soft palate, epiglottis, and aryepiglottic fold.

Induction

- Little risk of increased ICP with pituitary adenomas.
- No special technique if hormone replacement and volume status are adequate.

Maintenance

- Maintain normocarbia for pituitary surgery.
- Titrate narcotics and benzodiazepines carefully in pts with OSA secondary to GH-secreting tumors.

Extubation

- Routine (for nonpituitary surgery). May need CPAP postop if pt requires use at home for possible OSA.

Adjuvants

- Intraop DI treated with vasopressin 5 to 10 IU SQ or IM every 4–6 h

Postoperative Period

- Polyuria and polydipsia with dilute urine may indicate development of DI.
- Postop hypopituitarism may require steroid replacement therapy.

Anticipated Problems/Concerns

- Acromegalic pts should be treated as having difficult airways.
- Pts with GH deficiency may manifest hypoglycemia.
- Electrolyte abnormalities (K^+, Na^+, Ca^{2+}) and possible hypovolemia, predisposing to arrhythmias and CV instability.

Hypoplastic Left Heart Syndrome

Gianluca Bertolizio

Risk

- Frequency: 0.163–0.184 per 1000 live births
- 7–9% of all congenital heart diseases
- Approximately 1000 infants/y in USA
- Male to female: Up to 2:1
- 15% is associated with genetic syndromes, such as Turner syndrome, Jacobsen syndrome, trisomy 13, trisomy 18, and Smith-Lemli-Opitz syndrome

Perioperative Risks

- 60% prenatally diagnosed (18–22 wk)
- 90% mortality within the first month without operation
- 70% overall survival to adulthood
- 30% mortality within 30 d after stage I
- 10–15% interstage mortality

Worry About

- Premature closure of the DA and the presence of a restrictive PFO/ASD will cause a rapid decompensation of pt after birth.
- Severe hypoxemia due poor intracardial mixing or increased PVRs.
- Pulmonary edema due to pulmonary overcirculation and high LA pressure.
- Systemic and coronary hypoperfusion due to runoff (mainly diastolic) to the pulmonary circulation.
- High risk of myocardial ischemia.
- Aortic atresia + mitral atresia/stenosis subtypes have higher mortality.
- Possible presence of left ventriculocoronary fistulae.

Overview

- Secondary to a severe hypoplasia of the left heart structures (MV, AV, LA, LV, ascending aorta, aortic arch), which leads to different degrees of obstruction of LA and/or LV outflow tract. It is defined as single ventricle physiology, which has the following characteristics:
  - Complete mixing of the Qp and Qs.
  - Ventricular output = Qp + Qs.
  - Existence of two parallel circulations: The distribution of systemic and pulmonary blood flow is dependent on the relative resistances to flow.
  - $SaO_2 = SpaO_2$.
- The goal is to manage the PVR/ SVR ratio to maintain the Qp:Qs~1.
- Qp:Qs is calculated as the following = $(SaO_2 - SvO_2) / (SpvO_2 - SpaO_2)$.
- SvO_2 = mix venous saturation and $SpvO_2$ = pulmonary venous saturation. $SpvO_2$ = 100% if there is no lung disease.

Etiology

- It is a ductal-dependent circulation with complete mixing of blood through PFO or ASD.
- In a normal fetus systemic circulation, 90% of circulating blood flow is guaranteed by FO and DA. After birth, both DA and FO close. In the neonate with HLHS, blood cannot flow into the LV (MV atresia) or into the aorta (AV/aortic atresia); therefore it crosses the atrial septum through the PFO/ASD,

mixes with blood in the RA, and goes into the RV. From the RV it is pumped into the lungs via the PA and to the body via the open DA. Hence, the RV provides the cardiac output for both systemic and pulmonary circulations.

Usual Treatment

- At birth, children are kept on PGE_1 to maintain the DA open and permit systemic perfusion. If FO/ASD is restrictive, it may be emergently enlarged (atrial septostomy/Rashkind).
- Functional univentricular surgical repair consists of three stages:
  - Stage I: Norwood or DKS procedure within the neonatal period—aortic arch reconstruction + systemic-to-pulmonary shunt (modified Blalock-Taussing shunt, Sano conduit are the most common). Aortic reconstruction requires DHCA/RLFP.
  - Stage II: Bidirectional Glenn procedure at 6–8 mo of age.
  - Stage III: Fontan procedure between 18 mo–3 y.
- NB: Aortic arch reconstruction may be delayed until stage II. If so stage I usually consists in a hybrid procedure = PA banding + ductal stent. Other surgical variations exist.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult intubation due to associated syndromes		Facial dimorphism	Genetic test
CV	Decreased BP due to PGE_1 Poor RV function Poor atrial left to right shunt due restrictive PFO/ASD CHF (high LA pressure) Pulm Htn due to pulm overcirculation, neonatal high PVR	Difficulty feeding Need of inotropic support	Weak pulses at the lower limbs Tachycardia Diaphoresis Hypotension Tachypnea Hepatomegaly Metabolic acidosis	Cardiac ECHO, ECG, CXR, cardiac cath Cardiac MRI
RESP	Apnea due to PGE_1 Normal saturation 80–85% Pulm edema (Qp:Qs>1) Desaturation (Qp:Qs<1)	Apnea Increased O_2 requirement CPAP Intubation	Respiratory failure, rales Central cyanosis versus peripheral cyanosis	ABG, CXR Saturation SvO_2
GI	If decreased BP: Metabolic acidosis, mesenteric ischemia, hypoglycemia NEC Hypocalcemia if DiGeorge syndrome Liver immaturity	Abdominal distention Poor feeding Blood in stool Free air in peritoneum	Distended tense abdomen Edema of abdominal wall Tender abdomen	Coag, abdominal x-ray Flank NIRS LFT
RENAL	Renal failure secondary to decreased BP, diuretic therapy		Oliguria	Lytes, BUN, Cr UO, UA
CNS	Hypoglycemia, CNS hemorrhage	Increased fontanel pressure Decreased Hct	Increased fontanel size and tension	Head US Head NIRS

Key References: Graham EM, Bradley SM, Atz AM: Preoperative management of hypoplastic left heart syndrome, *Expert Opin Pharmacother* 6(5):687–693, 2005; DiNardo JA, Zvara DA: Congenital heart disease. In DiNardo JA, Zvara DA, editors: *Anesthesia for cardiac surgery,* ed 3, Oxford, 2007, Blackwell Publishing Ltd, pp 167–251.

Perioperative Implications

Preoperative Preparation

- Maintain PDA patency with PGE_1. Atrial septostomy (ultrasound guided or in interventional radiology) may be considered to improve intracardiac mixing and decompress LA.
- Inotropic support may be needed to maintain adequate CO. Systemic perfusion can be promoted by increasing PVR (hypoxia/normoxia, mild hypercarbia, mild acidosis, increased transpulmonary pressure).
- Pt may be sedated and intubated to decrease oxygen consumption and manage the PVRs. Atelectasis should be avoided because they promote intrapulmonary shunting and V/Q mismatch.
- Aiming for PaO_2 = 40–45 mm Hg, saturation = 80–85%, Sa-v difference 25–30%.
- Careful evaluation of signs of systemic hypoperfusion is warranted (myocardial ischemia, splanchnic hypoperfusion, cerebral hemorrhage).

Monitoring

- Five-lead cardiac monitoring.
- Preductal and postductal saturations.
- Cerebral NIRS ± flank NIRS.
- CVL: Know specific anatomy, including SVC variation.
- Arterial cath Usually femoral arterial line is preferred since a right mBTS will affect the right radial trace. Noninvasive BP on the upper limbs.
- Urinary cath.
- TEE.

Airway

- Associated congenital syndromes with airway anomalies.
- Pt may be already intubated. Nasal intubation may be preferred due to better stability and if TEE placement is planned.

Induction

- Absolute air bubble precaution.
- Induction may be carefully managed. Pt is a high risk of VT. Low aortic diastolic pressure (<30 mm Hg) and high heart rate make the heart susceptible of myocardial ischemia.
- Preinduction volume expansion may be indicated.
- Maintain HR, BP, and contractility.
- IV induction with high-dose opioids and NMB are recommended.
- Inhalational induction may be poorly tolerated and must be used judicially.
- Prolonged preoxygenation with FIO_2 1.0 may cause significant increase of pulmonary flow at expense of systemic blood flow (high Qp:Qs), causing systemic hypotension and coronary hypoperfusion.

Maintenance

- Maintain HR and contractility infusion of inotropes, such as dopamine and/or epinephrine.
- Ventilation should be adjusted to optimize PVR/SVR ratio. Usually PaO_2 = 40–45 mm Hg promotes minimal pulmonary vasoconstriction and provides cerebral dilatation. Low FiO_2 is recommended to avoid pulmonary vasodilation. Low mean airway pressures (high PIP, low RR) will decrease the transpulmonary pressure and may be needed to promote pulmonary blood flow.
- NIRS is indicated to monitor cerebral oxygenation.
- Flank NIRS may be used to monitor peripheral perfusion during DHCA/RLFP.
- A high Hct may help the splanchnic and cerebral oxygen delivery but will increase blood viscosity and PVR.
- Use of antifibrinolytic therapy should be weighed against the risk of shunt thrombosis.

Extubation

- Deferred in PICU

Postoperative Period

- PICU/CICU admission.
- Risk of bleeding.
- Risk of kinking/occlusion of the shunt.
- Risk of aortic obstruction.
- Maintain balanced circulation and treat low cardiac output syndrome:
  - SaO_2 = 75–80%, Sa-vO_2 = 25–30%, BP >60/30 = balanced Qp:Qs.
  - SaO_2 >85%, Sa-vO_2 >30%, decreased BP = overcirculated flow.
  - SaO_2 <75%, Sa-vO_2 25%–30%; increased BP = undercirculated flow.
  - SaO_2 <70%, Sa-vO_2 >30%, decreased BP = low cardiac output.
- Inotropic support (to maintain CO) and milrinone (to decrease PVR and improve systemic perfusion) are often needed.
- Inhaled nitric oxide (selective pulmonary vasodilator) may be necessary.
- Diastolic pressure is usually higher after the Sano conduit placement versus other shunts.
- After Stage I Norwood repair
  - Up to 45% develop laryngeal dysfunction, dysphagia, or GERD.
  - 10%–20% NEC.
  - Risk of periop cardiac arrest for non-cardiac surgeries: 22%–27%.

Hypothermia, Mild

Daniel I. Sessler

Risk

- Greater in infants and children
- Greater in longer, larger operations
- Similar in RA and GA

Perioperative Risks

- Surgical wound infections
- Coagulopathy
- Reduced drug metabolism
- Prolonged recovery and hospitalization
- Shivering and thermal discomfort

Overview

- Benefits:
  - Improved neurologic recovery in asphyxiated neonates
  - Decreases triggering and severity of malignant hyperthermia.
- Core temperature normally protected by responses that include sweating, vasoconstriction, and shivering.
- Typical doses of GA have little effect on the sweating threshold but decrease vasoconstriction and shivering thresholds 2–4° C, thus increasing the range of temperatures not triggering protective responses 10-fold from approximately 0.4–4° C.
- RA inhibits thermoregulatory control by preventing peripheral responses (such as vasoconstriction) and centrally by reducing afferent input.

Etiology

- Initial 0.5–1.5° C decrease in core temperature from core-to-peripheral redistribution of body heat.
- Subsequently, slow, linear decrease in core temperature from heat loss exceeding heat production.
- Finally, a core-temperature plateau results when thermoregulatory vasoconstriction decreases cutaneous heat loss and constrains metabolic heat to core thermal compartment.

Usual Treatment

- Forced-air is by far the most commonly used warming method, typically increasing mean body temperature 1° C/h.
- 1 L of crystalloid at 20°C or 1 U of blood at 4° C decreases mean body temperature approximately 0.25° C in adults. Fluid warming should be restricted to pts given large volumes of fluid (i.e., ≥2 L/h).
- Passive insulation (e.g., surgical drapes, cotton blankets) decreases heat loss 30%, which is usually insufficient to maintain periop normothermia.
- Airway heating and humidification is ineffective.

Assessment Points

System	Effect	Dx	Treatment
CNS	Ischemia protection Thermal discomfort	None Visual analogue scale	Induce and maintain hypothermia Active cutaneous warming
VASC	Precapillary dilation; reduced SVR Arteriovenous shunt constriction, increased BP, decreased HR	Associated with sweating Fingers feel cold, approximately 10 mm Hg increase in mean arterial pressure	Active or passive cooling Active cutaneous warming
MS (shivering)	Two-fold to three-fold increase in metabolic rate Pt discomfort Interference with monitoring	Visual inspection O_2 consumption	Prevent hypothermia Meperidine 10–25 mg IV Clonidine 75 mcg IV Active cutaneous warming
IMMUNE	Increased risk of surgical site infection	Clinical infections	Prevent hypothermia
HEME	10% increase/° C in blood loss	Bleeding time PT/ PTT falsely normal	Prevent hypothermia Defect probably not reversed by FFP and platelet transfusions
METAB (increased drug action)	MAC decreases approximately 5%/° C Decreased drug metabolism	Monitor drug action (rather than dose)	Titrate drug administration to desired endpoint Monitor twitch depression

Key Reference: Sessler DI: Perioperative thermoregulation and heat balance, *Lancet* 387: 2655–2664, 2016.

Perioperative Implications

Preoperative Preparation

- Active prewarming for 30–60 min helps prevent redistribution hypothermia.

Monitoring

- Four core temperature sites are accurate: pulm artery, distal esophagus, tympanic membrane (with a contact thermometer), nasopharynx.
- Three additional sites suitable except during cardiopulmonary bypass: mouth, axilla, bladder.
- Best site for postop temperature monitoring is the mouth.

Intraoperative Period

- Maintain normothermia (core temperature >36° C) unless otherwise indicated.
- Sufficient passive or active reduction of heat loss will prevent hypothermia; however, active warming is usually required.
- Once triggered, thermoregulatory vasoconstriction effective in preventing further core hypothermia.
- Community standard of care is to monitor core temperature in pts having general anesthesia lasting more than 30 min and to keep core temperature ≥36°C.

Postoperative Period

- Hypothermic pts should be rewarmed with forced air.
- Shivering and thermal discomfort can be specifically treated.
- Postop warming not a substitute for maintaining intraop normothermia.

Anticipated Problems/Concerns

- Hypothermia has been proven to cause numerous life-threatening complications and should be actively prevented unless therapeutic hypothermia is specifically indicated.

Hypothyroidism

John F. Butterworth

Risk

- Hypothyroidism may be present in 2-5% of the general population and is more common in women and the elderly.
- Approximately 3% of adults receive chronic thyroid replacement.

Perioperative Risks

- If inadequately treated, increased risk for hypothermia, hypotension, cardiac failure, and GI dysfunction.
- Periop mortality rate not increased unless overtly hypothyroid.
- Inadequate thyroid replacement associates with adverse obstetric outcomes and developmental delays in the offspring, but screening for hypothyroidism during pregnancy remains controversial.

Worry About

- Predisposition to hypothermia.
- Neuromuscular weakness may impair weaning from mechanical ventilation.

Overview

- Common condition, particularly in adult women.
- Elevated TSH concentration in blood is hallmark lab finding.
- Subclinical hypothyroidism (persistent increase in TSH despite normal T_4) sometimes present month to year before decreased T_4 concentration.
- Adequacy of T_4 replacement defined by TSH concentrations in the low-normal range.
- Total and free T_4 (and usually T_3) concentrations typically reduced.
- Symptomatic pts with TSH >10 mU/L should receive maintenance thyroid hormone replacement (T_4 0.8-2 mcg/kg daily).
- Pts presenting with severe, untreated hypothyroidism or myxedema coma may also demonstrate hypothermia, hypoventilation, hyponatremia, hypotension, heart failure, bowel obstruction, and hypoglycemia.

Etiology

- Hypothyroidism (decreased thyroid hormone secretion) most often results from primary disease of thyroid gland (most commonly autoimmune thyroiditis). Less frequently, it results from disorders of the pituitary gland or hypothalamus.
- Previous treatment for hyperthyroidism and previous total thyroidectomy are also relatively common causes of hypothyroidism.
- Pts with critical illness may have reduced T_4 and T_3 despite normal TSH concentrations (nonthyroidal illness syndrome) but usually do not require thyroid hormone replacement.
- Primary TSH deficiency may result from pituitary tumors and cysts or their treatment (either surgery or radiation), pituitary infiltration, necrosis, or infarction; secondary TSH deficiency may result from congenital deficiency of TRH, radiation therapy, infections, or tumors or cysts that impinge on the hypothalamic-pituitary portal circulation.

Usual Treatment

- Maintenance outpatient therapy for adults consists of oral T_4 0.1–0.2 mg (0.8-2 mcg/kg) daily.
- There may be a delay of up to 4 wk for TSH to stabilize after T_4 dosage adjustment ($T_{1/2}$ of T_4 about a wk).
- Chronic rifampin, carbamazepine, phenobarbital, and phenytoin, and increase T_4 dosage requirements by increasing metabolism or clearance of T_4.
- Pts with CAD should have T_4 replacement initiated at a reduced dose and only cautiously increased to avoid precipitating increased anginal symptoms.
- Myxedema coma may require use of IV T_3 (liothyronine) 0.15–0.3 mcg/kg every 6 h and IV hydrocortisone 0.5–1 mg/kg every 8 h to cover for possible hypothyroid-impaired adrenal response to stress.
- IV T_3 may also be indicated in other circumstances when peripheral conversion of T_4–T_3 is impaired (e.g., hypothermic cardiopulmonary bypass).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Puffiness below eyes, enlarged tongue	Snoring	Enlarged tongue	TSH, T_4 (or T_3) concentrations
CV	Bradycardia, decreased BP, heart failure	Palpitations, myocardial ischemia, arrhythmias, peripheral edema	Bradycardia, tachycardia	TSH, T_4 (or T_3) concentrations, ECG
RESP	Hypoventilation			TSH, T_4 (or T_3) concentrations, arterial P_{CO_2}, or venous HCO_3^-
GI	Ileus, weight gain	Constipation, ascites	Decreased bowel sounds	TSH, T_4 (or T_3) concentrations
RENAL	Decreased free water clearance	Fluid retention, edema	Edema	TSH, T_4 (or T_3) concentrations; serum Na^+ concentration
CNS	Obtundation, depression, muscular weakness, cold intolerance	Lethargy, weakness, mental slowness	Decreased deep tendon reflexes, impaired mental status examination	TSH, T_4 (or T_3) concentrations

Key References: Biondi B, Wartofsky L: Treatment with thyroid hormone, *Endocr Rev* 35(3):433–512, 2014; Fliers E, Bianco AC, Langouche L, et al.: Thyroid function in critically ill patients, *Lancet Diabetes Endocrinol* 3(10):816–825, 2015; Hennesey JW: The emergence of levothyroxine as a treatment for hypothyroidism, *Endocrine* 55(1):6–18, 2017.

Perioperative Implications

Preoperative Preparation

- Chronic thyroid replacement to maintain euthyroid state.
- Hypothyroid pts who are inadequately treated require different periop management from those who receive adequate maintenance T_4 therapy.
- If pt is receiving chronic thyroid replacement and is euthyroid, likely no additional concerns.
- Long $T_{1/2}$ of T_4 (approximately a week) permits oral T_4 to be withheld safely for several NPO days.

Monitoring

- Temperature
- Other monitors as indicated by surgery

Airway

- Rare cause of macroglossia with congenital hypothyroidism

Maintenance

- No effect of hypothyroidism on MAC for inhaled anesthetics.
- Keep the pt warm.
- Potential increased periop risk of heart failure, hypotension, and GI dysfunction (controversial).

Extubation

- Weaning from mechanical ventilation may be impaired with inadequate hormone replacement.

Adjuvants

- None needed (except in cases of myxedema coma, in which IV liothyronine and hydrocortisone may be indicated)

Anticipated Problems/Concerns

- Only those hypothyroid pts who have been inadequately treated with T_4 carry risks; those who chronically receive an appropriate dose of T_4 have almost no increased risk compared with other pts.
- Inadequately treated hypothyroidism can lead to lethargy and fatigue, weight gain, dementia, heart failure, respiratory insufficiency, fluid retention and edema, hyponatremia, clotting abnormalities, and generalized weakness.

Hypoxemia

Ana Fernandez-Bustamante

Risk

- All pts undergoing anesthesia and surgery (7–35% in large series have Pao_2 <60 mm Hg in OR or PACU).
- Pts with pulm disease, difficult airway management, severe hemodynamic instability.

Perioperative Risks

- Hypoxemia may lead to hypoxia and eventual severe neurologic/cardiac sequelae or death.

Worry About

- Inadequate delivery of O_2 to lungs and blood is the greatest concern to the anesthesiologist because it will lead to tissue hypoxia.
- Differential Dx is critical for successful causal treatment.
- Misinterpretation of certain clinical manifestations of hypoxemia (anxiety, tachycardia, dysrhythmias).

Overview

- Hypoxemia denotes low PaO_2 in blood (vs. hypoxia, which refers to inadequate delivery of O_2 to tissues).
- Hypoxemia is defined as resting PO_2 greater than two SD below normal for age and FIO_2 and SpO_2 less than 90%, PaO_2 less than 60 mm Hg on room air, and/or a fall in SpO_2 greater than 5%.
- Multiple symptoms and vital signs that should be considered possibly related to hypoxemia.

Etiology

- Decreased FIO_2: Failure to provide adequate inspired O_2 (e.g., O_2 supply failure, anesthesia machine failure, airway disconnect, pts at high altitude)
- Inadequate alveolar ventilation: Difficult airway management, low minute ventilation (respiratory depression or residual muscle paralysis in spontaneous breathing pt), severe laryngospasm/bronchospasm
- V/Q mismatch: Asthma, COPD, pulmonary embolism, pulm vascular disease, atelectasis, pneumonia, alveoli filled with blood or vomitus, FRC >closing capacity
- Diffusion problems: Very rare cause (massive pulm edema)
- R-to-L cardiac shunts: ASD, VSD (may not respond to increased FIO_2)
- Inadequate delivery of O_2 to tissues: Extremely low cardiac output, severe anemia, extremely decreased release of O_2 from Hb to tissue (left shift Hb dissociation curve: CO intoxication, metHb, severe hypothermia)

Usual Treatment

- Determine cause of decreased O_2 delivery and treat.
- Increase FIO_2 (may not help if hypoxemia is due to R-to-L shunts).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Altered mental status	Anxiety, restlessness Confusion, seizures		
CV	Sympathetic stimulation Htn Arrhythmia Bradycardia (late sign)	Htn	Tachycardia BP	ECG TEE
RESP	Cyanosis Atelectasis, evidence of aspiration, pneumonia		Tachypnea	SpO_2 ABG, low PaO_2 CXR

Key References: Blum JM, Fetterman DM, Park PK, et al.: A description of intraoperative ventilator management and ventilation strategies in hypoxic patients, *Anesth Analg* 110(6):1616–1622, 2010; Sanford TJ: Hypoxemia. In Fleisher LA, Roizen MF, editors: *Essence of anesthesia practice,* ed 3, Philadelphia, PA, 2011, Elsevier, p 210.

Perioperative Implications

Monitoring

- Routine: Pulse oximetry is mandatory; ABG if concerns.
- Capnography and hemodynamic monitoring may help with differential Dx.

Airway

- Must ensure patency and intact circuit at all times.

Maintenance

- Adequate FIO_2 and alveolar ventilation
- Adequate O_2 delivery to tissues (CO, Hb)

Anticipate Problems/Concerns

- Must have a high index of suspicion whenever SpO_2 decreases or any of the clinical subjective or objective signs and symptoms are present. Always assume the decreased SpO_2 does not reflect a problem with the pulse oximeter but signifies a real problem. Stable vital signs may not fully eliminate significant arterial hypoxemia.

IgA Deficiency

Jahan Porhomayon | Paul R. Knight III

Risk

- Most common immunodeficiency disorder.
- Incidence estimated to be 1:100 to 1:1000.
- More prevalent among European descendants.
- Most pts are clinically normal.
- Increased risk of allergies and anaphylaxis.
- Increased risk of malignancies.

Perioperative Risks

- Increased incidence of pulm complications, atopic disorders, and postop infections

Worry About

- Recurrent sinopulmonary infections leading to decreased pulm reserve
- Associated autoimmune disorders (e.g., lupus, DiGeorge syndrome)
- Associated GI disorders leading to volume depletion
- Anaphylactic reactions from transfusion of blood products containing IgA

Overview

- An immunodeficiency syndrome with increased susceptibility to nosocomial infection.
- Cell-mediated immunity is usually normal.
- Coexisting diseases may include atopy, recurrent sinopulmonary infection, GI disease, and autoimmune disease.
- Decreased synthesis or secretion of IgA.

Etiology

- Absence of IgA on mucosal surface.
- Decreased IgA blocking antibodies against environmental antigens.
- Associated with histocompatibility groups HLA-A1, HLA-B8, and HLA-Dw3.
- There have been several reported cases of acquired IgA deficiency.
- Usually decreased rather than absent lymphocyte IgA secretion.
- Overt clinical disease presentation may relate to changes in IgG subclass and/or compensatory IgM secretion.

Usual Treatment

- Do not treat with gamma globulin.
- Increased suspicion of infections and aggressive antibiotic therapy.
- Therapy directed toward specific coexisting disease(s).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Decreased reserve, hypovolemia	Dyspnea or exertion	Tachycardia, orthostatic hypotension	ECG, ECHO
RESP	Recurrent sinopulmonary infection, hemosiderosis, asthma	Decreased exercise tolerance	Wheezing, rales	CXR, PFTs, sinus x-rays
GI	Chronic gastroenteritis, malnutrition, malabsorption	Chronic diarrhea	Cachexia	Lytes, BUN, serum albumin
HEME	Nonspecific	Depends on the extent of coexisting diseases		Serum IgA, anti-IgA antibody, Coombs test
RENAL	Nonspecific	Varies in severity depending on the extent of coexisting diseases		BUN, Cr
CNS	Degenerative, demyelinating	Mental retardation associated with ataxia-telangiectasia		MRI

Key References: Tait AR, Knight PR: Anesthetic considerations for the immune compromised patient. In Lema MJ, editor: *Problems in anesthesia: anesthesia and cancer.* Philadelphia, PA, 1993, JB Lippincott, pp 375-391; Out TA, van Munster PJ, De Graeff PA, et al.: Immunological investigations in individuals with selective IgA deficiency, *Clin Exp Immunol* 64(3):510–517, 1986; Yel L: Selective IgA deficiency, *J Clin Immunol* 30(1): 10–16, 2010.

Perioperative Implications

Preoperative Preparation
- Consider antibiotic therapy.
- Work up any indication of infection.
- Optimize any underlying organ dysfunction and volume status.

Monitoring
- Consider invasive hemodynamic monitoring in debilitated pts.

Airway
- Strict aseptic technique
- Universal precautions
- May encounter difficult intubation in pts with associated rheumatoid arthritis

Induction
- Hypotension secondary to hypovolemia and/or decreased cardiac reserve
- Wheezing allergies relatively resistant to conventional therapy

Maintenance
- May require high inspired O_2.
- Regional anesthesia and careful titration of anesthetic agents due to potential underlying CV and pulm diseases.
- Use only thoroughly washed RBC transfusions.

Extubation
- Careful assessment of neuromuscular function due to potential drug-drug interaction

Adjuvants
- Depend on organ dysfunction

Postoperative Period
- May require intensive pulmonary therapy.
- Maintain strict antiseptic precaution.
- Increased suspicion of bacterial infection.

Anticipated Problems or Concerns
- Anaphylactic reaction from transfusions of blood or blood products containing IgA to individual with IgA antibodies.
- Asthmatic pt with IgA deficiency is relatively resistant to treatment.
- Increased risk of nosocomial infection.

Immune Suppression

Nader D. Nader | Paul R. Knight III

Risk
- The incidence of HIV infection has been stable in USA, at approximately 20–30 newly diagnosed infections per 100,000 population per y.
- 20–25% of HIV infected pts will require surgery.
- Major risk factors: Neutropenia, yeast overgrowth, and/or nosocomial colonization of skin and mucosa.

Perioperative Risks
- In one study of AIDS pts undergoing intraabdominal surgery, 22.2% 30-d mortality was reported.
- Mortality is greatest at the extremes of age.
- Greatest source of morbidity and mortality is secondary to infection.
- Pneumonia accounts for approximately 40% of all deaths.
- Increased incidence of postop pneumonia, wound infection, postop sepsis, respiratory insufficiency, SIRS, and hypotension due to cardiovascular instability.
- Increased healing time.

Worry About
- Nosocomial transmission of infection
- Interactions with other drugs (IV recreational drugs, antiviral agents)
- Transmission of pathogenic drug-resistant strains of microbial agents to medical personnel (e.g., new strains of tuberculosis)
- Decreased pulm reserve due to repeated infections
- Decreased myocardial reserve secondary to underlying disease and generalized poor health
- Translocation of intestinal bacteria due to severe mucositis

Overview
- Immune suppression can arise from multiple causes, both primary and acquired.
- In the intraop period, surgical trauma, anesthetic agents, blood transfusion with or without severe hemorrhage decreases the immune response.

Etiology
- Primary immune deficiency (most are familial).
- The very young have immature immune systems.
- Aging alters some cellular immune responses.
- Acquired:
  - Malnutrition, drugs (glucocorticoids, chemotherapy, antiviral), massive burns, or trauma
  - Cancers (leukemia, lymphoma, and multiple myeloma)
  - Infections (HIV stages 2–4, influenza, sepsis)
  - Smoking decreases respiratory defense mechanisms

Usual Treatment
- Selective use of antibiotic prophylaxis, antivirals (e.g., acyclovir), antifungal agents (e.g., fluconazole), or immune enhancement (e.g., immune globulin)
- Strict sterile procedures and universal precautions
- Fastidious personal hygiene

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEME	Anemia, neutropenia, lymphopenia, recurrent bacteremia, coagulation abnormality, and thrombocytopenia	Easily fatigued, recurrent fever, sweats and chills	Pale Presence of petechiae or purpura	Hct/ Hgb, WBC, plts, plasma proteins, coagulation studies, special lymphocyte counts (e.g., $CD4^+$ cells)
CV	Subacute bacterial endocarditis, decreased reserve, hypovolemia, drug-induced injury (e.g., arabinomycin), mycotic aneurysms, pericardial effusion, vasculitis, pulm Htn	Decreased exercise tolerance, dyspnea on exertion	Murmurs, orthostatic hypotension, abnormal heart rate	ECG, transthoracic ECHO
RESP	Recurrent acute pulm infections, pulm fibrosis, obstruction, chronic tuberculosis and/or fungal infections	Decreased exercise tolerance, dyspnea on exertion	Airway lesions, pneumonia	CXR and spirometry
GI	Chronic gastroenteritis, chronic malnutrition, severe mucositis, parasitic infections	Severe "cramping," dysphagia, odynophagia diarrhea	Cachexia, leukoplakia	Lytes, albumin, blood cultures
RENAL	Chronic pyelonephritis, bladder infections, chronic cystitis, drug-induced nephropathy (e.g., cyclosporine), end-stage renal pathology	Recurrent UTIs, frequency	Hematuria, pyuria	BUN, Cr, pyelogram, spiral CT imaging
CNS	Mycotic infarcts, AIDS, dementia, encephalopathy	Minor strokes	Focal deficits, decreased mental function	CT imaging of the head
MS	Osteomyelitis	Deep pain located over involved area	Point tenderness	X-ray imaging

Key References: Tait AR, Knight PR: Anesthetic considerations for the immune compromised patient. In Lema MJ (editor): *Problems in anesthesia: anesthesia and cancer.* Philadelphia, PA, 1993, JB Lippincott Company, pp 375-391. Fishman JA: Opportunistic infections—coming to the limits of immunosuppression? *Cold Spring Harb Perspect Med* 3(10):a015669, 2013.

Perioperative Implications

Preoperative Preparation
- Continue or initiate antibiotic therapy and immune therapy.
- Assess and optimize underlying organ system dysfunction (HIV-associated cardiomyopathy).
- Assess volume status and lytes due to chronic diarrhea.
- Involved assessment may be required (pulm function tests, transthoracic echocardiography).
- Identify timing of administration of immune suppressive drug(s).

Monitoring
- Consider arterial line, pulm arterial line, or other invasive hemodynamic monitors in severely debilitated pts.

Airway
- Strict aseptic technique and universal precautions when handling the airway

- Examination of upper airway for potentially obstructive lesions (i.e., Kaposi sarcoma)

Induction

- Chronic respiratory injury due to repeated lung infections may cause rapid desaturation.
- Hypotension due to decreased myocardial reserve and/or relative hypovolemia.
- Decreased drug requirements secondary to decreased plasma proteins.

Maintenance

- Increased inspired O_2 may be required due to chronic lung infections.
- Decreased myocardial reserve may require careful selection and titration of anesthetic agents or local or regional anesthesia for peripheral procedures.
- Preemptive pain management may protect against additional immune suppression.

Extubation

- Due to weakness and drug-drug interactions, return of strength should be carefully evaluated.

Adjuvants

- Transplantation and anticancer drug interactions need to be considered (e.g., cyclosporine and barbiturates, narcotics, muscle relaxants); bleomycin and O_2 administration.

Postoperative Period

- Respiratory adequacy should be carefully followed and may require ICU monitoring.
- Maintain careful antisepsis procedures for extended periods.

Anticipated Problems/Concerns

- Greatest intraop risk to these pts is infection; therefore strict hygienic practices are required.
- General state of nutrition, recurrent infections, and the underlying cause of the immune suppression all tend to generally decrease respiratory reserve and cardiovascular stability.
- Risk of transmission of drug-resistant pathogenic microbial agents to medical personnel (needlestick or respiratory [e.g., drug-resistant tuberculosis]). Follow CDC recommendations if exposed

Implantable Cardioverter-Defibrillators

Peter M. Schulman | Shital Vachhani | Marc A. Rozner

Epidemiology

- In USA, more than 300,000 people have an ICD and more than 180,000 ICDs are implanted annually, based on CMS registry data.
- Given current implant and survival rates, nearly 700,000 people in USA may have an ICD by the year 2020.
- ICD implant is indicated for any-cause cardiomyopathy with EF ≤35% and without evidence of dysrhythmia; thus some pts undergo ICD implantation for "primary prevention."
- All conventional ICDs can provide pacing for bradycardia; some pts are pacing dependent.
- Some ICDs also have atrial, RV, and LV pacing capability for CRT. LV leads can be transvenous in the coronary sinus or epicardial.
- Newer subcutaneous ICDs use a subcutaneous electrode instead of traditional transvenous or epicardial leads. These devices are less invasive but have limited functionality; for example, they have no permanent antibradycardia pacing capability and cannot deliver antitachycardia pacing.
- Premature ICD failure rates might approach 2%. For the ICD pt without evidence of pacing, determining battery function is difficult.*

Risk

- In USA, 450,000 pts/y suffer SCA; 550,000 new cases/y of CHF.
- ICD therapy for SCA, VT, and VF and primary prevention is superior than medical management.
- Associated diseases include cardiomyopathy, CAD, long QT syndrome, arrhythmogenic right ventricular dysplasia, Brugada syndrome, hypertrophic cardiomyopathy, and LV noncompaction. Some ICD pts also have sinus and/or AV node disease.

Perioperative Risks

- Robust data is lacking; however, the presence of an ICD might increase periop risk.
- Inappropriate HVT can induce tachydysrhythmia, injure the myocardium releasing troponin, and is associated with increased mortality.
- Incorrect interpretation of device type (i.e., confusing an ICD for a pacemaker) or events (i.e., pseudomalfunction) during the periop period might lead to pt harm.
- Risk might also be increased in these pts owing to associated disease(s).

Worry About

- EMI on the ICD's ventricular channel resulting in inappropriate HVT including shock(s) and/or antitachycardia pacing. For the pacing-dependent pt, EMI-induced ventricular oversensing with pacing inhibition can also result in asystole
- Intraop increase in ventricular pacing owing to EMI entering a dual chamber ICD and causing atrial lead oversensing and ventricular tracking
- Intraop increases in pacing rates owing to activation of the "exercise sensor," whether due to direct mechanical stimulation (such as preparation of the chest) or pressure on the device (personnel leaning). The cause of this undesirable tachycardia might be mistaken as inadequate anesthetic depth
- Failure to capture (i.e., pacing output without myocardial depolarization) due to inappropriate programmed parameters (i.e., inadequate safety margin), or abrupt increase in pacing threshold from myocardial ischemia/infarction, drug administration, or lyte shifts. Note that any or all chambers can undergo failure to capture with possible hemodynamic derangement, even without apparent outright pacing failure
- Magnet* placement will never change the pacing mode (i.e., produce asynchronous pacing) of an ICD and will change pacing rates only in ICDs from ELA (Sorin, Milan, Italy). Only Boston Scientific (BOS)§ ICDs emit ongoing tones confirming appropriate magnet placement. No ongoing confirmation of magnet placement is available in Medtronic, St Jude Medical§ (SJM), or Biotronik ICD. ICDs from BOS and St. Jude Medical can have their magnet switch disabled by programming. Indeed, some older ICDs from BOS (with the "GDT" or "CPI" x-ray code) can undergo permanent disabling of HVT by magnet placement
- Disabling HVT during central access procedures in the thorax to prevent inappropriate shocks due to guidewire contact with the RV lead. For 6 weeks after lead implant central venous catheterization in the thorax is relatively contraindicated

Overview

- Indications for initial ICD placement: SCA (including spontaneous or induced VT or VF), cardiomyopathy from any cause with LVEF ≤35%, long QT syndrome, arrhythmogenic RV dysplasia, or Brugada syndrome
- Tachydysrhythmia therapy in most conventional ICDs includes ATP, which uses less battery energy and is better tolerated (sometimes not even noticed) by pts. For ICDs programmed to deliver repetitive ATP, shock can be delayed for periods exceeding 1 min, and distinguishing between repetitive ATP on the monitor versus ventricular tachydysrhythmia can be difficult. Some ICDs will deliver ATP while charging, which will not delay shock
- Codes: The North American Society of Pacing and Electrophysiology (NASPE)/British Pacing and Electrophysiology Group (BPEG) generic defibrillator code has four positions. The first position refers to the chamber(s) shocked (A = atrium, V = ventricle, D = both, O = none). The second position refers to the chamber(s) where ATP is programmed (A, V, D, O). The third position identifies the detection method: either heart rate E = electrogram or hemodynamic (H) (although no hemodynamic sensors are currently in clinical use). The fourth position identifies chambers (A, V, D, O) where pacing for bradycardia has been programmed. The most robust form of this code uses only the first three positions and adds the five-position generic pacemaker code. For example, an ICD with anti–atrial fibrillation therapy and CRT might be DDE-DDDRV

Indications and Usual Treatment

- Primary prevention in a pt with LVEF ≤35% (and more than 40 d from an ischemic event or 3 mo from vascular intervention) who is receiving optimal medical therapy and has a reasonable expectation of survival with good functional capacity for >1 y
- Survivors of cardiac arrest presumably due to VT/VF, not associated with reversible factors, such as acute coronary syndrome
- Pts with inducible VT/VF by EP study and no reversible cause
- Treatment for LV cardiomyopathy should include (unless contraindicated) beta-blocker and ACE inhibitor/angiotensin receptor blocker therapy (see the ACC/AHA Heart Failure Guidelines). Many pts will also have statin, aspirin, antiarrhythmic, diuretic, nitrate, and/or digoxin therapy

*Some ICDs allow demonstration of battery function without interrogation:

Assessment Points

System	Effect	Assessment By Hx	PE	Test
CV	Myocardial ischemia LV dysfunction Heart rate (guidelines suggest <80 bpm) Frequency of ICD therapy Need for pacing	Angina symptoms Exercise tolerance, DOE	ECG, pulse S_3, rales	Nuclear imaging ECHO B-type natriuretic peptide ICD interrogation
RESP	Amiodarone toxicity	Exercise tolerance, DOE		SpO_2, CXR, PFTs, ABGs
ENDO	Amiodarone toxicity			TSH, T_4
RENAL	Renal insufficiency		Edema	BUN, Cr
NEURO	CV disease	Stroke, TIAs	Bruits	Carotid duplex
METAB	Reversible VT/VF	Diuretic Chemotherapy (platins)		Serum K^+ and Mg^{2+}

Key References: Rozner MA: Pacemakers and implanted cardioverter-defibrillators. In Miller RD, Eriksson LI, Fleisher LA, et al. editors: *Miller's anesthesia*, ed 7 Philadelphia, PA, 2009, Churchill Livingstone, pp 1387–1409; Schulman PM, Rozner MA, Sera V, Stecker EC: Patient with a pacemaker or implantable cardioverter-defibrillator, *Med Clin North Am* 97:1051–1075, 2013.

Perioperative Implications

Preoperative Preparation

- Prior to an elective procedure, a CIED care team assessment should be obtained. Comprehensive interrogation should be performed within 6 mo prior to scheduled surgery for an ICD and within 3 mo prior for any CRT device. For pts who have received HVT since the last interrogation, or those who are scheduled to undergo hemodynamically challenging surgery, interrogation might be indicated during the periop evaluation. Remaining battery life, tachycardia zones and therapies, pacing behavior, prior dysrhythmia treatment, and magnet behavior should be documented. Many ICDs (even those with dual chamber capability) are programmed to VVI pacing capability; for the pt with intact atria and AV node, periop care must be directed to prevent the sinus rate from falling below the VVI pacing rate because ventricular-only pacing will likely compromise hemodynamics. For the pt with hemodynamically advantageous pacing capability who is chronotropically incompetent or pacing dependent and undergoing a major procedure, consideration should be given to increasing the pacing rate.
- For ventricular multisite pacing (called cardiac resynchronization therapy), assurance that the LV pacing lead is functioning. If placement of a thoracic central venous cannulation is planned in a CRT pt, the position of the LV (coronary sinus) lead on the CXR should be noted because it may be dislodged during CVC insertion.
- Alternate defibrillation (and pacing modality [e.g., transvenous, transcutaneous]) for the pacing-dependent pt should be available. While transesophageal pacing might work as backup, it is contraindicated in any pt with an ICD or those with atrial fibrillation or AV nodal block.
- IV chronotropes (epinephrine, ephedrine).
- Discuss monopolar ESU precautions with surgeon and nursing staff. If monopolar ESU is planned, the ICD should have its HVT suspended for the procedure. Suspending HVT by applying a magnet† is sometimes possible and appropriate; however, it is important to ensure that the magnet mode is active and understand that magnet application can occasionally have unintended and untoward consequences.
- Placement of defibrillation pads should be considered, especially if a pt has been receiving HVT from the ICD.

Monitoring

- Mechanical pulse wave monitoring is required. It can be accomplished with pulse oximeter plethysmogram, any invasive hemodynamic monitoring modality, or Doppler technique.
- ECG monitoring is an ASA requirement, but EMI perturbs the signal, and monitors frequently report incorrect heart rates (both too high and too low).

Induction

- Succinylcholine or etomidate might lead to muscle fasciculation or myoclonus, resulting in pacing inhibition, increased rates, or false VT/VF detection, but these sequela have not been reported for ICDs. Succinylcholine-induced potassium fluxes theoretically can change pacing thresholds.

Maintenance

- Vigilant ECG/pulse monitoring
- Monopolar ESU cautery (i.e., the "Bovie") emits radiofrequency energy, potentially causing EMI, and resulting in inappropriate VT/VF detection (and HVT), as well as transient or permanent changes in ICD function. The most common problem is inhibition of pacing. Prevention includes use of bipolar-only ESU, use of pure unblended monopolar ESU, and placement of the ESU dispersive electrode so that the presumed current path of the ESU does not cross the pulse generator or leads. For all head and neck or contralateral breast surgery, the dispersive electrode can be placed on the shoulder contralateral to the CIED. For ipsilateral breast surgery, the dispersive electrode can be placed on the ipsilateral arm and the wire prepped into the field if needed
- Magnet†: Assuming that the magnet is appropriately placed and that the magnet mode is enabled, placement might be useful to suspend HVT. No ICD provides asynchronous pacing upon magnet application, and, except for ELA (Sorin) ICDs, no ICD will change its pacing rate in response. If interference from the ESU or other equipment creates hemodynamic instability, the use of this equipment should be transiently stopped. If possible the dispersive electrode should be relocated (for abdominal or pelvic surgery the pad could be moved to the other leg). If relocating the return pad is not possible or ineffective the ICD will require reprogramming

Postoperative Period

- Monitoring of mechanical pulse in the postop care unit.
- ICD interrogation/reprogramming required if ICD was reprogrammed preop; advisable if monopolar ESU used, any problems noted, or cardioversion/defibrillation has taken place.
- Some pts require pacing programming changes to optimize postop hemodynamics. These changes might include increasing the pacing rate, disabling battery saving features, and adjusting the AV delay.

Anticipated Problems/Concerns

- Inappropriate delivery of HVT, which typically occurs without warning and might be missed by intraop personnel
- Intraop failure to pace, most likely related to EMI from monopolar electrosurgery
- Periop pacing and sensing threshold changes
- Risks related to associated medical problems
- Iatrogenic misadventures resulting from misunderstanding of ICD pacing behavior
- BOS‡ ICDs will emit beeps if the magnet switch is enabled and the magnet is appropriately placed. A constant tone indicates that the ICD is disabled. No tone indicates magnet switch deactivation or a dead battery.
- ELA (Sorin) ICDs will change pacing rate to 90 bpm if battery is okay, 80 if elective replacement. However, the pt rate must be <90 (80) to observe this function. No change indicates battery or other failure.
- Medtronic ICDs will emit a tone for at least 15 sec when the magnet switch (nonprogrammable) is activated, even briefly, by a magnet. A warbling tone indicates a problem with the ICD, and no tone indicates a nonfunctioning device. Note that this tone cannot be used to verify appropriate placement of a magnet.

† MAGNET CAUTION: A magnet will never change the pacing mode of an ICD. Only ICDs from ELA (Sorin) will change pacing rate (to 90 bpm if battery is okay) upon magnet placement. For many ICDs (Boston Scientific‡and St Jude Medical‡), the magnet switch can be programmed "OFF." Only ICDs from Boston Scientific and its previous companies emit ongoing tones that identify correct placement of a magnet (except subcutaneous ICDs, which emit a tone for only 1 min following magnet application). Some older ICDs from Boston Scientific (with the "GDT" or "CPI" x-ray code) can undergo permanent disabling of tachycardia therapy by magnet placement.

‡ Boston Scientific owns the Guidant and CPI brands, and St Jude Medical owns the Pacesetter brand.

Infratentorial Tumors

Tod B. Sloan | Antoun Koht

Risk

- Highest incidence: Age 3–12 y and 55–65 y
- Two-thirds of childhood CNS tumors; approximately 3–5:100,000/y under age 19 y
- 15–20% of adult CNS tumors; incidence lower than in children

Perioperative Risks

- Very confined space, brain tolerates tumor poorly, leading to symptoms and less forgiving with surgery than supratentorial
- CSF obstruction with hydrocephalus common; ICP tolerated poorly

Worry About

- Increasing ICP and hydrocephalus
- Impaired protective airway reflexes and aspiration
- Irregular ventilation due to brainstem compression and swelling
- Impaired level of consciousness
- Cranial nerves abnormalities

Overview

- Survival 60% in children.
- Prognosis is poor with glioblastoma, and infiltrating brainstem glioma.
- Benign lesions, such as meningioma and acoustic neuroma, have low morbidity and mortality but may recur if resection is incomplete.
- Degree of head elevation influences venous pressure and incidence and severity of air embolism (sitting (worst) > prone > park bench/lateral position).

Etiology

- Primary intraaxial lesions are generally malignant; extraaxial lesions are typically benign.
- Children: Astrocytoma, medulloblastoma, and brainstem glioma are the most common in children ages 3–12 y.
- Less than 1 y old, most common are astrocytoma, cerebellar PNET medulloblastoma ependymoma, brainstem glioma.
- Less than 2 y old, most common are are medulloblastoma and low-grade glioma (70%).
- Pediatric cystic cerebellar astrocytoma is associated with 80% survival at 20 y.
- Adult: Most primary tumors are acoustic neuroma associated with NF-II and meningioma. (most >60 y are acoustic).
- Metastases: Lung and breast most common; vasogenic so ICP common. Metastases to cerebellum forms mass lesion.
- Differentiate from AVM and aneurysms.

Usual Treatment

- Surgical removal or debulking
- CSF diversion (ventriculostomy or shunt)
- Dexamethasone to decreased peritumor vasogenic edema
- Primary or adjuvant radiotherapy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Tonsillar herniation, cranial nerve compression	Dysphagia, change in voice tinnitus, vertigo	Gag dysfunction, hyperthermia, ipsilateral hearing impairment	Indirect laryngoscopy, hearing exam
CV/HEME	Progressive brainstem compression, ischemic cardiomyopathy		Cushing response: Htn, bradycardia, raised ICP, S_3 gallop, CHF	ECG, HCT, T&C
RESP	Progressive tonsillar herniation		Hyperventilation, irregular respirations, apnea	CT exam, MRI
RENAL/GI	Increased ICP	N/V (especially near fourth ventricle)		CT scan, MRI, glucose
CNS	Increased ICP	Listlessness, headache, nausea, drowsiness, diplopia	Papilledema, classic triad (headache, vomiting, ataxia), enlarged head, bulging fontanelle	CT scan, MRI
MS	Lesion in cerebellar hemisphere or midline	Truncal ataxia	Nystagmus hypotonia, limb ataxia intention tremor	Extraocular movement abnormalities

Key References: McClain CD, Soriano SG: Anesthesia for intracranial surgery in infants and children, *Curr Opin Anaesthesiol* 27(5):465–469, 2014; Francois A: Posterior fossa tumor surgery. In Mongan P, Soriano S, Sloan T, editors: *A practical approach to neuroanesthesia,* Philadelphia, PA, 2013, Lippincott Williams and Wilkins, pp 62–67.

Perioperative Implications

Preoperative Preparation

- Neurologic exam: Cranial nerve deficits
- Presence and status of EVD or VP shunt
- Patent foramen ovale avoid sitting position
- Assess volume status from decreased intake, vomiting, diuresis (will increase risk of hypotension if sitting)
- Avoid narcotic premedication or any respiratory depressants if risk of increased ICP
- Note use of steroids to reduce peritumoral edema
- Note: NF-I and -II, tuberous sclerosis, Von Hippel Lindau
- Surgical position, prone, sitting, lateral
- Tumors versus microvascular decompressions

Monitoring

- Goals are maintenance of adequate CNS perfusion and cardiorespiratory stability, detection and treatment of air embolism, and surgical brainstem compression.
- Monitor CPP (MAP-ICP), radial artery cath, transducer at ear level; watch for hypotension when sitting.
- Capnography, precordial Doppler US, right atrial cath for air embolism detection and retrieval (TEE if available).
- Auditory brainstem responses and facial nerve monitoring may reduce neural morbidity. SSEP, MEP, and multiple cranial nerves often monitored.
- Watch for deep breath from brainstem compression respiratory center, watch for Htn or BP decreases and arrhythmias from brainstem compression.
- ECG and pulse oximetry to watch for arrhythmias (bradycardia common but other sudden changes can be as diagnostic) from manipulation of brainstem cranial nuclei and dura (innervated by vagus nerve). Avoid treating with anticholinergic as eliminate heart rate as monitor of brainstem.
- If sitting position, precordial Doppler and CVP with tip at right atrium needed.
- Watch eyes if prone for pressure and prep solutions.
- Head flexion: Ensure two fingers' minimum distance from chin to chest.

Airway

- Verify appropriate ETT position after final positioning; avoid oral airways or large bite blocks to minimize tongue and soft tissue compression, postop airway swelling.
- Soft bite block between molars with MEP.
- Watch for ETT kinking with neck flexion (armored tube if indicated).

Induction

- Hypotension on induction can be offset by preinduction IV hydration.

Maintenance

- Positioning: Protect eyes, avoid kinking of jugular vein, carotid, vertebral artery when turning head.
- Preserve autonomic reflexes; avoid long-acting vasodilators.
- Monitor for changes in electrolyte balance due to loop and osmotic diuretics; replace diuresis if needed.
- Maintain normothermia, normovolemia, normotension, and normonatremic fluids.
- Watch for hypothermia with prolonged case (neuroendoscopy).
- Avoid hyperglycemia and hyperthermia.
- Controlled PPV; adequate hydration decreases risk of air embolism.
- Avoid NMB with cranial nerve and MEP monitoring.
- Limited inhalational agents <0.5 MAC with SSEP and MEP and consider TIVA if EP signals are weak.
- Consider infusions of short-acting opioids especially in cases of TIVA.
- Secure EMG leads for cranial nerves.
- Dose and redose antibiotics.
- Avoid anticholinergics and beta-blockers to mask CV changes with brainstem compression.

Extubation

- Pt should be awake, following commands, and showing return of protective airway reflexes (swallow); note possibility vocal cord paresis (CN X)

Adjuvants

- Short-acting vasopressors or vasodilators for maintenance of CV stability
- Antiemetics

Postoperative Period

- Suspect brainstem compression or hematoma if postop Htn or profound bradycardia persists in previously normotensive pt.
- Suspect brainstem injury if persistent hypotension or apnea.
- Avoid potent opioids that may produce ventilatory depression (hypercarbia) and decreased intracranial compliance.

Anticipated Problems/Concerns

- Intraop air embolism: Notify surgeon who should flood field and use bone wax; turn off N_2O if on; acute CPAP may help to find source; lay head down to level of heart if needed.
- Pts with higher-grade malignancy have greater likelihood of postop brain swelling.
- Postop inability to protect airway (loss of lower cranial nerves); watch for swallowing prior to extubation; use NG if question.
- Loss of resp drive with injury to brainstem resp center.
- Delayed awakening from pneumocephalus (tension possible requiring relief); also supratentorial hemorrhage when sitting.
- Massive tongue swelling and cervical spinal cord ischemia if sitting position.
- Loss of facial nerve (corneal ulceration from failed eye closing).
- Aseptic meningitis (blood irritating meninges).

Insulinoma

Molly B. Kraus | Jesse J. Muir | Molly Solorzano

Risk

- Most common functional islet cell tumor of pancreas
- Incidence: 1–4 per million population per year
- Mean age of onset: 47 y
- Presentation earlier (mean age 25 y) if part of MEN-1
- More common in females

Perioperative Risks

- Hypoglycemia

Worry About

- Preop and intraoperative hypoglycemia
- Post-excision rebound hyperglycemia (not always present and not reliable to validate completeness of resection)
- Possibility of multiple islet cell tumors or MEN-1 characterized by primary hyperparathyroidism, anterior pituitary adenomas, and tumors of the pancreas and duodenum

Overview

- 80–90% are <2 cm, solitary, and benign.
- Malignant lesions typically invade locally into surrounding structures or into the lymph nodes or liver
- Insulinomas are found equally distributed throughout the pancreas (i.e., head, body, and tail).
- 5–10% occur in the setting of MEN-1; increased risk of recurrence if associated with MEN-1.
- Presentation: Post-absorptive hypoglycemia, hypoglycemia after exercise, awakening at night to eat, and weight gain due to frequent meals to avoid hypoglycemic symptoms.
- Differential Dx: Factitious hypoglycemia, liver or metabolic disease, NIPHS.
- Dx strongly suggested by Whipple triad: (1) symptoms of hypoglycemia provoked by fasting; (2) blood glucose levels <50 mg/dL; and (3) relief of symptoms with glucose administration.
- Typically blood glucose <45 mg/dL, insulin level >6 uU/mL, and C-peptide elevated to >200 pmol/L (with undetectable ketones/betahydroxybutyrate).
- Gold standard for Dx: Measurement of plasma glucose, insulin, C-peptide, and pro-insulin during a 72-h fast with or without betahydroxybutyrate and absence of plasma levels of sulfonylurea. These tests in combination are sufficient to diagnose 97% of individuals.
- Preop localization techniques include CT, MRI, PET, endoscopic US, octreotide scintigraphy, selective mesenteric angiography with intra-arterial calcium stimulation, and hepatic venous sampling for plasma insulin.
- Preop imaging useful to evaluate for evidence of metastatic disease and to plan for the extent and type of surgery.
- Preop localization fails 10–27% of the time.
- Gold standard is firm biochemical Dx and selected preoperative imaging along with thorough pancreatic exploration and intraoperative US.
- In absence of preoperative localization and intraoperative detection, blind pancreatic resection is not recommended.
- Neurogenic symptoms are secondary to autonomic system discharge in response to hypoglycemia (anxiety, tremor, nausea, hunger, sweating and palpitations). Neuroglycopenic symptoms are secondary to CNS glucose deprivation (headache, lethargy, dizziness, diplopia, blurred vision, seizures, amnesia, confusion, and coma).

Etiology

- Unknown; most are solitary adenomas.
- 5–10% of insulinomas associated with the autosomal dominant MEN-1 syndrome; the gene causing MEN-1 is localized in band 11q13.

Usual Treatment

- Operative management is only curative option.
- Surgery includes inspection of the entire abdomen for evidence of metastatic disease, palpation of the entire pancreas and intraoperative US to localize the lesion.
- Laparoscopic enucleation is the treatment of choice for all benign insulinomas.
- Enucleation may be performed for lesions that are clearly localized preoperatively, near or at the pancreatic surface, and easily defined intraoperatively.
- Resection recommended for lesions that are multiple, near the pancreatic duct or major vessels, MEN-1 cases, and suspected malignancy (infiltrating tumor, puckering of surrounding soft tissue, distal dilation of pancreatic duct, or lymph node involvement).
- Medical management is reserved for those who are awaiting surgery, not a surgical candidate or have persistent symptoms despite surgery.
- Medical treatment consists of small frequent meals, diazoxide, verapamil, and octreotide.
- Octreotide is a somatostatin analogue that can relieve symptoms in 50% of pts.
- Octreotide should be used with caution because many insulinomas lack octreotide receptors. Treatment may fail to suppress insulin production and blunt compensatory growth hormone and glucagon response, leading to worsening hypoglycemia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RENAL	Renal stones if MEN-1	Renal colic	Flank pain	Serum Ca^{2+}
ENDO	MEN-1 Pituitary tumors	Renal colic Vision changes	Flank pain Signs of pituitary dysfunction	Parathyroid hormone, serum Ca^{2+} Skull x-rays and appropriate endocrine tests
	Insulinoma	Neurogenic symptoms: Hunger, sweating, and paresthesias (cholinergic) and anxiety, tremor, and palpitations (adrenergic) Neuroglycopenic symptoms: behavioral changes, death, confusion, vision changes, fatigue, seizure, loss of consciousness	Mental status exam	Fasting glucose, insulin levels, C-peptide
CNS	Symptoms of hypoglycemia	Neuroglycopenic symptoms	Mental status exam	Blood glucose

Key References: Mathur A, Gorden P, Libutti S: Insulinoma, *Surg Clin North Am* 89(5):1105–1121, 2009; Goswami J, Somkuwar P, Naik Y: Insulinoma and anaesthetic implications, *Indian J Anaesth* 56(2):117–122, 2012.

Perioperative Implications

Preoperative Preparation

- Maintain/optimize physiologic condition.
- Evaluate for MEN-1.
- Avoid severe hypoglycemia with frequent meals and avoidance of prolonged exercise.
- Diazoxide, octreotide, and verapamil to control hypoglycemia if necessary; should be continued the morning of surgery.
- Admit the night before and maintain on 10% dextrose infusion while NPO.
- Remove dextrose from IV solution just prior to entering the operative room.
- Monitor plasma glucose every 10-15 min.

Monitoring

- Measure plasma glucose every 10-15 min.
- Maintain plasma glucose >60 mg/dL.
- Consider arterial line and/or CVP to facilitate sampling ease.

Airway

- Nothing specific, although these pts may have significant weight gain.

Induction

- Propofol has not been shown to significantly affect the release of insulin or glucose regulation.

Maintenance

- Length of procedure highly variable.
- Careful attention to fluid status.
- Have dextrose solutions available to treat hypoglycemia.
- Goal should be to decrease cerebral metabolic rate.

Extubation

- Nothing specific

Anticipated Problems/Concerns

- It has been proposed that glucose solutions be avoided intraoperatively so that hyperglycemic rebound can be used to confirm tumor removal.
- More recent studies show that less than half of pts will have this rebound in the first 30 min following tumor removal, and therefore hyperglycemic rebound cannot be used as proof of complete tumor removal.
- Intraoperative handling of the tumor may cause severe hypoglycemia.
- Pneumoperitoneum during laparoscopy causes release of cortisol which stimulate glucose production.
- Intraoperative insulin assays may be an alterative.
- Pts who have hyperglycemic rebound and/or successful tumor removal can still have hypoglycemic episodes, so pts must be monitored for hypoglycemia in the postop period.
- Most patients are discharged home with normal fasting glucose levels.
- Postop complications include pancreatic duct leak causing pseudocyst, abscess, and/or fistula (octreotide can be used to decrease fistula output).

Intracranial Hypertension

Elizabeth Mahanna Gabrielli

Risk

- Incidence in USA: >50% of pts presenting with head trauma or other intracranial pathology (>600,000/y)
- Gender predominance: Only for certain etiologies (i.e., TBI and males)

Perioperative Risks

- Increased risk of herniation leading to subsequent brain infarction, disability, coma, and death

Worry About

- Controlling ICP and preventing brain ischemia/herniation
- CV and respiratory instability
- Coexisting injuries in trauma pts (occult cervical spine and intra-abdominal injuries)

Overview

- Intracranial compartment has fixed volume with three components (brain = 85%, CSF = 10%, CBV = 5%).
- Increased volume of one component (e.g., tumor, hydrocephalus, or hemorrhage) without compensatory decrease in another compartment elevates ICP, leading to ICH (ICP >20 mm Hg for >5 min typically, but individual patients' threshold for injury varies).
- ICH reduces CPP (CPP = MAP – ICP), causing brain ischemia and/or infarction.
- ICH causes ICP gradients that may extrude brain parenchyma through dural or bony passages, resulting in herniation. Subfalcine herniation compresses the anterior cerebral artery. Transtentorial herniation compresses the posterior cerebral artery and herniation from cranioectomy may compress the middle cerebral artery.
- Some anesthetic agents, hypercapnia, and hypoxemia increase CBF, increasing CBV and ICP. In cases of loss of autoregulation Htn may also increase CBF.

Etiology

- Abnormal increase in volume of parenchymal compartment, CSF or CBV, usually a secondary process accompanying other pathology (e.g., cerebral edema in TBI, cerebral infarct, tumor, inflammation; hemorrhage in TBI, ICH, SAH; hydrocephalus in intraventricular hemorrhage, compression of ventricles; decreased venous drainage as in cerebral venous thrombosis)

Usual Treatment

- Treatment of primary disease (e.g., removal of tumor, hematoma, or abscess; hemicraniectomy in middle cerebral artery syndrome).
- CSF drainage with either an external ventricular drain or lumbar drain.
- Secure airway if needed and control ventilation, avoid hypoxemia (PaO_2 >90 torr), and avoid hypercapnia and severe hypocapnia ($PaCO_2$ <30 torr).
- Establish stable hemodynamics (normotension but estimated CPP >60 mm Hg).
- Head elevation above heart and neutral neck position to promote cerebral venous return.
- Osmotic therapy (mannitol or hypertonic saline) to decrease brain parenchyma volume.
- Anesthetic infusion to decrease $CMRO_2$ after airway is secured.
- Corticosteroids (for vasogenic edema only as in neoplasm or abscess).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dysrhythmias, unstable vital signs Inferior wall myocardial ischemia		BP Pulse S_3 gallop	Tachycardia, bradycardia, prolonged QT interval, ECG, ECHO
RESP	Irregular breathing		Respiratory rate and pattern	
GI	Reduced gut motility	Vomiting		
RENAL	ADH disturbances: SIADH, central DI		Oliguria Polyuria	Urine Na, urine K, urine urea, urine Osm, serum lytes
CNS	Altered function	Headache, vomiting, unconsciousness	Neurologic deficits, papilledema	Direct ICP measurement (ventriculostomy, intracranial bolt)

Key References: Stevens RD, Shoykhet M, Cadena R: Emergency neurological life support: intracranial hypertension and herniation, *Neurocrit Care* 23(Suppl 2):S76–S82, 2015; Stocchetti N, Maas AI: Traumatic intracranial hypertension, *N Engl J Med* 370(22):2121–2130, 2014.

Perioperative Implications

Preoperative Preparation

- Judicious or no preoperative sedation due to risk of depressed ventilatory drive leading to hypoventilation and hypercapnia and increased ICP.
- Assess volume status.

Monitoring

- Consider arterial cath for BP monitoring and for serial ABGs to properly manage mechanical ventilation and control $PaCO_2$.
- Consider CVP monitor.
- Continue intracerebral multimodal monitoring (i.e., ICP, brain tissue oxygen, microdialysis, jugular venous saturation) if present.

Airway

- Neutral cervical spine position for tracheal intubation if traumatic injury
- Possible aspiration risk (emergency procedure or severe ICH)

Preinduction and Induction

- Neutral neck position and head elevation.
- Deep anesthetic level and complete muscle relaxation with NMBD at time of laryngeal intubation to avoid coughing, sympathetic response, and further increase in ICP.
- Maintain CV stability and CBF with the use of vasopressors as necessary.

Maintenance

- Hypnotic agent (either propofol or volatile anesthetic) and narcotic infusion.
- Maintain volatile anesthetic at less than 1 MAC; N_2O use is controversial.
- Normoventilation ($PaCO_2$ to 35–40 torr) and use PEEP to maintain FRC and oxygenation; avoid excessive PEEP.
- Maintain MAP such that estimated CPP >60 mm Hg and place transducer at the tragus.

Extubation

- Maintain tracheal intubation if concerns about postoperative respiratory function or persistent ICH; otherwise, prompt extubation for early neurologic evaluation.
- Avoid coughing and bucking on the tube.

Adjuvants

- Benzodiazepines, beta-blockers, and antihypertensives

Postoperative Period

- If ICH persists, continue stepwise approach to decrease ICP and maintain adequate ventilation and/or oxygenation, sedation, NMB, and mild hypothermia as necessary.

Anticipated Problems or Concerns

- Use isotonic crystalloid or colloid IV solutions to minimize cerebral edema.
- Renal dysfunction and severe hypovolemia are possible with mannitol; hypervolemia and acute CHF exacerbation are possible with hypertonic saline.

Acknowledgment

Thank you to Kevin J. Gingrich for his contribution to the previous version of this chapter.

Intraoperative Recall

G. Richard Benzinger

Risk

- Incidence in USA: 20 million anesthetics annually

Perioperative Risks

- Incidence is approximately 0.1% in general surgical population and increases to approximately 1% in high-risk populations.
- Procedure risk factors include OB surgery, cardiac surgery, trauma, and rigid bronchoscopy.
- Pt risk factors include prior awareness, significant CV disease, COPD, substance abuse, chronic opioid use, and chronic benzodiazepine use.
- Anesthetic risk factors include absent/low benzodiazepine premedication, absent/low halogenated agent, and dense NM blockade.

Worry About

- PTSD is a common sequela (up to 50% incidence).
- Awareness caused a significant fraction of closed claims against anesthesia personnel (1.9–12%).
- Many cases are preventable and identified as attributable to lapses in technique.

Overview

- Explicit recall: Conscious, articulable recollection of events when intended to be unaware.
- Implicit recall: Change in behavior attributable to perception of intraoperative events, but no explicit awareness. Much harder to study.
- Intraoperative awareness: Consciousness during presumed general anesthesia; does not necessarily lead to postoperative recall.
- Hemodynamic changes are neither sensitive nor specific signs of awareness.
- Processed EEG monitoring (such as BIS) may decrease incidence of awareness.
- Maintenance of adequate end-tidal halogenated agent (≥0.7 MAC, age adjusted) using audible alarms may decrease incidence of awareness.

Etiology

- Inadvertent awake paralysis usually due to drug labeling or administration error
- Other awareness frequently associated with light anesthesia: Intentional, unintentional, or equipment malfunction

Usual Treatment

- Discuss incident with pt postop.
- Offer psychiatric referral to all pts with recall as screening or treatment for PTSD.
- Preliminary work suggests that glucocorticoids may reduce development of PTSD when administered shortly after a traumatic event; consider administration in PACU if explicit recall is reported there.
- Benzodiazepines are not effective in producing retrograde amnesia; cannot use for rescue of awareness.

Assessment Points

System	Effect	PE	Test
CV	Htn Tachycardia		BP ECG
RESP	Tachypnea Bronchospasm Decreased compliance	Observation Auscultation	Respiratory rate PIP
CNS	Increased sympathetic tone Spontaneous movement	Lacrimation Diaphoresis Observation	Processed EEG, bispectral index End-tidal agent monitoring Postop interview

Key References: Mashour GA, Avidan M: Intraoperative awareness: controversies and non-controversies, *Br J Anaesth* 115(Suppl 1):i20–i26, 2015; Brice DD, Hetherington RR, Utting JE: A simple study of awareness and dreaming during anesthesia, *Br J Anaesth* 42(6):535–542, 1970.

Perioperative Implications

Preinduction, Induction, and Maintenance

- Counsel all pts about risk of awareness as part of routine consent process.
- Consider benzodiazepine premedication in all pts without contraindication; titrate dose to clinical effect.
- Avoid muscle relaxant if not indicated. If needed, titrate to avoid dense paralysis.

Monitoring

- Consider use of processed EEG monitoring in high-risk pts, especially those receiving total IV anesthesia.
- Keep inhaled agent ≥0.7 MAC with audible alarms in high-risk pts.
- Continue to monitor NM blockade.

General Anesthesia

- Consider redosing induction agent or using inhaled agents if time between induction and securing airway is prolonged.

Regional Anesthesia

- Counsel pts that awareness during regional anesthesia is expected, even with sedation.
- Limit incidental and alarming conversation during surgery with regional or any other anesthetic technique.

Postoperative Period

- Many pts with recall will not spontaneously report recall in the recovery room. Structured interviews reveal more cases. Serial interviews may improve surveillance further.
- Structured interview for recall:
  - Last thing remembered before sleeping?
  - First thing remembered after awakening?
  - Anything in between?
  - Remember any dreams?
  - Worst thing about anesthetic?

Anticipated Problems/Concerns

- High risk of serious psychiatric sequelae

Jaundice

Maggie Lesley | Aliaksei Pustavoitau | William T. Merritt

Risk

- Chronic liver disease consistently the ninth most common cause of death in USA
- Male to female ratio: 2:1
- African American to Caucasian ratio: 2:1

Perioperative Risks

- Jaundice per se poses no special risks; at least 25% present with severe pruritus.
- Risks are associated with coexisting or underlying conditions.
- Use of regional anesthesia limited by coagulopathy and ascites.

Worry About

- Biliary obstruction
- Chronic liver disease:
  - Hepatopulmonary syndrome and hypoxemia
  - Portopulmonary Htn
  - Hepatorenal syndrome
  - CV dysfunction (cirrhotic, alcohol)
  - Infection, protein-malnutrition
  - Encephalopathy (hepatic and alcoholic); cerebral edema
  - Portal Htn:
    - Esophageal varices (incompetent lower esophageal sphincter)
    - Ascites; renal dysfunction
  - Low systemic vascular resistance and hyperdynamic circulation
  - Bleeding
  - Inability to extubate at end of surgery
- Altered drug pharmacodynamics and pharmacokinetics
- Renal impairment
- Universal precautions
- Invasive monitoring

Overview

- Mostly unconjugated-excess production:
  - Hemolytic anemias (e.g., sickle cell anemia, β-thalassemia major)
  - Extravascular hemolysis (tissue infarction, large hematoma, hemorrhage into tissue, postoperative jaundice)
  - Ineffective erythropoiesis: Decreased hepatic uptake
  - Drugs (e.g., flavaspidic acid, novobiocin, some cholecystographic dyes)
  - Severe, prolonged fasting: Decreased conjugation

- Neonate: Physiologic jaundice of the newborn, breast milk jaundice, hypothyroidism, galactosemia
- Sepsis
- Acquired transferase deficiency: Drug inhibition (e.g., pregnanediol, chloramphenicol), hepatocellular disease (cirrhosis, hepatitis)
- Gilbert disease: Decreased glucuronyl transferase; usually mild but can transiently worsen during periods of stress
- Crigler-Najjar I (absent) and II (partial decrease) in glucuronyl transferase

- Mostly conjugated-decreased hepatic/extrahepatic excretion:
  - Hereditary and/or familial: Dubin-Johnson, Rotor syndromes, recurrent intrahepatic cholestasis (benign), gestational cholestatic jaundice (approximately 1:13,000 deliveries; third trimester; preeclampsia, nulliparity; twin; decreased plt)
  - Acquired: Sepsis; hepatocellular disease (drug- and viral-induced hepatitis), postoperative jaundice (pigment overload [transfusions, resorption of hematomas, hemolysis], hepatocellular damage [drugs, including halothane; shock], benign postoperative jaundice), drug-induced cholestasis (e.g., oral contraceptives, methyltestosterone)
    - Extrahepatic biliary obstruction (e.g., mechanical, from stones, stricture, tumor, pancreatitis)
  - Pseudojaundice:
    - Dietary carotenoids (primarily infants; excessive intake of vegetables, such as carrots and tomatoes), TPN-associated liver dysfunction
    - Poisoning (picric acid)

Usual Treatment

- No specific treatment outside of newborn period.
- For neonates: fluids, phototherapy, exchange transfusion, albumin, tin mesoporphyrin, and IV immunoglobulin Rx have been shown to decrease the level of unconjugated bilirubin below levels regarded to be toxic to the neonatal brain. The smaller and sicker the premature infant, the more aggressive the therapy needed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Duration	Yellow sclerae	
CV	Hyperdynamic Poss decreased SVR	General symptoms	Increased HR, decreased BP	
RESP	Cirrhotics have 6× increase in pulm Htn	Severe dyspnea, hypoxia, clubbing	Clubbing Cyanosis	ECHO; right-sided heart cath if indicated, usually for PAS ≥50
GI	Severe dysfunction Prolonged effects of most anesthesia drugs	General symptoms, reflux, ascites, varices, edema	Signs of chronic liver disease	LFTs Coagulation time Hgb, plt
ENDO/METAB	Decreased synthetic function, increased enzymes, decreases albumin, decreased hepatic coagulation factors; decreased clearance of toxins	General malaise symptoms Easy bruising and bleeding	Jaundice Ecchymoses Hematoma Ascites	LFTs Coagulation time NH_3, lactate
HEME	Decreased plt	Easy bruising and bleeding	Ecchymoses, hematoma	
DERM		Duration, evidence of bleeding	Yellow color	
RENAL	Decreased function Higher risk of postop renal impairment		Edema May be hypovolemic in obstructive jaundice	BUN, Cr; Cr may be spuriously lower with high bilirubin
CNS	Recurrent encephalopathy in cirrhosis Cerebral edema in fulminant hepatic failure Autonomic dysfunction	Mental status Duration of illness Abnormal autonomic function	Normal to encephalopathy/ comatose Orthostatic BP changes	Bilirubin interferes with cerebral near-infrared oximetry

Key References: Yang LQ, Song JC, Irwin MG, et al.: A clinical prospective comparison of anesthetics sensitivity and hemodynamic effect among patients with or without obstructive jaundice, *Acta Anaesthesiol Scand* 54(7):871–877, 2010; Vaja R, Barker RC: Drugs and the liver, *Anaesth Intensive Care Med* 13:71–74, 2011.

Perioperative Implications

- Drug: Decreased protein production leads to decreased albumin binding and more active drug.
  - Cimetidine and/or ranitidine: Clearance reduced, especially in pts with ascites, hypoproteinemia, and encephalopathy.
  - Benzodiazepines: Clearance of oxidative pathway markedly decreased; glucuronidation path (e.g., lorazepam) not greatly altered; excessive sedation in severe liver disease.
  - Narcotics: Meperidine clearance is severely affected; adverse affects of morphine can be increased.
  - Neuromuscular blockade: Succinylcholine activity may be prolonged somewhat because of decreased levels of pseudocholinesterase; decreased metabolism of vecuronium and rocuronium.
  - Miscellaneous: Phenobarbital and lidocaine have reduced clearance; diuretics may have reduced natriuretic efficacy.
  - Halogenated agents: Halothane should be avoided; association of enflurane with hepatic toxicity is less clear; isoflurane and sevoflurane are preferred agents in setting of liver disease and best preserves liver hemodynamics; reports of hepatic toxicity for both are rare.
  - Pregnancy: Jaundice may signal HELLP syndrome and pregnancy-induced Htn.
- Cardiac surgery: Jaundice occurs in approximately 20% post-CPB pts; risk factor for mortality.

Preoperative Preparation

- Hydration should be adequate; if chronic liver failure, may be total body fluid increased but intravascularly decreased.

Monitoring

- NMB: Dose muscle relaxants to effect and consider path of elimination.
- Invasive CV monitoring: Important for some procedures.

Airway

- May have bleeding disorder.

Induction

- Avoid benzodiazepines.
- Consider cricoid pressure if varices present.

Maintenance

- Be mindful of metabolic clearance paths.
- When practical, use drugs cleared chiefly by nonhepatic paths.

Extubation

- May have delay in awakening

Anticipated Problems/Concerns

- Inability to extubate immediately postoperatively due to prolonged action of NMB and sedative/hypnotic/narcotic medications

Jehovah's Witness Patient

Meg A. Rosenblatt | Alopi Patel

Risk

- More than 8 million members worldwide
- Headquarters in Brooklyn, New York; new world headquarters under construction in Warwick, New York

Perioperative Risks

- Possible morbidity and/or mortality from massive hemorrhage secondary to religious dogma banning members from accepting blood transfusions.
- Appropriate blood conservation measures (i.e., autologous blood salvage, normovolemic hemodilution, reduction of intraoperative and iatrogenic blood loss) in pts who do not accept autologous blood transfusions results in similar or better outcomes compared

with the population that does receive autologous blood transfusion.

Worry About

- Understanding the rights and desires of pt versus duty of physician in regard to blood or blood product administration.
- Trauma and emergency situations in which little time is available to discuss blood product transfusion.
- Competent adults are those who know the nature and consequences of their actions and such adults have the right to refuse specific therapies.
- *Parens patriae* ("parent of the nation") refers to the public policy power of the state and represents the duty and interest of the state to preserve the health of minors. Medicolegally, when a child's right to live and parental religious beliefs collide, the courts have consistently ruled that the child's welfare is paramount.

Overview

- Began as Bible study group in 1869 and adopted the name Jehovah's Witnesses (based on Isaiah 43:10–12) in 1931.
- Strict interpretation and adherence to Biblical passages, which forbid eating of blood. This is interpreted as prohibition of acceptance of blood products to sustain life because this may compromise their soul.
- Other medical restrictions were established over time, such as prohibition of organ transplants in 1967. However, vaccinations are deemed acceptable.
- In 1942 the Watchtower Society, the governing body of Jehovah's Witnesses, introduced the blood ban, which forbids members from accepting allogeneic blood products, including whole blood, RBCs, WBCs, platelets, and plasma.
- There is variability among members to the interpretation of the prohibition regarding blood. Jehovah's Witnesses may consider the use of one's own blood in the course of a medical procedure or therapy provided there is no advanced storage. They may accept fractions of plasma, such as albumin, rHuEpo, immunoglobulin, or factor concentrates.

Usual Treatment

- Discuss and document preoperatively the potential for life-threatening hemorrhage. Discuss and document therapies and interventions that would be acceptable to the pt.
- Seek evidence of an advance directive, an affidavit that confirms the pt's refusal to accept a transfusion (which promotes discussion and releases physicians/hospitals of responsibility for outcome of the pt's decision).
- Consider contacting a Jehovah's Witness Hospital Liaison Committee, which consists of a group of individuals trained to work as intermediaries in avoiding conflict between pts and physicians.
- Contact legal counsel if pt is a minor, unconscious, or an incompetent adult.
- Be aware that administration of blood products against a competent pt's wishes can be a prosecutable offense.

Assessment Points

System	Assessment by Hx	Test
HEME	Evaluate for treatable forms of anemia	Hg/Hct, folate, B_{12} levels, Fe, ferritin, transferrin saturation

Key References: Bodnaruk ZM, Wong CJ, Thomas MJ: Meeting the clinical challenge of care for Jehovah's witnesses, *Transfus Med Rev* 18(2):105–116, 2004; Lawson T, Ralph C: Perioperative Jehovah's witnesses: a review, *Br J Anaesth* 115(5):676–687, 2015.

Perioperative Implications

Preoperative Preparation

- Iron therapy, especially if evidence of decreased iron stores: Ferrous sulfate 325 mg PO daily or iron dextran 100–200 mg IV daily.
- Vitamin B_{12} 1 mg IV once daily.
- Folate 1-5 mg IV daily.
- Consider rHuEpo: 600 U/kg SQ for 21 d prior to surgery.
- Delay elective surgery until red cell mass is optimal.
- Consider anesthetic alternatives such as regional or neuraxial anesthesia.

Monitoring

- Minimize phlebotomies. Consider pediatric sampling tubes.
- Consider central venous line, pulm artery cath, and arterial line if high possibility of hemorrhage.

Intraoperative Considerations

Maintain Blood Volume

- Nonblood volume expanders (i.e., normal saline, lactated Ringer, PlasmaLyte A, hydroxyethyl starches, dextrans).
- Synthetic oxygen therapeutics (recombinant human hemoglobin).
- Hypervolemic or normovolemic hemodilution (maintain continuous circuit with pt) in the absence of CAD or Hg <7 g/dL.
- Blood salvage techniques (maintain continuous series with pt's circulation).
- Red cell substitutes include crystalloids, colloids, recombinant erythropoietin, and recombinant factor VIIa; in some cases human, animal, or synthetic hemoglobin may be acceptable.
- White cell substitutes include interferons and interleukins and should be considered on a case by case basis.
- Plasma may be substituted with albumin, immunoglobulin, cryoprecipitate, and/or clotting factors. Determine if acceptable with the pt before administering.

Maximize Oxygen Delivery

- Increase FIO_2.
- Hyperbaric O_2.
- Inotropic agents to augment cardiac index once volume resuscitated.

Prevention of Intraoperative Blood Loss

- Meticulous surgical technique and use of hemostatic surgical instruments.
- Avoiding blood loss is most effective in preventing mortality.
- Consider use of tourniquet if feasible for particular surgery.
- Consider use of antishock garments, such as pneumatic dressing.
- Laparoscopic, endovascular, or minimally invasive surgical techniques.
- Hypotensive anesthetic techniques.
- Preoperative angiographic embolization (i.e., uterine arteries for hysterectomy).
- Correct coagulopathies with pharmacologic agents (tranexamic acid, aminocaproic acid, desmopressin, recombinant factor VIIa).
- Hemostatic products containing blood fractions (fibrin glue/sealant, thrombin sealants)

Minimize O_2 Consumption and Demand

- Hypothermia 30–32° C (reduces O_2 consumption 50%); however, also a concern for hypothermia induced coagulopathy. Consider risks and benefits.
- Sedation, analgesia, paralysis.
- Acute hypervolemic hemodilution, CPB or ECMO, renal dialysis, and plasmapheresis.

Postoperative Considerations

- Consider postop ventilation with paralysis, sedation, and hypothermia for severe anemia.
- Consider PA catheter to measure and follow CO and SvO_2 to assess O_2 delivery and consumption without resorting to phlebotomy.
- Supplement with IV hyperalimentation, rHuEpo, and iron dextran.
- Avoid gastric ulceration with proton pump inhibitors.
- Consider progesterone for control in menstrual bleeding.

Jeune Syndrome (Asphyxiating Thoracic Dystrophy)

Anne M. Lynn | K. Karisa Walker

Risk

- Incidence in USA: 1:100,000-130,000 live births and prevalence of 2.6:100,000.
- No race or sex predilection.
- Skeletal survey by US after 14 wk gestation can detect defining deformities.
- Heterogeneous presentation, from mild to fatal.

Perioperative Risks

- 70–80% mortality in infancy for severe cases
- Respiratory failure from small thoracic cage and hypoplastic lungs; frequent infection in those with ciliary dysmotility
- Progressive renal disease with cystic lesions and periglomerular fibrosis
- Liver and pancreatic involvement with fibrosis and cysts

Worry About

- Hypoxic and/or hypercapnic respiratory failure.
- Barotrauma with positive pressure ventilation.
- Renal failure requiring careful fluid and electrolyte management and selection of nonrenally cleared muscle relaxants and opiates.
- Liver involvement, and rarely cirrhosis, may affect drug metabolism.

Overview

- Rare autosomal recessive disease with skeletal dysplasia and variable renal, hepatic, and eye abnormalities; variable involvement of CNS and GI systems.
- Overlap of findings with Ellis-van Creveld syndrome, short rib polydactyly syndrome, and oral-facial-digital syndromes.
- Poor survival beyond early infancy.
- Narrow, rigid thoracic cage due to short horizontal ribs, short limbs, underdeveloped iliac wings and acetabula and occasional polydactyly.
- Respiratory failure from restrictive thorax and hypoplastic lungs.
- Possible renal, hepatic, and pancreatic dysfunction if pt survives infancy.
- Chronic renal failure can lead to transplantation.
- Hepatic dysfunction can be controlled with ursodeoxycholic acid but those with severe portal Htn require liver transplantation.
- Occasional pulm Htn and cor pulmonale.
- Surgical enlargement of the thorax has been undertaken to increase chest wall compliance.

Etiology

- Autosomal recessive inheritance, variable phenotype
- Postulated involvement of chromosome 15q13 or *IFT80* gene on chromosome 3

Usual Treatment

- VEPTR thoracoplasty and external distraction thoracoplasty have been successful for Jeune syndrome.
- Older children may require surgery related to renal or hepatic failure or treatment of retinal pathology.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm Htn	Syncope	Increased second heart sound	ECG (RVH) ECHO
RESP	Stiff, small rib cage Hypoplastic lungs Ciliary dysfunction	Pneumonia/respiratory failure Assisted ventilation Asynchronous ventilation with agitation/crying	Small chest Horizontal ribs Cyanosis with crying	ABG CXR Oximetry
GI	Hepatic fibrosis/cysts Pancreatic fibrosis/cysts Foregut dysmotility/malrotation	Failure to thrive Metabolic anomalies Nausea, vomiting	Hepatomegaly	Abdominal US Bilirubin/ LFTs
RENAL	Cysts Nephritis	Polyuria, polydipsia		BUN, Cr, lytes, Ca^{2+}/PO_4, abdominal US
CNS	Occasional hydrocephalus Dandy-Walker malformation Retinal degeneration		Increased OFC (head circumference)	
MS	Short limbs and stature Polydactyly of hands and feet			X-ray of thorax, pelvis

Key References: Keppler-Noreuil KM, Adam MP, Welch J, et al.: Clinical insights gained from eight new cases and review of reported cases with Jeune syndrome (asphyxiating thoracic dystrophy), *Am J Med Genet A* 155A(5):1021–1032, 2011; Waldhausen JH, Redding GJ, Song KM. Vertical expandable prosthetic titanium rib for thoracic insufficiency syndrome: A new method to treat an old problem, *J Pediatr Surg* 42:76-80, 2007.

Perioperative Implications

Preoperative Preparation

- Assess ventilation.
- Evaluate for possible pulm Htn.
- Evaluate renal function and consider LFT.
- High index of suspicion for other organ system involvement.

Monitoring

- Consider arterial catheter.
- Consider central venous access.

Airway

- Small larynx requires smaller ETT size.

Induction

- Agitation may make respirations asynchronous (chest and/or abdomen), causing hypoxemia.

Maintenance

- Lung hypoplasia makes barotrauma high risk; maintain low peak airway pressures.

Extubation

- Ensure adequate ventilation before extubation; postop ventilation may be needed for a prolonged period, specifically after thoracoplasty.

Adjuvants

- Renal/hepatic function assessment guides selection of muscle relaxant and fluid management.

Anticipated Problems/Concerns

- Asynchronous ventilation during crying with hypoxia
- Barotrauma during assisted mechanical ventilation
- Renal and/or liver disease and drug metabolism
- Postoperative respiratory failure requiring ventilatory support

Juvenile Gaucher Disease (Type III/Subacute Neuronopathic)

Lance C. Atchley | Lee A. Fleisher

Risk

- Less than 1:100,000
- Autosomal recessive with no sex predominance
- Panethnic but more common in Northern Sweden and Palestinian town of Jenin

Perioperative Risks

- Abnormal platelet functioning and increased risk of bleeding
- Respiratory failure
- Seizure

Worry About

- Intraoperative blood loss and need for transfusion of PRBC, FFP, and platelets
- Perioperative continuation of anticonvulsant therapy and possible need to supplement
- GERD and aspiration
- Potential presence of restrictive or obstructive lung pathology
- Potential presence of pathologic fractures, including vertebrae
- Type IIIc disease: Intracardiac calcifications—mitral valve, aortic valve, ascending aorta, aortic arch, and coronary ostia

Overview

- Variable clinical expression and severity; presents along a continuum.
- Systemic involvement often present in all forms of Gaucher disease, including type III:
  - Splenomegaly, which may lead to anemia, thrombocytopenia, and leukopenia.
  - Platelet dysfunction independent of splenic involvement.
  - Decrease in coagulation factors.
  - Hepatomegaly.
  - Skeletal involvement, including bone marrow infiltration, osteonecrosis/osteoporosis, and pathologic fractures.
- Systemic involvement more common in type III disease:
  - Pulm involvement ,including interstitial lung disease, pulm Htn, or hepatopulmonary syndrome.
  - GERD with chronic aspiration.
- Specific to type III disease:
  - Slowly progressive neurologic symptoms.
  - Supranuclear horizontal gaze palsy is pathognomonic sign.
  - Seizures may be present.
  - Oculomotor apraxia.
  - Three subtypes:
    - Type IIIa: Myoclonus; dementia

- Type IIIb: Early onset of isolated horizontal supranuclear gaze palsy; aggressive systemic illness
- Type IIIc: Intracardiac calcifications—mitral valve, aortic valve, ascending aorta, aortic arch, and coronary ostia

Etiology

- Autosomal recessive deficiency of the lysosomal enzyme acid beta-glucosidase.
- Results in accumulation of glucosylceramide in various tissues, most often lysosomes of macrophages.
  - Can lead to macrophage clumping in liver, spleen, and bone marrow.
  - Hypersplenism may result in anemia, thrombocytopenia, and leukopenia.
  - May also accumulate in lungs, skin, conjunctiva, kidneys, and heart.
- Specific to type III (juvenile Gaucher):
  - Most common mutation is a variant of L444P, but other missense/null mutations may occur.
  - Type IIIa: No specific mutation.
  - Type IIIb: Predominantly homozygous mutation of L444P.
  - Type IIIc: Homozygous mutation of D409H.

Usual Treatment

- ERT

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Corneal opacity Oculomotor apraxia (see CNS) Anorexia	Visual disturbances Nutritional deficiencies Fatigue	Corneal deposits	
RESP	Interstitial lung disease Cor pulmonale Obstructive or restrictive pulmonary disease	Difficulty breathing Fatigue Dyspnea on exertion Chest pain	Rales and/or rhonchi on auscultation Expiratory wheezing Labored breathing	CXR, PFTs, ABG ECHO or right heart cath to evaluate cor pulmonale
CV	Present in type IIIc: Mitral valve calcification Aortic valve calcification Aortic calcifications Coronary ostia calcifications	Easy fatigability Dyspnea on exertion Decreased activity Chest pain	Heart murmur—may be diastolic or systolic	ECHO Chest CT ECG
GI	Splenomegaly Possible splenic infarction or rupture Hepatomegaly Possible liver fibrosis with resultant portal hypertension and liver failure	Usually painless splenomegaly but could present as painful if splenic infarction or rupture occurs Postprandial gastric fullness possible	Hepatosplenomegaly on palpation	AST, ALT, alk phos, albumin, total protein, bilirubin, calcium, phosphorus Abdominal US Abdominal CT
RENAL	Variable proteinuria Possible renal insufficiency			Urinalysis BUN/Cr
CNS	Horizontal supranuclear gaze palsy Convulsive crises Ataxia Oculomotor apraxia Seizures Dementia Myoclonus	History of the occurrence of any of the aforementioned effects	Careful eye examination for oculomotor apraxia or gaze palsy	CT scan of head
HEME	Thrombocytopenia (most common) Platelet dysfunction Anemia Leucopenia Coagulation factor deficiency	Abnormal bleeding Easy bruising	Petechiae Ecchymosis	CBC, differential PT/ INR, PTT Platelet function assay Clotting time Iron, ferritin, transferrin Vitamin B_{12}
MS	Osteopenia Osteoporosis Bone marrow infiltration Pathologic fractures Avascular necrosis	Chronic pain Easy fracturing "Bone crises"	Bony deformity Painful palpation Painful ROM Restricted ROM Short stature possible	X-ray DEXA Bone marrow biopsy MRI CT scan

Key References: Tobias JD, Atwood R, Lowe S, et al.: Anesthetic considerations in the child with Gaucher disease, *J Clin Anesth* 5(2):150–153, 1993; Martins AM, Valadares ER, Porta G, et al.: Recommendations on diagnosis, treatment, and monitoring for Gaucher disease, *J Pediatr* 155(Suppl, 4):S10–S18, 2009.

Perioperative Implications

Preoperative Preparation

- Assessment of platelet function, platelet count, hemoglobin, and coagulation factors.
- Preparation for potential transfusion needs, including PRBC, FFP, and platelets.
- Measurement of serum anticonvulsant levels to ensure that these levels are within therapeutic range.
- Liver function testing.
- ECG and consider ECHO, especially if concern for type IIIc disease.
- Consider ranitidine and metoclopramide preop given increased risk of GERD.
- Consider CXR and ABG and PFTs in pts with pulm involvement.
- Consider antisialagogue for pts with copious oral secretions.
- Enzyme replacement therapy in the preoperative period has shown to decrease organomegaly and improve hematologic abnormalities in adult disease and may also be of benefit in juvenile disease.

Monitoring

- Standard ASA monitoring with consideration for more invasive monitoring depending on procedure, with specific attention to risk of blood loss

Airway

- Pts may present with restrictive or obstructive airway disease.
- Copious secretions may be present.
- Airway obstruction could occur with induction if pt has bulbar involvement with resultant poor control of pharyngeal musculature and/or infiltration of upper airway with glycolipids.
- Pathologic vertebral fractures should be of consideration for potential cervical instability.
- Few reports of airway management difficulties; however, thorough preoperative evaluation with consideration for possible difficulties should be performed.

Induction

- Consider rapid sequence induction with cricoid pressure in pts with significant GERD.
- Special care when positioning due to increased risk of pathologic fracturing.
- Special care with padding bony prominences due to increased risk of pressure necrosis in pts with severe CNS involvement and malnutrition.

Maintenance

- No specific advance of one technique over the other
- Choice of muscle relaxant more controversial given CNS involvement, but no reported adverse effects with use of succinylcholine

Extubation

- Ensure airway protective reflexes are intact prior to extubation due to increased risk of GERD and aspiration

Adjuvants
- Careful consideration to increased bleeding risk if considering regional anesthesia.
- Must obtain bleeding time, coagulation studies, and platelet count prior to performing regional anesthesia.
- Parenteral opioids are acceptable.

Postoperative Period
- Extended postoperative monitoring for 24 h with pulse oximetry
- May require frequent suctioning and positioning especially with more severe CNS dysfunction
- Continue anticonvulsive therapy
- May require PRBC and/or FFP transfusion for continued bleeding

Anticipated Problems/Concerns
- Intraoperative hemorrhage with the potential for continued hemorrhage in the postop period
- Respiratory failure and pulmonary complications in pts with lung involvement
- Aspiration
- Seizures

Kartagener Syndrome

Nancy C. Wilkes

Risk
- KS, first described in 1933, is part of a larger family of diseases classified as PCD.
- The triad of KS consists of bronchiectasis, chronic sinusitis, and situs inversus; it has an incidence estimated at 1:15,000–40,000 births.
- The disease is likely underdiagnosed because a limited amount of centers have resources to provide an accurate diagnosis.
- No known predilection for race or gender.
- Symptoms more prevalent in children in the first decade of life.

Perioperative Risks
- Morbidity: Lung infection, pulm edema, atelectasis, sinusitis

Worry About
- Pulm function and anatomy.
- Airway obstruction due to ineffective clearance of secretions.
- Bronchiectasis, which can lead to cor pulmonale, amyloidosis, and pulm edema and is usually found in the middle or lower lobes in KS pts, as opposed to the upper lobes in cystic fibrosis pts.
- Chronic disease with variable onset.
- Chemical injury from aspiration in left lung, which is the larger lung in pts with KS.
- Unintended bronchial intubation with single-lumen ETT, resulting in nonventilation of right lung (in those with pulm inversion).
- Left-sided double-lumen tubes may occlude orifice of left upper lobe.
- Nasal catheters relatively contraindicated because of risk of paranasal sinusitis and ear infections.
- Increased susceptibility to overall infection due to impaired neutrophil chemotaxis.

Overview
- Complete situs inversus (including dextrocardia).
- PCD resulting in chronic respiratory tract infections, bronchiectasis, and sinusitis.
- Approximately half of patients with PCD have situs inversus and thus are classified as having KS.

Etiology
- Congenital defect in synthesis of various parts of cilia (dynein arms, radial spokes, nexin links, microtubules) that results in abnormal/dyskinetic ciliary movement.
- Ciliated epithelium covers most areas of the upper resp tract, including the nasal mucosa, paranasal sinuses, middle ear, eustachian tube, and pharynx. The lower resp tract contains ciliated epithelium from the trachea to the resp bronchioles.
- Autosomal recessive inheritance pattern; genetically heterogeneous with multiple chromosomes likely responsible for phenotype.

Usual Treatment
- Aerosol administration to reduce secretion viscosity
- Antimicrobial therapy for chronic resp tract infections and sinusitis
- Surgical intervention for persistent bronchiectasis
- Conventional and assisted airway clearance techniques (chest physiotherapy, PEP mask, forced oscillation techniques, exercise programs, and physical activity)
- Nasal steroid sprays
- Inhaled bronchodilators and anti-inflammatory medications to treat bronchospasm

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dextrocardia		Right-sided heart tones	CXR, ECHO, ECG
RESP	Bronchiectasis Ciliary dyskinesia	Dyspnea Cough Halitosis	Decreased breath sounds, rhonchi, crackles, wheezes	CXR, bronchoscopy, spirometry, bronchography
IMMUNO	Chronic pansinusitis, nasal polyposis Bronchitis	Nasal drainage, morning sore throat Cough, mucus production	Frontal and maxillary tenderness Rhonchi	CT sinuses Sputum and tracheal aspirate for culture and Gram stain
	Pneumonia Otitis media	Cough, fever Earache, hearing loss	Rales, rhonchi Erythematous tympanic membrane	CXR, SpO_2 Audiometry, tympanotomy

Key References: Leigh MW, Pittman JE, Carson JL, et al.: Clinical and genetic aspects of primary ciliary dyskinesia/Kartagener syndrome, *Genet Med* 11(7):473–487, 2009; Mathew PJ, Sadera GS, Sharafuddin S, et al.: Anaesthetic considerations in Kartagener's syndrome–a case report, *Acta Anaesthesiol Scand* 48(4):518–520, 2004.

Perioperative Implications

Preinduction
- Consider omitting anticholinergics and cough suppressants from preanesthetic medication.
- Chest physiotherapy, bronchodilators, and incentive spirometry are often beneficial.
- Treat underlying pulm infections.
- Immunize against influenza A and pneumococcal organisms.

Monitoring
- In dextrocardia, position of ECG leads should be the mirror image of normal, as should that of paddles of external defibrillation, cardioversion, and pacing.
- Because the great vessels and thoracic duct are likely to be reversed, consider cannulation of the internal jugular vein from the left.
- Pulm artery cath should be oriented in anticipation of a clockwise direction of migration.
- Pregnant pts with KS should be positioned in right uterine displacement rather than left.

Induction and General Anesthesia
- Emphasize aseptic technique secondary to abnormal neutrophil chemotaxis.
- Aim for nontraumatic airway manipulation to avoid possible infection.
- Humidify inspired gases.
- Inhalation injury usually occurs in left lung, which is also larger lung.
- Bronchial intubation with a single-lumen ETT usually involves left side.
- Right bronchial suctioning will be more difficult to perform with nonangulated suction cath.
- Left-sided double-lumen tubes may occlude orifice of left upper lobe.
- When lung isolation is needed, consider tracheal intubation first with a bronchial blocker in the appropriate bronchus.
- If a double-lumen tube is required, consider inserting a left-sided tube with the bronchial tube on the right; the endobronchial stylet and the upper part of tube must be bent 180 degrees from original orientation prior to insertion such that the normal curvature of the oropharynx is still followed. The same principles apply to use of a right-sided tube.
- Extubation of the trachea should occur as soon as possible after the patient meets common extubation criteria.

Regional Anesthesia
- Use regional or local anesthetic techniques when possible to avoid airway manipulation and complications and to preserve resp muscle function intraop and postop.

Postoperative Period
- Consider nonnarcotic analgesia and/or epidural analgesia for postop pain.
- Avoid excessive sedation and encourage early ambulation to aid in clearance of airway secretions
- Chest physiotherapy, bronchodilators, and incentive spirometry may be beneficial.
- Oral airway preferred over nasal airway secondary to increased risk of sinusitis.

Anticipated Problems/Concerns
- Lung infection is common as result of ciliary dyskinesia.
- Fluid overload can precipitate cor pulmonale and pulm edema.
- Avoid nasal cath and/or airways to minimize chances of paranasal sinusitis.

Kawasaki Disease

Kumaran Senthil | Todd J. Kilbaugh

Risk
- Incidence in USA: 20 hospitalizations per 100,000 children
- Most commonly in pts <3 y of age
- Asian and Pacific Islanders have a higher rate, implying an unknown genetic effect
- Infants <6 mo and children >5 y have a higher risk of developing coronary artery lesions

Perioperative Risks
- Risk of myocarditis, valvular disease, pericardial effusions, and arrhythmias during the acute phase, defined as within 2 wk of fever onset.
- Coronary artery thromboembolic events from coronary artery aneurysm, stenosis, or obliteration can develop subacutely, usually within 6 wk of fever onset, and can become chronic concerns.

Worry About
- Acute coronary syndrome in pts with history of KD with coronary artery pathology
- Diminished left ventricular ejection fraction in 20% of cases during acute phase
- Oral mucous membrane inflammation during acute phase
- Vomiting and abdominal pain with risk of aspiration
- Aseptic meningitis from KD or as a potential side effect from IVIG therapy

Overview
- Acute febrile illness characterized by medium vessel vasculitis that mimics an infectious process, with the potential risk of myocarditis, pericardial effusions, and arrhythmias in the acute phase and development of coronary artery aneurysms subacutely.
- KD is clinically diagnosed by at minimum of 5 days of high fever and with at least four of the following criteria, or fewer if coronary artery lesions are present:
  - Swelling of hands and feet or redness of palms and soles.
  - Polymorphous rash.
  - Bilateral limbic sparing conjunctival injection.
  - Strawberry tongue, cracked lips, or erythematous oropharynx.
  - Cervical adenopathy with greatest node ≥1.5 cm in diameter.
- Atypical KD does not meet all of the clinical criteria for a complete diagnosis but meets some, with additional lab findings, such as elevated liver enzymes, decreased albumin, anemia, or sterile pyuria.
  - Atypical KD is more common in infants and older children and therefore is associated with greater risk for development of coronary artery lesions.
- Treated with high-dose IVIG and aspirin, preferably before day 10 of fever to limit coronary pathology.
- Risk of developing coronary artery lesions is approximately 3–5% of those treated with IVIG and 25% of those untreated.

Etiology
- No known etiology.
- Theories include viral illness, toxin-mediated process, or infectious trigger leading to vasculitis in predisposed pts.

Usual Treatment
- High-dose IVIG and high-dose aspirin within 10 d of illness to minimize risk of coronary artery lesions.
- If fevers recur, most clinicians consider another course of IVIG after 48 h from initial administration.
- Japanese data supports use of corticosteroids, but no supporting evidence in USA populations.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Conjunctival Injection Oral/mucosal inflammation Cervical adenopathy	Pain	Conjunctivitis, but sparing the limbus Strawberry tongue, cracked lips	
RESP	Pleural effusions Pulmonary nodules or interstitial infiltrates	Dyspnea	Tachypnea, dullness to percussion Dry crackles	CXR, US CT scan if other imaging is insufficient
CV	Congestive heart failure via myocarditis, pericardial effusions Valvular abnormalities, arrhythmias Coronary artery abnormalities Medium vessel noncoronary aneurysms	Exertional dyspnea, chest pain, abdominal pain Exertional chest pain	Tachycardia, S_3, distant heart sounds, hepatomegaly Tachycardia, systolic or diastolic murmur Palpable pulsatile masses	ECG, CXR, ECHO ECG, Holter monitoring, echocardiography ECHO, coronary angiography US
GI	Hydrops of the gallbladder	N/V, diarrhea, jaundice	RUQ tenderness, scleral icterus, hepatomegaly	RUQ ultrasound, LFT, GGT, bilirubin
CNS	Aseptic meningitis Anterior uveitis	Irritability, lethargy, headache Visual changes	Meningismus, photophobia, phonophobia	Lumbar puncture Slit lamp evaluation
HEME	Anemia Thrombocytosis (after first wk)	Fatigue	Pallor	CBC, reticulocyte count
DERM	Polymorphous exanthem		Starts as perineal desquamation, progresses to diffuse, erythematous, maculopapular	

Key References: Son MF, Newburger JW: Kawasaki disease, *Pediatr Rev* 34(4):151–162, 2013; Morrison JE, Anderson M, Chan KC, et al.: A 15-year review of children with Kawasaki's Syndrome having general anesthesia or deep sedation, *Paediatr Anaesth* 15(12):1053–1058, 2005.

Perioperative Implications

Preoperative Preparation
- If no diagnosis of undiagnosed protracted fever with rash, consider diagnosis of KD and potentially delay nonemergent cases until adequate cardiac evaluation.
- Assess cardiac status.
- In acute phase, concern for myocarditis and pericardial effusion with potential for development of acute heart failure.
- For pts with history of KD, assess coronary status and determine risk of developing myocardial ischemia.
- Assess need for rapid sequence intubation if active nausea or vomiting or risk for aspiration.

Monitoring
- Arterial line if indicated; insert with ultrasound guidance to evaluate for possible noncoronary arterial aneurysms.

- ECG with lead II and V5 monitoring to assess for ST segment changes.
- Consider attaching defibrillator/cardioversion pads if Hx of significant arrhythmias.

Airway
- Consider rapid sequence intubation for risk of aspiration.
- Assess for difficult airway secondary to friable oral and pharyngeal mucosal surfaces.

Preinduction and Induction
- If compromised cardiac status, induction with minimal alterations in afterload and preload.
- If known severe CAD, maintain afterload to preserve coronary perfusion pressure.
- If clinically significant pleural effusions, expect loss of functional residual capacity and faster desaturation.

Maintenance
- Avoid fluid overload for pts with depressed cardiac function.
- Avoid hypotension in pts with significant coronary disease.
- In acute phase, highly febrile pts may have a greater anesthetic need and insensible fluid loss.

Extubation
- Period with greatest myocardial oxygen consumption and vigilance for cardiac decompensation

Postoperative Period
- Continued ECG for myocardial ischemia or signs of heart failure.
- Consider perioperative troponin trending if concern for subclinical myocardial ischemia based on exam or ECG findings.

Anticipated Problems/Concerns
- If acute myocardial ischemia from coronary thromboembolic event, consider cardiac cath with angioplasty and stenting.
- If CHF develops in the setting of fluid overload or evidence of myocardial ischemia, consider transport to ICU for continued monitoring and treatment.

Klippel-Feil Syndrome

Ronald S. Litman | Lee A. Fleisher

Risk
- Incidence estimated at 1:40,000 live births (but milder cases go unrecognized).
- Slight female predilection (63%).

Perioperative Risks
- Cervical spine instability and cardiopulmonary complications.
- Often occurs in association with other clinical syndromes (e.g., fetal alcohol, Goldenhar).

Worry About
- Exacerbation of cervical spine instability during airway maneuvers, endotracheal intubation, and subsequent positioning.

Overview
- Congenital abnormality consisting of the following triad of findings: Fusion of two or more cervical vertebrae, low posterior hairline, cervical immobility.
- Type 1: Extensive fusion of many cervical vertebrae; type 2: Fusion at only one or two cervical interspaces; type 3: Fusion in the cervical spine and in the lower lumbar spine.
- Severity ranges from mild (often not recognized until late in life) to severe (recognized at birth because of obvious deformity).
- Careful preop assessment of cervical spine anatomy and degree of instability.
- Review of systems for other congenital abnormalities: Renal dysfunction (64%), scoliosis (60%), deafness (30%), Sprengel scapular deformity (25–35%), congenital heart disease (4.2–14%), mental deficiency, pulmonary disability, and cleft lip and palate.

Etiology
- Unknown

Usual Treatment
- Symptomatic; depends on organ system involvement

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Head and neck immobility		Decreased ROM of cervical spine, low posterior hairline, webbed neck, facial asymmetry, cleft palate, torticollis, vocal cord dysfunction	Flexion/extension radiographs of cervical spine Consider MRI of cervical spine
CV	Bradyarrhythmias and AV conduction pathway abn (due to CNS malformations) Cardiac defects (most commonly VSD)	Syncope	Murmurs	ECG, ECHO
RESP	Central alveolar hypoventilation, pulmonary agenesis or hypoplasia, restrictive lung disease (due to severe scoliosis)	Sleep apnea, snoring, difficulty breathing		ABG CXR (if symptomatic)
RENAL	Urinary tract abn, renal agenesis, ureteral duplication			BUN, Cr if indicated, renal US
CNS	Hindbrain abnormality (e.g., syringomyelia, Arnold-Chiari malformation) Mental retardation, deafness, strabismus	Peripheral neurologic dysfunction (e.g., weakness, paresthesias, paraplegia, quadriplegia)	Neurologic exam	
MS	Scoliosis, Sprengel deformity (scapular elevation), hypermobility of cervical spine, spondylosis/decreased mobility of cervical spine		Exam of spine and shoulders	X-rays if indicated

Key References: Stallmer ML, Vanaharam V, Mashour GA: Congenital cervical spine fusion and airway management: a case series of Klippel-Feil syndrome, *J Clin Anesth* 20(6):447–451, 2008; Hase Y, Kamekura N, Fujisawa T, et al: Repeated anesthetic management for a patient with Klippel-Feil syndrome, *Anesth Prog* 61(3):103–106, 2014.

Perioperative Implications

Preoperative Preparation
- Careful and complete evaluation of cervical spine anatomy and instability and of other major organ system abnormalities

Monitoring
- Depends on pt's physical condition

Airway
- If indicated, awake intubation using maneuvers to stabilize cervical spine; complete immobility with use of fiberoptic intubating bronchoscope ideal

Preinduction/Induction
- Depends on pt's physical condition

Maintenance
- Careful positioning of head and neck with maintenance in neutral position

Extubation
- Depends on extent of cervical spine pathology and respiratory compromise

Adjuvants
- No special considerations

Anticipated Problems/Concerns
- Exacerbation of preexisting cervical spine instability leading to neurologic deterioration

Lambert-Eaton Myasthenic Syndrome

Ahmed Alshaarawi | Jeffrey R. Kirsch

Risk

- Unknown true incidence. Few studies of very specific regions outside USA report prevalence between 0.48 and 3.42 per million.
- 60–84% of LEMS patients have SCLC.
- LEMS mostly affects middle-aged adults, with rare occurrence in children.

Perioperative Risks

- Increased risk for fall when ambulating, due to proximal lower extremities weakness
- Hypotension due to autonomic dysfunction
- Prolonged emergence secondary to persistent muscle weakness
- Respiratory compromise or collapse after extubation

Worry About

- Failing extubation, necessitating unplanned ICU admission.
- Exacerbation of muscle weakness postoperatively.
- Concomitant presence of SCLC may complicate respiratory function.

Overview

- Autoimmune disorder affecting the presynaptic NMJ.
- Most patients present with slow progressive lower extremities muscle weakness.
- LEMS is different from MG:
  - LEMS affects the proximal lower extremities more than MG.
  - Primarily affects presynaptic mechanisms, whereas MG primarily affects postsynaptic mechanisms.
  - Muscle weakness transiently resolves with activities in LEMS.
  - LEMS is strongly associated with SCLC.
- Pathophysiology: Antibodies attack VGCC, diminishing the release of calcium and subsequent reduction in the release of acetylcholine in the presynapse.

Etiology

- LEMS is an autoimmune disease. IgG antibodies target the P/Q type VGCC at the presynaptic endplate of the NMJ.
- The strong prevalence of SCLC in patients with LEMS suggests the presence of the same antigen in SCLC and at the presynaptic NMJ.
- Cerebellar degeneration may be present in some patients with LEMS. This is likely due to the presence of the P/Q type VGCC in the cerebellum.
- Acetylcholine is necessary for the autonomic function and its reduction in LEMS may result in autonomic nervous system dysfunction.

Usual Treatment

- First line treatment with 3,4-diaminopyridine, which blocks potassium at the neurosynapse, allowing for the release of acetylcholine. It also directly facilitates neurotransmission at VGCC.
- Removing or treating the SCLC tumor may be considered if diaminopyridine is ineffective in alleviating symptoms.
- In cases of severe weakness prednisone and azathioprine may be added to treatment therapy. This treatment must be initiated slowly because it may cause acute weakness prior to having their positive impact.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Ptosis	Drooping of eyelid	Cranial nerve assessment	Symptoms reported by pt
RESP	Respiratory weakness	Dyspnea	Supplemental O_2 dependence Difficulty taking deep breaths	PFTs, including inspiratory force measurements. Phrenic nerve stimulation recordings CXR, CT scan
CNS	Autonomic dysfunction	Dry mouth Erectile dysfunction	Reduced saliva Impotence	Symptoms reported by pts
MS	Proximal lower limbs weakness	Aching, fatigued or stiff muscles affecting gait	Depressed or absent DTRs	Plasma levels of P/Q type VGCC antibodies Electromyography

Key References: Titulaer MJ, Lang B, Verschuuren JJ: Lambert–Eaton myasthenic syndrome: from clinical characteristics to therapeutic strategies, *Lancet Neurol* 10(12):1098–1107, 2011; Weingarten TN, Araka CN, Mogensen ME, et al.: Lambert-Eaton myasthenic syndrome during anesthesia: a report of 37 patients, *J Clin Anesth* 26(8):648–653, 2014.

Perioperative Implications

Preoperative Preparation

- Confirm adequate respiratory function. Verify use of supplemental oxygen at home.
- Prepare for possible ICU admission if unable to extubate due to muscle weakness.
- Consider use of monitored anesthesia care or regional anesthesia whenever possible instead of general anesthesia.
- Assess baseline strength of extremities.

Monitoring

- Standard monitoring
- Arterial line in patients presenting with respiratory compromise or significant autonomic dysfunction
- Nerve stimulation monitoring

Airway

- Avoid intubation whenever possible.
- Consider use of supraglottic airway instead of endotracheal intubation to avoid muscle relaxation.

Preinduction and Induction

- Depolarizing and nondepolarizing muscle relaxants can be used if muscle relaxation is required.
- If unable to avoid endotracheal intubation, consider intubating without muscle relaxants. Avoid neuromuscular relaxants whenever possible. Remember that inhaled anesthetics each have efficacy in neuromuscular blockade.

Maintenance

- Both IV and inhalational anesthetics have been given safely to LEMS pts. Vigilance to administer minimum requirements of anesthetics will likely minimize perioperative complications.
- Hypotension may occur as a result of autonomic dysfunction; vasopressors may be given as boluses or continuous infusion.
- Pts on prednisone should receive a perioperative dose of hydrocortisone.

Extubation

- Ensure return of safe cognitive function, muscle strength, and ventilatory function before extubation.

Postoperative Period

- Judicial use of opioids in the PACU to avoid respiratory compromise.
- Increased susceptibility to respiratory failure and reintubation.
- Consider continued monitoring of pulse oximetry after discharge from PACU.

Anticipated Problems/Concerns

- Muscle weakness
- Respiratory compromise

Landouzy-Dejerine Dystrophy (Facioscapulohumeral Muscular Dystrophy)

Francis Veyckemans

Risk

- Prevalence estimated to be 1:20,000
- Affects equally males and females
- Third most common familial myopathy after myotonic dystrophy and Duchenne muscular dystrophy

Perioperative Risks

- No greater risk of malignant hyperthermia than normal population.
- Possible risk of acute rhabdomyolysis if succinylcholine and/or a halogenated agent is used. However, the dystrophin-glycoprotein complex is not involved in Landouzy-Dejerine dystrophy, and no case of anesthesia-induced rhabdomyolysis has been reported so far.
- Perioperative respiratory complications
- Supraventricular paroxysmal tachycardia

Worry About

- Muscle weakness

Overview

- Muscular dystrophies are a heterogeneous group of genetic muscle disorders leading to progressive weakness and muscle wasting. They were grouped together based on a common histologic picture: variations in fiber size and areas of muscle necrosis

progressively replaced with fat or connective tissue. They are classified based on three phenotypic considerations: predominant distribution of affected muscles, whether facial muscles are affected or not, and mode of inheritance.

- Its clinical presentation varies widely. Approximately 30% of people with a mutation do not present any clinical sign; this could be due to mosaicism. For those presenting with clinical signs, the distribution of muscle weakness varies widely. Two main clinical forms are described below.
- Congenital or infantile form: Facial muscles are affected before 5 years of age, and the muscles of the shoulder and hip girdle around 10 years: muscular involvement is bilateral and symmetric, resulting in apparent facial diplegia and poor expression of emotions. Sensorineural hearing loss is common. Hyperlordosis and scoliosis appear in late childhood and adolescence.
- Usual form: Muscular involvement is asymmetric and starts during adolescence. The first signs affect the face and the shoulder girdle: difficulties drinking with a straw, pursing the lips or whistling, inability to close the eyes (risk of keratitis during sleep), and protruding lips (tapir mouth). All muscles of the shoulder are affected but the deltoid is usually spared, which results in a preserved deltoid bulk despite surrounding muscles atrophy: this produces scapular winging when the arms are abducted. The foot dorsiflexors and the hip are affected later and result in stepping and difficult walking (need for a cane). Weakness of abdominal wall muscles is frequent and can result in some abdominal wall protrusion. The following signs are also frequent: (1) early onset and bilateral sensorineural hearing loss, which varies from mild to moderate; (2) bilateral retinal exudative telangiectasia, called Coats disease, with marked tortuosity of retinal arterioles. Respiratory muscle involvement is usually mild, but severe cases can result in early onset and progression of severe restrictive pulmonary dysfunction, and cor pulmonale. A few cases of hypertrophic cardiomyopathy and cardiac arrhythmias (mainly supraventricular paroxysmal tachycardia) have been observed.
- The evolution is slow and progressive: 20% become wheelchair bound, and less than 5% of pts end up with some form of ventilation support during sleep.
- Paraclinical examinations: CPK: Normal or mildly elevated (<1500 UI/L); RFT: Restrictive pattern in severe forms; EMG: Myopathic changes.

Etiology

There are currently two different known genetic causes of LDD:

- Type 1 [OMIM 158 900] is the most frequent (85% of cases); it is caused by a shortening of the D4Z4 zone in the subtelomeric region of chromosome 4q (4q35.2). This zone is usually hypermethylated and includes tandem repeats of a fragment containing a DUX4 (nuclear protein) open reading frame. The normal number of these repeats varies between 11 and 100: it is lower than 10 in case of myopathy but results in insufficient repression of the usually silent DUX4 gene only if there is a functional pLAM sequence nearby. In this case the degree of chromosomal shortening is correlated with the severity of the disease ,and its earlier age of onset
- Type 2 [OMIM 158 901] is due to a mutation of a gene on chromosome 18p11.32 encoding for protein SMCHD1: this produces a hypomethylation of chromosomes 4 and 10, including both alleles of the D4Z4 zone and has the same consequence on repression of DUX4 gene

Usual Treatment

- Supportive. Some experimental trials are ongoing.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS	Muscle weakness: Poor facial, expression, inability to close eyes, weakness in shoulder girdle	Usual activities? Chronic muscle or joint pain?	Eye closure? Ability to perform head lift maneuver? Shoulder girdle amyotrophy Cough?	CPK: Normal or mildly elevated Neuromuscular monitoring: Use unaffected muscle!
RESP	Involvement: Usually mild			PFT
CV	Rarely: Atrial dysrhythmias, hypertrophic cardiomyopathy			ECG Cardiac ECHO if ECG abnormal or murmur
HEENT	Hearing loss			

Key References: Mercuri E, Muntoni F: Muscular dystrophies, *Lancet* 381(9869):845–860, 2013; Nitahara K, Sakuragi T, Matsuyama M, et al.: Response to vecuronium in a patient with facioscapulohumeral muscular dystrophy, *Br J Anaesth* 83(3):499–500, 1999.

Perioperative Implications

Preoperative Preparation

- ECG: If it shows any abnormality (e.g., rhythm, conduction) a transthoracic cardiac echography is useful (cardiomyopathy, pulm Htn secondary to chronic cor pulmonale?). Check SpO_2 on room air and, if you anticipate using muscle relaxants, whether the pt is able to perform the head lift maneuver in order to know if clinical assessment of adequate muscle reversal will be possible. A diagnosis of LDD should not hide the usual preoperative concerns (e.g., allergies, hemostasis, smoking habits, venous access). Pt should be allowed to enter the OR with hearing aids, if any.

Monitoring

- ASA standards
- Neuromuscular monitoring, use a muscle group that is not or only minimally dystrophic and checking its baseline TOF ratio before administering any muscle relaxant.
- Central venous access: Ultrasound-guided jugular or subclavian vein catheterization is recommended because muscular atrophy in the head and neck region makes usual surface landmarks less reliable.
- Locoregional anesthesia: Hyperlordosis could make neuraxial blocks more difficult to achieve; regarding peripheral nerve blocks, regional amyotrophy and dystrophy increase muscular echogenicity and could make nerve identification more difficult.
- Obstetrics: There seems to be an increased risk for breech presentation in mothers with LDD.

Airway

- Although no case of difficult mask ventilation/intubation has been reported in LDD, the upper airway should be carefully assessed because, in addition to factors independent of LDD (e.g., retrognathism), facial muscle atrophy could result in reduced mouth opening and neck mobility.

Induction

- All induction agents can be used; susceptibility to malignant hyperthermia is not greater than in the normal population, but LDD is considered to be phenotypically similar to Duchenne and Becker muscular dystrophies and could thus carry a risk of acute rhabdomyolysis in case of exposure to succinylcholine and or halogenated agents. However, very few cases of uneventful use of enflurane or sevoflurane have been reported. Great care should be given to eye protection.

Muscle Relaxants

- Succinylcholine is best avoided as in any muscle disease; in individual case reports on the use of vecuronium and atracurium, normal sensitivity and faster recovery were observed; rocuronium has been used without problem and reversed with sugammadex.

Maintenance

- TIVA with propofol has been used successfully; see Induction regarding the use of halogenated agents.

Extubation

- Awake, ideally after a period of pressure support ventilation

Postoperative Period

- Chest physiotherapy
- Pain management: Should be titrated to effect, as for any other pt; in severe forms, overnight stay in PACU or ICU is a wise option.
- Chronic pain: Chronic muscle and joint pain is not unusual.

Anticipated Problems/Concerns

- Postop muscle weakness and respiratory failure in severe cases

Latex Allergy

Robert H. Brown

Risk

- Myelomeningocele (25–50%)
- Congenital urologic anomalies (25–50%)
- Healthcare workers (3–17%)
- Atopic individuals (6–11%)
- General population (0–6%)

Perioperative Risks

- Anaphylactic reaction leading to hypotension, bronchospasm, and CV collapse

Worry About

- A latex allergy is a type I immediate hypersensitivity reaction. Life-threatening anaphylaxis can be the first manifestation of the reaction. Latex-containing medical products are common throughout most medical environments.

Overview

- Type I (immediate) hypersensitivity reaction: Immune-mediated and involve IgE-specific latex proteins. Exposure can occur by either direct contact or through inhaled airborne particles. Symptoms can be localized or generalized, mild to life-threatening and including pruritus, hives, angioedema, wheezing, hypotension, tachycardia, and CV collapse.
- Type IV (delayed or contact dermatitis) hypersensitivity reaction: Cell mediated, occurs 24–48 h after exposure, and is localized. Symptoms include localized pruritus, swelling, and blisters.
- Increase in latex allergies coincided with the advent of universal precautions and the increased use of latex examination gloves, many with high allergen content.
- Exposure can occur both by contact and by inhalation of latex-containing powder.
- Considered to represent approximately 10% of all anaphylactic reactions reported for pts while under anesthesia.
- Increased risk with repeated exposures.
- Reaction caused by cross-linking latex specific IgE on mast cells, leading to degranulation and release of both immediate and delayed inflammatory mediators.
- Dx includes a Hx consistent with a latex reaction (e.g., time, exposure), nonspecific blood markers (e.g., serum mast cell tryptase), serology testing (RAST testing), and skin testing where available.

Etiology

- Exposure with subsequent sensitization in at-risk individuals is the usual etiology of a latex allergy. At-risk individuals commonly have identified risk factors, such as atopy, food allergies, and/or a Hx of multiple surgeries.

Usual Treatment

- Avoidance of exposure should be the primary consideration.
- There is no evidence any premedications can prevent or attenuate a type I hypersensitivity reaction.
- In cases of an anaphylaxis reaction, treatment includes stopping the exposure, intravascular volume expansion, epinephrine as needed to support BP, bronchodilators to treat bronchospasm. Antihistamines and corticosteroids are distant secondary therapies.
- A latex-safe environment, one with minimal latex allergen, insufficient to elicit a latex allergic reaction, should be considered for all healthcare locations.

Assessment Points

System	Assessment by Hx	PE	Test
CV	Hypotension, tachycardia, CV collapse	Tachycardia, vasoconstriction	ECG, BP
PULM	SOB, stuffy nose, cough, elevated airway pressures	Wheezing, accessory muscle use	Auscultation, spirometry, airway pressure
DERM	Pruritus, edema	Hives, urticaria, erythema, swelling	Visual exam
HEENT	Red, itching eyes	Angioedema	Visual exam
GI	Cramps, N/V, diarrhea		

Key References: Mertes PM, Demoly P, Malinovsky JM: Hypersensitivity reactions in the anesthesia setting/allergic reactions to anesthetics, *Curr Opin Clin Immunol* 12(4):729–735, 2012; Dewachter P, Mouton-Faivre C, Hepner DL: Perioperative anaphylaxis: what should be known? *Curr Allergy Asthma Rep* 15(5):21, 2015.

Perioperative Implications

- Ask all pts about any Hx of an allergy or reactions to latex products.
- Do not attempt to prevent with premedications.
- Provide a latex-safe environment, including the preop, intraop, and postop environment.
- If latex allergic reaction suspected, make sure the postop environment is latex safe.

Anticipated Problems/Concerns

- Many latex-sensitized individuals are unaware of their allergic status.
- 10% of anaphylactic reactions under anesthesia are presumed due to a latex reaction.
- Maintain vigilance with regard to potential inadvertent latex exposures.
- Consider allergic reaction if hypotension is unresponsive to usual pressor agents.

Lesch-Nyhan Syndrome

Roberta Hines

Risk

- X-linked recessive disorder due to deficiency on the enzyme HGPRT, resulting in the buildup of uric acid
- Incidence ~5.2 per million male births (where symptoms appear)

Perioperative Risks

- Hyperuricemia and hyperuricosuria (gout)
- Airway problems secondary to scarification from self-mutilation (lip and finger biting)
- Involuntary writhing
- Repetitive movement of arms and legs
- Impairment of renal function due to obstructive uropathy

Worry About

- Aspiration pneumonia (poor muscle control).
- May have associated megaloblastic anemia (poorly utilized vitamin B_{12}).
- Drug metabolism and prolonged drug effects secondary to metabolic defect and impaired renal function.

Overview

- Pts are usually mentally subnormal.
- Pts exhibit characteristic pattern of compulsive self-mutilation, spasticity, and choreoathetosis.
- Primary biochemical defect is almost complete absence of HGPRT.
- Enzyme defect leads to excessive purine production and elevated uric acid concentrations.

Etiology

- Genetic disease inherited as X-linked recessive trait (female carriers generally asymptomatic)

Usual Treatment

- No specific treatment of enzyme deficiency.
- Benzodiazepines frequently used to control self-mutilation and spasticity (baclofen may be helpful).
- Gene therapy possibility.
- Gabapentin.
- Gout can be treated with allopurinol.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Distortion of airway structures due to self-mutilation		Examine airway	
CV	Htn, CAD Adrenergic pressor response to stress is absent	Angina, angina-equivalent symptoms, PND	Displaced PMI S_3	ECG Pharmacologic stress testing Coronary angiography and ECHO
RESP	Aspiration pneumonia	SOB following vomiting episode	Rales Wheezing	CXR
GI	Vomiting Athetoid dysphagia	Dysphagia		
RENAL	Decreased renal function due to obstructive uropathy			BUN Cr IVP
CNS	Mental retardation Seizure disorders Decreased MAO activity		Mental status questioning	EEG Mental function tests
MS	Spasticity, contractures		ROM	

Key References: Williams KS, Hankerson JG, Ernst M, et al.: Use of propofol anesthesia during outpatient radiographic imaging studies in patients with Lesch-Nyhan syndrome, *J Clin Anesth* 9(1):61–65, 1997; Salhotra R, Sharma C, Tyagi A, et al.: An unanticipated difficult airway in Lesch-Nyhan syndrome, *J Anaesthesiol Clin Pharmacol* 28(2):239–241, 2012.

Perioperative Implications

Preoperative Preparation
- Antacids.
- H_2 blockers.
- Metoclopramide.
- IV access may be difficult.

Monitoring
- Routine
- ST-segment analysis if CAD present

Airway
- Rapid-sequence induction.
- Avoid succinylcholine.
- Awake fiberoptic intubation.

Preinduction/Induction
- Premedication where appropriate to help with behavioral issues.
- Avoid agents with renal metabolism (adjust dosing).

Maintenance
- Avoid agents with renal toxicity.
- No one agent or technique shown superior.
- Administer exogenous catecholamines with caution (due to associated Htn).

Extubation
- Awake to avoid aspiration

Adjuvants/Postoperative Period
- Make some space accessible to avoid injury to child.
- Benzodiazepines for spasticity.

Anticipated Problems/Concerns
- Hx unavailable or inaccurate because of retardation

Leukemia

Dilipkumar K. Patel | Nathan Poiro

Risk
- Estimated 318,389 individuals living with leukemia or in remission in USA
- Estimated 54,270 new cases and 24,450 deaths of leukemia in 2015
- Males >females
- ALL greater in children (median age of diagnosis 14 y)
- CML, CLL, and AML common in adults and diagnosed in sixth and seventh decades

Perioperative Risks
- Immunocompromised pt, tumor lysis syndrome (metabolic derangement), tumor compression of organs (anterior mediastinal mass), neutropenia (anemia, coagulopathy), hyperviscosity, oral mucositis, sequelae of cytotoxic agents (immunocompromised state, respiratory failure, cardiovascular failure), opportunistic infection, and sepsis
- Hematoma and/or bleeding, thromboembolism, diffuse alveolar hemorrhage from thrombocytopenia and splenic sequestration of platelets

Worry About
- Myelosuppression: Thrombocytopenia, anemia, and neutropenia
- Bone marrow suppression with NO; rare potential for malignant hyperthermia in ALL
- Upper airway edema, anterior mediastinal mass (paralysis, supine position)
- Pleural effusion, pneumonitis, and pulm fibrosis
- Tumor lysis syndrome (especially with dexamethasone), hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia, and renal failure
- Remote anesthesia location, airway difficulty, equipment, and monitoring

Overview
- Four main types of leukemia: ALL, AML, CLL, and CML. No staging system for leukemia.
- From 2004 to 2010, the 5-year relative survival rates overall: CML—59.9%, CLL—83.5%, AML—25.4%, ALL—70%, ALL—93% for children <5 y.
- Usually outpatient treatment, but may require GA or MAC for bone marrow biopsy, bone marrow harvest, central venous access/port placement, lumbar puncture (diagnostic and intrathecal chemotherapy), HSCT, bronchoscopy, pericardiocentesis, and radiation therapy.
- Mortality remains high post HSCT secondary to sepsis, pulmonary complications, and GVHD.

Etiology
- Largely unknown. Greaves hypothesis (in utero mutation and secondary delayed viral exposure).
- Strong suspicion that leukemia and lymphoma are virus-induced (e.g., EBV). Associated with genetic disorders (e.g., Down syndrome).
- Chronic exposure to benzene (primarily from tobacco smoke), extraordinary doses of radiation, and secondary malignancy from certain cancer therapies can be causes of the leukemia.
- Breastfeeding for 6 mo or more could lower childhood leukemia risk.

Usual Treatment
- Treatment varies with type of leukemia, age, and phase (beyond the scope of this chapter)
- Supportive treatment: Antimicrobial, blood transfusion, nutrition, and pain control
- Newer approaches: Monoclonal antibody, experimental cancer vaccines, donor lymphocyte infusion, gene therapy, autologous and allogeneic transplantation, and stem cell transplantation
- AML:
  - Ara-C
  - Anthracyclines: Daunorubicin, idarubicin + cytarabine
  - Gemtuzumab ozogamicin: ATRA
  - Arsenic trioxide: Vinca alkaloids: vincristine/vinblastine
  - Bone marrow transplant
- CML:
  - HSCT
  - Tyrosine kinase inhibitors: Imatinib mesylate (initial treatment of choice)
- Nilotinib
  - Dasatinib
  - Busulfan
  - Hydroxyurea
  - Interferon alfa, allopurinol
  - Splenectomy, radiation, bone marrow transplant
- CLL:
  - Cyclophosphamide
  - Corticosteroid
  - Fludarabine
  - Cytarabine
  - Bendamustine, rituximab
  - Alemtuzumab
  - Radiotherapy
- ALL:
  - Imatinib, clofarabine, L-asparaginase, daunorubicin, vincristine, dexamethasone, doxorubicin, cytarabine (ara-C)
  - Radiation therapy, intrathecal chemotherapy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Ulceration, oral lesions	Dysphagia, pain	Airway assessment	
CV	Rare: Pericardial effusion, conduction defects, murmurs, CHF Mediastinal mass	Dyspnea, fatigue	Narrow pulse pressure, pericardial friction rub, cardiomegaly	CXR, CT scan, ECG, ECHO
GI	Hepatosplenomegaly hypoalbuminemia	Loss of appetite Weight loss	Hepatosplenomegaly	Albumin
HEME	Anemia Leukostasis Thrombocytopenia	Weakness, easy fatigue,	Pallor Ecchymoses Petechiae, easy bruising, nose-bleeds	CBC Bone marrow aspirate results
RENAL	Renal failure from tumor lysis syndrome (acute loss of tumor)	Decreased UO	Decreased UO	BUN/Cr, hyperkalemia ↑ phosphate, ↑ or ↓ Ca^{2+}
CNS	Cranial nerve infiltration (very rare), meningeal leukemia (less common in adults), vincristine neuropathy	Cranial nerve palsies, clouding of mental status, peripheral neuropathy	Weakness	EMG
MS	Infiltration of bony cortex and periosteum, synovial membranes	Bone pain	Bone swelling	X-ray CT scan

Key References: Bryan JC, Jabbour EJ: Management of relapsed/refractory acute myeloid leukemia in the elderly: current strategies and developments, *Drugs Aging* 32(8):623–637, 2015; Latham GJ: Anesthetic considerations for the pediatric oncology patient—part 2: systems-based approach to anesthesia, *Paediatr Anaesth* 20(5):396–420, 2010.

Perioperative Implications

Preoperative Preparation

- Assess volume status, CBC, electrolytes, renal function, N/V, diarrhea, and oral mucositis.
- Review sign and symptoms and imaging reports of mediastinal mass for compromised airway.
- Airway assessment: Oral mucosal ulceration, edema, fibrosis, and neck mobility.
- Neutropenia precaution: Periop isolation, aseptic technique for safe port access, avoidance of per rectum medication and probe.

Monitoring

- Routine

Airway

- Signs of dysphagia, ulcerations, and airway bleeding from chemotherapy and candidiasis.
- Oral leukemia lesions can occur prior to or during therapy.
- Anterior mediastinal mass: Risk of difficult intubation, ventilation, and compromise hemodynamic. Fiber optic intubation, inhalation induction, and rigid bronchoscopy may be required; lateral or prone position may help with ventilation. Avoid muscle relaxants.
- Chronic radiation: Potential for difficult airway; high-dose or chronic radiation to oral cavity, head, and neck cause fibrosis and stiffness of soft tissue resulting in limited mouth opening and neck extension.
- Post radiation changes: Affecting airway mucosal fibrosis, subglottic edema, and supraglottic and subglottic narrowing or stenosis may complicate the airway management.
- Leukemic infiltration of tonsils and adenoids, retropharyngeal lymph nodes, and cervical lymphadenopathy may cause airway obstruction and difficulty in intubation and ventilation.

Induction

- Brief heparinization and thrombocytopenia may influence choice of local, spinal, or epidural
- MAC or deep sedation with propofol and remifentanil infusion preferred over propofol alone
- GA may require in younger pediatric age with special equipment and monitoring in various remote anesthesia locations, such as radiation therapy suite

Maintenance/Extubation

- Routine inhalation technique or TIVA
- Low FIO_2 for during and after bleomycin therapy
- Prophylaxis for N/V
- Multimodal pain management

Anticipated Problems/Concerns

- Risk of infection; aseptic technique with placement of all lines.
- Dexamethasone may precipitate tumor lysis syndrome; anesthesia provider should communicate with oncology team before using dexamethasone for N/V prophylaxis in high-risk pts.
- Caution required for subclinical cardiomyopathy, pericardial effusion, airway management, and pulmonary dysfunction after chemotherapy and radiation therapy.
- Use of epidural blood patch for treatment of PDPH is controversial; may increase risk for infectious complication and CNS leukemia spread.
- Blood products: CMV depleted, irradiated blood, platelets; careful with doses and GVHD.
- ICU admission: Cardiorespiratory failure, pleural effusion, pneumonia, sepsis, compromised airway, GVHD following HSCT, pulmonary complications, and multiple organ failure.

Liddle Syndrome

Taiwo A. Aderibigbe | Lee A. Fleisher

Risk

- Extremely rare but described in a variety of populations
- True incidence and prevalence unknown

Perioperative Risks

- Chronically untreated Htn

Worry About

- Undiagnosed cerebrovascular, CV, and/or renal disease secondary to chronic Htn
- Worsening of hypokalemia with hyperventilation and nasogastric suctioning
- Hypokalemia-induced dysrhythmias and potentiation of NMB

Overview

- Monogenic AD gain-of-function mutation in the ENaC resulting in early onset Htn, hypokalemia, and metabolic alkalosis with suppressed plasma renin activity; resembles primary aldosteronism but aldosterone excretion is markedly suppressed (also known as "pseudoaldosteronism").
- Htn results from volume expansion due to increased Na^+ reabsorption via the constitutively active ENaC; urinary secretion of K^+ and H^+ occurs to balance out movement of electrical charges, resulting in a hypokalemic metabolic alkalosis.
- Presentation is variable.
  - Htn may not be early in onset or severe.
  - Hypokalemia may be absent.
  - Family history is not reliable, as spontaneous mutations have been reported.

Etiology

- ENaC is a membrane-bound ion channel located on the apical membrane of the principal cell in the distal tubule, which is selectively permeable to sodium ions; their activity is normally regulated by aldosterone.
- ENaC is composed of three subunits: α, β, and γ.
- NEDD4, a ubiquitin ligase enzyme, negatively modulates ENaC via ubiquitination.
- Gene mutations resulting in deletions or alterations of the carboxy-terminus of the β or γ subunits (located on chromosome 16p) make NEDD4 binding impossible; this prevents channel degradation and removal, resulting in the constitutive activity of ENaC.

Usual Treatment

- Amiloride or triamterene therapy (direct ENaC inhibitors) with a low-sodium diet.
- Kidney transplantation is curative.
- Htn and hypokalemia are not responsive to mineralocorticoid antagonists (e.g., spironolactone) because the increased activity of ENaC is not mediated by aldosterone.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn (LVH with diastolic dysfunction, MI/CHF if long standing), dysrhythmias	Angina, poor exercise tolerance, palpitations	Two-flight walk, ability to lie flat, chest auscultation, peripheral edema check	ECG, ECHO, CXR
RENAL	Decreased serum K^+, nephropathy	Constipation, fatigue, muscle weakness/pain		K^+, BUN/Cr

Key References: Hansson J: Liddle's syndrome: review of the clinical disorder and its molecular genetic basis, *Endocrinologist* 10(4):229–236, 2000; Hayes NE, Aslani A, McCaul CL: Anaesthetic management of a patient with Liddle's syndrome for emergency caesarean hysterectomy, *Int J Obstet Anesth* 20(2):178–180, 2011.

Perioperative Implications

Preoperative Preparation

- Treatment of Htn; ideally normalization of <140/90 mm Hg would occur prior.
- Assessment of cardiac function (ECG, CXR, possible ECHO).
- Assessment of renal function (specifically BUN/Cr).
- Assessment of electrolyte balance (specifically K^+) and associated clinical symptoms.

Monitoring

- Continuous ECG to monitor myocardial ischemia and hypokalemic dysrhythmias

Airway

- No airway changes expected

Induction

- Labile hemodynamics in pts with longstanding Htn requires careful titration of induction medications.
- Caution using drugs dependent on renal excretion.

Maintenance

- Higher mean arterial pressure goals tend to be required.
- Monitor fluid balance; renal insufficiency is possible, and untreated pts are volume-overloaded.
- Possible prolongation of NMB due to hypokalemia.
- Lyte monitoring/replacement if symptomatic prior or ECG changes are present; hyperventilation and nasogastric suctioning can worsen hypokalemia.

Extubation

- Pts are prone to excessive tachycardia and Htn; exclude typical causes such as pain, agitation, hypoxia, and hypercarbia before treating.

Postoperative Period

- Adjuvant Htn therapy often required
- Lyte monitoring

Anticipated Problems/Concerns

- Untreated cerebrovascular, CV, and renal disease

Lipidemias

Alan David Kaye | Erik M. Helander | Rachel J. Kaye | Lien Tran

Risk

- Prevalence in USA: 13.1% in people >20 y.
- Prevalence highest among Hispanics.
- Cigarette smoking is a risk factor.
- Incidence highest among men ≥45 y and women ≥55 y.
- Htn is a risk factor.
- Low HDL (<40 mg/dL) is a risk factor.
- Family Hx of premature CHD in first degree relative (male <55 y or female <65 y) is a risk factor.

Perioperative Risks

- Pancreatitis with hypertriglyceridemia
- Stroke and transient ischemic attacks
- Myocardial ischemia, infarction, CHF

Worry About

- Angina of increasing frequency or severity and new-onset angina
- Peripheral atherosclerosis
- Worsening or new-onset CHF
- TIAs

Overview

- Hypertriglyceridemia, hypercholesterolemia, lipodystrophy: Köbberling-Dunnigan syndrome (familial lipodystrophy of limbs and trunk, autosomal dominant) may lead to macrosomia; familial generalized lipodystrophy (Berardinelli-Seip syndrome: autosomal recessive) leads to macrosomia.
- Hypolipidemia: LDL deficiency (autosomal recessive abetalipoproteinemia, autosomal dominant familial hypobetalipoproteinemia); normotriglyceridemic abetalipoproteinemia (LDL absent); autosomal recessive Tangier disease (severe deficiency of HDL); secondary to cancer, myeloproliferative disorders, liver failure familial hypoalphalipoproteinemia (HDL deficiency).

Etiology

- Autosomal dominant or recessive inheritance
- Secondary to systemic illness (i.e., primary hypothyroidism, nephrotic syndrome, and extrahepatic obstruction of bile)

Usual Treatment

- Cholestyramine and colestipol inhibit absorption of bile acids derived from cholesterol.
- Neomycin blocks cholesterol absorption.
- Diet and exercise.
- Thyroid hormone clears LDL.
- Fish oils (omega-3 fatty acids) reduce triglyceride levels.
- Nicotinic acid inhibits VLDL and LDL production; also an HDL-raising drug.
- Fibric acids clofibrate and gemfibrozil to increase catabolism of triglyceride-rich lipoproteins.
- Niacin/statin combination therapy promotes optimal lipid values for several at-risk pt populations.
- Statins inhibit HMG CoA reductase; these are the mainstay of lipid-lowering therapy, reducing risk for ASCVD.

Assessment Points

System	Effect	Assessment by Hx	PE	System
HEENT	Tangier disease		Lobulated, bright orange-yellow tonsils Hepatosplenomegaly Peripheral neuropathy (in 50% of pts)	Lipoprotein profile
CV	Myocardial ischemia and infarction Left ventricular dysfunction	Angina or its equivalents Dyspnea, edema, exercise intolerance, MI	Displaced PMI S_3 S_4	ECG, CXR, stress testing, ECHO, coronary angiography
RESP	CHF	Dyspnea, orthopnea, cough	Rales and rhonchi	CXR
RENAL	Impaired renal perfusion	Nighttime urinary frequency		BUN, Cr
CNS	Cerebrovascular atherosclerosis	TIAs	Carotid bruit	Carotid US and angiography

Key References: Stone NJ, Robinson JG, Lichtenstein AH, et al.: 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *J Am Coll Cardiol,* 63(25 pt B):2889–2934, 2014; Hindler K, Shaw AD, Samuels J, et al.: Improved postoperative outcomes associated with preoperative statin therapy, *Anesthesiology,* 105(6):1260–1272, 2006.

Perioperative Implications

Preoperative Preparation
- Assess for CAD and peripheral vascular disease.
- Beta-blockers and nitrates given periop as tolerated.
- Statins have been associated with improved postop outcomes.

Monitoring
- Consider pulm artery catheter, transesophageal ECHO in the presence of large fluid shifts, history of ischemia, and high-risk surgery.

Airway
- Pts may have large head and neck and be overweight, making intubation difficult.

Maintenance
- Avoid hypothermia and anemia.
- Monitor for ischemia and cardiac failure.
- Insulin increases activity of lipoprotein lipase and releases FFAs.
- Sympathetic stimulation, stress, and catecholamines release FFAs.
- Spinal or epidural anesthesia and beta-blockers reduce FFA levels.
- Heparin releases two triglyceride hydrolases: lipoprotein lipase inhibited by protamine, and hepatic lipase resistant to protamine.

Extubation
- During noncardiac surgery, this may be time of greatest risk for ischemia.

Adjuvants
- Depend on lipid-drug binding and end-organ disease

Postoperative Period
- High incidence of ischemia, tachycardia, and MI for several days after noncardiac surgery.
- Treat pain, hemodynamic, and biochemical abnormalities.

Anticipated Problems/Concerns
- Concerns are related to atherosclerotic disease.

Long QT Syndrome

Regina Linganna | Lee A. Fleisher

Risk
- Prevalence of cLQTS: Approximately 1:5000 live births.
- Incidence of cLQTS: 1 in 10,000.
- 60–70% of those diagnosed are females.
- Males under 10 y of age have the highest mortality.
- Pts usually present in childhood with a cardiac event.

Perioperative Risks
- Torsades de pointes
- Sudden cardiac death

Worry About
- Sympathetic stimulation with laryngoscopy, pain, etc.
- Electrolyte abnormalities: hypokalemia, hypocalcemia, and hypomagnesemia

Overview
- cLQTS is diagnosed when the corrected QT interval is >500 ms in the absence of other causes
- Jervell and Lange-Nielsen syndrome is cLQTS associated with deafness; Romano-Ward syndrome is cLQTS without deafness
- aLTQS is most commonly drug induced or caused by an electrolyte abnormality
- Pathophysiology: Arrhythmogenic prolongation of the QT interval caused by mutated genes encoding the cardiac myocyte ion channels

Etiology
- Most common gene mutations: LQT1, LQT2, and LQT3.
- aLTQS primarily prolongs the QT interval by blockade of the rapid delayed I_{Kr}, encoded by *HERG*.
- Drug-induced: succinylcholine, ketamine, atropine, quinolone and macrolide antibiotics, dexmedetomidine, and ondansetron.

Usual Treatment
- Beta-blockade is the first line treatment
- In pts who are symptomatic despite beta-blockade, AICD implantation may be considered

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Torsades de pointes Ventricular fibrillation Sudden cardiac death	Convulsions, syncope	Tachycardia Tachycardia	ECG ECG
CNS	Syncope	Loss of consciousness	Neurologic exam	
METAB	Electrolyte abnormalities			Electrolyte panel Ca^{2+}, Mg^{2+}, K^{+}

Key References: Havakuk O, Viskin S: A tale of 2 diseases: the history of long-QT syndrome and Brugada syndrome, *J Am Coll Cardiol* 67(1):100–108, 2016; Owczuk R, Wujtewicz, Zienciuk-Krajka E, et al.: The influence of anesthesia on cardiac repolarization, *Minerva Anesthesiol* 78(4):483–495, 2012.

Perioperative Implications

Preoperative Preparation
- Elicit family history of sudden cardiac death or congenital deafness.
- 12-lead ECG.
- Ensure maintenance of beta-blockade.
- Ensure availability of defibrillator.
- Avoidance of spinal anesthesia superior to the level of T10 due to the increase in sympathetic tone of the unanesthetized fibers.

Monitoring
- Standard ASA monitors
- Adequate IV access for resuscitation should pt convert to lethal arrhythmia

Airway
- Pt needs to be deeply anesthetized before manipulation of the airway to reduce sympathetic discharge with laryngoscopy.

Preinduction/Induction
- Adequate anxiolysis prior to entering the OR to reduce sympathetic discharge associated with preop anxiety

Maintenance
- Multimodal analgesia for adequate intraop and postop pain control
- Avoidance of hypothermia and associated shivering
- Avoidance of hyperthermia to reduce sympathetic discharge associated with fever
- Avoidance of medications that further prolong the QT duration
- Avoidance of hypokalemia, hypomagnesemia, and hypocalcemia

Extubation
- Consider deep extubation of these pts to reduce sympathetic discharge with emergence.

Postoperative Period
- Continue standard ASA monitors.
- Adequate pain control.

Anticipated Problems/Concerns
- Conversion to lethal arrhythmia secondary to electrolyte abnormality, sympathetic stimulation, or medications that prolong the QT duration

Ludwig Angina

Kristen Burton | John Kissko III

Risk

- Main risk factor is odontogenic infection, especially of the second and third molars (90% of all cases). Other factors include dental and gingival disorders, bacterial infection of the floor of the mouth, peritonsillar abscess, IV drug abuse, mandible fracture, tongue piercing, sialadenitis, and puncture wounds of the floor of mouth.
- Infrequently encountered with contemporary oral hygiene practices and antibiotics.
- Often occurs in otherwise healthy pts but predisposing factors include immunosuppressed states, diabetes mellitus, alcoholism, acute glomerulonephritis, systemic lupus erythematosus, and aplastic anemia.

Perioperative Risks

- Airway obstruction and respiratory distress, aspiration pneumonia secondary to inability to handle secretions, sepsis, descending mediastinitis, subphrenic abscess, empyema, and cervical or mandibular osteomyelitis

Worry About

- Airway obstruction, sepsis, jugular venous thrombosis, pneumothorax, pericardial/pleural effusions, infection of carotid sheath structures, descending necrotizing mediastinitis occurring via the retropharyngeal space and carotid sheath

Overview

- Potentially lethal, rapidly spreading cellulitis of the bilateral submandibular space, which is comprised of the sublingual and submaxillary spaces. Five characteristics: Submandibular cellulitis; involvement of more than one space; progression of cellulitis to gangrene; extension of cellulitis to connective tissue, fascia, and muscles; and spread of cellulitis by continuity and not via the lymphatics. Infection often starts as a periapical dental abscess of the second and third mandibular molars (the roots of these teeth penetrate the mylohyoid ridge such that any abscess or dental infection has direct access to the submaxillary space) usually with elevation and posterior displacement of the tongue. Infection may spread to adjacent neck tissues and the thorax, causing airway obstruction and other serious complications, including mediastinitis.
- Presents with painful neck swelling, laryngeal edema, tooth pain, dysphagia, dyspnea, fever, and malaise. Neck swelling and protruding or elevated tongue are seen in the vast majority. Stridor, trismus, cyanosis, and tongue displacement suggest impending airway crisis.

Etiology

- Most commonly results from bacterial infection: Usually polymicrobial but also *Streptococcus viridans* and *Staphylococcus aureus*. Less commonly from *Bacteroides, Fusobacterium, Actinomyces*, or *Haemophilus influenzae*.

Usual Treatment

- Early airway control: Administration of IV dexamethasone (antiinflammatory) and nebulized epinephrine (reduction of airway obstruction)
- Antibiotics: Penicillin, clindamycin, metronidazole
- Surgical decompression

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway edema, elevation, and posterior displacement of tongue	Dysphagia, dyspnea, pain	Stridor, drooling, cyanosis, tongue displacement, altered airway anatomy, redness and swelling of neck and face, trismus, poor mouth opening	MRI/CT with IV contrast, ultrasound if abscess present
PULM	Pneumonia, pneumothorax, empyema, pleural effusion, subphrenic abscess	Pleuritic pain, cough, dyspnea, generalized SOB	Unequal breath sounds, tachycardia, cyanosis, tactile fremitus	CXR, CT Thoracentesis for pleural effusion and empyema
CV	Pericardial effusion, hypovolemia	Poor PO intake, hypotension	Fever, orthostatic hypotension, tachycardia, arrhythmia, decreased CO, JVD	Blood cultures, fluid gram stain and culture, ECHO, pericardiocentesis

Key References: Kremer MJ, Blair T: Ludwig angina: forewarned is forearmed, *AANA J* 74(6):445–451, 2006; Farish SE: Ludwig's angina. In Bagheri SC, Bell RB, Khan HA editors: *Current therapy in oral and maxillofacial surgery*, Philadelphia, PA, 2012, Saunders, pp 1092–1098.

Perioperative Implications

Preoperative Preparation

- Ensure availability of fiberoptic bronchoscope, video laryngoscope, and surgical airway equipment with personnel trained in their use.

Preinduction/Induction

- For fully developed Ludwig, direct laryngoscopy is associated with a high rate of failure, and any airway instrumentation may itself cause obstruction and bleeding, leading to acute deterioration in respiratory status and the need for emergency tracheostomy.
  - Elective, awake tracheostomy using local anesthesia is the preferred method of airway management in pts with fully developed Ludwig.
  - In cases not fully advanced, consider awake nasal fiber optic intubation.
- An initial dose of 10 mg of IV dexamethasone followed by 4 mg every 6 h helps to decrease edema and cellulitis. Nebulized epinephrine (1 mL of 1:1000 diluted in 5 mL of 0.9% saline) is also believed to help to relieve upper airway obstruction. Pt must be maintained in sitting position, and surgeon should be immediately available for tracheostomy.
- The first attempt should be performed by the most experienced operator, and induction should occur after airway has been secured. For mild cases that have not progressed, one may elect to do an inhalational induction but the majority of cases require awake intubation and then induction. Muscle relaxation should occur after endotracheal intubation is accomplished..

Monitoring

- Standard monitors.
- Large-bore IV access should be obtained. Central line placement in the neck is not advised.

Maintenance

- Avoid nitrous oxide in case of pneumothorax.

Adjuvants

- IV steroids and nebulized epinephrine as previously discussed

Extubation

- Based on intraop findings; consider continued intubation postop until edema resolves

Postoperative Period

- Monitoring in a critical care setting; consider extubation as previously discussed.

Anticipated Problems/Concerns

- Blind nasotracheal intubation should not be attempted in Ludwig angina given the potential for bleeding and abscess rupture.

Lyme Disease

Ahmed M. Darwish | Philip D. Lumb

Risk

- Approximately 30,000 new cases are reported to the CDC each year; however, this number is likely underestimated. The CDC is currently conducting research, and preliminary results suggest the number of new cases to be around 300,000.
- Lyme disease is the most commonly reported vector-borne illness in USA. In 2013 95% of confirmed Lyme disease cases were reported from 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, and Wisconsin. Reported cases of Lyme disease are most common among boys aged 5–9 y. Incidence was highest among children aged 5–14 y; a disproportionate increasing trend was observed in children and in young males compared with other demographic groups. The majority of pts had onset in June, July, or August.
- Gender predilection: Male (53.4%).
- Children <15 y; adults 30–59 y.

Perioperative Risks

- Increased risk of dysrhythmias and CHF in pts with cardiac involvement.

Worry About

- Cardiovascular: Volume overload, CHF, and AV block
- Neurologic: Hyperkalemia from muscular weakness or paralysis, facial muscle paralysis (Bell palsy), peripheral neuropathy and muscle weakness, meningitis, and confusion

Overview

- Stage 1: Early localized infection; chills, fever, headache, lethargy, muscle pain, erythema migrans (rash spreads centrifugally; lesion usually occurs at site of bite) in 68% of pts.
- Stage 2: Early disseminated infection; arthritis, aseptic meningitis, cranial neuritis (Bell palsy), and peripheral radiculoneuritis are neurologic manifestations.
  - Carditis occurs in 4–8% of pts during this stage of disease.
  - Second- and third-degree AV block and myocarditis may be documented by ECG and heart failure; symptoms resolve in days to weeks.
- Stage 3: Late persistent infection; over time 60% of pts with untreated infection will develop intermittent bouts of arthritis, with severe joint pain and swelling. Large joints are most often affected, particularly the knees. In addition, up to 5% of untreated pts may develop chronic neurologic complaints months to years after infection. These include shooting pains, numbness or tingling in the hands or feet, and problems with concentration and short-term memory.
- Approximately 10–20% of pts with Lyme disease have symptoms that last months to years after treatment with antibiotics. These symptoms can include muscle and joint pains, cognitive difficulties, sleep disturbances, or fatigue. The cause of these symptoms is not known, but according to current research, these symptoms are not due to ongoing infection with *Borrelia burgdorferi*. This condition is referred to as PTLDS. There is some evidence that PTLDS is caused by an autoimmune response, in which a person's immune system continues to respond, doing damage to the body's tissues, even after the infection has been cleared. Studies have shown that continuing antibiotic therapy is not helpful and can be harmful for persons with PTLDS.

Etiology

- Lyme disease is caused by the spirochete *B. burgdorferi*, which is transmitted by the tick *Ixodes dammini*.

Usual Treatment

- Early doxycycline prevents infection in high percentages of pts. Amoxicillin, cefuroxime, and ceftriaxone are also effective. Pts with certain neurologic or cardiac forms of illness may require IV treatment with drugs, such as ceftriaxone. Antibiotic therapy for 10–21 up to 28 d generally aborts stages 2 and 3. Pts may benefit from a second 4-wk course of therapy.
- Vaccine available for adults.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	AV node block CHF	Palpitations Fatigue Dyspnea Dizziness with exercise	Bradycardia Tachycardia	ECG ECHO
RESP	Dyspnea	SOB	Rales	CXR
DERM	Erythema chronicum migrans	Erythematous annular lesions	Erythematous circular rash	
CNS	Meningitis Bell palsy Radiculoneuritis	Headache Cognitive impairment Memory deficit	Cranial nerve facial palsy Numbness, tingling Muscular weakness	Serology Lumbar puncture EMG
MS	Arthritis	Joint pain and swelling Musculoskeletal pain	Swelling of one or a few joints Erythema of joints	

Key References: Shapiro ED: Clinical practice. Lyme disease, *N Engl J Med* 370(18):1724–1731, 2014; Gupta B, Agrawal P, D'souza N, et al.: Anaesthetic management and implications of a case of chronic inflammatory demyelinating polyneuropathy, *Indian J Anaesth* 55(3):277–279, 2011.

Perioperative Implications

Preoperative Concerns

- Ensure antibiotic Rx and cure of carditis prior to all but emergency operations.

Monitoring

- Consider invasive monitoring with an arterial line based on cardiac manifestations.

Airway

- Routine

Preinduction/Induction

- Avoid depolarizing muscle relaxants.

Maintenance

- Routine

Extubation

- Usually routine but might be delayed due to generalized muscle weakness

Adjuvants

- Avoid depolarizing muscle relaxants on induction because of hyperkalemia.

Postoperative Period

- Depends on the cardiac and neurological manifestations of the disease if present

Anticipated Problems/Concerns

- Pts may develop dysrhythmias or CHF.

Lymphomas

Wajid M. Khan | Donal J. Buggy

Risk

- 5.3% of all cancers; 55.6% of all blood cancers (USA National Institutes of Health Registry)
- Per annum risk 2.9:100,000 population (European Age-Standardized Incidence UK, 1993–2012)

Perioperative Risks

- Tumor: Mechanical obstruction, compression effect on organs systems (e.g., airway or bowel obstruction)
- Systemic effects: Myelosuppression including immunosuppression, anemia, thrombocytopenia, paraneoplastic syndromes
- Cachexia

Overview

- Group of blood cell tumors developed from lymphatic tissues
- WHO classification: Prognosis depends upon correct diagnosis and classification based on the Revised European-American Lymphoma Classification five types

Etiology

- Epstein-Barr virus, family history, autoimmune disorders, immunosuppressant, and pesticides

Usual Treatment

- Low-grade lymphomas: Radiation and rituximab.
- High-grade lymphomas: R-CHOP (**R**ituximab, **C**yclophosphamide, **H**ydroxydaunorubicin, **O**ncovin (vincristine), **P**rednisone or **P**rednisolone), and stem cell transplantation).
- R-Maxi-CHOP is used in mantle cell lymphoma and is given in 21-day intervals, alternating with R-HDAC (rituximab + high-dose cytarabine).
- Hodgkin lymphoma: Radiation alone.

Toxicity of Chemotherapeutic Agents

Chemotherapy Treatment	Indication	Toxicity
Anthracyclines (e.g., daunorubicin, doxorubicin)	Hodgkin lymphoma	Myocarditis, leukopenia
Alkylating agents (e.g., cyclophosphamide, ifosfamide)	Lymphoma, solid tumors	Hemorrhagic cystitis, left ventricular dysfunction, immunosuppression, hyponatremia
Bleomycin	Hodgkin lymphoma	Pneumonitis, pulmonary fibrosis
Platinum analogues (e.g., carboplatin, cisplatin)	B-lymphoma	Bone marrow suppression, neurotoxicity/ototoxicity/nephrotoxicity
Monoclonal antibodies (rituximab)	B-cell lymphoma	Cytokines release syndrome, anaphylaxis, interstitial fibrosis

Assessment Points

System	Effects	Assessment by Hx	PE	Test
HEENT	Obstruction, mediastinal mass, tracheomalacia	Dysphagia, odynophagia	SVC obstruction signs, neck ROM	CXR, CT thorax indirect laryngoscopy
RESP	Pneumonitis, pulmonary fibrosis	Poor exercise tolerance	Auscultation	PFTs, CXR, ABGs
CV	Myocarditis, left ventricular dysfunction	Exertional dyspnea, PND, orthopnea	Signs of CHF, Pemberton sign	ECG, CXR, ECHO
RENAL	Nephrotoxicity	Orthostatic hypotension, swelling, somnolence	Edema, pallor, ascites	BUN, Cr, lytes
HEME	Anemia, pancytopenia	Tiredness, SOB	Pallor, tachycardia	FBC, bone marrow biopsy
CNS	Leptomeningeal disease	Headache, CN abnormalities	Nerve palsy, weakness	CT, MRI, lumbar puncture
GI	Aspiration	Regurgitation, dyspepsia	Palpable mass	CT, MRI

Key References: Swerdlow SH: *World Health Organization classification of tumours*, ed 4, Geneva, 2008, World Health Organization; Cullen M, Steven N, Billingham L, et al.: Antibacterial prophylaxis after chemotherapy for solid tumors and lymphomas. *N Engl J Med* 353(10):988–998, 2005.

Perioperative Implications

Preoperative Preparation
- Aspiration prophylaxis; Assess and prepare for airway challenge and cardiopulmonary status.

Monitoring
- Depending upon condition of pt and level of surgery

Airway
- Rule out mediastinal masses; possible difficult intubation.

Induction
- May be hypovolemic with limited cardiopulmonary reserves as per disease severity.
- Consider deep inhalation induction with sevoflurane and O_2 initially to evaluate whether lower airway instruction occurs: if so, wake pt up and reevaluate.

Maintenance
- CV instability and obstructive or restrictive pulmonary disease

Extubation
- Risk of tracheal collapse, airway obstruction, and aspiration

Postoperative Period
- May require HDU/ICU admission.

Anticipated Problems/Concerns
- Airway challenges: Mechanical obstruction (tumor mass effect)
- High risk of thromboembolism, DVT, infection, and bleeding

Lysosomal Storage Disorders

Jacqueline Cade

Risk
- Individually rare, but as a group the incidence is approximately 1:8000.

Perioperative Risks
- Difficult airway management
- Cardiac or respiratory failure
- Hemorrhage

Worry About
- Difficult or failed intubation
- Coexisting cardiac or respiratory disease
- Difficult vascular access
- Neurologic involvement and pt cooperation

Overview
- Lysosomal storage disorders are rare, inherited, metabolic connective tissue disorders (often autosomal recessive) with variable anesthetic risk.
- Caused by a variety of mutations in lysosomal enzymes in macrophages, impairing normal cellular debris scavenging.
- Retained debris thus accumulates in various tissues throughout the body.
- Includes MPS types I to VII and lipid storage disorders (including Tay-Sachs and Gaucher disease).
- Depending on disease type and severity, many die in early childhood; others can expect to survive well into adulthood.
- MPS most feared from anesthetic point of view primarily due to airway issues (thus the primary focus of this chapter is on these conditions).

Usual Treatment
- Many of these conditions have no specific treatment, and therapy is targeted towards improving quality of life.
- Some more recent success with enzyme replacement therapy (depending on specific condition) and stem cell transplant.

Assessment Points

System	Effect	History	PE	Tests
HEENT (most effects in MPS pts, less so in those with lipid storage disorders)	Facial dysmorphism Macroglossia Micrognathia Enlarged supraglottic tissues Narrowed nasopharynx Excessive secretions Short neck Cervical spine stenosis Floppy or malformed tracheal cartilage High, elongated epiglottis	Previous anesthesia records, history of difficult airway (note usually gets worse with age)	Facial features Mallampati score Thyromental distance Neck ROM Anterior anatomical landmarks	Cervical spine imaging (plain films, MRI)
RESP	Sleep apnea Restrictive lung disease Recurrent URTIs	Snoring, apneic episodes Hx of lung disease	Coarse facial features, macroglossia Pectus excavatum	Sleep study LFTs
CV	Valvular insufficiency (especially mitral and aortic) Cardiomyopathy Cor pulmonale (less common)	Exercise tolerance	CV examination	ECG ECHO 6-min walk test
MS	Flexion deformities Myopathy Short stature Overweight	Variable mobility ranging from independent to wheelchair-bound		
CNS	Developmental delay Neurobehavioral problems Cognitive impairment Visual or hearing loss	Variable spectrum according to specific condition. Some are cognitively intact.		
HEME	Hepatosplenomegaly Possible bleeding tendency Lymphadenopathy, pancytopenia (lipid storage disorders)		Abdominal exam	Baseline full blood count and coagulation profile

Key References: Stuart G, Ahmad N: Perioperative care of children with inherited metabolic disorders, *Contin Educ Anaesth Crit Care Pain* 11(2):62–68, 2010; Cade J, Jansen N: Anesthetic challenges in an adult with mucopolysaccharidosis type VI, *A Case Rep* 2(12):152–154, 2014.

Perioperative Implications

Preoperative Preparation

- Tertiary center with ICU facilities ideal.
- Experienced anesthesia team.
- Consult previous anesthesia records.
- Multidisciplinary team approach (pediatrician, geneticist, and orthopedic or neurosurgeon if cervical spine an issue).
- Optimize: No concurrent infection, consider investigations as appropriate (ECG, ECHO, sleep study, lung function tests, cervical spine imaging), continue enzyme replacement therapy if pt already on it.

Lines

- May have claw deformities (implications for radial arterial lines and peripheral IV lines)

Airway

- Pre-med: Avoid sedatives. An antisialagogue, such as glycopyrrolate, is useful.
- Equipment: Difficult airway equipment prepared, including fiberoptic bronchoscope, video laryngoscope, surgical airway equipment, and second anesthetist.
- Bag-mask ventilation: Can be difficult because prone to obstruction; oropharyngeal airway may not help due to elongated epiglottis.
- Laryngoscopy: Cervical stenosis may limit safety of neck manipulation, and direct laryngoscopy may be difficult. Narrow trachea may necessitate smaller tube.
- Nasal intubation: Narrow nasopharynx may make nasal intubation difficult. Some success with nasopharyngeal airways to relieve airway obstruction during induction, but choose smaller size and beware bleeding from prominent nasal turbinates.
- Bronchoscopy: Consider awake fiber optic intubation if feasible and older pt. Variable success with both inhalational induction maintaining spontaneous ventilation and asleep fiber optic techniques in children. Confirming endotracheal placement with bronchoscope can be misleading due to abnormal tracheal anatomy.
- Surgical airway: Short, stiff neck can make identification of anatomical landmarks for surgical airway difficult. ENT surgeon present if high risk.
- LMA may be useful to relieve obstruction or as a conduit for intubation.

Maintenance

- Ventilation management for restrictive lung disease if present (higher RR, low TV).
- Careful pressure care and padding, especially if pt has flexion deformities.
- Maintain normothermia, especially if coexisting myopathy.

Drugs

- Consider routine dexamethasone, particularly in children (thickened glottic tissues more prone to swelling).
- Risk of hyperkalemia with suxamethonium if pt has prolonged immobility or significant myopathy.
- Ensure nondepolarizing relaxants are fully reversed prior to attempted extubation (use nerve stimulator or consider sugammadex if available).
- Care with opioids and other long-acting sedative drugs. Consider regional analgesia and multimodal approach.
- May have increased bleeding tendency; judicious use of anticoagulants.

Extubation

- Extubate fully awake, reversed, and with minimal or no airway swelling; consider leaving exchange wire in older pts if extreme difficulty encountered with intubation.

Postoperative Period

- Consider ICU/HDU.
- Longer monitoring in recovery room for postextubation complications.
- Risk for postop pulm edema.

Malignant Hyperthermia and Other Anesthetic-Induced Myodystrophies

Michael R. King | Ronald S. Litman

Risk

- Incidence of MH impossible to know because of lack of reporting mechanisms; Malignant Hyperthermia Association of the US hears of approximately 1–2 cases per week in North America.
- More common in males (approximately 2:1).
- Family Hx of MH or unexplained death during surgery associated with MH occurrence.

Perioperative Risks

- Mortality with MH unknown. Malignant Hyperthermia Association of the US hears of approximately 1–2 deaths directly related to MH every 1–2 years.
- Occurrence of MH reduced by avoidance of triggering agents in MH susceptible individuals, and use of succinylcholine only when indicated.
- Immediate availability of dantrolene has greatly reduced morbidity and mortality from MH.
- Myopathies associated with MH are those associated with mutations in RYR1; most common is central core disease.
- Some obscure myopathies associated with risk of MH when caused by mutations in RYR1, STAC3, or CACNL1A3 genes. These include

King-Denborough syndrome (RYR1), multiminicore disease (RYR1), congenital myopathy with cores and rods (RYR1), congenital fiber type disproportion (RYR1), Native American myopathy (STAC3), and hypokalemic periodic paralysis (CACNL1A3).
- Pts with unexpected severity of rhabdomyolysis in response to hot environment, exercise, or statin administration may have increased chance of MH susceptibility. These occurrences probably unmask RYR1 inheritance.
- Myopathies associated with hyperkalemic cardiac arrest following administration of succinylcholine: Duchenne and Becker muscular dystrophies; also reports of arrest with volatile agents only.
- Other neuromuscular diseases not associated with MH susceptibility include mitochondrial myopathies, Noonan syndrome, Freeman-Sheldon syndrome, and osteogenesis imperfecta.
- Muscle rigidity can be seen in all myotonias following succinylcholine administration.

Worry About

- Unexplained increase in $PETCO_2$, hyperthermia, tachycardia, or tachypnea (if spontaneous breathing) during GA with triggering agents
- Generalized muscle rigidity with or without trismus sensitive indicator for development of MH
- Recrudescence of MH in 25% of cases despite treatment

Overview

Malignant Hyperthermia

- No phenotypic signs predict MH susceptibility other than previous Hx of MH or family Hx or unexplained elevated CK.
- Hypermetabolic disorder manifested by increased CO_2 production and O_2 consumption, acidosis, hyperkalemia, myoglobinuria/myoglobinemia, rhabdomyolysis, tachycardia, tachypnea, increased $ETCO_2$, and hyperthermia (if severe leads to DIC).
- Dx by CHCT of biopsied muscle is most sensitive and specific. Sensitivity is approximately 80%; specificity close to 100%.
- DNA testing available in USA and in many centers in Europe. Sensitivity is approximately 50%, specificity close to 100%.
- Information for provider and pt available through the Malignant Hyperthermia Association of the US, Sherburne NY (www.mhaus.org, 607-674-7901).

Other Anesthetic-Induced Myodystrophies

- Pts with muscular dystrophy may develop hyperkalemic cardiac arrest with succinylcholine and rarely with potent volatiles only.
- Signs of dystrophy subtle; may not be apparent in young children.
- Obtain muscle specimens for dystrophin analysis; blood or other tissue for mutation analysis.
- Test for CK elevation in suspicious cases.

Etiology

Malignant Hyperthermia

- Autosomal dominant mutation, most often in ryanodine receptor (RYR-1 gene on chromosome 19).
- Resulting defect allows uncontrolled intracellular calcium release from sarcoplasmic reticulum when triggered, increasing muscle and metabolic activity.

Other Anesthetic-Induced Myodystrophies

- Muscular dystrophies: Heterogeneous X-linked mutations.

Usual Treatment

Malignant Hyperthermia

- D/C triggering agents.
- Hyperventilate patient with 100% O_2.
- Dantrolene 2.5 mg/kg IV; continue treatment for at least 24 h at 1–2 mg/kg every 4–6 h
- Treat metabolic acidosis; actively cool.
- Increase fluids 1.5 to 2 times maintenance to maintain UO 1–2 mL/kg; diuretics if necessary.
- Assess for hyperkalemia and treat appropriately.
- Monitor for DIC.
- For additional guidance call MH hotline at 800-MH–HYPER.

Other Anesthetic-Induced Myodystrophies

- Treat for hyperkalemia (IV calcium, albuterol, bicarbonate, hyperventilation).

Assessment Points

System	Effect	Assessment by Hx and PE	Test
HEENT	Masseter muscle rigidity		ABG/acidosis Hypercarbia Myoglobinuria
CV	MH: Tachycardia, arrhythmias AIMs: Sudden bradycardia VFIB, asystole	Htn/hypotension	Mixed venous and ABG: increased $ETCO_2$, myoglobinuria, hyperkalemia
RESP	Tachypnea	Tachypnea	Increased $ETCO_2$
MS	Generalized rigidity	Developmental delay Muscle weakness	CK Muscle biopsy contracture test and histology DNA testing
RENAL	Renal failure	Low UO Dark urine	Myoglobin in serum and urine, serum potassium
DERM	Vasoconstriction heat	Mottled appearance (late) Hot skin Sweating	Core temperature

Note: The caffeine/halothane contracture test is used to assess MH susceptibility.

Key References: Rosenberg H, Pollack N, Schiemann A, et al.: Malignant hyperthermia: a review, *Orphanet J Rare Dis* 10:93, 2015; Larach MG, Gronert GA, Allen GC, et al.: Clinical presentation, treatment, and complications of malignant hyperthermia in North America from 1987 to 2006, *Anesth Analg* 110(2):498–507, 2010.

Perioperative Implications

Perioperative Preparation for Known Malignant Hyperthermia

- Purge machine with 100% O_2 15–20 min prior to case. Newer anesthesia workstations (e.g., Drager Fabius) require longer period of purging (>60 min for some models).
- Avoid triggers (succinylcholine, all potent volatile agents).
- Safe GA: Propofol, ketamine, dexmedetomidine, nitrous oxide, barbiturates, all nondepolarizing muscle relaxants, opioids, benzodiazepines, local anesthetics.
- Consider RA (epidural, spinal, regional block) or monitored anesthesia care. Use TIVA if GA needed.
- Anesthesia machine:
  - Change circuit and bag.
  - Tape over vaporizers to remind not to use.
  - O_2 flow at 10 L/min for 15–20 min prior to use.
  - Insertion of charcoal filters reduces flush time to several min.
- Ensure availability of dantrolene.
- If working in ambulatory center, prearranged transfer protocol and blood gas analysis.

Monitoring

- Standard monitors plus core temperature if case expected to last more than 30 min. Core temperature monitoring decreases mortality compared with skin or no temperature monitoring due to improved detection.
- Increased CO_2 production/increased $ETCO_2$ is a sensitive early sign in the mechanically ventilated pt (tachypnea develops in the spontaneously ventilated pt).

Perioperative Implications in Other Anesthetic-Induced Myodystrophies

- Some pts with DMD and Becker dystrophy have developed hyperkalemia with MH triggers.
- Avoid succinylcholine in pts with myotonia and most other myopathies and neuromuscular disorders involving muscle atrophy.

Anticipated Problems/Concerns

- Sudden cardiac arrest in PACU.
- Myoglobinuria and renal failure.
- Postop rhabdomyolysis, follow CKs.
- Hyperkalemia.
  - Postop muscle pain or weakness and persistently elevated CK.
  - Have pt enter the North American MH Registry of Malignant Hyperthermia Association of the US (MHreg.org).

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Malnutrition

Jeffrey D. Roizen

Risk

- Rate approximately 5% in general population and 10–20% in surgical pts; increases to 40% or more in severely ill hospital admissions.
- Risk increases with severity of underlying disease, presence of malignancy (especially GI), and advancing age (in older [>75 y] hip fracture pts baseline on presentation is 30%).
- Hospitalized pts lose an average of 5% body weight over the course of admission.

Perioperative Risks

- Postop complications are significantly higher in the malnourished.
- Severe undernutrition may result in CHF, respiratory failure, and immunologic dysfunction.

Worry About

- Need for early postop nutritional supplementation, particularly enteral if possible.
- Infection risk: Care should be taken with invasive procedures and sterile technique.
- Intraop problems may include low cardiac output and respiratory failure.

Overview

- Results from inadequate intake of macronutrients (carbohydrate, protein, fat); referred to as PCM.
- There are two types of PCM:
  - MF-PCM, which results in uniform loss of fat and muscle mass in all tissues and a concomitant loss of H_2O in proportion to nonaqueous mass.
  - Stress-induced HAF-PCM, which results from neurohumoral modulation leading to depletion of visceral protein (in excess of muscle mass) and fat and is associated with an expansion of extracellular fluid compartment. Stress may be surgery, infection, inflammation, trauma, or neoplasia.
  - In hospitalized pts, marasmic kwashiorkor type (i.e., wasting of muscle and fat with hypoalbuminemia) is most common.

Etiology

- Decreased dietary intake: Advanced age, physical debilitation, GI-related illnesses, neck mass
- Increased metabolic demands and nutrient loss: stress (physical and psychological), disease states (particularly GI and respiratory illness, such as emphysema), infections, burns, liver failure
- Conditions associated with N/V
- Malignant conditions, especially those involving the GI tract

Usual Treatment

- Early PO intake postop is advantageous, especially in GI malignancies; enteral intake reduces infections.
- Enteral nutrition via G-tube or J-tube preferable to TPN if direct PO intake not possible but gut can still be use (e.g., esophageal surgery).
- TPN value is inconclusive but probably indicated in severe malnutrition states. TPN reduces noninfectious complications but increases infectious complication rates in most studies.

Assessment Points

System	Effect	Assessment by Hx	Test
CV	Decreased preload and stroke volume		ECHO
RESP	Decreased FRC and diaphragmatic activity		CXR Expiratory spirogram
GI	Decreased gastric motility Gastric ulceration Gastric and intestinal atrophy	Anorexia, vomiting	Generally not needed
GENERAL	Malnutrition	Preadmission weight loss >10% of body weight in 6 mo or 5% in 1 mo, edema, anorexia, vomiting, diarrhea, decreased food intake, chronic illness	BMI <20 kg/m^2 Voluntary hand-grip test Anthropometric measurements (midarm muscle circumference or triceps skinfold thickness: both <15th percentile of reference data)
IMMUNE	Impaired cell-mediated immunity Surgical wound infection and sepsis		Abnormally low lymphocyte count (<1500/mm^3) Anergy to a battery of four or five standard skin antigens
RENAL	Decreased body mass Decreased Cr clearance and impaired ability to concentrate urine	Decreased UO	Serum Cr/BUN
HEPAT	Decreased protein synthesis		Decreased serum albumin (<3.5 mg/dL) and decreased serum transferrin (<200 mg/dL)
PNS	Decreased peripheral nerve conduction and sensory abnormalities	Tingling and numbness in extremities	Generally not needed

Key Reference: Corish CA, Kennedy NP: Protein-energy undernutrition in hospital in-patients, *Br J Nutr* 83(6):575–591, 2000.

Perioperative Considerations

Preinduction

- Use of a malnutrition risk assay (e.g., Nutrition Risk Score/Mini Nutritional Assessment); Mini Nutritional Assessment score <17/30 = protein-energy malnutrition) for screening will help to identify at-risk pts.
- Nutritional and caloric supplementation in the days before surgery may be beneficial if possible.
- Consider prophylaxis for aspiration of gastric contents if GI process is responsible for malnutrition (e.g., malignancy, obstruction).

Monitoring

- Routine

Induction

- If respiratory muscle weakness or fatigue is suspected, avoidance of long-acting NMDBs may be prudent.

Maintenance

- Pts receiving TPN should continue to receive it in the OR because abrupt discontinuation may result in severe hypoglycemia. Many sources recommend a rate reduction of 50% intraop. Alternatively, TPN may be replaced with dextrose during surgery.
- Standard hydration and UOP monitoring.

Extubation

- Respiratory muscle failure may preclude early extubation; careful attention to respiratory status warranted in PACU.

Adjuvants

- Hepatic drug metabolism may be impaired.
- Decreased binding (volume of distribution) of protein-bound drugs in hypoalbuminemic pts.

Anticipated Problems/Concerns

- Because edema is prominent feature of HAF-PCM, interpretation of anthropometric measurements like arm circumference may be unreliable.
- Serum markers like albumin, transferrin, and prealbumin can be unreliable in a wide array of disease states and do not correlate well with outcomes and complications.
- Pts with end-stage chronic obstructive lung disease usually have malnutrition; initiation of feeding periop may precipitate acute respiratory failure and refeeding syndrome (electrolyte/nutrient abnormalities associated with refeeding; most dangerous is hypophosphatasia but also thiamine deficiency, decreased K, decreased Mg, decreased Na, and decreased P).

Marfan Syndrome

George Silvay | Joshua A. Heller

Risk

- Prevalence is estimated at 1:5000 people.
- Inherited as autosomal dominant trait, though 25% of cases are sporadic.
- The 2010 Ghent Nosology for Marfan Syndrome guides Dx, heavily prioritizing aortic root dilation, ectopia lentis, and family history.

Perioperative Risks

- Aortic rupture and dissection, mitral valve prolapse, mitral or aortic valve regurgitation, arrhythmias, pneumothorax, restrictive lung disease, and chest wall and spine deformity

Worry About

- Ascending aortic dissection and rupture
- Mitral and aortic valvular insufficiency
- Myocardial ischemia due to medial necrosis of coronary arteries
- Dyspnea, reduced functional residual capacity increased risk of pneumothorax

Overview

- Connective tissue disorder typically inherited via autosomal dominant genetics. Pathophysiology is complex but characterized by a defect of collagen synthesis, which decreases tensile strength and elasticity of connective tissue. CV, particularly aortic, manifestations are most responsible for reduced life expectancy, but the disorder has pansystemic implications.
- CV manifestations are most lethal. Pts commonly diagnosed and monitored via transthoracic echocardiography.
- Invasive management recommended for type A dissection, type B dissection with severe pain, ischemia, rapid aortic growth, or large aortic diameter. Prophylactic surgery recommended when aortic root exceeds 50 mm or 46 mm in setting of adverse family history, severe valvular involvement, rapid aortic dilation, or planned pregnancy.
- Ocular manifestation that is most defining is ectopic lentis, which is the subluxation of the lens
- Pts may have a high-arched palate, crowded teeth, abnormal skull shape, malar hypoplasia, or retrognathia. Pts are at risk for spontaneous pneumothorax, restrictive lung disease, and obstructive sleep apnea.
- Musculoskeletal features include increased length of long bones, joint laxity, scoliosis, pectus excavatum and carinatum, laxity of cervical spine, and lumbar dural ectasia.

Etiology

- Mutation in *FBNI*, the gene on chromosome 15 that encodes fibrillin-1, is an extracellular matrix glycoprotein. Fibrillin-1 normally binds TGFβ. Decreased functional fibrillin-1 leads to excess TGFβ, which is thought to lead to a cascade of inflammatory degradation of elastic fibers and extracellular matrix.
- The 2010 Revised Ghent Nosology defines diagnostic criteria for Marfan syndrome, including data from aortic imaging, genetic testing, family history, and physical examination.

Usual Treatment

- Pts are prescribed beta-blocker therapy and potentially ACE-inhibitor or ARB therapy to reduce aortic wall stress and potentially growth rate. The American Heart Association has recommendations for physical activity limitations because straining and Valsalva actions can worsen aortic wall stress.
- Regular follow-up by a cardiologist is necessary to monitor heart and aorta; and elective aortic root, aorta, and valve repair common to avoid catastrophic complications.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Ectopia lentis	Myopia	Retinal detachment, lens subluxation	Ophthalmoscopy
CV	Aortic dissection Myocardial ischemia	Chest pain Angina		MRI, ECHO, CT ECG Stress testing Angiography
	Arrhythmias	Palpitations	Heart rate Chest auscultation	Holter monitor Electrophysiology
RESP	Restrictive lung disease Obstructive sleep apnea	Dyspnea Snoring Decreased functional capacity	Scoliosis Abnormal airway exam	Pulm function testing CXR Sleep study
MS	Tall stature Joint hypermobility Recurrent joint dislocation Hernias TMJ dysfunction		Chest wall deformity Elevated arm to height ratio	

Key References: Radke RM, Baumgartner H: Diagnosis and treatment of Marfan syndrome: an update, *Heart* 100(17):1382–1391, 2014; Castellano JM, Silvay G, Castillo JG: Marfan syndrome: clinical, surgical, and anesthetic considerations, *Semin Cardiothorac Vasc Anesth* 18(3):260–271, 2013.

Perioperative Implications

Preoperative Preparation

- Antibiotics for SBE prophylaxis if a prosthetic valve or other indication from 2007 AHA Guidelines.
- Consider periop beta-blockade to mitigate increases in aortic wall tension.
- Consider large-bore IV access and transfusion capacity in case of vascular rupture if vascular manipulation possible.

Monitoring

- Standard ASA monitoring, and consider transesophageal echocardiography and CNS monitoring (such as cerebral oximetry)
- Invasive monitoring as appropriate for planned surgery

Airway

- High-arched palate, crowded teeth, and retrognathia are characteristic.
- Potential cervical laxity and instability with extension.
- Potential for TMJ dislocation with direct laryngoscopy.
- If a known aortic aneurysm, consider fiber optic bronchoscopy to inspect for compression of respiratory tract.

Preinduction/Induction

- Meticulous hemodynamic control to avoid increases in aortic wall tension
- Careful positioning to avoid dislocations

Maintenance

- No specific technique is known to be superior. Hemodynamic vigilance is critical.

Extubation

- Avoid sudden swings in hemodynamics because this may increase aortic wall tension and sheer forces.
- Be cognizant of risk of myocardial ischemia.

Adjuvants

- Adequate pain management is important.
- Pts may have different dose response to neuraxial medication due to lumbar dural ectasia, which may have significance for dosing and distribution of local anesthetic.

Anticipated Problems/Concerns

- CV: Aortic dissection, mitral or aortic regurgitation, myocardial ischemia, and cardiac arrhythmias
- Respiratory: Difficult airway, high pneumothorax risk, and restrictive lung disease with thoracic deformity

Mastocytosis

Pascale Dewachter | Claudie Mouton-Faivre

Risk

- Rare clinical condition with an estimated incidence at 1:150,000.

Perioperative Risks

- Not an allergic disease.
- Not a risk factor of IgE-mediated drug allergy.
- Mast cell degranulation induced by various nonspecific triggers with subsequent histamine and other mediators (e.g., tryptase, leukotrienes, prostaglandins) release may result in periop clinical features involving the skin and the cardiovascular system.
- Bronchospasm usually does not occur.
- Periop course is usually uneventful when nonspecific triggers for mast cell release are avoided. Periop complications have been reported only in a few cases.

Worry About

- Main concern: Avoid nonspecific mast cell degranulation.

Overview

- Heterogeneous group of disorders characterized by an abnormal increase in tissue mast cells.
- It is classified into seven categories according to the World Health Organization consensus, which differ by the onset time of the disease (childhood or adulthood), the phenotype (cutaneous or systemic), and the clinical presentation (indolent or aggressive).
- CM, the most common phenotype, is limited to the skin. The most frequent skin presentation is consistent with *urticaria pigmentosa* in both adults (mainly monomorphic variant) and children (polymorphic variant). Other types, such as CM with bullous forms, are almost uniquely seen in children. CM is mainly reported during childhood and often resolves after puberty.
- SM infiltrates the bone marrow and other organs with or without skin involvement. Six forms of SM have been described and include indolent SM, which is the most common clinical presentation with a good prognosis, and aggressive SM with severe organ infiltration, SM with hematologic disease, mast cell leukemia, and mast cell sarcoma with a poor prognosis. SM is mainly reported during adulthood.
- Mast cell degranulation can be induced by various nonspecific triggers, such as physical pressure of skin lesions (mechanical irritation, tourniquet use), surgery itself (especially the digestive tract which is a rich source of mast cells), histamine-releasing drugs, extreme temperature (hypothermia, hyperthermia), pain, and emotional factors.
- Mast cell degranulation: Histamine, tryptases, PGD2, LTC4, and various cytokines.
- Tryptases are neutral serine proteases stored predominantly in mast cells. Pro-α tryptase reflects mast cell burden, whereas mature β-tryptase is preferentially stored in mast cell granules and released during mast cell activation.
- Total tryptase level at baseline reflects pro-α tryptase and correlates with total body mast cell burden. Tryptase level greater than 20 μg/L is associated with SM, but lower levels may be seen. Tryptase levels are less than 20 μg/L in most CM.
- Common symptoms include itching, flushing, erythema, diarrhea, abdominal pain, headache, and fatigue.
- Periop clinical features may involve the skin (erythema, rash, flushing) and cardiovascular system (hypotension, infrequently cardiovascular collapse). Life-threatening condition is extremely rare.
- CV symptoms induced by nonspecific triggers may occur in SM and CM, especially in those with excessive spreading of skin disease (diffuse CM).
- Care management is guided by the clinical presentation according to the Ring and Messmer scale. Fluid therapy should be initiated with crystalloids or colloids. Use epinephrine when required (i.e., grade III reaction according to the Ring and Messmer scale).
- In case of periop immediate hypersensitivity:
  - Measure tryptase level (will then be compared with pt's baseline level).
  - Perform skin tests (at least 4 wk later) with all drugs injected just before the occurrence of immediate hypersensitivity to prove that the clinical reaction was related to mastocytosis itself and not to drug allergy.
- Main concern: Avoid mast cell degranulation.

Etiology

- Mutation (codon D816V) in the tyrosine kinase receptor c-kit (protein involved in mast cell survival).

Usual Treatment

- H_1-receptor antagonists: Nonsedating drugs (e.g., cetirizine).
- H_2-receptor antagonists: Ranitidine, famotidine.
- Proton pump inhibitor (omeprazole) if H_2-receptor antagonist is ineffective for abdominal pain.
- Leukotriene inhibitor or disodium cromoglycate for GI symptoms.
- Psoralen combined with PUVA.
- Calcium supplementation, bisphosphonate, and estrogen replacement during postmenopause.
- Interferon.
- Targeted therapy, such as imatinib (tyrosine kinase inhibitor), in some pts.
- Splenectomy may improve survival in severe clinical forms.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Urticaria pigmentosa, mastocytoma, DCM, TMEP	Itching, erythema, flushing	Darier sign	Lesional skin biopsy
CV	Hypotension, CV collapse	Prior episodes? Potential triggers?		Serum tryptase compared to baseline tryptase level Skin tests
GI	Abdominal pain, diarrhea, PUD, malabsorption		Hepatosplenomegaly	GI biopsies
CNS	Headache, depression, moods symptoms			
MS	Osteopenia, osteoporosis, pathologic fractures, MS musculoskeletal pain			Bone densitometry, x-ray, CT
HEME	Myeloid or lymphoid leukemia			Bone marrow biopsy

Key References: Valent P, Escribano L, Broesby-Olsen S, et al.: Proposed diagnostic algorithm for patients with suspected mastocytosis: a proposal of the European Competence Network on Mastocytosis, *Allergy* 69(10):1267–1274, 2014; Dewachter P, Castells MC, Hepner DL, et al.: Perioperative management of patients with mastocytosis, *Anesthesiology* 120(3):753–759, 2014.

Perioperative Implications

Preoperative Period

- H_1- and H_2-receptor antagonists are usually recommended.
- Avoid known triggers that have precipitated prior episodes and potential triggers, such as pharmacologic, psychologic, and mechanical factors and temperature changes.
- Check for the pt's tryptase baseline before surgery (in case of periop immediate hypersensitivity, it is important to compare the tryptase level after immediate hypersensitivity to the pt's baseline level).

Monitoring

- Routine monitors

Induction/Maintenance

- Preoxygenation: Bullae may occur in any of the skin lesions with mechanical pressure from a facemask in CM. This feature is mostly limited to the first few years of life.
- Following agents can be used:
  - Benzodiazepine: Midazolam.
  - Hypnotics: Etomidate, ketamine, propofol, thiopental.
  - Halogenated gases, nitrous oxide.
  - Local anesthetics: Amide- and ester-type.
  - NMBAs: Succinylcholine, rocuronium, vecuronium, cis-atracurium, suxamethonium.
  - Analgesic: Acetaminophen (paracetamol).
  - Opioids: Alfentanil, fentanyl, remifentanil, sufentanil, and morphine (titration).
  - Plasma substitutes: Albumin, gelatin, HEA.
  - Other agents: Oxytocin, protamine, aprotinin (biologic glue), ondansetron, chlorhexidine, povidone iodine, dyes and contrast agents.
- The following histamine release agents are not recommended:
  - NMBAs: Atracurium, mivacurium.
  - Analgesic: Nefopam.
- Maintenance phase: Maintain normothermia, including warmed anesthetic gases, fluid therapy, and blood components transfusion.

Extubation

- Reversal of neuromuscular blockade, including atropine and neostigmine or sugammadex, according to the NMBA used

Other Types of Anesthetics

- There is no role to avoid regional or neuraxial anesthetics in mastocytosis.

Postoperative Period

- Continue with analgesics and usual treatment.

Anticipated Problems/Concerns

- Histamine release due to mast cell degranulation induced by histamine release drugs or surgical procedures
- Ambulatory surgery; no evidence to contraindicate ambulatory surgery in mastocytosis

Mediastinal Masses

Ashish C. Sinha

Risk

- Usually a congenital lesion, occurring at 1:5000; no gender bias
- Benign or malignant; cysts or aneurysms that arise from the lung, pleura, or another structure of anterior mediastinum; middle mediastinum: LN enlargement and vascular masses, posterior mediastinum: neurogenic tumors and esophageal abnormalities. In children, neurogenic tumors or cysts are common.
- Lymphoma (Hodgkin or NHL), thymoma, germ cell tumor, granuloma, bronchogenic cancer, thyroid tumors (retrosternal goiter), bronchogenic cysts, and cystic hygroma.

Perioperative Risks

- Periop mortality is rare.
- Sudden CV collapse from inability to ventilate or oxygenate.
- Hypotension or tamponade.
- Increased dyspnea (orthopnea) or cough when supine (increased risk of airway complications).
- Syncopal symptoms or pericardial effusion (increased risk of CV complications).
- Major airway complications in these pts are now more likely to occur in the postanesthetic care area rather than in the OR.

Worry About

- Inability to get on cardiopulmonary bypass rapid enough to avoid permanent neurologic damage
- Superior vena cava syndrome with airway edema and increased bleeding
- Recurrent laryngeal nerve injury
- Pts at risk with cough and pain, dyspnea and dysphagia, superior vena cava syndrome, tracheal deviation, Horner syndrome, cyanosis, mediastinal widening, and hoarseness

Overview

- Severity of symptoms does not predict intraop course.
- Airway obstruction or hemodynamic compromise has occurred with induction of GA, intubation, muscle relaxation, position change, and after extubation.
- Pts may present with Sx that include chest pain or fullness, dyspnea, cough, sweats, superior vena cava obstruction, hoarseness, syncope, or dysphagia.
- Pts can be asymptomatic and have a mass diagnosed on a screening chest radiograph or CT scan.

Etiology

- Adults: 97% malignant, 80% metastatic bronchogenic carcinomas; 17% lymphomas (50% of lymphomas have mediastinal involvement); 20% thymomas (50% malignant, 35% associated with myasthenia gravis).
- Pediatric: 8% malignant, 16–36% NHL, and 54–81% Hodgkin lymphomas, bronchial cysts, and teratomas.
- Superior vena cava syndrome in 6–7% of lung cancer.
- Others include parathyroid or thyroid tumors; lymphoid tumors; teratomas; aortic aneurysms; esophageal achalasia or diverticula, diaphragmatic hernia.

Usual Treatment

- For tissue diagnosis, biopsy under local anesthetic.
- If no tissue can be obtained or pt is uncooperative, approach is selective radiotherapy sparing some tumor for later diagnosis; if not diagnostic, then biopsy under GA.
- Surgical resection for some tumors.
- Anesthesia complications are usually fewer after radiation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible tracheal compression by mass, bulky nodal disease	Dysphonia, dysphagia, coughing paroxysms when supine or orthopnea	Palpable neck mass, wheezing, stridor	Indirect laryngoscopy, CXR, CT scan, MRI, pulm flow volume studies
CV	SVC syndrome, compression of PA, cardiac failure	Dyspnea, fatigue, syncope, peripheral edema, crackles, headache, chest pain, SOB	Facial or neck swelling, upper body edema, cyanosis, increased JVP, hypotension	CXR, ECHO, ECG, stress ECHO, CT/MRI
CNS	Recurrent laryngeal nerve compression, spinal cord compression	Stridor, dysphonia, focal symptoms based on point of compression	Anatomical distortion of neck or thorax	CXR, CT
RESP	Decreased lung volumes, bronchial compression, obstructive pneumonia	SOB, increased respiratory rate, dyspnea, cough	Wheezing, distant breath sounds, hypoxemia, pedal edema	PFTs, ABG, CXR, DL_{CO}

Key References: Blank RS, de Souza DG: Anesthetic management of patients with an anterior mediastinal mass: continuing professional development, *Can J Anaesth* 58(9):853–867, 2011; Fischer GW, Cohen E: An update on anesthesia for thoracoscopic surgery, *Curr Opin Anaesthesiol* 23(1):7–11, 2010.

Perioperative Implications

Preoperative Preparation

- Consider (including pediatric pts) an IV prior to induction (lower extremity if SVC syndrome).
- All pts should have a CXR and a chest and neck CT scan prior to any surgical procedure to plan airway management.
- Those with PA or heart compression may need cardiopulmonary bypass (check availability prior to induction with cannulation sites prepped and draped).
- Studies of flow-volume loops have shown a poor correlation with the degree of clinical airway obstruction and have not demonstrated usefulness in managing these pts.
- Reserve use of premedication except for anticholinergic.

Monitoring

- Consider intra-arterial, central venous, or PA cath.
- If SVC syndrome, insert central venous access or PA cath via femoral vein.

Airway

- Tracheal or distal compression; may become obstructed with induction and muscle relaxation.
- Maintain spontaneous ventilation throughout procedure unless ETT is below obstruction.
- Pts who are symptomatic in supine position are best induced sitting or semi-sitting.
- Awake fiber optic intubation may be skipped if asymptomatic in supine position and CXR and/or CT scan do not reveal airway obstruction or compression.
- If in doubt, consider awake fiber optic bronchoscopy to rule out obstruction or compression.
- If compression seen in thoracic trachea, consider a single lumen armored ETT with its tip distal to the compression.
- If compression is at level of carina or distal, endobronchial intubation or a double-lumen endobronchial tube is recommended.

Preinduction/Induction

- May develop airway obstruction with inability to ventilate.
- May develop hypoxia from obstruction of pulm artery and blood flow to lungs.
- If muscle relaxants are required, assisted ventilation should first be gradually taken over manually to ensure that positive-pressure ventilation is possible and only then can a short-acting muscle relaxant be administered.
- Development of airway or vascular collapse at induction demands immediate awakening.

Maintenance

- Consider local anesthesia; otherwise consider keeping pt breathing spontaneously.
- If obstruction occurs, consider altering pt's position; attempt rigid bronchoscopy, median sternotomy, or femorofemoral cardiopulmonary bypass.

Extubation

- Deep extubation during spontaneous breathing recommended; try to minimize straining, coughing, or bucking which would all increase intrathoracic pressure.
- Observe in a monitored bed for several h after extubation to detect and treat delayed airway obstruction.

Anticipated Problems/Concerns

- Airway obstruction with the inability to ventilate.
- Vascular compression with hypotension, hypoxia, and arrest.
- Consider radiation and/or chemotherapy before surgery.
- If GA required, consider inspection of tracheobronchial tree with fiber optic bronchoscopy.
- If GA required, maintaining spontaneous ventilation preferable.
- The most useful information for the anesthesiologist to guide management of these pts comes from the pt's Hx and the chest imaging.
- Special problems in pediatric populations: Anesthetic deaths have mainly been reported in children, possibly due to the more compressible cartilaginous structure of the airway or because of underestimation of the severity of the airway compression in children due to the difficulty in obtaining a clear Hx of positional symptoms. Even with proper management, children with tracheobronchial compression more than half cannot be safely given GA. Further increasing risk in pediatric pts, securing the distal airway with awake fiber optic intubation and placement of an ETT distal to a tracheal obstruction, an option for some adults with masses compressing the midtrachea, is not an option in most children.

Acknowledgment

I wish to thank Dr. Frank Gencorelli for his work on this chapter in the earlier edition of this book.

Mesothelioma

Srinivasan Rajagopal | John R. Moyers

Risk

- Incidence in USA: Approximately 2000–3000 new cases annually and decreasing. Increasing incidence in developing countries due to poor regulation of asbestos in mining and industrial use
- Attributable mortality: 14 deaths per million in USA
- Male to female ratio: 3–6:1
- 0.16% of all malignancies

Perioperative Risks

- Usually discovered in geriatric male undergoing lung biopsy
- Pleural effusion
- General debilitation from malignancy

Worry About

- Previous needle biopsy of lung and thoracentesis make pneumothorax a concern.

Overview

- Diffuse malignant mesothelioma arises from the mesothelial surface of the pleura, peritoneum, and pericardium and the tunica vaginalis of the testis.
- 80–90% percent originate from the pleura.
- Peak incidence 20–40 y after asbestos exposure.
- Usual onset of symptoms at age 55–70 y.
- Median survival after onset of symptoms is approximately 18 mo.

Etiology

- Diffuse mesothelioma related to asbestos exposure in 12–93% of cases
- Also associated with radiation therapy, erionite exposure, chronic inflammation and fibrosis, and other agents

Usual Treatment

- Treatment has been controversial and largely ineffective.
- Therapy has consisted of combinations of radiation to hemithorax, chemotherapy, and sometimes surgery (parietal pleurectomy and decortication or extrapleural pneumonectomy).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Tracheal displacement Superior vena cava syndrome			Lateral and AP CXR
CV				ECG, ECHO
RESP	Pneumothorax	Cough, chest pain, increased SOB		ABG, PFTs (for lung resections) CXR (post biopsy; in expiration)
	Restrictive lung disease	Dyspnea with exercise	Percussion and auscultation of chest	
GI	Weight loss, debilitation, peritoneal tumors	Past body weights		CT scan of abdomen (not for periop care) Albumin (for degree of malnutrition) CBC (for malnutrition)
ENDO	Not associated with paraneoplastic syndromes			

Key References: Rusch VW: Diagnosis and treatment of pleural mesothelioma, *Semin Surg Oncol* 6(5):279–284, 1990; Ng J, Hartigan PM: Anesthetic management of patients undergoing extrapleural pneumonectomy for mesothelioma, *Curr Opin Anaesthesiol* 21(1):21–27, 2008.

Perioperative Implications

Preoperative Preparation

- Usually come to surgery for lung biopsy via thoracoscopy or open-lung biopsy; some pts are scheduled for pleuropneumonectomy.
- Assess pulmonary status; size of effusion, no pneumothorax.
- Pt often had one or more recent needle biopsies of lung or thoracenteses.
- Review radiographic studies for size and location of tumor.

Monitoring

- Routine monitors
- Resp system via stethoscope, SpO_2, and $PETCO_2$
- Intra-arterial catheter for complex surgical procedures

Airway

- Look for tracheal and mediastinal displacement on radiographic studies.

Induction

- Propensity for hypoxia, particularly from restrictive lung disease.

Maintenance

- High FIO_2 may be necessary.
- One-lung ventilation.
- Lateral positioning.

Extubation

- Ensure pt meets extubation criteria.

Adjuvants

- Pain control after thoracoscopy or thoracotomy
- No special considerations for muscle relaxants, reversal agents, local anesthetics, or special drug interactions

Postoperative Period

- Monitor ventilation and oxygenation.
- Pain relief; consider epidural or spinal analgesia after thoracotomies.
- May have air leak postop.

Anticipated Problems/Concerns

- Anesthesia with one-lung ventilation for a geriatric pt with incurable malignancy.
- Recent lung biopsy and thoracentesis prior to surgery and potential for complications from those procedures, including pneumothorax and dehydration.
- With extrapleural pneumonectomy, a possibility of massive blood loss, dysrhythmias, and hemodynamic instability during pericardial window and patch.
- Effective pain relief and monitoring of resp function postop.
- Consider ICU stay for those undergoing complex procedures.

Methemoglobinemia

Tiffany Sun Moon

Risk

- Incidence within USA: Rare
- Gender prevalence: None
- Socioeconomic or ethnic prevalence: None

Perioperative Risks

- Inadequate O_2 carriage and delivery to tissues.
- Hemolysis may be induced by methylene blue, especially in pts with G6PD deficiency.

Worry About

- Percent of MetHb. Symptoms vary and depend on the level of MetHb present: Cyanosis appears when MetHb reaches 10–20%. Tachycardia and tachypnea can appear when MetHb reaches 20–50%. CV collapse, coma, and seizures can occur when MetHb reaches 50–70%. Death may occur at MetHb levels >70%

Overview

- MetHb is produced when Hb is oxidized and Fe^{2+} is converted to Fe^{3+} so that Hb cannot bind O_2, and the O_2-Hb dissociation curve is shifted to the left.
- Hereditary forms due to cytochrome b5 reductase deficiency or abnormal hemoglobin M.
- Acquired methemoglobinemia is largely due to oxidizing medications, including local anesthetics (benzocaine, prilocaine), antibiotics (dapsone), and nitrites. Toxic dosages can vary between individuals. Other medications and drugs (e.g., cocaine) have also been known to cause methemoglobinemia.

Etiology

- Endogenous mechanisms (NADH-MetHb reductase and NADPH-MetHb reductase) normally maintain MetHb levels to <1%. Oxidizing agents convert Hb to MetHb and can overwhelm protective mechanisms, resulting in toxic methemoglobinemia.

- Diagnosis:
  - An ABG with co-oximetry (spectrophotometry), which uses multiple wavelengths of light to determine the amount of normal versus abnormal Hb (e.g., MetHb, COHb), is necessary.
  - Keys to diagnosis are a discrepancy between pulse oximeter saturation and measured Pao_2 (Spo_2 <90% while Pao_2 >70 mm Hg) and hypoxia that does not improve with increasing FIO_2.
  - "Chocolate brown" blood may be seen.

Usual Treatment

- Supportive (ventilation, CV support); discontinuation of the offending agent
- Pts without G6PD deficiency: Methylene blue (a transient false decrease in SpO_2 may be seen after administration)
- Pts with G6PD deficiency: Ascorbic acid (methylene blue causes hemolysis)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Tachypnea, dyspnea, hypoxia	Exposure to oxidizing drugs	RR	Co-oximetry
CV	Tachycardia, arrhythmias, death if MetHb >70%	Exposure to oxidizing drugs	HR	Co-oximetry

Key References: Cortazzo JA, Lichtman AD: Methemoglobinemia: a review and recommendations for management, *J Cardiothorac Vasc Anesth* 28(4):1043–1047, 2014; Guay J: Methemoglobinemia related to local anesthetics: a summary of 242 episodes, *Anesth Analg* 108(3):837–845, 2009.

Perioperative Implications

Preoperative Preparation

- Because medications are the most frequent cause of acquired methemoglobinemia, a complete medication Hx should be sought, including OTC medications.

Monitoring

- Traditional pulse oximeters that use two wavelengths of light will not detect MetHb. Spo_2 values are inaccurate and trend toward 85% because MetHb absorbs equally at 660 and 940 nm.
- Newer "pulse co-oximeters" can detect MetHb levels and have accurate SpO_2 values.

Airway

- Routine

Induction

- Routine

Maintenance

- Routine

Extubation

- Severe methemoglobinemia may preclude extubation until levels fall to normal.

Adjuvants

- Methylene blue or ascorbic acid to treat; avoid further administration of oxidizing agents.

Postoperative Period

- Rebound methemoglobinemia can occur for up to 24 h, so pts should have MetHb levels closely monitored and additional treatment given if necessary.

Anticipated Problems/Concerns

- Oxygen-carrying capacity is decreased proportional to the concentration of MetHb present. Pts with preexisting conditions (e.g., CAD, PVD, anemia) may have tissue hypoxia even with lower levels of MetHb, necessitating earlier treatment.

Mitochondrial Disorders

Sau Yee Chow

Risk

- Incidence 4–7:100,000; might be under-reported

Perioperative Risks

- CNS: Facial and bulbar weakness, mental retardation, seizures, learning disabilities, deafness, visual impairment, and stroke-like episodes
- CVS: Cardiomyopathy and cardiac conduction defects
- Respiratory: Weakness of muscles of respiration and respiratory failure
- Other: GI disturbances, diabetes mellitus, exocrine pancreatic insufficiency, lactic acidosis, liver failure, and renal tubular defects

Overview

- Characterized by pathologic mitochondrial dysfunction in oxidative phosphorylation.
- Variable clinical presentation due to numerous possible mutations in genes coding for the electron transport chain proteins or the ancillary machinery involved in oxidative phosphorylation.
- Cardinal features of progressive muscles weakness and exercise intolerance.
- Prognosis is variable, ranging from functional impairment to death.

Etiology

- Defects of:
  - Mitochondrial DNA (maternal inheritance)
  - Nuclear DNA (autosomal dominant or recessive mendelian pattern)

Usual Treatment

- Alleviate symptoms (e.g., anticonvulsant therapy for seizures).
- Dietary modifications: Avoid fasting, addition of midchain triglycerides.
- Avoidance of toxins (e.g., alcohol, cigarette smoke).
- Vitamins and supplements to improve efficacy of ATP generation and antioxidant to slow progression of disease: Coenzyme Q10, levocarnitine, riboflavin.
- Avoidance of physiologic stress: Cold, heat, starvation, lack of sleep.
- Current treatment and medications for mitochondrial disorder.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Aspiration risk	Abnormal speech, recurrent aspirations, aspiration pneumonias	Bulbar palsy speech pattern	Videofluoroscopic swallowing study
CV	Cardiomyopathy, cardiac conduction abnormalities	Effort tolerance, palpitations, syncope, thromboembolic stroke	Signs of heart failure, abnormal heart rate	ECG Consider transthoracic ECHO, stress testing
RESP	Poor lung function, possible aspiration pneumonia	Effort tolerance, ability to cough, symptoms to suggest pneumonia	Looking for consolidation	Baseline ABG CXR Lung function test (spirometry)
CNS	Acute neuromuscular decompensation	Triggers and manifestation, current neurologic status, preexisting deficits, prior strokes	Neuro exam	Review any previous MRI brain scans available
METAB	Acute metabolic decompensation	Triggers and manifestation, severity and frequency		Consider baseline ABG and serum lactate levels

Key References: Shipton EA, Prosser DO: Mitochondrial myopathies and anaesthesia, *Eur J Anaesthesiol* 21(3):173–178, 2004; Chow SY, Woon KL: General anesthesia for adults with mitochondrial myopathy, *A A Case Rep* 4(5):52–57, 2015.

Perioperative Implications

- No clinical trials studying the effects of anesthetic agents and techniques and incidence of intraop and postop complications in pts with mitochondrial disorders. The current available data consist of level 4 evidence.

Preoperative Preparation

- Communication with the pt's neurologist is crucial; a targeted preop assessment should be done because the organ systems affected in mitochondrial disorders are highly variable among individuals.
- Optimize nutritional state and pulmonary function.
- Consider premedication with prokinetic agents and nonparticulate antacid.
- Continue all medications and supplements for mitochondrial disorder up to day of surgery.
- Minimize duration of fasting, ensure normoglycemia, and avoid dehydration; list as first case of the day.
- Risk counseling.

Induction

- RSI in pts at high risk of aspiration.
- Consider avoidance of depolarizing neuromuscular blockers in view of risk of hyperkalemia.
- Reasonable to consider use of rocuronium with sugammadex available on standby.
- Propofol has been associated with decoupling of oxidative phosphorylation; experience is scarce on whether it should be avoided, but has been used successfully.

Monitoring

- Standard mandatory monitoring.
- Consider intra-arterial line: Continuous BP monitoring for pts with cardiomyopathy, early detection of arrhythmias, and frequent blood sampling for electrolytes, lactate, and glucose.
- Consider temp monitoring, especially for prolonged procedures greater than 2-h duration.
- Urinary cath to monitor urine output for adequacy of organ perfusion and fluid balance.
- Neuromuscular monitoring (unpredictable response to nondepolarizing neuromuscular blockers, aids timing of reversal and extubation).

Maintenance

- The association between mitochondrial myopathy and malignant hyperthermia remains unproven in current literature. Malignant Hyperthermia Association of the United States recommends volatile agents not be routinely avoided and succinylcholine to be used with care
- Consider increasing depth of inhalational and concurrent use of remifentanil to avoid depolarizing neuromuscular blockers
- Concerns: Acute decompensation with lactic acidosis, electrolyte abnormalities, acute encephalopathy, neuromuscular weakness, and cardiac dysfunction or arrhythmias.
- Avoid IV fluids containing lactate.

Extubation/Postoperative Period

- Ensure adequate reversal of neuromuscular blockers and extubate awake.
- Comanagement with neurologist.
- Avoid postop respiratory compromise; early and aggressive chest physiotherapy and early mobilization.
- Avoid decompensation: ensure adequate hydration, maintain normoglycemia and normothermia, and monitor for and correct electrolyte abnormalities.
- Adequate analgesia; use of multimodal approach.
- Appropriate postop placement; high dependency ward or ICU as indicated.
- Thromboembolic prophylaxis as appropriate.

Mitochondrial Myopathy

Jerry H. Kim | Jeremy M. Geiduschek

Risk

- More common than previously thought. Prevalence ranges from 1:7000–15,000.
- Occurrence is usually sporadic or maternally inherited.

Perioperative Risks

- Metabolic acidosis
- Respiratory and cardiac insufficiency/failure
- Delayed emergence

Worry About

- Respiratory failure following sedation.
- Consider aspiration risk.
- Metabolic acidosis.
- Hypotension during induction.

Overview

- Clinically heterogeneous collection of diseases with myopathy of mitochondrial origin as common trait. Defects can be in electron transport, fatty acid, and amino acid metabolism.
- Commonly associated with encephalopathy.
- Nomenclature rapidly changing to reflect discovery of specific genetic mutations. The following all are mitochondria-based disorders that may include a myopathic component: Kearns-Sayre syndrome (KSS); Pearson syndrome (PS); maternally inherited Leigh syndrome (MILS); late-onset Leigh syndrome; mitochondrial encephalomyopathy, lactic acidosis, and stroke-like symptoms (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); Leber hereditary optic neuropathy (LHON); chronic progressive external ophthalmoplegia (CPEO); and neuropathy, ataxia, and retinitis pigmentosa (NARP).
- Onset is variable. Most severe phenotypes present in infancy.
- Most common symptom is muscle weakness, and most common sign is lactic acidosis, resulting from the inefficient metabolism of pyruvate and shift to anaerobic respiration.
- Muscle biopsy often used for suspected cases. Hallmark is appearance of ragged red fibers.
- Biochemical analysis of mitochondria often needed to make exact diagnosis.
- Anesthetic sensitivity may manifest as decreased MAC of inhaled anesthetics (e.g., complex I disorders), increased respiratory insufficiency from sedatives and narcotics, and decreased hepatic clearance or renal excretion of IV agents.

Etiology

- Genetic variation in either mtDNA or nDNA.
- Large-scale mtDNA deletions (e.g., KSS, PS, PEO) are most often acquired sporadically.
- Single-base mtDNA changes (e.g., MELAS, MERRF, MILS, LHON) are often inherited maternally and usually affect mitochondrial protein synthesis (via mRNA, tRNA, or rRNA) or components of the electron-transport chain (i.e., complex I, III, IV, V).
- Single-base nDNA changes (e.g., late-onset Leigh syndrome) are often inherited in mendelian patterns (autosomal dominant or recessive).

Usual Treatment

- Supportive measures
- Dietary vitamins and supplements, coenzyme Q

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dysphagia	Coughing, choking, aspiration with feeding	Sialorrhea	Swallow study
CV	Cardiomyopathy Conduction defects (KSS)	Symptoms of CHF	Murmur, gallop, crackles	CXR, ECHO ECG, exercise testing (VO_2 max)
RESP	Disorganized respiratory muscle effort	Hypoventilation, hypoxia following sedative use	Rhonchi	CXR
GI	Chronic diarrhea Exocrine pancreatic failure (PS)	Dehydration Steatorrhea		Serum lytes
ENDO/METAB	Lactic acidosis Hepatic insufficiency	N/V Prolonged Rx effects	Hyperventilation	Serum lactate, CSF pyruvate/lactate ratio
GU	Renal tubular defects (PS), nephropathy	Urinary changes		Urinalysis Serum BUN, Cr, lytes
CNS	Encephalopathy (MILS) Ophthalmoplegia (CPEO, KSS) Stroke (MELAS) Seizure (MELAS, MERRF) Retinopathy, ataxia (NARP), blindness (LHON), deafness	Developmental delay Poor visual tracking Poor coordination Vision loss	Decreased ROM of extraocular mm Decreased visual acuity, ptosis Focal neurologic deficits Signs of seizures Pigmented retinas	Head CT or MRI Ophtho exam
PNS	Peripheral neuropathy	Weakness, clumsiness	Decreased strength	
MS	Hypotonia, weakness Myoclonus (MERRF)		Decreased strength	Muscle biopsy (ragged red fibers)

Clinical findings listed above may be characteristic of one or more mitochondrial myopathies. A specific disorder may follow in parentheses if the finding is a primary feature.
Key Reference: Niezgoda J, Morgan PG: Anesthetic considerations in patients with mitochondrial defects, *Paediatr Anaesth* 23(9):785–793, 2013.

Perioperative Implications

Preoperative Preparation
- Assess for cardiomyopathy and conduction defect.
- Preop anticholinergic for excessive oral secretions.
- Avoid prolonged fasting and dehydration, which can worsen acidosis.
- When possible, start IVF at NPO time, allow for late (2 h prior) clear fluid intake, and book as first case.

Airway
- Possible aspiration risk

Monitoring
- Routine, assuming no severe cardiomyopathy or CHF
- Consider BIS monitor prior to induction for possible increased anesthetic sensitivity

Induction
- Avoid lactate-containing IVF (e.g., lactated Ringer).
- Consider dextrose-containing IVF (e.g., 2–5% dextrose in normal saline).
- Avoid succinylcholine for uncharacterized myopathy or in face of neuropathy.

Maintenance
- Many techniques have been used safely.
- Avoid prolonged infusion of IV anesthetics, especially propofol, which is a known electron transport chain decoupler, due to worsened acidosis and reduced ATP production.
- Hepatic and renal insufficiency may increase IV anesthetic half-life and prolong elimination.
- If NMB agent is required, consider careful titration with shorter-acting agents.
- Implement aggressive temp control; recommend active warming techniques.
- Avoid tourniquets.

Extubation
- Muscle weakness and anesthetic sensitivity may delay extubation.

Regional Anesthesia
- Used successfully, but caution in those with underlying cardiac conduction block.
- Local anesthetics have potential to decouple electron transport chain.

Postoperative Period
- Close monitoring of respiratory function.
- For cases of longer duration, consider serum electrolytes or blood gas to assess acidosis.
- Some have reported increased incidence of PONV.

Anticipated Problems/Concerns
- Generally not associated with MH; however, scenario of critical ATP depletion may lead to muscular contraction mimicking MH.
- Although succinylcholine is not contraindicated as in Duchenne or Becker MD, acidosis and neuropathy may predispose to accentuation of hyperkalemia.

Mitral Regurgitation

Luiz Maracaja | Raj K. Modak

Risk
- Mitral regurgitation affects more than 2 million people in USA.
- Incidence of moderate/severe mitral regurgitation: Nearly 20% for age >55 y.
- Mitral valve prolapse is the primary form of myxomatous degeneration of the valve.
- Mitral valve prolapse is the most frequent diagnosed valve abnormality.
- Incidence in females is slightly higher than in males.

Perioperative Risks
- Acute mitral regurgitation
- Atrial arrhythmias (tachycardia, atrial fibrillation, atrial flutter)
- LV dysfunction yielding reduced cardiac output, acute CHF, pulm edema, and acute RV failure
- Bacterial endocarditis

Worry About
- Worsening symptoms of fatigue, orthopnea, dyspnea on exertion
- Acute or chronic mitral regurgitation
- New-onset atrial fibrillation
- Hemodynamic instability in setting of poor LV function and acute MI

Overview
- The mitral valve allows one-way blood flow through the left heart.
- During diastole, it acts as an open conduit for blood flow from the LA to the LV During systole, it closes preventing backflow while the heart contracts.
- With mitral regurgitation, retrograde flow occurs from the LV to the LA during systole. This can occur as an acute or chronic process.
- The acute form results in sudden elevations in LA pressure. Elevated pressures in the pulm vasculature resulting in pulm edema and RV strain and possible failure.
- Chronic mitral regurgitation is tolerated well. LV hypertrophy is followed by dilation and failure. Similar changes in the RV and pulm circulation occur, as in the acute form, but are better tolerated over the longer time period.
- As a general rule, the more precipitous the onset, the more significant the sequelae.

Etiology
- Acute: Myocardial ischemia or MI causing papillary muscle dysfunction, ruptured chordae causing a flail mitral valve from infarction or endocarditis, trauma, prosthetic valve dysfunction.

- Chronic: Include acute processes over longer time, myxomatous degeneration, ischemic heart disease, dilated cardiomyopathy, rheumatic disease, lupus, congenital valvular disease, LA myxoma. All forms can be accelerated by systemic Htn.

Usual Treatment

- Medical therapy: Afterload reduction, CHF regimens, arrhythmia control, endocarditis prophylaxis
- Pharmacology: Includes Angiotensin inhibitors, hydralazine, cardiac glycosides, diuretics, nitrates, antibiotics
- Surgical therapy: Mitral valvuloplasty (repair), annuloplasty, mitral valve replacement (mechanical and tissue)
- Transcatheter mitral valve interventions: Edge-to-edge repair/enhanced coaptation, chordal repair, annuloplasty, mitral valve implantation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Mitral regurgitation LA enlargement	Fatigue, exertional or nocturnal dyspnea	Pansystolic and late systolic murmur, rales	Doppler ECHO, 2D/3D ECHO 2D-ECHO ECG
	AFIB	Palpitations, defibrillation, anticoagulation	Irregular rhythm, bruises	ECG, PT/INR
	RV failure	Peripheral swelling, RUQ pain, tenderness	Ankle edema, hepatomegaly, hepatojugular reflux	Cardiac cath 2D and Doppler ECHO
	Cardiomegaly		Displaced posterior MI	CXR, 2D ECHO
RESP	CHF, pulm edema	Dyspnea, orthopnea	Gallop, rales	CXR
GI	Congestive hepatopathy	Bleeding with minor trauma	Bruises	PT, PTT, LFTs
RENAL	Decreased perfusion Diuretic-induced Decreased K^+, Mg^{2+}	Oliguria Palpitations	 Muscle weakness Decreased reflexes	Decreased BUN, Cr Serum K^+, Mg ECG
MS	Cachexia	Weight loss	Muscle wasting	Decrease weight

Key References: Bhattacharyya S, Khattar R, Chahal N, et al.: Dynamic mitral regurgitation: review of evidence base, assessment and implications for clinical management, *Cardiol Rev* 23(3):142–147, 2015; Al-Atassi T, Malas T, Mesana T, et al.: Mitral valve interventions in heart failure, *Curr Opin Cardiol* 29(2):192–197, 2014.

Perioperative Implications

Preoperative Preparation

- Antibiotic prophylaxis.
- Manage anticoagulation issues related to atrial fibrillation and the possible use of regional techniques.
- Optimize HR issues related to AFIB.
- Optimize symptoms related to CHF.
- TEE with 3D imaging is essential for disease classification, surgical planning, and post-intervention valve assessment.

Monitoring

- In procedures with expected wide variations in BP, direct arterial BP monitoring should be considered, especially with moderate or severe mitral regurgitation.
- In settings of LV failure, a pulm artery cath or TEE may be useful in assessing changes and guiding pharmacologic therapy.

Airway

- Avoid hypoxemia and hypercarbia, which maintains the lowest pulm vascular resistance and reduces risk of RV failure.

Preinduction/Induction

- "Faster, Fuller, Forward."
- Avoid bradycardia, maintain high-normal preload, reduce afterload.
- Maintain stoke volume by avoiding myocardial depression and AFIB.

Maintenance

- Cardiac and pulm goals, same as induction.
- Avoid excessive PEEP, which reduces preload.
- If possible, follow cardiac output, using pharmacology as needed.
- Regional anesthetic techniques may be considered because they help to reduce afterload; however, caution is recommended in the setting of impaired LV function.

Extubation

- Airway management to avoid hypoxia and hypercarbia inducing RV strain and failure
- Requires vigilance on BP management to avoid Htn
- Transcatheter MV procedures slowly evolving to monitored anesthetic delivery without need for general endotracheal anesthesia

Adjuvants

- No known drug interaction problems

Postoperative Period

- Pain management critical to avoid hypertensive episodes.
- Both scheduled and pt-controlled analgesia useful for pain control.
- Fluid shifts and intraop volume management may alter LV function and antiarrhythmic blood concentrations.
- New onset AFIB.
- Consideration for pacemaker use: new-onset bradycardia and heart block related to manipulation and device insertion via direct pacing wires or transvenous pacing device.
- Consideration for restarting anticoagulation for chronic AFIB.

Anticipated Problems/Concerns

- High periop risk is best predicted by impaired LV function, symptoms of both LV and RV dysfunction.
- Htn can acutely worsen mitral regurgitation, causing CHF and pulm edema.

Mitral Stenosis

Albert T. Cheung | Tarang Safi

Risk

- Bimodal age distribution: 20–39 y and 50–60 y.
- Mitral stenosis is 2–3 times more common in women and is the most common valve disease affecting pregnant women.
- Most common among immigrants to USA from regions where rheumatic fever is prevalent (e.g., Middle East, Asia, Latin America).

Perioperative Risks

- Increased risk of periop cardiac complications, including infectious endocarditis, pulm edema, resp failure, HF, tachyarrhythmias, new-onset AFIB or atrial flutter, embolic stroke of cardiac origin (0.7–0.9% risk of stroke after cardioversion)

Worry About

- Fluid status
- Paroxysmal AFIB or flutter
- Pregnancy
- Limited ability to increase cardiac output in response to increased metabolic demands or intravascular volume expansion
- Tachycardia, AFIB, or atrial flutter decreases atrial emptying by decreasing the duration of diastole
- Cardiomyopathy, pulm Htn, RV failure, hepatic dysfunction, tricuspid regurgitation, and associated aortic valve disease
- Pulm edema

Overview

- The normal mitral valve has an area of 4–6 cm^2. Symptoms start when the mitral valve area is reduced to 1.5 cm^2. Diastolic emptying of blood from the LA into the LV is impaired critically when the mitral valve area is <1 cm^2.
- MS can be classified as at risk for MS (Stage A), progressive MS (Stage B), asymptomatic severe MS (Stage C), or symptomatic severe MS (Stage D), based on the presence of dyspnea on exertion, exercise intolerance, diastolic doming and commissural fusion of the mitral valve leaflets, left atrial enlargement, and pulm Htn.
- Transmitral pressure gradient varies directly with blood flow across the valve; acute increases

in cardiac output or venous return to the heart increases the mitral valve gradient and increases LA and pulm venous pressures. Pulm edema occurs when the pulm venous pressure is >pulm capillary oncotic pressure.
- Elevated left atrial pressure leads to pulm venous Htn, left atrial dilation, left atrial thrombosis, AFIB, pulm Htn, RV failure, and tricuspid regurgitation.
- Symptoms of mitral stenosis can be elicited by conditions (fluid overload, exercise, pregnancy, sepsis, operation) that demand an increase in cardiac output or diastolic blood flow across the mitral valve.
- Deformity of the mitral valve apparatus may cause mitral stenosis in combination with mitral regurgitation or LV dysfunction.

Etiology

- Congenital heart disease (rare).
- Mitral valve repair with restrictive ring annuloplasty (rare).
- Acquired mitral stenosis is sequela of rheumatic carditis developing after group A streptococcal pharyngitis.
- Rheumatic carditis produces exudative and inflammatory lesions that lead to fibrosis, calcification, thickening, and commissural fusion of the mitral valve apparatus.
- Acquired prosthetic mitral stenosis from structural valvular deterioration after bioprosthetic mitral valve replacement or mechanical prosthetic valve dysfunction after mechanical mitral valve replacement.

Usual Treatment

- Anticoagulation to decrease risk of thromboembolic events in pts with AFIB, prior embolic event, or left atrial thrombus
- Digoxin, beta-blockers, or calcium channel blockers to control ventricular rate in pts with AFIB
- Diuretic therapy for symptomatic pulm edema, CHF, or RV failure
- Percutaneous balloon valvotomy in pts without extensive valve calcification, leaflet restriction, leaflet thickening, moderate-severe mitral regurgitation, left atrial thrombus, or involvement of the subvalvular apparatus
- Mitral valve replacement, repair, or open valvotomy in pts with symptomatic severe MS and MVA ≤1.5 cm^2
- Transcatheter valve-in-valve mitral valve replacement in high-risk surgical pts with bioprosthetic mitral stenosis

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Mitral stenosis	DOE, NYHA class Chest pain or tightness	Diastolic murmur	ECHO Cardiac cath
	AFIB	Palpitations	Irregular pulse	ECG
	Pulm Htn	DOE	Sternal heave Prominent S_2	CXR
RESP	Pulm edema	DOE Orthopnea Paroxysmal nocturnal dyspnea Hemoptysis	Tachypnea Rales Wheezes	CXR
GI	Cardiac cirrhosis		Hepatomegaly	LFTs
RENAL	Fluid retention Diuretic therapy	Dependent edema	Pedal edema	Serum lytes
CNS	Embolic stroke	Neurologic deficits, TIAs	Focal neurologic deficits	Head CT scan, TEE
HEME	Bleeding	Anticoagulation therapy	Ecchymosis	INR, PT, PTT

Key References: Nishimura RA, Otto CM, Bonow RO, et al.: 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines, *Circulation* 129(23):e521–e643, 2014; Weiner MM, Vahl TP, Kahn RA: Case scenario: cesarean section complicated by rheumatic mitral stenosis, *Anesthesiology* 114(4):949–957, 2011.

Perioperative Implications

Preoperative Preparation

- Determine if pt is a candidate for percutaneous balloon valvotomy.
- Optimize fluid status of pts in CHF.
- Control ventricular rate in pts with AFIB.
- Replete K^+ in pts with hypokalemia on digoxin therapy.
- Antibiotic prophylaxis for infectious endocarditis according to guidelines.
- Keep pt calm using reassurance, anxiolytics, and analgesics.
- Assess the risk of bleeding in anticoagulated pts and correct the prolonged PT (INR) with FFP if necessary.

Monitoring

- ECG to detect paroxysmal AFIB or flutter.
- Consider arterial catheter for continuous BP monitoring and ABG sampling.
- Consider CVP line, PA catheter, or TEE to measure pulm artery pressure, assess RV function, and guide intravascular volume management when large fluid shifts are anticipated.

Preinduction/Induction

- Cautious administration of drugs that decrease myocardial contractility, increase HR, or cause vasodilation.
- Hypoventilation and hypoxia may worsen pulm Htn and RV failure.
- Positive inotropic drugs may precipitate pulm edema.

Maintenance

- Control fluid administration.

Extubation/Postoperative Period

- Provide adequate analgesia.
- Increased risk of postop resp failure.

Adjuvants

- Consider regional anesthesia or periop epidural anesthesia and analgesia, especially for labor and delivery in the pregnant pt with mitral stenosis.
- Inhaled NO or epoprostenol for RV failure associated with pulm Htn.

Anticipated Problems/Concerns

- Pts have a limited ability to increase their cardiac output.
- Acute pulm edema is precipitated by increased cardiac output, increased HR, pregnancy, anxiety, fluid overload, exercise, and postop mobilization of sequestered (third space) interstitial and extracellular fluid.
- Bleeding in anticoagulated pts.

Mitral Valve Prolapse

Jessica L. Brodt | Albert T. Cheung

Risk

- Believed to be most common form of valvular heart disease, with an incidence of 2–3% in the general population. MVP is a progressive disease that begins in middle age and affects both men and women.
- Most common cause of chronic primary MR.
- Disease severity varies widely. Complications related to the disease are a consequence of arrhythmias, infective endocarditis, and progressive severity of MR with associated LV dysfunction.

Perioperative Risks

- Acute HF or exacerbation of chronic HF as a consequence of MR
- Embolic stroke
- Arrhythmias
- Sudden cardiac death

Worry About

- Severity of MR
- Severity of associated LV dysfunction and HF
- AFIB, embolic stroke, sudden cardiac death
- Associated conditions: Marfan syndrome; Ehlers-Danlos syndrome, osteogenesis imperfecta, pseudoxanthoma elasticum, aneurysms-osteoarthritis syndrome, or hypertrophic cardiomyopathy

Overview

- Severity of disease varies widely based on the clinical and diagnostic criteria used to establish the diagnosis.
- MVP is defined by echocardiography as isolated prolapse of the mitral valve leaflets ≥2 mm beyond the mitral valve annular plane into the LA during systole. The myxomatous degeneration causing MVP is characterized by leaflet thickening, leaflet redundancy, chordal elongation, or chordal rupture. MRI may demonstrate scarring or fibrosis of the papillary muscle or inferobasal segments of the LV
- Structural changes lead to weakness and deformity of the valve apparatus. Annular dilation, stretching of leaflets and chordal elongation impair leaflet coaptation causing progression of MR.
- Fibrosis or scarring of the valve apparatus may increase the risk of ventricular arrhythmias or sudden cardiac death.
- Rupture of weakened chordae results in a flail leaflet and produces acute severe MR.
- Chronic MR causes progressive atrial dilation, eccentric LV hypertrophy, HF, and AF.
- MVP syndrome is MVP associated with a spectrum of nonspecific symptoms, including atypical chest pain, palpitations, exertional dyspnea, exercise intolerance, syncope, anxiety, lean body habitus, electrocardiographic repolarization abnormalities, and sudden cardiac death. A pathophysiologic link between genetics and the molecular biology of disease expression for MVP and its syndromes has yet to be fully defined.
- Onset of HF symptoms, LV dysfunction (ejection fraction <50% or end-systolic diameter >40 mm) and pulm Htn worsen pt prognosis. AF, left atrial enlargement, leaflet thickening (>5 mm), flail segments, and age >50 y is associated with worsening disease.

Etiology

- Familial (autosomal dominant, genetics not completely defined) or sporadic occurrence.
- Inherited connective tissue disorders.
- Myxomatous degeneration caused by dysregulation of collagen and elastin matrix protein synthesis and degradation.

Usual Treatment

- No treatment if asymptomatic or in pts with MVP syndrome without severe MR.
- Medical therapy with ACE inhibitors, beta-blockers, angiotensin receptor antagonists, aldosterone antagonists, and diuretics in pts with significant MR or HF (see Mitral Regurgitation or Heart Failure).
- Antiarrhythmic and anticoagulation therapy in pts with AF (see Atrial Fibrillation).
- Mitral valve repair recommended in pts with symptomatic severe MR or if asymptomatic with moderate LV dysfunction. Valve repair is reasonable in asymptomatic pts with preserved LV size and systolic function if expected mortality rate is <1% and likelihood of successful repair >95%. Mitral valve repair preferable to mitral valve replacement when a successful and durable repair can be achieved

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	MVP	Atypical chest pain	Mid- and late-apical nonejection systolic clicks	ECHO
	MR	DOE	Mid- to late-apical systolic murmur	ECHO
	AFIB	CHF	Irregular pulse	CXR
	Infectious endocarditis	NYHA class	Embolic phenomena	ECG
		Palpitations		TEE, blood culture
		Fever, chills		Cardiac MRI
CNS	Stroke	Neurologic deficits	Focal neurologic signs	Head CT scan
		TIAs		TEE
MS	Connective tissue disorders		Pectus excavatum	
			Scoliosis	
			Lean stature	

Key References: Delling FN, Vasan RS: Epidemiology and pathophysiology of mitral valve prolapse. New insights into disease progression, genetics, and molecular basis, *Circulation* 129(21):2158–2170, 2014; Frogel J, Galusca D: Anesthetic considerations for patients with advanced valvular heart disease undergoing noncardiac surgery, *Anesthesiol Clin* 28(1):67–85, 2010.

Perioperative Implications

Preoperative Preparation

- Assess presence and severity of MR.
- Assess for signs and symptoms of HF.
- Prophylactic antibiotics for endocarditis only indicated in pts with prior episode of IE.

Monitoring

- Routine.
- Consider invasive hemodynamic monitoring for major operations in pts with symptoms, severe MR, and/or LV dysfunction.

Preinduction/Induction/Maintenance

- Avoid Htn and acute increases in sympathetic tone.
- Consider regional anesthesia.

Adjuvants

- Interventions that increase BP, myocardial contractility, preload, or sympathetic tone may increase severity of MVP, MR, or the risk of chordal rupture.
- Antihypertensives, afterload reducing agents, and positive inotropic drugs are effective for increasing cardiac output in pts with significant MR.

Extubation and Postoperative Period

- Avoid Htn and acute increases in sympathetic tone.

Anticipated Problems/Concerns

- Htn and intravascular volume expansion may increase severity of MVP, worsen the degree of MR, and increase the risk of pulm edema and acute exacerbation of HF.
- Presence of severe MR, LV dysfunction, or associated connective tissue disease may alter routine management of pts with isolated MVP (see Mitral Regurgitation).
- Risk of sudden cardiac death among predominantly young females with MVP who have frequent ECG repolarization abnormalities.

Mobitz I (Second-Degree Atrioventricular Block)

James R. Zaidan

Risk

- Occurs after inferior MI or occasionally in trained athletes or in normal, sleeping people.
- Incidence varies based on etiology.

Perioperative Risks

- Without associated heart disease and without symptoms, should not present undue risk during anesthesia (e.g., in trained athletes).
- If occurs secondary to inferior MI, periop risk depends on extent of ischemic area.

Worry About

- Advancing to a higher-degree block if ischemic zone extends to anterior wall.
- Papillary muscle dysfunction may occur.

Overview

- Found usually in presence of CAD.
- Block generally occurs in AV node, resulting in normal QRS complexes.
- ECG reveals progressive lengthening PR intervals at decreasing increments and progressively shortening RR intervals leading to regular atrial rhythm and irregular ventricular rhythm.
- Bradycardia usually responds to atropine.

Etiology

- Acquired, usually with MI
- Increased resting parasympathetic tone relative to resting sympathetic tone

Usual Treatment

- Specific therapy in absence of heart disease not necessary unless pt is symptomatic.
- Treatment of an infarction-related Mobitz I block includes observation and medical therapy with atropine.
- Temporary pacing is necessary only if a medically unresponsive pt is symptomatic.
- Permanent pacing seldom required and considered only in persistently blocked, symptomatic pts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Commonly no Sx Bradycardia on occasion	Exercise tolerance Angina SOB	Signs of CHF and decreased perfusion	ECG CXR
RENAL	Likely normal			Renal function testing?
CNS	No effect or decreased perfusion of CNS	No Sx or only mild Sx: Fainting, dizziness	Normal Bruits	PE Carotid US

Key References: Epstein AE, DiMarco JP, Ellenbogen KA, et al.: 2012 ACC/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society, *J Am Coll Cardiol* 61(3):e6–e75, 2013; Coumbe AG, Haksuh N, Newell MC, et al.: Long-term follow-up of older patients with Mobitz type 1 second-degree atrioventricular block, *Heart* 99(5):334–338, 2013.

Perioperative Implications

Preoperative Preparation
- Consider availability of transcutaneous pacing.

Monitoring
- Based on coexisting disease.
- Observe for and prepare to treat tertiary block when positioning PA cath in pt with Mobitz I block.

Airway
- None

Induction and Maintenance
- Regional or general.
- No contraindications to any standard anesthetic drugs.
- Intraoperative processes and drugs that increase atrial rate could decrease ventricular rate.

Extubation
- None

Adjuvants
- Cautious use of drugs that slow AV conduction

Anticipated Problems/Concerns
- Extension of infarcted area with higher-degree block and CHF

Mobitz II (Second-Degree Atrioventricular Block)

James R. Zaidan

Risk
- Occurs after anterior infarction and can quickly proceed to third-degree heart block

Perioperative Risks
- Risk of developing third-degree block

Worry About
- Rapid development into third-degree block, which requires temporary transvenous pacing

Overview
- Unlike Mobitz I block, Mobitz II block is located in bundle of His or bundle branches, resulting in lengthening QRS duration.
- PP and RR intervals are constant, and PR intervals are constant prior to the dropped QRS complex.

Etiology
- Acquired; usually associated with MI

Usual Treatment
- Temporary pacemaker insertion should be considered soon after onset of this block because third-degree block commonly occurs.
- Pacing does not improve survival.
- Atropine usually does not improve conduction.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Bradycardia	Exercise tolerance Angina SOB	Signs of CHF and decreased perfusion	ECG CXR Other tests as indicated
GU	Likely normal			Renal function testing?
CNS	Decreased perfusion of CNS	Fainting, dizziness	Normal? Bruits	PE Carotid US

Key References: Epstein AE, DiMarco JP, Ellenbogen KA, et al.: 2012 ACC/AHA/HRS focused update incorporate dinto the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society, *J Am Coll Cardiol* 61(3):e6–e75, 2013; Arias MA, Sánchez AM: Obstructive sleep apnea and its relationship to cardiac arrhythmias, *J Cardiovasc Electrophysiol* 18(9):1006–1014, 2007.

Perioperative Implications

Preoperative Preparation
- Evaluation of CAD important.
- Likely a transvenous pacemaker will be in place.
- Transcutaneous pacing should be available if temporary transvenous pacing was not established prior to induction of anesthesia.

Monitoring
- Based on severity of heart disease and extent of infarcted area.
- Prepare to treat third-degree block when positioning a PA cath.

Airway
- None

Induction and Maintenance
- No contraindications to any standard anesthetic drugs.
- Any intraop process or drug increasing atrial rate could worsen block and decrease ventricular rate.

Adjuvants
- Cautiously use drugs that slow conduction through AV node unless they also slow SA nodal rate and allow 1:1 AV conduction and increased ventricular rate.
- First-degree AV block will persist if 1:1 conduction occurs.

Morbid Obesity

Ashish C. Sinha

Risk

- Incidence in USA: Approximately 5% morbidly obese

Perioperative Risks

- Increased morbidity and mortality versus normal BMI from resp and cardiac issues

Worry About

- Challenging procedures: IV start, intubation, ventilation, epidural cath placement.
- Restrictive pattern of resp disease, hypoxemia, larger O_2 demand, small FRC; OSA is common, with associated cardiac issues.
- Htn: Systemic and pulm.
- DM.
- NASH.
- Reflux, hiatal hernia, and depression.

Overview

- Defined by BMI (weight in kg/height in m^2); >30 obese; >35 morbidly obese
- Cardiac and resp issues mainly due to size; large body mass to be perfused and oxygenated; increased cardiac strain and resp effort of breathing; OSA common; increased sensitivity to narcotics
- Depression common

Etiology

- Disputed role of genetics, mainly environmental and nutritional habits; essentially a form of severe malnourishment

Usual Treatment

- Medical treatment includes psychological counseling, along with decreased calorie consumption with increased exercise, if physically able.
- Surgical treatment includes gastric banding, Roux-en-Y, sleeve gastrectomy, or intestinal bypass.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn Pulm	Fatigue, dyspnea	Auscultation, increased heart size, ±rales	BP, ECG, CXR
	Htn Cardiac failure Coronary disease	Dyspnea, fatigue, syncope including JVP, peripheral edema, hepatomegaly, crackles	Auscultation, palpation, auscultation	CXR, ECG, ECHO ECG, ECHO
		Chest pain, SOB		ECG, stress ECHO Coronary angiogram
RESP	Restrictive disease	SOB, including resp rate, decreased exercise tolerance	Rapid shallow breathing, hypoxemia, large neck, redundant soft tissue in neck	PFT, ABG, CXR, Hg, pulse oxygen for room air saturation
	OSA	Hx of snoring, periods of apnea in sleep, nonrestful sleep, daytime somnolence and tiredness Different screening tests (STOP-BANG)	Large neck, redundant soft tissue in neck	Overnight sleep study for apnea hypopnea index $PaCO_2$ as predictor
NEURO	Depression	Hx	Question and answers, survey instruments	By psychologist and/or psychiatrist
HEENT	Potentially difficult intubation	Mallampati, upper lip bite test	Evaluation for large tongue, small interdental distance, limited ROM	
GI	NASH NIDDM	Hepatomegaly, icterus, ascites Polyphagia, polyuria, polydipsia	Palpation	LFT, PT, PTT, BUN, Cr UA, BS, GTT, HgA1c

Key References: Sinha AC: Some anesthetic aspects of morbid obesity, *Curr Opin Anaesthesiol* 22(3):442–446, 2009; Nishiyama T, Kohno Y, Koishi K: Anesthesia for bariatric surgery, *Obes Surg* 22(2):213–219, 2012.

Perioperative Implications

Perioperative Preparation

- All medications except for DM.
- Avoid sedation, unless benefit outweighs risk of postop resp depression.
- Consider prophylactic preop IVC filter placement if risk of DVT is high.
- Preop carbohydrate loading isoosmolar drink 2 to 3 h prior to surgery may benefit postop insulin resistance, nitrogen, and protein loss and decrease LOS.

Monitoring

- Routine with ± arterial cath if cardiac status dictates or ultra obese (BMI >70 kg/m^2 or weight >200 kg)
- If severe cardiac or resp disease, ABG
- UO
- Central venous access if peripheral access difficult, or CVP or pulm pressures need to be monitored for cardiac disease

Airway

- Position at 30-degree head elevated (HELP) to improve probability of intubation with direct laryngoscopy; BMV difficult in 10–15% and intubation difficult in 1–2%
- Minority of pts may need awake FOI
- Prepare for difficulty with multiple airway options, such as laryngeal masks and video laryngoscopes and short-acting drugs

Induction

- Preoxygenate with pressure support if possible; complete denitrogenation.
- Rapid sequence with cricoid pressure should be considered.

Maintenance

- Drug dosing: Lipophilic dosed to real body weight; lipophobic to IBW or LBM.
- Desflurane preferable due to complete and rapid recovery; avoid nitrous; TIVA has advantages if high risk of PONV.
- Consider opioid free or low opioid intraop; use such adjuncts as NSAIDs, acetaminophen, pregabalin, lidocaine infusions, α-2 agonists.
- Appropriate goal-directed fluid infusion based on deficit, losses, and UO.
- Ventilation: Start at TV 6–8 mL/kg IBW; RR 12–14/m; PEEP 8–10; adjust as needed, recruitment helps atelectasis, volume or pressure control.

Extubation

- Wide awake, no residual volatile agent, normocapnic, responsive with appropriate resp effort and partially sitting up; consider cyclodextrin for NMB reversal.

Postoperative Period

- Rapid placement on CPAP or BiPAP decreases atelectasis.
- Good analgesia with IV PCA, NSAIDs and local infiltration with LA and rapid mobilization helps resp function and decreases DVT.

Moyamoya

Francine S. Yudkowitz

Risk

- Occurs in both children and adults, peak age at 5 y and 40 y, respectively
- Female-to-male ratio of 1.8:1
- Highest incidence in Japanese and Asian populations; familial occurrence 10%

Perioperative Risks

- Stroke

Worry About

- Hypocarbia and hypercarbia
- Adequate cerebral blood flow
- Hypotension
- Hypothermia

Overview

- In Japanese, moyamoya means "puff of smoke," which describes the angiographic appearance of collaterals between internal and external carotid arteries.
- Chronic progressive cerebrovascular disease consisting of concentric stenosis or occlusion of the distal internal carotid arteries and large vessels of the circle of Willis with prominent basal collateral vessels.
- Histopathology shows eccentric intimal thickening by fibrous tissue, smooth muscle cell hyperplasia, and luminal thrombosis
- The most common presentation in children and adults is ischemic stroke.

- In contrast to children, adults may also present with intracranial hemorrhage.
- TIA, headache, and seizures are other presenting symptoms.
- Symptoms are precipitated by activities that involve hyperventilation that results in hypocarbia (e.g., crying, exercise).

Etiology

- Poorly understood but probably involves both genetic and environmental factors
- Autosomal dominant with low penetrance or polygenic mode
- Moyamoya disease (congenital): Vasculopathy without known associated risk factors, usually bilateral
- Moyamoya syndrome: Vasculopathy with other known associated conditions (e.g., sickle cell disease, neurofibromatosis, SLE, Graves disease, trisomy 21, prior radiation therapy to head or neck, brain tumors, and tuberculous meningitis)

Usual Treatment

- Medical:
  - Does not stop progression.
  - Antiplatelet agents (e.g., aspirin, ticlopidine).
  - Vasodilators (e.g., calcium channel blockers).
  - Rheologic therapy (e.g., pentoxifylline).
- Surgical:
  - Direct: Superficial temporal artery to middle cerebral artery (STA-MCA) bypass; also known as extracranial-intracranial bypass.
  - Usually done in adults, technically difficult in children.
  - Indirect: EDAS. Scalp or temporal artery is placed onto the arachnoid surface of the brain. Collaterals occur over time.
  - Usually done in children; combined with STA-MCA bypass in adults.
  - EMS: Temporalis muscle is attached to brain surface.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Decreased CBF Seizures	TIAs, strokes	Neuro deficits	CT/MRI/MRA EEG

Key References: Parray T, Martin TW, Siddiqui S: Moyamoya disease: a review of the disease and anesthetic management, *J Neurosurg Anesthesiol* 23(2):100–109, 2011; Chui J, Manninen P, Sacho RH, et al.: Anethetic management of patients undergoing intracranial bypass procedures, *Anesth Analg* 120(1):193–203, 2015.

Perioperative Implications

Preoperative Preparation

- Assess for associated abnormalities.
- Review of chronic medications. Continue antiseizure and calcium channel blocker.
- Premedication:
  - In children, anxiolysis may be beneficial to avoid hyperventilation from crying.
  - Caution with sedatives and opioids that may result in hypercarbia.

Monitoring

- Arterial line for BP monitoring and blood gas analysis

Induction

- Inhalation or IV.
- Avoid hyperventilation and hypoventilation.
- Avoid hypotension that will impair CBF.
- Avoid muscle relaxants that release histamine or cause hemodynamic changes.

Maintenance

- Balanced anesthesia or total IV anesthesia.
- Nitrous oxide use is controversial.
- Maintaining cerebral and systemic hemodynamics is paramount.
- Avoid cerebrovasodilators.
- Minimize increases in $CMRO_2$ with adequate levels of anesthesia during painful stimuli.
- Ensure adequate CBF by avoiding hypotension, hypocarbia, and hypercarbia.
- Maintain normovolemia to hypervolemia.
- Maintain normothermia with warming blanket if needed.

Postoperative Period

- Monitor for hypoventilation to avoid hypercarbia-induced neurologic symptoms.
- Provide adequate analgesia.
- Maintain normotension, normocarbia, normovolemia, and normothermia.

Anticipated Problems/Concern

- TIA/stroke
- Intracranial hemorrhage
- Infection

Mucopolysaccharidoses

Megan A. Brockel | James J. Fehr

Risk

- All forms of MPS are autosomal recessive except MPS II (also known as Hunter syndrome), which is X-linked recessive (only males affected).
- Estimated incidence in USA: 1:30,000.

Perioperative Risks

- MPS pts are at increased anesthetic risk (most complications are associated with airway obstruction), and surgery is associated with a high mortality rate.

Worry About

- Airway obstruction, difficult airway management, cardiac pathology, obstructive and restrictive lung disease, cervical instability, spinal canal narrowing with cord compression

Overview

- MPSs are a group of rare, inherited, progressive lysosomal storage diseases caused by a lack of lysosomal enzymes required to break down glycosaminoglycans, resulting in their accumulation in tissues and organs.
- Children may appear normal at birth but begin developing symptoms by 1 y of age.
- Diagnosis is made by clinical features and increased urine mucopolysaccharides.
- Typical clinical manifestations include coarse facial features, impaired vision and hearing, airway abnormalities, cardiac problems, pulm disease, organomegaly, cervical instability, spinal cord compression, joint contractures, growth impairment, and hernias.
- Some types are associated with cognitive impairment.
- Several different subtypes are described, with differing clinical manifestations, rates of progression, and anesthetic implications:
  - Type IH (Hurler): Considered the prototypic and most severe subtype of MPS I, it is characterized by coarse facial features and airway narrowing, leading to difficult intubation, cardiac involvement, hepatosplenomegaly, atlantoaxial subluxation, joint stiffness, and contractures.
  - Type IH/S (Hurler-Scheie): Characterized by macrocephaly, micrognathia, and mental capacity ranging from mild deficiency to normal intelligence.
  - Type IS (Scheie, formerly classified as type V): Characterized by mandibular prognathism, normal intelligence, aortic insufficiency, and joint stiffness.
  - Type II (Hunter): Characterized by coarse facial features and airway narrowing leading to difficult intubation, severe mental deficiency, valvular heart disease, hepatosplenomegaly, joint stiffness, and dwarfism.
  - Type III (Sanfilippo): Characterized by mildly coarse facial features and severe mental deficiency.
  - Type IV (Morquio): Characterized by mildly coarse facial features, aortic regurgitation, restrictive lung disease, atlantoaxial instability and narrowing of the spinal canal, and joint laxity.

Etiology

- Lack of lysosomal enzymes required to break down glycosaminoglycans results in their intracellular accumulation in tissues throughout the body, leading to progressive alteration of cellular structure and function.

Usual Treatment

- Life expectancy is decreased in pts with MPS but has improved with the introduction of HSCT and ERT, both of which have beneficial effects on pulm function.
  - HSCT must be performed early in the disease course (before developmental deterioration begins); it can prevent and/or reverse many clinical features of MPS (it appears to reduce airway complications in children treated at less than 2 y of age).
  - ERT is generally initiated later and also improves airway patency but does not cross the blood brain barrier and therefore cannot preserve CNS function.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Macroglossia, adenotonsillar hypertrophy, tracheobronchomalacia	Symptoms of sleep-disordered breathing	Airway exam including neck range of motion	X-ray, sleep study
CV	Valvular disease (most common cardiac pathology), coronary artery disease, heart failure, arrhythmias, pulm Htn	Exercise tolerance, history of angina	Auscultation for murmurs, exam for signs of heart failure	ECG, ECHO, CXR
RESP	Restrictive lung disease, obstructive sleep apnea (can lead to pulm Htn and cor pulmonale)	Exercise tolerance, symptoms of sleep-disordered breathing	Auscultation, exam for chest wall deformities	PFTs, sleep study, CXR
CNS	Spinal canal narrowing with spinal cord compression, atlantoaxial instability from odontoid hypoplasia	Neurologic symptoms	Neck range of motion	X-ray, CT, MRI

Key References: Walker R, Belani K, Braunlin E, et al.: Anaesthesia and airway management in mucopolysaccharidosis, *J Inherit Metab Dis* 36(2):211–219, 2013; Wheeler M, Cote C, Todres D: The pediatric airway. In Cote J, Lerman J, Todres D, editors: *A practice of anesthesia for infants and children,* ed 4, Philadelphia, PA, 2009, Elsevier, pp 237–278.

Perioperative Implications

Preoperative Preparation

- A thorough discussion with pt and family regarding the anesthetic and operative risk should occur prior to any surgical procedure.
- Anxiolysis with benzodiazepines can be helpful in a lower-than-normal dose (reducing the dose is especially important in those with obstructive sleep apnea).
- Antisialagogues may useful to reduce secretions, and many pts will require fiberoptic bronchoscopy to secure the airway.

Intraoperative Considerations

- A careful induction (either inhalational or IV) with preservation of spontaneous ventilation is often safest, as severe obstruction can develop with any sedation.
- A nasopharyngeal airway, an LMA, or lateral positioning may be helpful to maintain airway patency.
- Fiberoptic bronchoscopy or videolaryngoscopy is often the safest way to place an endotracheal tube (especially in those with unstable cervical spines).
- MPS pts often require a smaller-sized endotracheal tube than would be expected for age.
- Even a surgical tracheostomy can be very challenging owing to the tendency of MPS pts to have short necks and thickened soft tissues.
- Neurophysiologic monitoring should be considered for those at risk for spinal cord compression.

Postoperative Period

- Extubation should take place with the pt fully awake, adequately oxygenating and ventilating, and moving purposefully in a setting where all the personnel and equipment necessary to reintubate are readily available.

Anticipated Problems/Concerns

- Most serious anesthetic complications result from severe airway obstruction.
- Involvement of the cardiac and pulm systems can also increase anesthetic challenges and risks.

Multiple Endocrine Neoplasia Type 1 and 2

Mary A. Blanchette

Risk

- Neoplastic syndromes inherited in an autosomal dominant pattern; variable penetrance and rare incidence. Syndromes involve more than one endocrine gland.
- MEN tumors and their effects may be underdiagnosed and unrecognized when pt presents for nonrelated surgery (MEN 2a and 2b associated with pheochromocytoma).
- Medullary carcinoma of thyroid (MEN 2a and 2b) is inherited, with almost 100% penetrance; prophylactic thyroidectomy is recommended. Genetic screening tests are available.

Perioperative Risks

- See specific syndrome topics; risk related to functional components of tumors.

Overview

- MEN 1 "Werner syndrome" includes parathyroid hyperplasia (95%), anterior pituitary tumors (30%), pancreas (insulinoma, glucagonoma) (50%), and gastrinoma ("Zollinger-Ellison") (20–60%).
- MEN 2 has three distinct clinical subtypes: 2a, 2b, and FMTC.
- MEN 2a: "Sipple syndrome" includes medullary carcinoma of the thyroid (97%), parathyroid hyperplasia (20%), pheochromocytoma (50%).
- MEN 2b: Extremely rare subtype (5% of all MEN 2 syndrome) includes medullary carcinoma of thyroid, pheochromocytoma, neuromas of oral mucosa, intestinal ganglioneuromas, marfanoid body habitus, rare parathyroid hyperplasia.

Etiology

- MEN 1/2: Autosomal dominant, variable penetrance. MEN 1 caused by mutation in MEN-1 gene (tumor suppressor/regulatory); men and women equally affected. MEN 2 caused by oncogenic mutation in c-Ret gene (regulatory). Incidence of MEN 2a >FMTC >MEN 2b.

Usual Treatment

- MEN 1: Parathyroid hyperplasia; treat hypercalcemia medically; surgical resection of hyperplastic tissue with parathyroid reimplantation. Pituitary adenoma; prolactinoma (58%) treated medically with dopamine agonist, growth hormone adenoma/acromegaly (23%), and nonsecreting adenoma (10%); treated surgically with transsphenoidal resection. Pancreatic tumors treated surgically with glucose management (insulinomas); gastrinoma treated medically, then surgery.
- MEN 2a: Parathyroid hyperplasia; treat as in MEN 1. Medullary carcinoma treated with total thyroidectomy and neck dissection. Pheochromocytoma pts must be medically optimized with alpha-adrenergic blockade first, then beta-blockade, before surgical resection of tumor is attempted, otherwise high morbidity and mortality. Pts with Hx of pheochromocytoma and parathyroid hyperplasia should have prophylactic total thyroidectomy.
- MEN 2b: Treatment for medullary carcinoma is total thyroidectomy; pheochromocytoma. Same treatment as in MEN 2a.

Assessment Points

Type	Effect	Assessment by Hx	PE	Test
MEN 1	Parathyroid hyperplasia (assoc nephrolithiasis) Pancreatic tumors (insulinoma, glucagonoma), gastrinoma Ant pituitary tumor (prolactinoma, GH tumor, ACTH/Cushing)	Family Hx of endocrine tumors Fatigue, muscle weakness, flank pain, renal stones, Hx pathologic fractures Diaphoresis, palpitation, abdominal pain Diarrhea, reflux, dyspepsia Headache, visual changes	Htn Neck nodule Altered mental status Flank tenderness Tremor, mental status changes (hypoglycemia) Visual field defect Acromegaly (GH) Cushingoid habitus	NIBP and ECG Serum calcium Sestamibi scan, PTH level, neck CT, bone density, BUN/creatinine, pelvic x-ray Serum glucose, lytes, CT/MRI Endoscopic US Head CT/MRI metabolic panel, specific hormone level
MEN 2a AND 2b	Pheochromocytoma	Family Hx, episodic sweating, palpitations, anxiety, tremor	Htn (paroxysmal), arrhythmia	CT/MRI, NIBP ECG/consider ECHO, 24-h urine for catecholamines, metanephrines
	Medullary cancer of thyroid Parathyroid adenoma (see MEN I)	Can be asymptomatic Family Hx Hx urinary stones Symptoms of hypercalcemia	Thyroid mass Neck nodule	Calcitonin levels Serum calcium, serum PTH level, BUN/Cr Pelvic x-rays

Key References: Chen H, Sippel R, O'Dorisio MS, et al.: The North American Neuroendocrine Tumor Society consensus guidelines for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer, *Pancreas* 39(6):775–783, 2010; Grant F: Anesthetic considerations in the multiple endocrine neoplasia syndromes, *Curr Opin Anaesthesiol* 18(3):345–354, 2005.

Perioperative Implications (Men 1)

Monitoring

- Parathyroid surgery: ECG signs of hypercalcemia (arrhythmias, prolonged PR, short QT), consider using EMG ETT for monitoring recurrent laryngeal nerve intraop. Unpredictable response to muscle relaxants with hypercalcemia, monitor the TOF. PTH levels; significant decrease expected post successful resection; monitor calcium level postop.
- Pituitary adenomas: Tight BP control; acromegalics may have impaired ulnar circulation to hand which increases risk morbidity from radial a-line; monitor urine output (risk for DI, SIADH)
- Insulinoma surgery: Requires tight, careful blood glucose control; increased risk hypoglycemia periop; arterial line
- Gastrinomas: Arterial line; pts at risk for labile BP

Airway

- Acromegaly: Increased risk of difficult mask airway and intubation; also increased incidence of sleep apnea; have difficult airway equipment ready
- Parathyroidectomy: Risk of surgical damage to recurrent laryngeal nerve, and vocal cord paresis periop (risk of hoarseness to stridor to complete airway obstruction if bilateral)

Maintenance

- Parathyroidectomy: Draw post-resection PTH levels to confirm removal of tumor
- Insulinomas and gastrinomas: Monitor volume status, glucose, and BP control
- Pituitary adenomas: Usually transsphenoidal approach; tight BP control; watch UO

Perioperative Implications (Men 2)

Monitoring

- Pheochromocytoma: Standard ASA monitors, arterial line, CVP, UO.
- Total thyroidectomy: Standard ASA monitors. Consider use of EMG ETT to monitor recurrent laryngeal nerve intraop. Postop PTH levels to check for adequate parathyroid function.
- Parathyroidectomy: See MEN 1 section.

Airway

- Thyroidectomy and parathyroidectomy: Review ENT preop evaluation, including ENT's fiber optic exam of larynx, CT/MRI scans, sestamibi localization scans for potential mass effects of tumor on airway; also note baseline vocal cord function. Communicate with surgeon for plan

Maintenance

- Pheochromocytoma: Tight BP control before and during resection (anesthetics, nipride, phentolamine, esmolol, calcium channel blockers, epidural infusions); after adrenal ligation, BP support with fluid boluses, prn pressors (NE, phenylephrine). Monitor glucose.
- Thyroidectomy: If using EMG ETT, avoid muscle relaxants.
- Parathyroidectomy: See MEN 1.

Adjuvants

- Pheochromocytomas: Require adequate preop treatment to control BP, HR, and restore blood volume (10–14 d alpha-adrenergic blockers [e.g., phenoxybenzamine, prazosin], hydration, then initiate beta-blockade)
- Hyperparathyroidism with symptomatic hypercalcemia: Preop hydration; diuresis with furosemide; consider biphosphonates, calcitonin, or glucocorticoids

Anticipated Problems/Concerns

- MEN 1: Parathyroidectomy: Postop hypocalcemia, recurrent laryngeal nerve damage/VC paresis, neck hematoma/airway compromise. Transsphenoidal pituitary adenoma resection: Hypopituitarism, SAIDH/DI. Acromegaly: Potential difficult airway. Pancreas tumors: Hyperglycemia/hypoglycemia. Gastrinoma/VIPoma: Labile BP
- MEN 2: Pheochromocytoma; malignant Htn and labile BP, increased risk of CVA, and MI

Multiple Myeloma

Ryan J. Kline | Gregory Bordelon | Alan David Kaye | Amit Prabhakar

Risk

- Represents 1.6% of all new cancer cases in USA; estimated 26,850 new cases in 2015.
- Estimated 11,240 deaths, or 1.9% of all cancer deaths in USA in 2015.
- Incidence: 7.5:100,000 white males; 4.5:100,000 white females; 15.1:100,000 black males; 11.2:100,000 black females; 7.9:100,000 all races male; 5.1:100,000 all races female (based on 2008 to 2012 data).
- Race: 1.1% of all malignancies in white population; 2.1% of all malignancies in black population.
- Male to female ratio: 3:2.
- Age: Median age 68 y in men, 70 y in females; most frequently diagnosed between 65 and 74 y (28.2%).
- Increased risk among those with MGUS.
- Fourteenth leading cause of cancer death.
- Survival: Median survival 3 y; 100% fatality rate; median age of death 75 y; 46.6% 5-y survival.

Perioperative Risks

- Pts typically anemic.
- Pathologic fractures occur with this disease; careful positioning and padding essential.
- Coagulopathy common with thrombocytopenia, thrombocytopathy, and decreased functional plasmatic coagulation factors.
- Renal failure is the most common cause of mortality; concern for anesthetics with renal elimination.
- Hypercalcemia common and can cause morbidity and mortality.
- Infection risk real, especially if pt has recently had a stem cell transplant.

Overview

- Part of a spectrum ranging from MGUS to plasma cell leukemia (malignancy of antibody forming cells).
- Also known as plasmacytosis, myelomatosis, or Kahler disease; classified within non-Hodgkin lymphomas.
- Proliferation of plasma cells results in functioning peripheral blood cells and leads clinically to
  - Impaired production of blood cells >pancytopenia (leucopenia anemia thrombocytopenia).
  - Formation of plasmacytoma (mass), leading to lytic lesions in bone.
  - Impaired immunity (humoral) >infections.
  - Increased plasma cells (antibody-forming cells) >amyloidosis (soft tissue, lungs, kidneys) and hyperviscosity.
- Presenting signs: High sedimentation rates, anemia, signs of coagulopathy.
- Renal failure from toxic immunoglobulin deposition in renal tubuli most common cause of mortality; 10% of pts develop amyloidosis.

Etiology

- Genetic instability: Translocation at 14q32 and/or deletion of chromosome 13, leading to either neoplastic plasmacytes producing either a monoclonal immunoglobulin (IgG, IgA, IgD) or isolated light chains (Bence Jones plasmacytoma)
- Environmental and occupational causes
- Radiation (increased incidence in survivors of the atomic bombing of Nagasaki)

Usual Treatment

- Alkylating chemotherapeutic agent
- Immunomodulatory drugs: thalidomide, lenalidomide, or pomalidomide
- Stem cell transplantation
  - Autologous
  - Allogenic
- Glucocorticoids
- Interferon alpha-2b
- Protease inhibitors
  - Bortezomib: inhibitor of 26S proteasome >inhibition of proteasome in myeloma
  - Carfilzomib: inhibitor of 20S proteasome >increase in polyubiquitinated proteins

Treatment of Complications

- Bone disease-related pain: Opioid preparations, immediate- and extended-release formulations, lidoderm patches, diclofenac topical products; radiation (refractory pain and cord compression), surgical intervention
- Anemia: Iron, B_{12}, folate, erythropoietin, transfusion
- Infection: Vaccination against *Streptococcus pneumoniae*, *Haemophilus influenzae*, H1N1, seasonal flu; antibiotics; IV immune globulin
- Hypercalcemia: IV fluid and corticoid steroid, bisphosphonates (if unresponsive to hydration), calcitonin, furosemide
- Renal failure: Treatment of dehydration, hypercalcemia, and hyperuricemia; chemotherapy (e.g., vincristine, doxorubicin); alkaline diuresis; trial of plasma exchange in acute evolving renal failure; hyperviscosity syndrome; exchange of plasma (plasmapheresis)

Assessment Points

System	Clinical Manifestations	Signs and Symptoms	Anesthetic Implication
MS	Bone pain Pathologic fracture	Usually lumbar 95% more than one side	Positioning to prevent fracture
HEME	Bleeding and bruising Coagulopathy Normochromic normocytic anemia Capillary fragility	Secondary to thrombocytopenia Absorption of clotting factor Weakness Purpura Dark circles (raccoon-like) around eye, secondary to prolonged Valsalva	Availability of FFP and plts Increased transfusion requirements, ventilator management
METAB	Hypercalcemia Infection Hyperviscosity	Confusion, somnolence, constipation, nausea, thirst, bone pain Secondary to humoral immunity of normality Epistaxis Visual disturbance Carpal tunnel Headache Somnolence, bruisability	Increased fluid requirements, maintenance of adequate urine output Antibiotic coverage Preoperative: plasmapheresis, increased fluid requirement intraop Temperature maintenance to prevent microvascular sludging
CNS/PNS	Spinal cord compression Meningitis Carpal tunnel Peripheral neuropathies Stroke (hyperviscosity)	Signs of weakness and numbness of extremities	Positioning of pt Diligent use of muscle relaxants Avoidance of depolarizing muscle relaxants
RENAL	Renal insufficient/failure	Secondary to direct tubular injury Amyloidosis Involvement by plasmacytoma	Adequate hydration
RESP	Pneumonia Respiratory insufficiency	Secondary to rib fracture	Extubation problems Pneumothorax intraop
HEENT	Amyloidosis	Macroglossia Skin lesions of lips	Airway problems

Key References: Kyle RA, Rajkumar SV: Multiple myeloma, *N Engl J Med* 351(18):1860–1873, 2004; Palumbo A, Gay F: How to treat elderly patients with multiple myeloma: combination of therapy or sequencing, *Hematology Am Soc Hematol Educ Program* 566–577, 2009, http://dx.doi.org/10.1182/asheducation-2009.1.566.

Perioperative Implications

Preoperative Preparation

- Recombinant erythropoietin increases Hgb and decreases transfusion requirement
- Antibiotics and gammaglobulin prophylaxis

Airway

- May be difficult due to macroglossia

Maintenance

- Regional anesthesia is contraindicated due to bony lesions, coagulopathy, and neurologic deficit.
- Unpredictable pharmacokinetic of protein-bound drugs.

Postoperative Period

- Continue adequate hydration.
- Aggressive pulmonary toilet.
- Treat specific complication (refer to Treatment of Complications section).

Anticipated Problems/Concerns

- Careful positioning to prevent fractures

Multiple Organ Dysfunction Syndrome

Zerlina Wong | Jesse M. Raiten

Risk

- Most common cause of death for pts in ICU
- Incidence 11-40% of adult ICU pts
- Risk factors: (1) Severe illness at time of ICU admission; (2) severe sepsis or infection at time of ICU admission; (3) old age
- Associated with trauma, sepsis, shock, male sex, African American race, chronic health conditions, malnutrition, use of immunosuppressants

Perioperative Risks

- Labile hemodynamics
- Difficulty with oxygenation and ventilation
- Malnutrition
- Altered drug metabolism

Worry About

- Volume status
- Drug metabolism
- Antibiotic selection
- Difficulty cross-matching blood products
- Transfusion reactions

Overview

- MODS is a dynamic process; clinical course and causes are highly variable.

- Defined by the presence of altered organ function in an acutely ill pt such that homeostasis cannot be maintained without intervention.
- A potentially reversible physiologic derangement involving two or more organ systems not involved in the original disorder as cause for ICU admission.

Etiology

- Septic shock is the main cause of MODS in the ICU.
- Represents a failure of homeostasis resulting from dysfunction of the neuroendocrine and immune systems.
- A combination of tissue hypoxia, exaggerated inflammatory response, and end-organ damage from ischemia and necrosis, resulting in macrovascular and microvascular changes.

Usual Treatment

- Requires a multimodal approach using a combination of source control, supportive care, and prevention of further complications.
- Fluid and blood products: Consider guidelines for sepsis and septic shock.
  - CVP 8–12 mmHg.
  - MAP 60–65 mmHg.
  - Hemoglobin 7.0–9.0 g/dL.
- Vasopressors and inotropic support: Consider guidelines for sepsis and septic shock.
  - Norepinephrine first line.
  - Epinephrine and vasopressin may be added if necessary.
- Respiratory management: Consider guidelines for pts with ARDS.
  - Tidal volumes 6 mL/kg of ideal body weight.
  - Plateau pressure goals less than 30 cm H_2O.
  - PEEP for alveolar recruitment.
- Endocrine and metabolic support:
  - Stress steroids in refractory septic shock.
  - Tight serum glucose control less than 180 mg/dL.
- Renal replacement and acid-base support: Dialysis to correct electrolyte abnormalities, acidosis, uremia, and volume overload in pts with kidney failure.
- Antimicrobial support: Initial broad spectrum antibiotics with narrowing as culture results are available.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Delirium Altered mental status Cognitive loss	Lethargy, agitation Confusion, coma	Glasgow coma score Mental status exam	CT scan Full set of labs, nutrition markers, ABG
RESP	Abnormal gas exchange Pulm edema ALI, ARDS	Dyspnea, tachypnea Increasing O_2 requirement Intubation	Cyanosis, diaphoresis Rhonchi, rales, wheezing	CXR, CT scan ABG, bronchoscopy ± bronchoalveolar lavage
CV	Myocardial depression Reduced vascular tone Left ventricular failure, right ventricular failure Pulm Htn	Dyspnea Hypotension	Tachycardia, hypotension Arrhythmias—VTach, VFIB Edema, increased JVP	ECG, TTE, TEE PA cath: SvO_2, CVP, PAOP Cardiac output
GI	Bleeding, stress ulcers Hepatic failure, coagulopathy Hyperbilirubinemia Cholestasis, steatosis	Bloating, diarrhea Constipation Malnutrition Acute pancreatitis	Abdominal pain Jaundice Melena, hematochezia	Albumin (low), amylase LFT PT, PTT, INR
HEME	Pancytopenia Coagulopathy DIC	Thrombocytopenia Bruising	Jaundice, pallor Petechiae	CBC + differential Leukopenia BM biopsy
RENAL/ METAB	Renal failure Lyte abnormalities Glucose intolerance	Oliguria, ATN Renal failure requiring CRRT or IHD	Edema Oliguria Anuria	Lytes Ca^{2+}, Mg^{2+}, phosphate, albumin, transferrin

Key References: Ramírez M: Multiple organ dysfunction syndrome, *Curr Probl Pediatr Adolesc Health Care* 43(10):273–277, 2013; de Montmollin E, Annane D: Year in review 2010: critical care—multiple organ dysfunction and sepsis, *Crit Care* 15(6):236, 2011.

Perioperative Implications

Preoperative Preparation

- Ensure blood product availability.
- Evaluate ventilator dependency; consider traveling with the ICU ventilator.
- Thorough review of preop data (labs, cardiac evaluation, end-organ function).

Monitoring

- All standard intraop monitors (NIBP, temp, CO_2 monitoring, ECG).
- High likelihood of invasive monitors (arterial line, CVP).
- Consider intraop TEE to better assess cardiac function and volume status.
- Foley cath to monitor urine output.

Airway

- High likelihood pt is already on mechanical ventilation.
- Avoid alveolar derecruitment.
- Consider need for ICU ventilator if difficulty oxygenating/ventilating.

Preinduction/Induction

- Inhalational induction via in situ ETT if present.
- Avoid induction agents causing significant myocardial depression (propofol).
- Be prepared to provide increased hemodynamic support after addition of anesthetic agents.

Maintenance

- Frequent assessment of ventilation, oxygenation, hemoglobin, and acid-base equilibrium.
- Maintain ICU ventilator settings/strategy as appropriate.
- Judicious fluid management (avoid volume overload, pulmonary edema, heart failure).
- Maintain normothermia.

Extubation

- Likely remain on mechanical ventilation after surgery

Postoperative Period

- Close monitoring of oxygenation, ventilation, hemodynamic and volume status.
- Consider diuresis if excess volume administered intraop.
- Anticipate prolonged effects of sedatives and analgesics as a result of end organ failure.
- Wean vasopressors as tolerated; continue supportive care until organs are able to recover.

Anticipated Problems/Concerns

- Recovery from MODS can take weeks to months.
- Organs may not return to their original baseline function.
- Mortality is high; with many unanswered questions about the mechanisms causing MODS and the most effective therapeutic approach; these topics are areas of active research.

Multiple Sclerosis

Sabry Khalil | Armin Schubert

Risk

- Affects more than a half million people in USA, with almost 10,000 new cases every year.

Perioperative Risks

- Worsening of symptoms due to stress or infection
- Aspiration related to bulbar involvement
- Postop mechanical ventilation

Worry About

- Hyperkalemia related to succinylcholine.
- Fever that could exacerbate the disease.
- Pt may come to surgery medically unoptimized.

Overview

- A chronic progressive inflammatory T-cell–mediated demyelinating disease that affects the CNS, with periods of remission and exacerbation.
- Commonly affects more women than men (ratio of >2:1) and peaks between ages 20–40; however, it can also affect children (<0.5%) and the elderly.

Etiology

- Pathogenesis is not fully clear; immunologic, viral (EBV, HHV-6), and environmental factors are involved. The disease is more common in areas away from the equator. Sun exposure and vitamin D may play a role. MS is more common in white than black Americans. HLA associations are present (e.g., A3, B7).

Usual Treatment

- Disease-modifying agents: Interferon beta, glatiramer acetate, natalizumab, fingolimod hydrochloride, dimethylfumarate, and teriflunomide. Flu-like symptoms, elevated liver enzymes, neutropenia, and cardiac arrhythmias (fingolimod) are common side effects.
- Immunosuppressive agents: Mitoxantrone can be cardiotoxic. Other agents include cyclophosphamide, corticosteroids, and IV immunoglobulins.
- Symptomatic treatment: For spasticity, depression, neuropathic pain. This includes baclofen, SSRIs, and gabapentin. Continue all these medications.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Lhermitte sign	Visual disturbances due to optic neuritis	Neck flexion induces electrical sensation	
CNS	Neurologic sequelae	Neurologic symptoms	Uhthoff sign (worsening symptoms by increased body temperature, e.g., with exercise)	MRI CSF analysis
PSYCH	Depression			

Key References: Makris A, Peperopoulos A, Karmaniolou I: Multiple sclerosis: basic knowledge and new insights in perioperative management, *J Anesth* 28(2):267–278, 2014; Dorotta IR, Schubert A: Multiple sclerosis and anesthetic implications, *Curr Opin Anaesthesiol* 15(3):365–370, 2002.

Perioperative Implications

Preoperative Preparation

- Ask pt if symptoms are stable and when he or she last visited the neurologist. Pay special attention to any bulbar symptoms and respiratory system. Inform pt of possible postop mechanical ventilation if significant respiratory compromise is evident.
- Carefully review list of medications and their possible side effects and drug interactions.
- Avoid stressors that exacerbate the disease. This includes pain, anxiety, infection, and hyperthermia.
- Premedicate with midazolam, as it decreases stress. It is believed also to decrease core body temperature through inhibition of tonic thermoregulatory vasoconstriction.
- For unknown reasons, MS is stable during pregnancy but worsens postpartum.
- Consider aspiration prophylaxis.

Monitoring

- Depends on other comorbidities and the risk of surgery. Pay special attention to temperature.

Airway

- Consider RSI to avoid aspiration or awake fiberoptic intubation for difficult airway.

Preinduction/Induction

- Titrate medications slowly on induction, as there could be an element of autonomic dysfunction.
- If RSI is needed, it is advisable to avoid succinylcholine for possible myopathy-induced hyperkalemia. For ECT, sugammadex can reverse rocuronium very rapidly.
- Spinal anesthesia may exacerbate the disease; better to avoid it. Epidural is safe; however, it is prudent to avoid higher concentrations of local anesthetics. Avoid epinephrine-containing local anesthetics for peripheral nerve blocks to avoid potential vasoconstriction-induced neuropathy.
- IV lidocaine can worsen MS, especially eye symptoms.
- Use multimodal analgesia, especially for pts with pain issues. There is increased risk of OSA and less commonly central apnea ("Ondine's curse").
- Consider stress dose of steroids if pt chronically uses high doses.

Maintenance

- Stress on normothermia.
- Inhalational anesthetics and NO are safe to use.
- Careful padding of extremities to avoid exacerbation of peripheral neuropathies.
- Response to muscle relaxant is variable. Titrate to TOF.

Extubation

- Fully awake extubation is preferred, with careful attention to clearing secretions.

Adjuvants

- Duration of most NMBs is shortened by phenytoin and carbamazepine.

Postoperative Period

- Adequate pain control; avoid emotional stressors; avoid overheating the pt; consider incentive spirometry for pts with respiratory dysfunction.

Anticipated Problems/Concerns

- Postop mechanical ventilation
- Aspiration

Multisystem Organ Failure, Lung Dysfunction in

Muhammad Azam

Risk

- 200,000 new cases of ARDS occur annually in USA.
- 0.2% of general surgical pts develop ARDS postop.

Perioperative Risks

- Hypoxemia, hypercarbia, hemodynamic instability.
- ARDS hypoxemia requires ventilator management using high PEEP to achieve adequate oxygenation.
- High PEEP may impede right atrial/right ventricular preload.
- Lower RV preload can reduce stroke volume and cardiac output. This can lead to alveolar hypoperfusion, thus inhibiting carbon dioxide elimination and further worsening hypercarbia and respiratory acidosis.
- Mechanical ventilation modes, such as inverse ratio and pressure control, target oxygenation rather than carbon dioxide elimination, resulting in permissive hypercarbia.
- Mechanical ventilation may cause breath stacking, which can also cause hemodynamic instability.
- Acidosis and dysrhythmias worsen hemodynamic instability.

Worry About

- Mortality: 40% among ARDS alone; >90% for MODS, involving three or more organ failures.
- Poor prognostic factors: Advanced age, impaired immunity, poor prior functional status, resistant organisms, MODS despite adequate therapy.
- Severity of ARDS by Berlin criteria as graded by oxygenation ratio (PaO_2/FiO_2): Mild ≤300 mm Hg; moderate ≤200 mm Hg; severe ≤100 mm Hg.

Overview

- Lung dysfunction in MODS is either ARDS or ALI.
- ARDS is more severe than ALI.
- MODS exists when altered organ function in the acutely ill requires medical intervention for homeostasis.

Etiology

- Pulm conditions (pneumonia, lung contusion)
- Nonpulmonary (sepsis, trauma, transfusions, pancreatitis, DIC)

Usual Treatment

- Mechanical ventilation ARDS.net protocol:
  - Mode: Assist control.
  - Tidal volume 6 mL/kg of predicted body weight (length for predicted body weight).
  - Plateau pressure ≤30 cm H_2O.
  - Higher PEEP levels in sepsis-induced moderate/severe ARDS.
  - Link FiO_2 and PEEP levels.
  - Daily awakening and spontaneous breathing trials.
  - Use of bundles to include head-of-bed elevation, oral hygiene.
- Management of severe sepsis and shock:
  - Early recognition and treatment.
  - Microbiology cultures, timely appropriate antibiotics, source control.
  - Fluid boluses with crystalloids.
  - Measure lactate; follow lactate clearance.
- Titrate vasopressor (norepinephrine) to MAP ≥65 mm Hg.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Hypoxemia Hypercarbia	Acute respiratory distress	Tachypnea Crackles	ABGs, CXR, lactate, bronchoalveolar lavage, $ScvO_2$
CV	Shock state Dysrhythmias	Hypotension	Tachycardia, S_3 gallop Irregular rhythm	ECG, troponin, brain natriuretic peptide, ECHO
RENAL	Acute injury or failure	Oliguria/anuria	Edema	Basic metabolic panel, fractional excretion of sodium, UA, renal US
HEPAT	Shock liver	Jaundice	Ascites Bruising	INR, bilirubin, LFTs, NH_3, liver US
GI	Ileus	Nausea Vomiting Constipation	Distension Decreased bowel sounds	KUB Abdominal CT Bladder pressures
CNS	Altered mental status	Acute onset	Low score on GCS	CT brain, MRI, LP, ICP monitor, EEG
HEME	Anemia Thrombocytopenia	Bleeding Bruising	Pallor Purpura	CBC, fibrinogen/FDP
ENDO	Hyperglycemia Hypoadrenalism	Increased blood glucose Decreased blood pressure	Polyuria Shock state	Blood glucose Adrenal functional tests

Key References: Blum JM, Stentz MJ, Dechert R, et al.: Preoperative and intraoperative predictors of postoperative acute respiratory distress syndrome in a general surgical population, *Anesthesiology* 118(1):19–29, 2013; Dellinger RP, Levy MM, Rhodes A, et al.: Surviving sepsis campaign: international guidelines for management of severe sepsis and shock: 2012, *Crit Care Med* 41(2):580–637, 2013.

Perioperative Implications

Preoperative Preparation

- Associated risk factors:
  - ASA class 3–5
  - Emergency surgery, multiple anesthetics, renal failure, COPD
  - High Paw and FiO_2
  - High volume of crystalloids

Airway

- Secure and stabilize endotracheal tube/tracheotomy.
- Consider ICU/transport ventilator for mechanically ventilated pt with high PEEP or FiO_2 (10 cm H_2O, 50%) or inhaled agents with nitric oxide.
- Avoid prolonged circuit disconnection, especially with higher levels PEEP, due to risk of rapid and potentially irreversible hypoxemia caused by alveolar derecruitment.
- Severe ARDS hypoxemia may require prone mechanical ventilation.
- Continue inhaled agents and nitric oxide/prostacyclin.

Monitoring

- Invasive lines including arterial lines, central line, PA catheter, hemodialysis lines, PICC lines.
- Verify dose and indications for all infusions.
- Maintain drains and mechanical devices (chest tubes, temporary pacer wires, external pads, extracorporeal membrane oxygenator, intra-aortic balloon pump, ventricular assist devices).

Preinduction/Induction

- Intraop medication challenges:
  - Induction agents may cause hypotension (propofol), tachycardia (ketamine), worsen survival in sepsis (controversially, etomidate).
  - Paralytic agent risks include hyperkalemia (succinylcholine) and prolonged neuromuscular blockade activity. If organ-dependent elimination (consider organ independently eliminated cisatracurium or sugammadex for reversing rocuronium).
  - Antimicrobial choice based on best evidence, local microbiome, specific findings, allergies, and pt status.

Maintenance

- Opiates titrated for analgesia.
- Benzodiazepines may prolong emergence and have been associated with delirium.
- Inhalational anesthetics titrated as indicated.
- Vitals, clinical picture, and labs guide fluids, products, and vasopressors.

Extubation

- Delayed emergence or instability precludes immediate extubation.
- Plan and coordinate with surgical, anesthesia, and ICU team to continue all supportive measures.
- Anticipate repeat surgeries in burns, exploratory laparotomies, vascular injuries, skeletal and spinal trauma, compartment syndromes.
- Avoid hypothermia which delays emergence and in trauma is associated with worse outcome.
- Provide safe transport and comprehensive report.

Adjuvants

- Dexmedetomidine GTT has sedative and analgesic properties and is less likely to cause delirium.

Anticipated Problems/Concerns

- Anticipate worsening of ARDS immediately postop.
- Tracheotomy if low GCS and frequent ongoing surgical procedures.
- Ventilator-associated pneumonia risk increases with duration of mechanical ventilation and in pts emergently intubated.
- Critical illness polyneuropathy, steroids, and neuromuscular blockade unpredictably prolong significant skeletal muscle weakness.
- Extended illness and immobility predispose to DVT, cath-associated urinary tract infections, central line–associated bloodstream infections, intestinal bleeding, malnutrition, delirium, decubitus ulcers, and so forth.

Myasthenia Gravis

Lee A. Fleisher | Cecil O. Borel

Risk

- Prevalence of myasthenia gravis in USA is estimated at 14 to 20 per 100,000 population; there are approximately 36,000–60,000 cases in USA.
- Affects all races.
- Male:female ratio: 2:1.

Perioperative Risks

- Postop NM ventilatory failure
- Postop pneumonia due to poor cough and secretion clearance

Worry About

- Preop optimization of muscle strength
- Anticholinesterase medications, steroids, plasmapheresis
- Inspiratory muscle weakness due to residual paralysis from nondepolarizing NM blocking agents.
- Exacerbation of underlying bulbar (airway) musculature weakness.
- Increased sensitivity to hypoventilation with narcotic analgesics.

Overview

- Characterized by weakness and fatigability of skeletal muscles.
- Muscle strength improves similarly in both myasthenia gravis and nondepolarizing blockade after administration of anticholinesterase drugs.

Etiology

- Autoimmune disease of the NM junction mediated by reduction in number of acetylcholine receptors at the NM junction.

Usual Treatment

- Anticholinesterase medications (pyridostigmine, Mestinon)
- Immunosuppression: Steroids, azathioprine
- Plasmapheresis
- IVIG
- Thymectomy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NM	Peripheral muscle weakness	Easy fatigability	Arm adduction times <1 min	Repetitive nerve stimulation
RESP				
(Airway)	Bulbar weakness	Difficulty swallowing	Head lift <5 s	Formal swallowing evaluation
(Ventilation)	Inspiratory muscle weakness	Orthopnea, breathlessness	Paradoxical insp motion	NIF <30 cm H_2O FVC <1000 mL
(Ventilatory drive secretion clearance)	CO_2 retention Weak cough	Morning headache Recurrent pneumonia	Reduced ventilation of bases	ABG CXR

Key References: Borel CO, Hanley DF: Muscular paralysis—myasthenia gravis and polyneuritis. In Parrillo JE, Bone RC (eds): *Critical care medicine: principles of diagnosis and management.* Philadelphia, 1994, Mosby Year Book, pp 1193–1215; Sungur Z, Sentürk M: Anaesthesia for thymectomy in adult and juvenile myasthenic patients, *Curr Opin Anaesthesiol* 29(1):14–19, 2016.

Perioperative Implications

Preoperative Preparation

- Anticholinesterase medications:
  - Hold 2–4 h preop
  - Postop: IV neostigmine may be used to replace pyridostigmine, PO 1 mg IV/60 mg PO or start IV neostigmine 1 h before emergence at 1/30–1/60 the daily pyridostigmine dose infused over 24 h.
- Steroid maintenance.

Monitoring

- Routine.
- TOF twitch monitor if short-active nondepolarizers are used.
- NM recovery at the adductor pollicis muscle may not reflect the recovery of all muscles.

Induction/Intubation

- Consider inhalational anesthetic breathe-down techniques
- Consider intubation without muscle relaxation using propofol/remifentanil maintenance.
- Minimize or avoid the use of muscle relaxants.
- Total IV analgesia or inhalational anesthesia.

Extubation

- Consider sugammadex if muscle relaxants are given.
- Check NIF (>30 cm H_2O), head lift, cough, gag reflex; ensure full return of twitch.

Adjuvants

- Avoid or minimize use of nondepolarizing muscle relaxants.
- Depolarizing relaxants may have increased or decreased efficacy.
- Consider epidural analgesic, particularly for thymectomy.

Anticipated Problems/Concerns

- Postop ventilatory failure, pneumonia, aspiration
- Cholinergic crisis if excess anticholinesterase medications are given

Mycoplasma pneumoniae Infection

Carlos A. Puyo

Risk

- Endemic/pandemic worldwide every 3–5 y.
  - Outbreaks likely during summer and early fall.
  - Affects persons of all ages.
  - Long incubation periods of 1–3 wk.
  - Transmitted person to person via aerosols.
  - Frequent in closed and semiclosed communities.
- Common cause of upper and lower respiratory infections.
  - Up to 40% of community-acquired pneumonias, "walking pneumonia."
  - Up to 5% of bronchiolitis in children.
  - 3–10% of adults may develop bronchopneumonia.
  - Clinical manifestations similar to *Chlamydophila pneumonia, Streptococcus pneumonia,* and respiratory viruses.
  - Fulminant pneumonia may occur in children with sickle cell disease (functional asplenism), Down syndrome, and immunosuppressive conditions.
- Extrapulmonary complications in 25% of pts infected with *Mycoplasma pneumoniae.*

Perioperative Risks

- No periop risk data; hemolytic anemia, DIC, and cross-reacting cold agglutinins are of concern, especially if CPB is required.
- Hyper-reactive airway disease.

Worry About

- Multisystem organ dysfunction

Overview

- Clinical manifestations of respiratory involvement are mediated by activity of cytoadherence on the airway epithelium and include
  - Sore throat, hoarseness, fever, cough (pertussis-like).
  - May play a role in asthma, COPD.
  - Conjunctivitis, headache, chills, coryza, myalgias, earache, and generalized malaise are common.
- Extrapulmonary manifestations are the result of direct invasion or immune reactivity.
- Dx:
  - Hx and clinical manifestations: Unspecific upper respiratory symptoms.
  - CXR: Diffuse reticular infiltrates in perihilar and lower lobe regions; bilateral in 20% of cases.
  - Pathology: Ulceration, edema, ciliary loss, bronchioalveolar inflammatory cell infiltration.
  - Culture: Incubation period of several wk; sensitivity around 60%; not practical for routine diagnosis.
  - Serology: Current or recent infection likely if antibody titer increase ≥fourfold.
  - Cold agglutinins: IgM within 1–2 wk after initial infection; titers ≥1:32 correlate with severity of lung involvement.
  - PCR: RNA-amplification techniques are highly sensitive and indicate viable bacterium.

Etiology

- *M. pneumoniae*: Slow-growing bacterium; requires human host for survival

Usual Treatment

- Antibiotic treatment will shorten respiratory symptoms.
- Macrolides, tetracyclines, and fluoroquinolones. Macrolide resistance has been reported.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Otitis Retinitis Conjunctivitis	Ear symptoms may affect 30%	Mucosal congestion	
RESP	Tracheobronchitis Pneumonia Asthma	Failure to respond to treatment with sulfonamide or penicillin	Persistent cough Expiratory wheezes	CXR Sputum
CV	Pericarditis Pericardial effusion Cardiac tamponade	Incidence 1–8.5%	Distant heart sounds S_3, JVD	ECG, ECHO
	Myocarditis	Approximately 50% will develop cardiac symptoms within 16 mo of *M. pneumonia* infection	Pericardial rub	Tap effusion
CNS	Aseptic meningitis Meningoencephalitis Transverse myelitis Guillian-Barré Peripheral neuropathy Cerebellar syndrome	Incidence 7% Children more likely to die or have severe neurologic deficits	Focal or general neuro symptoms, diplopia, coma	CSF Elevated cytokines IL-6, IL-8 MRI Serology
HEME	Hemolytic anemia Cold agglutinins DIC	More common in children Likely due to cross reactive antibodies	Peripheral cyanosis	IgG Free Hgb Coombs
DERM	Maculopapular Vesicular rash Stevens-Johnson syndrome	May affect up to 25%	Rash, but needs to rule out rash due to antibiotics	*M. pneumonia* has been detected in cutaneous lesions
RENAL	Glomerulonephritis Tubulointerstitial nephritis IgA nephropathy Paroxysmal cold Hemoglobinuria	Brisk hemolytic anemia		UA Renal biopsy IgG, IgM, IgA

Key Reference: Waites KB, Balish MF, Atkinson TP: New insights into the pathogenesis and detection of *Mycoplasma pneumonia* infections. *Future Microbiol* 3(6):635–648, 2008.

Perioperative Implications

Preoperative Preparation

- Routine physical examination: Emphasis on respiratory, CNS, CV, and HEME systems
- Respiratory: Increased minute ventilation, low saturation; prolonged ventilation may be required.
- CNS: Document preexistent neuropathy.
- CV: JVD; rule out tamponade physiology.
- HEME: Hemolysis and anemia. If cold agglutinins are suspected, determine temperature range and titers.
- If surgery is nonurgent, consider postponing it until active issues resolved.

Monitoring

- Invasive monitoring necessary if respiratory and CV concerns

Airway

- Desaturation is possible due to decreased FRC
- High incidence of hyper-reactive airway disease

Maintenance

- Normothermia is essential to avoid cold agglutinins. Warm all fluids and humidify airway.
- If hemolysis develops: Optimized UO, alkalinized urine, and use diuretics.

Extubation

- Clear mental status, good respiratory mechanics, able to clear secretions

Anticipated Problems/Concerns

- Respiratory distress secondary to asthma, COPD, high O_2 requirements may result in prolonged intubation.
- Neurologic deficit may delay extubation.
- CPB/cold agglutinins may result in circuit obstruction and impair myocardial protection.

Myelomeningocele

Marla B. Ferschl | Mark D. Rollins

Risk

- Incidence in USA: 1.7–10:10,000 live births.
- 70,000–100,000 individuals with myelomeningocele living in USA.
- Central Asian and Latin American countries have the highest incidence.
- Risk of myelomeningocele is 20 times higher in subsequent pregnancies.
- Reduced dietary folic acid, as well as antiepileptic medication exposure (valproic acid, carbamazepine), in early pregnancy also increases risk.

Perioperative Risks

- Fetal surgery:
  - Intraop fetal distress/demise.
  - Preterm labor/delivery.
  - Risk of nonobstetric surgery during pregnancy.
  - Maternal hemorrhage.
  - Chorioamnionitis.
  - Uterine dehiscence; all future pregnancies require delivery by cesarean.
- Neonatal surgery:
  - Infection.
  - Apnea.
  - Hemorrhage and insensible fluid losses.

Worry About

- Fetal surgery:
  - Intraop fetal monitoring
  - Fetal stress and movement during repair
  - Intraop fetal distress/demise and need for resuscitation
  - Inadequate uterine relaxation
  - Maternal pulm edema
  - Maternal postop pain control
- Neonatal surgery:
  - Meningitis/sepsis if not closed within 72 h after birth
  - Latex exposure
  - Apnea, vocal cord paresis, or swallowing difficulties with the Chiari II malformation

Overview

- Failure of neural tube to close in third to fourth wk of gestation.
- Results in herniation of the nerve roots, meninges, and CSF in a fluid-filled sac.
- Most frequently occurs in lumbar or sacral portion of spinal cord but can occur anywhere along length of cord.
- Pts most often have loss of sensation and motor function below the level of the lesion.
- Bowel and bladder incontinence is common; pts require clean intermittent urinary catheterization to fully evacuate their bladder and avoid chronic renal disease.
- Hydrocephalus is a frequent complication, 85–90% of pts require ventriculoperitoneal shunting; shunts

carry lifelong morbidity because they can malfunction or become infected.
- The Chiari II malformation, which includes a small posterior fossa, as well as downward displacement of the medulla, cerebellum, and fourth ventricle into the spinal canal, is present in the majority of pts. This manifests as
  - Headache and/or neck pain.
  - Irregular breathing or periods of apnea.
  - Swallowing difficulties.
  - Vocal cord paresis.
- Tethered cord is also a common finding and should be suspected when progressive deterioration in motor or bowel/bladder function is noticed.
- Intelligence is often low normal, and many pts with myelomeningocele have learning disabilities.

Etiology

- Due to failure of primary neurulation
- Due to a variety of genetic, environmental, and/or intrauterine exposures
- Severity worsened by intrauterine exposure of neural tissues to amniotic fluid

Usual Treatment

- Postnatal repair: Closure of the neural tube and overlying skin within 72 h after birth
- Prenatal repair: Available at specialized fetal treatment centers worldwide
  - Prenatal treatment occurs during the second trimester (19–26 wk gestational age) and involves a maternal general anesthetic for laparotomy, hysterotomy, and fetal repair. In addition, fetal resuscitation drugs are available, intraop fetal monitoring is used, and intramuscular opioids and muscle relaxants are typically provided to the fetus.
  - Prenatal repair may prevent further neural tissue damage and reduce the incidence of hydrocephalus requiring a ventriculoperitoneal shunt. A multi-institutional RCT has noted benefit to prenatal repair.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Hydrocephalus Increased IOP Vocal cord paralysis	Headache Choking	Increased head circumference Papilledema Vocalization	Ultrasound MRI Fiberoptic bronchoscopy
RESP	Aspiration pneumonia OSA Restrictive lung disease	Cough Fever Snoring, apnea	Tachypnea, hypoxia Lung field consolidation Scoliosis	CXR and hypoxia Polysomnography Spine radiographs, measurement of Cobb angle
CV	ASD/VSD Critical CHD	Dyspnea	Murmur Crackles Cyanosis	Antenatal or postnatal ECHO
GI	Bowel incontinence, constipation	Constipation	Abd distention	Abdominal imaging
CNS	Hydrocephalus Chiari II malformation Tethered cord Cognitive delay Loss of sensory and motor function below level of lesion	Headache, irritability Headache, back pain, scoliosis	Increasing head circumference, papilledema Diplegia Worsening sensory or motor function	Head ultrasound, MRI demonstrating ventriculomegaly, downward displacement of hindbrain MRI spine Neurocognitive testing Neurologic exam
RENAL	Neurogenic bladder	Bladder incontinence		Serum creatinine level Renal and bladder US
MS	Kyphosis, scoliosis Club feet		Scoliosis, compromised cardiac and pulm function. Feet turned inward	Spine radiographs, measurement of Cobb angle Lower extremity radiogaphs

Key References: Sandler AD: Children with spina bifida: key clinical issues. *Pediatr Clin North Am* 57(4):879–892, 2010; Ferschl MB, Ball R, Lee H, et al.: Anesthesia for in utero repair of myelomeningocele. *Anesthesiology* 118(5):1211–1223, 2013.

Perioperative Implications

Preoperative Preparation

- Fetal surgery:
  - Maternal history and physical exam.
  - Fetal workup (MRI, ECHO) to exclude other anomalies and determine fetal weight and lesion location.
  - Maternal lumbar epidural (L2-3) placed and test-dosed.
  - Maternal premedication with a nonparticulate antacid and rectal indomethacin for tocolysis.
  - Preparation of maternal and fetal blood products; fetal blood must be type O-negative, irradiated, leukocyte depleted, CMV negative, and cross-matched against the mother.
- Neonatal surgery:
  - Birth history and physical exam.
  - Cardiac evaluation (antenatal or postnatal) to exclude concurrent congenital heart disease.
  - Preparation of type-matched and cross-matched blood products.

Monitoring

- Fetal surgery:
  - Large-bore peripheral IVs ± arterial line.
  - Continuous fetal monitoring with ultrasound.
- Neonatal surgery:
  - Standard ASA monitors ± arterial line.
  - Consider preductal and postductal oxygen saturation monitoring.

Airway

- Fetal surgery:
  - Rapid-sequence intubation with succinylcholine.
- Neonatal surgery:
  - Endotracheal intubation required.
  - Pts with a Chiari II may have more pronounced vagal tone; consider atropine pretreatment before direct laryngoscopy.

Preinduction/Induction

- Fetal surgery:
  - Left uterine displacement preinduction.
  - Confirm fetal well-being preinduction.
  - Fetal medications prepared and transferred to scrub nurse in sterile fashion (rocuronium 2–3 mg/kg + fentanyl 10 mcg/kg, epinephrine 10 mcg/kg, atropine 20 mcg/kg).
  - Prepare neonatal resuscitation equipment if there is a plan for delivery in the event of fetal distress.
- Neonatal surgery:
  - Consider lateral positioning or supine positioning on a foam donut to avoid pressure on myelomeningocele sac during intubation.
  - IV or inhalational induction appropriate; consider nondepolarizing muscle relaxant.
  - Latex-free OR environment to avoid sensitization.

Maintenance

- Fetal surgery:
  - High-dose volatile agent for adequate uterine relaxation (2–3 MAC); may consider supplemental IV anesthesia with remifentanil/propofol and also administration of IV nitroglycerin infusion if uterine tone remains high
  - Use of vasoactive medications (phenylephrine, ephedrine, glycopyrrolate) to maintain maternal blood pressure within 10% of baseline
  - Restrict IV fluids to <2 L to avoid maternal pulm edema
  - Load magnesium 4-6 g IV once uterine closure begins for tocolysis
  - Discontinue volatile agents once magnesium load is complete; continue 1-2 g/h magnesium following load; activate epidural
- Neonatal surgery:
  - Volatile anesthetic agent titrated appropriately; MAC requirements less in the neonate
  - IV opioids titrated for analgesia
  - Use of dextrose-containing IV fluids to maintain normoglycemia
  - Meticulous attention to temperature to avoid hypothermia, with use of warm ambient room temperature, forced air warming blankets, and/or radiant warmers

Extubation

- Fetal surgery:
  - Carefully assess for residual neuromuscular blockade if nondepolarizing medications are given to the mother because magnesium potentiates blockade.
  - Extubate once fully awake.
- Neonatal surgery:
  - Consider postop intubation because pts are at risk for postop apnea due to their age, as well as for the Chiari II malformation.
  - If intraop extubation is planned, make sure pt is fully awake with regular breathing pattern.

Postoperative Period

- Fetal surgery:

- Continued monitoring of uterine activity and fetal HR.
- Pt-controlled epidural analgesia.
- Neonatal surgery:
  - Pt should avoid supine position for 14 d.
  - Carefully titrate opioids with continuous monitoring in intensive care setting.

Anticipated Problems/Concerns

- Fetal surgery: Delivery for this and future pregnancies requires cesarean section due to high risk of uterine rupture.
- Neonatal surgery: Pt may require concurrent placement of ventriculoperitoneal shunt at time of surgery or may require shunt placement at a later date if head circumference continues to enlarge.

Myocardial Contusion (Blunt Cardiac Injury)

Andrew L. Rosenberg

Risk

- Incidence unknown, in part due to absence of clear diagnostic criteria/test
- 2 million motor vehicle accidents/y, with ~40% involving closed chest injury
- 20–70% incidence by clinical criteria
- 16–20% incidence by autopsy
- Motor vehicle > falls > crush injuries
- Males >females (5:1)
- Commotio cordis a rare form of BCI due to low impact chest injury (sports) causing sudden death

Perioperative Risks

- Abnormal ECG
- Nonspecific ST-T wave changes (70% of trauma pts)
- Q-wave and ST-segment elevation
- 7–17% false negative
- 60% false positive
- Ventricular arrhythmias, most common in cases of contusion
  - Trifascicular conduction block.
- Other cardiac conditions: Thrombosed or lacerated coronary arteries in spasm, ventricular hypofunction, pericardial effusion/tamponade, pericarditis, valvular insufficiency (left-sided >right), ventricular wall rupture (including septum)
- Possible increased risk of cardiac complications (arrhythmias, hypotension) with increased CK-MB troponins and abnormal ECHO
- No evidence of increased mortality assoc with GA

Worry About

- Malignant ventricular arrhythmia (acute and delayed)
- Cardiac conduction blocks include complete heart block
- Hemopericardium
- Volume status
- Acute hypotension
- Delayed myocardial rupture
- Associated injuries: Pulm contusion, hypoxemia, injuries to the thoracic aorta, flail chest
- Attribution of hemodynamic instability to myocardial contusion versus occult hemorrhage elsewhere

Overview

- Traumatic injury with hemorrhagic, well-circumscribed lesions of partial or full thickness from myocardial contusion.
- Usually affecting the RV but can be multichambered.
- BCI frequently seen in severe blunt chest trauma and after CPR and precordial thumps, but difficult to definitively diagnose.
- Incorporation of clinical suspicion, anginal chest pain unrelieved by nitrates, ECG—especially ventricular dysrhythmia, CK-MB, troponin I and T levels; 2D ECHO for Dx.
- Amount of malignant arrhythmias may be proportional to the severity of myocardial contusion.

Etiology

- Mechanical contusion of myocardium from posterior sternum.
- Ram effect from increased transdiaphragmatic pressure or sudden deceleration.
- Automobile accident most common cause, representing ~15% of cases.
- Falls ~10%.
- Crash, sports-related assaults ~15%.

Usual Treatment

- Supportive
- Adequate volume replacement

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Ventricular contusion	Angina-like chest pain unrelieved by nitrates Dyspnea	Chest wall, sternal tenderness Hypotension with severe dysfunction S_3 Rales	Serial ECG Increased troponin I and T within 6 h ECHO SPECT MRI
	Arrhythmia	Palpitations, dizziness, syncope	Pulse	ECG monitoring
	Valvular disruptions	Dyspnea	Auscultatory murmurs	ECG
	Coronary artery injury: thrombosis, laceration, spasm	Chest pain		Angio
	Effusion/tamponade	Chest pain	Pericardial friction Diminished heart sounds Distended neck veins	TTE 2D cardiography PA catheter
RESP	CHF Pulm contusion	Dyspnea Orthopnea Chest tightness	S_3 Rales Wheezing Tachypnea	CXR O_2 saturation

Key References: Clancy K, Velopulos C, Bilaniuk JW, et al.: Screening for blunt cardiac injury: an Eastern Association for the Surgery of Trauma practice management guideline, *J Trauma Acute Care Surg* 73(5 Suppl 4):S301–S306, 2012; Moore EE, Malangoni MA, Cogbil TH, et al.: Organ injury scaling. IV: thoracic vascular, lung, cardiac, and diaphragm, *J Trauma* 36(3):299–300, 1994.

Perioperative Implications

Preoperative Preparation

- FAST is usual first imaging and diagnostic choice to rule in/out pericardial effusion (hemopericardium being the major concern).
- 2D ECHO or abnormal TEE predict periop hypotension and/or valve/septum disruption.
- Assess volume and ensure adequate volume replacement.
- Assess and treat associated concurrent injuries.
- No evidence for benefit of prophylactic antiarrhythmic agents.
- The Cardiac Injury Scale (American Association for Surgery of Trauma) may be useful for quality, scoring, research purposes, and objective measures.

Monitoring

- Continuous ECG for arrhythmias.
- Consider PA cath for large fluid shift operations or pts with signs of LV dysfunction.
- Increased risk of periop arrhythmias without increased mortality.

Airway

- Evaluate for associated airway injury.

Preinduction/Induction

- Adequate volume replacement.
- Hypotension more likely with large contusions; avoid cardiodepressant induction agents.
- Extra attention to avoid hypoxia; care required with increased mean airway pressure ventilator strategies (e.g., PEEP).

Maintenance

- No one agent or technique shown to be superior.
- Avoid known pulm vasoconstrictors: catecholamine, hypoxia, acidosis, histamine-releasing agents ($MgSO_4$, mivacurium).
- Consider high inspired O_2 if there is a contusion.
- NO can aggravate pulm Htn.
- Elevations in PVR may unmask RV failure.
- Increased LV filling pressures and decreased cardiac output often reflect hypovolemia or are secondary to RV failure, not LV failure.

Extubation
- May leave pt intubated if concerns for resp failure and hypoxia.

Adjuvants
- Combination of appropriate intravascular volume replacement and vasodilators (nitroglycerin) for pulm Htn

Postoperative Period
- Delayed hypoxia from pulm injury common and can cause pulm Htn leading to hypotension if RV is severely contused

Anticipated Problems/Concerns
- Variable diagnostic criteria, total CK-MB >50 U/L and ≥5% total CK.
- Possible higher risk of cardiac complications with increased CK-MB.
- Almost any arrhythmia may be reported, especially conduction delays; more severe contusion associated with increased malignant ventricular arrhythmia.
- Watch for RV failure leading to increased LV pressure but decreased LV diastolic filling.

Myocardial Ischemia

Dennis T. Mangano | Michael F. Roizen

Risk
- Incidence in USA: 1.5 million/y develop acute MI; about 50% are silent (without enough symptoms to cause a medical visit); decreased rate of death in the United States balanced by increased population has kept MI numbers constant since 1970 despite increased population; worldwide, the incidence of MI is 9 million/y.
- Some 12 million individuals in USA have narrowing of 70% or more of one or more coronary arteries; among unselected pts over age 40 years, 1.4% have MIs; cardiac death occurs in 1.7%.
- Risk is higher among those of European, Indian, and African American heritage than among Japanese, but the environment of North America equalizes risks.
- Risk is highest in pts with known other atherosclerotic disease (including prior MI): smokers (3.5-fold increase); hypertensives (threefold increase); diabetics (4-fold increase); hypercoagulable or chronic inflammatory diseases (threefold increase); stressed, divorced, or unstable marriage (2.5-fold increase); with wt gain since age 20 years (1.5-fold increase for each 5-kg increase); increased LDL cholesterol in those who do not exercise (0.5% increase for each 1% increase above 100 mg/dL); who do not drink or take vitamin D or aspirin; whose parent died of CAD at <40 y of age (1.4- to 2.5-fold increase); age (threefold increase per decade over 50), family Hx (1.1-fold to 2.4-fold increase)

Perioperative Risks
- Periop CV complication (MI, CHF, RHF, arrhythmia requiring Rx) increases the risk ninefold.
- 2-y survival: Rate in high-risk pt with periop MIsch is 25% versus 85% for those without periop MIsch.
- Inadequate coronary perfusion (1–6% reinfarction rate with general surgery; higher with vascular/thoracic/upper abd surgery); lower with cataract/prostate/peripheral surgery with single-limb anesthesia only.
- Can lead to increased left or right ventricular compliance and CHF and dysrhythmias.
- Can lead to inadequate perfusion of other organs and their insufficient function (brain, kidney, liver, gut).

Worry About
- Postop period if stressed by perturbations that increase demand (pain, sepsis, fever, hypervolemia and hypovolemia, and tachycardia), or limit supply (thrombosis, hyperviscosity states, diseases limiting pulm function and gas exchange [restrictive, obstructive, parenchymal], Hct <28%)

Overview
- Condition of inadequate supply of O_2 and nutrients to myocardial cells relative to need associated with the increased stress of periop period,
- Treatment and prophylaxis of this and related disorders consume 10–20% of total health expenditures. Periop CV complications double with MIsch, with threefold reduction in 2-year survival and threefold increase in periop costs for major surgery.
- Major foci of clinical and basic studies are to decrease incidence and risks from concern over risk-benefit ratio and cost-effectiveness, identifying high-risk pts prior to surgery and segregating them for prior therapy (smoking cessation, control of Htn, hypercholesterol states, hypercoagulable states, PTCA, CABG) or increased periop vigilance and care (PA lines, TEE, ICU care, prophylactic pain therapy).

Etiology
- Known atherosclerotic risks (genetic predisposition, smoking, Htn, diabetes, divorced or unstable marriage, inflammation, hypercoagulable states, increase LDL or decrease HDL cholesterol, weight gain)
- Known conditions that increase periop demands on heart (tachycardia: 2-fold greater for HR >90, 11-fold greater for HR >110); or limit supply (vasospastic states; $PaCO_2$ <25; Hct <28%; hyperviscosity and hypercoagulable states; inadequate O_2 exchange)

Usual Treatment
- Decrease atherogenic risk factors.
- Decrease periop demands on the heart.
- Consider preop segregation for statin or aspirin (162.5mg) and nitrate therapies, antispasmodic and sympatholytic therapies, PTCA or CABG considerations, or stepped up postop care of increased monitoring, intensive normalization of hemodynamics, more prophylactic pain therapies. See the algorithm in second Key Reference below the Assessment Points.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Plaques in other areas	Risk factor search: Smoking stain, hypercholesterolemic lesions	McArdle earlobe	
CV	Decreased left or right ventricular compliance Decreased pump function arrhythmias Autonomic pain	SOB, DOE, angina, reduced exercise tolerance, palpitations, PND	HR/BP prior to and after two-stair climb; S_3; rales; JVD; use character and rhythm	ECG, CXR, stress ECHO or dipyridamole thallium or ambulatory Holter, troponins, and myeloperoxidase tests
RESP		Nocturnal cough, orthopnea		
RENAL	Perfusion insufficiency	Nocturia Erectile dysfunction (male) Loss of ability to achieve orgasm (female)		BUN/Cr
CNS	Autonomic pain syndromes Other atherosclerotic syndromes	Pain in neck or left arm History of stroke or TIA	CNS and cranial nerve exam	Carotid Doppler, testing of ANS

Key References: Jeremias A, Kaul S, Rosengart TK, et al.: The impact of revascularization on mortality in patients with nonacute coronary artery disease, *Am J Med* 122(2):152–161, 2009; Fleisher LA, Fleischmann KE, Auerbach AD, et al.: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, *Circulation* 130(24):2215–2245, 2014; Practice advisory for the perioperative management of patients with cardiac rhythm management devices: pacemakers and implantable cardioverter–defibrillators, *Anesthesiology* 103(1):186–198, 2005.

Perioperative Implications

Preoperative Preparation
- Consider segregation procedures and prophylactic regimens (see Usual Treatment); continue concurrent aspirin, adrenergic, and antilipidemic therapies; optimize blood sugar control.

Monitoring
- ST-T waves of area of myocardium identified as at risk (or II and V_5) (II especially for CNS surgery); ST-segment trend analysis.
- Consider TEE and arterial line and approaches to intensive normalization of hemodynamics.
- Management of arrhythmia control devices.

Airway
- Routine

Induction
- Without hemodynamic disturbance and especially with control of HR

Maintenance
- Tachycardia or hypovolemia and Hct <28 can precipitate ischemia.
- No agent with demonstrated outcome superiority.
- Intensively normalize hemodynamics and HR.

Extubation
- In nonstressful fashion for pt without compromising supply of O_2 to myocardium
- Aggressive stepped pain therapy recommended; alpha$_2$-adrenergic agonist recommended by some

Adjuvants
- CHF decreases liver blood flow and clearance of drugs requiring hepatic metabolism (such as lidocaine).
- β-adrenergic receptor antagonists and nitrates can be associated with profound hemodynamic disturbances if there are drug interactions or sudden preload, afterload, or contractility perturbations (such as rapid onset of spinal anesthesia).

Anticipated Problems/Concerns
- Preop and postop periods at least as great a cause of morbidity as intraop period.
- Restart antianginal and antiplaque therapies (i.e., statins, CO Q10, aspirin, DHA) and physical activity rehab program as soon as possible postop if D/C preop.
- Consider compassionate anxiety-relieving yet aggressive preop consultation and intensive stepped pain prophylaxis consultations postop.

Myocarditis

Ronak Shah

Risk
- Incidence of idiopathic or viral myocarditis in the general population is unknown.
- Infectious and noninfectious causes; viruses are the most common.
- Pts with autoimmune diseases are at increased risk.

Perioperative Risks
- If pt develops DCM: EF <35% increased risk of MACE.
- Atrial arrhythmia if significant mitral regurgitation is present.
- Postop respiratory failure secondary to pulm edema.

Worry About
- Acute cardiovascular decompensation.
- New-onset atrial or ventricular arrhythmias, complete heart block, or an acute MI–like syndrome.
- Worsening of chronic HF.
- Chest pain in acute myocarditis can result from an associated pericarditis or occasionally from coronary artery spasm.
- Sudden death occurs in ~12%.

Overview
- Inflammatory infiltrative process targeting the myocardium.
- Usually due to viral infection and/or a postviral immune-mediated response.
- Virus or infectious agent enters myocytes.
- Viral replication and cell necrosis initiate a response from host's immune system.
- Immune response declines with elimination of virus and ventricular function recovers.
- However, the autoimmune processes persist independently of detection of the virus genome in the myocardium, leading to the chronic phase, characterized by myocardial remodeling and development of DCM.
- DCM is enlargement of RV and LV with hypertrophied muscle fibers but no increase in size of the free wall of the septum; this gives the heart a spherical shape.
- The heart is 2–3 times larger than normal and systolic function is impaired.

Etiology
- Endomyocardial biopsies have implicated multiple viruses, such as coxsackievirus B, adenovirus, parvovirus B19, and even HCV.
- Bacterial causes include *Chlamydia trachomatis*, *Corynebacterium diphtheriae*, *Legionella pneumophila*, *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *Streptococcus aureus*, and *Streptococcus pneumoniae*.
- Other noninfectious causes include hypersensitivity and toxic reactions to medications.
- Autoimmune diseases such as giant cell myocarditis, hypereosinophilic syndrome, Kawasaki disease, lupus erythematosus, lymphofollicular myocarditis, rheumatoid arthritis, sarcoidosis, scleroderma, and ulcerative colitis place pts at higher risk.

Usual Treatment
- For acute DCM, treatment focus is supportive therapy for LV dysfunction.
- Most pts will improve with a standard HF regimen that includes ACEIs pr ARBs, beta blockers, and diuretics.
- Complete heart block and bradycardia are treated with a temporary pacemaker.
- If etiology is autoimmune-related, treatment includes immunosuppression therapy specific for the disease.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Lymphadenopathy if caused by viral/bacterial infection and sarcoidosis	Hx of fever, chills, upper respiratory tract infections	Enlarged cervical lymph nodes if progressed to DCM, JVD	Blood and sputum cultures, immunologic assays for viral infections
RESP	Pulm edema if HF develops	Dyspnea, frothy sputum Exercise intolerance and fatigue	Tachypnea, rales on auscultation	CXR, ABG analysis
CV	LV dysfunction, with LV dilatation and subsequent RV overload with chronic HF Atrial and ventricular arrhythmias	Orthopnea, chest pain, peripheral edema, fatigue, palpitations, and hepatomegaly	Tachycardia or irregularly irregular S_3 gallop Distant heart sounds Cardiomegaly (broad and displaced point of maximal impulse, RV heave)	Labs: Cardiac enzymes (troponin I or T) indicators for cardiac myonecrosis Viral antibody titers Rheumatologic screening ECHO to exclude other causes of HF and assess extent of cardiac dysfunction Coronary cath: rule out ischemic causes ECG: ST, QRS/QT prolongation, diffuse T-wave inversions, AV conduction defects and ventricular arrhythmias. Cardiac MRI Endomyocardial biopsy

Key References: Kaur H, Khetarpal R, Aggarwal S: Dilated cardiomyopathy: an anaesthetic challenge, *J Clin Diagn Res* 7(6):1174–1176, 2013; Daabiss MA, Hasanin A: Perioperative anesthetic management of a case with severe dilated cardiomyopathy, *Oman Med J* 25, 2010, doi:10.5001/omj.2010.20.

Perioperative Implications

Preoperative Preparation
- If acute cardiac decompensation presents with myocarditis, consider delaying surgery.
- Continue and optimize HF regimen (except for ACE inhibitors).
- Consider ECHO/CXR if there is a change in functional clinical status.
- If present, cardiac pacemaker should be evaluated.

Monitoring
- Consider invasive monitoring such as arterial line and pulm artery catheter, depending on type of surgery and condition of pt.
- Consider intraop TEE if significant hemodynamic changes occur.

Airway
- HF pts can present with frothy secretions resulting from pulm edema.

Preinduction/Induction
- Pts with DCM are extremely sensitive to cardiodepressants.
- Narcotic-based technique (EF <30%) is preferred to minimize cardiac depression.
- Also consider ketamine (<0.5 mg/kg) and etomidate.

Maintenance
- Conducted under general anesthesia.
- Fluid balance regulated to avoid hypervolemia and hypovolemia.
- Acute LV failure is more sensitive to the depressant effects of volatile agents.
- Afterload reduction in DCM is key as it will improve regional and global indices of ventricular relaxation and EF during anesthesia when myocardial depression is significant.

Adjuvants
- Hemodynamic instability can be treated with low-dose inotrope and vasodilator.

Anticipated Problems/Concerns
- Prolonged intubation secondary to pulm edema/hemodynamic instability.
- If LV function worsens despite optimal medical management, consider mechanical circulatory support, such as ventricular assist devices or ECMO, as a bridge to transplantation or recovery.

Myoclonic Epilepsy With Ragged Red Fibers

Diana Ayubcha | Taras Grosh

Risk

- Prevalence: 1:400,000
- Maternal inheritance; less commonly a spontaneous mitochondrial gene mutation in those without family Hx

Perioperative Risks

- Lactic acidosis
- Cardiac/respiratory insufficiency/failure
- Delayed emergence

Worry About

- Respiratory failure following sedation.
- Consider aspiration risk.
- Lactic acidosis.
- Seizures.

Overview

- Mitochondrial myopathy most commonly characterized by cerebellar ataxia, myoclonus, epilepsy, lactic acidosis, hearing loss, peripheral neuropathy, and short stature.
- Excess lactic acid load leads to nausea, vomiting, abdominal pain, fatigue, and tachypnea.
- Most commonly maternal inheritance; less commonly results from a new mutation in a mitochondrial gene in those without a family Hx.
- Onset is in late adolescence through early adulthood.
- Muscle biopsy with hallmark appearance of ragged red fibers.
- DNA point mutation results in mutation of respiratory chain complexes I + IV.
- Inability to process lactate-containing fluids.
- Anesthetic sensitivity may manifest as decreased MAC of inhaled anesthetics, with increased respiratory insufficiency from sedatives and narcotics.

Etiology

- Most common mutation is the m.8344A>G mutation in the mitochondrial DNA gene, MT-TK, which encodes mitochondrial transfer (t)RNA lysine.
- Muscle biopsy shows ragged red fibers with deficient activity of COX, and presence of COX deficient vessels with SDH stain.

Usual Treatment

- Anticonvulsant (valproic acid, phenobarbital)
- Myoclonus therapy (clonazepam, tizanidine)
- Multivitamins (CoQ-10, CoQ-6, B-complex, L-carnitine)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Sensorineural hearing loss Optic atrophy Pigmentary retinopathy	Hearing loss Vision loss	Decrease visual acuity	Hearing exam Ophtho exam
CV	Cardiomyopathy Conduction defects (WPW)	Symptoms of CHF Palpitations, dizziness, lightheadedness	Murmur, gallop, crackles	CXR, ECHO, ECG, exercise testing (VO_2 max)
RESP	Disorganized respiratory muscle effort	Hypoventilation, hypoxia, following sedative use	Rhonchi	CXR
GI	Swallowing impairment, GI dysmotility	Dysphagia, bloating, N/V		Barium swallow, Endoscopy, manometry
ENDO/METAB	Lactic acidosis DM	N/V Polyuria Polydipsia Polyphagia	Hyperventilation Orthostatic hypotension	Serum lactate, serum electrolytes, serum pyruvate, HbA_{1C}
CNS	Epilepsy, cerebellar ataxia, Dementia Intention tremor Degenerative changes in CNS, psychomotor regression	Developmental delay Vision loss Poor balance/coordination	Focal neurologic deficits Signs of seizure	Head CT/MRI, EEG
PNS	Peripheral neuropathy	Weakness Dysesthesias	Decreased strength, distal sensory loss, decreased DTR	Monofilament, tuning fork
MS	Myopathy myoclonus Spasticity	Weakness, involuntary twitching of extremities, stiffness, muscle spasms	Decreased strength, decreased ROM, muscle contractures	EMG, serum CK Ragged red fibers on SDH stain
OTHER	Short stature Lipomas (near the neck)			

Key References: Vilela H, Garcìa-Fernández J, Parodi E, et al.: Anesthetic management of a patient with MERRF syndrome, *Pediatr Anaesth* 15(1):77–79, 2005; Baum VC, O'Flaherty JE: MERRF syndrome. In Baum VC, O'Flaherty JE, editors: *Anesthesia for genetic, metabolic, & dysmorphic syndromes of childhood*, ed 3, Philadelphia, 2015, Wolters Kluwer, pp 283–284.

Perioperative Implications

Preoperative Preparation

- Assess cardiac involvement.
- Avoid prolonged fasting and dehydration because it worsens acidosis.
- Correct preop acidosis.
- When possible, start IV fluid (avoid lactate-containing fluids; bicarbonated Ringer is OK) at NPO time, allow for late (2 h prior) clear intake, and book as first case.
- H+P limitations (hearing loss, dementia).
- Assess medication list; anticonvulsants and myoclonus medications will affect sensitivity to certain anesthetics.
- Ensure most recent dose of anticonvulsant has been administered.
- Determine frequency, severity, and triggering factors of seizures.

Airway

- Aspiration risk

Monitoring

- Routine, assuming no severe cardiomyopathy or CHF.
- Consider BIS monitor prior to induction for possible increased anesthetic sensitivity.
- Longer procedures consider arterial line for intraop

Induction

- Avoid lactate-containing IVF (i.e., lactated Ringer).
- Avoid succinylcholine risk of uncharacterized myopathy/neuropathy leading to exaggerated hyperkalemia.
- Avoid etomidate as this has the highest incidence of CNS excitatory activity.

Maintenance

- Ensure normoglycemia, normothermia, normotension, normovolemia and optimal oxygenation (factors known to influence existing or latent lactic acidosis).
- Avoid propofol infusion as this leads to disruption of the electron transport chain worsening acidosis and reduced ATP production.
- Short-acting NMB if required (carefully titrated) but better to avoid if possible.
- Aggressive temp control; active warming techniques.
- Opioids carefully titrated with caution for increased risk of respiratory depression. Avoid meperidine secondary to strong association with myoclonus and seizure activity.
- Possible increased sensitivity to halogenated agents but can be used safely.
- Reduce spontaneous ventilation and natural airway, preventing muscle fatigue and respiratory failure.
- Severe lactic acidosis can be treated with dichloroacetate (15 mg/kg IV over 30 min) which stimulates pyruvate dehydrogenase which converts lactate to pyruvate.

Extubation

- Muscle weakness and anesthetic sensitivity may delay extubation.

Regional/Neuraxial

- Local anesthetics have potential to uncouple electron transport chain worsening lactic acidosis but have been used successfully.

Postoperative Period

- Close monitoring of respiratory function.
- Longer duration procedures: Consider obtaining lytes or ABG to assess for acidosis.

Anticipated Problems/Concerns

- Generally not associated with MH; however, critical ATP depletion may precipitate muscular contraction, mimicking MH.
- Although succinylcholine is not contraindicated (as in Duchenne or Becker MD), acidosis and neuropathy may predispose to hyperkalemia.

Myotonia Dystrophica (Myotonic Dystrophy, Steinert Disease)

Amir Elhassan | Paul J. Delahoussaye | Alan David Kaye

Risk

- Incidence of approximately 1:8000.
- Incidence of the congenital form is higher, with an incidence of 1:100,000 compared with adult-onset form.

Perioperative Risks

- Operative/anesthetic and postop morbidity and mortality are increased and not proportional to severity of disease.
- High incidence of cardiopulmonary complications, including sudden death, cardiac failure, and cardiomyopathy.

Worry About

- Increasing frequency of symptoms
- Signs of respiratory or cardiac decompensation

Overview

- Degenerative disease of skeletal muscles. It consists of a triad of characteristic features, including frontal baldness, cataracts, and mental retardation.
- It can be variable in presentation. Some are asymptomatic, whereas more severe congenital manifestations include mental retardation and respiratory insufficiency.
- Typically the onset of symptoms in second and third decades of life with progressive muscular weakness and wasting, most common in the cranial and distal limb muscles (e.g., temporalis and masseter muscle atrophy, known as "hatchet face" and "limb muscles"). There may be diminished deep tendon reflexes and muscles of the vocal cord apparatus resulting in nasal speech. A proximal muscle variant has recently been recognized. Death frequently occurs in the fifth or sixth decade of life and is usually related to cardiopulmonary complications, including sudden death from conduction abnormalities, cardiomyopathy, and/or CHF.
- There is often persistent contracture after cessation of stimulation or voluntary contraction of the muscle. This inability of the skeletal muscle to relax is diagnostic. EMG is corroborative and pathognomonic and it shows continuous low-voltage activity with high-voltage, fibrillation-like potential bursts.
- Myotonic dystrophy is an intrinsic disorder of skeletal muscle linked to a myotonin-protein kinase gene on chromosome *19q13.2*. A defect in Na^+ and Cl^- channel function produces electrical instability of the muscle membrane and self-sustaining runs of depolarization. Abnormal metabolism of calcium may be seen.

Etiology

- Myotonic dystrophy is inherited via an autosomal dominant trait. It occurs from an abnormal expansion of the nucleotide CTG on chromosome 19, which codes for a serine-threonine protein kinase. Variable gene expressivity can be seen within the same family in which one member can have minimal affects and another be severely affected. Anticipation is seen with inheritance, and the longer the CTG repeat, the more severe the disease is.

Usual Treatment

- Quinine, procainamide, phenytoin, tocainide, mexiletine (depress Na^+ influx)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Visual disturbance Speech/swallowing impaired		Presenile cataract, ptosis, strabismus, retinal pigmentation Generalized weakness of pharyngeal, mandibular (and thoracic) musculature Dysarthria, facial weakness Expressionless facies	Exam by ophthalmologist
CV	Dysrhythmias Cardiomyopathy	CHF uncommon but may occur with pregnancy	Delayed intraventricular conduction Heart block, hypotension Up to 20% with mitral valve prolapse, sudden death	ECG ECHO, Holter Cardiology consult
RESP	Restrictive lung disease Chronic aspiration Central hypoventilation	Weak cough Dyspnea Hx of pneumonia	Wasting of sternocleidomastoid muscles; respiratory muscle weakness Lungs intrinsically normal; decreased VC, decreased ERV, increased CO_2	PFTs ABG
GI	High aspiration potential Delayed esophageal and gastric emptying Gastric dilation/atony Increased incidence of cholelithiasis	Weak swallowing ability		
ENDO/IMMUNE	Testicular atrophy DM Decreased thyroid function Adrenal insufficiency Frontal balding Malignant hyperthermia		Thyroid nodules Decreased immunoglobulins	Blood/urine glucose tests Thyroid function tests
CNS	Mental retardation Associated with central sleep apnea and hypersomnolence Emotional abn		Myotonic handgrip (delayed, incomplete release), increased CK in serum Myotonia can be initiated or worsened by exercise or cold temp; decreased DTR	EMG CK
GYN	Pregnant pt is a challenge. Respiratory function threatened by decreased FRC and myotonic weakness, which may be exacerbated by pregnancy. Seems to be added risk for uterine hemorrhage at delivery due to uterine atony and retained placenta. C-section may be safer.			

Key References: Aldredge LM: Anaesthetic problems in myotonic dystrophy. A case report and review of the Aberdeen experience comprising 48 general anesthetics in a further 16 patients, *Br J Anaesth* 57:1119–1130, 1985; Mathieu J, Allard P, Gobeil G, et al.: Anesthestic and Sugrical complications in 219 cases of myotonic dystrophy, *Neurology* 49(6):1646–1650, 1997.

Perioperative Implications

Preoperative Preparation

- Ensuring NPO status (increased aspiration) and recent ECG.
- No preop analgesics or sedatives and caution with benzodiazepines.
- Warm ambient room air in OR may decrease incidence and severity of myotonia.
- Routine monitoring.

Airway

- Propensity for frequent jaw dislocation
- Potential inability to secure airway because of jaw muscle spasm

Preinduction/Induction

- Risk for aspiration of gastric contents.
- Induction: Gaseous; avoid slow metabolizing hypnotics; use lower doses on propofol.
- Relaxation: Avoid succinylcholine (link to malignant hyperthermia, severe extended contractures); use short-acting nondepolarizing agents at lower doses; recovery may be prolonged.
- May be hard to differentiate from onset of MH.

Maintenance

- Myotonia may be precipitated by drugs (e.g., propofol, succinylcholine, anticholinesterases, halothane, neuroleptics, liquid paraffin), physical factors (e.g., cold, shivering), surgical manipulation, or electrocautery.
- Avoid K^+-containing fluids.
- Regional or local anesthesia acceptable but will not block myotonic response.
- Regional ± TIVA may be preferable when suitable extubation.
- Beware of airway obstruction because of jaw muscle weakness.
- Delayed recovery from anesthetic common.

Extubation

- Beware of airway obstruction because of jaw muscle weakness.
- Delayed recovery from anesthetic common.
- Sugammadex has been described in literature with successful reversal of steroidal NMBs.

Adjuvants

- Increased sensitivity to ventilatory depressant effects of all premedicants, sedatives, and opioids.

- Reversal agents can theoretically precipitate skeletal muscle contraction by facilitating depolarization of NMJ, but adverse responses do not predictably occur.

Postoperative Period

- Increased sensitivity to respiratory depressant effects of opioids or sedatives, including epidural opioids
- Postop pain to be managed with NSAIDs, regional blocks, and acetaminophen if possible
- Pulm complications due to poor cough possible
- Cardiac and respiratory monitoring and early chest physiotherapy

Anticipated Problems/Concerns

- If myotonia develops intraop, neither GA nor RA nor NMBs will attenuate it. Local infiltration of involved muscles may help. Even asymptomatic pts may have some degree of cardiomyopathy. Beware of premature extubation, and consider postop ventilation.
- 57% of these pts have conduction defects, with one-third having primary block unresponsive to atropine. It is advisable to have antiarrhythmics and transthoracic pacing readily available as many anesthetic agents can increase vagal tone.
- For numerous reasons, it is advisable to avoid GA (e.g., myocardial depressants, conduction effects, link to malignant hyperthermia). Pts should have procedures done with RA if at all possible.

Myxoma

Rebecca Y. Klinger | Solomon Aronson

Risk

- Although primary cardiac tumors are rare (<0.01%), myxoma is the most common type (50%).
- 75% develop in LA, with most attached to the interatrial septum.
- Rarely develop in ventricles.
- More common in females (70%).

Perioperative Risks

- May be friable and may embolize (30–40% of pts)
- LV- or RV-inflow obstruction with resultant hypotension
- May simulate pulm Htn and/or constrictive pericarditis physiology

Worry About

- Hypotension due to obstruction of ventricular inflow and/or incompetence of tricuspid (right) or mitral (left) valve, may be positional.
- Tumor flips on a stalk across valves, causing stenotic and/or incompetent symptoms.
- RV hypertrophy can occur because of longstanding left ventricular–inflow obstruction.
- There is the possibility of pulm or systemic embolization.

Overview

- Is a true neoplasm and distinct from a thrombus
- Usually polypoid, pedunculated with a 1–2 cm stalk, and round with smooth margins
- Typically grows very slowly before the patients becomes symptomatic (10–20 y)

Etiology

- Typically arises from the endocardium and rarely extends deeper.
- Polyhedral cells with small nuclei are separated by an afibrillar, eosinophilic myxomatous stroma that is predominantly a mucopolysaccharide.
- Although benign, this tumor rarely can undergo malignant degeneration.

Usual Treatment

- Surgical, usually curative
- Cardiopulmonary bypass required
- Median sternotomy, atriotomy with transseptal approach through fossa ovalis
- Resection including the root of the pedicle and the full thickness of the adjacent septum and then ASD closure

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Mitral or tricuspid stenosis or insufficiency syndromes	Edema and CHF	Atrial enlargement Systolic murmur (regurgitation) Diastolic murmur (stenosis)	ECHO, ECG, CXR CT, MRI
RESP	Pulmonary emboli (right)	DOE and cough	Rales, wheezing, and increased P_2	ECHO, CXR, ECG
GI		CHF	Hepatic enlargement	Hepatic enzymes (if symptoms of CHF)
RENAL	Emboli (left)			Urinalysis Cr clearance
CNS	Stroke (left)	CNS dysfunction	CNS dysfunction	ECHO
GENERAL	Constitutional symptoms	Fever and malaise	Weight loss	ESR, CRP, Hct (anemia)

Key References: Reynen K: Cardiac myxomas, *N Engl J Med* 333(24):1610–1617, 1995; Essandoh M, Andritsos M, Kilic A, Crestanello J: Anesthetic management of a patient with giant right atrial myxoma, *Semin Cardiothorac Vasc Anesth* 20(1):104–109, 2016.

Perioperative Implications

Preoperative Preparation

- Differential Dx: Mitral stenosis/insufficiency (left), tricuspid stenosis/insufficiency (right), constrictive pericarditis, pulm Htn, and subacute bacterial endocarditis.
- Mitral stenosis: Hemodynamic aim is to keep pt in normal sinus rhythm with adequate preload and high-normal afterload (see Mitral Stenosis).
- Mitral insufficiency (regurgitation): Hemodynamic aim is to keep HR normal or fast and to vasodilate.
- Hemodynamics can mimic any or all of the above, depending on load-dependent variables prevailing in the cardiac cycle at the time (e.g., preload, afterload, HR)

Monitoring

- Routine monitors otherwise needed for cardiopulmonary bypass (e.g., standard ASA monitors, temperature, ECG, coagulation, Foley).
- Intra-arterial catheters.
- Beware of central line with right-sided atrial myxoma (may cause dislodgment of friable debris as pulm emboli); TEE guidance (bicaval view) of guidewire placement may be helpful.
- TEE: Most sensitive way to guide hemodynamic management and assess the therapeutic approach.

Airway

- Routine

Preinduction/Induction

- Pt may develop hypotension if preload is decreased or HR is increased; best managed with a vasopressor (no or judicious use of inotropes).
- Insert a central venous catheter carefully and avoid a PA catheter in pt with a right-sided tumor.
- Intraop TTE is helpful/diagnostic (before induction) if there is concern about right inflow obstruction exacerbated by PPV and for monitoring of IV fluid administration.
- Avoid/treat atrial dysrhythmias.
- Have a surgical team present on induction in case of CV collapse.
- Initiate PPV carefully.

Maintenance

- May dislodge pieces during CPB venous cannulation; direct assessment of anatomy, physiology, and even placement of venous cannulas should be guided by TEE.
- If pedunculated, a tumor may obstruct inflow tract, and hemodynamics may present as low BP, low CO, or increased CVP (right)/increased PCWP (left).

Extubation

- Expect separation from CPB with minimal support and overall excellent recovery with primary myxomatous lesion.
- Extubation criteria should be based on myocardial protection techniques and post-CPB bleeding risk.
- Early extubation consideration is reasonable.

Postoperative Period

- Beware of residual ASD (as tumors typically originate in the atrial septum in the region of the fossa ovalis).
- Beware of conduction and rhythm disturbances (esp. in pediatric pts).
- Symptoms of pulm Htn usually regress quickly.

Anticipated Problems/Concerns

- Hypotension with inadequate preload when the lesion obstructs ventricular inflow

Narcolepsy

Alexander Tzabazis

Risk

- Prevalence approximately 1:2000
- Women and men equally affected
- Prevalence higher in Japan (1:600)

Perioperative Risks

- Potential for masking or mimicking periop complications
- Potential deleterious interactions between drugs for narcolepsy and drugs administered periop

Worry About

- There is little evidence that pts with narcolepsy actually have an increased periop risk.
- Theoretical concerns are:
  - Potential drug interactions with anesthetics leading to
    - Hemodynamic changes.
    - Altered anesthetic requirements.
    - Increased risk of serotonin syndrome.
  - Periop narcoleptic episodes mimicking or masking other anesthesia complications (e.g., delayed emergence or postop residual curarization).

Overview

- Chronic neurologic sleep disorder
- Onset usually in adolescence
- May take years to be diagnosed (polysomnography and multiple sleep latency test)
- Classic symptoms: Excessive daytime sleepiness, cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations (nocturnal sleep disruption)
- Excessive daytime sleepiness:
  - Daytime sleep episodes occurring at inappropriate times
  - Difficult to avoid falling asleep
  - Frequently rationalized
  - Differential Dx: OSA, sleep deprivation
- Cataplexy:
  - Sudden decrease in muscle tone
  - Usually partial (e.g., affecting only facial or neck muscles)
  - May be complete, with fall risk; pts are fully conscious
  - Both partial/complete can be triggered by emotions (e.g., periop anxiety)
  - Can last up to 60 min
- Hallucinations:
  - Hypnagogic (during transition from waking to sleep) or hypnopompic (during transition from sleep to waking)
  - Often visual but may also be auditory, tactile, or multisensory
  - May be misdiagnosed as mental illness
- Sleep paralysis:
  - Inability to move during sleep onset or offset
  - Pt fully conscious
  - Breathing unaffected
  - May occur in conjunction with hallucinations
- Other symptoms:
  - Automatic behavior (performing routine tasks without conscious awareness)
  - Memory lapses
  - Secondary psychological symptoms (e.g., depression)

Etiology

- Multiple etiologies, at least partially genetic (HLA-DR and HLA-DQ).
- Decreased concentrations of neurotransmitter (hypocretin, also known as orexin) in lateral hypothalamus.
- Undetectable levels of hypocretin in CSF of most pts.
- Current theory favors an autoimmune process that attacks hypocretin-producing neurons (possibly triggered by upper airway infections).

Usual Treatment

- Modafinil:
  - Usually first line for sleep attacks, MOA unknown.
  - Low abuse potential, favorable side-effect profile.
  - Less effect on blood pressure compared with amphetamines.
  - Less rebound hypersomnolence upon withdrawal.
  - Armodafinil: R-enantiomer with longer half-life of 10–15 h.
  - Small studies suggest that modafinil may improve recovery from general anesthesia by making pts feel less fatigued or worn out and more alert; whether this also holds if modafinil if taken chronically needs to be determined.
- Amphetamines/methylphenidate:
  - Second line for sleep attacks.
  - Methamphetamine for pts with severe sleepiness.
  - Methylphenidate usually well tolerated; half-life of 3–4 h, but sustained release formulations available.
  - Emerging evidence suggests that amphetamines administered chronically for medical indications can/should be continued for elective surgery.
  - In case of hypotension, direct-acting vasopressors (phenylephrine or epinephrine) should be used, since response to indirect-acting vasopressors (ephedrine) will be attenuated secondary to catecholamine depletion.
- Sodium oxybate:
  - To treat nighttime insomnia and dyssomnia, thus decreasing excessive daytime sleepiness and cataplexy.
  - Risk of respiratory depression (black-box warning).
  - May worsen OSA, especially in conjunction with sedative hypnotics or other CNS depressants.
  - Half-life 3–4 h.
- TCAs:
  - Imipramine, clomipramine, and protryptyline are used to treat cataplexy.
  - Unfavorable side-effect profile (e.g., anticholinergic, orthostatic hypotension, antihistaminergic, leading to sedation).
  - Increased risk of periop hypotension.
  - Potential of tachycardia/dysrhythmia with coadministration of ketamine, meperidine, and local anesthetics with epinephrine.
- SSRIs:
  - Fluoxetine and venlafaxine are less potent in treating cataplexy compared with TCA but have a favorable side-effect profile.
  - Theoretical concerns for serotonin syndrome: Mild: Tachycardia, myoclonus, restlessness, dilated pupils, anxiety, diaphoresis; Severe: Muscle rigidity, hyperthermia, multiorgan failure).
  - Periop drugs with potential SSRI interaction: Fentanyl, metoclopramide, 5-HT3 antagonists, meperidine, linezolid, methylene blue.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Reduced concentration of neurotransmitter hypocretin in lateral hypothalamus May have altered anesthetic requirements	Excessive daytime sleepiness, cataplexy, hallucinations, sleep paralysis		Polysomnography, multiple sleep latency test, reduced hypocretin concentration in CSF
HEENT	Increased risk of airway obstruction in pts on sodium oxybate			
CV	Side effects of medications: TCAs Amphetamines	Orthostatic hypotension Catecholamine depletion and profound hypotension		BP change on standing
MS	Sleep paralysis, cataplexy	Ask about frequency and severity		

Key References: Leschziner G: Narcolepsy: a clinical review, *Pract Neurol* 14(5):323–331, 2014; Burrow B, Burkle C, Warner DO, et al.: Postoperative outcome of patients with narcolepsy. A retrospective analysis, *J Clin Anesth* 17(1):21–25, 2005.

Perioperative Implications

Preoperative Preparation

- Review medications and ask about the typical frequency and presentation of narcoleptic attacks (duration), cataplexy (partial vs. complete), sleep paralysis (duration).
- It is considered safe to continue medications for narcolepsy for elective surgery, even chronically used methamphetamine.
- Especially in outpatients on sodium oxybate, consider avoiding longer-acting sedatives such as midazolam.

Monitoring

- For potential change in anesthetic requirements, consider using an EEG monitor.
- For hemodynamic changes in pts on methamphetamine and/or TCAs, low threshold for placing arterial catheter.
- Use relaxometry to differentiate between residual curarization and cataplexy/sleep paralysis.
- Use direct-acting vasopressors (phenylephrine) to treat hypotension in pts on methamphetamine.
- Effect of direct-acting vasopressors may be enhanced in pts on TCAs.

Airway

- No special concerns

Induction and Maintenance

- Hemodynamic changes in pts on methamphetamine and/or TCAs (see Monitoring).
- Fentanyl, metoclopramide, and 5-HT3 antagonists increase risk for serotonin syndrome in pts on SSRIs (clinical relevance unknown).

Extubation

- Cataplexy/sleep paralysis may mimic postop residual curarization.

Adjuvants
- Consider using local anesthetic without epinephrine for local infiltration/nerve blocks.

Postoperative Period
- Cataplexy/sleep paralysis may mimic postop residual curarization.
- Hallucinations may be misdiagnosed as postop/emergence delirium.
- Consider longer than usual PACU stay or ICU admission (overnight) for pts on sodium oxybate, depending on length of case, sedatives/hypnotics administered intraop, and expected opioid requirements postop (increased risk for airway obstruction/respiratory depression and death).
- If shivering occurs in pts on SSRIs, meperidine may trigger serotonin syndrome.

Anticipated Problems/Concerns
- Retrospective study with 10 pts and 27 elective procedures under general anesthesia and endotracheal intubation showed no increase in periop complications; in this study only pts who received their narcolepsy medication (five of them were on methamphetamine, none on modafinil or sodium oxybate) before the procedure were included.
- Although existing literature suggests that pts with narcolepsy do not have an increased risk for periop complications, clinical suspicion—especially for narcoleptic drug-anesthetic interaction and narcoleptic symptoms complicating the periop course—must be maintained.

Necrotizing Enterocolitis

Robert M. Insoft | Jeffrey D. Roizen

Risk
- Most common life-threatening intestinal surgical emergency in the newborn.
- Occurs predominantly in premature infants, with 75% in infants weighing <1500 g.
- Increasing incidence in term and near-term neonates as well.

Perioperative Risks
- CV instability, acidosis, shock, bowel ischemia, bacteremia, patent ductus arteriosus, polycythemia

Worry About
- Persistent metabolic acidosis and intestinal perforation are ominous signs.

Overview
- Presents commonly with generalized signs of sepsis, including glucose instability, hypothermia, apnea, feeding intolerance, and metabolic acidosis.
- The terminal ileum is most commonly involved, followed by the distal small bowel and ascending colon. Bowel ischemia may lead to gangrene of the bowel with perforation as well as peritonitis, CV and respiratory collapse, shock, and death.
- Multisystem failure commonly involves the respiratory, CV, renal, and hepatic systems. Abnormal elevated inflammatory mediators, such as TNF, IL-6, and PAF, are associated.
- In severe cases, the abdominal wall may be erythematous, signifying intestinal perforation and peritonitis.
- Pneumatosis intestinalis is evident as a linear collection of air and hydrogen gas in the wall of a dilated loop of bowel; it may extend into the portal venous circulation.

Etiology
- Associated with bowel ischemia, enteral feeds, infection, and prematurity. Clearest link is with prematurity, leading to the theory that an underlying developmental immaturity of bowel is potentially the initiating problem leading to this life-threatening condition.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Shock PDA	Pulm edema, RDS, shock	Murmur BP/HR	ABG, BP UO
RESP	RDS	Apnea or tachypnea		ABG CXR
ID	Sepsis	Bacteremia Peritonitis	Abdominal wall cellulitis, peritonitis	Blood and peritoneal fluid cultures
GI	Peritonitis, bloody stools, malabsorption	Large feeding residuals, bilious emesis	Residuals, guaiac stools	Lytes, bowel sounds, KUB examination Temperature instability
RENAL	Prerenal failure		UO, BP	BUN, Cr
HEME	DIC Polycythemia	Bleeding		Hct, plt count, fibrinogen PT/PTT

Key Reference: Henry MC, Moss RL: Necrotizing enterocolitis, *Annu Rev Med* 60:111–124, 2009.

Perioperative Implications

Preoperative Preparation
- Most neonates can be treated medically with fluid resuscitation, antibiotics, ventilatory support, and hyperalimentation.
- Surgery is indicated for pneumoperitoneum from intestinal wall perforation, intestinal gangrene (detected by abdominal paracentesis), and the presence of portal vein gas. Other indications include clinical deterioration, abdominal wall erythema, and an unresolved ileus.
- Discontinue enteral feeds and insert NG tube connected to suction for intestinal decompression.
- Therapeutic goals include normalization of vital signs and ensuring adequate oxygenation and ventilation (e.g., tracheal intubation, mechanical ventilation, adequate perfusion).
- Ensure vigorous fluid resuscitation to keep up with third-space losses from peritonitis and sepsis.
- Correct metabolic acidosis (achieved through fluid resuscitation).
- Inotropic agents such as dopamine and dobutamine may be required to optimize cardiac output.
- Correct coagulopathy with FFP, plts, and packed RBCs.
- Administer broad-spectrum antibiotics, with anaerobic coverage highly considered as well.

Monitoring
- Routine plus glucose and lytes

Induction/Maintenance
- Potent anesthetic agents are poorly tolerated.
- A carefully titrated narcotic and muscle relaxant technique is satisfactory.
- N_2O is usually avoided because of its potential for causing bowel distention.
- Fluid resuscitation (lactated Ringer solution, 5% albumin, and sometimes packed RBCs) is actively carried out during surgical procedures.

Postoperative Period
- Closely monitor in NICU for ongoing fluid requirements as third-space loss continues.
- Prolonged TPN is often required.
- Stricture formation leading to partial or total bowel obstruction is a common complication in both medically and surgically treated neonates.
- Short-bowel syndrome can occur, leading to long-term complications.

Anticipated Problems/Concerns
- Hypovolemia and bowel ischemia
- Acidosis, shock, and death

Necrotizing Fasciitis

Hernando Gomez | A. Murat Kaynar

Risk

- Incidence in USA: Approximately 9–11.5 cases of invasive streptococcal infections, from which 1–1.8 die each year
- STSS and NF, each comprising an average of 6–7% of these invasive cases, with an associated mortality of 35–50% for STSS and 29% for NF
- Predisposing risk factors: Diabetes, peripheral vascular disease, alcoholism, IV drug abuse, immunosuppression, obesity, or malnourishment

Perioperative Risks

- Shock, hypoperfusion, organ dysfunction, and hyperglycemia or hypoglycemia
- MODS and death

Worry About

- Making an early diagnosis and beginning treatment (which always includes surgical debridement) accordingly, which is the single most important factor to decrease morbidity and mortality
- STSS and septic shock
- Multiple organ dysfunction, including pulmonary (ARDS), renal, hepatic failure, and hematologic (DIC)
- Postop ICU often required

Overview

- NF constitutes one of the two severe manifestations of GAS, along with STSS, and often is associated with it during its initial presentation.
- NF is a common cause of CV collapse, shock, and hypoperfusion, which could be aggravated by the anesthetics. High suspicion is important to ensure early detection and treatment of hypovolemia and hypoperfusion. A suitable anesthetic procedure should be planned. Aggressive and continuous assessment of the CV status is required to have a stable hemodynamic state during sepsis.
- Despite the low incidence of the disease, prompt recognition is important given its devastating consequences, not only as a major cause of mortality but also morbidity, including
  - Organ failure with long-term requirement of support therapy (i.e., dialysis, home O_2)
  - Physical disfiguration and amputations causing physical and psychological disability
  - Acute and chronic pain syndromes (difficult to control)

Etiology

- Polymicrobial (including *Staphylococcus aureus*, *Escherichia coli*, enterobacteria, *Clostridium* spp., *Peptostreptococcus*, *Fusobacterium*, and *Bacteroides* spp.) in 70% of cases; GAS, which is causal in 30% of cases
- Skin and soft-tissue infections (majority of cases at 80%) and contaminations from distant sources (bacteremia) (20% of cases)

Usual Treatment

- Early diagnosis and repeated surgical excision of necrotic tissues are often required.
- Adequate antibiotic coverage is based on cultures and sensitivities.
- Support of organ systems, metabolism, and nutrition are necessary.
- Hyperbaric O_2 therapy is still under study.

Assessment Points

System	Effect	Assessment by Hx	Physical Examination	Test
CV	Vasodilation, hypovolemia early after local symptoms (i.e., 24–48 h)	Dizziness, alteration in mental status	Signs of dehydration, orthostatism, tachycardia, hypotension	Hemodynamic monitoring
HEME	DIC, hemorrhage, leukocytosis	Petechiae, skin discoloration	Bleeding, poor coagulation, fever, chills, myalgias	Hgb and Hct, clotting evaluation with platelets, PT/PTT, fibrinogen, fibrin split products, CBC
RENAL	Prerenal and acute renal failure	UO	Signs of hypovolemia	Urinalysis with specific gravity, Na excretion, serum creatinine and BUN
PULM	ALI/ARDS	None	Hypoxia, increased work of breathing	ABG with low P/F ratios <300
DERM/SOFT TISSUE	Inflammation, necrosis, blistering	Hx of skin/soft-tissue injury (i.e., insect bite, contusion, ingrown nail)	Pain, erythema, edema, cellulitis with rapid progression to bluish discoloration, blisters, subcutaneous crepitus	Congelation biopsy, with fascia involvement.

Key References: Hakkarainen TW, Kopari NM, Pham TN, et al.: Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes, *Curr Probl Surg* 51(8):344–362, 2014; Durrani MA, Mansfield JF: Anesthetic implications of cervicofacial necrotizing fasciitis, *J Clin Anesth* 15(5):378–381, 2003.

Perioperative Implications

Preoperative Preparation

- Establish large-bore venous access promptly and optimize CV status and perfusion. Anticipate additional fluid loss from exposed debrided areas and large fluid shifts.
- Note type and cross.
- Consider ketamine 1–2 mg/kg versus etomidate 0.2 mg/kg as induction agent. Watch for CV depression during induction. Anticipate the potential for adrenal insufficiency with etomidate.
- Provide adequate pain control.
- Consider procedure contaminated and use all recommended infection control guidelines.

Monitoring

- Establish invasive CV monitoring (CVC and A-line), PPWF, echocardiography, and temperature monitor.
- Clotting studies, CBC, and chemistry-7.
- Pulm airway pressures, tidal volumes, and ABGs.
- Perfusion to end organs: $ScvO_2/SvO_2$, lactate, and base excess.

Preinduction/Induction

- Hydrate aggressively with crystalloids/colloids.
- Establish invasive CV monitoring (CVC and A-line). Preoxygenate adequately.
- Aspiration prophylaxis.
- Do not delay antibiotics.

Maintenance

- Monitor volume status (CVP/SVV/PPWF/UO) and perfusion adequacy to optimize accordingly, including volume responsiveness; consider requirement of vasopressors (such as norepinephrine).
- Monitor blood loss, coagulopathy, and electrolyte imbalance and replace accordingly.
- Avoid hypothermia; monitor for fever.
- Watch for the presentation of bacteremia during/after debridement (hypotension, tachycardia, and fever).
- Consider delaying extubation according to CV/pulm status.
- RA: Do not use in the acute setting. Only use it in the absence of shock, occult shock, hemorrhage, and significant coagulopathy. Usually adequate in later stages of the disease while still requiring surgical management.
- Spinal versus epidural: Use is dependent on affected region and length of the procedure.
- Anticipate important loss of sympathetic tone in the setting of potential hypovolemia.
- Do not use if anesthetic application implies puncture through potentially contaminated site.

Postoperative Period

- Potential requirement for continued intubation to maintain adequate oxygenation and to be admitted to ICU
- Must be directed at obtaining adequate end-organ perfusion (establish invasive CV monitoring [CVC and arterial line], PPWF, ECHO [volume status and cardiac contractility]; obtain ABG, $ScvO_2/SvO_2$, lactate, and base excess)
- Optimize support according to pt requirements (i.e., CVVH, HD, and mechanical ventilation)

Anticipated Problems/Concerns

- Pts are often in septic shock, hypovolemic, or hypoperfused to begin with. Optimize CV and perfusion status in preinduction and be cautious during induction. Always consider associated comorbidities.
- Surgical debridement, combined with antibiotic therapy, is the only strategy to decrease poor outcomes. Do not delay surgical intervention. Surgical procedures may include amputation of limbs, which if delayed may cause uncontrolled systemic involvement and response.
- Complications such as organ failure (acute kidney injury 80% or ARDS 50%) and bacteremia (60%) are the rule, not the exception. Be prepared to support failing organs and troubleshoot acute destabilizations.
- Pts may require additional surgical interventions such as diverting colostomies or urinary diversions to avoid further contamination.
- Specific complications may arise depending on the location of NF.

Nelson Syndrome

Girija Prasad Rath | Vikas Chauhan

Risk

- Incidence: Reported in 8–44% of pts following bilateral adrenalectomy for Cushing disease
- More likely in pts with younger age and pregnancy

Perioperative Risks

- Lyte imbalances
- DI
- Vision loss
- Challenges specific to type of surgery

Worry About

- Panhypopituitarism
- Volume status imbalance
- Steroid supplementation

Overview

- The first case of Nelson syndrome was reported in 1958 by Dr. Del Nelson, who named this condition.
- It is also known as post-adrenalectomy syndrome and occurs as result of bilateral adrenalectomy performed for treatment of Cushing disease.
- It can develop as long as 24 y after a bilateral adrenalectomy, but the mean age of presentation is 15 y after the adrenalectomy.
- Nelson syndrome differs from Cushing disease in that the hypercortisolism cannot occur because of the adrenalectomy, and a pituitary tumor is known to be present.
- The pathophysiology of Nelson syndrome is poorly understood. It possibly occurs due to release of the negative feedback that would otherwise suppress high cortisol levels, in turn leading to restoration of CRH production by the hypothalamus going on to stimulate corticotroph neoplasia.
- The signs and symptoms of Nelson syndrome are due to the effects of raised ACTH (more than 154 pmol/L) and the pressure of the tumor on surrounding structures, inhibiting release of other pituitary hormones, and thereby leading to panhypopituitarism. The symptoms include hyperpigmentation, headache, and visual disturbances. Increased urine output may suggest development of DI.
- ACTH levels are markedly elevated in Nelson syndrome and because of an exaggerated ACTH response to CRH.
- Other tests for hormones to assess panhypopituitarism may be done. Thyroid-function tests, prolactin levels, and IGF-1 IGF-BP3 measurement; measure gonadotropin levels in adolescents showing pubertal arrest and urine osmolality and specific gravity to rule out DI.
- No clear guideline is provided for periop glucocorticoid replacement, although serum cortisol values less than 3.6 µg/dL should be treated with supplementation.

Etiology

- Exact pathogenesis remains unclear.
- After a bilateral adrenalectomy is performed, cortisol levels are no longer normal, and it increases CRH production.
- The loss of partial cortisol inhibition because of the adrenalectomy allows the pituitary tumor to secrete tremendous amounts of ACTH and may promote growth of the adenoma.

Usual Treatment

- Radiotherapy
- Surgical resection of pituitary tumor, transsphenoidal or transcranial
- Pharmacologic agents along with surgery: pasireotide, temozolomide, and octreotide

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Eyes	Reduced visual acuity	Ophthalmoscopy	Visual field testing
CV	Hypovolemia, hypotension, and tachycardia		Orthostatic hypotension Volume status and BP	Steroid supplementation
GI	Hyperaldosteronism	Anorexia, N/V		Hypokalemia, hyponatremia, hypovolemia
ENDO	Increased ACTH Decreased LH and FSH Decreased TSH Decreased GH	Increased pigmentation Decreased sexual function and amenorrhea Increasing weight, cold intolerance, depression, constipation, and sleep disturbances Fatigue	Diminishing secondary sexual features Myxedema	FSH, LH levels TSH, free T_3, T_4, IGF-1
CNS	Headache			MRI (brain)
RENAL	Decreased vasopressin	Increased UO	Decreased BP and hypovolemia	Hypernatremia, decreased urine specific gravity

Key References: Barber TM, Adams E, Ansorge O, et al.: Nelson's syndrome. *Eur J Endocrinol* 163(4):495–507, 2010; Mehta M, Rath GP, Singh GP: Anaesthesia for Nelson's syndrome, *Middle East J Anaesthesiol* 20(2):313–314, 2009.

Perioperative Implications

Preoperative Preparation

- Serum lyte correction
- Fluid replacement and volume status management
- Hormonal replacement to treat panhypopituitarism
- Periop steroid supplementation
- DI management, if present

Monitoring

- Invasive arterial catheter
- Frequent ABGs and lytes

Airway

- Avoid succinylcholine and hyperkalemia.

Maintenance

- Maintenance of normocarbia for pituitary surgery
- Management of hemodynamic fluctuations during transsphenoidal surgery
- Titration of anesthetic agents to prepare for early extubation

Extubation

- Before extubation, ensure the pt is fully awake and able to maintain airway reflexes.
- Blood may be present in the stomach despite pharyngeal packing.

Adjuvants

- Esmolol and labetalol during epinephrine use during nasal packing

Anticipated Problems/Concerns

- Unstable hemodynamics
- Possible lyte changes and DI
- The possibility of difficult extubation with bleeding through the nose packing

Neurofibromatosis

R. Ryan Field | Zeev N. Kain

Risk

- NF-1 birth incidence: 1:3000
- NF-2 birth incidence: 1:25,000
- Schwannomatosis incidence: 1:40,000

Perioperative Risks

- Depend on tumor extent and location

Worry About

- Difficult intubation
- Intraop Htn
- Intraop tachycardia

Overview

- NF-1, formerly known as von Recklinghausen disease, is a relatively common, neurologic genetic disorder with variable clinical presentation. It involves multiple organs, such as the skin and peripheral nervous system, which serve as sites for tumors and hamartomas.
- Hallmarks include café-au-lait spots (more than 6 that are >1.5 cm in diameter), Lisch nodules (benign iris hamartomas), axillary and groin freckling, and multiple neurofibromas.
- Laryngeal and tracheal compression may occur secondary to associated tumors.

- Surgery may be indicated for NF-1 pts with tumors (e.g., neurofibromas, pheochromocytoma), tibial pseudarthrosis, scoliosis, and/or vascular abnormalities.
- NF-2, also known as MISME, is a genetic disorder with bilateral vestibular schwannomas, cataracts, hearing loss, and cranial nerve, meningioma, spinal astrocytoma, and ependymoma tumors.

Etiology

- NF-1 and NF-2 are both autosomal dominant; about 50% of cases represent new mutations.
- The gene for NF-1 resides on the long arm of chromosome 17, *17q11.2*.
- The gene for NF-2 resides on chromosome 22.

Usual Treatment

- Radiation and surgical treatment for various tumors involved

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT*	Pharyngeal compression Laryngeal compression Vocal cord and arytenoid involvement Airway obstruction	Dyspnea, dysphonia, stridor, and voice changes	Evaluation of the airway	X-ray CT of neck
CV	Renal vascular Htn Pheochromocytoma Autonomic dysfunction	Headache and perspiration		BP/HR Urinary catecholamines
RESP*	Restrictive lung disease Cor pulmonale Interstitial lung disease Hypoxemia	Exercise tolerance	Cyanosis Clubbing	CXR ECG ABG PFTs (rare)
GI	Carcinoid tumor			
GU*	Obstruction and uremia			
CNS	Mental retardation Seizures Intracranial tumors and increased ICP Paraspinal tumors			MRI of brain and spine for neuraxial technique
MS*	Kyphoscoliosis Macrocephaly Craniofacial dysplasia Cervical dislocation Pectus excavatum			X-ray of the neck

*In severe cases.

Key References: Hirsch NP, Murphy A, Radcliffe JJ: Neurofibromatosis: clinical presentations and anaesthetic implications, *Br J Anaesth* 86(4):555–564, 2001; Fox CJ, Tomajian S, Kaye AJ, et al.: Perioperative management of neurofibromatosis type 1, *Ochsner J* 12(2):111–121, 2012.

Perioperative Implications

Preoperative Preparation

- Evaluation of the airway for laryngeal, pharyngeal, and mediastinal masses in NF-1.
- Increased skeletal abnormalities including scoliosis should be considered in NF-1.
- Frequent end-organ vasculopathies impair or alter end-organ function and reserve in NF-1.
- Controversially, NF-1 may be associated with hypertrophic obstructive cardiomyopathy.

Monitoring

- Routine
- Arterial line monitoring for pheochromocytoma and/or vascular stenoses/aneurysms

Airway

- Consider awake fiberoptic intubation or awake tracheotomy if laryngeal and pharyngeal involvement or known mediastinal mass is present.

Preinduction/Induction

- Consider potential for increased ICP.
- Consider potential of vascular stenoses and/or aneurysms, including risk of ischemic infarct.
- Consider potential of restrictive scoliotic lung disease.

Maintenance

- Maintain cardiovascular stability and optimize ventilation.

Extubation

- Routine considerations

Postoperative Period

- Pain management may be critical and challenging.

Regional Anesthesia

- Asymptomatic paraspinal neurofibromas can make identification and entry into epidural and subarachnoid spaces very difficult. Preemptively carefully examine the back.
- Paraspinal and intracranial tumors are exacerbated during pregnancy.
- Consider potential for epidural hematoma, tumor trauma, and brainstem herniation.
- Recommend MRI of brain and spine for tumor assessment before using a neuraxial technique.

Anticipated Problems/Concerns

- Difficult airway
- Presence of pheochromocytoma or vascular abnormality
- Potential for increased ICP with expanding intracranial tumor
- Difficult epidural or spinal placement; potential for complications due to tumor involvement

Neuroleptic Malignant Syndrome

Lyndsay M. Hoy | Lee A. Fleisher

Risk

- Incidence of 0.01–0.02%
- Mortality rate of 10%
- 2000 cases of NMS diagnosed annually in USA hospitals
- Pharmacologic:
  - Typical/"first generation" antipsychotic
  - Rapid dose titration/switching agents/abrupt medication withdrawal/high cumulative dose
  - IM depot/IV administration
  - Multiple concurrent antipsychotics or antipsychotic with lithium/carbamazepine
- Demographic/miscellaneous:
  - Advanced age
  - Psychiatric/medical comorbidities
  - Anemia
  - Dehydration/malnutrition
  - Pt history of NMS
  - Hot climate/high ambient temperature

Perioperative Risks

- Pulm aspiration
- Cardiovascular lability
- Rhabdomyolysis

Worry About

- Potentially life-threatening if left untreated
- Increased risk of recurrence in pts requiring chronic antipsychotic therapy with Hx of previous NMS

- Increased off-label use of antipsychotics
- Differentiating NMS from serotonin syndrome, malignant hyperthermia, drug-induced extrapyramidal reactions, and substance-abuse withdrawal

Overview

- Rare, iatrogenic hypermetabolic reaction characterized by fulminant or insidious development of muscular rigidity, altered sensorium, dysautonomia, and high fever.
- Triggered by antidopaminergic agents or DA agonist withdrawal.
- More common in pts with psychiatric Hx of schizophrenia, schizoaffective disorder, bipolar disorder, mental retardation, Parkinson disease, dementia, and psychosis.
- Despite declining frequency likely due to more widespread recognition and earlier diagnosis/treatment, NMS remains a significant source of morbidity and mortality for pts taking antipsychotics.
- Shares striking clinical similarities with but is otherwise pathophysiologically distinct from malignant hyperthermia; to date, no definitive evidence demonstrating that NMS increases the risk of malignant hyperthermia under general anesthesia.

Etiology

- Central D_2 receptor antagonism triggers a cascade of disrupted DA receptor–mediated signaling pathways with resultant autonomic dysregulation and end stage hypermetabolic syndrome.
- Known triggering scenarios include DA antagonists, DA-agonist withdrawal, and GABA-agonist withdrawal.

- Once NMS is diagnosed and the triggering agent discontinued, NMS is generally self-limited, and full resolution can be expected to occur within 1 wk to 10 d, with appropriate supportive therapy.

Usual Treatment

- Dx of exclusion; rule out alternate causes of symptoms.
- Immediate discontinuation of triggering medication.
- Consider use of benzodiazepines, dantrolene, DA agonists, or electroconvulsive therapy.
- Supportive care including airway protection, hemodynamic stabilization, temperature regulation, fluid resuscitation, and lyte correction as indicated.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dystonia	Increased facial tone with involuntary contractions Excess saliva	Oculogyric crisis, trismus, blepharospasm, dysarthria, and dysphagia Sialorrhea Facial flushing	
RESP	Pulm aspiration Hypoxemia Acute pulm edema Pulm embolus	Respiratory distress Dyspnea	Lung-field consolidation Tachypnea	CXR and CT scan ABG Bronchoalveolar lavage V/Q scan
CV	Dysautonomia Reversible dilated cardiomyopathy	Diaphoresis, chest pain, dyspnea, and palpitations	Tachydysrhythmias and labile BP	ECG, ECHO, and coronary angiogram
CNS	Delirium Hyperthermia Extrapyramidal symptoms Metabolic encephalopathy	Disorientation Fever	Altered mental status and agitation Choreiform/dyskinesia	CT/MRI CSF analysis and EEG
RENAL	Myoglobinuria Acute kidney failure Metabolic acidosis	Dark-red urine	Oliguria	Electrolytes, UA, BUN, and Cr
HEME	Leukocytosis DIC			CBC Fibrinogen and coagulation

Key References: Strawn JR, Keck PE Jr, Caroff SN: Neuroleptic malignant syndrome, *Am J Psychiatry* 164(6):870–876, 2007; Mustafa HI, Fessel JP, Barwise J, et al.: Dysautonomia: perioperative implications, *Anesthesiology* 116(1):205–215, 2012.

Perioperative Implications

Preoperative Preparation

- Conduct a thorough review of home medications/inpatient regimen with particular attention to antipsychotics and confirmation of date/time of last dose.
- If concern exists for active NMS, postpone any elective procedure until pt is clinically stable.

Monitoring

- Arterial line if indicated
- Urine output for myoglobinuria

Airway

- Anticipate copious secretions w/ possible dysphagia and muscular rigidity in pts with active NMS.
- Consider full stomach precautions.

Preinduction/Induction

- Pt may exhibit exaggerated hemodynamic response to induction medications and volatile agents.

Maintenance

- Vigilant management of blood pressure and volume status
- Neuromuscular blockade to reverse severe muscular rigidity if indicated
- Diuresis

Extubation

- Keep intubated if concern for airway protection exists.

Postoperative Period

- May require a higher level of care

Anticipated Problems/Concerns

- Periop autonomic dysfunction
- Increased risk for aspiration and periop pulm complications
- Clinical presentation similar to malignant hyperthermia but with no pharmacologic crossover

Niemann-Pick Disease

Thomas Schilling | Alf Kozian

Risk

- Incidence in live births: 1:100,000-120,000
- Affects equally males and females of all ethnic groups
- NP-D type A frequent in the Ashkenazi-Jewish population
- No curative therapy, although several symptomatic manifestations are treatable
- Associated with a decrease in life expectancy, although many pts survive until late adulthood

Perioperative Risks

- NP-D pts require a multitude of diagnostic and therapeutic procedures (e.g., medical imaging, lumbar puncture, intrathecal chemotherapy injection, auditory brainstem response measurements, and skin biopsies). General anesthesia with endotracheal intubation is often required.
- Pts at increased risk of aspiration, especially those with severe lung involvement, recurrent aspiration, and chronic cough.
- Perianesthetic morbidity includes need for tracheal reintubation; pneumonitis, hypothermia, and seizures.

Worry About

- Severe visceral, pulmonary, and neurologic involvement
- Hepatomegaly, ascites, coagulation disorders, and hypersplenism with thrombocytopenia

- Alterations of liver function and in some cases, liver cirrhosis and liver failure
- Rarely causes spontaneous splenic rupture
- Recurrent respiratory infections are common; prior episodes of aspiration

Overview

- It is classified into the neurovisceral lysosomal lipid-storage disease group (types A–D).
- Two distinct entities exist: acid sphingomyelinase deficiency (type A and B) and loss-of-function mutations in either the *NPC1* or *NPC2* genes (C and D).
- Age of clinical onset varies widely.
- Broad clinical spectrum ranges from a rapidly fatal disorder in neonates to an adult onset chronic neurodegenerative disease, a mix of visceral and neurologic deficits including vertical gaze palsy, ataxia, dystonia, dysphagia, seizures, and progressive dementia.
- With systemic disease, hepatosplenomegaly can be severe.
- Lung involvement can be present and results from severe neurologic impairment and associated dysphagia, recurrent aspirations, and thoracic muscle weakness.

Etiology

- Autosomal recessive lysosomal storage disorders
- Mutations in the *SMPD1* gene (types A and B) resulting in sphingomyelinase deficiency with progressive accumulation of sphingomyelin in systemic organs and brain, and secondary accumulation of other lipids
- Historically, categorized into a severe, acute neuronopathic form (A), and a nonneuronopathic form (B), also intermediate cases
- Extremely variable degree of systemic involvement depending on age of discovery; retarded body growth (common); often delayed skeletal age and puberty
- Vomiting and diarrhea in first months of life; failure to thrive often motivating a first consultation, leading to the discovery of a usually prominent hepatosplenomegaly (80% of pts); additionally, hypotrophy, dysmorphia, brownish skin pigmentation, macular halo, and cherry-red spots, which are typical
- Further hypotonia, progressive loss of acquired motor skills, increasing spasticity, abolished deep-tendon reflexes, joint/limb pain, bruising, headache, abdominal pain, and diarrhea
- NP-D type C, which involves alterations in the intracellular transport of endocytosed cholesterol and accumulation of unesterified cholesterol in lysosomes and endosomes due to mutations in either the *NPC1* (95% of families) or *NPC2* genes
- Hypercholesterolemia with marked decrease of HDL cholesterol (common); complex lipid storage observed in extra neural tissues
- Pulmonary involvement:
  - Common at all ages, with widely variable impairment of respiratory function ranging from dyspnea on exertion (frequent) to oxygen dependency
  - CXR: Reticulonodular pattern, interlobular septal thickening, ground-glass density; in adults with a long follow-up, pulm involvement (often the main complaint)

Usual Treatment

- Management remains largely symptomatic.
- Gastrostomy is often required.
- Splenectomy is seldom necessary and should be avoided.
- Pts who progress to liver failure require liver transplantation.
- Neurologic manifestations of NP-D C: Miglustat; cataplexy often responds to protriptyline, clomipramine, or modafinil.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway difficulties Intubation problems Aspiration	Dyspnea	Barrel chest, very short neck Neck mobility diminished Degeneration of the cervical vertebral column Mental–zygomatic distance reduced Muscle contractures, extensive degeneration of bone, joint in the vertebral column	Mallampati score (limited)Thyromental distance Neck mobility
CV	Reduction of overall left ventricular function Poor diastolic function by lipid storage CAD Pulm arteriovenous fistulas Pulm Htn	Poor exercise tolerance Angina pectoris CHF symptoms	Two-flight walk 6-min walking test	ECG CXR ECHO Cath coronary angiography Spiroergometry
RESP	Decrease in lung volume and FRC Interstitial lung disease Lipoid pneumonia Recurrent aspiration Hypoxemia	Cyanosis, clubbing, fine crackles Recurrent lung infections Dyspnea (increasing breathlessness) Chronic cough Respiratory failure	Inspection, auscultation	Chest x-ray Body plethysmography Lung biopsy High-resolution CT Flexible bronchoscopy Broncho-alveolar lavage
HEPAT/GI	Hepatomegaly, liver damage Drop in hepatic blood flow Changes in drug metabolism Coagulopathy Hepatopulmonary syndrome Splenomegaly Neonatal cholestatic jaundice	Dysphagia Ascites Gastroparesis Anterior abdominal wall elevation	Inspection, palpation	US scan of the abdomen Liver enzymes Thrombocyte count and function Routine lab tests often not helpful
RENAL/ENDO	Nothing specifically known			
CNS	Neurodegeneration Progressive dementia	Transient consciousness Vertical supranuclear gaze palsy Seizure Cerebellar ataxia Dystonia, dysphagia	Neurologic/mental status Cognitive function tests	EEG Brain MRI Auditory brainstem potential Lumbar puncture Psychometric assessment
PNS	Progressive damage to the PNS with demyelization	Motor pathologies Horizontal saccadic eye movements Speech difficulties Cataplexy	PNS examination	Clinical exams: HSEM, cognition, ambulation, swallowing, hearing deficit, and speech delay Muscle tone and strength tests, motor reflexes, assessment of movement, and swallowing testing
MS	Anatomic disorders	Generalized developmental disturbances		

Key References: Patterson MC, Hendriksz CJ, Walterfang M, et al.: Recommendations for the diagnosis and management of Niemann-Pick disease type C: an update, *Mol Genet Metab* 106(3):330–344, 2012; Miao N, Lu X, O'Grady NP, et al.: Niemann-Pick disease type C: implications for sedation and anesthesia for diagnostic procedures., *J Child Neurol* 27(12):1541–1546, 2012.

Perioperative Management

Preoperative Preparation

- Assess extent of visceral and neurologic involvement, as well as the cardiac and volume status.
- Check liver enzymes, lipids, and respiratory function, as well as the coagulation status and function of thrombocytes.
- Pt with severe lung disease, recurrent aspiration, and chronic cough at risk of aspiration; consider antacid therapy.
- Check for possible regional anesthesia.
- Majority are ASA class III.
- Maintain anticonvulsants.

Monitoring

- Airway and oxygen saturation
- Noninvasive blood pressure

- ECG: Myocardial ischemia; possible CHF if volume overload and LV dysfunction is present
- Temperature monitoring

Induction

- Consider rapid sequence induction.
- Swallowing secretions: Consider anticholinergic agents.
- Cave hypovolemia; CV dysfunction makes BP and HR fluctuate.

Maintenance

- Inhalational anesthetics (sevoflurane and nitrous oxide) and sedatives (midazolam and propofol) were used.
- >2.0 MAC sevoflurane and hyperventilation can be associated with epileptiform activity on EEG.

Extubation

- CV and pulm-drive insufficiencies (common with neuropathies)
- Aspiration risk

Adjuvants

- Regional/neuraxial anesthesia possible despite neurodegeneration

Postoperative Period

- Possible tracheal reintubation, hypothermia, and seizure
- Can keep pt in ICU/PACU overnight

Anticipated Problems/Concerns

- Increased intraabdominal pressure and decreased FRC
- Decreases in oxygen saturation
- Hypothermia
- Gastroparesis

Noonan Syndrome

Jiri Horak | Alexander Fort | Lee A. Fleisher

Risk

- Incidence between 1:1000-2500 live births
- Incidence consistent worldwide
- Equal distribution between genders

Perioperative Risks

- Airway
- Cardiovascular
- Hematologic
- Infectious

Worry About

- Difficult airway
- Cardiovascular complications
- Bleeding
- Endocarditis

Overview

- Key features include facial anomalies, neck webbing, short stature, chest deformity, spinal deformity (e.g., scoliosis, atlanto-occipital fusion, cervical fusion), congenital heart disease (e.g., pulmonic stenosis, hypertrophic obstructive cardiomyopathy), bleeding diathesis, mental retardation.
- Congenital heart disease may include pulmonic stenosis (in 80% of cases); hypertrophic obstructive cardiomyopathy (20–30%). Less common lesions include ventricular septal defect, tetralogy of Fallot, aortic stenosis, coarctation of the aorta, Ebstein malformation, total anomalous pulm venous return, and patent ductus arteriosus.
- Increased incidence of cancers, especially hematologic, with roughly a 3.5-fold increased risk.

Etiology

- Primarily an autosomal dominant disorder; however, sporadic cases are reported.
- Mutation on the PTPN11 gene on chromosome 12 in roughly 50% of cases.
- Also associated with mutations in genes that are part of the RAS/RAF/MEK/ERK signal transduction pathway (regulators of cell growth).

Usual Treatment

- Repair congenital cardiac defects.
- Administer growth hormone.
- Treat hematologic disorders.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Facial deformity Atlanto-occipital or cervical instability or fusion	Instability Pain	Limited neck range of motion	Cervical spine x-ray
RESP	Chest wall deformity Restrictive lung disease Pulm edema	Dyspnea	Tachypnea Crackles	CXR CT scan PFTs ABG
CV	Congenital heart disease (repaired or unrepaired, most commonly HOCM or PS)	Dyspnea Orthopnea Exercise intolerance Syncope Arrhythmias	Tachycardia Murmur S_3/S_4 Displaced PMI JVD	ECG ECHO Cardiac cath
GI	Hepatic congestion Hepatosplenomegaly Decreased appetite Gastroparesis	Abd pain N/V Failure to thrive Weight loss	RUQ tenderness/fullness Jaundice	LFTs RUQ US Albumin/prealbumin
ENDO	Growth hormone supplementation	Glucose intolerance Hypertension Dyslipidemia		BMP Lipid profile
CNS	Mental retardation Seizures	Developmental delay		Mental status exam
HEME	Bleeding disorder Hematologic malignancy	Easing bruising Epistaxis Bleeding gingiva GI bleed Fatigue	Pallor Petechiae Hematochezia Melena	CBC with differential Coagulation profile Bleeding time Fibrinogen vWF Factor levels
MS	Scoliosis Joint laxity	Restrictive lung disease	Spinal curvature	Lumbar/thoracic spine x-ray PFTs
METAB	Lyte abnormalities from zmalnutrition	Fatigue Weight loss ECG changes		BMP/Mg/Ph ECG

Key Reference: Aggarwal V, Malik V, Kapoor PM, et al.: Noonan syndrome: an anesthesiologist's perspective, *Ann Card Anaesth* 14(3):214–217, 2011.

Perioperative Implications

Preoperative Preparation
- Assessment of cardiac function (ECG, ECHO).
- Pulm function testing if significant chest deformity.
- Thorough airway evaluation.
- Prophylaxis for potential subacute bacterial endocarditis.
- Appropriate blood products and adjuncts should be available (e.g., desmopressin).
- Prevent preop anxiety.

Monitoring
- Arterial line, central line, and PA cath if indicated
- TEE if there are significant cardiovascular abnormalities

Airway
- Advanced airway equipment must be available, including fiberoptic bronchoscope.

Preinduction/Induction
- In case of hypertrophic obstructive cardiomyopathy, maintain preload/afterload and avoid tachycardia.
- Developmental delay may make IV placement or awake intubation challenging or impossible; consider preop sedatives when appropriate.

Maintenance
- Inhalational agents or total IV anesthesia depending on the case

Extubation
- Assess adequacy of ventilation/oxygenation if significant cardiac/pulmonic abnormalities.

Adjuvants
- Regional anesthesia when appropriate; thorough hematologic assessment prior to any intervention

Postoperative Period
- Cardiovascular monitoring
- Close monitoring for bleeding
- Increased risk for subacute bacterial endocarditis

Anticipated Problems/Concerns
- In many pts, Noonan syndrome may go undiagnosed or misdiagnosed; therefore thorough preop assessment is vital.
- Thorough cardiovascular assessment is vital, as many pts undergo surgery for congenital cardiac defects.
- Difficult airway is common; advanced airway devices must be readily available.

Obsessive-Compulsive Disorder

Andrew J.D. Cameron | Bradley K.W. Ng

Risk
- Lifetime prevalence is 1–3%, with bimodal onset in childhood and late adolescence/early adulthood
- Males and females affected equally

Perioperative Risks
- Drug interactions, notably risk of serotonin syndrome in pts on serotonergic agents such as SSRIs and clomipramine
- Anxiety/panic attacks
- OCD-related behavior interfering with preop and postop instructions

Worry About
- Serotonin syndrome
- Coexistent psychiatric illness
- Anxiety/panic attacks
- Behaviors triggered by OCD complicating recovery (e.g., noncompliance with bedrest, interference with dressings.)
- Nutritional status if coexistent with an eating disorder

Overview
- Characterized by obsessions and/or compulsions (both usually occur together).
- Obsessions: Repetitive and persistent behaviors and unwanted thoughts or urges that pts recognize as being a product of their own mind, which cause distress and/or anxiety.
- Compulsions: Ritualistic behaviors or mental acts, which aim to either ab olish or decrease the obsessions or prevent a dreaded event; they are excessive and not realistically relevant to the adverse event.
- Often associated with comorbid psychiatric illness (approximately 50%), including anxiety disorders, mood disorders, body-dysmorphic disorder, eating disorders, and alcohol dependence.
- Low rates of remission if untreated; significant numbers of pts do not receive adequate and evidence-based pharmacotherapy and psychotherapy.

Etiology
- Twin/family studies show some genetic predisposition.
- Exact etiology remains unclear.

Usual Treatment
- Psychotherapy; The best evidence is for exposure and response-prevention therapy and cognitive therapy.
- SSRIs (usually at high doses): Fluoxetine, paroxetine, sertraline, and fluvoxamine.
- Clomipramine, a tricyclic antidepressant.
- For treatment-resistant cases: Other antidepressants, antipsychotics (e.g., risperidone, aripiprazole) and anticonvulsants (e.g., lamotrigine, topiramate), which are used off license.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Anxiety	Subjective anxiety	Vigilance, tachycardia	Not required

Key References: Grant JE: Obsessive-compulsive disorder, *N Engl J Med* 371(7):646–653, 2014; Buckley NA, Dawson AH, Isbister GK: Serotonin syndrome, *Br Med J* 348:g1626, 2014.

Perioperative Implications

Preoperative Preparation
- Review mental status, including any concurrent psychiatric illness.
- Review nutritional status if pt has a concurrent eating disorder.
- Review pt's psychiatric medications, including high-dose antidepressants.
- Review pt's ability to follow and comply with any preop instructions and preparations; a family member or support person may be helpful in some circumstances.
- Ask about stressors and discuss how to minimize them (e.g., pt obsessed with cleanliness could be shown equipment in sterile packs).
- Ask about compulsive behaviors and plan accordingly (e.g., pts with a background of excoriation [skin picking] may interfere with their wounds; wounds should be dressed in a way that makes them inaccessible to pt).
- Consider liaison with a psychiatrist or a psychiatric review in pts with severe OCD or if a number of challenges are identified preop.

Intraoperative Period
- Pts on medication for OCD are at risk of serotonin syndrome if given a second serotonergic medication. These include opioids (fentanyl, hydrocodone, meperidine, morphine, oxycodone, and tramadol), cocaine, methylene blue, and ondansetron.
- Consider strategies to avoid opioids (regional anesthesia and nonopioid analgesics).

Postoperative Period
- If pt is on serotonergic medication, monitor for serotonin syndrome; watch for altered mental state (e.g., agitation, confusion), neuromuscular excitation (e.g., clonus, hyperreflexia, myoclonus, rigidity), and autonomic excitation (e.g., hyperthermia, tachycardia).
- In addition to the above-listed drugs, avoid dextromethorphan and ergotamine.
- Consider closer nursing observation and/or a private room.
- Consider short-term anxiolytics or sedation if the pt's rituals or anxiety pose a major barrier to recovery.
- Consider early involvement of a psychiatrist or psychiatric team if available in the hospital.

Anticipated Problems/Concerns
- Preop anxiety: Consider premedication with midazolam 7.5 mg PO 1 h before the procedure.
- Postop anxiety/panic attacks or problematic rituals: Administer prn benzodiazepines and arrange a psychiatry consultation.
- Serotonin syndrome if the pt is on medication; the risk is generally higher than for pts being treated for anxiety/depression due to the high doses required to treat OCD.

Occipital Encephalocele

James Joseph Thomas

Risk

- Most frequent type of encephalocele in North America and Western Europe
- Incidence in North America: 1:3000–10,000 live births
- Worse prognosis compared with frontal encephaloceles

Perioperative Risks

- Seizures
- Hydrocephalus
- Cranial nerve deficits
- Poor feeding
- Spasticity
- Blindness

Worry About

- Positioning concerns
- Coexisting congenital anomalies, especially renal and facial
- Difficult airway
- Elevated ICP
- Body temperature changes
- IV access
- Blood loss
- Hemodynamic disturbances

Overview

- Herniation of brain, meninges, and/or CSF through a skull defect (cranium bifidum) that is usually covered with skin
- One of the three most common neural tube defects
- Cranial nerve deficits, poor sucking and feeding, spasticity, blindness, seizures, or developmental delay
- May be associated with hind-brain anomaly (Chiari III malformation), in which herniating occipital/cerebellar tissues distort the posterior fossa structures
- Associated conditions include:
  - Hydrocephalus (30–50%)
  - Corpus colossal abnormalities (18%)
  - Cerebral dysgenesis (13%)
  - Seizures
  - Meckel Gruber syndrome
  - Occipital encephalocele
  - Microcephaly
  - Microphthalmia
  - Polycystic kidneys
  - Ambiguous genitalia
  - Polydactyly
  - Cleft lip and palate
  - Other malformations

Etiology

- Unknown
- Isolated encephaloceles showing no familial inheritance
- Possibly a syndrome with an autosomal recessive pattern or inheritance
- Usually obvious at birth, with many diagnosed prenatally using fetal US or fetal MRI

Usual Treatment

- Requires surgical management, usually in infancy, by a pediatric neurosurgeon directed by the type of neural tissue protruding from the skull.
- Gliotic and malformed neural elements can be amputated.
- Staged repair may be necessary to return normal tissue to the cranial vault.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway Difficult positioning Cleft lip/palate Microphthalmia Microcephaly	Obstruction and location Mass location Poor suckling Small head	Chin and tongue size Lips and mouth Small eyes	 CT, MRI
RESP	Respiratory failure Aspiration	Dyspnea Dyspnea	Tachypnea, desaturations Tachypnea, desaturations	CXR, CT, ABG CXR
CV	Congenital anomalies	Sweating, poor feeding, lethargy	Murmur, cyanosis	ECG, ECHO
GI	Dysphagia Aspiration	Emesis Respiratory failure	Feeding tube Tachypnea, desaturations	Swallow study Swallow study, CXR
CNS	Seizures Increased ICP	Irritability, lethargy Irritability, lethargy	Cushing triad	EEG, LP CT, MRI, LP
RENAL	Polycystic kidneys			US, lytes
MS	Polydactyly	Extra fingers and toes		

Key References: Alexiou GA, Sfakianos G, Prodromou N: Diagnosis and management of cephaloceles, *J Craniofac Surg* 21:1581–1582, 2010; Mahajan C, Rath GP, Dash HH, et al.: Perioperative management of children with encephalocele: an institutional experience, *J Neurosurg Anesthesiol* 23(4):352–356, 2011.

Perioperative Implications

Preoperative Preparation

- Thorough Hx and PE
- Availability blood products

Monitoring

- Arterial line.
- Two large IVs; consider a central line if IV access is inadequate.
- UP.
- Temperature monitoring.
- Prone positioning.
- Blood glucose.

Airway

- Potentially difficult mask ventilation and intubation; have difficult intubation equipment immediately available
- Supine positioning can be difficult; may need to secure the airway in a lateral position or with the pt elevated and heavily padded to avoid compression of the sac.

Preinduction/Induction

- Maintain spontaneous ventilation.
- Mask induction may be preferred.

Maintenance

- Sudden CSF leaks can cause severe hemodynamic instability and electrolyte imbalances.
- Sudden ICP changes can occur and can result in cardiac arrest.
- Maintenance of normothermia is imperative.
- Pneumocephalus can cause delayed wakening.

Extubation

- Extubate awake in the OR versus intubating in the ICU

Postoperative Period

- Monitor for hydrocephalus and increased ICP.
- Maintain normothermia.
- Maintain glucose control.
- Structural derangement of the respiratory control center can contribute to apnea.

Anticipated Problems/Concerns

- Ongoing concern for hydrocephalus; the pt may require a VP shunt.
- Ongoing concern for seizures; consider prophylaxis with anticonvulsants.
- Developmental delay is more common with sacs containing brain tissue; expect worse prognosis for occipital encephaloceles.
- Brainstem dysfunction can occur resulting in apnea and/or gastric aspiration due to a lack of gag reflex.
- Metabolic and electrolyte disturbances, hemodynamic instability, and septic shock can contribute to nonresuscitable cardiac arrest in these pts.

Occlusive Cerebrovascular Disease

Lashmi Venkatraghavan

Risk

- Worldwide, 15 million people suffer a stroke each year.
- Prevalence of stroke in USA: Approximately 3%.
- Incidence of stroke in USA: 795,000 annually, including 600,000 new cases and 115,000 recurrences.
- China has the highest rates of mortality (19.9%), followed by Africa and South America.

Perioperative Risks

- Risks for stroke:
  - Cardiac and carotid surgery: CABG = 1–5%; CEA < 3%
  - Noncardiac surgery: Major general surgery 0.08–0.7%; orthopedic 0.2–0.9%; major peripheral vascular reconstruction = 0.3–3%

Worry About

- Cerebral ischemia
- Myocardial ischemia (CAD, the leading cause of morbidity following CEA)
- Cognitive decline (long-term effects of poor perfusion)
- Control of coexisting Htn, DM, CAD, and OSA

Overview

- Two main clinical presentations:
  - Pts with known occlusive CVD undergoing carotid or cerebral revascularization; risk factors include CAD/CHF; stroke in evolution, frequent TIAs; severe Htn; stenosis; COPD; OSA, diabetes, and poor cerebral collateral flow; age >70 y; and intraluminal thrombus. Criteria for pt selection and acceptable periop morbidity and mortality rates are now well established for CEA and carotid stenting.
  - Pts with known or possible CVD presenting for other surgery; risk factors vary with age and type of surgery. The peak incidence of periop stroke is on postop d 2, and the median is between 2–9 d. Periop stroke carries higher mortality than stroke does in nonsurgical settings (26% vs. 12.2%). In pts with previous stroke, mortality rate after periop stroke is around 87%.

Etiology

- Most common cause of occlusive CVD is atherosclerosis that can be divided into three main categories of conditions: extracranial carotid artery (15–20%), intracranial cerebral arteries (10%), and vertebrobasilar arteries (8%).
- Nonatherosclerotic causes of occlusive CVD include fibromuscular dysplasia, cervical artery dissection, moyamoya disease, and vasospasm.
- Risk factors incl age, Htn, DM, smoking, and OSA.
- High incidence of concomitant CAD, PVD, and OSA.
- Two main mechanisms of ischemia are thromboembolism and hemodynamic.

Usual Treatment

- Medical treatment: Smoking cessation, BP control (target is <140/90 mm Hg), statins (LDL <100 mg/dL), and antiplatelet drugs (especially ASA, clopidogrel)
- Interventional:
  - Surgical: CEA, vessel-to-vessel bypass for intracranial stenosis
  - Endovascular: Intraarterial thrombolysis with or without mechanical thrombectomy, angioplasty with or without stenting

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Possible positional cerebral ischemia	Sx of cerebral ischemia with head movements	Neck ROM	
CV	Htn Vasculopathy LV dysfunction and CHF	Exercise tolerance Angina, MI, CHF Claudication	Arterial BP S_3 Peripheral pulses	ECG, CXR ECHO Stress test
RESP	COPD caused by smoking Irritable airway OSA	Dyspnea Chronic cough Smoker	Wheezing Accessory muscles	CXR? ABG? PFTs, sleep studies
ENDO	Possible diabetes			Glucose
RENAL	Possible nephropathy	Diabetes, Htn		Cr, urea
CNS	Cerebral ischemia	TIA, stroke	Neurologic deficits	Duplex US Angiogram (CT, MR, or conventional), PET, or CT perfusion study

Key References: O'Brien M, Chandra A: Carotid revascularization: risks and benefits. *Vasc Health Risk Manag* 10:403–416, 2014; Chui J, Manninen P, Sacho RH, et al.: Anesthetic management of patients undergoing intracranial bypass procedures. *Anesth Analg* 120(1):193–203, 2015.

Perioperative Implications

Preoperative Preparation

- Neurologic assessment.
- Optimized control of coexisting Htn, CAD, diabetes, and COPD.
- Establish pt's normal BP range.
- Preop antiplatelet therapy for pts undergoing endovascular treatment.

Monitoring

- Arterial catheter and ST-segment monitoring.
- Consider neurologic monitor for CEA or intracranial bypasses: EEG, SSEP, transcranial Doppler, cerebral oximetry, or regional anesthetic (CEA) with the awake pt (if practical).
- Carotid angioplasty with stent is usually performed with the pt awake, whereas intracranial angioplasty is performed under GA.
- Conscious sedation has better outcomes than GA for intraarterial thrombolysis and mechanical thrombectomy for acute stroke.

Induction/Maintenance

- Maintain hemodynamic stability based on preop BP range.
- Maintain normocapnia based on preop pH and $PaCo_2$.
- Intraop anticoagulation and neuroprotection if indicated.
- Light IV sedation often administered during angioplasty.
- Embolic stroke or severe, vagal-mediated bradycardia can accompany carotid dilation during angioplasty.

Extubation

- Smooth emergence: avoid straining on ETT.
- Be prepared to manage hemodynamic instability and airway during emergency neuro assessment.

Postoperative Period

- Adequate analgesia and supplemental O_2.
- Awake pt allows early and frequent neurologic evaluation.
- Monitor airway/neck circumference.
- Avoid postop cerebral hyperperfusion; treat hypertension aggressively.

Anticipated Problems/Concerns

- Most pts with CVD also at high risk for CAD and often need CABG: hence, the controversy on the combined versus staged approach to CABG and CEA. Recent evidence suggests that the combined approach remains an option.
- Timing of surgery after TIA or stroke: Impaired cerebral autoregulation and vasomotor reactivity to CO_2 usually persists up to 6 mo after acute stroke. Nonurgent surgeries should be delayed for 3–6 mo after ischemic stroke. For urgent surgeries, meticulous BP management with monitoring for cerebral ischemia is indicated.
- Carotid revascularization can be performed within 2 wk of an ischemic event except in pts with large hemispheric infarction who are at risk for reperfusion injury or hemorrhagic conversion. These procedures should be delayed for a period of 6 wk or longer.
- Caution regarding use of succinylcholine in pts with previous paretic CVA.

Opitz-Frias Syndrome (The G Syndrome)

Roberta Hines

Risk

- Overall incidence not reported
- Very rare congenital disorder

Preoperative Risks

- Very high risk of recurrent pulm aspiration; hypoplasia of both pulm and vascular components of one lung (pulm hypoplasia)
- High mortality rate in infancy

Worry About

- NM dysfunction of laryngoesophageal apparatus
- Laryngotracheoesophageal cleft or fistula
- Difficult tracheal intubation due to assoc craniofacial deformity
- Assoc congenital anomalies (Htn, hypospadias, wide eyes, cleft lip, cleft palate, cryptorchidism, imperforate anus, cardiac deficits)

Overview

- Also known as the hypospadias-dysphagia syndrome.
- Emergency presentations are for cardiopulmonary resuscitation, upper respiratory obstruction, severe respiratory stridor, regurgitation, aspiration.
- Presence of one hypoplastic lung.
- Laryngeal hypoplasia.
- Laryngotracheoesophageal cleft or fistula.
- Anticipate very difficult tracheal intubation.
- Thorough preop cardiac evaluation; need to assess for cardiac abnormalities (possible ECHO).
- Any male infant presenting for tracheoesophageal fistula with genital defect should be suspected.
- Classically: Weak, hoarse cry

Etiology

- X-linked recessive inheritance.
- Autosomal dominant inheritance or new mutation.
- Partial male sex limitation.
- Autosomal recessive inheritance, high parenteral consanguinity.
- Females can be equally or nearly as severely affected as males.

Usual Treatment

- Prophylactic gastrostomy
- Feeding jejunostomy
- Cervical esophagostomy if infant is unable to swallow
- Prophylactic antibiotics (for pulm infection)

Assessment Points

System	Effect	Assessment by Hx	PE	Tests
HEENT	Cleft lip/palate (35%) Ankyloglossia Micrognathia	Feeding difficulties, speech anomalies	Short lingual frenulum	
CNS	Dolichocephaly (20%) Large metopic sagittal suture and anterior fontanel	Mental dysfunction, prominent forehead	"Cone-head" Palpation	CT (if indicated)
FACIES	Hypertelorism/telecanthus (90%) Mongoloid palpebral fissures Strabismus	Mother-related disease	Large nasal bridge downslanting	Facial x-ray
CV	Congenital heart defects (40%) (ASD, VSD, PDA, coarctation of aorta)	Failure to thrive	Auscultation	ECG, TEE, ABG
RESP	Agenesis, hypoplasia of one lung Tracheoesophageal cleft, fissure Hypoplasia of vocal cord Tracheomalacia Short trachea, high carina	Polyhydramnios on delivery Coughing, choking, cyanosis Hoarse, weak cry Stridorous respirations	Auscultation Tracheal stenosis	CXR Bronchogram Esophagogram
GI	Achalasia of the cardia (70%) NM dysfunction of esophagus	Dysphagia		Esophagogram (if indicated) Cinefluoroscopy of swallowing (if indicated)
GU	Hypospadias with descended testis Ureteral stenosis or duplication		Perineal or penoscrotal	Nephrogram

Key Reference: Bershof JF, Guyuron B, Olsen MM: G syndrome: a review of the literature and a case report. *J Craniomaxillofac Surg* 20(1):24–27, 1992.

Perioperative Implications

Preoperative Preparation

- Evacuation of the stomach with NG tube (if pt has gastrectomy open to air)
- Feeding: Clear water or apple juice (standard NPO guidelines)
- Consideration of H_2 blocker
- No atropine IM or metoclopramide preop
- Sodium citrate through NG tube
- Complete cardiac evaluation
- Assessment of renal function
- Not appropriate for outpatient or same-day process
- IV access 24 h before surgery to reduce stomach content

Monitoring

- All standard monitors
- Invasive arterial pressure if indicated owing to procedure or unstable hemodynamics

Airway

- Tubes smaller than normal secondary (as assessed by age) to laryngeal hypoplasia

Preinduction

- Warm OR.
- Decompress stomach with suction.
- Atropine and succinylcholine backup.

Induction

- Maintain spontaneous respiration.
- Danger of regurgitation and aspiration requires careful inhalation induction.
- Cricoid pressure should be applied.
- Atropine 20 mcg/kg at induction to prevent bradycardia during intubation.

Maintenance

- Hand ventilation (low PPV).
- Avoid hypothermia.

Extubation

- Based on pt's lung condition and preop assessment and/or lung function

Adjuvants

- All medications can be used (no contraindication to IV or inhaled anesthesia).

Anticipated Problems/Concerns

- Regurgitation and pulm aspiration. Difficult tracheal intubation. Increased incidence of pneumothorax. High mortality rate in infancy.
- Unanticipated cardiac issues.
- Difficult to assess recovery from anesthesia owing to associated mental conditions.

Osteoarthritis

Anuj Bhatia | Philip Peng

Risk

- Most common type of arthritis with significant disease burden.
- Globally, affects 9.6% of men and 18% of women ≥60 y old and is ranked as top 11th cause of disability (global years lived with disability).
- Common presentations are pain, stiffness, and limitation of movement.
- Most commonly affected joints are the knees (41%), hips (19%), small hand joints (30%), and facet joints in the spine.

Perioperative Risks

- Associated conditions: Obesity, DM, hypothyroidism, hyperparathyroidism, and gout
- Concomitant medication: Acetaminophen, NSAIDs, COX-2 inhibitors, and intraarticular steroid injections
- Airway: Rarely affected (neck or jaw)

Worry About

- Obesity and geriatric population
- Positioning concerns due to joint pain and stiffness
- Possible associated metabolic conditions (DM and hypothyroidism) or sleep apnea
- Adverse effects of medications: NSAIDs: Platelet function; effect on cardiovascular, renal, and GI systems. Steroid injections: HPA and immunity suppression, hyperglycemia, hypertension, myopathy, osteoporosis. Acetaminophen: Liver function. Opioids: Daily analgesic requirements may need to be escalated throughout periop treatment

Overview

- Pathologic features of OA: Focal areas of damage to the articular cartilage, new bone formation at the joint margins (osteophytes), changes in the subchondral bone (subchondral cysts), variable degrees of synovitis, and thickening of the joint capsule
- Radiologic features of OA: Joint-space narrowing, osteophytes, subchondral cysts, intra-articular osseous bodies, and subchondral bone collapse (late finding)
- Risk factors: Age, female sex, obesity, trauma, and high-impact activities/sports

Etiology

- Autosomal dominant in some with co-segregation of OA with a mutation in type II procollagen gene

Usual Treatment

- Conservative therapy: Weight loss; PT; exercise and lifestyle change to maintain function and mobility; analgesics (acetaminophen and NSAIDs)
- Injections: Intra-articular steroid or viscosupplement injections
- Arthroscopic surgery; joint preserving (osteotomy/resurfacing) or replacement surgery

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Rare C-spine involvement	Pain	Neck ROM	Usually not needed C-spine x-rays
CV	Age-related changes	Exercise tolerance may be limited by joint changes	HR and tolerance to two-flight stair climb	ECG CXR ECHO
RESP	Sleep apnea	Daytime somnolence and morning headache		Sleep study
GI	Sensitivity to NSAIDs	Gastric upset		
ENDO	Associated diabetes			FBS
CNS	Age-related changes	TIAs or stroke		
MS	Multiple joint involvement	Joint pain	Joint ROM	
RENAL	Age-related changes			Cr

Key References: National Clinical Guideline Centre (UK): *Osteoarthritis: care and management in adults.* Clinical Guideline CG177, United Kingdom, 2014, Commissioned by the National Institute for Health and Care Excellence; Zhang Y, Jordan JM: Epidemiology of osteoarthritis, *Clin Geriatr Med* 26(3):355–369, 2010.

Perioperative Implications

Preoperative Preparation

- Common surgical procedures: Arthroscopy and arthroplasty
- IV access, airway management, and neuraxial anesthesia: May be difficult
- Checking platelet function
- Consideration of regional anesthetic techniques
- Evaluation for periop steroid supplementation in pts who have received multiple steroid injections recently

Monitoring

- Routine

Airway

- Assess neck ROM.

Induction

- Age-related considerations: elderly pts may have slow circulation times, CV disease, and fluctuations in BP.

Maintenance

- Position with consideration of other joint involvement.

Extubation

- No special considerations

Adjuvants

- Elderly pts may be more sensitive to opioids; NSAIDs may be contraindicated.

Postoperative Period

- Consider continuous regional technique with local anesthetic and/or opioids for pain management.

Anticipated Problems/Concerns

- Usually neck and airway normal
- Concomitant risk factors, especially obesity and aging
- Often involving several joints with pain and decreased ROM
- Regional anesthesia preferable over general anesthesia

Osteogenesis Imperfecta

Klaus Morales dos Santos

Risk

- Incidence: OI occurs in 1:10,000-20,000 live births.

Perioperative Risks

- Owing to the fragility of bones, caution is needed in positioning or transporting these pts.
- Excessive neck extension may lead to fracture.
- Scoliosis may cause difficulty with regional anesthesia.
- High risk for difficult intubation.
- Temperature control; tendency toward hyperthermia due to a hypermetabolic state.
- Cardiac events (pts may have cardiac abnormalities).
- Consider advanced monitoring in case of cardiac lesions (valvulopathy).
- Coagulopathy may be present owing to reduced collagen-induced platelet aggregation.

Worry About

- Difficult mask ventilation due to bone deformities
- Difficult intubation
- Temperature regulation
- Positioning and monitoring

Overview

- Inherited disease of connective tissue with tendency to bone fractures
- Brittle teeth (dentinogenesis imperfecta), blue sclerae, progressive deafness
- Bone fragility leading to major complications

Etiology

- There are now 10 types of OI; most are due to a dominant mutation in one of the two genes encoding collagen type 1 (*COL1A1* and *COL 1A2*).
- Most cases are genetically heterozygous.
- There are mild and severe forms; type II is incompatible with life.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Atlantooccipital dislocation Dentinogenesis imperfecta	Bone fragility	Abnormal oral cavity	Cervical x-ray
CV	Valvulopathies	SOB, cyanosis	Murmur, gallop	ECHO
RESP/GI	Restrictive pulm disorders		Dyspnea, thoracic deformities	CXR Spirometry
MS	Scoliosis Thoracic deformities			
CNS	Growth retardation			

Key References: Oakley I, Reece LP: Anesthetic implications for the patient with osteogenesis imperfecta, *AANA J* 78(1):47–53, 2010; Libman RH: Anesthetic considerations for the patient with osteogenesis imperfecta, *Clin Orthop Relat Res* 159:123–125, 1981.

Perioperative Implications

Preoperative Preparation
- Difficult airway management
- Peripheral IV lines difficult to place

Monitoring
- Avoid noninvasive BP monitoring because of the risk of fractures.
- Pay particular attention to temperature control and neuromuscular blockade.
- Avoid fast-acting relaxants; fasciculation can lead to bone fractures.
- Continuous temperature monitoring is mandatory under general anesthesia.

Airway
- LMA available.
- Fiberoptic bronchoscope ready to use before induction.
- A wide assortment of laryngoscope blades and ETTs should be available

Preinduction/Induction
- Sedation in a monitored setting.
- Rigid control of temperature.

Maintenance
- Monitor neuromuscular blockade.

Extubation
- Pt should preferably be extubated awake.

Anticipated Problems/Concerns
- Heart disease may be present, mainly valvulopathies; refer to cardiac assessment before inducing anesthesia.
- Airway management may be difficult.
- Repeated visits to the OR are frequent; try to avoid latex contact to prevent allergy.
- Avoid anesthesia in the ambulatory setting.

Osteoporosis

David B. Albert | Lee A. Fleisher

Risk
- Most common metabolic bone disease in USA
- All elderly pts of European descent considered at risk
- Non-Hispanic white women and Asian women at highest risk
- Estimate is that over 200 million people worldwide are at risk. Approximately 30% of all postmenopausal women in USA and Europe have osteoporosis.
- At least 40% of these women and 15–30% of men will sustain one or more fragility fractures in their remaining lifetimes.
- Female incidence >male incidence: 3:1.
- Postmenopausal women with small frames and low weight especially vulnerable.
- Risk factors for osteoporosis, such as advanced age and reduced bone density, have been established by virtue of their direct and strong relationship to the incidence of fractures; however, many other factors have been considered risk factors based on their relationship to bone density value as a surrogate indicator of osteoporosis. Risk factors include advanced age, female sex, white or Asian ethnicity, family Hx of osteoporosis, body weight less than 127 lb, amenorrhea, late menarche, early menopause, nulliparity, physical inactivity, alcohol and tobacco use, androgen or estrogen deficiency, and calcium deficiency.
- Secondary osteoporosis is attributable to diseases (hyperparathyroidism, rheumatoid arthritis, sarcoidosis, thalassemia, idiopathic scoliosis, multiple myeloma, thyrotoxicosis) and drugs (lithium, anticonvulsants, excessive alcohol use, excessive thyroxine, prolonged unfractionated heparin use [>6 mo of >15,000 IU/d], glucocorticoids, cytotoxic drugs).

Perioperative Risks
- Pneumonia
- Coexisting metabolic or endocrine disorders
- Fractures

Worry About
- Positioning because of increased risk of bone fractures
- Vertebral fractures: Vertebral compression fractures associated with increased morbidity/mortality.
- Hip fractures: Significantly increased risk of morbidity/mortality in first year after fracture; men more vulnerable than women
- Pulm function/restrictive disease, especially if kyphosis present

Overview
- Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility.
- Imbalance between bone resorption and formation causes loss of bone substance, resulting in bone fractures.
- Most common fracture sites: Vertebral body, neck of femur, distal radius, proximal humerus, pelvis.
- 1.5 million fractures due to osteoporosis occur each y: Spine (700,000), hip (300,000), wrist (200,000).
- Women who have sustained a hip fracture have a 10–20% higher mortality than would be expected for their age.
- Severe kyphosis common.
- Type I (postmenopausal) osteoporosis: Women 15–20 y after menopause; vertebral and Colles' fractures most common.
- Type II (age-related) osteoporosis: Men and women ≥70 y; hip and vertebral fractures most common; also pelvis, humerus, and femur.
- Biphasic pattern of bone loss:
  - Slow phase occurs in both sexes beginning at age 40 y; 0.6–1% per y affecting cortical and trabecular bone.
  - Accelerated phase in women after menopause; 2–3% per y affecting cortical bone; 4–6% per y for trabecular bone.

Etiology
- Insufficient accumulation of bone mass during skeletal growth.
- Age-related factors: Decreased bone formation at cellular level begins in the fourth decade and becomes more severe with age. Age-related increase in parathyroid function with age-related decrease in calcium absorption.
- Menopause: Accelerated phase of bone loss results from estrogen deficiency.
- Sporadic factors: Twofold increased risk with cigarette smoking and high alcohol consumption.

Treatment
- Vitamin D and calcium.
- SERMs: Raloxifene.
- Bisphosphonates: Alendronate, risedronate.
- Human recombinant PTH: Teriparatide.
- Calcitonin.
- Discontinue glucocorticoid (if osteoporosis due to chronic use).
- Surgical stabilization of fractures: Kyphoplasty/vertebroplasty for spinal fractures; ORIF for fractures of the hip or wrist.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Osteoporosis of skull Vertebral fractures	Pain		Skull x-ray Neck x-ray
RESP	Kyphosis	Dyspnea	Dowager's hump	Flow-volume loop ABG
ENDO	Parathyroid function Decreased in type I Increased in type II Calcium absorption decreased Metabolic disorders of vitamin D			Ca^{2+}
MS	Back pain Loss of height Spinal deformity Fractures	Acute back pain Remittance and recurrence until chronic	Dowager's hump Loss of height Multiple fractures	X-ray Vertebral bone density

Key References: O'Connor KM: Evaluation and treatment of osteoporosis, *Med Clin North Am* 100(4):807–826, 2016; Guay J, Parker MJ, Gajendragadkar PR, et al.: Anaesthesia for hip fracture surgery in adults, *Cochrane Database Syst Rev* 2:CD000521, 2016.

Perioperative Implications

Preoperative Preparation

- Move and position carefully owing to risk of bone fractures.
- Pulm function tests are indicated if kyphoscoliosis is present.
- Consider preop cervical x-rays if indicated by thorough evaluation of cervical spine. Document range of motion. Document any preop neurologic deficits.
- Detailed Hx to determine coexisting metabolic/endocrine disorders.

Monitoring

- Routine.
- Consider arterial line and frequent ABG if pulm disease or pneumonia is present.

Airway

- Cervical fractures may require neck stabilization and fiberoptic intubation.
- Acromegaly may occur with osteoporosis.

Musculoskeletal

- Vertebral collapse may make spinal/epidural anesthesia more difficult.

Anticipated Problems/Concerns

- Susceptible to fracture with routine positioning and moving.
- Restrictive lung disease if scoliosis is present may impair oxygenation.

Otitis Media

Caroline D. Fosnot

Risk

- Age: Highest incidence occurs between 6–24 mo of age; incidence subsequently declines, except for an increase at the time of school entry (between 5–6 y of age).
- Day care attendance.
- Tobacco smoke and air pollution.
- Other factors: Poor social/economic conditions, cooler seasons (fall and winter), altered host defenses, and diseases with associated craniofacial abnormalities (cleft palate and Down syndrome).

Perioperative Risks

- Active or concurrent disease: Upper or lower respiratory infections, which may increase risk of airway reactivity, laryngospasm, bronchospasm, periop O_2 requirement, and postop mechanical ventilation
- Inherent risks of associated craniofacial abnormality may predispose to airway obstruction and/or difficult airway management
- N/V related to the infection, antibiotic therapy, and vestibular imbalance
- Chronic issues:
  - Chronic or recurrent OM can cause hearing loss (usually conductive) that may lead to problems in development of speech, language, and cognitive abilities in the child. In chronic/advanced disease, preop and postop communication may become impaired.
  - Rare but serious complications include mastoiditis, petrositis, labyrinthitis, meningitis, epidural abscess, brain abscess, lateral sinus thrombosis, cavernous sinus thrombosis, subdural empyema, and carotid artery thrombosis.
  - Pts with fever ≥38°C and/or concurrent disease, including upper and lower respiratory infections and associated challenges with general anesthesia/airway manipulation.
  - Pts with associated vestibular, balance, and motor dysfunctions.
  - Pts with adenotonsillar hypertrophy or craniofacial abnormality that may predispose to more severe airway obstruction and/or difficult airway management.

Overview

- AOM is a common infectious disease. It is defined by the presence of fluid in the middle air, accompanied by acute signs of illness, and signs or symptoms of middle ear inflammation, which is restlessness, pain, agitation, and decreased hearing in younger children.
- OME is defined by the presence of middle ear fluid without acute signs of illness or inflammation of the middle ear mucosa. OME may be caused by allergies but usually occurs after AOM. Chronic OME typically leads to a conductive hearing loss.
- OM is most prevalent in infancy, but it can occur at all ages.

Etiology

- Pathogenesis: ETD usually from nasal congestion associated with an upper respiratory infection or allergic rhinitis leads to negative pressure and accumulation of secretions in the middle ear. The middle ear secretions serve as a growth medium for viruses and bacteria that colonize the upper respiratory tract resulting in suppuration and clinical signs of OM.
- Most common bacterial pathogens in OM are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.
- Most common viral pathogens in OM are RSV, rhinoviruses, influenza viruses, and adenoviruses.

Usual Treatment

- Analgesics for the pain associated with swelling of the tympanic membrane (otalgia): Ibuprofen, acetaminophen, and auralgan (topical anesthetic drops)
- Antimicrobial therapy:
  - First-line therapy is amoxicillin (80–90 mg/kg orally per d divided into 2 doses). Others incl cephalosporins (cefuroxime, ceftriaxone), macrolides (erythromycin, azithromycin), and trimethoprim sulfa sulfamethoxazole.
  - Should be administered to any child younger than 6 mo.
  - Should be administered to children 6 mo to 2 y in whom the Dx of AOM is certain or if the Dx is uncertain but the illness is severe (moderate to severe otalgia or fever ≥39°C). If the Dx is uncertain and illness is not severe, the child may be observed without treatment with antibiotics.
  - Should be administered to pts older than 2 y if the Dx is certain and illness is severe. When the Dx is certain but illness is not severe, observation alone is an option.
- AOM usually resolves in 24–72 h with appropriate antimicrobial therapy; however, fluid may persist for weeks to months despite treatment. Placement of tympanostomy tubes is performed for pts with persistent middle ear effusion or severe and recurrent episodes of otitis media (>6 antibiotic courses/y). Adenoidectomy may be indicated in selected pts, and if chronic ETD is a major contributing factor.
- Prevention is an important management strategy for OM: Minimize risk factors (smaller day care groups and decrease smoke exposure), administer vaccines (influenza and pneumococcal), and encourage breastfeeding for at least 3 mo and ideally for 6 mo (diminishes colonization of the nasopharynx by bacterial pathogens and increased negative pressure in hypopharynx drain middle ear through ET).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL	Pt age varies	Childhood vs. adult Dx	Find comorbidities	As indicated
HEENT	Nasal secretions Middle ear fluid/drainage Hypertrophic tonsils and adenoids T&A	Allergy vs. infection Acute vs. chronic OM; ear pain and ear tugging OSA, mouth breathing, snoring	Clear vs. green mucus Fever vs. afebrile, inflamed tympanic membrane (red, opacified, bulging, and immotile) vs. fluid level Inspection	Eosinophil smear Tympanogram
RESP	Cough Laryngo-tracheomalacia Pneumonia	Dry vs. wet OSA/feeding difficulty Fever, cough, dyspnea	Upper vs. lower tract symptoms Retractions and stridor Fever, tachypnea, and crackles	Pulse ox Bronchoscopy Pulse oximetry, CXR, CBC
GI	NPO status and reflux Hx	Clear vs. fatty liquid	Tolerating clears; content	None
CNS	Developmental status Hearing (usually conductive loss) Complications of untreated OM (such as meningitis)	Developmental Hx Delayed speech and cognition Fever, headache, mental status changes, photophobia	Congenital anomalies Fever, Brudzinski and Kernig signs, and meningismus	Genetic testing, Audiometry MRI, lumbar puncture, cultures
DERM	Eczema	Allergy/steroid Hx	Allergic/nonallergic rash	Skin biopsy

Key References: Hoffmann KK, Thompson GK, Burke BL, et al.: Anesthetic complications of tympanostomy tube placement in children. *Arch Otolaryngol Head Neck Surg* 128(9):1040–1043, 2002; Bowatte G, Tham R, Allen KJ, et al.: Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis. *Acta Paediatr* 104(Suppl 467):85–95, 2015.

Perioperative Implications

Preoperative Preparation

- Lower respiratory tract pathology or pneumonia may warrant further evaluation and case rescheduling; runny nose (rhinorrhea) is usually not an indication for case cancellation.
- Children: Avoid oral premed for myringotomy and PETs alone (short surgical time); consider parental presence for induction; allow comfort object in the OR; developmentally appropriate review of procedures; consider preop oral acetaminophen to give the analgesic regimen time to work.
- Adult: IV midazolam or fentanyl before induction; topical local anesthetic drops in ear may be indicated.

Monitoring

- Standard ASA monitors; skin temperature probe
- Precordial stethoscope very helpful

Airway

- Children: Inhalation induction and mask airway maintenance for straightforward cases.
- Adults: IV induction with mask airway or LMA maintenance.
- Oral and/or nasal airways as indicated.
- Preparation for intubation if obstruction is present or as the case direction changes.
- Maintenance.
- Volatile anesthetic in oxygen with NO usually sufficient.
  - 70/30 N_2O/O_2 plus 8% sevoflurane for induction, followed by 50/50 N_2O/O_2 plus 4% sevoflurane for maintenance until first tube in place.
  - Turn off anesthetics at second myringotomy to avoid prolonged anesthesia for short operation.
- Consideration of IV propofol infusion to maintain spontaneous ventilation if laryngoscopy/bronchoscopy is also planned.
- Otherwise as required for additional operative procedures after PETs are placed.

Extubation

- Routine precautions and criteria

Adjuvants

- Determined by the course and complexity of operation(s) to be performed
- PETs are frequently placed before other procedures (cleft lip/palate repair, auditory evoked potentials)

Postoperative Period

- Postop analgesia: Multimodal approach
  - Children: "Belly" analgesia first (bottle, cup, juice, comfort); consideration of nasal fentanyl and/or oral acetaminophen if rectal not given intraop
  - Adults: IV/oral analgesics as needed; antiemetic may be needed more so than in children
- Emergence delirium: Nasal or IV clonidine or dexmedetomidine (an option for children)
- Slow introduction of PO fluids; limited volume if possible
- Plans to reunite child with parent and/or proxy after pt is settled in the PACU

Anticipated Problems/Concerns

- Separation of child and parent and/or proxy: Have a guardian present for induction, oral midazolam if appropriate.
- Separation from child's comfort object: Label the object with pt's name.
- Charting vital signs and maintaining anesthesia record in a short case with much to do: An assistant or electronic medical record is helpful.
- Difficulty maintaining mask airway: Use LMA and ET intubation.
- Laryngospasm: Hold positive pressure, IM/IV succinylcholine and/or atropine, propofol if IV present, possible ET intubation
- Antibiotics: Start PIV if required.
- Ear drops applied by the surgeon: Can sting if the pH is basic.
- Unanticipated pathology includes cerumen impaction, cholesteatoma, other tumors, and ossicular dislocation.
- Excessive bleeding (ear canal trauma): Apply topical epinephrine.
- Small external ear canals: Change type of PE tube used.
- Unable to place PE tube because of prior scarring: Abandon the case.
- PE tube falls into middle ear space: Surgical retrieval is required

Pacemakers

Peter M. Schulman | January Y. Tsai | Marc A. Rozner

Risk

- In USA, over 3 million people have an implantable cardiac PM, and more than 400,000 PMs are implanted annually.
- In addition to a right atrial and right ventricular lead, some PM pts with cardiomyopathy also have left ventricular pacing capability via a transvenous coronary sinus or epicardial lead (this configuration is called CRT-P).
- Because all conventional ICDs provide antibradycardia pacing, that section of this book applies to these pts as well.*
- The incidence of pts with a PM or ICD (collectively called CIEDs) presenting for surgery is substantial.

Perioperative Risks

- Robust data are lacking; however, the presence of a PM might increase periop risk owing to
  - Associated medical problems.
  - Incorrect interpretation of device type (i.e., confusing a PM for an ICD) or events (i.e., pseudomalfunction).
  - Inappropriate periop management, especially for the pacing-dependent pt.
  - Lack of familiarity with new technology, such as LCP.

*MAGNET CAUTION: A magnet will never change the pacing mode or create asynchronous pacing in an ICD. Only ICDs from ELA (Sorin) will change the pacing rate (to 90 bpm if the battery is OK) upon magnet placement. For many ICDs (Boston Scientific and St Jude Medical),† the magnet switch can be programmed "OFF." Only ICDs from Boston Scientific and its previous companies emit ongoing tones that identify correct placement of a magnet (except subcutaneous ICDs, which only emit a tone for 1 min following magnet application). Some older ICDs from Boston Scientific (with the "GDT" or "CPI" x-ray code) can undergo permanent disabling of tachy therapy by magnet placement. Boston Scientific owns the Guidant and CPI brands, and St Jude Medical owns the Pacesetter brand.

Worry About

- Intraop decrease in pacing rate and/or asystole from EMI: induced ventricular oversensing and pacing inhibition in the pacing-dependent pt.
- Intraop increase in ventricular pacing owing to EMI entering a dual chamber PM and causing atrial lead oversensing and ventricular tracking
- Intraop increases in pacing rates resulting from activation of the "exercise sensor," whether because of direct mechanical stimulation (such as preparation of the chest) or pressure on the device (personnel leaning). Cause of this undesirable tachycardia: Possibly mistaken as inadequate anesthetic depth and inappropriately treated with antichronotropic agents
- Failure to capture (i.e., pacing output without myocardial depolarization) because of inappropriate programmed parameters (i.e., inadequate safety margin), or abrupt increase in pacing threshold from myocardial ischemia/infarction, drug administration, or electrolyte shifts. (Note that any or all chambers can undergo failure to capture with possible hemodynamic derangement, even without apparent outright pacing failure.)
- Hemodynamics being degraded by magnet* placement; magnet placement, which typically (but not always) produces asynchronous pacing at 85–100 bpm (depending upon the brand, model, and programming) and shortens the AV interval to 100 ms in some devices; magnet application to a Medtronic Micra leadless PM, which has no effect and is not programmable; magnet application to a St Jude Nanostim leadless PM, which will provide VOO (asynchronous ventricular) pacing at 100/min for 8 cycles, 90/min assuming the battery status normal, and 65/min if the battery status is "elective replacement indicated, assuming that the magnet sensor is programmed 'ON'"
- Thoracic central line placement in a pacing-dependent pt where the guidewire meets the ventricular lead causing over sensing and pacing inhibition; thoracic central line placement that could cause dislodgement of a new CIED lead because the procedure is relatively contraindicated for at least 6 wk following new lead implant. (Note that spontaneous dislodgement of coronary sinus leads occurs in over 10% of pts.)

Overview

- Indications for permanent pacing: Symptomatic failure of impulse formation (sinoatrial disease), symptomatic failure of impulse conduction (AV block), hypertrophic or dilated cardiomyopathy, and long QT syndrome
- Indications for temporary pacing (usually reversible issue): After cardiac surgery, treatment of drug toxicity resulting in dysrhythmias, certain dysrhythmias complicating MI, and bridge to permanent placement
- Nomenclature: Five positions of the North American Society of Pacing and Electrophysiology (NASPE)/British Pacing and Electrophysiology Group (BPEG) generic pacing code, with the first position referring to the chamber(s) paced (A = atrium, V = ventricle, and D = both, O = none); the second position referring to the chamber(s) sensed (A, V, D, and O), the third position identifying the response to sensed events (I = inhibit, D = dual chamber pacing and tracking); the fourth position being "R" if the CIED increases its rate in response to "exercise" or "O" if rate responsiveness is programmed off; and the fifth position identifying a multisite (A = biatrial, V = biventricular, or D = both) CIED

Etiology

- Congenital electrical disease
- Acquired: Mainly idiopathic or resulting from necessary antiarrhythmic drug therapy; neurally mediated syncope (less common indication); other etiologies include AV ablation, CAD, MI, post-cardiac surgery, dilated infiltrative, or hypertrophic cardiomyopathy, inflammatory disease, infection, neoplasm, and radiation

Usual Treatment

- An in-office PM check should occur at least annually, and telephonic checks should occur quarterly. As the PM pulse generator approaches end of life, monthly checks are recommended.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Dysrhythmia PM	PM indication	ECG/pulse	Preop PM check; CXR unnecessary to evaluate a properly working device except for multisite pacing device
	Palpitations	Exacerbating cause(s), such as arm movement, body position, or exercise	PM pocket manipulation while monitoring PM; arm movement, flexion/extension of shoulder	PM telemetry
	Exercise intolerance	Exercise tolerance, angina, symptoms of CHF	Two-flight walk	Walk test to ensure correct settings of rate response sensor
ENDO	Atrial tachydysrhythmias	Hypothyroidism, hyperthyroidism		TSH, free T_4
CNS	Other causes of syncope	TIA, CVA	Bruits	Carotid Doppler exam
Code	**Indication**	**Function**	**Perioperative Management**	
VVI	Ventricular bradycardia without need for preserved AV conduction	Demand ventricular pacing	Magnet* utilization might be helpful to produce asynchronous (VOO) pacing 85–100 bpm; Magnet* effect can depend upon programming	
VVIR	Ventricular bradycardia without need for preserved AV conduction and chronotropic incompetence	As above, but adjusts the pacing rate to allow somewhat physiologic response to exercise	PM may sense perioperative changes (e.g., mechanical stimulus or respiratory rate) and respond by increasing pacing rate; the etiology of the faster pacing rate might be misinterpreted as pain or device malfunction.	
DDD	Bradycardia when AV synchrony can be preserved	Provides more physiologic response and maintains AV concordance	Magnet* utilization might be helpful to produce asynchronous (DOO) pacing 85–100 bpm; magnet* effect can depend upon programming	
DDDR	Pts requiring AV synchrony and have chronotropic incompetence	Allows somewhat physiologic response to exercise, and maintains AV concordance	PM may sense perioperative changes (e.g., mechanical stimulus or respiratory rate) and respond by increasing pacing rate; the etiology of the faster pacing rate might be misinterpreted as pain or device malfunction	

Key Reference: Rozner MA: Implantable cardiac pulse generators: pacemakers and cardioverter-defibrillators. In Miller RD, Cohen NH, Eriksson LI, et al., editors: *Miller's anesthesia*, ed 8, Philadelphia, 2015, Elsevier, pp 1460–1486; Schulman PM, Rozner MA, Sera V, et al.: Patient with a pacemaker or implantable cardioverter-defibrillator, *Med Clin North Am* 97:1051–1075, 2013.

Perioperative Implications

Preoperative Preparation

- Before an elective procedure, a CIED care team assessment should be obtained. Comprehensive interrogation should be performed within 12 mo before scheduled surgery for a properly working PM system (or perhaps during preop evaluations for surgery expected to be hemodynamically challenging), and within 3 mo before for any CRT device. Remaining battery life, pacing behavior, and magnet response should be documented.
- Many pacing systems (either PM or ICD) have VVI pacing capability; for the pt with intact atria and an AV node, periop care must be directed to prevent the native sinus rate from falling below the VVI pacing rate because ventricular-only pacing could compromise hemodynamics.
- For the pt who is chronotropically incompetent or pacing dependent and undergoing a major procedure, consider increasing the pacing rate.
- For ventricular multisite pacing (called CRT-P), ensure the LV pacing lead is functioning. If placement of a thoracic central venous cannulation is planned in a CRT pt, the position of the LV (coronary sinus) lead on the CXR should be noted because it may be dislodged during central venous cath insertion.
- Alternate pacing modality (e.g., transvenous, transcutaneous) for the pacing-dependent pt should be available. Even though transesophageal pacing might work as backup, its use is contraindicated in CIED pts, as well as atrial fibrillation and AV nodal block.
- IV chronotropes (epinephrine, ephedrine) should be immediately available.
- Discuss monopolar ESU precautions with surgeon and nursing staff. If monopolar ESU will be used

superior to the umbilicus in a pacing-dependent pt, the PM should be programmed to an asynchronous pacing mode. Programming a PM to an asynchronous pacing mode by applying a magnet* is usually possible and sometimes appropriate; however, it is important to ensure that the magnet mode is active and understand that magnet application can occasionally have unintended and untoward consequences.

Monitoring

- Mechanical pulse wave monitoring is required. It can be accomplished with the pulse oximeter plethysmogram, any invasive hemodynamic monitoring modality, or Doppler technique.
- ECG monitoring is an ASA requirement, but EMI perturbs the signal, and monitors frequently report incorrect heart rates (both too high and too low).

Induction

- Succinylcholine or etomidate might lead to muscle fasciculations or myoclonus, resulting in pacing inhibition or increased rates. Succinylcholine-induced potassium fluxes theoretically can change pacing thresholds. No consensus has been reached about the use of these drugs, and appropriately monitored pts should receive appropriate care.

Maintenance

- Monitor ECG/pulse vigilantly.
- Monopolar ESU cautery (i.e., the "Bovie") emits radiofrequency energy, potentially causing EMI, and resulting in transient or permanent changes in PM function. The most common problem is pacing inhibition. Prevention includes the use of bipolar only ESU and pure unblended (CUT MODE) monopolar ESU, and placement of the ESU current return dispersive electrode so that the presumed current path of the ESU does not cross the pulse generator or leads. For all head and neck or contralateral breast surgery, the dispersive electrode can be placed on the shoulder contralateral to the CIED. For ipsilateral breast surgery, the dispersive electrode can be placed on the ipsilateral arm, and the wire prepped into the field if needed.
- Magnet*: Assuming that the magnet is appropriately placed and that the magnet mode is enabled, placement might be useful to convert the PM to an asynchronous pacing mode to prevent asystole from EMI-induced pacing inhibition. However, the asynchronous pacing rate (which depends on manufacturer and battery status) must be greater than the pt's own rate, or competition will result. Atrial competition usually just lowers the blood pressure, but ventricular competition can lead to R-on-T pacing and induce ventricular tachycardia. Some PMs will change the AV delay to 100 ms, which might compromise hemodynamics in some pts.

Postoperative Period

- Monitor the mechanical pulse in the postop care unit.
- Interrogation/reprogramming is required if the PM was reprogrammed before surgery, and it is advisable if monopolar ESU is employed, any problems are noted, or cardioversion/defibrillation has occurred.
- Some pts require programming changes to optimize postop hemodynamics. These changes might include increasing the pacing rate, disabling battery saving features, and adjusting the AV delay.

Anticipated Problems/Concerns

- Intraop failure to pace, most likely related to EMI from monopolar ESU
- Periop pacing and sensing threshold changes
- Risks related to associated medical problems
- Iatrogenic misadventures resulting from misunderstanding of pacing system behavior

Paget Disease

Annie Santi | Lee A. Fleisher

Risk

- Second most common bone disorder after osteoporosis.
- Most common in individuals of Anglo-Saxon descent; men > women
- Prevalence increases with age and can be as high as 9–15% in people >80 y; average age at diagnosis in USA is 58.
- Within USA, prevalence is highest in the Northeast and lowest in the South.

Perioperative Risks

- Bleeding
- Cardiovascular disease
- CNS structures at risk

Worry About

- Excessive blood loss and transfusion requirement
- Potential difficult airway
- High-output heart failure
- Increased ICP

Overview

- Disorder of markedly accelerated bone resorption with excessive formation of bone with abnormal structural integrity, which may predispose to pathologic fracture or cause impingement of surrounding structures.
- Pathophysiology: Early: Exaggerated osteoclastic activity and accelerated bone resorption, resulting in the formation of abnormal bony matrix. Meanwhile bone marrow is replaced by fibrous connective tissue and blood vessels. Late: Pagetic bone becomes large and sclerotic, with reduced tensile strength.
- Typically affected are pelvis, femur, spine, skull, tibia; disease may be limited to one bone (monostotic) or affect many (polyostotic).
- Pain is the most common presenting complaint.
- Radiographic findings include osteolytic and osteosclerotic lesions; "cotton wool" appearance of skull, cortical and trabecular thickening, hyperostosis, bowing of tibia/femur; technetium bone scan is the most sensitive diagnostic tool for determining sites and extent of PD.
- Serum alkaline phosphatase is usually elevated, and the degree of elevation correlates with extent of disease and level of pagetic activity; serum calcium and phosphate are typically normal.
- Risk of progression to neoplasm <0.5%.

Etiology

- The majority of cases are idiopathic; however, a strong genetic component exists in a subset of pts with familial PD; 15–30% of PD pts have a positive family history, which correlates with more severe disease; inheritance is typically in an autosomal dominant pattern with high penetrance.
- Individuals who have first-degree relatives with PD can have up to a 7-fold to 10-fold higher risk.
- Most common mutation is in a gene encoding a scaffold protein, with important effects on osteoclast differentiation and function.
- There is controversial evidence that a viral etiology may play a role in the development of disease in pts already genetically predisposed to PD.

Usual Treatment

- Bisphosphonates are first-line therapy, with remission rates varying from months to years depending on the agent; these drugs inhibit osteoclast activity and bone resorption; therapeutic response is measured by serum alkaline phosphatase levels.
- Calcitonin also inhibits osteoclast activity and has a more rapid onset but is overall less effective, with high rates of recurrence upon drug withdrawal; its use is mostly limited to pts intolerant of bisphosphonates or with renal insufficiency.
- Antipagetic therapy can cause hypocalcemia; adequate calcium intake and vitamin D levels must be ensured.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mandibular sclerosis	Jaw pain, mobility	Poor mouth opening	X-ray
RESP	Thoracic bony deformity	Chest wall pain		CXR, spirometry
CV	High output heart failure Valvular disease (i.e., aortic stenosis) Conduction abnormalities	Dyspnea Syncope, exertional chest pain	Tachycardia, dyspnea, edema SEM Heart block	TTE ECG
CNS	Increased ICP Spinal stenosis	Headache Radiculopathy	Papilledema	CT, MRI, X-ray
MS	Bony enlargement Reduced tensile strength of bone	Pain, fracture	Enlarged skull Bowing of lower extremities	Technetium bone scan X-ray Serum alkaline phosphatase
METAB	Hypocalcemia (typically on antipagetic drugs) Vitamin D deficiency			Ca^{2+}, Mg^{2+}, phosphate, serum 25-OHD, PTH

Key References: Tucci J: Preoperative management of Paget's disease. In Aaron RK, editor: *Diagnosis and management of hip disease,* Switzerland, 2015, Springer, pp 159–184; Tetzlaff J, Benedetto P: Skin and bone disorders. In Fleisher LA, editor: *Anesthesia and uncommon diseases,* ed 6, Philadelphia, PA, 2012, Saunders, pp 319–349.

Perioperative Implications

Preoperative Preparation

- Perform a thorough review of systems to identify coexisting disease in this older pt population and a thorough airway exam, including assessment for atlantoaxial instability; obtain radiographs if necessary.
- Check lytes, serum alkaline phosphatase; CBC for baseline hemoglobin.
- Echocardiography to assess cardiac function and potential sclerotic valvular disease (calcific disease of the aortic valve is most common); ECG to assess to conduction abnormalities; assess for ICP and obtain additional imaging if necessary.
- Ensure blood availability.
- If elective procedure, make sure that antipagetic therapy is instituted preop.

Monitoring

- Invasive BP monitoring may be appropriate.
- Neuromonitoring may be required for procedures involving the spine.

Airway

- Advanced airway equipment may be required for pts with significant cervical spine and/or mandibular disease; fiberoptic intubation may be indicated.

Preinduction/Induction

- If significant cardiovascular or valvular disease is present, aggressive BP management may be required during induction, including the use of cardiac neutral induction agents.
- Neuraxial anesthesia may be difficult if significant spine involvement is present
- Avoid medications contraindicated in pts with increased ICP.

Maintenance

- The majority of pts will be >50 y and may therefore require a lower MAC of anesthesia; there are no specific interactions between anesthetic agents and PD.
- Avoid medications that can increase ICP; can consider hyperventilation if ICP is an issue.
- Maintain normotension and avoid tachycardia in pts with cardiac disease; manage fluids carefully; maintain normothermia to decrease bleeding.

Extubation

- If pt has a difficult airway, it is crucial to avoid the need for emergent reintubation.

Postoperative Period

- Multimodal analgesia will be necessary, as some pts may have chronic pain at baseline due to pagetic activity.
- Mobility may be difficult depending on the extent of disease involvement.
- Lyte monitoring and telemetry may be indicated.
- Postop pulm toilet is important, given an elderly population, especially if there is thoracic involvement.

Anticipated Problems/Concerns

- Risk of injury during positioning.
- Sclerotic bone may be more difficult to manipulate and can prolong surgical time.
- IV access may be challenging if vessels are calcified.

Pancreatitis

Benjamin Rubin | Alexandria Piedmont

Risk

- Incidence of AP varies from 4.9–73.4 cases per 100,000 worldwide.
- Prevalence of CP has recently been estimated at 12–45 cases per 100,000, although its true prevalence is unknown.

Perioperative Risks

- Most mortality occurs with surgery for complications of severe pancreatitis: 10–30%
- Risk of nonpancreatic surgery probably dependent on severity of attack

Worry About

- Severe hypovolemia secondary to sequestration of fluid in the retroperitoneal space
- Lyte abnormalities, including hypocalcemia, hyperglycemia, and acidosis
- Systemic complications such as alcohol withdrawal, ARDS, acute renal failure, DIC, multisystem organ failure, and sepsis

Overview

- AP involves an intense inflammatory response caused by the release of activated pancreatic enzymes, with resultant tissue destruction as well as the loss of fluid and electrolytes.
- AP diagnosis requires at least two of three criteria: amylase and/or lipase >3 times the upper limit of normal, abdominal pain consistent with disease, and/or characteristic abdominal imaging.
- AP is most commonly a mild self-limited disease; it is occasionally severe, with renal, pulm, coagulatory, and septic complications.
- CP results from inflammatory cell infiltration, formation of granulation tissue and fibrosis, and loss of pancreatic parenchyma, leading to exocrine and endocrine insufficiency.

Etiology

- Acute: Most common risk factors are gallstones and excessive alcohol consumption. Others include post-ERCP, drugs, viral infections, metabolic disorders, and abdominal trauma.
- Chronic: In adults, chronic alcohol use accounts for 70% of cases. In children, genetic diseases and anatomic defects are more likely.

Usual Treatment

- In most cases, nonspecific and supportive only.
- Adequate volume replacement and correction of electrolyte abnormalities.
- Intensive care of organ system failures.
- Parenteral opioid analgesia.
- Thromboprophylaxis.
- Early nutritional support; enteral better than parenteral.
- Pts with AP and concurrent acute cholangitis should undergo ERCP within 24 h of admission.
- Rarely, judiciously timed open or endoscopic surgery to drain abscesses or debride necrotic tissue.
- For biliary AP, timing of cholecystectomy dependent on severity.
- CP is primarily managed medically.
- Endoscopic/surgical management of CP is aimed at decreasing pain and treating associated complications, such as strictures (biliary and pancreatic), ductal leaks, intraductal calculi, or pseudocysts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	Orthostatic dizziness Cold	Lying and sitting BP and HR Hypotension Oliguria	BUN/Cr Hct (hemoconcentration)
RESP	ARDS	Dyspnea Tachypnea	Chest exam may be nonspecific	ABG CXR
GI	Ileus GI bleed	N/V Hematemesis		
ENDO	Hyperglycemia			Serum glucose
HEME	DIC		Bleeding	PT/PTT, plts FSP, fibrinogen Hct
RENAL	ARF Hypocalcemia		Tetany	BUN/Cr Serum Ca^{2+}
CNS	Psychosis Encephalopathy		Mental status	

Key References: Inui K, Yoshino J, Miyoshi H, et al.: New developments in diagnosis and non-surgical treatment of chronic pancreatitis. *J Gastroenterol Hepatol* 28(Suppl 4):108–112, 2013; Tenner S, Baillie J, DeWitt J, et al.: American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastorenterol* 108(9):1400–1415, 2013.

Perioperative Implications

Preoperative Preparation

- Assess and correct volume status, hypocalcemia, hyperglycemia, and acidosis.
- For a pt with CP and intractable pain, determine current pain regimen. Consider thoracic epidural for postop pain.

Monitoring

- Consider bladder catheter to monitor urinary output.
- Consider arterial cath if there is need for blood draws or hypovolemia
- Consider CVP or PA cath for monitoring of volume status

Airway

- Routine management

Induction

- Peritoneal irritation frequently leads to ileus and increased risk of aspiration.
- Anticipate hypovolemia.

Maintenance

- CV instability due to massive sequestration of fluid; depending on severity, >10 L of isotonic fluid may be required over 24 h.

Extubation

- Will likely require postop mechanical ventilation

Adjuvants

- Multiple possible interactions of protein-bound drugs, especially if the pt is malnourished or undergoing alcohol withdrawal

Anticipated Problems/Concerns

- Pts with AP presenting for abdominal surgery are typically critically ill and require intensive care postop to manage hypovolemia, ARDS, DIC, acute renal failure, and sepsis.
- Hypoglycemia and hyperglycemia are life-threatening risks after pancreatectomy.
- Alcohol withdrawal can be life-threatening.

Papillomatosis

Christina Iliadis | Lee A. Fleisher

Risk

- Incidence of recurrent respiratory papillomatosis (RRP) in USA estimated at 4.3:100,000 among children and 1.8:100,000 among adults.
- Vertical transmission during delivery is believed to be the major mode of transmission for juvenile-onset recurrent respiratory papillomatosis (JORRP).
- Case reports show malignant transformation of RRP to squamous cell carcinoma.
- Children diagnosed with JORRP at <3 y of age tend to have more aggressive disease.
- Adult-onset recurrent respiratory papillomatosis (AORRP) typically presents in the fourth decade of life.

Perioperative Risks

- Mask ventilation or intubation difficult due to obstruction from papilloma.
- Increased risk of complete obstruction during induction or with muscle paralysis.
- Upper airway obstruction from laryngeal papillomatosis associated with pulm Htn.

Worry About

- Laryngeal papilloma prolapse causing complete airway obstruction; unable to ventilate or intubate, leading to hypoxia and cardiac arrest
- Airway fire from CO_2 laser therapy during surgical resection

Overview

- The term papillomatosis describes multiple papillomas, or benign epithelial tumors found on the epidermis and mucous membranes.
- RRP can be further classified into adult onset (>18 y of age) or juvenile onset (age <10 y).
- Papillomas are caused by HPV.
- The hope with HPV vaccine is to prevent transmission of the virus to neonates, reducing the incidence of RRP and oropharyngeal cancers associated with HPV.
- Can have highly recurrent nature in children (HPV-11), requiring repeated exposure to anesthesia and surgical treatment
- Laryngeal papillomas may be found on vocal cords, epiglottis, pharynx, or trachea.

Etiology

- Most commonly caused by human papillomaviruses 6 and 11, rarely HPV-16 or HPV-18

Usual Treatment

- No current cure.
- Surgical debulking is the standard treatment, usually requiring multiple procedures.
- CO_2 laser is frequently used. (Laser plumes can contain viral particles.)
- Adjuvant therapy includes cidofovir injections; interferon therapy (topical versus IV).
- Prevention/treatment of gastroesophageal reflux may improve control of RRP.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vocal cord dysfunction Obstruction of airway	Dysphonia, stridor Hoarseness	Stridor with no change with position RR, cyanosis, increased respiratory effort	Exam with flexible fiberoptic nasopharyngoscope Endoscopy, biopsy
RESP	Tachypnea, cyanosis if impending respiratory failure, extralaryngeal spread can present as lung nodules, pneumonia, bronchiectasis	Declining pulmonary status	Decreased BS, use of accessory muscles	CXR or CT may provide additional info
GI	Malnutrition, dysphagia	Failure to thrive, feeding difficulties	Malnutrition, dehydration	
CV	Pulm Htn, RV failure		Peripheral edema, hepatomegaly	ECG, ECHO
MS/DERM	Cutaneous lesions	Could have widespread manifestation in immunocompromised host	Warty growths	Biopsy

Key References: Li SQ, Chen JL, Fu HB, et al.: Airway management in pediatric patients undergoing suspension laryngoscopic surgery for severe laryngeal obstruction caused by papillomatosis, *Paediatr Anaesth* 20(12):1084–1091, 2010; Taliercio S, Cespedes M, Born H, et al.: Adult-onset recurrent respiratory papillomatosis: a review of disease pathogenesis and implications for patient counseling, *J Am Med Assoc Otolaryngol Head Neck Surg* 141(1):78–83, 2015.

Perioperative Implications

Perioperative Preparation

- Important to coordinate care between ENT and anesthesia.
- Perform thorough preop airway evaluation with a flexible fiberoptic nasopharyngoscope to determine severity of airway obstruction.
- Have advanced airway equipment available.
- Consider anticholinergic meds to decrease secretions and prevent bradycardia from hypoxia.
- Caution with premedication if pt hoarse or has stridor with concern for worsening airway obstruction.
- Minimize risk of gastric content aspiration: H_2 blockers, promotility agents

Monitoring

- Standard monitoring

Airway

- Have ET tubes of several sizes (generally smaller for age) on hand in case a papilloma is obstructing glottic opening.
- Prepare for tracheotomy.
- Spontaneous ventilation is preferred to avoid having to deliver positive pressure when pt is apneic; also provides increased visualization for surgeons.
- Flexible fiberoptic to visualize airway
- Other anesthetic airway techniques include jet ventilation and apneic ventilation techniques; however, there is a risk for hypoxia and hypercarbia.
- Exercise caution with paralytic agents; ensure ability to ventilate via facemask before using.

Induction

- Maintain spontaneous ventilation when possible.
- Mask induction or IV induction with propofol, lidocaine atomizer to help prevent laryngospasm.
- Be prepared for cricothyrotomy or tracheotomy if obstruction occurs.

Maintenance
- Maintain anesthesia with propofol, short-acting opioids, and/or volatile inhalational agents depending on technique used.
- Avoid paralytic agents if possible.
- Pt is usually placed in microlaryngeal suspension for surgical procedures.

Extubation
- Use caution and assess for bleeding or edema.
- Suction thoroughly and extubate awake to prevent aspiration and laryngospasm.
- At the end of procedure, ET tube is usually placed while the pt is given time to wake up from anesthesia.

Adjuvants
- Consider dexamethasone for swelling of airway mucosa from repeated intubations or resections.

Postoperative Period
- Some pts will require humidified oxygen or nebulized racemic epinephrine if stridor occurs in PACU.
- Monitor SpO_2 for desaturation; some pts may require reintubation.

Anticipated Problems/Concerns
- When using CO_2 laser therapy, must use laser-safe ETT to prevent ignition from laser.
- Use of jet ventilation is common for ENT procedures. Concern for dissemination of HPV particles into distal airway and barotrauma from jet ventilator.
- Important to debulk as much pathology as possible while preserving normal tissue to prevent scarring and airway stenosis over time with repeated surgical therapy.

Parkinson Disease (Paralysis Agitans)

Stacie Deiner | Jess Brallier

Risk
- Advanced age
- 1% of population >65 y
- No difference in distribution by gender

Perioperative Risks
- Hemodynamic instability, hypotension, arrhythmias
- Aspiration and upper airway obstruction from poor coordination of upper airway muscles
- Laryngospasm
- Postop confusion and hallucinations

Worry About
- Exacerbation of PD symptoms triggered by dopamine antagonists such as metoclopramide; also phenothiazines, butyrophenones
- Potential drug interactions: MAOIs; meperidine

Overview
- Pathophysiology: Symptoms result from the loss of dopaminergic cells in the pars compacta region of the substantia nigra reticulata. This loss upsets the normal balance between dopaminergic inhibition and cholinergic excitation.
- At least two of the following clinical manifestations are required for the diagnosis of PD: postural instability, bradykinesia, resting tremor, and rigidity. Other common features include depression, anxiety, sensory abnormalities, anosmia, autonomic dysfunction, cognitive impairment, and sleep disturbances.

Etiology
- Etiology unknown; possible genetic predisposition; possible neurotoxin involvement.

Usual Treatment
- Pharmacologic: The goal of current medical therapies is to maintain motor function and quality of life by restoring the dopaminergic/cholinergic balance in the striatum and blocking the effect of Ach.
  - Dopamine precursors
    - l-Dopa (a prodrug converted to dopamine in the brain): Mainstay of therapy, ameliorates all major clinical features of parkinsonism. Often helpful for hyperkinesias. Levodopa treatment is characterized by "on" periods of symptom amelioration and possible dyskinesias followed by "off" periods with decreasing therapeutic levels of dopamine and return of symptoms.
    - Carbidopa: Inhibits dopa decarboxylase, the enzyme responsible for the conversion of levodopa to DA. Limits breakdown of levodopa outside the CNS and increases the effectiveness of levodopa while also minimizing side effects.
    - Sinemet: Combination of carbidopa/levodopa.
  - DAs: Less effective than levodopa in relieving signs/symptoms of PD but less likely to cause dyskinesia and the on-off phenomenon. These drugs include ergot alkaloids (bromocriptine, cabergoline, lisuride), and nonergot alkaloids (pramipexole, ropinirole, rotigotine).
  - Anticholinergics: Trihexyphenidyl benztropine—more helpful for tremor and rigidity; generally less effective than DA drugs.
  - Antivirals: Amantadine—given for mild parkinsonism. Used alone or in combination with anti-Ach. Unclear mechanism of action. Improves all clinical features of PD.
  - MAO-B inhibitors: Selegiline—inhibits breakdown of DA and enhances antiparkinsonian effect of levodopa. May reduce the on-off phenomenon.
  - COMT inhibitors: Entacapone and tolcapone—help sustain plasma levels of levodopa. Decreases the dose and response fluctuations due to carbidopa/levodopa (Sinemet).

Surgical
- Lesioning: Historically, surgical intervention was primarily limited to lesioning of deep brain structures. The idea was that permanent lesioning would remove stimuli due to abnormal CNS activity (thalamotomy, used to treat tremor; pallidotomy, used to treat levodopa-induced dyskinesia/antiparkinsonian effects).
- Although affording some clinical benefits, such operations were also shown to result in permanent side effects, such as paresis, confusion, quadrantanopsia, gait disturbances, dysarthria, and hypersalivation.
- Such surgeries were associated with high complication rates and no possibility of lowering anti-PD drugs. These procedures are rarely performed today, having been replaced by DBS.
- DBS: In the late 1980s it was discovered intraop that high-frequency electrical stimulation could produce the same functional effect as surgical lesioning. This introduced DBS as a primary treatment modality. DBS has revolutionized the treatment of PD.
- The CNS targets of DBS include the ventralis intermedius nucleus (VIM), the subthalamic nucleus (STN), and the globus pallidus (GPi). However, the effects of VIM DBS on the other symptoms of PD (akinesia, rigidity, bradykinesia, etc.) are short-lived or nonexistent. GPi or STN DBS is used to treat these other symptoms.

Assessment Points

System	Effect and Assessment by Hx and PE	Test
ANS	Difficulty with salivation, micturition, temperature regulation, GI function	
CNS	General muscle rigidity, akinesia, tremor, confusion, depression, hallucination, speech impairment	CT, MRI
RESP	Upper airway dysfunction: Retained secretions, atelectasis, respiratory infections, aspiration pneumonia (most common cause of death) Other complications: Postextubation laryngospasm, postop respiratory failure	CXR, CT lung
GI	Dysphagia, esophageal dysfunction, constipation, weight loss, sialorrhea	
ENDO	Abnormal glucose metabolism	Glucose metabolism

Key References: Deiner S, Hagen J: Parkinson's disease and deep brain stimulator placement, *Anesthesiol Clin* 27(3):391–415, 2009; Osborn IP, Kurtis SD, Alterman RL: Functional neurosurgery: anesthetic considerations, *Int Anesthesiol Clin* 53(1):39–52, 2015.

Perioperative Implications of Deep Brain Simulation Surgery

Preoperative Preparation
- A complete assessment of the extent of the pt's PD and other medical comorbidities should occur.
- A full explanation of what to expect with each step of the procedure is imperative and, when possible, should occur prior to the day(s) of surgery. DBS procedures are most often staged, with lead placement performed on one day and the generators placed on another.
- The pt's ability to cooperate should be assessed, and he or she should be mentally prepared to have part of the procedure performed while awake.
- Hold Parkinson medications on the morning of surgery.
- Avoid or limit medications that can affect the microelectrical recordings (MER) used to guide DBS lead placement or suppress PD tremor (i.e., benzodiazepines).

Monitoring
- ASA standard monitoring modalities.
- An arterial line is indicated when severe tremor precludes accurate use of a noninvasive cuff or in pts with significant medical comorbidities.
- Possible use of Foley catheter.

Intravenous Access
- One peripheral IV line is generally sufficient (usually a 20- or 18-gauge catheter).

Airway
- Access to the airway is limited due to the presence of the stereotactic head frame. In the case of an airway emergency, supraglottic airways and ultimately the head frame key (used to remove the frame) should be immediately available.

Intraoperative Period
- DBS surgery requires the pt to be secured in a stereotactic head frame and awake for a portion of the operation. This allows for superior identification of the brain areas involved in the pathology by maximizing the quality of MER and pt cooperation.
- Many practitioners use an awake-asleep-awake technique with sedation utilized during burr-hole creation, interrupted during lead placement and MER, and restarted during surgical closure. A scalp nerve block is performed at the very beginning of the procedure in order to provide analgesia throughout the operation.
- It is important to select anesthetic agents that minimally affect MER quality, tremor, and pt cooperation.
  - Dexmedetomidine (alpha-2 agonist): Has minimal effect on MER, provides sedation while preserving pt cooperation, minimal resp depression, and does not suppress PD tremor.
  - Propofol: Short duration of action, easily titratable. MER and tremor return to baseline with discontinuation of infusion.
  - Opioids (fentanyl and remifentanil): These have minimal effect on MER and suppress PD tremor. Resp depression precludes their use in high doses.
  - Benzodiazepines: Reduce quality of MER. Can cause respiratory depression, suppress PD tremor, and can impair pt cooperation.
- Optimize pt comfort while positioning.
- Complications of DBS surgery:
  - Intracranial hemorrhage (highlights importance of stringent blood pressure control)
  - Seizure
  - Venous air embolism
  - Infection
  - Pneumocephalus

General Anesthesia
- Reserved for pts who cannot tolerate awake procedure (pediatric pts, uncooperative pts).
- The major concerns are that GA can diminish intraop MER used to ensure proper lead placement. GA also inhibits macrostimulation testing by eliminating tremor and preventing pt cooperation and feedback (another tool used by surgeons to ensure proper lead placement).
- Recent studies suggest that the concerns surrounding GA for lead placement may be overstated. Sizable studies have demonstrated successful lead placement under GA and that MER can still be successful as long as anesthetic agents are carefully titrated.
- Additional randomized controlled trials are needed to objectively evaluate the role of GA for DBS cases.

Perioperative Implications for Non–Deep Brain Simulation Surgery

Preoperative Preparation
- Continue PD medications the morning of surgery
- Administer PD medications via OG/NG tube at regularly scheduled intervals during surgery to prevent exacerbation of parkinsonism.

Monitoring
- ASA standard monitoring modalities

Airway
- Aspiration risk
- Upper airway obstruction

Induction
- Many PD pts are exquisitely sensitive to the cardiovascular and respiratory depressant effects of many anesthetic agents. These pts may require dose adjustments. Titrate carefully. Propofol, etomidate, and ketamine are all appropriate.

Maintenance
- Exaggerated vasodilatation and cardiodepressant effects with volatile anesthetics
- Nondepolarizing NMB drugs well tolerated but mask tremor
- Enhanced opioid-induced muscle rigidity following fentanyl administration
- Increased risk of neostigmine-induced bronchoconstriction

General Anesthesia
- May see transient appearance of otherwise pathologic neurologic reflexes (hyperreactive stretch reflexes, ankle clonus, Babinski reflex, decerebrate posturing) on emergence

Regional Anesthesia
- Advantageous
- Diphenhydramine useful for sedation

Postoperative Period
- Confusion, delirium, hallucinations common
- Shivering common

Anticipated Problems/Concerns
- Be aware of all parkinsonian medications and possible drug interactions, particularly with MAO inhibitors.
- Avoid drugs that exacerbate parkinsonism (phenothiazines, butyrophenones, and metoclopramide).
- Use caution with airway management, especially keeping in mind postextubation laryngospasm and respiratory failure.

Paroxysmal Atrial Tachycardia

David Amar

Risk
- May be seen in ICU pts and is indistinguishable from paroxysmal SVT
- Digitalis toxicity, acute lyte or acid-base imbalance
- Incidence of 2% in the periop period (excluding AF)
- No racial prevalence and all age groups
- May be seen with mitral valve prolapse, especially in females

Perioperative Risks
- Rapid heart rate impairs LV filling and may adversely affect LV function in pts with LV failure, hypertrophic cardiomyopathy, and aortic or mitral stenosis.
- Cerebrovascular disease.

Worry About
- Syncope ~15% on initiation or abrupt termination of rapid SVT.
- Syncope may also indicate AF and rapid conduction over an accessory pathway.
- Hypotension in pts with systolic or diastolic dysfunction.
- Chest pain in pts with CAD.
- ST-T segment changes common with rapid rates and reduced coronary filling even with normal coronaries.
- VF in WPW pts who develop AF.
- Digoxin level, lyte, and acid-base status.

Overview
- PAT is among a larger group of narrow (<120 ms) QRS-complex tachycardias defined by the ACC/AHA/ESC task force to include PSVT, AF/flutter, permanent junctional tachycardia and focal atrial tachycardia, and macro-reentrant tachycardia.
- Rapid atrial arrhythmias, primarily AF, occur after any major surgery in pts >45 y of age (2–4%) but with a greater incidence after cardiac (25–45%) or thoracic (4–27%) surgery. Such arrhythmias peak 2–3 d after surgery. Acute postop events such as pneumonia or ARDS may increase the incidence.
- Causes are multifactorial and include autonomic imbalance (sympathetic and vagal excess), oxidative stress, and atrial myocardial inflammation. Predisposing factors include atrial fibrosis, left atrial enlargement, and diastolic dysfunction.
- Common mechanisms of narrow complex tachycardias in the periop period:
  - Reentrant rhythms: AV nodal reentrant tachycardia, AV reciprocating tachycardia through accessory pathway, AF/flutter (most common; seen in over 90% of pts).
  - Unifocal or ectopic atrial tachycardia.
  - Multifocal atrial tachycardia in pts with chronic pulm disease.
- A wide-complex tachycardia (QRS >120 ms) may represent either VTach or SVT with abnormal conduction. Adenosine is suggested as first-line therapy if the arrhythmia is monomorphic, regular, and hemodynamically tolerated because adenosine may help convert the rhythm to sinus and may help in the diagnosis. When doubt exists, it is safest to assume any wide-complex techycardia is VTach. The failure to correctly identify VTach can be potentially life threatening, particularly if misdiagnosis results in VTach being treated with verapamil or diltiazem.

Etiology
- Reentrant rhythms.
- AV nodal reentry: Reentrant pathway within the AV node. Most common form of PAT; seldom associated with organic heart disease.
- Accessory pathway–mediated: Reentrant rhythm that involves an accessory pathway from atrium to ventricle. In sinus rhythm, the bypass tract may cause a preexcitation pattern on ECG (WPW syndrome: short P-R interval and delta wave on ECG) or may not be apparent.
- Unifocal atrial tachycardia arising from a single atrial muscle site other than SA node; associated with catecholamine excess states (uncontrolled pain, light anesthesia) or digitalis toxicity (triggered activity with variable AV block).
- Multifocal atrial tachycardia arising from multiple atrial sites, usually seen in pts with pulm disease or CHF.

Usual Treatment
- Initial therapy: Vagal maneuvers (i.e., Valsalva, carotid massage [avoid in known carotid disease or with presence of bruit] or applying ice-cold wet towel to the face) should be initiated to terminate the arrhythmia.

- IV adenosine (especially in diagnosis of wide-complex tachycardia that could be VTach or if WPW or preexcitation is suspected) or CCBs (diltiazem or verapamil) are the drugs of choice but beta-blockers may also be used. Adenosine may provoke bronchospasm in pts with reactive airway disease, with excessive (prolonged) bradycardia in patients taking carbamazepine, or in denervated heart transplant pts. Higher doses of adenosine may be needed in pts taking methylxanthines (i.e., theophylline). Adenosine may initiate AF in 1–15% of pts; it is usually transient.
- The goal of second-line therapy is to achieve ventricular rate control and possible conversion when PAT does not respond or rapidly recurs after adenosine. IV digoxin is not effective unless CHF is present.
- When AV nodal block is unsuccessful, electrical cardioversion is considered. If infeasible or unsuccessful, antiarrhythmic agents may also be used. When LV function is preserved, IV options include procainamide and amiodarone. The proarrhythmic potential of these agents makes them less desirable than AV nodal blockade. In patients with poor LV function, IV amiodarone is preferred.
- Pts with accessory pathway reentrant rhythms who develop AF are at risk for VFIB; this scenario is exacerbated by agents that reduce the accessory bundle refractory period (digoxin, CCBs, beta-blockers, and adenosine). Hence WPW pts who experience AF should not receive AV nodal blockers. IV procainamide and amiodarone are preferred agents to slow the rate and achieve conversion.
- Multifocal and unifocal PAT: Correct underlying hypoxia and lyte imbalance. Therapy: Electrical cardioversion and procainamide are not effective. Effective IV agents available for use include AV nodal blockers (CCBs, beta-blockers) and amiodarone. Although digoxin slows the ventricular rate, toxicity may provoke automatic atrial tachycardia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	WPW AV nodal reentry Symptomatic unifocal atrial tachycardia	Palpitations, diaphoresis Hypotension, chest pain	Prominent jugular venous pulsations	ECG (150–250 bpm, abnormal P waves preceding QRS, rarely discernible) Electrophysiologic studies, ECHO
NEURO	Rapid arrhythmia	Fatigue, presyncope or syncope		
RESP	Rapid arrhythmia	Dyspnea	Rales, wheezes	CXR
RENAL	Atrial dilation	Polyuria		BNP, BUN/Cr

Key References: Page RL, Joglar JA, Caldwell MA, et al.: 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, *J Am Coll Cardiol* 67:e27–115, 2016; Amar D. Perioperative atrial tachyarrhythmias, Anesthesiology 97:1618–1623, 2002.

Perioperative Implications

Preoperative Preparation

- If possible, continue CCBs and beta-blockers periop to avoid withdrawal-associated arrhythmias.
- Correct hypoxemia and lyte imbalance.
- Consider guideline-driven prophylactic regimens for high-risk pts undergoing cardiac or thoracic surgery.
- Pts with recurrent arrhythmias may be taking drugs such as flecainide, propafenone, amiodarone, or dofetilide for prevention.
- Pts with refractory arrhythmias have usually had electrophysiologic studies and catheter ablation procedures.

Monitoring

- Continuous intraop and postop ECG monitoring in high-risk pts

Induction/Maintenance/Extubation

- Aim for effective postop analgesia.
- Consider beta-blockers in hyperadrenergic postop patients whose cardiac output is adequate.

Anticipated Problems/Concerns

- Transient side effects with adenosine include flushing, dyspnea, and chest pain. Adenosine may provoke hypotension, especially in patients with borderline hemodynamic status.
- Wide-complex rhythms: Adenosine may be used if the rhythm is confirmed by other means to be supraventricular in origin. The use of adenosine to discriminate VT from SVT is now discouraged owing to vasodilatory side effects (worsened hypotension) in pts with VT.
- Diltiazem is highly effective but may be associated with transient hypotension; this can be minimized with slow titration of the drug, α-agonists, and correction of hypovolemia.

Patent Ductus Arteriosus

Aris Sophocles | Mark Twite | Jeffrey D. Roizen

Risk

- Full-term infants: 1:2000
- Preterm infants: 8:1000
- Highest in preterm and low–birth-weight infants
- Female-to-male ratio: 2:1
- Associated with congenital rubella infection and genetic defects, including trisomy 21, CHARGE, and a familial recurrence rate of 3%

Perioperative Risks

- Surgery: Hemorrhage; hemodynamic instability, especially in premature and low–birth-weight neonates; single-lung ventilation resulting in hypoxia, atelectasis, and pneumothorax; injury to the recurrent laryngeal nerve; chylothorax; ligation of the incorrect vessel (aorta or pulm artery); thoracic scoliosis over the long term
- Closure by an occluding device via cardiac cath: Obstruction of the pulm artery and/or aorta from the occluding device, arrhythmias, incomplete closure, and embolization of the device

Worry About

- Premature infant: Lung disease and high mechanical ventilator settings, hemodynamic instability after duct closure due to poor cardiac reserve
- Term infant and young child: Preop dehydration, ability to tolerate single-lung ventilation, postextubation stridor due to injury to the recurrent laryngeal nerve, postop analgesia
- Older child and adult: Pulm Htn

Overview

- Preterm and low–birth-weight infants: PDA may cause CHF and worsening of chronic lung disease, which makes weaning from mechanical ventilation difficult.
- Term and older infants: PDA may be asymptomatic or associated with failure to thrive, recurrent resp infections, and CHF.
- A "silent duct" is a small PDA detected on echocardiography, with no murmur heard.
- PDA leads to an increased risk of endocarditis.

Etiology

- Normal: The arterial duct is the connection between the pulm artery and the aorta; it shunts blood away from the lungs during fetal development in utero. The duct normally constricts shortly after birth owing to the postnatal drop in circulating prostaglandin levels as well as the rise in systemic O_2 tension. Constriction is followed by permanent duct closure due to the hypertrophy of endothelial and smooth muscle cells and eventual formation of the ductal ligament.
- PDA: In preterm infants the ductal muscle layer is thin and poorly contractile; it has a poor constrictor response to changes in arterial oxygen tension.

Usual Treatment

- Medical management: Neonates often receive a trial of ibuprofen or indomethacin. These act by inhibiting prostaglandin-forming COX enzymes. Adverse drug effects include renal dysfunction and NEC.
- Surgical management:
  - Bedside left lateral thoracotomy: Reserved for critically ill ventilated pts who have failed medical therapy.
  - Operated left-lateral muscle-sparing thoracotomy or video-assisted thoracoscopic surgery: For a stable child, technique is surgeon's preference, with most children receiving a thoracotomy. Candidates are usually not suitable for device closure (less than 8 kg) or unusual duct anatomy.
  - Cardiac cath lab: Reserved for children weighing more than 8 kg owing to the size of the femoral sheaths through which the occluding device is introduced. Large PDAs are occluded with an Amplatzer device and small PDAs are occluded with coils.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CHF	FTT, difficulty feeding	"Machinery" murmur Wide pulse pressure Bounding pulses Pulsus bisferiens	ECHO
	Pulm Htn		Tachycardia Diaphoresis	
RESP	Pulm edema	Recurrent respiratory infections Increased O_2 requirement	Worsening mechanical ventilation parameters Rales	CXR
GI	NEC	Abdominal distention Poor feeding Blood in stool Free air in peritoneum	Distended tense abdomen Edema of abdominal wall Tender abdomen	Abdominal x-ray
RENAL	Oliguria	Decreased UO due to decreased renal blood flow		Serum chemistry
CNS	CNS hemorrhage	Increased fontanel pressure Decreased Hct	Increased fontanel size and tension	Head US

Key Reference: Jacobs JP, Giroud JM: Evolution of strategies for management of the patent arterial duct, *Cardiol Young* 17(Suppl 2):68–74, 2007.

Perioperative Implications

Preoperative Preparation

- Surgery:
  - Unstable neonate, bedside: Cross-matched blood at bedside, adequate IV access with extension tubing. Caretakers must be familiar with ventilator function and settings and must check current running infusions (TPN, vasopressors).
  - Stable child: Cross-matched blood in the OR.
- Cardiac cath lab: Routine setup for general ET anesthesia.

Preinduction/Induction

- Unstable neonate: Induce with fentanyl (10–30 mcg/kg)
- Stable child in cath lab/OR: Premedication and mask induction

Monitoring

- Standard ASA monitors.
- Unstable neonates require an arterial line for continuous BP measurement and blood gas analysis and central venous access for inotrope drug delivery.
- Stable older children do not require invasive monitoring.

Airway

- Critically ill neonates are already intubated and ventilated. Check tube size for leak and confirm position on CXR.
- OR cases: Intubate for single-lung ventilation (right main stem, a single-lumen ETT, bronchial blocker, or double-lumen tube).
- Cath lab cases: Young children often require intubation; older cooperative children may be treated with a natural airway.

Maintenance and Extubation

- Critically ill neonate, bedside: Fentanyl and paralytics; patient should remain intubated at the end of the procedure.
- Stable child, OR: Balanced anesthetic technique with the goal of early extubation and adequate analgesia (consider regional techniques).
- Stable child, cath lab: Balanced anesthetic technique and extubate at the end of the procedure. Analgesic requirements are minimal and related to the femoral vessel puncture sites.

Adjuvants

- Antibiotic prophylaxis for all cases (usually cefazolin 30–50 mg/kg)

Postoperative Period

- Adequate analgesia

Anticipated Problems/Concerns

- Critically ill neonates: Often require a transient increase in BP and respiratory support.
- Stable children: Postop surgical ligation via a thoracotomy; such patients may have atelectasis from single-lung ventilation and also thoracotomy pain.

Patent Foramen Ovale

Ronit Lavi | Daniel Bainbridge

Risk

- Incidence: 25–30% at autopsy.
- Atrial septal aneurysm (a deformity of the septum that results in deviation of the septum more than 15 mm into either atrium) is associated with at least 50% of PFOs and is considered an additional risk factor for stroke.

Perioperative Risk

- Unclear if a PFO increases the risk of stroke or cognitive dysfunction in the periop period.

Worry About

- R-to-L shunting of blood leading to profound hypoxemia
- Paradoxical embolization of air, blood clot, or tissue fragments, potentially resulting in stroke

Overview

- The foramen ovale directs oxygenated blood returning from the placenta and into the right atrium across the intra-atrial septum to the left ventricle.
- As right-sided pressures decrease after birth, the foramen ovale flap is pressed against the septum secundum.
- This results in the fusion of the ovale flap to the septum secundum; irreversible closure of the ovale occurs in 75% of pts.
- Diagnosed by:
  - Right heart cath, with the ability to cross a guide wire across the atrial septum.
  - TEE is considered the "gold standard" imaging technique, using a contrast agent (bubble study) and provocative technique (Valsalva maneuver).
  - TCD is less invasive than TEE with similar sensitivity but reduced specificity.
  - TTE: Sensitivity 50% of TEE, with similar specificity.
- See also Atrial Septal Defect.

Etiology

- Unknown what, if any, risk factors predispose to patent foramen ovale
- A higher incidence of PFO was found in pts who suffer migraine with aura; unclear whether this represents coexistence or a causal relationship between the two entities.

Usual Treatment

- Anticoagulation has not been shown to reduce cryptogenic stroke.
- Percutaneous closure for pts with history of cryptogenic stroke.
- Surgical closure in pts who are not candidates for percutaneous closure.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Rarely RV overload secondary to chronic L-to-R shunting	Fatigue, abdominal pain	Hepatic enlargement, elevated JVP, peripheral edema	ECG showing right axis deviation ECHO showing large RV PFO
CNS	Assoc with cryptogenic stroke, migraine	Hx of migraine headache, stroke unrelated to carotid Dx, AFIB		

Key References: Sukernik MR, Mets B, Bennett-Guerrero E: Patent foramen ovale and its significance in the perioperative period, *Anesth Analg* 93(5):1137–1146, 2001; Kutty S, Sengupta PP, Khandheria BK: Patent foramen ovale: the known and the to be known, *J Am Coll Cardiol* 59(19):1665–1671, 2012.

Perioperative Implications

Preoperative Preparation
- Deairing of all IV lines/syringes.
- No indication for antibiotic prophylaxis.
- Use regional technique when possible as a sole anesthetic or in combination with GA for pain control.

Monitoring
- TEE and/or TCD to check for PFO has been advocated, especially for pts undergoing surgery in the sitting position or when the surgical field is above the level of the right atrium.

Airway
- Careful airway assessment, optimal pt positioning, and all necessary airway management tools available

Induction
- Proper preoxygenation avoid hypoxemia, hypercarbia, and acidemia
- Five-lead ECG and low threshold for arterial line cath to monitor BP, metabolic balance, and oxygenation throughout the case and in PACU.
- Avoid systemic hypotension/pulm Htn, as this increases the potential for R-to-L shunting.
- If appropriate, use an induction regimen that maintains or decreases PVR and maintains systemic vascular resistance, sinus rhythm, and contractility.

Maintenance
- Avoid high peak airway pressures during PPV as rapid changes in pressure may predispose to R-to-L shunting.
- If hypoxemia worsens with PEEP, suspect shunt.
- Laparoscopic procedures with increased intra-abdominal pressure might not be tolerated.

Extubation
- Hypercarbia and/or hypoxia may predispose to R-to-L shunting. Extubate when pt is fully awake and obeys commands.
- Smooth emergence is indicated to prevent shunting.

Postoperative Period
- Pulm embolus in the postop period may present as severe hypoxemia with preserved systolic blood pressure owing to an increase in R-to-L shunting.
- Adequate pain control with a multimodal approach and/or regional anesthesia as indicated.

Anticipated Problems/Concerns
- Intraoperative and postop hypoxemia.
- Potential increased risk for periop TIA/stroke.
- Positive-pressure ventilation and laparoscopic procedures with increased intra-abdominal pressure; neurosurgery, orthopedic surgery, thoracic surgery, and cardiac procedures might precipitate R-to-L shunt with hypoxemia.
- Atrial arrhythmia should be managed promptly to decrease the chance of shunt and embolism.
- Excessive pain might increase the chances of developing shunt; an adequate pain control regimen should be in place.
- All lines should be de-aired and special air-trapping filters used.
- Insertion and removal of a central line impose a higher risk for air embolism.

Pemphigus

Megan K. Werntz | Brandon M. Togioka

Risk
- Incidence in USA: 0.1–0.5:100,000 per y for pemphigus vulgaris (the most common form of pemphigus)
- Individuals from ages 40-60 y most commonly affected.

Perioperative Risks
- Infection, sepsis
- Electrolyte abnormalities and dehydration, with extensive lesions

Worry About
- Volume status with oropharyngeal lesions and decreased oral intake
- Skin and/or pharyngeal blisters (lesions may be limited to the oropharynx), sloughing of mucosa, bleeding produced by airway manipulation
- Consequences of steroid treatment (e.g., hypertension, hyperglycemia, gastric or duodenal ulceration, myopathy, infection, psychic disturbances, osteoporosis) or immunosuppressive therapy (bone marrow suppression, susceptibility to opportunistic infections and cancer)

Overview
- An autoimmune intraepidermal blistering disease of the skin and mucous membranes. Oral lesions are most common. Blisters rupture easily but heal slowly.
- There are four types: Pemphigus vulgaris (most common and severe form), pemphigus pemphigus foliaceus, IgA pemphigus, and paraneoplastic pemphigus.
- The 5-y mortality is 5–15% for treated pemphigus vulgaris. The most common cause of death is infection, usually with *Staphylococcus aureus*.
- Occasionally pemphigus can coexist with other autoimmune diseases, a thymoma (with or without myasthenia gravis), or malignancies.

Etiology
- Autoimmune disease, in which autoantibodies are produced against cell adhesion molecules (desmosomal glycoproteins) on keratinocytes. Immune response leads to separation of epidermal keratinocytes and blistering.
- Uncommonly, pemphigus is drug-induced, associated with malignancy, or related to infection.

Usual Treatment
- Corticosteroids (most common therapy).
- Azathioprine and mycophenolate are the most commonly used immunomodulatory agents.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral and pharyngeal erosions and blisters	Painful swallowing Decreased oral intake	Oral lesions	Albumin Na^+
ENDO	Hyperglycemia (due to steroids)			Glucose
CV	Htn (due to steroids)		BP	
RESP	At risk for pneumonia	Fever, cough, sputum	Diminished breath sounds, dullness to percussion	CXR
GI	Gastric or duodenal ulcer (due to steroids)	Epigastric pain	Dark stool	Guaiac fecal occult blood test
MS	Myopathy (due to steroids or association with myasthenia gravis)	Fatigability, weakness		
DERM	Skin and mucous membrane blisters	Painful skin lesions	Blisters/denuded skin	BMP

Key References: Mahalingam TG, Kathirvel S, Sodhi P: Anaesthetic management of a patient with pemphigus vulgaris for emergency laparotomy, *Anaesthesia* 55(2):160–162, 2000; Bansal A, Tewari A, Garg S, et al.: Anesthetic considerations in pemphigus vulgaris: case series and review of literature, *Saudi J Anaesth* 6(2):165–168, 2012.

Perioperative Implications

Preoperative Preparation
- Pts may require supplemental steroids.
- Secure IV lines with cloth bandage or suture (avoid tape) and place on lesion-free areas.

Monitoring
- Ensure careful placement of monitors and extra padding under pressure points and BP cuff.

Airway
- Airway management may become more difficult if tissue manipulation leads to bleeding.
- Consider lubricating mask and laryngoscope blade (Macintosh may be less traumatic than Miller blade) to decrease friction (potentially with hydrocortisone cream or ointment).
- Consider small ETT and inflate cuff only minimally; suture ETT or use tube holder instead of taping.
- Consider avoiding LMA owing to risk of pharyngeal trauma.
- Consider use of video laryngoscope for assessment of bullae during intubation.

Preinduction/Induction
- Lubricate eyes; consider goggles instead of tape.
- Use gentle bag mask ventilation.

Maintenance
- Regional anesthesia preferred (when appropriate) to avoid airway manipulation.
- Consider single-shot blocks (spinals or peripheral blocks) to avoid tape.
- Local infiltration is probably contraindicated owing to risk of blister formation.

Extubation
- Minimize coughing during extubation and provide gentle oropharyngeal suctioning.

Postoperative Period
- Gentle pt repositioning.
- Treat pruritus aggressively and avoid pain management that can cause itching.

Adjuvants
- Consider need for steroid supplementation.

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Pericardial Effusion

Austin J. Peters | Jeffrey R. Kirsch

Risk

- Occurs rarely
- May be seen after open-heart surgery or PTCA.
- Blood and/or serous
- May be caused by infection: Viral, bacterial, or fungal
- May have a neoplastic etiology: Lymphoma, leukemia
- Can occur after acute MI, especially transmural
- Can be due to trauma
- Gender predominance: More common among men than women

Perioperative Risks

- If undiagnosed, tamponade leading to CV collapse is possible, with a low probability of determining the cause antemortem.
- Risk of CV collapse, especially with induction and institution of positive-pressure ventilation.

Worry About

- Hypovolemia
- Limited filling of cardiac chambers

Overview

- Effusion is found in the sac surrounding heart; if severe, it can restrict filling of the heart.
- Ventricular filling is depressed in both the RV and the LV.
- Fluid bolus and inotropes are beneficial but do little to improve CO.
- CO becomes more dependent on heart rate.
- For proper treatment, surgical drainage must be implemented.

Etiology

- Postsurgical and cath procedures
- During or after viral, bacterial, or fungal infection
- Postinflammatory process: Acute transmural inflammation, SLE, rheumatoid arthritis
- Uremia
- Neoplastic
- Trauma

Usual Treatment

- Drainage, either percutaneous or open.
- Medical management is generally ineffective.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tamponade limiting CO Hypotension Arrhythmias	Chest pain	Neck veins HR BP	TTE/TEE Equalization of all pressures in heart (cath) ECG
RESP	Decreased CO on institution of IPPB (mechanical ventilation)	Dyspnea Change in BP on institution of mechanical ventilation	Pulsus paradoxus: Large decrease in BP with inspiration Decreased O_2 sat	Pulm artery, RA/LA pressures
METAB	Metabolic acidosis			ABG

Key References: Adler Y, Charron P, Imazio M, et al.: 2015 ESC Guidelines for the diagnosis and management of pericardial diseases, *Eur Heart J* 36(42):2921–2964, 2015; Grocott HP, Gulati H, Srinathan S, et al.: Anesthesia and the patient with pericardial disease, *Can J Anaesth* 58(10):952–966, 2011.

Perioperative Implications

Preoperative Preparation

- Appropriate monitoring before induction.
- Preoxygenation is not always effective.
- Hemodynamic goals: Full (fluid), fast (maintain or increase HR), tight (maintain or increase SVR).
- Consider draining transthoracically if hemodynamic compromise is severe.
- Consider prepping and draping prior to induction with surgeon ready.
- PPV may significantly worsen hypotension, resulting in shock and death.
- Consider placing external defibrillator patches prior to induction of anesthesia.

Monitoring

- Arterial line is indicated as BP may change suddenly; sampling of Hct for bleeding and acid-base status in state of low cardiac output is useful.
- Consider a PA cath; useful for diagnosis and following surgical treatment. If pressures are not relieved by surgical drainage, question the original diagnosis.
- TEE is more useful than PA monitoring.

Induction/Maintenance

- Do not decrease preload or heart rate.
- Consider initiating invasive hemodynamic monitoring before induction.
- Monitor hemodynamics: If stable, slowly titrate small doses of propofol vs. etomidate.
- Consider inhalational induction if evidence of tamponade.
- Ketamine is advocated for new tamponade situations.
- Maintain spontaneous ventilation if possible; initiation of PPV may cause severe CV compromise due to decreased filling of RV and LV.

Treatment Approach

- For hemorrhage after open-heart surgery, reopen the sternum to explore for sources of bleeding, which is usually relieved by releasing the first few sutures.
- TTE-guided pericardiocentesis.
- Infections and/or neoplasia: Subxiphoid pericardial window.
- Insertion of a pericardioscope enables visualization of the pericardium and can serve to obtain biopsies.

Adjuvants

- Depend on etiology

Extubation

- Depending on etiology, consider awake extubation or postop mechanical ventilation.

Anticipated Problems/Concerns

- Many different causes, all with different sequelae.
- Hypotension on induction of anesthesia or positive pressure ventilation.

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Pericarditis, Constrictive

Elizabeth Y. Zhou

Risk

- Dense changes in pericardium can be caused by scarring induced by a single episode of acute pericarditis or by prolonged exposure to an inflammatory process.
- 18% of pericardiectomies are attributed to previous cardiac surgery, which may explain the increase in number of cases of CP since the mid-1990s.

Perioperative Risks

- Heart failure, atrial arrhythmia, MI
- Abnormal drug metabolism secondary to liver failure
- Intraop major hemorrhage
- Postop respiratory failure

Worry About

- Hemodynamic instability due to limited filling or myocardial depression.
- When providing GA, be prepared for CPB.
- Right heart failure and volume overload.
- Differentiate from restrictive cardiomyopathy by various signs and symptoms as well as ECHO.

Overview

- CP is an inflammation of the pericardium, leading to impaired filling of the ventricles and reduced ventricular function.
- Restriction of the pericardium results in increased ventricular interdependence and a reciprocal relation between the filling of the left and right heart.
- During spontaneous ventilation, transtricuspid blood flow is increased, resulting in increased filling of the RV. This will lead the septum to shift to the left and to decrease LVEDV, with subsequent hypotension and pulsus paradoxus.
- During expiration, the septum is shifted to the right. Opposite changes take place during mechanical ventilation.
- Pts present with dyspnea, fatigue, orthopnea, and right heart failure with jugular venous congestion and chest pain, hepatomegaly, and ascites.
- Cardiac cath with hemodynamic assessment is considered the "gold standard." However, comprehensive echocardiography with Doppler assessment is usually necessary to confirm CP and exclude restrictive cardiomyopathy.

Etiology

- In developed countries, idiopathic or viral infections are the most common cause of CP, followed by cardiac surgery and mediastinal irradiation.
- Bacterial infectious causes (e.g., TB, staphylococci, group A and B streptococci, and gram-negative rods) are more common in underdeveloped countries.
- Less common causes are uremia, connective tissue disorders, and drug reactions.
- Idiopathic, neoplastic, postirradiation or uremic CP accounts for most cases of CP that require surgery.

Usual Treatment

- In advanced stages, the standard treatment is pericardiectomy. Both median sternotomy and left thoracotomy approaches are used.
- Pericardiectomy has been associated with relatively high early mortality/morbidity and low long-term survival. Predictors of poor prognosis include DM and high transmitral early diastolic velocity, which may reflect high left atrial pressure resulting from severe pericardial constriction.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Lymphadenopathy if the CP is caused by viral or bacterial infection, cyanosis	Hx of fever, chills, upper resp tract infections	Enlarged cervical lymph nodes, jugular venous distention	Blood and sputum cultures, immunologic assays for viral infections
RESP	Pulm edema if heart failure develops	Dyspnea, dry cough	Tachypnea, rales on auscultation	CXR, ABG analysis
CV	Right and left heart failure, arrhythmia, hypotension	Dyspnea, orthopnea, chest pain, peripheral edema, fatigue, palpitations, and hepatomegaly	Tachycardia, muffled and distant heart sounds, friction rub, apical pulse not palpable	MRI and CT scans ECG, low voltage and ectopic AT. Increased CVP (W shape). Cath showing "square root sign," increased ratio of RV to LV systolic area on inspiration versus expiration Doppler ECHO: Restrictive LV diastolic filling, E/A >0.8, ventricular septal motion abnormality with respiration, mitral medial e′ > 8, annulus reversus, hepatic vein expiratory end-diastolic reversal velocity/forward flow velocity >0.8
MS	Muscle atrophy, myositis if there is an underlying connective tissue disorder	Significant weight loss and muscle wasting	Clinical evidence of weakness	CPK to rule out myositis; specific tests if connective tissue disorder is suspected

Key References: Schwefer M, Aschenbach R, Heidemann J, et al.: Constrictive pericarditis, still a diagnostic challenge: comprehensive review of clinical management, *Eur J Cardiothorac Surg* 36(3):502–510, 2009; Welch T, Oh J: Constrictive pericarditis: old disease, new approaches, *Curr Cardiol Rep* 17(20):1–7, 2015.

Perioperative Implications

Preoperative Preparation

- Cardiac medications including antidysrhythmics should be continued.
- Minimize bradycardia and myocardial depression and minimize decreases in afterload and preload.

Monitoring

- Have invasive monitoring available, including arterial line and monitoring for CVP. A PA cath is recommended because of occurrence of low CO syndrome after surgery.
- Intraop TEE is of significant help.

Maintenance

- Conducted under GA.
- Narcotic-based technique is preferred.
- Intraop hemodynamic goals are adequate preload, maintenance of sinus rhythm, and rate control if sinus rhythm cannot be maintained.

Adjuvants

- Inotropic support is indicated if there is evidence of ventricular dysfunction.
- Because of limited ventricular diastolic filling, CO is rate-dependent. Consider pacing to improve CO.
- Most pericardiectomies are done without the need for CPB, but CPB should be on standby.

Anticipated Problems/Concerns

- MI, major intraop hemorrhage due to myocardial perforation, atrial and ventricular arrhythmias, and worsening of heart failure.

Peripheral Vascular Disease

Elizabeth A. Valentine

Risk

- Prevalence of PVD is 3–20%; and increases with age.
- Risk factors: Nonwhite race, male gender, older age, smoking, DM, Htn, hyperlipidemia, and CRI.
- Risk of MACE approximately 5–7% per year; correlates with the severity of PVD.

Perioperative Risks

- Prevalence of concomitant CAD or CVD is in the range of 40–60%.
- Vascular surgery associated with greater cardiac morbidity (periop MI in 4–15%) and mortality (>50% of periop deaths) than other, noncardiac surgery.

Worry About

- Increase in afterload from cross-clamping on major vasculature may precipitate myocardial ischemia or ventricular failure.
- Release of cross-clamp and revascularization of ischemic extremity may result in profound hypotension.
- Risk for hemorrhage from major vasculature.
- Increased risk of MACE in the periop period.

Overview

- Imbalance between oxygen supply and demand results in tissue ischemia.
- Symptoms range from intermittent claudication to rest pain to tissue loss.
- Critical limb ischemia (CLI) manifests when arterial blood flow is insufficient to meet basal metabolic demands of resting tissue.

Etiology

- Atherosclerosis is the most common etiology of PVD.
- Less commonly: Arteritis (Takayasu, giant cell, thromboangiitis obliterans, or polyarteritis nodosa), thromboembolic disease, fibromuscular dysplasia, aneurysmal thrombosis, vascular tumor, prior trauma/irradiation, popliteal entrapment, popliteal artery cyst, pseudoxanthoma elasticum.

Usual Treatment

- Aggressive medical management of risk factors and lifestyle/exercise programs generally prevent progression of disease (remains stable in 70–80% of pts, worsens in 10–20%, and progresses to CLI in 1–2%).
- Decision for surgery for intermittent claudication is based on individualized assessment of risks/benefits of procedure, success of medical/lifestyle interventions, and overall impact on quality of life.
- CLI associated with a higher risk of limb loss without revascularization and nearly always warrants surgical intervention.
- Surgical options include open or endovascular repair.
- No differences in short- or long-term mortality between open and endovascular techniques.
- Lower perioperative morbidity with endovascular repair at the expense of a higher rate of reintervention in the long term.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CARDIO	Htn	Usually asymptomatic; may have signs of urgency/emergency	Normal if treated S_4 if longstanding Htn/ LVH	Baseline vital signs ECG TTE Exercise or pharmacologic stress test Radionuclide studies
	CAD	Angina or equivalent, may be asymptomatic	May detect new murmur or signs and Sx of heart failure	Coronary angiography
	CHF	Exercise intolerance Sx of heart failure	S_3, JVD, rales, hepatomegaly	
VASC	Occlusive lesions	Claudication	Cool, mottled extremities Ulcer or gangrene Decreased pulses	ABI Peripheral angiography Abdominal US/CTA/MRA
	May have concomitant AAA	Abd pain, may be asymptomatic	Pulsatile abdominal mass	
RESP	Concurrent tobacco abuse May have COPD	DOE Chronic cough Home O_2/inhaler requirement	Decreased breath sounds Prolonged expiration Wheezes Focal rales may indicate superinfection	CXR ABG PFTs
RENAL	CRI	Need for HD/PD	Edema	BUN/Cr Baseline lytes
ENDO	DM and assoc effects such as peripheral and autonomic neuropathy, nephropathy	Attention to CV, PNS for ANS and other evaluation	Obesity (in DM type II) Retinopathy Cardiomegaly Foot ulcers	Fasting blood sugar (acute control) HgbA1C (long-term control)
CNS	Cerebrovascular disease	Stroke/TIA symptoms Scotoma	CNS exam Search for carotid bruits	CT/MRI brain Doppler or angio (if indicated)

Key References: Norgren L, Hiatt WR, Dormandy JA, et al.: Inter-society consensus for the management of peripheral arterial disease (TASC II), *J Vasc Surg* 45(Suppl S):S5–S67, 2007; Anton JM, McHenry ML: Perioperative management of lower extremity revascularization, *Anesthesiol Clin* 32(3):661–676, 2014.

Perioperative Implications

Preoperative Preparation

- Aggressive management of medical comorbidities
- Continue ASA, beta-blocker, ACE-I, and statin periop. Maintain normoglycemia and encourage smoking cessation.
- Clinical symptomatology may make functional status difficult to ascertain. Consider preop stress test for pts with poor or unknown functional status.

Monitoring

- ST-segment analysis for myocardial ischemia.
- Consider invasive arterial pressure monitoring, particularly for open procedures.
- Central pressure monitoring rarely indicated.

Airway

- Open procedures successfully performed with GA (ETT vs. LMA), neuroaxial anesthesia, or RA.
- Endovascular procedures typically performed under MAC with a natural airway.

Preinduction/Induction

- Tachycardia increases myocardial oxygen demand and decreases myocardial oxygen supply (less time in diastole)
- Htn increases LV stress; hypotension risks decreased perfusion of likely hypertrophied LV.

Maintenance

- No significant outcomes or differences between anesthetic techniques, even for pts with more severe disease or CLI.
- Neuroaxial techniques may increase vascular blood flow, improve graft patency rates, and decrease need for reintervention.
- Endovascular repairs typically performed under light sedation to allow for pt cooperation.

Extubation

- Sympathetic stimulation and resultant hypertension/tachycardia are to be avoided.

Adjuvants

- Neuroaxial catheters can be used for adjuvant pain control and may have benefits for graft patency. Risk/benefit of neuroaxial anesthesia must be weighed against need for periop anticoagulation.

Anticipated Problems/Concerns

- Periop complications include graft occlusion, MACE, hemorrhage, postoperative delirium, and pulm, renal, and wound complications.

Pertussis (Whooping Cough)

Luiz Maracaja | Raj K. Modak

Risk

- Increasing prevalence 1976 (lowest) vs. 2012, 1010 vs. 41,880 cases (14 deaths in infants aged <12 mo).
- Substantial morbidity and mortality in USA children despite high childhood vaccination rates.
- Incidence highest for infants <1 y of age (23% of all cases).
- Adolescent group 10–19 y (33% of all cases).
- Incidence of death highest for infants <6 mo of age (91% of all deaths).
- Incidence greater among females than males (54%).
- Incidence greater among whites than minorities (90%).
- If unimmunized, 90% susceptibility following exposure to index case.
- Only 2% of adult population is protected against pertussis.
- Tdap vaccine coverage is 56% among adolescents and <6% among adults.

Perioperative Risks

- Most common complications occurring in those <6 mo of age: Hospitalization (69%), pneumonia (13%), seizures (2%), encephalopathy (<2%)
- Common complications in adults: Cough-related incontinence (28%), syncope (6%), pneumonia (5%), rib fractures (4%), hospitalization (3%)

Worry About

- Infectivity and contagion
- Secretions, pneumonia, altered mucociliary function, apnea, and decreased pulm reserves causing hypoxemia
- Postop complications related to coughing

Overview

- Pertussis is an acute respiratory infection caused by *Bordetella pertussis*.
- Transmission occurs by respiratory droplets with a 7-d to 10-d incubation period.
- Organism releases multiple toxins that damage the epithelial cells of the respiratory tract.
- Characterized by three phases: Catarrhal (cold symptoms), paroxysmal (cough symptoms), convalescence (persistent or episodic cough).
- Infectivity highest in catarrhal and early paroxysmal phases.
- Adolescents and adults display milder symptoms that may be indistinguishable from less serious causes of URI/LRI.
- Immunization in childhood has decreased but not eliminated incidence.
- Vaccine estimated 80–85% effective after three exposures, usually given as combination Tdap vaccine.
- Increased in incidence in adolescence (age 10–19), indicating a need for booster immunization.

- In October 2012, the ACIP recommended administration of Tdap during each pregnancy irrespective of the pt's prior history of immunization. Vaccinations given to pregnant women will stimulate the development of maternal antipertussis antibodies that will pass through the placenta, likely providing the newborn with protection against pertussis in early life protecting the mother from pertussis around the time of delivery, making her less likely to become infected and transmit pertussis to her infant. Optimal timing for Tdap administration is between 27–36 wk of gestation for maximal maternal antibody response and passive antibody transfer to the infant, although Tdap may be given at any time during pregnancy. However, the maternal antipertussis antibodies are short-lived.

Etiology

- *B. pertussis*, a fastidious gram-negative pleomorphic or rod bacillus.
- A whooping cough syndrome can also be caused by *Bordetella parapertussis*, *Chlamydia trachomatis*, and many adenoviruses.

Usual Treatment

- Infectivity and contagion control
- Most effective treatment occurs in the catarrhal and early paroxysmal phases.
- Macrolides (erythromycin, azithromycin, clarithromycin) and trimethoprim-sulfamethoxazole.
- Cough suppression: Dextromethorphan and codeine; expectorant: guaifenesin.
- Corticosteroids and β_2 agonists have an unclear role in the paroxysmal stage.
- In some cases hospitalization may be required to suppress cough, institute antibiotic treatment, monitor for apnea and hypoxemia, and provide general nutrition.
- Intensive care treatment may be needed for severe sequelae of pneumonia, seizures, and encephalopathy.
- Antibiotic therapy is not recommended in the convalescent phase.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Upper airway obstruction	Difficulty feeding Difficulty breathing	Rhinorrhea Lacrimation Conjunctivitis	Nasal culture DFA
CV	High O_2 consumption	Irritability	Tachycardia	ECG
RESP	Cough V/Q mismatch Hypoxemia Pneumonia	Apnea, SOB Tachypnea, rales	Inspiratory whoop Cyanosis Rales	Culture and DFA Pulse oximetry, ABG CXR
GI	Poor oral intake Posttussive emesis Fatty liver Cough-induced hernias	Dehydration Inability to retain food Inguinal hernias	Altered turgor Weight loss Hepatomegaly Reducible hernias	Weigh on scale LFTs
RENAL	Hypovolemia	Oliguria	Altered turgor	BUN, Cr, FEN_a,
CNS	Seizures Encephalopathy	Seizure type Altered neuro logic status	Seizure type Neuro logic exam	EEG, CT, MRI LP, glucose, ammonia, BUN
ID		Immunization Hx Physical contacts		Culture and DFA

Key References: Centers for Disease Control and Prevention (CDC): National, state, and local area vaccination coverage among adolescents aged 13–17 years—United States, 2009, *MMWR Morb Mortal Wkly Rep* 59(32):1018–1023, 2010; Centers for Disease Control and Prevention (CDC): Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) in Pregnant women and persons who have or anticipate having close contact with an infant aged <12 months—Advisory Committee on Immunization Practices (ACIP), 2011, *MMWR Morb Mortal Wkly Rep* 60(41):1424–1426, 2011.

Perioperative Implications

Preoperative Preparation

- Postpone elective surgery until pt is noninfectious and symptom-free; uncomplicated disease resolves in 6–10 wk.
- Emergency surgery based on risks and benefits.
- Infectivity and contagion control with isolation precautions.
- Usage of disposable anesthesia circuit system.
- If possible, optimize respiratory function and nutrition prior to surgery.
- If in early phases, consider premedication with topical or oral decongestants (ephedrine, pseudoephedrine, xylometazoline) to reduce upper airway secretions; β_2 agonists (albuterol, metaproterenol) to minimize risk of bronchospasm.
- Optimize preop volume status to protect from dehydration.
- Premedication with respiratory depressants may increase risk of hypoxemia.

Monitoring

- Arterial cath may be useful in scenarios of impaired oxygenation or for frequent blood gas sampling.

Airway

- Acute and chronic coughing increase the risk of upper and lower airway edema with possible obstruction.
- Nasal and tracheal secretions increase the risk of laryngospasm and bronchospasm.
- Inspissated secretions can cause hypoxemia by mucous plugging and atelectasis, barotrauma by airway obstruction, and an inability to ventilate by ET due to obstruction.

Preinduction/Induction

- In some scenarios, RA may be favorable.
- Inhalational techniques with pungent agents should be avoided.
- Avoid agents associated with coughing.
- Usage of IV or topical lidocaine may decrease tracheal irritation and coughing.

Maintenance

- Keep pt warm and hydrated.
- Airway humidity should be controlled with a passive device to minimize humidity loss; or use an active humidifier that warms and humidifies the airway gases.
- Controlled ventilation allows optimal oxygenation and minimizes atelectasis.
- Consider PEEP for alveolar recruitment.
- Be prepared to contend with airway secretions and suction the ETT as needed; saline-moistened secretions are more readily removed.

Extubation

- Oral and tracheal suctioning should be performed with anticipation of copious secretions.
- Consider the use of preemergence bronchodilator treatment to minimize bronchospasm.
- Emergence techniques using NO may carry an increased risk of postextubation hypoxemia.
- An H_2 blocker should be considered with postop N/V prophylaxis to minimize risk of aspiration of acidic gastric contents.

Postoperative Period

- Control of infectivity and contagion with isolation precautions should be maintained.
- Supplemental O_2 therapy should include the use of a humidifier.
- Aggressive pulm toilet.
- Monitoring for apnea and hypoxia is needed.
- Regional techniques for pain management may be useful in avoiding serious respiratory complications related to IV analgesics.

Anticipated Problems/Concerns

- All contacts—including family, other pts, and hospital personnel—are at risk for infection.
- High risk of respiratory insufficiency due to hypoxemia from tissue damage, edema, and secretions.
- Infants at higher risk than adults for sequelae and death.

Pheochromocytoma

Michael F. Roizen

Risk

- Incidence in USA: 0.03–0.04% (~80,000) by autopsy of nonselected individuals.
- Prevalence: 0.1–0.3% of individuals with sustained Htn have pheochromocytoma. At least 20% are now diagnosed when the tumor is incidentally found during abdominal MRI or CT for other reasons.
- Race with highest prevalence: Caucasian.

Perioperative Risks

- In the case of emergency (life-threatening trauma, ruptured viscus), use α- and β-blockers and nitroprusside and keep pt in ICU until worst pain has passed or adrenergic control is achieved.
- Risk of hypertensive crisis is increased with bleeding into myocardium, brain, or kidney or with ischemia.
- Mortality rate of 0–3% even if pt is appropriately prepared for tumor resection and in "good" hands for adrenalectomy; it may be higher for undiscovered cases undergoing nonadrenal surgery.
- 25–50% of those who die in hospital of pheochromocytoma crisis do so during induction of anesthesia, during stressful periop periods, or during labor and delivery, often in surgery for other problems
- Associated with cholelithiasis and renal stones.

Worry About

- Pheochromocytoma (catecholamine excess) crisis with hemorrhage/infarcts in vital organs.
- Major goal is to avoid pheochromocytoma crisis; preop and intraop goals in management of extra-adrenal surgery are same as for adrenal surgery. If adrenergic blockade is not present prior to surgery, try to delay operation until pt has an appropriate degree of α-blockade. Judge appropriate blockade by:
  - No BP readings >165/90 mm Hg for 48 h
  - Presence of orthostatic hypotension, but BP on standing should not be <80/45 mm Hg
  - ECG free of ST-T changes
  - Absence of other signs of catecholamine excess and presence of signs of α-blockade

Overview

- Tumor of catecholamine-producing tissue (90% in adrenals). Painful (stressful) events in daily living or if a pt is less than perfectly anesthetized cause exaggerated stress response. Even small stresses can lead to blood catecholamine levels of 2000 to 20,000 pg/mL. However, infarction of tumor, with release of products onto retroperitoneal surfaces or pressure causing release of products, can result in blood levels of 200,000–1 million pg/mL, a situation that should be anticipated during tumor resection.
- Endocrinopathy associated with CV disease: Tachycardia, CHF, dysrhythmias (AFIB).
- Need α-blocker prior to β-blocker unless vasoconstrictive effects of latter go unopposed, thereby increasing risk of dangerous Htn. β-blockade is suggested if persistent arrhythmias or tachycardia fail to resolve with α-blocker or are aggravated by α-blocker.
- If α-blockade is used appropriately, risk of crisis diminished by >90%.
- Calcium channel blockers (nicardipine) are second in frequency for preparation, and metatyrosine is used as an alternative for malignant pheochromocytoma or for rapid preparation, but it has major adverse effects, including somnolence, movement disorder, and orthostatic effects and may be best confined to use in the hospital. These drugs, both phenoxybenzamine and metatyrosine, have recently become much more expensive.

Indications and Usual Treatment

- 60–90% of cases arise spontaneously and 10–40% are familial (autosomal dominant genetics involving chromosome 7 implicated in many).
- Associated with MEA IIA (medullary thyroid carcinoma; primary hyperparathyroidism) and IIB (medullary thyroid carcinoma and mucosal neuromas) with mutation often at chromosome location 17q11.2.
- Associated with neurofibromatosis, von Hippel–Lindau disease (retinal and cerebellar hemangioblastoma), ataxia-telangiectasia syndrome, Sturge-Weber syndrome, with mutation often at the VHL gene localized to chromosome 3p25–26.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Nasal stuffiness (from α-adrenergic blockade)		
CV	Htn; dysrhythmias; AFIB, sinus tachycardia, mitral valve prolapse; CHF, myocardial fibril necrosis or myocarditis	SOB, poor exercise tolerance, palpitations, Htn (50% sustained, 40% paroxysmal)	Standard exam including BP measurement for 1 min in stressful environment plus orthostatic maneuvers with BP/HR measured for 1 min	ECG, ECHO (if cardiomyopathy is suspected)
GI	90% of tumors adrenal or abdominal	Weight loss, diarrhea Dehydration	Palpation of abdomen can trigger crisis	No different from normal
HEME		Mild polycythemia, thrombocytopenia (secondary to reduced intravascular fluid)		Hgb (reduced polycythemia is a way to judge volume expansion by α-blocker)
GU	Renal stones from dehydration			
CNS	Increased catecholamine effects	Headache, tremor, anxiety, lowered pain threshold, fatigue		
METAB	Associated with hyperparathyroidism	Glucose intolerance from α-adrenergically induced gluconeogenesis and reduced insulin secretion		Insulin Rx often before Dx is made; Ca^{2+}

Key References: Witteles RM, Kaplan EL, Roizen MF: Safe and cost-effective preoperative preparation of patients with pheochromocytoma, *Anesth Analg* 91(2):302–304, 2000; Amar L, Servais A, Gimenez-Roqueplo AP, et al.: Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma, *J Clin Endocrinol Metab* 90(4):2110–2116, 2005; Lenders JW, Duh QY, Eisenhofer G, et al.: Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline, *J Clin Endocrinol Metab* 99(6):1915–1942, 2014.

Perioperative Implications

Preoperative Preparation

- Prehydrate liberally over 6–60 d if CV status will tolerate it; expand with high salt/fluid diet while increasing α-adrenergic blockade over 7–60 d (some use calcium channel blockers, but increased complications are associated with this process epidemiologically).

Monitoring

- Temperature.
- Arterial line placement prior to induction is difficult and painful but desired because of variations in BP.
- PA cath or TEE if CV system severely affected; CVP used in a minority of cases.

Anesthetic Technique

- No technique/group of agents associated with a better outcome; use of droperidol controversial; agents that block reuptake (ketamine) or cause catecholamine release might be avoided.

Induction/Maintenance

- Prehydrate liberally if CV status will tolerate it.
- Gentle induction with nitroprusside infusion plugged into an IV line and running slowly.
- Dopamine infusion in reserve for ready use.
- Painful or stressful events often cause an exaggerated response due to release of catecholamines from nerve endings that are "loaded" by the reuptake process.

Postoperative Period

- If catecholamine-producing tumor has been removed or α-adrenergically blocked, do not chase or force a high UO with large crystalloid infusions; pts have tendency to develop CHF because they have been on endogenous inotropes for many years.
- Early mobilization and deep breathing a must but fraught with difficulty; disturbed mentation often follows the removal of catecholamines for a lengthy period.

Adjuvants

- Drug interactions possible with chronic antiadrenergic agents, such as between verapamil or diltiazem and β-blockers in depressing AV nodal conduction if pt is chronically or acutely receiving a β-blocker or has decreased clearance of phenytoin, barbiturates, rifampicin, chlorpromazine, or cimetidine.

Anticipated Problems/Concerns

- Important to interview family members and perhaps advise them to inform their future anesthesiologists about the potential for such a familial disease.

Physiologic Anemia and the Anemia of Prematurity

Jeffrey D. Roizen

Risk

- Physiologic anemia, occurring 6–8 wk after birth, is a normal process in term infants.
- Anemia of prematurity is a pathologic anemia occurring in preterm infants. Extent of prematurity and comorbidities correlate with extent of anemia.

Perioperative Risks

- Term infants with physiologic anemia tolerate minor surgery well.
- Premature infants must be evaluated for symptoms due to anemia that may contribute to increased risk of preop events.

Worry About

- Major surgery occurring at the physiologic nadir of anemia may require blood transfusion.
- Preterm infants with anemia undergoing physiologic stress due to surgery are at risk for tachycardia, tachypnea, lactic acidosis, and periop apnea and bradycardia.

Overview

- Physiologic anemia is normal response to extrauterine life. Nadir at 9th–12th wk of life, Hgb level varies 9–11 g/dL.
- In preterm infants, nadir occurs at 4–8 wk of life and may decrease to 8 g/dL.
- Anemia of prematurity may be asymptomatic or give rise to nonspecific symptoms such as tachycardia, tachypnea, lethargy, pallor, apnea and bradycardia, poor feeding, poor growth, and lactic acidosis.

Etiology

- Transition to extrauterine life includes requirement for increased oxygen to bind to hemoglobin (HbO_2 saturation 50% in utero, 95% ex utero). Fetal hemoglobin with high oxygen affinity starts to be replaced with low-oxygen-affinity adult hemoglobin.
- Survival of neonatal erythrocytes is shorter than that of adult erythrocytes. Hemoglobin decreases until oxygen needs are greater than supply. Production of EPO is triggered and erythropoiesis increases.
- Rapid growth in infants causes a rapid increase in blood volume, resulting in hemodilution. Growth is more rapid in preterm than term infants.
- Preterm infants have more severe anemia because the less sensitive hepatic oxygen sensor triggers EPO production until 40 wk PCA. After 40 wk PCA, an extremely sensitive renal oxygen sensor takes over triggering and production of EPO.
- Iron storage occurs in the last trimester; therefore, premature infants are relatively iron deficient and have difficulty increasing iron stores by feeding.
- Extent of prematurity correlates with the amount of blood loss due to blood sampling.

Usual Treatment

- No treatment required in term infants.
- Preterm infants benefit from prevention: Reduction of blood draws, appropriate dietary supplementation, and erythropoietin therapy.
- Treatment of anemia of prematurity with blood transfusion occurs when symptoms of reduced O_2 supply are present. Symptoms include continued need for mechanical ventilation, apnea and bradycardia, tachycardia (>180 bpm for 24 h), inadequate weight gain, metabolic acidosis, or anticipation of major surgery.

Assessment Points (Apply to Preterm Infants Only)

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia	Review of VS trends	Tachycardia	± ECG
RESP	Apnea/bradycardia	Number of episodes; treatment required or spontaneous resolution		

Key References: Aher S, Malwatkar K, Kadam S: Neonatal anemia, *Semin Fetal Neonatal Med* 13(4):239–247, 2008; Bishara N, Ohls R: Current controversies in the management of the anemia of prematurity, *Semin Perinatol* 33(1):29–34, 2009.

Perioperative Implications

Preoperative Preparation

- Timing of elective blood-losing surgery depends on Hgb levels.

Monitoring

- Routine

Airway

- None

Preinduction/Induction

- Routine

Extubation

- Recent Hx of apnea and bradycardia: Consider delaying extubation to allow metabolism of anesthetic agents and sedatives.

Adjuvants

- Spinal anesthesia, when appropriate, may be beneficial in preterm infant.

Postoperative Care

- Consider monitoring preterm infant for apnea and bradycardia for 24 h.

Anticipated Problems/Concerns

- Anemia is a significant risk factor for postop apnea in preterm infant undergoing surgery and anesthesia.

Pickwickian Syndrome

Aaron M. Fields | Ryan E. Rubin

Risk

- Affects 5–10% of morbidly obese pts
- Usually associated with long-standing obesity

Perioperative Risks

- Markedly greater risk among the morbidly obese vs. pts with normal BMI.
- With intraabdominal or intrathoracic procedures lasting more than 2 h, there is approximately 40% of serious morbidity.

Worry About

- Hypoventilation
- Hypercarbia
- Hypoxemia
- Polycythemia, thrombophlebitis, and subsequent pulm embolism
- Pulm Htn
- Hypersomnolence
- Biventricular cardiac failure

Overview

- Pickwickian syndrome, or OHS, is defined as the combination of obesity (BMI above 30 kg/m^2), hypoxia during sleep, and hypercapnia.
- Morbidly obese pts who hypoventilate due to sleep apnea and severe restrictive ventilatory disorder have permanent pulm Htn, acidosis, and polycythemia because of their chronic hypoxemia and CO_2 retention.
- OHS is usually associated with systemic Htn and acompensatory increase in circulating blood volume, leading to right and left ventricular failure.
- Two subtypes are recognized, depending on the nature of the disordered breathing detected on further investigation. The first is OHS in the context of obstructive sleep apnea; this is confirmed by the occurrence of five or more episodes of apnea, hypopnea, or respiration-related arousals per h (high apnea-hypopnea index) during sleep. The second is OHS primarily due to "sleep hypoventilation syndrome;" this requires a rise of CO_2 levels by 10 mm Hg (1.3 kPa) after sleep compared to awake measurements and overnight drops in O_2 levels without simultaneous apnea or hypopnea. Overall, 90% of all people with OHS fall into the first category and 10% in the second.
- On physical exam, characteristic findings are the presence of a raised jugular venous pressure, a palpable parasternal heave, a heart murmur due to tricuspid regurgitation, hepatomegaly, ascites, and leg edema.

Etiology

- Work of breathing is increased as adipose tissue restricts the normal movement of the chest muscles and makes the chest wall less compliant, causing the diaphragm to move less effectively. Respiratory muscles are fatigued more easily, and airflow is impaired by excessive tissue in the head and neck area.

- Under normal circumstances, central chemoreceptors in the brain stem detect decreased pH and respond by increasing the respiratory rate; in OHS, the ventilatory response is blunted.
- Episodes of nighttime acidosis due to sleep apnea lead to renal compensation with retention of bicarbonate.
- Nighttime apnea leads to hypoxia, causing hypoxic pulm vasoconstriction. This vasoconstriction, in turn, leads to pulm Htn as well as right ventricular failure and remodeling.
- The chronically low O_2 levels in the blood also lead to increased release of erythropoietin, causing polycythemia.

Usual Treatment

- Weight loss through diet and exercise (which is rarely successful) or bariatric surgery
- NIPPV
- Uvulopalatopharyngoplasty
- Tracheostomy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway access	Snoring	Poor visualization	X-ray of neck may be helpful
CV	Biventricular failure CAD	Dyspnea, poor exercise tolerance Angina, poor exercise tolerance	Venous engorgement, S_3 and S_4, dyspnea	ECG, ECHO, CXR ECG, stress ECHO, angio
RESP	Hypoventilation	Dyspnea, sleeping upright Poor exercise tolerance	Rapid shallow breathing, cyanosis	ABGs, Hct, CXR

Key References: Olson A, Zwillich C: The obesity hypoventilation syndrome, *Am J Med* 118:948–956, 2005; Chau EH, Lam D, Wong J: Obesity hypoventilation syndrome: a review of epidemiology, pathophysiology, and perioperative considerations, *Anesthesiology* 117(1):188–205, 2012.

Perioperative Implications

Preoperative Preparation

- Consider pulm function tests with bronchodilator to determine whether a reversible restrictive component exists.
- Assess for bronchitis/pneumonia, which can be improved with pulm toilet and antibiotic therapy.
- Assess myocardial and volume status using a central venous catheter or PA cath.
- Consider maintaining pt in a semisitting position to avoid sudden shifts of volume to central circulation and pulm edema.

Monitoring

- Consider an arterial line for frequent monitoring of ABGs.
- Maintain adequate respiratory volumes and pressures.
- Consider PAC or transesophageal ECHO to monitor filling volumes and wall motion.

Airway

- Awake intubation frequently required.
- Laryngoscopy can sometimes be facilitated by elevating the shoulders and head on a bolster.

Induction

- Do not expect to ventilate pt adequately by mask. Establish airway first.

Maintenance

- Pts may have to remain in reverse Trendelenburg position to allow adequate ventilation.

Extubation

- Perform with pt in sitting position without residual sedation.
- Ensure adequate tidal volume and consider preop levels of CO_2 retention in making decision to extubate, as a normal CO_2 level may not be attainable.

Adjuvants

- Regional anesthesia only if pt is able to maintain ventilation
- Residual sedation or narcosis may preclude early extubation.

Postoperative Period

- Consider prophylaxis for thromboembolism; early ambulation may minimize pulm and thromboembolic complications.
- Pts may be extremely sensitive to the respiratory depressant effects of benzodiazepines and narcotics.

Anticipated Problems/Concerns

- All those problems associated with morbid obesity apply to Pickwickian pts.
- Early ambulation may minimize pulm and thromboembolic complications.
- Prepare the pt for a possibly prolonged course of postop mechanical ventilation, especially after upper abdominal procedures.

Pierre Robin Sequence

Charles B. Cauldwell

Risk

- 1:8500-14,000 live births; PRS nonsyndromic in about 40% of cases.
- Syndromic PRS most commonly associated with Stickler, velocardiofacial, and Treacher-Collins syndromes.

Perioperative Risks

- Chronic airway obstruction, respiratory distress, hypoxia.
- Malnutrition due to feeding difficulties, GE reflux.
- Congenital heart defects with syndromic PRS.

Worry About

- Airway obstruction
- Difficult intubation

Overview

- An anomaly consisting of micrognathia (or retrognathia), glossoptosis (posterior displacement of the tongue), and varying degrees of airway obstruction as well as feeding difficulties; cleft palate may be present but is not diagnostic.
- Airway obstruction, which may be multilevel, can lead to hypoxia and /or cyanosis.
- Feeding problems associated with malnutrition, reflux, and aspiration.
- In nonsyndromic PRS, if hypoxia and malnutrition are overcome, obstruction may improve secondary to mandibular growth by the time the pt reaches several mo of age.

Etiology

- Nonsyndromic PRS associated with a defect in gene SOX9, a chondrogenic regulator.
- Syndromic PRS associated with multiple genetic syndromes involving multiple defective genes.

Usual Treatment

- Prone positioning, lavage feeding may treat 70% successfully.
- Nasopharyngeal airway is the next level of intervention,
- Glossopexy or mandibular distraction osteogenesis to relieve airway obstruction and allow growth.
- Tracheostomy for multilevel airway obstruction or failure of previous surgery.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway obstruction	Respiratory distress OSA	Micrognathia Stridor, retractions	Sleep study CT, MRI
CV	Congenital defects Pulm Htn	 Cyanotic episodes Tachypnea	Murmur Desaturation	ECG ECHO CXR SpO_2
RESP	Hypoxia Aspiration pneumonitis	Tachypnea	Retractions Stridor	SpO_2 CXR
GI	Failure to thrive	Feeding problems GE Reflux	Wt	Weight gain Reflux study
CNS	Hypoxia	Seizures Developmental delay		

Key References: Côté A, Fanous A, Almajed A, et al.: Pierre Robin sequence: review of diagnostic and treatment challenges, *Int J Pediatr Otorhinolaryngol* 79(4):451–454, 2015; Cladis F, Anand K, Grunwaldt L, et al.: Pierre Robin sequence: a perioperative review, *Anesth Analg* 119(2):400–412, 2014.

Perioperative Implications

Preoperative Preparation
- Avoid sedative premedication.
- Consider atropine as antisialagogue and to maintain heart rate.

Monitoring
- Pulse oximeter and precordial stethoscope are important.

Airway
- Intubation may be very difficult.
- Consider awake placement of an LMA or intubation in neonates.
- Airway management and intubation may become easier with age in isolated PRS.

Preinduction/Induction
- Spontaneous ventilation is recommended, usually inhalational induction.
- Consider oral or nasopharyngeal airway if obstruction occurs.
- Have difficult airway cart available, with multiple scopes and light wand.
- Consider use of LMA with fiberoptic bronchoscope and exchange catheter.
- Have surgeon in OR capable of performing rigid bronchoscopy and/or tracheostomy at induction.

Extubation
- Thorough evaluation before postop extubation in the OR. If extubation is chosen, pt must be fully awake and should recover in the ICU.

Adjuvants
- Muscle relaxants, if used, should be administered after intubation and reversed if extubation is planned. Minimize use of opioids intraop unless long-term intubation is planned.

Anticipated Problems/Concerns
- Airway obstruction during all phases of anesthesia is very common. Chronic airway may lead to opioid sensitivity intraop and postop.

Pituitary Tumors

Lauren K. Dunn | Edward C. Nemergut

Risk
- 10% of diagnosed brain neoplasms
- Peak incidence fourth to sixth decade of life

Perioperative Risks
- Related to specific hormone-related effects, including difficult airway management; cardiovascular complications (hypertension, coronary artery disease, cardiomyopathy); respiratory compromise (obstructive sleep apnea); and endocrine and lyte abnormalities

Worry About
- Airway management: Difficult mask ventilation and intubation, especially in acromegaly and Cushing disease
- Cardiovascular risk: Htn, CAD, cardiomyopathy
- Respiratory complications: Obstructive sleep apnea and postop ventilatory support
- Endocrine abnormalities: Acromegaly, hyperthyroidism, Cushing disease, panhypopituitarism, postop DI
- EleLyte abnormalities: Hypernatremia secondary to DI
- Rarely, management of elevated ICP

Overview
- Tumors classified by size (macroadenoma >1 cm vs. microadenoma <1 cm) and hormone secretion (functioning vs. nonfunctioning).
- Functioning tumors present with symptoms of hormone excess.
- Nonfunctioning tumors are more likely to be macroadenomas and present with symptoms of mass effect: headache, visual loss (bitemporal hemianopsia), and hypopituitarism.
- Pts rarely present with elevated ICP owing to obstruction of the third ventricle.

Etiology
- Disease and secreted hormones: Acromegaly, growth hormone; Cushing disease, ACTH; gonadotroph, FSH and luteinizing hormone LH; prolactinoma, prolactin; thyrotrophic, TSH
- May occur in MEN 1 syndrome with pancreatic and parathyroid neoplasms.

Usual Treatment
- Medical therapy for treatment of systemic effects of functional tumors: Acromegaly, somatostatin analog (octreotide, lanreotide), growth hormone antagonists (pegvisomant); Cushing disease, ketoconazole, metyrapone (block cortisol synthesis); prolactinoma, dopamine agonist (bromocriptine, cabergoline); thyrotropic, somatostatin analog (octreotide, lanreotide) or propylthiouracil
- Tumor resection via transsphenoidal approach (endoscopic endonasal or sublabial)
- Gamma knife radiosurgery

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Acromegaly: Bone and soft tissue hypertrophy Cushing disease and thyrotropic adenoma: Exophthalmos		Enlarged facial bones, tongue and mandible, laryngeal and pharyngeal thickening, glottic narrowing, possible recurrent laryngeal nerve injury	Indirect laryngoscopy, fiberoptic laryngoscopy
CV	Acromegaly: Htn, CAD, CM Cushing disease: Htn, septal and LV hypertrophy Thyrotropic adenomas: Palpitations, arrhythmias	Chest pain, dysrhythmias, diastolic heart failure Diastolic dysfunction	BP, S_3 and S_4 heart sounds, peripheral edema, JVD	ECG, ECHO, CXR ECG ECG
RESP	Acromegaly and Cushing disease: OSA	Snoring, daytime somnolence		Sleep study
ENDO	Acromegaly: DM type 2 Cushing disease: DM type 2, hypercortisolism Prolactinoma: Infertility, amenorrhea, galactorrhea, impotence (male) Nonfunctioning macroadenoma: Panhypopituitarism		Truncal obesity, striae, moon facies	Preop labs: Metabolic panel (sodium, calcium, glucose), TSH, thyroxine, serum cortisol, ACTH, insulin-like growth factor-1, testosterone, LH, FSH, prolactin, pregnancy test
CNS	Optic chiasm compression	Visual field deficit		Visual field testing
MS	Acromegaly: Bone and soft tissue overgrowth Cushing disease: Osteoporosis, truncal obesity, myopathy	Pathologic fractures, weakness, fatigue	Enlarged hands and feet, cervical spine changes Proximal muscle weakness	
DERM	Cushing disease: Fragile skin	Easy bruising	Striae	

Key References: Miller BA, Ioachimescu AG, Oyesiku NM: Contemporary indications for transsphenoidal pituitary surgery, *World Neurosurg* 82(6S):S147–S151, 2014; Nemergut EC, Dumont AS, Barry UT, et al.: Perioperative management of patients undergoing transsphenoidal pituitary surgery, *Anesth Analg* 101(4):1170–1181, 2005.

Perioperative Implications

Preoperative Preparation

- Hormone replacement therapy for panhypopituitarism
- "Stress dose" steroid is often unnecessary, but the prudent practitioner should be aware of the risk of absolute or relative hypocorticalism and be prepared to treat if necessary.

Monitoring

- Consider invasive arterial monitoring if BP cuff size is inadequate or in pts with significant cardiac disease
- Acromegalic pts may have compromised ulnar blood flow; place radial arterial line with caution.
- Theoretical risk of VAE due to head up positioning. No reports of VAE-related morbidity or mortality and additional monitors (i.e., end-tidal nitrogen or precordial Doppler) not typically required.

Airway

- A standard ETT or oral RAE tube is acceptable.
- Be prepared for difficult airway in acromegalic pts; 20% of those with Mallampati class 1 and 2 airways are difficult to intubate.
- If macroglossia is present, intubation with intubating LMA or fiberoptic bronchoscope difficult. Consider awake fiberoptic intubation.

Induction

- Consider rapid sequence induction in pts with GERD or DM and delayed gastric emptying.

Maintenance

- Infiltration of nasal mucosa with local anesthetic and epinephrine may cause dysrhythmias and hypertension.
- Choice of anesthetic to facilitate rapid emergence; propofol, remifentanil, or volatile anesthetics are all reasonable.
- Muscle relaxation to provide immobile surgical field and reduce risk of CSF leak, visual field or vascular injury.
- Injury to carotid artery may result in significant blood loss, but this is uncommon. Deliberate Htn may facilitate repair.
- Valsalva maneuver may be used to check for CSF leak.

Extubation

- Suction stomach and oropharynx to remove blood and irrigation fluid.
- Perform awake extubation with pt in seated position to minimize risk of airway obstruction or aspiration.

Postoperative Period

- Prophylaxis for and treatment of PONV.
- Treat headache pain with opioids, NSAIDs, or acetaminophen.
- Monitor serum sodium and UOP for development of DI or SIADH (rare).
- Postop visual field testing is important, as injury optic nerves may result in catastrophic loss of vision.
- Complications include cranial nerve palsy and CSF leak.
- Screen for hypopituitarism and replace hormones as needed.

Adjuvants

- Use opioids cautiously in pts with OSA.
- Treat hemodynamic instability with α_1- and β-blockers.

Anticipated Problems/Concerns

- Airway management
- Hemodynamic instability and risk of myocardial ischemia
- OSA and need for assisted ventilation postop

Acknowledgment

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Placenta Previa

Courtney G. Masear | Karen S. Lindeman

Risk

- Incidence: 1:200-250 pregnancies
- Highest incidence with multiparity, repeat C-section or other uterine surgery, prior placenta previa, advanced maternal age, tobacco use, cocaine use, male fetus

Perioperative Risks

- Maternal mortality is <1%.
- Fetal complications: Prematurity (45% of deliveries at <37 wk); mortality increased 3 to 4 times.
- Life-threatening hemorrhage of mother or fetus.
- Fetal hypoxia.

Worry About

- Blood loss, hypovolemia.
- Increased risk of aspiration due to pregnancy or recent oral intake.
- Higher risk of placenta accreta, increta, and percreta, possibly requiring hysterectomy.
- Fetal compromise from inadequate intervillous blood flow.
- Preterm labor: Concomitant tocolytic therapy can alter hemodynamic response to hemorrhage.

Overview

- Placental implantation in advance of fetal presenting part.
  - Placenta previa: Placenta overlies cervical os.
  - Low-lying placenta: Placenta is near but not overlying the os.
- Often presents as painless vaginal bleeding in the second or third trimester.
- Diagnosis confirmed by transvaginal ultrasound ("gold standard") by measuring distance from internal cervical os to placental edge.

Etiology

- Unknown

Usual Treatment

- Expectant management.
- In pts with low-lying placenta, mode of delivery depends on distance from placental edge to internal cervical os.
  - >2 cm: Can undergo trial of labor.
  - 1-2 cm: Controversial, but consider trial of labor.
  - <1 cm: C-section.
- Uncomplicated placenta previa, stable without bleeding: Planned C-section at 36 wk.
- Persistent hemorrhage: Emergency C-section.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway edema	Pregnancy	Mallampati class	
CV	Hypovolemia, anemia	Amount of bleeding	Tachycardia, hypotension	Hb/Hct
RESP	Reduced FRC	Pregnancy		
GI	Full stomach, decreased lower esophageal sphincter tone	Reflux symptoms		

Key References: Scavone BM: Antepartum and postpartum hemorrhage. In Chestnut DH, editor: *Obstetric anesthesia: principles and practice*, ed 5, Philadelphia, PA, 2014, Saunders, pp 881–914; Silver RM: Abnormal placentation: placenta previa, vasa previa, and placenta accreta, *Obstet Gynecol* 126(3):654–668, 2015.

Perioperative Implications

Preoperative Preparation

- Anesthetic plan:
  - Stable placenta previa or low-lying placenta without bleeding: neuraxial anesthesia (epidural, spinal, or CSE) for elective C-section.
  - Active hemorrhage: Emergency C-section under general anesthesia.
- Nonparticulate oral antacid premedication.
- Assess volume status.
- Crossmatch blood and consider transfusion if there is active bleeding.
- Two large-gauge IV lines; consider central venous access.

Monitoring

- Standard ASA monitors.
- Consider arterial monitoring if pt is hemodynamically unstable.

Airway

- Airway edema may make intubation more difficult; have appropriate equipment available.
- Full-stomach precautions.

Preinduction/Induction

- Preoxygenate with four vital capacity breaths of O_2.
- Consider awake or rapid-sequence induction.
- Rapid-sequence induction agent plus succinylcholine; induction agent depends on hemodynamic status.
- Low-dose propofol.
- Ketamine (1 mg/kg).
- Etomidate (0.3 mg/kg).

Maintenance

- Low-concentration inhalational agent (0.5–0.75 MAC) ± N_2O (≤50%) before delivery.
- Potent inhalational anesthetics relax the uterus.
- FIO_2 less than 1.0 with use of N_2O results in less dissolved O_2 in maternal blood.
- NO_2 with IV opioid and benzodiazepine after delivery; consider low concentration of potent inhalational anesthetic for additional amnesia.
- Monitor intravascular volume; massive transfusion protocol may be required. One PRBC, one FFP, one plt pheresis pack per 6 U of PRBC/FFP. Protocol comes from trauma literature but not yet studied for obstetrics.

Extubation

- Extubate awake.

Adjuvants

- Oxytocin, methylergonovine, prostaglandin $F_2\alpha$ to enhance uterine contraction and decrease bleeding after delivery

Postoperative Period

- Monitor hemodynamic and volume status.
- Monitor for coagulopathy in pts with hemorrhage and massive transfusion.

Anticipated Problems/Concerns

- Intrapartum and/or postpartum hemorrhage
- Urgent induction of anesthesia
- Fetal distress

Plagiocephaly

Amy O. Soleta

Risk

- Obstetric factors: Primigravidy, assisted delivery, low birth weight, preterm birth
- Infant factors: Limited neck ROM, male sex, larger CSF spaces, preference to sleep with head turned to one side.
- Infant care factors: Spends most time in supine position without variable head positions, firmer mattress, less time in prone position and/or upright, exclusively bottle-fed.
- Observed in 5–48% of healthy newborns.

Perioperative Risks

- Minimal risk if plagiocephaly is isolated and pt is presenting for unrelated surgical procedure
- Increased risk if pt is presenting for cranial vault remodeling due to failed conservative therapy

Worry About

- Association with syndrome and/or other craniofacial abnormalities
- Potential for difficult airway
- Significant blood loss during surgical correction

Overview

- Cranial malformation characterized by asymmetric flattening of a portion of the skull
- May lead to postural torticollis

Etiology

- External pressure on malleable skull leads to plagiocephaly.
- Unilateral body/head positioning of infant during first 6 wk of life.
- Infants aged 2–4 wk have maximally deformable skulls.

Usual Treatment

- Prevention: Parental counseling to alternate head position when placing infant supine to sleep and to vary positions when infant is awake, with time spent upright, lateral, and prone.
- Conservative treatment with repositioning of infant for mild cases.
- Helmeting to reshape skull for more severe cases or if not improved by 6 mo of age.
- Physical therapy to treat associated positional torticollis.
- Most children show dramatic improvement in head shape by age 2–3 y.
- Surgical correction if severe or failed conservative and orthotic treatment by age 12–15 mo.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Abnormal head shape, torticollis	Positioning	Flattened skull, head turned to one side	CT scan
CNS	Elevated ICP, orbital pressure, developmental delay*	Irritability, lethargy Headache, seizures	Papilledema	CT head

*Severe cases only.

Key References: Beretta F, Talamonti G, D'Aliberti G, et al.: Surgical indications and treatment for cranial occipital anomalies. In Villani D, Meravigla MV, editors: *Positional plagiocephaly*. Switzerland, 2014, Springer International Publishing, pp 79–95; Cladis F, Grunwaldt L, Losee J: Anesthesia for plastic surgery. In Davis P, Cladis F, Motoyama E, editors: *Smith's anesthesia for infants and children*, ed 8, Philadelphia, 2011, Elsevier, pp 826–829.

Perioperative Implications for Surgical Correction

Preoperative Preparation
- Thorough history to evaluate for associated syndrome or craniofacial abnormality.
- Type and crossmatch for PRBCs.
- Prepare parents for long surgery, postop swelling of face, potential for continuing intubation postop, and need for blood transfusion.

Monitoring
- Standard monitors
- Arterial line
- UO

Airway
- Potentially difficult if there are additional craniofacial abnormalities or severe torticollis is present

Preinduction/Induction
- Premedication with oral or intranasal anxiolytic as needed
- Standard inhalational induction

Maintenance
- Standard inhalational agents.
- Monitor Hgb/Hct.
- Consider use of antifibrinolytic agent and cell saver.

Extubation
- Long duration of procedure and large volume fluid and blood administration can lead to postop airway edema, low threshold for remaining intubated.

Postoperative Period
- Pediatric ICU
- Potential for continued blood loss, coagulopathy
- Risk of cerebral edema
- Adequate pain management
- Potential for difficult reintubation due to facial and airway edema

Anticipated Problems/Concerns
- Risk of venous air embolism during skull removal

Pneumocystis jirovecii Pneumonia

Neal H. Cohen

Risk
- PJP is a respiratory infection seen in immunocompromised pts, usually associated with a CD4 cell count <500/μL.
- Can affect pts with both acquired and congenital immunodeficiency syndromes.
- Seen in both males and females and all age groups.
- Often associated with chronic HIV infection, particularly if not treated with HAART.

Perioperative Risks
- Respiratory failure often necessitating mechanical ventilatory support with high airway pressures even when ventilating with low tidal volumes; often accompanied by severe dyspnea independent of gas exchange.
- Hemodynamic instability associated with induction of anesthesia, initiation of positive pressure ventilation.
- Pneumothoraces.
- Persistent expiratory airflow reduction after resolution of acute infection.
- Bronchiectasis, lung cysts.
- Often associated with other comorbidities related to immune deficiency.

Worry About
- Progressive respiratory failure with diffuse bilateral interstitial infiltrates.
- Pneumothoraces, either spontaneous or associated with positive-pressure ventilation.
- Persistent pulm dysfunction.
- Common cause of nonproductive cough, dyspnea, fevers in immunosuppressed pt
- Associated with other opportunistic infections, particularly CMV and *Candida albicans* esophagitis.
- Toxicity from therapy with sulfa antimicrobials, including methemoglobinemia, anemia, leukopenia, and severe skin rashes.
- High incidence of drug resistance.

Overview
- Indolent disease; can progress to severe respiratory failure.
- May be cause for nonproductive cough in high-risk pt.
- High incidence of spontaneous pneumothoraces.
- Extrapulmonary sites of *Pneumocystis* infection are rare.
- May be associated with other infections (tuberculosis, bacterial, viral, fungal) and malignancies (Kaposi sarcoma, lymphoma) in immunosuppressed pts.

Etiology
- *P. jiroveci* (previously *carinii*), originally characterized as a parasite, is now classified as a fungus.
- Organisms reside in the lungs, usually as latent infection; activated in an immunosuppressed host.
- High prevalence of antibodies to *P. jirovecii* in nonimmunosuppressed humans, suggesting that most individuals are "colonized" early in life.
- Human-to-human transmission has not been documented.

Usual Treatment
- Chemoprophylaxis for PJP: TMP/SMX.
  - Second-line agents: Dapsone; pentamidine, systemic and aerosolized; atovaquone.
- Treatment for PJP:
  - TMP-SMX is the mainstay.
  - Corticosteroids (strongly recommended but conflicting data on value of steroids, particularly for non-HIV pts).
  - Alternative antimicrobial therapy: Pentamidine, clindamycin plus primaquine, dapsone plus trimethoprim, atovaquone.
  - Supportive respiratory care including positive-pressure ventilation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oropharyngeal lesions	Fever, chills, sweats	Circumoral, acral, and mucous membrane lesions	
CV	Intravascular volume deficits Cardiomyopathy	Fluid intake, syncope, respiratory rate	Hemodynamic lability Distended neck veins Abnormal heart sounds	Orthostatic BP changes
RESP		Cough, usually nonproductive Progressive dyspnea Hemoptysis	Tachypnea Breath sounds, prolonged expiratory phase Exam often normal though coarse breath sounds common	ABG PFTs Transbronchial biopsy Gallium scan of lung LDH
GI	Hepatopathy Bowel lesions	Often associated with wt loss, other infections causing diarrhea, GI symptoms	Hepatosplenomegaly	LFTs
HEME	Anemia, leukopenia Coagulopathy			CBC Clotting studies
RENAL	Nephropathy, oliguria	Oliguria		BUN, Cr
CNS	Encephalitis, meningitis	CNS changes	Abnormal mental status	

Key References: Travis TJ, Hart E, Helm J, et al.: Retrospective review of *Pneumocystis jirovecii* pneumonia over two decades, *Int J STD AIDS* 20(3):200–201, 2009; *Centers for Disease Control and Prevention*: Pneumocystis pneumonia. <http://www.cdc.gov/fungal/diseases/pneumocystis-pneumonia/>, (Accessed 01.06.16.)

Perioperative Implications

Preoperative Preparation

- Ensure adequacy of oxygenation, ventilation, acid-base balance.
- Assess pulmonary function, particularly expiratory phase of respiration.
- Evaluate for evidence of other opportunistic infections.
- Review CXR for evidence of infiltrates, abscesses, cystic lesions or cavitations, bullae, pneumothorax, effusions.

Monitoring

- If treated with sulfa drugs, confirm presence or absence of metHb.
- Interpret SpO_2 with caution if metHb present; measure SaO_2 by cooximeter.

Airway

- Minimize airway pressures, tidal volume.
- Consider local anesthesia to upper airway to manage increased airway reactivity.

Induction

- Maintain adequate PaO_2.
- Minimize airway pressures; risk of pneumothorax.
- Ensure adequate intravascular volume.
- Monitor for hypotension associated with positive-pressure ventilation, myocardial depressants.

Maintenance

- Ensure adequate oxygenation, ventilation.
- Minimize airway pressures.
- Administer bronchodilators.

Extubation

- May be delayed.
- Prolonged ventilatory support often required.

Postoperative Period

- Ensure adequate oxygenation, ventilation.
- If mechanically ventilated, minimize airway pressures using low-tidal-volume ventilation.
- Maintain intravascular volume; optimize myocardial function.
- Continue anti-*Pneumocystis* therapy; consider other antiviral agents.

Anticipated Problems/Concerns

- Deterioration of respiratory status; prolonged respiratory failure.
- Pneumothorax; may require surgical repair if tube thoracotomy unsuccessful.
- Nosocomial infections and associated viral infections.
- Monitoring oxygenation with pulse oximeter may be inaccurate if pt treated with dapsone or primaquine.
- Drug resistance.

Pneumonia, Community-Acquired

Emily J. MacKay

Risk

- Incidence of CAP requiring hospitalization is 24.8:10,000 individuals.
- Incidence is 9 times higher among those 65 y of age or older (compared with age group 18–49).
- Incidence is 25 times higher among those 80 y of age or older (compared with age group 18–49).

Perioperative Risks

- Intraop decrease in FRC could worsen the severity of hypoxemia.
- Prolonged mechanical ventilation.

Worry About

- Irritable airway at increased risk for laryngospasm
- Hypoxemia

Overview

- CAP is defined as involving no history of hospitalization within 90 d of onset of symptoms.
- The responsible pathogen is identified in approximately 40% of cases.

Etiology

- Viruses (23%):
  - Human rhinovirus most common (9%)
  - Influenza (6%)
  - HMPV, RSV, and parainfluenza viruses; coronaviruses and adenovirus
- Bacteria (11%):
  - *S. pneumoniae* most common (5%)
  - *M. pneumoniae*, *L. pneumophila*, and *C. pneumoniae* second most common (4%)
  - *Staphylococcus aureus* (1%)
  - Enterobacteriaceae (1%)
- Bacteria plus virus (2%)
- Fungus or mycobacteria (1%)

Viral pathogens:

- Human rhinovirus
- Influenza (A or B)
- HMPV
- RSV
- Parainfluenza virus

Bacterial pathogens:

- *Streptococcus pneumoniae* (gram-positive cocci in chains)
- *Mycoplasma pneumoniae* (small bacterium, Mollicutes, no peptidoglycan cell wall [no stain])
- *Legionella pneumophila* (gram-negative, aerobic, non-spore-forming)
- *Chlamydia pneumonia* (gram-negative, small)
- *Staphylococcus aureus* (gram-positive cocci in clusters)
- Enterobacteriaceae (gram-negative, enteric)

Usual Treatment (Empiric)

- Combination therapy: Beta-lactam (third-generation cephalosporin) plus macrolide. For example (70-kg pt):
  - Ceftriaxone (third-generation): 1.5 g q8h plus azithromycin 500 mg q24h
  - Cefotaxime (third-generation): 2 g q8h plus azithromycin: 500 mg q24h
- Monotherapy: Fluoroquinolone
  - Levofloxacin: 750 mg daily
  - Moxifloxacin: 400 mg daily

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Upper respiratory infection Tracheobronchitis Pneumonia	Sore throat, rhinorrhea, headache, myalgias Cough: Nonproductive Cough: Productive, shortness of breath, fever	Inflammation of nasal turbinates Erythematous soft palate Inspiratory wheeze Focal or nonfocal crackles on lung auscultation	Nasopharyngeal swab Rapid strep test CXR, sputum sample CXR, sputum sample

Key References: Jain S, Self WH, Wunderink RG, et al.: Community-acquired pneumonia requiring hospitalization among US adults, *N Engl J Med* 373(5):415–427, 2015; Futier E, Constantin JM, Paugam-Burtz C: A trial of intraoperative low-tidal-volume ventilation in abdominal surgery, *N Engl J Med* 369(5):428–437, 2013.

Perioperative Implications

Preoperative Preparation

- Elective procedure: Delay surgery for at least 6 wk.
- Urgent or emergent procedure: Proceed with caution.
- If sputum purulent, send for sputum culture.
- Ensure that appropriate antibiotic therapy is initiated.
- Bronchodilator must be available in the OR.

Monitoring

- Routine.
- Consider arterial line for serial blood gas analysis.

Airway

- At risk for rapid desaturation secondary to shunt
- At risk for laryngospasm and bronchospasm secondary to inflammation

Induction

- Ensure adequate depth of anesthesia prior to airway instrumentation (increased risk of bronchospasm).
- Use neuromuscular blockade (increased risk of laryngospasm).

Maintenance

- Inhalational anesthesia has benefit of bronchodilation.
- Consider avoiding desflurane (increased risk of airway reactivity).
- Consider protective lung ventilation strategy intraop (i.e., tidal volume of 6–8 mL/kg ideal body weight, PEEP ≥5 cm H_2O, maintain plateau pressure <30 cm H_2O).

Extubation

- Awake and following commands
- Vital capacity >15 mL/kg ideal body weight
- Adequate analgesia to accommodate aggressive pulmonary toilet

- High-risk procedure (e.g., open abdominal, thoracotomy, trauma exploratory laparotomy) plus pneumonia; strongly consider prolonged mechanical ventilation.

Adjuvants
- Bronchodilator (albuterol).
- Maintain scheduled antibiotic dosing in addition to periop antibiotics.

Postoperative Period
- Increased risk for reintubation
- If pt remains intubated, maintain intraop mechanical ventilation settings.

Anticipated Problems/Concerns
- Increased airway reactivity
- Impaired oxygenation secondary to shunt
- At risk for prolonged mechanical ventilation

Pneumonia, Ventilator-Associated

Emily J. MacKay

Risk
- Incidence of VAP is 1.2–8.5:1000 ventilator days; occurs in 9–27% of intubated mechanically ventilated pts
- Risk greatest in the first 5 d of mechanical ventilation
- Increased risk: Male sex; admission for trauma; underlying disease severity; surgery; previous antibiotic exposure

Perioperative Risks
- Intraop decrease in FRC can worsen the severity of hypoxemia.
- Preop high levels of PEEP can lead to decreased preload and hypotension.

Worry About
- Atelectasis and derecruitment of alveoli
- Hypoxemia
- Mucus plugging of main or intermediate bronchi

Overview
- VAP is defined as pneumonia occurring in mechanically ventilated pts 48–72 h after endotracheal intubation.
- Implications of ETT placement:
  - Suppression of cough reflex leading to microaspiration around ETT cuff.
  - Pooling of secretions around cuff.
  - Biofilm coating ETT, including gram-negative and fungal organisms.
  - Impaired mucociliary clearance of secretions.
- Microbiology:
  - Early VAP (≤4 d on ventilator): Organisms usually sensitive to antibiotics.
  - Late VAP (≥5 d on ventilator): Increased risk of organisms resistant to antibiotics.

Etiology
- Early VAP bacteria:
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - MSSA
  - Antibiotic-sensitive enteric gram-negative bacilli: *Escherichia coli, Klebsiella pneumoniae, Enterobacter* spp., *Proteus* spp., *Serratia marcescens*
- Late VAP bacteria:
  - MDR bacteria: MRSA, *Acinetobacter, Pseudomonas aeruginosa,* ESBL
  - Oropharyngeal bacteria: *Streptococcus viridans, Corynebacterium,* coagulase-negative *Staphylococcus, Neisseria* spp.
  - Polymicrobial infection
  - Fungal infection
- VAP pathogen incidence:
  - *P. aeruginosa* (24.4%)
  - *S. aureus* (20.4%; half MSSA and half MRSA)
  - Enterobacteriaceae (14.1%): *Klebsiella. E. coli, Proteus* spp., *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp.
  - *Streptococcus* spp. (12.1%)
  - *Haemophilus* spp. (9.8%)
  - *Acinetobacter* spp. (7.9%)
  - *Neisseria* spp. (2.6%)
  - *Stenotrophomonas maltophilia* (1.7%)
  - Others (4.7%): *Corynebacterium, Moraxella, Enterococcus,* fungi
- MDR organisms' potential mechanisms:
  - *Pseudomonas*
    - Upregulation of efflux pumps (pump antibiotic out).
    - Lower expression of outer membrane porin channel (antibiotic cannot get in).
    - Beta-lactamases (break beta-lactam ring on beta-lactam antibiotics, rendering antibiotic inactive).
  - *S. aureus:* Lower affinity for beta-lactam antibiotics by production of penicillin-binding protein.
  - Enterobacteriaceae: Plasmid mediated production of beta-lactamases that destroy extended-spectrum beta-lactam drugs (ESBLs). ESBLs can also cause crossover resistance to aminoglycosides in addition to extended-spectrum beta-lactams.

Usual Treatment (Empiric)
- Local antibiogram for hospital is *extremely important* (to show differing incidence of organisms)
- Early-onset VAP (≤4 d): Potentially treat with limited spectrum antibiotics for 8 d.
- Late-onset VAP (≥5 d): Requires broad-spectrum antibiotic for 10–14 d.
- Deescalation is extremely important to limit the development of MDR organisms.
- Antibiotic options for early-onset bacterial VAP (70-kg pt):
  - Monotherapy: Second- or third-generation cephalosporin (e.g., cefuroxime [second], 1.5 g q8h; ceftriaxone [third], 2 g daily; cefotaxime [third], 2 g q8h)
    OR
  - Monotherapy: Fluoroquinolone or levofloxacin, 750 mg daily; moxifloxacin, 400 mg daily
    OR
  - Combination therapy: Aminopenicillin plus beta-lactamase inhibitor (e.g., ampicillin plus sulbactam, 3 g q8h)
    OR
  - Monotherapy: Carbapenem (e.g., ertapenem)
- Antibiotic options for late-onset bacterial VAP (triple therapy required) (70-kg pt):
  - Third- or fourth-generation cephalosporin (e.g., ceftazidime [third], 2 g q8h; cefepime [fourth], 1–2 g q8h)
    OR
  - Carbapenem (e.g., imipenem plus cilastatin 500 mg q6h or 1 g q8h; meropenem, 1 g q8h)
    OR
  - Beta-lactam/beta-lactamase inhibitor (e.g., piperacillin plus tazobactam, 4.5 g q6h)
    PLUS
  - Aminoglycoside (e.g., amikacin, 20 mg/kg per d; gentamicin, 7 mg/kg per d; tobramycin, 7 mg/kg per d)
    OR
  - Antipseudomonal fluoroquinolone (e.g., ciprofloxacin, 400 mg q8h; levofloxacin: 750 mg daily)
    PLUS
  - Coverage for MRSA (e.g., vancomycin, 15 mg/kg q12h; linezolid, 600 mg q12h)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Tracheobronchitis Pneumonia	Cough: Productive Ventilator-dependent respiratory failure, fever, increased WBC	Inspiratory wheeze Focal or nonfocal crackles on lung auscultation	CXR, endotracheal aspirate CXR, endotracheal aspirate, bronchoalveolar lavage

Key References: Kalanuria AA, Zai W, Mirski M: Ventilator-associated pneumonia in the ICU, *Crit Care* 18(2):208, 2014; Futier E, Constantin JM, Paugam-Burtz C, et al.: A trial of intraoperative low-tidal-volume ventilation in abdominal surgery, *N Engl J Med* 369(5):428–437, 2013.

Perioperative Implications

Preoperative Preparation
- Intubated pt
- Assess mechanical ventilation settings in the ICU; if PEEP ≥10 cm H_2O utilize ICU ventilator for transport and intraop.
- Consider having inhaled nitric oxide or epoprostenol available.
- Ensure that appropriate antibiotic therapy is initiated for VAP (especially if MDR organisms suspected).

Monitoring
- Arterial line for serial blood gas analysis.
- Consider central line.

Airway
- Ensure that ETT is secure.
- Suction ETT.

Induction
- With ETT already in place, proceed cautiously with inhalational induction.

Maintenance
- Inhalational anesthesia has benefit of bronchodilation.
- Maintain protective lung ventilation strategy intraop (i.e., tidal volume of 6–8 mL/kg ideal body weight, PEEP ≥5 cm H_2O, maintain plateau pressure <30 cm H_2O)
- Limit intraop IV fluids.

Extubation
- Intubated preop VAP pt; low threshold for ongoing mechanical ventilation.
- If considering extubation:
  - Rapid shallow breathing index <75 breaths/tidal volume (L) per min
  - Vital capacity >15 mL/kg ideal body weight
  - If arterial line available, PaO_2 >80 mm Hg on an FiO_2 <40%

Adjuvants
- Bronchodilator (albuterol).
- Inhaled nitric oxide.
- Inhaled epoprostenol.
- Maintain scheduled antibiotic dosing in addition to periop antibiotics.

Postoperative Period
- If intraop mechanical ventilation settings do not require high levels of PEEP, transport pt with oxygen and ambu bag with PEEP valve.
- If intraop mechanical ventilation settings are complex, transport pt with ICU ventilator.
- If ICU ventilator was utilized intraop, transport pt with ICU ventilator.

Anticipated Problems/Concerns
- Impaired oxygenation secondary to shunt
- Hemodynamic instability
- Impaired RV function in the setting of high PEEP or increased PVR

Poliomyelitis

David P. Martin | Luke Van Alstine

Risk
- Acute disease eradicated in USA and most of Europe owing to effective vaccination (last USA case reported in 1979 and last case in the western hemisphere in Peru in 1991).
- Small parts of Africa and Asia still have areas of endemic wild-type poliovirus with less than 200 cases reported globally in 2014.
- Hundreds of thousands of survivors still live in USA with varying degrees of deficit.
- Postpolio syndrome is a constellation of signs and symptoms that constitute a synergy between normal aging and the decreased neuromuscular reserve and musculoskeletal effects of polio itself.

Perioperative Risks
- Potential predisposition to respiratory complications (such as aspiration and postop respiratory failure), chronic pain syndromes, altered sensitivity to muscle relaxants and anesthetics, and positioning challenges.
- Hyperkalemia with succinylcholine is a risk if there is significant muscle denervation.

Worry About
- Weakness of the pulmonary or swallowing muscles, which are believed to be at greatest risk for postsurgical complications.
- Polio survivors often underestimate or minimize their degree of weakness.
- Postpolio syndrome may predispose pts to respiratory difficulties, sleep apnea, swallowing impairment, and impaired ability to deal with temperature changes.

Overview
- Caused by the poliovirus, a subtype of the human enterovirus C group.
- The virus is transmitted most commonly via fecal-oral contamination but can also be transmitted by pharyngeal spread during outbreaks.
- Most infected individuals are asymptomatic (primary or "minor" viremia) but a small percentage (<10%) will go on to develop a "major" viremia characterized by the typical viral symptoms ranging from malaise to fever and nausea/vomiting. A fraction of these individuals (<1%) will develop selective destruction of motor neurons, leading to weakness (paralytic polio).
- Weakness is often asymmetric and varies from one muscle group to another.
- The virus can also affect other neurons, including the brain stem, which can lead to respiratory insufficiency and bulbar dysfunction.
- Bulbar involvement can include dysphagia, dysarthria, and difficulty controlling secretions.

Etiology
- Spread of poliovirus to the CNS is not well understood. It can spread laterally to other neighboring motor neurons and/or via transneuronal spread through the axon.

Usual Treatment
- Treatment is supportive, ranging from mechanical ventilation for respiratory failure to pain management and physical therapy.
- Many pts deal with long-term sequelae, from chronic weakness and pain to potential development of postpolio syndrome later in life, for which treatment is again supportive.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	OSA	Snoring Daytime somnolence	Neck circumference Htn	Sleep study
RESP	Respiratory failure Aspiration risk	Dyspnea Pneumonia	Tachypnea	CXR, PFTs ABG
CNS	Muscle denervation Bulbar weakness Opioid tolerance	Difficulty swallowing	Weakness	EMG Swallow study
MS	Weakness Disability Chronic pain	Gait Mobility aids	Joint contractures ROM	Radiographs

Key References: Jubelt B: Polio and infectious diseases of the anterior horn. In Shefner JM, editor. Waltham, MA, 2016, *UpToDate*. www.uptodate.com/contents/polio-and-infectious-diseases-of-the-anterior-horn. (Accessed 01.06.16.); Van Alstine LW, Gunn PW, Schroeder DR, et al.: Anesthesia and poliomyelitis: a matched cohort study, *Anesth Analg* 122(6):1894–1900, 2016.

Perioperative Implications

Preoperative Preparation
- Thorough preop physical and exam looking for signs/symptoms of respiratory insufficiency, bulbar dysfunction, OSA, chronic pain, or neurologic deficits.
- Consider PFTs if respiratory insufficiency is known preop.

Monitoring
- As appropriate for planned procedure.
- Consider postop oximetry.

Airway
- Evaluate for neurologic deficits, which can limit airway options if there is cervical involvement.
- Potential for unrecognized difficult airway due to bulbar dysfunction and/or OSA.

Preinduction/Induction
- May need special positioning if neurologic deficits or contractures are present.
- Avoid succinylcholine if pt has significant muscle denervation.

Maintenance
- Individualized; no specific technique identified as safer than any other for these pts.

Extubation
- Be mindful of bulbar dysfunction, which can lead to postextubation difficulties.
- OSA may be present; close monitoring postop is recommended.

Adjuvants
- Many of these pts deal with chronic pain and may have a tolerance to opioids; this subgroup may benefit from procedure-specific regional anesthesia.

Anticipated Problems/Concerns
- Respiratory: Pulm insufficiency and/or OSA, which are often unrecognized or not diagnosed.
- Neurologic: These pts commonly have long-standing neurologic deficits and/or contractures.
- Pain: Chronic pain common; pt may have opioid tolerance.

Polycythemia Vera

Steven M. Frank

Risk

- Prevalence: 22:100,000; twice as high among men as women.
- Higher prevalence in Jewish people of European origin.
- Prevalence increases with advancing age (rare in those <30 y).

Perioperative Risks

- Risk of deep venous thrombosis, pulmonary emboli
- Risk of coronary, cerebral thrombosis/ischemia
- Increased histamine release and prostaglandin production

Worry About

- Hyperviscosity from increased Hct
- Preop treatment should include phlebotomy to Hct of ≤45%
- Increased plt count and plt aggregation
- Thrombotic complications: MI, stroke, deep venous thrombosis, Budd-Chiari syndrome
- Bleeding diathesis

Overview

- A chronic myeloproliferative disease characterized by increased red blood cell mass.
- Often WBC and plt counts are increased.
- The resulting hyperviscosity of blood predisposes to thrombosis.
- Symptoms: Headaches, erythromelalgia (pain in hands/feet), pruritus.
- Predisposed to gouty arthritis, peptic ulcer disease.
- Accompanied by palpable splenomegaly.

Treatment

- Although incurable, treatment increases life expectancy from 1–2 y to 20 y
- Phlebotomy is first-line therapy
- Low-dose aspirin (81 mg/d) is often given to reduce thrombotic risk.
- Hydroxyurea (Hydrea): The most commonly used myelosuppressive agent for PV. Helps reduce both Hct concentration and plt count.
- Ruxolitinib (Jakafi): A Janus-associated kinase inhibitor, approved by the US FDA for treatment of pts with PV who have had an inadequate response to hydroxyurea or are intolerant of it.

Etiology

- Unclear, but a mutation in the *JAK2* (Janus kinase 2 gene) increases response to erythropoietin.
- Normal oxygen saturation (if low, may be secondary polycythemia).
- Low erythropoietin levels (if high, may be secondary polycythemia).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Headaches, tinnitus, blurred vision or blind spots, dizziness or vertigo		
CV	Increased intravascular volume	Angina, coronary artery microthrombus	Reddened, purplish skin	Increased Hgb, Hct, red cell count Hct: >46% in women >52% in men May have increased WBC and plt count
RESP/HEME	Absence of hypoxemia	Poor exercise tolerance Smoking, high altitude not a cause Often asymptomatic	Signs/symptoms of pulm emboli	Normal arterial oxygen saturation *JAK2* mutation in blood cells
GI	Splenomegaly Budd-Chiari syndrome Peptic ulcer disease	Symptoms of liver disease secondary to Budd-Chiari syndrome	Splenomegaly	Liver enzymes
RENAL	Potential renal thrombosis			
ENDO	Low EPO levels			Bone marrow: Hypercellular, low iron stores
CNS		Headaches		
PNS	Erythromelalgia (pain in hands/feet)			
MS	Itching, gouty arthritis	Fatigue	Extremity edema, signs of DVT Bleeding, bruising in 25%	DVT assessment by US or venogram

Key References: Leukemia and Lymphoma Society: Polycythemia vera facts. FS13:1-7. <https://www.lls.org/sites/default/files/file_assets/FS13_PolycythemiaVera_FactSheet.pdf>, 2015 (Accessed 01.06.16); Finazzi G, Barbui T: How I treat patients with polycythemia vera, *Blood* 109(12):5104–5111, 2007.

Perioperative Implications

Preoperative Preparation

- Preop phlebotomy
- Hydration for hemodilution
- May benefit from periop hematology/oncology consult
- For low-risk blood loss cases, may continue aspirin, weighing the risk of thrombosis versus bleeding

Monitoring

- ST-segment changes for myocardial ischemia
- Large-bore access to facilitate additional phlebotomy

Induction/Maintenance

- Both RA and GA are options
- Caution with neuraxial anesthetics if there is a bleeding diathesis

Intraoperative Management

- Intraop hemodilution to reduce thrombotic risk
- Some pts at risk for increased bleeding and transfusion

Postoperative Period

- Increased risk for thrombosis and bleeding diathesis.
- Aggressive DVT prophylaxis is important.

Anticipated Problems/Concerns

- Vigilance for prevention, diagnosis, and treatment of thrombotic events
- Also must be prepared to treat bleeding diathesis
- Treat symptoms: Itching, fatigue, angina, heart failure, gout
- PV pts at greater risk for thrombosis than for secondary polycythemia

Polymyositis

Daniel Abraham | Lee A. Fleisher

Risk

- Annual incidence in USA: 5.5:1,000,000, most prevalent among black women
- Annual incidence around the world: 1.9-7.7:1,000,000, although comprehensive epidemiologic data are lacking

Perioperative Risks

- Delayed recovery from muscle relaxation
- Aspiration pneumonitis
- Cardiac arrhythmias
- CHF

Worry About

- Increased risk of aspiration
- Respiratory muscle and/or diaphragmatic weakness
- Hyperkalemia following succinylcholine use; sensitivity to NMB
- Interstitial lung disease, progressive fibrosis, and/or difficulty with ventilation/oxygenation
- Cardiomyopathy with heart failure
- Chronic use of therapeutic steroids and anti-immunologic medications

Overview

- Rare form of an acquired inflammatory myopathy affecting adults and rarely children.
- Can often mimic many other myopathies and is a diagnosis of exclusion.
- Pts present with progressive and symmetric proximal muscle weakness.

- Diagnosis confirmed by analysis of serum muscle enzymes, EMG findings, and muscle biopsy (most definitive test).
- A careful family history, medication list review, physical exam, blood test, and muscle biopsy are all crucial because they may help to exclude an alternative diagnosis, such as an inherited muscle disease or toxic myopathy.

Etiology

- An autoimmune etiology is suspected and hypothetically supported by an association with other autoimmune or connective tissue diseases and a response to immunotherapy.
- Drugs—especially D-penicillamine, statins, or zidovudine—may also trigger an inflammatory myopathy.
- Several viruses—including coxsackie, influenza, mumps, CMV, and Epstein-Barr virus—may also have an association.

Usual Treatment

- Treatment focuses on controlling inflammatory response through immunosuppression.
- Steroids, with prednisone as first-line agent.
- Immunosuppressive drugs, which include azathioprine, methotrexate, mycophenolate mofetil, rituximab, cyclosporine, tacrolimus, cyclophosphamide.
- IVIG.
- Physical therapy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Neck muscles weakness	Headache Head drop	Neck ROM Head lift	EMG
RESP	Inspiratory muscles weakness Interstitial lung disease Aspiration pneumonitis	Dyspnea Chronic cough Limited exercise tolerance	Dyspnea/tachypnea Wheezing Hypoxia	PFTs CXR, CT scan ABG Bronchoscopy
CV	Conduction abnormalities CHF	Chest pain Dyspnea Palpitations	Arrhythmia Edema Inspiratory crackles	ECG TTE Stress test
GI	Pharyngeal muscle weakness	Dysphagia	Regurgitation Aspiration	Endoscopy CXR
CNS	Systemic manifestations	Malaise Fever	Hyperthermia	
HEME	Raynaud phenomenon	Cold digits	Digit vasospasm	
DERM	Only seen with concomitant disease, dermatomyositis	Rash	Erythematous and raised papules on extensor surfaces Heliotrope rash	Muscle/skin biopsy
MS/RHEUM	Proximal muscle weakness Arthralgias or arthritis Calcinosis of subcutaneous tissue Coexisting rheumatologic disorder (scleroderma, SLE)	Myalgia Muscle tenderness Skin ulceration Joint swelling	Muscle weakness, atrophy Delayed reflexes	CPK, CK, ALT, AST, LDH Autoantibodies EMG Joint x-ray Muscle biopsy

Key References: Strauss KW, Gonzalez-Buritica H, Khamashta MA, et al.: Polymyositis and dermatomyositis: a clinical review, *Postgrad Med J* 65(765):437–443, 1989; Gunusen I, Karaman S, Nemli S, et al.: Anesthesia management for cesarean delivery in a pregnant woman with polymyositis: a case report and review of literature, *Cases J* 2:9107, 2009.

Perioperative Implications

Preoperative Preparation

- Assess cardiovascular and pulm status.
- Consider use of RA in order to limit GA and use of NMB; there are some case reports of successful and safe neuraxial techniques and limited reports on peripheral nerve blockade.
- Concomitant steroid therapy and necessity of stress doses should be considered.

Monitoring

- Arterial line if indicated (either owing to CHF or frequent blood draws for ABG)
- TOF peripheral nerve stimulation with NMB use (consider baseline stimulation before NMB given)
- Foley catheter for urine output assessment if pt has cardiac disease

Airway

- Consider rapid sequence intubation if pt has dysphagia.

Induction

- Avoid use of succinylcholine (may cause hyperkalemia).
- Volatile agents and succinylcholine may serve as a trigger malignant hyperthermia and should be avoided in pts with baseline elevated CPK levels.
- If not necessary, avoid nondepolarizing NMB due to increased sensitivity (vecuronium and pancuronium associated with prolonged neuromuscular paralysis).
- Consider use of remifentanil to aid with intubation/for hypokinesis.

Maintenance

- Volatile anesthetics may potentiate the effects of muscle relaxation.
- Consider total IV anesthetic technique.
- Antagonism to NMB may cause additional muscle weakness and/or cardiac dysrhythmias.
- Consider stress-dose steroids.
- Avoid overuse of narcotics.
- Keep pt euvolemic to avoid heart failure.

Extubation

- If NMB is used, confirm complete reversal using twitch monitor and confirm full strength of pt with head lift (if able to do so preop).
- Confirm that pt is completely awake and able to breathe independently of ventilator prior to extubation.
- Consider NIF test to assess adequacy of strength of ventilation.

Postoperative Period

- If possible, keep head of bed elevated to assist with pulm function and to avoid an aspiration event.
- Increased susceptibility to infection if on immunosuppression.

Anticipated Problems/Concerns

- May need ICU stay postop to wean off ventilator.
- Pain control management; avoid overuse of narcotics, which may lead to oversedation and/or apnea.
- May need continued dose of stress dose steroids through periop period.
- Volume shifts may complicate cardiac status.
- Consider swallow study before oral intake to avoid unanticipated dysphagia and an aspiration event.

Pompe Disease

Sheri Jones Oguh | Lee A. Fleisher

Risk

- Combined incidence (infantile vs. late-onset): 1:40,000.
- Infantile form has higher incidence in African-American and Chinese populations.
- Late-onset disease has a higher incidence in the Netherlands.

Perioperative Risks

- Respiratory insufficiency
- Aspiration pneumonia
- Pulm edema
- Myocardial ischemia

Worry About

- Respiratory insufficiency, which may require prolonged mechanical ventilation
- Myocardial ischemia
- Arrhythmias, sudden death

- GE reflux, aspiration pneumonia
- Difficult extubation and ventilator dependence

Overview

- Only glycogen storage disease that is also a lysosomal storage disease.
- Deficiency of lysosomal enzyme acid-α glucosidase.
- Lysosomal glycogen accumulates in several organ systems, most importantly cardiac, skeletal, and smooth muscle.
- Clinical features are mostly neuromuscular.
- Two major forms: Infantile versus late-onset.
- Infantile presents with cardiomyopathy, hypotonia, and muscle weakness ultimately leading to death secondary to cardiorespiratory failure within the first year of life.
- Cardiomyopathy usually not seen in late-onset variants, which can present at any age. Usually characterized by muscle weakness followed by muscles of respiration and diaphragm. Respiratory failure is usually cause of death or severe morbidity.
- Pts with late-onset Pompe disease usually present with slowly progressive myopathy, which can be mistaken for limb girdle muscular dystrophy.
- Measurement of GAA activity in skin fibroblasts is the current gold standard test to confirm diagnosis.

Etiology

- Disorder of acid α-glucosidase.
- Disease severity correlates inversely with residual acid α-glucosidase activity.
- Autosomal recessive inheritance pattern.

Usual Treatment

- Enzyme therapy can be helpful in infantile variants, improving cardiac and respiratory function
- Supportive therapy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Weakness of muscles of inspiration and diaphragm	Open-mouth breathing, decreased gag reflex	Macroglossia	
RESP	Atelectasis (compression of bronchi by enlarged heart), Weakness of muscles of inspiration and diaphragm, decreased vital capacity, diaphragmatic dysfunction	Dyspnea Open-mouth breathing, protrusion of tongue (may mimic macroglossia) Frequent pulm infections, aspiration pneumonia Sleep apnea, morning headaches, somnolence Weak cough, use of accessory muscles	Decreased breath sounds	CXR Pulm function tests (e.g., FEV_1) Polysomnography ABG
CV	Biventricular hypertrophy, short PR interval (interference with specialized conducting tissues) Cardiomegaly LV dysfunction Cardiomyopathy with or without left ventricular outflow obstruction	Palpitations, CHF symptoms Exercise intolerance	Murmur, gallop, arrhythmias	ECG CXR ECHO 24-h Holter monitoring
GI	Weakness of oropharyngeal muscles	Difficulty chewing/swallowing, failure to thrive GE reflux	Underweight, macroglossia, decreased gag reflex Hepatomegaly	
CNS	Glycogen accumulation in skeletal, cardiac, and smooth muscle	Muscle weakness, hypotonia, developmental delay, gross motor delay, loss of early motor milestones		
HEME	Elevated CK, LDH, AST, ALT May reflect enzymes released from muscle			CK
MS	Glycogen accumulation	Myopathy Exercise intolerance Limb-girdle weakness Gait abnormalities		EMG, muscle biopsy

Key References: Kishnani PS, Steiner RD, Bali D, et al.: Pompe disease diagnosis and management guideline, *Genet Med* 8(5):267–288, 2006; McFarlane HJ, Soni N: Pompe's disease and anaesthesia, *Anaesthesia* 41(12):1219–1224, 1986.

Perioperative Implications

Preoperative Preparation

- Assess myocardial, respiratory, and volume status.
- Consider regional anesthetic techniques.

Monitoring

- Arterial line if indicated.
- Consider CVP or PA catheter if indicated.
- ECG with focus on ST segments; pulse oximetry.
- Capnography.

Airway

- Macroglossia
- Impaired gag reflex

Preinduction/Induction

- Avoid hypotension, as this can precipitate arrhythmias from ischemia due to a hypertrophied LV.
- Maintenance of normal coronary perfusion pressure is of utmost importance.
- Maintain a higher filling pressure for adequate preload and a normal to high systemic vascular resistance to ensure effective coronary perfusion.
- Consider ketamine, as it maintains SVR and contractility and is less likely to reduce preload.
- Etomidate is another consideration.
- Inhalation agents should be used cautiously and in pts with a lesser degree of cardiac hypertrophy.
- High induction doses of propofol should be avoided.
- Pts may be more sensitive to neuromuscular blockade.
- Malignant hyperthermia precautions should be followed.

Maintenance

- If neuromuscular blockade required, choose one that has the least amount of cardiac depressant ability and shortest duration.
- Beta blockers must be used carefully, as there is anecdotal evidence of sudden death in the pediatric population.
- Avoid drastic changes in volume status (hypovolemia vs. fluid overload).

Extubation

- Period with the greatest O_2 demands

Postoperative Period

- Impaired cough predisposes pt to atelectasis and aspiration pneumonia.
- Chronic CO_2 retention and hypoxemia.
- Sleep disordered breathing due to supine position and effect of sleep on respiratory control mechanism.
- Important to focus on pulm toilet, bronchodilators.
- Supplemental O_2 versus CPAP may be required to treat hypoxemia.

Anticipated Problems/Concerns

- Myocardial ischemia.
- Respiratory insufficiency.
- Decreased CO.
- Pulm infections should be treated aggressively.

Portal Hypertension

Michael A. Hall | Guarav Malhotra

Risk

- Hepatic cirrhosis has a prevalence of about 1–3:1000.
- At the time of diagnosis of cirrhosis, 50% of pts will already demonstrate sequelae of portal hypertension.
- Also, in the setting of schistosomiasis (mainly in developing countries), portal vein thrombosis, Budd-Chiari syndrome, or congestive hepatopathy may be seen in pts with congestive heart failure.

Perioperative Risks

- Multifactorial increase in risk of coagulopathy:
  - Risk of thrombocytopenia caused by splenic sequestration of platelets due to congestion of the spleen.
  - Splenic sequestration may compound thrombocytopenia caused by decreased synthesis of thrombopoietin in the liver.
  - Underlying hepatic synthetic dysfunction can also lead to decreased synthesis of clotting factors.
- Ascites may increase intra-abdominal pressures, increasing aspiration risk and compromising pulmonary function.
- Risk of total body volume overload in pts with ascites who have been chronically retaining sodium and water.
- Risk of hypotension from both decreased effective circulating volume as well as decreased vascular resistance in chronically vasodilated state.
- Risk of hypoxemia in pts with HPS.
- Risk of development of acute RV dysfunction in pts with portopulmonary hypertension.
- Risk of kidney injury due to reduced renal perfusion, leading to HRS.
- Risk of development of HE in the periop period.

Worry About

- Aspiration risk from increased intra-abdominal pressure in pts with ascites or from full stomach in pts with active upper GI/variceal bleeding.
- Hypotension from derangements of intravascular volume, peripheral vasodilation, hemorrhage, sepsis, or myocardial dysfunction.
- Sepsis from spontaneous bacterial peritonitis or increased bacterial translocation from intestines (leading to urinary tract infection or pneumonia). Prophylactic antibiotics are recommended for endoscopic procedures for variceal bleeding that would otherwise not have required antibiotics.
- Increased blood loss due to coagulopathy and platelet dysfunction as well as splanchnic congestion in intra-abdominal surgery.
- Potential for worsening of underlying hepatic disease during the periop period.
- Changes in drug pharmacokinetics and pharmacodynamics given increased volume of distribution and impaired liver metabolic function.

Overview

- Direct cause of many of the complications of hepatic cirrhosis.
- Causes derangement of nearly every organ system.
- Increases periop morbidity and mortality to a variable degree depending on type of surgery. For example, cirrhotic pts undergoing abdominal surgery have an estimated mortality of up to 30%.
- Pts can present for any of a number of elective and emergency surgeries, including cholecystectomy, endoscopy for GI bleeding, hernia repair (abdominal hernias exacerbated by ascites), colorectal surgery for diverticular disease, thoracoscopy for hepatic hydrothorax, liver resection for cancer, and finally (curative) liver transplantation.
- The model for end-stage liver disease (MELD) score has been shown to be useful in predicting surgical risk of morbidity and mortality, with a 14% increase in mortality for every 1-point increase in MELD score above 8. The pt's bilirubin, INR, and serum creatinine are used in calculating the MELD score.

Etiology

- Although a variety of diseases and disease states can cause portal hypertension, the initial insult is always an increase in pressure within the portal vein caused by an obstruction to flow from the portal vein to the right atrium. This obstruction can be prehepatic (portal vein thrombosis), intrahepatic (hepatic cirrhosis, most common), or posthepatic (Budd-Chiari syndrome or congestive hepatopathy).
- HVPG can be used to diagnose and grade portal hypertension. Portal hypertension is present when HVPG is >5 mmHg. Complications usually begin at HVPG >10 and acute variceal bleeding at HVPG >12.
- In an attempt to alleviate increased pressures, the splanchnic endothelium increases production of vasodilators and vascular endothelial growth factor and decreases sensitivity to vasoconstrictors.
- Vasodilation leads to increased arterial inflow into the splanchnic system, increasing portal vein flow, and further increasing portal pressures. Increased portal flows and pressures leads to increased interstitial tissue hydrostatic pressure and the development of ascites.
- Increased pressure and angiogenesis lead to the formation of portosystemic collateral venous beds, which manifest as esophageal varices, portal-hypertensive gastropathy, and hemorrhoids.
- Collateral flow, bypassing the liver, increases systemic exposure to splanchnic vasodilators, causing HPS as well as the hyperdynamic syndrome of cirrhosis. Collaterals also lead to hyperammonemia and development of HE.

Usual Treatment

- Currently, most treatments are aimed at specific sequelae of portal hypertension.
- Treatments specifically targeting portal pressures include nonselective beta blockers, placement of TIPS, and liver transplantation.
- Ascites is primarily treated with salt restriction and diuretics. Large-volume paracentesis can be used for tense ascites and to provide symptomatic relief.
- Peritoneal venous shunts (such as Denver shunt) may be used in pts who have ascites refractory to medical therapy.
- Esophageal varices can be treated endoscopically for both prophylaxis and control of acute variceal hemorrhage.
- Pts with type II HRS will sometimes require hemodialysis while waiting for liver transplant.
- Portopulmonary Htn will sometimes require pulm vasodilators such as sildenafil and epoprostenol.
- HPS may require supplemental oxygen while waiting for liver transplant.
- HE is treated with lactulose and oral antibiotics (rifaximin) but may require hospitalization and supportive care while waiting for clinical improvement.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hyperdynamic circulation Hypotension Intravascular volume depletion	Dyspnea on exertion Orthostasis	Vital signs (tachycardia), orthostatic signs	Monitor BP and HR Low SVR
RESP	V/Q mismatch in HPS Hepatic hydrothorax	Dyspnea	Vital signs (low SpO_2) Decreased breath sounds, dullness to percussion at lung base (most commonly on right)	Monitor SpO_2, PaO_2 on ABG Increased A-a gradient
GI	Ascites Esophageal varices Acute variceal hemorrhage Portal-hypertensive gastropathy Splenomegaly	Abdominal distention Hematemesis Melena BRBPR Abdominal pain	Abdominal distention, positive fluid wave, Palpable spleen Heme-positive stool Caput medusa	Abdominal US, abdominal CT Upper endoscopy, Measurement of HVPG
RENAL	Hypervolemic hyponatremia, HRS type I (acute) and type II (chronic)	Oliguria Peripheral edema Abdominal distention	Edema or exam consistent with ascites	Lytes, especially sodium; serum Cr, especially compared with pt's baseline BUN
HEME	Thrombocytopenia Platelet dysfunction	Easy bruising/bleeding	Petechiae Bleeding from venipuncture sites	CBC Coagulation studies Thromboelastogram
CNS	HE Cerebral edema	Severity ranges from confusion to disorientation to coma	GCS Signs of intracranial Htn or herniation Asterixis	Serum ammonia CT of head if concern for cerebral edema or herniation ICP monitoring (must be weighed against risk of hemorrhage in coagulopathic pts)

Key References: Kiamanesh D, Rumley J, Moitra VK: Monitoring and managing hepatic disease in anaesthesia, *Br J Anaesth* 111(Suppl 1):i50–i61, 2013; Malik SM, Ahmad J: Preoperative risk assessment for patients with liver disease, *Med Clin North Am* 93(4):917–929, 2009.

Perioperative Implications

Preoperative Preparation

- Control underlying disease as well as possible (i.e., sobriety for alcoholic cirrhosis, stress-dose steroids for autoimmune hepatitis).
- Risk stratify pt based on MELD score; use platelet count as an indicator of severity of portal hypertension.
- Correction of hyponatremia preop to avoid rapid increases intraop.
- Optimize diuretic regimen for pts with ascites to control hypervolemia.
- Assess and correct coagulopathy, with appropriate additional product available to the OR for intraop administration.

Monitoring

- Standard monitors.
- Urinary catheter for UOP monitoring.
- Frequently will require arterial catheter for continuous BP monitoring as well as stroke volume variation to determine volume status and ventricular loading conditions.
- Although CVP is known to be a poor indicator of volume status, central access can be helpful for transfusion as well as administration of vasoactive and inotropic medications.

Airway

- With ascites or acute variceal hemorrhage, aspiration precautions and RSI indicated.

Induction

- May see hemodynamic instability in pts with recent hemorrhage or in sepsis.
- May need to adjust choice and dosage of anesthetic drugs to account for renal dysfunction and underlying hepatic dysfunction.
- If considering regional anesthesia, attention should be paid to pt's coagulation status.

Maintenance

- Must be cognizant of dosing adjustment for renal and hepatic dysfunction.
- Active warming to avoid hypothermia and potentiation of coagulopathy.
- In abdominal surgery that drains a large volume of ascites, rapid fluid shifts can require the administration of albumin to maintain intravascular volume.
- Pts with HPS may require high FiO_2 and high PEEP to maintain oxygenation; however, this may need to be balanced with PEEP compromising venous blood return.

Extubation

- Requires full reversal of neuromuscular blockade, as duration of action of neuromuscular blockers may be altered.
- Ensure that pt fully awake and protecting airway before extubation without new or worsened encephalopathy.

Postoperative Period

- Pain control with PCA or oral opioids, again acknowledging altered metabolism.
- Regional anesthesia can be helpful as long as not contraindicated by coagulopathy.
- Watch for acute decompensation of either hepatic or renal function caused by decreased hepatic or renal blood flow while under general anesthesia.
- Risk for development of HE, especially if administered benzodiazepines.

Anticipated Problems/Concerns

- Aspiration risk in presence of ascites or acute variceal hemorrhage.
- Hemodynamic instability due to derangement of volume status, sepsis, or myocardial dysfunction.
- Pts susceptible to acute decompensation of renal function.
- Multifactorial risk for increased blood loss intraop.

Postoperative Encephalopathy, Metabolic

Steven Roth | Lee A. Fleisher

Risk

- Pts undergoing any surgical procedure are at risk. It is especially of concern following brain or cardiac surgery or interventional neuroradiology procedures and in pts with COPD, cancer, renal or hepatic failure, and those with lyte abnormalities.
- Post–liver transplant.
- No gender predominance.

Perioperative Risks

- Aspiration, fluid and lyte imbalances, circulatory failure, hypoxia, insulin use

Worry About

- Suspect in any pt who fails to awaken or awakens more slowly than expected following GA.
- Evaluate for the presence currently or earlier in the periop period of severe hypotension, hypoxemia, fluid and lyte disorders, cancer, renal or liver dysfunction, and thyroid abnormalities.
- Seizures, increasing intracranial pressure; persistent coma may result.

Overview

- Altered state of consciousness that becomes apparent in the perioperative period.
- Pts may fail to awaken after GA for these reasons: Anesthesia-associated narcotics, inhalational anesthetics, benzodiazepines, hypnotics (may impair consciousness), brain injury. Direct surgical intervention (e.g., occlusion of major intracranial vessel, intracranial hemorrhage, edema) may result in impaired consciousness, or embolization to a major artery may occur (e.g., during or after cardiac surgery, interventional neuroradiology procedures).
- Metabolic abnormalities: Circulatory failure, hypoxia, insulin use, hepatic and renal insufficiency. Lyte abnormalities can result in failure or slowness to awaken. In all cases, Dx should proceed quickly in order to treat underlying cause before severe brain injury results.
- Could be confused with delirium.

Etiology

- Anoxic-ischemic encephalopathy.
- Hypercapnic encephalopathy ($PaCO_2$ >70 mm Hg).
- Hypoglycemic encephalopathy (glucose ≤30 mg/dL).
- Hyperglycemic coma (glucose ≥450 mg/dL; Osm >319 $mOsm/mm^3$).
- Acute hepatic encephalopathy: Liver failure.
- Uremic encephalopathy: Renal failure.
- Other brain injuries: SIADH, seizures.
- Electrolyte imbalance: Hypokalemia or hyponatremia, hypercalcemia.
- Endocrine: Thyrotoxicosis, hypothyroidism.
- Drug and/or toxin exposure; use a drug and/or toxicology screen.

Usual Treatment

- Depends on the etiology (see Assessment Points)

Assessment Points

Etiology	Examples	Diagnosis	Treatment
ENDO	Hyperthyroid Hypothyroid	Thyrotoxicosis Myxedema	PTU Thyroid hormone replacement
ANOXIC-ISCHEMIC	Cardiac arrest Prolonged shock Hypoxemia	Obvious from clinical course	Reverse acute event Decrease cerebral edema, maintain BP, decrease temperature?, prevent seizures
HYPERCAPNIC	Narcotic-induced Severe COPD, sleep apnea	Increased heart rate and BP Increased end-tidal or arterial Pco_2	Reverse narcotic Mechanical vent to decrease Pco_2
HYPOGLYCEMIC	Insulin overdose Ethanol ingestion Neonatal (idiopathic)	No IVF and PO ingestion From Hx and alcohol level Decreased blood glucose	IV glucose (D50)
HYPERGLYCEMIC	Hyperosmolar nonketotic coma Ketoacidosis	Suspect in known diabetic Ketones in blood, urine Acidosis	Insulin, correct acidosis and fluid volume deficit
ION DISTURBANCES	Decreased Na^+ Decreased K^+	Serum Na^+ <125 mmol/L (e.g., SIADH) Serum K^+ <2.5 mEq/L Severe muscle weakness	Hypertonic saline (caution) NaCl and diuretics K^+ replacement
RENAL	Renal failure		
HEPAT	Hepatic encephalopathy		

Key References: Bozbora A, Coskun H, Erbil Y, et al.: A rare complication of adjustable gastric banding: Wernicke's encephalopathy, *Obes Surg* 10(3):274–275, 2000; Brown EG, Douglas VC: Moving beyond metabolic encephalopathy: an update on delirium prevention, workup, and management, *Semin Neurol* 35(6):646–655, 2015.

Perioperative Implications

- Correct ion and fluid disturbances.
- Normalize blood glucose.
- Optimize organ function (e.g., renal, hepatic).
- Adequate hormone replacement.
- Search for drug/toxin exposure (sedative/hypnotics; ethanol and its street substitutes, such as ethylene).

Posttransplant Lymphoproliferative Disorder

Tamas Seres

Risk

- Cumulative incidence over 5 y: 1–2% in liver, 1–3% in kidneys, 2–6% in heart, 2–9% in lung, and 11–33% in intestinal or multiorgan transplants
- Major risk factors:
  - EBV positive serology in the recipient (multisystem PTLD)
  - EBV negative recipient and EBV-positive donor (PTLD limited to allograft tissue)
  - The degree of T-cell immunosuppression (induction with OKT3, ATGAM, thymoglobulin, and maintenance with tacrolimus)
- Additional risk factors:
  - Time after transplant (highest incidence during the first y)
  - Recipient age (<25 y)
  - Ethnicity (Caucasians)
- Overall survival rates ranging between 25–35%

Perioperative Risks

- Increased risk of airway or bowel obstruction and hemodynamic compromise
- Increased risk of dysfunction of the transplanted organs
- Increased risk for infection and CNS involvement

Worry About

- Enlarged tonsils and cervical adenopathy increasing difficulty of airway
- Thoracic adenopathy complicating intubation, ventilation, and cardiac output
- Pulm involvement causing decreased oxygenation and/or ventilation
- Dysfunction of the transplanted kidneys, liver, or heart
- GI involvement manifesting as N/V or bowel obstruction
- CNS involvement manifesting as mental status change or increased ICP
- Immunosuppression causing an increased rate of infection

Overview

- Lymphoproliferative disorders are among the most serious and potentially fatal complications of chronic immunosuppression in organ transplant recipients.
- These tumors are mostly B-cell-type large-cell lymphomas. Extranodal involvement occurs in 30–70% of these cases as a localized tumor in either the transplanted organ or another site, such as the GI system, lungs, skin, liver, and CNS.

Etiology

- B lymphocytes, infected by EBV, proliferate in the setting of immunosuppression, where T-cell immune surveillance is significantly decreased.

Usual Treatment

- Reduction of immunosuppression, rituximab, cytotoxic T-cell infusions, and radiation (CNS).
- Surgery may be necessary to debulk large masses and relieve bowel obstructions.
- Chemotherapy for disseminated unresponsive disease.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Cervical adenopathy Pharyngitis Enlarged tonsils with pseudomembranous appearance Otitis media Sinusitis Laryngeal edema	Difficulty swallowing Sore throat Headache Facial pain, ear pain Difficulty talking or breathing	Lymphadenopathy Tonsillar enlargement Spotty, erythematous tonsils Otitis media Tenderness over sinuses Drooling; tripod position Difficulty of breathing	CT Hx and physical exam Serologic test for EBV
RESP	Lung nodules Pleural effusions Hilar and mediastinal adenopathy	SOB Orthopnea	Decreased breath sounds Crackles, egophony	CXR CT
CV	HF	SOB, tires easily Edema	New murmur, crackles Pitting edema	ECHO ECG
GI	Liver dysfunction, Bowel obstruction, Bowel perforation, Tumors anywhere in GI tract	N/V Abdominal pain and discomfort Distention Swelling, tenderness over graft site	Jaundice Abdominal distention Tenderness over graft Rebound tenderness	LFTs Abdominal x-ray, CT US
RENAL	Renal insufficiency or failure	Decreased UO Swelling	Pitting edema, Crackles	BUN, Cr, lytes
ID	Mononucleosis syndrome Generalized lymphadenopathy Sepsis	Fatigue, fever	Elevated temperature	CBC, serology for EBV
CNS	Brain tumors	Headache LOC Seizure	Stupor, coma Seizure	CT, MRI

Key References: Friedberg JW, Aster JC: Epidemiology, clinical manifestations, and diagnosis of post-transplant lymphoproliferative disorders. In Freedman AS, Brennan DC, editors: Waltham, MA, 2015, UpToDate. www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-of-post-transplant-lymphoproliferative-disorders. (Accessed 01.06.16); Pinyavat T: Posttransplant lymphoproliferative disorder. In Houck PJ, editor: *Handbook of pediatric anesthesia*, New York, 2015, McGraw Hill, pp 166–168.

Perioperative Implications

Preoperative Preparation

- Difficult airway techniques; consider GE reflux precautions.
- Evaluate the need for blood products and specific antibiotics.
- Evaluate the function of the transplanted organs.
- Consider stress-dose steroids if receiving steroids.
- Consider side effects of the immunosuppressant medications.

Monitoring

- Consider invasive monitoring in the event of organ failure or mediastinal mass.
- Consider ICP monitor as indicated for CNS involvement.

Airway

- Consider awake fiberoptic techniques if upper airway edema or masses or mediastinal masses are present.

Preinduction/Induction

- Induction agents should be chosen based on organ function. Cyclosporine can potentiate the effect of succinylcholine.
- A mediastinal mass can compress the aorta and SVC, leading to significant hypotension if pt is supine. Consider sitting or semisitting induction.
- Consider lower extremity for volume resuscitation if a large mediastinal mass is present.

Maintenance

- Keep the pt breathing spontaneously in case of significant airway obstruction.
- If a mediastinal mass is present, keep the pt in semisitting position and turn to lateral or prone position if hemodynamics become compromised.

Extubation

- Risk of airway obstruction if airway is manipulated during surgery

Postoperative Period

- Airway edema can become a problem.
- Continue stress-dose steroids.

Anticipated Problems/Concerns

- Airway obstruction and hemodynamic compromise
- Dysfunction of transplanted organs
- Mental status change or increased ICP in CNS involvement

Prader-Willi Syndrome

Navil F. Sethna

Risk

- Prevalence: 1:25,000
- Incidence: 1:10,000-15,000
- Racial prevalence: None
- Gender predominance: Similar frequency in both sexes and all races
- Most common syndromic form of obesity, affects 350,000–400,000 individuals worldwide
- Annual death rate is 3% versus 1% in the general population, primarily due to respiratory arrest

Perioperative Risks

- Infantile hypotonia, hypoventilation, and breathing difficulty
- Potential for difficult intubation and aspiration risk
- Worsening of obstructive/central sleep apnea and abn ventilatory responses to hypoxia, hypercarbia, and bronchospasm
- Bradycardia, ventricular arrhythmias (PVCs)
- Postop resp insufficiency
- Potential risk of rhabdomyolysis with succinylcholine
- Aberrant thermoregulation: Hyperthermia and MHS-like syndrome
- Glucose intolerance or DM

Worry About

- Abn short and restricted neck mobility, limited mouth opening and difficult intubation
- Poor vascular access and intraop positioning
- Systemic and pulm Htn, conduction defects, RBBB cor pulmonale, and dilated cardiomyopathy
- Restrictive lung disease (obesity, kyphoscoliosis) and reactive airways

Overview

- Presents in two stages: Infantile central hypotonia, FTT, and delayed developmental milestones. Childhood stage presents with obesity (BMI >97th percentile in a child and ≥30% in an adult), skeletal abn (dysmorphic, short stature, short hands and feet, scoliosis), hypogonadism, and hypothalamic dysfunction.
- Restrictive pulmonary disease results from muscle weakness, obesity, and kyphoscoliosis. It starts in early childhood and is present in 80–90% of pts >30 y of age.
- CV system: Htn in 17–32%; myocardial hypotrophic hypokinetic syndrome.
- Central thermodysregulation: May develop hyperpyrexia.
- Cognitive problems: Mild to moderate mental retardation. Mean IQ in 60s–70s; some individuals have normal intelligence.
- Behavior problems of oppositional behavior, emotional lability, aggressive and violent behavior; obsession with food and compulsion to eat. Psychosis found in 5–10% of adults.
- High threshold for pain.

Etiology

- A complex genetic disorder; paternally inherited via 15q11–q13 deletion (65–70%), maternal uniparental disomy 15 (20–30%) and imprinting defect (1–3%). GH deficiency.

Usual Treatment

- Early intervention and education: Physical, occupational, speech, and behavioral therapies
- Weight and dietary management; low-calorie diet and regular physical therapy
- GH replacement therapy
- Nighttime CPAP for severe OSA

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS (Craniofacial)	Facial dysmorphia, poor mask fit	Snoring, nystagmus, viscous and sticky saliva	Dental crowding and caries Micrognathia, short neck with limited movement	Imaging scans
CV	Htn Pulm Htn Cor pulmonale Cardiomyopathy	Headache Exertional and at rest Dyspnea, exertional intolerance Dyspnea, exertional intolerance	High diastolic BP Lung rales Tachypnea, orthopnea, systemic venous congestion, gallop sounds	ECG, CXR, renal function ECG, CXR, ECHO ECG, CXR, ECHO
RESP	Alveolar hypoventilation Increased airway responsiveness Increased work of breathing Upper airway obstruction	Snoring and interrupted sleep, daytime somnolence, exertional dyspnea, wheezing	Fatigue, limited upper airway access, short neck, limited mobility of neck	PFT, room air ABG CXR Polysomnography for severe OSA Difficult airway scoring
ENDO (Diabetes I or II)	Increased risk for CVS, CHF and autonomic dysfunction	Hyperglycemia/hypoglycemia, osmotic diuresis	Dysfunction of CVS, renal and peripheral neuropathy	Periop blood glucose Other test related to end-organ involvement

Key References: Angulo MA, Butler MG, Cataletto ME: Prader-Willi syndrome: a review of clinical, genetic, and endocrine findings, *J Endocrinol Invest* 38(12):1249–1263, 2015; Lirk PC, Keller J, Colvin J, et al.: Anaesthetic management of the Prader-Willi syndrome, *Eur J Anaesthesiol* 21(10):831–833, 2004.

Perioperative Implications

Preoperative Preparation

- Owing to obsessive hyperphagia, only a well-supervised pt should be considered NPO.
- Oral metoclopramide and cimetidine.
- Assess airways difficulty, CV and pulm status, and blood glucose.
- Effective premedication to ensure a cooperative pt during awake/sedated intubation and induction of GA.

Monitoring

- Standard ASA monitors. Consider direct intra-arterial BP measurement if the noninvasive cuff does not fit. Continuous temp monitoring for instability.
- Frequent checking of ABGs, UO, and central venous or pulm artery pressure for major surgery.

Airway

- Elective awake intubation if difficult airway is anticipated; increasing neck circumference, a Mallampati score of ≥3, micrognathia, and limited mouth opening

Induction

- Gastric regurgitation due to delayed gastric emptying and hiatal hernia.
- Be prepared to manage a situation where ventilation and/or intubation are not possible. The degree of obesity is only one factor among others that makes visualization of the glottis problematic.
- Semisitting position improves FRC and preoxygenation.
- Slow IV induction with propofol and remifentanil or fentanyl with cisatracurium to facilitate intubation.

Maintenance

- Sevoflurane or desflurane with remifentanil infusion and cisatracurium. These inhaled agents are least soluble and allow rapid recovery from GA. No specific drug or combination is recommended; the aim is rapid emergence. Avoid long-acting opioids and substitute with IV NSAIDs and/or acetaminophen.
- Regional anesthetic techniques are desirable alone or to supplement GA and provide postop analgesia to reduce the need for opioids.

Extubation

- Decision is dictated by the severity of obesity, assoc risks such as OSA, and the extent of the surgical procedure. Early tracheal extubation is desirable.

Adjuvants

- Hydrophilic drugs (e.g., muscle relaxants are calculated by lean body mass). Lipophilic drugs (e.g., fentanyl) are calculated in mg/kg of body weight.

Postoperative Period

- Severe obesity is associated with more atelectasis during, immediately after, and for 24 h following GA as compared with nonobese pts. CPAP or BiPAP may be necessary to maintain patent airways, particularly during sleep and for those with severe OSA. These pts are highly sensitive to opioid-induced resp depression.

Anticipated Problems/Concerns

- Monitor for OSA and alveolar hypoventilation in ICU/PACU. Monitor hyperglycemia and/or hypoglycemia, hyperthermia, and arrhythmias.
- Early ambulation and thromboembolic precautions.

Preeclampsia

Shobana Bharadwaj | Lester C. Chua

Risk

- 2–8% of all pregnancies
- Nulliparous, or multiparous with previous preeclampsia/eclampsia Hx, advanced maternal age
- Increased with Hx of obesity, chronic htn, diabetes, renal disease, SLE, thrombophilia

Perioperative Risks

- Increased risk of fetoplacental or maternal deterioration necessitating (often operative) delivery.
- Increased risk of fetal death.
- Preeclampsia and eclampsia account for about 15% of maternal and perinatal deaths.

Worry About

- Hypertensive crisis leading to intracerebral bleed or LV failure.
- Increased interstitial volume leading to edema.
- Maternal hypotension producing placental hypoperfusion.
- Renal dysfunction progressing to acute renal failure.
- Thrombocytopenia may contraindicate regional anesthetic.
- Eclampsia (seizure in a severely preeclamptic pt) necessitating difficult tracheal intubation.
- Placental abruption.
- Risks associated with preterm delivery.

Overview

- Early onset (<34 wk gestation): High rate of recurrence, strong genetic component, high risk of adverse outcome.
- Late onset (<34 wk gestation): Higher incidence, maternal metabolic predisposition.
- Marked by Htn, proteinuria (spot urine protein/Cr ratio >0.3).
- Maternal hyperdynamic state with diastolic dysfunction, leading to acute cardiorespiratory deterioration.
- Proteinuria: Sign of deteriorating renal function and widespread endothelial damage.

- Edema: Increasing total body water, proteinuria, Htn; lead to increasing interstitial edema and decreasing intravascular volume.
- Hematologic: Widespread endothelial damage often leads to thrombocytopenia.
- Epigastric/RUQ pain: Ominous sign of liver subcapsular edema and possible rupture. Delivery should be urgently effected.
- HELLP: Poor fetoplacental prognostic sign.
- Headache: Seizure may be impending.

Etiology

- Heterogenous disease of unknown etiology.
- Immune maladaptation causing placental angiogenesis dysfunction.
- Imbalance in circulating mediators of vascular tone and response (e.g., thromboxane vs. prostacyclin) from endothelial damage.
- Systemic inflammatory response from placental oxidative stress.
- Microangiopathy leading to endothelial change, platelet consumption, hemolysis.

Usual Treatment

- Prevention with daily low-dose aspirin beginning in second trimester has had limited success.
- Delivery becomes cure.
- In-hospital therapy: Antihypertensives, seizure prophylaxis with magnesium sulfate (therapeutic blood levels of 5–7 mg/dL), and support of maternal perfusion.
- Neuraxial analgesia for labor: Reduces catecholamine response to pain, increasing placental perfusion.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Edema		Airway exam	
CV	Systemic vasoconstriction Decreased intravascular volume Diastolic dysfunction		BP JVD Rales UO	ECG CXR ECHO Hct
RESP	Pulm edema	Dyspnea Chest discomfort	Rales/rhonchi Cyanosis	SaO_2 CXR ECHO
GI	Hepatic subcapsular edema	Epigastric/RUQ pain	Enlarged liver edge	LFT
HEME	Thrombocytopenia DIC	Easy bruising	Petechiae, gingival bleed Spontaneous hemorrhage	Platelet count Coag panel/TEG
RENAL	Increased capillary permeability	Weight gain	Nondependent edema Oliguria	Urinary protein Cr clearance Serum uric acid
CNS	Seizure Intracerebral hemorrhage Cerebral edema/posterior reversible encephalopathy syndrome	Headache Blurred vision Seizure	Retinal edema CNS exam Deep tendon reflexes	CT scan/MRI
OB	Decreased placental perfusion Placental abruption	 Vaginal bleeding	Fetal growth restriction FHR (lack of variability, late decelerations or bradycardia)	FHR monitoring BPP Doppler velocimetry FHR monitoring

Key Reference: Gogarten W: Preeclampsia and anaesthesia. *Curr Opin Anaesthesiol* 22(3):347–351, 2009; Chestnut DH, Wong CA, Tsen LC, et al. (editors): *Chestnut's obstetric anesthesia: principles and practice*, 5th edition, Philadelphia, PA, 2014, Elsevier.

Perioperative Implications

Antepartum Management

- Optimize maternal perfusion while lowering systemic diastolic BP to <110 mm Hg.
- Ensure therapeutic blood magnesium sulfate level.
- Maternal and fetal surveillance.
- Decisions on the timing/route of delivery; corticosteroids for fetal lung maturity if preterm.

Monitoring

- Consider intraarterial cath for extremes of BP.
- Consider transthoracic ECHO, CVP, or PA cath for oliguria/pulm edema.
- Fetal heart monitoring.

Airway

- Often difficult secondary to edema.
- Prepare for emergent airway.

Preinduction/Induction

- Neuraxial analgesia/anesthesia induces venodilation. Maintain maternal perfusion with judicious use of intravascular volume and (often) small, incremental prn doses of IV low-dose phenylephrine (by bolus or infusion) or IV ephedrine.
- Rapid-sequence induction of anesthesia, titrating IV antihypertensive drugs or rapid-acting opioids to blunt pressure response to intubation.

Maintenance

- Hemorrhage at delivery may lead to dramatic hypotension.
- Avoid ergot alkaloids.
- Titrate antihypertensive agents.

Extubation

- Extubate awake; control pressure response

Adjuvants

- Magnesium sulfate for seizure prophylaxis and increased UBF; IV antihypertensive drugs (most often hydralazine, labetalol, nifedipine, or nicardipine antepartum); rarely other inotropic support if demonstrable LV dysfunction; $PGE_1/PGF_{2\alpha}$ for uterine atony

Postoperative Period

- Risk for developing pulm edema, sustained Htn, stroke, VTE, seizures
- Effective postcesarean analgesia beneficial in BP control

Anticipated Problems/Concerns

- Maternal Htn causes maternal morbidity/mortality; maternal hypotension causes fetoplacental hypoperfusion.
- Eclampsia, intracranial hemorrhage associated with CNS residua, hepatic subcapsular hematoma.

Pregnancy, Ectopic

Lawrence C. Tsen

Risk

- Implantation of a fertilized oocyte outside the uterine cavity.
- 1.3–2.4% of all pregnancies, but rate is increasing due to risk factors and better diagnostic methods.
- Risk factors: High-tubal surgery, prior ectopic pregnancy, use of an IUD, interutero exposure to diethylstilbestrol, moderate assisted reproductive technologies, pelvic inflammatory disease, smoking, tubal pathology; maternal age >40 y.
- Fallopian "tubal" pregnancy is most common (97–99%).

Perioperative Risks

- Leading cause of pregnancy-related maternal deaths in first trimester; 4–10% of all pregnancy-related deaths.
- Mortality rate has declined from 1.15 to 0.5 maternal deaths per 100,000 live births owing to improved detection and treatment. Deaths are 6.8 times more common among African Americans and 3.5 times more common among women >35 y.
- Highest mortality with intraabdominal and interstitial tubal pregnancies because of increased fetal size, blood flow, and subsequent tissue involvement.

Worry About

- Death principally due to hemorrhage, shock, and renal failure
- Blood availability; may need type-specific or O-negative blood
- Full-stomach/aspiration risk
- Physiologic changes of pregnancy (see Pregnancy, Intra-Abdominal)
- Effects of CO_2 insufflation and steep Trendelenburg position on ventilation in the case of laparoscopy

Overview

- Primary concerns for airway, intravascular volume, and blood/coagulation management.
- Approach similar to that in the case of a trauma pt with profound hypovolemia.
- Dx made by history, physical (pelvic pain, 95%; amenorrhea, 75%; uterine bleeding, 60–80%); β-hCG (higher sensitivity of radioimmunoassay method) and ultrasound. 70% are diagnosed prior to rupture.
- Differential Dx: Appendicitis, any intraabdominal infection or process.

Etiology

- Mechanical factors: Salpingitis, peritubal adhesions, previous ectopic, prior tubal surgery, multiple prior abortions
- Functional factors: External ovum migration, menstrual reflux, altered tubal motility

Usual Treatment

- Surgical therapy is indicated if ectopic has ruptured or if there is hemodynamic instability/severe symptoms, if diagnostic laparoscopy is required, or there is a suspected heterotopic (i.e., simultaneous extrauterine and uterine) pregnancy.
  - Tube-preserving surgery (i.e., salpingotomy, partial salpingectomy, transampullary expression) may be considered based on bleeding intensity, size and damage, infertility and Hx of prior tubal pregnancy, and pt's wishes; tube preservation can result in retained tissue (4–15%).
  - Salpingectomy indicated if uncontrolled bleeding or marked tubal destruction.
- Medical management with methotrexate (administered IM single or multidose) ± leucovorin IM. Success rate is 63–97%.
- Combined surgical/medical management: Direct injection of drugs (e.g., methotrexate, potassium, or hyperosmolar glucose) into the ectopic implant by US guidance.
- Expectant management: Primarily used for small ectopics; follow β-hCG.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Snoring/difficult airway	Airway exam	
CV	Hypovolemia secondary to hemorrhage	Orthostatic dizziness	Vitals, neck veins, orthostatic vitals Weak thready pulse Vasoconstriction, cold legs and arms	
HEME	Blood loss secondary to rupture Hemoperitoneum/vaginal bleeding	Vaginal bleeding Orthostatic dizziness	Orthostatic vitals	Hct
CNS	Hypoperfusion altering mental status and urine production	History of CNS symptoms	CNS exam	BUN/Cr UA

Key Reference: Mukul LV, Teal SB: Current management of ectopic pregnancy, *Obstet Gynecol Clin North Am* 34(3):403–419, 2007.

Perioperative Implications

Preoperative Preparation

- Assess volume status using clinical and laboratory measures.
- Place two large-bore peripheral IV lines.
- Check blood availability; O-negative, but type-specific preferable.
- Consider full stomach risks.
- Discuss antibiotic use.

Anesthetic Technique

- GA: Preferred with unstable pt, ruptured ectopic, anticipated laparoscopy, or regional contraindication.
- RA: Consider in hemodynamically stable pt; spinal or epidural at T_2–T_4 level.

Monitoring

- Use standard monitors; consider EEG (BIS, Sedline), particularly if pt is unstable.
- Consider arterial line if pt is unstable, requires aggressive blood replacement, or offers poor access for venous lab tests.
- Consider bedside coagulation monitor (TEG, ROTEM)

Airway

- Alternative airway equipment and devices available; first attempt is the best attempt.
- Rapid-sequence induction and intubation.

Induction/Maintenance

- Propofol; consider etomidate or ketamine if pt is unstable; consider anxiolytic medication.
- Maintenance with O_2 plus inhalational volatile agent, opioid, and muscle relaxants.
- Pt may have uncorrected hypovolemia and full stomach.
- Surgical technique:
  - Laparotomy for ruptured ectopic, hemoperitoneum, or uncontrolled bleeding. Pfannenstiel or low midline approach; abdominal opening may release tamponade, involving severe hypotension.
  - Laparoscopy: Infraumbilical incisions with risk of organ injury with Veress needle insertion. Peritoneal insufflation with CO_2 to <18 mm Hg; potential CO_2 embolus.
  - Dissection: Depends on location of ectopic and degree of bleeding.

Definitive Surgery

- Salpingectomy, ipsilateral oophorectomy: Used for ruptured or interstitial implantation
- Salpingotomy: Used for unruptured or <2 cm ectopic, allows for fallopian tube conservation and use of laparoscope
- Approximate duration: 1–2 h
- Anticipate large hemodynamic and fluid shifts with ruptured ectopic
- Closure: Minimal if laparoscopy; low midline or Pfannenstiel 15–20 min

Extubation

- Awake

Postoperative Period

- Blood loss may be extensive; check Hct.
- Pain score: 4–6 laparoscopy, 5–8 laparotomy.
- PCA or neuraxial opioids; local anesthetic agents if regional ± neuraxial narcotics.

Anticipated Problems/Concerns

- CV: Instability from massive hemorrhage from ruptured ectopic
- GI: Gastric dilation 3%, thrombophlebitis 3%, pulm embolism 2%, ureteral injury/stenosis 1% with laparotomy
- Hematologic: Anemia, coagulation deficit, hemostasis, transfusion reaction
- Infection: Postop infection, abscess
- Musculoskeletal: Postop shoulder and chest pain from unabsorbed gas and peritoneal irritation (30%)
- Pulm: Pulm edema, TRALI, TACO
- Renal: Acute renal insufficiency

Pregnancy, Intra-Abdominal

Nathaniel N. Hsu

Risk

- Incidence in USA: 11:100,000 live births and 9:1000 ectopic pregnancies.
- Higher incidence in African Americans, Asians, and immigrant populations from third-world countries.
- Risk factors include PID, tubal damage, intrauterine contraceptive devices, assisted reproductive techniques, previous ectopic, and previous pelvic surgery.
- Maternal mortality 100 times that of intrauterine pregnancy.
- Perinatal mortality ranges from 40–95%.

Perioperative Risks

- Misdiagnosis prior to delivery is not uncommon, and a high index of suspicion is important for Dx. In one case series, only 6 of 10 pts were diagnosed preop.
- Massive hemorrhage may occur anytime in the periop setting.

Worry About

- Severe hemorrhage depending on location of placental implantation in the abdomen.
- Decreased placental perfusion and oligohydramnios, leading fetal growth restriction, pulmonary hypoplasia, and anatomic deformities.

Overview

- Defined as implantation in the peritoneal cavity, not including the fallopian tubes, ovaries, or ligaments.
- Early pregnancy may be normal and subsequently presenting with midtrimester abdominal pain, N/V, shock, partial bowel obstruction, and vaginal bleeding.
- Differential Dx includes abruptio placentae, placenta previa, uterine rupture, pelvic inflammatory disease, and bowel obstruction. MRI is better than US diagnosis. US may miss diagnosis in >50% of cases.
- Exsanguinating intraabdominal bleeding can occur at any time.
- No abnormal trend in serial hCG values compared to that seen in tubal pregnancies.

Etiology

- Often results from a missed ruptured tubal ectopic pregnancy.
- Fertilized ovum may implant anywhere in the peritoneal cavity, including uterine surface, adnexa, abdominal organs, and diaphragm.

Usual Treatment

- Emergency diagnostic laparoscopy or exploratory laparotomy with delivery of the fetus. However, expectant management has been successful in case reports with very close monitoring.
- Excision of placenta can result in life-threatening hemorrhage but, leaving it in situ, may yield higher infectious risk.
- Methotrexate or arterial embolization can be used to accelerate placental involution.
- Rare phenomena may occur where an unrecognized abdominal pregnancy dies and calcifies leading to formation of lithopedion or "stone baby."

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hemorrhage	Postural dizziness, shortness of breath	Hypovolemia, hypotension, tachycardia	Hgb, Hct
GI	Bowel obstruction GI bleed if bowel implantation	N/V, abdominal pain, distended rigid abdomen	GI bleed	Abdominal x-ray, CT, MRI, abdominal US
CNS			Decreased consciousness if massive hemorrhage	

Key References: Kunwar S, Khan T, Srivastava K: Abdominal pregnancy: methods of hemorrhage control, *Intractable Rare Dis Res* 4(2):105–107, 2015; Arendt KW: Problems of early pregnancy. In Chestnut DH, Wong CA, Tsen LC, et al., editors: *Chestnut's obstetric anesthesia: principles and practice*, 5th edition, Philadelphia, PA, 2014, Elsevier, pp 340–357.

Perioperative Implications

Preoperative Preparation

- Assess volume status and optimize maternal cardiovascular status, usually with intravascular volume replacement.
- Obtain large bore IV access, draw blood to assess hematocrit, and type and crossmatch.

Monitoring

- Urethral cath to monitor urine output.
- Consider invasive monitoring (arterial cath and/or central venous cath).

Induction

- GA with rapid-sequence using ketamine or etomidate if there is concern for significant hypotension in response to propofol

Maintenance

- Monitor for hemorrhage and resuscitate with crystalloid/blood products as needed.

Extubation

- May need to delay extubation for postop care.
- Extubate awake.

Postoperative Period

- May require multidisciplinary ICU for those who had massive transfusion or significant hypotension

Anticipated Problems/Concerns

- Massive hemorrhage, DIC.
- If massive blood transfusion is needed, be aware of possible dilutional thrombocytopenia and need for coagulation factor replacement.

Pregnancy, Maternal Physiology

Stephanie R. Goodman

Risk

- Estimated 6.4 million pregnancies in USA, resulting in 4.1 million live births per year.
- Pregnancy rate is 102 pregnancies per 1000 women between the ages of 15–44 y.

Perioperative Risks

- Maternal mortality rate is 28 deaths per 100,000 live births in USA, with 210 deaths per 100,000 live births in the world.
- Hemorrhage, hypertension, and embolic disorders are leading causes of maternal deaths.
- Risks of maternal mortality include advanced maternal age, obesity, multifetal pregnancies, C-section, and African American race.

Worry About

- Difficult airway, including inability to intubate and ventilate due to maternal wt gain, breast enlargement, and swelling of oropharyngeal tissues (incidence of failed intubation 1:280 vs. 1:2230 in nonpregnant pts).
- Hypoxemia occurs more quickly during periods of apnea due to decreasing FRC and increasing O_2 consumption.
- Aortocaval compression causing decreased uteroplacental perfusion and FHR late decelerations.
- Hypercoagulability causing DVT/PE.
- Obesity as an independent risk factor for adverse pregnancy outcomes.

Overview

- Physiologic changes occur during pregnancy to allow maternal adaptation to the demands of the growing fetus and supporting placental unit and ultimately to facilitate labor and delivery.
- These changes affect almost every organ system and influence the anesthetic and periop management of the pregnant woman.
- Adjust drug doses and administration schedules to compensate for increased volume of distribution, decreased peak plasma drug concentration, increased elimination $T_{½}$, and increased renal excretion.

Etiology

- Profound increases in hormonal concentrations, especially progesterone
- Mechanical effects of an enlarging uterus
- Increased metabolic demand
- Presence of the low resistance placental circulation

Usual Treatment

- Normal spontaneous vaginal delivery
- C-section

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Capillary engorgement/swelling of nasal and oral pharynx, larynx, trachea Vocal cords and arytenoid edema	Epistaxis Voice changes Difficult nasal breathing/ congestion	Careful airway exam Temporomandibular distance Mallampati class Neck ROM	Sleep study for OSA
CV	CO, SV, HR, ejection fraction increased SVR, BP decreased Third and fourth heart sounds Systolic ejection murmur Tricuspid and pulmonic regurgitation Peripheral edema	Palpitations Dizziness/presyncope	Auscultation of heart Pulse BP	ECG, ECHO
RESP	Tidal volume, respiratory rate increased FRC decreased Minute and alveolar ventilation increased PaO_2 increased, $PaCO_2$ decreased Elevated diaphragm	Dyspnea	Auscultation of lungs RR	CXR, ABG, PFTs (all rarely needed)
GI	Decreased lower esophageal sphincter tone Decreased gastric emptying (only in labor) Decreased gallbladder emptying	GE reflux Gallstones		Endoscopy, RUQ US
RENAL	Increased RBF, GFR, Cr clearance Decreased bicarbonate	Increased drug clearance		Decreased BUN, Cr, bicarbonate
HEME	Much increased plasma volume, increased RBC volume Increased coagulation factors (I, VII, VIII, IX, X, XII), increased clotting Increased platelet turnover, fibrinolysis Decreased albumin, α_1 acid glycoprotein	Physiologic anemia Leg pain, dyspnea Gestational thrombocytopenia	Pale, nail beds Homan sign for DVT	Hg, Hct PT/PTT, lower extremity Doppler, V/Q scan, spiral CT Plt count, TEG
CNS	Decreased MAC Increased pain threshold			
ENDO	Increased insulin resistance Enlarged thyroid, decreased TSH		Palpation of thyroid gland	Glucose Normal free T_3 and T_4
MS	Increased lumbar lordosis Increased joint mobility	Back pain		

Key References: Gaiser R: Physiologic changes of pregnancy. In Chestnut DH, editor: *Obstetric anesthesia: principles and practice,* ed 4, Philadelphia, PA, 2009, Mosby, pp 15–36; May L: Cardiac physiology of pregnancy, *Compr Physiol* 5(3):1325–1344, 2015.

Perioperative Implications

Preoperative Preparation

- Large-bore IV; consider a second IV if pt is at increased risk for bleeding.
- Consider use of nonparticulate antacids and/or metoclopramide to decrease gastric acid and volume.
- Keep pt with left uterine displacement to relieve aortocaval compression.
- Good oropharynx exam to assess likelihood of difficult intubation.
- Recommend NPO 6–8 h prior to elective surgery.

Monitoring

- Routine

Preinduction/Induction

- Need access to difficult airway equipment, including FOB, LMAs, and video laryngoscopes.
- Use a short or stubby-handled laryngoscope, especially in obese parturients.
- Avoid nasal intubation due to increased risk of bleeding.
- Preoxygenate with 100% O_2 at high-flow rates.
- Use rapid sequence induction and cricoid pressure (Sellick maneuver) to decrease passive regurgitation of gastric acid into oropharynx.
- ETT preferred to LMA to adequately protect against aspiration.
- Pseudocholinesterase activity reduced, but recovery from succinylcholine usually not prolonged.
- Decreased doses of induction agents needed.

Maintenance

- Adjust ventilation to maintain $PaCO_2$ around 30 mm Hg.
- Decreased MAC for inhalation anesthetics.
- Avoid high dose inhalation agents due to uterine atony.
- High doses of opioids and/or benzodiazepines given prior to delivery can cause resp depression in the neonate.

Extubation

- Awake without residual NM blockade

Regional Anesthesia

- Spinal, epidural, and combined spinal-epidural are all possible techniques and usually preferred over GA for surgical delivery, especially in the obese pt or one with apparent difficult airway.
- Decreased dose of spinal or epidural local anesthetic achieves the same dermatomal level as higher doses in nonpregnant adults.
- Pharmacologic sympathectomy can cause severe hypotension at term.
- Reduced response to vasopressors.

Postoperative Period

- Pain can be treated with a combination of NSAIDs and preservative-free spinal or epidural morphine or IV PCA if GA is used.
- Use compression stockings, prophylactic heparin, and/or early ambulation to lower the risk of DVT/PE.
- Most physiologic changes of pregnancy resolve 6–8 wk postpartum.

Anticipated Problems/Concerns

- Mallampati scores worsen during the progress of labor, so the airway must be examined immediately prior to induction of GA.
- Uterine artery blood flow is 500 mL/min at term, so obstetric hemorrhage can become life-threatening very quickly.
- Increased risk of C-section with obesity is a common and increasing problem.

Pregnancy-Induced Hypertension

Onyi C. Onuoha

Risk

- Although the true incidence of PIH remains unknown, it is believed to complicate about 6–10% of pregnancies, contributing to one of the major causes of maternal, fetal, and neonatal mortality and morbidity.

Perioperative Risks

- Short-term maternal risks: CNS dysfunction, hepatocellular injury/hemorrhage, thrombocytopenia, acute DIC, oliguria, pulmonary edema, cerebrovascular events (hemorrhage, encephalopathy), placental abruption, acute renal failure, progression to PEC, or EC and death.
- Short-term fetal risks: Severe intrauterine growth restriction, small for gestational age, preterm birth, low birth weight, oligohydramnios, hypoxia-acidosis, neurologic injury, and intrauterine and perinatal death.

Worry About

- Prompt recognition: When PIH is complicated by PEC, EC, or superimposed forms
- Timely response: With pharmacologic treatment or delivery of fetus/placenta when crucial
- High risk of uteroplacental insufficiency despite elevated maternal BP
- Multiple organ/system-based complications associated with PIH (see Assessment Points table)

Overview

- Broadly defined as BP ≥140/90 mm Hg obtained on at least two occasions at least 4 h apart. PIH is further classified into four categories:
- Chronic Htn: Htn before pregnancy, noted <20 wk gestation (suspect if Htn persists beyond 6 mo postpartum)
- Gestational Htn: BP >140/90 but <160/110 mm Hg after 20 wk gestation in previously normotensive pt. Increased BP in the first 24 h postpartum but normalization of BP within 10 d; no proteinuria, no other associated symptoms, no abnormal lab findings/blood tests
- PEC-EC:
  - PEC: Htn at ≥20 wk gestation + proteinuria (≥300 mg protein in 24-h urine collection)
  - PEC with severe features: Htn at ≥20 wk gestation + any of the following (new onset): Severe Htn (BP ≥160/110 mm Hg); persistently severe cerebral or visual disturbances; thrombocytopenia, <100,000/mm^3; HELLP syndrome; elevated liver enzymes, >2× upper limit normal; pulm edema; serum creatinine, >1.1 mg/dL; or doubling serum creatinine (in the absence of other renal disease)
- Superimposed PEC:
  - Superimposed PEC: Exacerbation of previously controlled CHTN (escalating BP meds) and/or new-onset/increased proteinuria
  - Superimposed PEC with severe features: Exacerbation of previously controlled CHTN despite treatment with severe features/symptoms (cerebral/visual changes, persistent epigastric pain, pulm edema, and lab findings, as discussed previously)

Etiology

- Multifactorial disease process with multiple theories about its pathogenesis. Mechanism is not fully understood. However, a central theory suggests abnormal placental implantation, vascularization, and function.
- Immune factors (auto-antibodies, oxidative stress, natural killer-cell abnormalities) cause placental dysfunction and impaired placental perfusion, stimulating the placental release of antiangiogenic and inflammatory mediators, which eventually initiate maternal endothelial dysfunction and organ damage.

Usual Treatment

- Primary goals include BP control (maintenance of uteroplacental perfusion) and prevention of seizures.
  - Mild-to-moderate Htn: Hypertensive disorders in pregnancy without evidence of severe features <37 wk of gestation (e.g., CHTN, gestational Htn, PE, or superimposed PE without severe features) call for expectant management. In the absence of severe features, antihypertensive therapy is only reserved for chronic Htn. Delivery is suggested if "category described previously" is ≥37 wk gestation (38 wk for chronic Htn).
  - Severe Htn: Hypertensive disorders in pregnancy *with* evidence of severe features ≤34 weeks of gestation call for aggressive management. Consider magnesium sulfate for seizure prophylaxis and corticosteroids for fetal lung maturity. Delivery is suggested if "category described previously" is >34 wk gestation. Delivery should not be delayed, regardless of gestational age, if maternal condition is unstable: this includes cases complicated by uncontrollable severe Htn, any of the severe features, evidence of nonreassuring fetal status, or fetal demise.
- Antihypertensive agents recommended in pregnancy include acute-lowering agents (for severe Htn):
  - Labetalol (onset: 5–10 min, dose: 20 mg IV, 40–80 mg every 10 min, max dose: 300 mg or continuous infusion: 1–2 mg/min)
  - Hydralazine (onset: 10–20 min, dose: 5–10 mg IV every 20 min, max dose: 30 mg)
  - Nifedipine (onset: 5–10 min, dose: 10 mg PO, repeat in 30 min, × 2 doses prn, 10–20 mg every 4–6 h up to max dose: 240 mg in 24 h)
- Antihypertensive agents recommended in pregnancy for long-term treatment include oral agents (for chronic Htn in outpatient settings):
  - Labetalol (dose: 200–2400 mg daily in 2–3 divided doses)
  - Nifedipine (dose: 30–120 mg daily)
  - Methyldopa (0.5–3 g daily in 2–3 divided doses)
  - Hydrochlorothiazide (25–100 mg daily): Second-line agent
- Prophylactic agents recommended for PIH in pregnancy include low-dose aspirin (which inhibits the synthesis of prostaglandins and the biosynthesis of plt thromboxane A_2).
- Agent recommended for seizure prophylaxis in PEC-EC is magnesium sulfate (loading dose: 4–6 g IV over 20–30 min, maintenance dose: 1–2 g/h, continued 24 h postpartum; therapeutic concentration range: 4–8 mEq/L).

Assessment Points*

System	Effect	Assessment by Hx	PE	Test
CV	Vasospasm, increased SVR Decreased circ BV, decreased IV volume Decreased oncotic pressure (decreased alb) Hyperdynamic, increased CO mostly	Decreased exercise tolerance Lightheadedness Decreased UO, dizziness	Increased BP + other signs of hypovolemia (increased HR, decreased mental status, increased RR, decreased UO)	BP cuff, pulse ox, ECG monitoring UA, 24-h output BUN, uric acid, Cr, albumin
RESP	Increased airway edema Increased risk of pulm edema	Hoarseness, stridor Dysphonia, SOB	Lung auscultation (rales, crackles), snoring	Airway exam CXR (if symptomatic)
HEME	Decreased plt count Hemolysis ± DIC (liver involvement)	Bleeding diathesis	Epistaxis Bleeding gums Easy bruisability Bleeding from sites	Hgb + coagulation studies: Plts, PT, PTT, fibrinogen; ± function if decreased plt (bleeding time, ±TEG) Peripheral blood smear (rule out HELLP), LDH, haptoglobin
RENAL	Oliguria or anuria Proteinuria Increased BUN, Cr, uric acid	Decreased UO		UA, 24-h urine protein collection Comprehensive metabolic panel (e.g., albumin, BUN, serum Cr)
HEPAT	Increased liver enzymes HELLP	Epigastric pain	Jaundice RUQ tenderness	Liver function tests (e.g., transaminases—ALT, AST; alkaline phosphatase)
CNS	Impaired CNS autoregulation; vasogenic edema, posterior reversible leukoencephalopathy syndrome	Persistent headaches Visual changes	Diplopia, blurry vision, scotomata Hyperreflexia (DTR)	Rule out posterior reversible leukoencephalopathy syndrome —MRI, CT (if concerning diagnosis)

*Especially in severe gestatational Htn, PEC, or EC.

Key References: Moussa HN, Arian SE, Sibai BM: Management of hypertensive disorders in pregnancy. *Womens Health (Lond)* 10(4):385–404, 2014; Lambert G, Brichant JF, Hartstein G, et al.: Preeclampsia: an update. *Acta Anaesthesiol Belg* 65(4):137–149, 2014.

Perioperative Implications

Preoperative Preparation

- Control BP with pharmacologic agents, and institute anticonvulsant therapy for seizure prophylaxis as needed.
- Examine the airway and evaluate coagulation status.
- Careful intravascular repletion could minimize the severe hypotension seen with regional or general anesthesia. If in doubt, consider TTE to quantify volume status.

Monitoring

- Basic monitoring should include measuring BP by noninvasive method, ECG, pulse rate, pulse oximetry, and UO measurements.
- Invasive BP monitoring with the use of an intra-arterial cath may be necessary in unstable pts with severe PEC or EC; pts needing frequent ABG measurements; pts requiring potent pharmacologic treatment for malignantly increasing BPs; or pts with significant body habitus (obesity) without the availability of an appropriate BP cuff size.
- Repetitive physical exam (e.g., DTRs) and measurement of Mg^{2+} blood levels for pts on magnesium sulfate for antiseizure prophylaxis.

Induction

- Early neuraxial analgesia (epidural) is often the preferred anesthetic technique for delivery (unless contraindicated or unstable); it may relieve vasospasm, decrease circulating catecholamines, improve uteroplacental perfusion, and decrease airway catastrophe risk.
- With the need for general anesthesia in the setting of severe gestational Htn, PEC, and/or EC:
  - Pharmacologic agents should be used to minimize the sympathetic response from direct laryngoscopy and endotracheal intubation.
  - Avoid the use of ketamine for induction due to its sympathetic effects.
  - Airway edema may complicate optimal mask ventilation and rapid-sequence intubation. Various sizes of endotracheal tubes should be available.
  - With the anticipation of a difficult intubation, consider the use of airway adjuncts (e.g., videolaryngoscopy) or an awake/anesthetized fiberoptic endotracheal tube placement. A difficult airway cart should always be in close proximity.

Maintenance

- Use of magnesium sulfate in the management of PEC-EC can contribute to the loss of uterine muscle tone, hence increasing the risk of uterine atony and postpartum hemorrhage. Consider the use of additional uterotonics after delivery. Avoid the use of methylergonovine maleate if possible.
- Reduce the dosage of muscular relaxants when used in conjunction with magnesium sulfate due to the potentiation of neuromuscular relaxant effects. Continuous monitoring with a peripheral nerve stimulator should be utilized.

Extubation

- If evidence of thrombocytopenia prior to placement of epidural, consider rechecking platelet count prior to removal of cath.
- Ensure that pt fulfills all "extubation criteria" prior to extubation.

Postoperative Period

- Pts with PIH are still at risk for progression to PEC and EC after delivery. Seizure prophylaxis with magnesium sulfate may be continued after delivery (48 h postpartum).
- Triage: Consider the need for ICU monitoring post delivery if concerned or if pt is unstable.

Preterm Infant

Meredith Anne Kato

Risk

- Births at less than 37 post conceptual wk (PCW) rose sharply from 1990 to 2006 in USA due to the increase in assisted reproductive technology and multiple gestation. It has been slowly declining in the ensuing years.
- In 2013, 11.4% of all live births were <37 PCW; 3.4% were <34 PCW.
- 67% of all infant deaths occur among the premature. Babies born at less than 32 wk are 88 times more likely to perish compared to full-term babies.
- Neonates have the highest periop morbidity and mortality among pediatric pts, with premature infants carrying the highest risk.

Perioperative Risks

- Laryngospasm
- Hypothermia
- Hypoglycemia
- Massive blood loss
- Rapid onset hypoxia
- Bradycardia, poor cardiac output
- Apnea

Worry About

- Occult congenital abnormalities
- Difficult intubation, vascular access
- Cardiac decompensation
- Persistent or reversion to fetal circulation and high pressures in the pulmonary vascular tree
- High airway pressures
- Oxygen toxicity
- Medication or dilution errors
- Pain control
- Transport disaster (extubation or hemodynamic compromise)

Overview

- Immature organ systems present very specific challenges to the anesthesiologist.
- Cardiac physiology is different in the premature and early neonate. The heart has fewer and disorganized contractile elements. Muscle cells contain fewer mitochondria. With low compliance, cardiac output is dependent upon heart rate. Yet, parasympathetics dominate predisposing to bradycardia. The premature heart is exquisitely sensitive to drops in serum calcium levels.
- Fetal lungs have inadequate surfactant production up until about 34–36 wk. The lungs are stiffer, harder to ventilate, and prone to atelectasis. They are vulnerable to volutrauma and barotrauma, which can lead to chronic pulmonary compromise.
- High pressure caused by an ill-fitting endotracheal tube against the trachea can lead to post extubation stridor or potentially subglottic stenosis.
- Babies have a higher oxygen demand and a lower oxygen reserve (FRC), but it is important not to over-oxygenate. Premature infants produce fewer antioxidants against the oxygen free radicals produced during oxygen therapy. Oxygen therapy is associated with retinopathy of prematurity and bronchopulmonary dysplasia.
- Hepatic metabolism of drugs is immature in the premature infant, which alters pharmacokinetics.
- Glucose homeostasis is immature. Glycogen stores are low, predisposing to hypoglycemia. These babies also frequently have dextrose or total parenteral nutrition infusions, which puts them at risk of iatrogenic hyperglycemia. These pts are also relatively insulin resistant.
- Hypothermia is common and can occur rapidly. Premature babies have immature mechanisms for heat homeostasis; they burn brown fat in "nonshivering thermogenesis."
- Premature kidneys have a lower glomerular filtration rate and a decreased ability to concentrate urine. Renal clearance of drugs is lower.
- The coagulation cascade of healthy neonates is immature but "functionally balanced." In sick babies, however, this immaturity may predispose them to coagulopathies leading to bleeding (intraventricular hemorrhage) or thrombotic events.
- Compared to an adult, the larynx is more cephalad, the epiglottis is omega shaped, the glottis lies at an angle, and the narrowest part of the airway is subglottic.
- The risk of postop apnea is high, especially with concomitant anemia (HCT <30%). It is usually mixed central and obstructive and made worse by anesthetics. The risk of apnea is greater than 1% in babies born before 35 wk who have not yet reached 54 PCW and in babies born before 32 wk who have not yet reached 56 PCW. It is important to monitor these babies postop. There is some evidence that spinal anesthesia without additional sedatives is somewhat protective against postop apnea.
- Common problems in critically ill premature infants include congenital abnormalities causing cardiac, respiratory, gastrointestinal, renal or hepatic insufficiency, intraventricular hemorrhage, necrotizing enterocolitis, hernias, or retinopathy of prematurity. These can be the reasons these babies come to the OR, or can complicate surgery done for another reason.

Etiology

- Etiology for prematurity is multifactorial and incompletely understood. Risk factors include:
  - Maternal factors including previous preterm birth, race, extremes of age, substance abuse, including smoking, multiple gestation, obesity, infection, and anemia
  - Fetal factors including congenital anomalies, intrauterine growth restriction, and male sex

Usual Treatment

- Optimization in a NICU setting, including respiratory care, nutrition, hemodynamic support, treatment of infection, and surgical correction or palliation of congenital abnormalities

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult or lost airway	Previous intubation, presence of syndrome (e.g., Pierre Robin, Treacher Collins, Klippel-Feil, Goldenhar)	Dysmorphic, micrognathia	Imaging or genetic testing as needed
CV	Cardiac decompensation	Feeding difficulties, cyanotic spells, vital signs, volume status	Cyanosis, poor saturation, murmur, edema	ECHO, ECG, cardiac cath, vital signs including preductal and postductal oxygen saturation, skin turgor
RESP	Respiratory failure	Feeding difficulties, cyanotic spells, vital signs	Air hunger, use of accessory muscles or instability on vent	Pulse oximetry, ABG
RENAL	Hypovolemia or volume overload, renal insufficiency	Review of intake and output and UO	Skin turgor, fontanel	Basic metabolic labs
HEME	Postop apnea, poor tolerance of blood loss, arrest	Recent blood loss or phlebotomy, previous episodes of apnea, Hx of treatment with caffeine	Pallor, air hunger	CBC

Key References: Spaeth JP, Kurth CD: The extremely premature infant (micropremie). In Coté CJ, Anderson BJ, Lerman J, editors: *Cote and Lerman's a practice of anesthesia for infants and children,* ed 5, Philadelphia, 2013, Elsevier; Jones LJ, Craven PD, Lakkundi A, et al.: Regional (spinal, epidural, caudal) versus general anaesthesia in preterm infants undergoing inguinal herniorrhaphy in early infancy. *Cochrane Database Syst Rev* 6:CD003669, 2015.

Perioperative Implications

Preoperative Preparation

- Look for dysmorphic features, micrognathia, and obvious congenital abnormalities.
- Listen for a heart murmur and have a low threshold for obtaining an ECHO. Obtain a feeding history; breast or bottle feeding is the "stress test" of the neonate.
- Make sure pt is metabolically optimized; check basic labs, especially potassium, calcium, and glucose. Consider getting an ABG.
- Warm the room.
- Calculate estimated blood volume (approximately 95 mL/kg) and maximum allowable blood loss (EBV × [HCT initial – HCT minimum]/HCT initial).
- Calculate doses of all medications and consider unit syringes; avoid drug errors.
- Prepare emergency drugs (atropine, succinylcholine, calcium, epinephrine). Consider drips of epinephrine, dopamine, or milrinone.
- De-air all lines; check and recheck.
- For all but the simplest cases, have an active type and cross. For high-risk procedures, have blood in the room. There is generally very little lead time between unexpected surgical bleeding and the need to transfuse.
- If coming from the ICU, transport with backup emergency airway supplies, warmer, and drugs. Check and recheck endotracheal tube position and IV patency before leaving and upon arrival to the OR.

Monitoring

- In addition to standard monitors, consider preductal and postductal pulse oximetry to watch the effect of a PDA on systemic circulation.
- Consider arterial line for continuous BP and for frequent checks of glucose, electrolytes, and hematocrit. Obtain central access if the risk of needing vasoactive drips is high.

Airway

- Always have an LMA for emergencies. Have an advanced airway device if the baby has a history of a difficult intubation or looks dysmorphic.
- Position with a shoulder roll; the large head relative to the rest of the body tends to flex the neck when supine.
- Prepare multiple sizes of tubes and oral airways.
- Preoxygenate.
- Check for an air leak at <20 cm H_2O.
- Consider a nasal tube if a prolonged intubation is anticipated.
- Check and recheck tube position throughout the case. The distance between a mainstem intubation and perfect positioning can be cm or even mm.
- Watch for kinking of the tube.

Induction

- As with any pt, the acuity of the illness will dictate the anesthetic plan.
- IV and arterial line access can be very difficult in these pts.
- Inhalational induction with sevoflurane is reasonable in a relatively healthy baby undergoing a minor procedure. IV induction is more common, however.
- Consider atropine 20 mcg/kg, fentanyl 2 mcg/kg, rocuronium 0.6 mg/kg for induction.

Maintenance

- For maintenance, consider a fentanyl infusion, low-dose inhalational agent, and nondepolarizing paralytic.
- Reduce oxygen levels and maintain saturations between 88–95% to avoid oxygen toxicity.
- Avoid hypercarbia and acidosis, as both raise pressure in the pulmonary arterial tree.
- Check and recheck the tube for dislodgement or kinks throughout the case.
- Maintain normothermia. While it is easy for pts to get cold, it is also very easy to overheat them with warming devices.
- Warm fluids and blood products if given. Consider "spinning" blood in a blood salvage device (CellSaver) to warm and reduce potassium load.
- Run dextrose containing maintenance fluids or keep TPN running. Check glucose during long cases.
- Be careful not to overtransfuse or fluid overload. Use measured aliquots of fluid and blood products.
- Monitor blood loss; communicate with the surgeons.
- Beware of "monitor failure." Loss of multiple monitors may indicate serious decompensation.

Extubation

- Consider postop location when planning extubation; keep intubated for long transports to ICU.
- If extubating, reverse paralytic.

Postoperative Period

- Consider overnight monitoring for any preterm baby who has not yet reached 56 PCA. Caffeine or theophylline can help attenuate the risk of postop apnea.
- Pain management should include opioids, acetaminophen, and nonpharmacologic adjuncts, along with nonnutritive sucking, breastfeeding, and maternal contact.
- Do not use ketorolac in premature infants.

Anticipated Problems/Concerns

- Difficult IV access
- Postop apnea
- Long transport hazards
- Under-resuscitation or over-resuscitation

Protein C Deficiency

Charles Weissman

Risk

- Congenital deficiency. Homozygote is estimated at 1:500,000-750,000 live births. Occurs when gene coding for protein C on both chromosomes #2 is affected.
- Heterozygote ~0.2–0.4% of healthy population; 2–5% in pts with DVT.
- Acquired deficiency also seen.

Perioperative Risks

- Pts with protein C deficiency are at risk for venous thrombosis and pulm embolism (immobility, endothelial damage, and decreased blood flow during periop period may be triggers).

Worry About

- Increased incidence of thrombophlebitis and pulm embolism
- Thrombosis of other vessels, such as intracerebral and coronary arteries, can occur.

Overview

- Protein C is a vitamin K–dependent protein found in blood and synthesized in the liver.
- Activated after forming a complex with thrombin on endothelial cell receptor thrombomodulin; facilitated by binding to endothelial cell protein C receptors.
- Inhibits blood coagulation by proteolytic inactivation of factors V and VIII.
- Protein S is a cofactor of protein C.
- Stimulates fibrinolysis possibly by neutralizing plasminogen activator inhibitors
- Deficiency causes hyperthrombotic state
- During SIRS and sepsis, there is decreased synthesis of protein C.

Etiology

- Inherited: Autosomal dominant with variable expressivity
- Homozygotes develop life-threatening visceral vessel thrombosis or purpura fulminans (massive cutaneous necrosis) in early neonatal period.

- Heterozygotes may develop venous thrombosis and thromboembolism (rare prior to age 20 y). Protein C levels are 35–65% of normal.
- Acquired causes: Hepatic dysfunction, vitamin K deficiency, DIC

Usual Treatment

- Heterozygotes:
  - If acute thrombosis, start heparinization (heparin or high-dose LMWH).
  - Long-term anticoagulation with warfarin in pts with Hx of thrombosis. (Heparin therapy should be continued until warfarin is at therapeutic levels to prevent skin necrosis.)
  - Acute thrombosis may require transfusions of FFP to increase protein C levels.
  - During pregnancy, treat with LMWH during and for 4–6 wk after delivery.
- Homozygotes: Periodic FFP or purified protein C concentrate transfusions to provide protein C.
- Acquired:
  - Vitamin K deficiency: Parenteral vitamin K
  - DIC: Treatment of underlying cause

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Retinal vein thrombosis	Hx of vision problems	Ophthalmoscopic exam	
CV	MI Angina Peripheral arterial disease	Hx of MI, angina Peripheral vascular thrombosis	Peripheral pulses	ECG
RESP	Pulm embolism	Hx of previous pulm embolism		
GI	Mesenteric thrombosis	Hx of bowel infarction		
HEME	Thrombophlebitis	Hx (and family Hx) of thrombophlebitis, pulm embolism	Exam of veins in legs, evidence for lower extremity postthrombotic syndrome	Screen for hypercoagulable state: PTT, proteins C and S, factor V Leiden, antiphospholipid antibody, antithrombin 3
RENAL	Renal vein and artery thrombosis	Hx of renal problem		BUN/Cr Urine protein
DERM	Necrosis	Cutaneous necrosis after warfarin is begun	Cutaneous necrosis	
CNS	Intracerebral artery thrombosis	Hx of CVA, TIA	Neurologic exam	

Key References: Goldenberg NA, Manco-Johnson MJ: Protein C deficiency, *Haemophilia* 14(6):1214–1221, 2008; Lipe B, Ornstein DL: Deficiencies of natural anticoagulants, protein C, protein S and antithrombin, *Circulation* 124(14):c365–c368, 2011.

Perioperative Implications

Preoperative Preparation

- For homozygotes and symptomatic heterozygotes, FFP and protein C concentrates can be administered to increase protein C levels.
- Warfarin can be stopped a few days before surgery to allow PT to return to normal range and heparin administered until surgery.
- Intermittent pneumatic compression stocking can be placed prior to induction of anesthesia.

Airway

- Some have suggested that the ETT cuff not be inflated to prevent tracheal venous thrombosis.
- In neonates, there should be an audible leak.

Preinduction/Induction

- RA preferable if possible

Maintenance

- Special attention can be paid to positioning to reduce venous and arterial stasis.
- Maintain adequate hydration to reduce thrombosis risk.
- Have propensity to thrombose central venous cath, so minimize use. If cath required, continually ensure patency.
- FFP and/or protein C concentrates should be given to pts with prior thrombotic manifestations and for prolonged operations.

Adjuvants

- Intermittent pneumatic compression stockings can be used.
- Postop heparinization should be started as soon as deemed safe.

Anticipated Problems/Concerns

- Increased risk of thrombosis, especially thrombophlebitis and pulm embolism
- When switching from heparin anticoagulation to warfarin, heparin should be continued until warfarin has achieved therapeutic effect to decrease risk of skin necrosis.

Pulmonary Atresia

Nirvik Pal | Mark T. Nelson

Risk

- PA/IVS occurs in 3% of all CHD and has a prevalence of 0.07:1000 live births.
- PA/VSD occurs in 3.4% of all CHD.
- 20% of all cases of TOF are physiologically similar to PA/VSD due to extreme pulm artery stenosis.
- Males are affected more than females.

Perioperative Risks

- RV failure (due to volume overload, pressure overload or both)
- Hypoxemia (leading to metabolic acidosis)
- Myocardial ischemia secondary to aberrant coronary circulation

Worry About

- RV-dependent coronary circulation in PA/IVS (rapid boluses of fluid through central line may precipitate myocardial ischemia).
- Maintain a patent ductus arteriosus (continue prostaglandin infusion).
- "Suicide RV" is sudden release of pulm valve obstruction leading to hyperdynamic RV and subpulmonic obstruction of RV outlet. Treatment involves a β blockade.
- Hyperventilation and hyperoxia when excess "pulmonary-steal," leading to low cardiac output syndrome and necrotizing colitis (maintain oxygen saturation to 70–80%), mainly in PA/VSD.

Overview

- Physiologically, PA/IVS and PA/VSD present as two extremes of the same spectrum. Usually associated with other cardiac lesions (e.g., patent foramen ovale, patent ductus arteriosus, possible VSD, ASD).
- PA/IVS often presents with varying extent of RV maldevelopment, TV hypoplasia and stenosis, and RV-dependent coronary blood flow (due to abnormal coronary arteries arising from sinusoids in the RV outlet musculature).
- PA/VSD, on the other hand, the RV by virtue of 'flow-growth phenomenon due to the presence of VSD, enjoys more blood flow and as a result is more completely developed. However, due to the reduced pulm blood flow in PA/VSD, MAPCA develop compensating for the limited blood flow in the maldeveloped PA.

Etiology

- Congenital

Usual Treatment

- Prostaglandin E_1 infusion
- Surgical correction
- Infective endocarditis prophylaxis
- Palliative therapy

Surgical Treatment

- With PA/VSD (usually RV well developed), goal is "two-ventricle repair":
  - Implement a staged repair with BTS early on, followed by VSD closure and valved RV-PA conduit (Rastelli procedure).
  - If multiple MAPCAs present, then implement "unifocalization" (surgically creating a neopulmonary artery by fusing all MAPCAs), followed by VSD closure and valved conduit from RV to neo-PA (Rastelli procedure).
- With PA/IVS (often RV maldeveloped and coronary artery obstruction), goal is "two-ventricle repair," if possible, or else "single-ventricle repair" and eventual heart transplantation. Monitor size/development of RV and extent of coronary artery malformation/obstruction:
  - For adequate RV size for future growth and no coronary malformation, transannual RV outflow patch or radiofrequency assisted valvotomy and dilatation and a systemic-to-PA shunt for future "two-ventricle repair."
  - For small RV (monopartite) and/or coronary malformation, RV outflow patch or dilatation not recommended so as to maintain high RV pressure necessary for coronary blood flow. Stage surgery with BTS, Glenn shunt, total cavo-pulmonary connection (single-ventricle repair), and/or heart transplant.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	RV failure Hypoxemia/metabolic acidosis	SOB	Cyanosis	ECG: RA enlargement, ECG-QRS axis 30–90° CXR: Decreased pulm vascular markings ABG ECHO: PV annulus size, flow across PV, TV size and function, RVOT obstruction, ductus arteriosus, PA anatomy Cardiac cath: Confirm ECHO findings and detect state of coronary blood flow, MAPCAs
RESP	Decreased pulm blood flow	SOB	Tachypnea	ECHO, cardiac cath
SYSTEMIC	Signs of RV failure	Hepatomegaly		

Key References: Malhotra SP, Hanley FL: Surgical management of pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals: a protocol-based approach, *Semin Thorac Cardiovasc Surg Card Surg Annu* 12:145–151, 2009; Mi YP, Chau AK, Chiu CS, et al.: Evolution of the management approach for pulmonary atresia with intact ventricular septum, *Heart* 91(5):657–663, 2005.

Perioperative Implications

Preoperative Preparation

- Ascertain physiologically predominant PA/IVS versus pulm valve stenosis or PA/VSD versus TOF.
- Cath suite intervention versus surgical intervention.
- Patency of ductus arteriosus.
- Maintain pulm blood flow.
- Avoid hyperoxia and hyperventilation in PS/VSD.
- RV dysfunction.
- Presence of RV-dependent coronary circulation.
- Type of shunt to be performed.
- Which systemic artery is to be used for shunt? Avoid during CVP attempts.
- Degree of hypoxemia, metabolic acidosis.

Monitoring

- Standard ASA monitors.
- A-line:
  - Use umbilical artery if good trace.
  - For radial artery, use opposite side of shunt.
  - Use partial clamping of subclavian artery for BTS, with the same implication for pulse oximeter placement and preductal and postductal pulse oximeter.
- CVP for resuscitation drugs.
- Temp/warmers.
- Bubble precaution.

Airway

- ET

Preinduction/Induction

- Continue prostaglandin infusion (0.03–0.1 µg/kg per min) in ductal dependent pts.
- Inhalational induction may be chosen to relax RV infundibulum versus IV ketamine to maintain vascular resistance, depending on presenting predominant physiology and physician preference.
- $ETCO_2$ may significantly underestimate $PaCO_2$ due to limited pulm blood flow.
- Goals: Decrease PVR (to help maintain pulm blood flow), and maintain normal SVR (to avoid desaturation and hypoxemia due to shunt reversal of L-to-R shunt across the VSD by drop in SVR) in PA/VSD.
- Avoid increases in pulm vascular resistance (coughing, bucking; increased PEEP; increased CO_2; decreased PO_2).
- Avoid extreme hyperoxia/hypocarbia in PA/VSD, as this may result in increased L-to-R shunting and systemic hypotension.

Maintenance

- Normothermia
- Normal filling volumes
- Normal myocardial contractility
- Aiming for early extubation

Extubation

- As early as reasonably safe

Postoperative Period

- Pediatric cardiac ICU.
- Continue prostaglandin infusion after palliative repair.

Anticipated Problems/Concerns

- Palliative surgery only
- Definitive procedure later (e.g., Fontan, Rastelli)
- Progressive hypoxemia: Inadequate BT shunt flow or ductus closure

Pulmonary Embolism

Ronald G. Pearl

Risk

- Incidence of pulmonary embolism in USA: 600,000/y
- No racial predilection
- Risk factors same as those for DVT

Perioperative Risks

- Presents a risk for hypoxemia and right heart failure.
- Periop mortality of 50–90% for acute thromboendarterectomy and of ~10% for chronic thromboendarterectomy.
- Postop pulm embolism in up to 1% of surgical pts.
- Pulm embolism accounts for 20–30% of deaths associated with pregnancy.

Worry About

- Recurrent pulm embolism (30% mortality if not treated)
- Right heart failure and CV collapse
- Hypoxemia
- Hemorrhage in pts on anticoagulants or thrombolytics

Overview

- Pulm embolism found in ~20% of autopsied pts.
- Clinical presentation may range from asymptomatic to chest pain and hypoxemia to CV collapse depending on magnitude of the embolus.
- Signs (tachycardia, tachypnea, calf swelling) and symptoms (dyspnea, pleuritic chest pain, calf pain) have low sensitivity and specificity.
- Most pts have DVT (and surgical pts may have pelvic vein thrombi).
- Dx should be based on positive CT pulm angiography after use of a validated clinical decision rule; pulm angiogram should no longer be used.
- Negative D-dimer test excludes Dx in selected low probability pts.

Etiology

- Acquired disease.
- Risk factors present in almost all pts include age >40 y, obesity, malignancy, recent surgery, trauma, pregnancy, immobilization, estrogen use, prior Hx of DVT, and hypercoagulable state (factor V Leiden, deficiency of protein C, protein S, or antithrombin III).

Usual Treatment

- Therapy decreases mortality from 30% to <5%.
- LMWH overlaps with warfarin sodium (INR 2–3) for most pts; use unfractionated heparin (PTT 1.5–2.5× normal) in cases of creatinine clearance <20–30 mL/min, high risk of bleeding, or extremes of weight; use fondaparinux if history of HIT.
- Nonvitamin K-dependent oral antagonists for initial and chronic use are as effective and may have decreased bleeding risk.
- Thrombolytic therapy for massive pulm embolism (hypotension).
- Vena caval filter if pt cannot receive anticoagulants.
- Surgical or catheter thrombectomy in selected cases of acute massive pulm embolism.
- Consider reduced dose thrombolytics or catheter-directed thrombolysis in intermediate-high risk pts (normotensive with RV dysfunction).
- Surgical thromboendarterectomy in selected cases of chronic thromboembolic pulm Htn.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	RV failure	Syncope Dyspnea Palpitations	↑ JVP; RV heave Hypotension Tachycardia Hepatojugular reflux	ECG CT pulm angiography ECHO
RESP	Pulm infarction V/Q abnormality Pain from pleural irritation	Hemoptysis Chest pain Shoulder pain Dyspnea Orthopnea	Tachypnea Pleural rub Wheezing	CXR, SaO_2 ABG Lung V/Q scan CT pulm angiography
CNS	Syncope	Syncope		
MS	Phlebitis	Hx DVT Leg edema Leg pain	Leg edema Inflammation Palpable cord	Compression ultrasonography Impedance plethysmography CT scan

Key References: van der Hulle T, Dronkers CE, Klok FA, et al.: Recent developments in the diagnosis and treatment of pulmonary embolism, *J Intern Med* 279(1):16–29, 2016; Banks DA, Pretorius GV, Kerr KM, et al.: Pulmonary endarterectomy: Part II. Operation, anesthetic management, and postoperative care, *Semin Cardiothorac Vasc Anesth* 18(4):331–340, 2014.

Perioperative Implications

Preoperative Preparation

- Preop Rx with heparin/LMWH and sequential compression devices, which decrease incidence of periop DVT and PE.
- If active DVT, consider preop vena caval filter.

Monitoring

- Consider PA catheter.
- TEE may demonstrate RV dysfunction and PA thromboembolism.

Airway

- None

Preinduction/Induction

- May develop hypotension due to RV failure.

Maintenance

- Adequate preload essential to RV function.
- Systemic vasoconstrictors for hypotension due to RV failure.
- Inhaled vasodilators (NO, prostacyclin) for refractory RV failure.
- Consider ECMO if cardiac arrest.

Extubation

- None

Regional Anesthesia

- Appropriate, especially if compatible with continued anticoagulation.

Postoperative Period

- Resume anticoagulation as soon as possible (or use IVC filter).

Anticipated Problems/Concerns

- RV failure with systemic hypotension may be initial presentation of PE or may develop with recurrent PE.
- Consider PE in all postop pts with unexplained hypoxemia or hypotension.

Pulmonary Fibrosis, Idiopathic

Andrew Oken

Risk

- Present in ~42.7–63:100,000 and incidence is ~16.3:100,000 in USA; more common with increasing age, with majority >55 y.
- Occurrence higher in males than females; risk factors include smoking, exposures, increasing age, family history, chronic reflux, environmental, viral, and genetics.

Perioperative Risks

- Dependent on degree of underlying lung disease and associated comorbidities.
- Pulm Htn, H/O PE, OSA, CKD, CAD, and NYHA class 2 or above are all associated with increasing periop risk for pulmonary failure.
- Obesity (which further reduces lung volumes and worsens ventilation-perfusion mismatch), hypercarbia, and respiratory failure.
- Preop functional status and exercise capacity; risks include albumin <3.5 mg/dL, smoking, COPD, asthma, and FEV_1 <80%.
- Neurologic impairment and immunosuppressive therapy.
- ABG (PaO_2/FiO_2, 225 mm Hg).
- Type of surgery and location (proximity to the diaphragm), especially thoracic surgery for cancer or lung biopsy, along with anesthetic type and surgical duration (>3–4 h).

Worry About

- Progressive respiratory failure, pulm Htn, and potential RV failure
- Postop pneumonia and respiratory failure; prolonged ventilation
- Increased morbidity and mortality, especially in high-risk pts undergoing thoracic procedures

Overview

- IPF, also known as cryptogenic fibrosing alveolitis, is a chronic and progressive fibrosing interstitial pneumonia of unclear etiology.
- Natural history reveals untreated IPF to have an unpredictable course with an insidious progressive nature and deterioration in physical function and capacity, along with a decline in FVC.
- Pts may also present with acute decompensation.
- Prognosis is poor and associated with ~25% survival at 5 y from time of diagnosis and median survival ~3 y from time of diagnosis.
- Morbidity and mortality can occur in approximately ~3–4% following lobectomy and ~11.6% following pneumonectomy.

Etiology

- Unclear, but possible association with smoking, chronic aspiration, and viral infection.
- Important to rule out common misdiagnoses of interstitial lung diseases (e.g., infectious, drug related, exposures [specifically asbestos], hypersensitivity pneumonitis, rheumatoid arthritis, and systemic sclerosis, and usual interstitial pneumonia).
- Clinical course, presentation, and severity variable from pt to pt.

Usual Treatment

- Smoking cessation and active and aggressive management of COPD with bronchodilators, antibiotics, chest physical therapy, and steroids if indicated for persistent wheezing and airflow limitation.

- Pulmonary rehabilitation should include inspiratory muscle training and pt education, supplemental oxygen, and vaccination for seasonal influenza and pneumococcus.
- No current FDA-approved therapy has been shown to be efficacious in IPF, and consequently management includes primarily supportive care, as described previously.
- Some clinical benefit is described with medications pirfenidone and nintedanib in terms of potentially slowing disease progression.
- Lung transplantation is a possible consideration, but mainstay of therapy more commonly involves aggressive management of associated comorbidities.
- A multitude of pharmacologic trials, including a broad spectrum of medications (cytotoxic agents, antifibrotic agents, anti-inflammatory and immunosuppressive agents, and PDEinh), have unfortunately not proven beneficial and in fact were often associated with intolerable toxicities.
- Pts may present on these medications, and therefore it is important to have an awareness of them and review them preop.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	RV strain and failure, pulm Htn and cor pulmonale	Easy fatigue and swelling peripherally	Edema in legs and feet and hepatic congestion	ECG, ECHO, and consider RV heart cath
RESP	Diminished pulm capacity and function	Progressive shortness of breath and diminished functional capacity Dry persistent cough	Inspiratory crackles, clubbing of digits; rapid and shallow breathing; absence of signs of acute/chronic infection	PFTs (restrictive physiology with low lung volumes and decreased DLCO); CXR (diffuse patchy fibrosis and pleural based honeycombing), 6-min walk test, oximetry, hypoxemia
GENERAL	Metabolic wasting and weight loss, malnourishment	Diminished exercise and functional capacity	Progressive weight loss	Albumin
RENAL	Renal insufficiency			Cr, Cr clearance

Key Reference: King TE Jr, Pardo A, Selman M: Idiopathic pulmonary fibrosis. *Lancet* 378 (9807):1949–1961, 2011.

Perioperative Implications

Preoperative Preparation

- Review systems. It is important to thoroughly investigate through questioning and appropriate testing for associated comorbidities that may be optimized to improve potential for periop success. One must be vigilant to address all coexisting disease to the extent possible.
- Assess pulm physiologic reserve to guide periop risk discussion.
- Consider common misdiagnoses that may be treatable preop if surgery is elective (e.g., bronchitis/pneumonia, bronchospasm, PE, exposures).
- Evaluate progression of disease as assessed by longitudinal measurements: FVC, TLC, DLCO, oximetry, 6-min walk test.
- Risk is further increased for periop pulm insufficiency if:
  - Obesity BMI >27 kg/m^2
  - Smoking within 8 wk of surgery
  - Productive cough or wheezing within 5 d of surgery
  - FEV_1/FVC ratio <70% and $PaCO_2$ >45 mm Hg
- Consider need for ICU and invasive hemodynamic monitoring/management periop.
- Aggressive management of COPD, smoking cessation, steroids, and antibiotics as indicated.

Monitoring

- Routine ASA monitors plus consideration of invasive hemodynamic monitors and/or TEE as dictated by pt status, pulm Htn, RV and LV functional status, and case type/duration.
- Consider possible need for postop ventilation in the ICU and ABG monitoring for weaning from ventilator support.
- Type and duration of surgery will affect the rate of postop pulm insufficiency. Proximity to the diaphragm and intrathoracic procedures are the most likely to result in postop respiratory complications.

Airway

- If intubation is necessary, proceed with meticulous antiseptic technique to minimize risk for postop respiratory infection.

Maintenance

- Low tidal volume lung protective strategies intraop to minimize postop respiratory complications.
- Judicious intraop fluid management.
- High FiO_2 likely required to maintain adequate oxygenation.
- If pulm Htn is present, then use additional consideration/preparation for treatment and hemodynamic management for RV failure and pulm Htn.
- Efforts to minimize bronchospasm and optimize bronchodilation: beta-adrenergics, steroids, potent inhalational agent, and adequate anesthetic depth.

Extubation

- Respiratory mechanics and physiology impaired by inhalational anesthetics, narcotics, NMB agents, interscalene block, and high neuraxial blocks, and therefore particular caution regarding residual respiratory depression and muscle weakness on emergence.
- Ensure pt is fully awake and strong with return of baseline respiratory mechanics and particular attention to completely reverse residual muscle relaxant effects.
- If postop ventilation is required, consider early extubation if able to minimize complications of prolonged intubation and ventilation.
- Use bronchodilators and steroids as indicated
- Careful titration of opioids but inadequate treatment of surgical pain will contribute to splinting and insufficient respiratory effort, so consider adjuvants as able.

Adjuvants

- NSAIDs, beta-adrenergic agents, and steroids.
- Consider neuroaxial and/or regional anesthetic technique if possible to minimize requirements for neuromuscular blockade and potentially avoid airway instrumentation and ventilation and to assist in postop pain management.
- Judicious intraop fluid management.
- Vasopressor and inotropic support may possibly be required.
- Consider iNO, or prostacyclin or nebulized iloprost for pts with pulm Htn.

Postoperative Period

- Confusion and decreased LOC secondary to hypoxia and hypercarbia.
- Periop respiratory insufficiency and failure; prolonged intubation/ventilation.
- Low threshold for postop observation in the ICU
- Consider NIPPV or CPAP assistance.
- Nasogastric decompression to potentially improve respiratory mechanics and minimize rates of pneumonia and atelectasis.
- Nutrition: Consider early TPN support, especially in malnourished pts and those in whom prolonged hospitalization is likely.
- Early ambulation and lung expansion maneuvers.
- Adequate but cautious pain control.
- DVT prophylaxis.

Anticipated Problems/Concerns

- Pulm insufficiency; reintubation/ventilation for respiratory failure
- Pulm Htn and RV failure leading to LV decompensation and hemodynamic compromise

Pulmonary Hypertension

Michael Wollenberg | Jeffrey D. Davis

Risk

- Relatively uncommon disease process, with an estimated incidence of 1–5:100,000.
- Frequently identified as a contributing cause of death in USA, resulting in 6.5:100,000 deaths (2010).
- Left heart disease underlies 60–85% of pHTN cases.
- Primary pulmonary disease (e.g., COPD/OSA) is the second most common etiology.
- Chronic thromboembolic disease causes pHTN in 2–4% of pts after acute PE.
- Primary PAH is rare but most amenable to medical therapy.

Perioperative Risks

- RV failure
- Atrial tachyarrhythmias
- Hemodynamic instability

Worry About

- Hypoxia/hypercarbia: Causes pulm vasoconstriction and decreases myocardial contractility, which can lead to RV pressure and volume overload and ultimately RV failure.
- PE: Consider urgent intervention (surgical or thrombolytics) if hemodynamically unstable.
- Hypotension: Decreases RV perfusion and preload, which can worsen failure.
- Atrial tachyarrhythmias: Atrioventricular coupling ensures adequate preload.
- Sympathectomy (if neuraxial blockade present): Disrupts RV homeometric autoregulation in addition to systemic vasodilation.

Overview

- Defined by mean PA pressure (MPAP): ≥25 mm Hg
  - Mild: 25–40 mm Hg
  - Moderate: 41–55 mm Hg
  - Severe: >55 mm Hg
- pHTN is often occult but presents symptomatically with increasing DOE (graded by NYHA classification).
- Diagnosed with RHC.
- PA pressures can be estimated on ECHO by utilizing the modified Bernoulli equation and maximal velocity of the TR jet, if present. (RV systolic pressure >40 mm Hg, which roughly correlates to MPAP >25 mm Hg.)
- Primary periop morbidity and mortality results from RV failure, organ hypoperfusion, and arrhythmias.

Etiology

- WHO classification:
  - PAH: Idiopathic, heritable, drug/toxin-induced, HIV, connective-tissue disease
  - Due to left heart/valvular/congenital heart disease
  - Due to primary lung disease (e.g., COPD, interstitial lung disease, OSA)
  - Chronic thromboembolic pHTN
  - Unclear multifactorial mechanisms: Incorporating chronic hemolysis, metabolic diseases, rheumatologic disorders

Usual Treatment

- Avoid hypoxia/hypercapnia.
- Maintain adequate coronary blood flow (potential role for norepinephrine, vasopressin).
- Maintain sinus rhythm.
- In RV failure, support the right heart with inotropes (dobutamine, milrinone), judicious volume management, and decrease pulm vascular resistance.
- Consider pulm artery cath.
- There is a potential role for nitric oxide and inhaled prostacyclins in acute management of decompensation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Right heart failure	Poor exercise tolerance	Dependent edema, JVD, systolic murmur (TR)	RHC (gold standard), TTE, TEE, ECG, 6-min walking distance
	Left heart failure, MR/MS, AR/AS, congenital heart disease	DOE, orthopnea, PND	Rales, S_3, cold extremities, prolonged capillary refill	TTE, TEE, ECG, CXR, nt-Pro-BNP
RESP	COPD, sarcoidosis, interstitial pulm fibrosis, chronic thromboembolic pulm disease	DOE, fatigue, cough	Rales, wheezes	CXR, PFTs, sleep study, VQ scan, CT pulm angiogram
	OSA	High STOP-BANG score	Large neck (>40 cm circumference)	Sleep study
GI	Portopulmonary Htn	ETOH abuse, IVDU	Ascites, effusions	Liver US
IMMUNE	Lupus, scleroderma, HIV			ANA, HIV

Key References: Pilkington SA, Toboada D, Martinez G: Pulmonary hypertension and its management in patients undergoing non-cardiac surgery. *Anaesthesia* 70(1):56–70, 2015; Hosseinian L: Pulmonary hypertension and noncardiac surgery: implications for the anesthesiologist. *J Cardiothorac Vasc Anesth* 28(4):1064–1074, 2014.

Perioperative Implications

Preoperative Preparation

- Optimize RV function with inotropes, vasodilators, and diuresis as needed.
- Optimize any comorbidities that contribute to pHTN (most commonly COPD and left heart dysfunction).
- PAH: Determine if responsive to vasodilators during RHC.

Monitoring

- Consider awake arterial line for beat-to-beat BP monitoring at induction and ABGs intraop.
- Consider PA cath or TEE in pts with severe pHTN or right heart failure; useful to guide optimization of cardiac output, to optimize of volume status, to monitor for RV overload, and to monitor for response to pulm arterial vasodilators.
- PA catheter findings suggest RV failure: Uptrending CVP, unexplained decline in PA systolic pressures, unexpected increase in PA diastolic pressures, or decline in PA pulse pressure.

Preinduction/Induction

- Avoid hypoxia (oxygen is a direct pulm vasodilator), hypercarbia, and acidosis.
- Avoid hypothermia (causes pulm vasoconstriction).
- Avoid high peak inspiratory pressures/excessive PEEP (decreases RV preload).
- Maintain appropriate SVR and coronary perfusion with pressors (norepinephrine or vasopressin preferred).
- Sevoflurane provides the least pulm vasoconstriction.
- All inhaled and many IV anesthetic agents are direct cardiac depressants.
- Avoid nitrous oxide (myocardial depressant and increases pulm vascular resistance).

Maintenance

- Goal: Maintain gradient between aorta and RV with vasopressors and inotropes (MAP >65, PVR/SVR ratio <0.5 [or preop ratio], CI >2.2).
- Norepinephrine and vasopressin increase SVR >PVR.
- Dobutamine and milrinone improve R heart contractility while causing pulm artery vasodilatation (and systemic vasodilatation).
- Epinephrine increases RV contractility, and low doses (<0.02 mcg/kg per min) decrease pulm arterial pressures through primary β2 agonist effects.
- Vasodilators (sildenafil, prostacyclins, inhaled NO) have a role in PAH but must be balanced with hypotension due to systemic vasodilation.

Extubation

- Consider extubation in OR if usual respiratory and hemodynamic criteria are met.
- Withdrawal of PEEP on RV preload may induce volume overload and acute decompensation.
- Hypercarbia and hypoxia may occur post extubation.
- BiPAP/CPAP postextubation provide PEEP and may prevent hypercarbia/hypoxia.

Postoperative Period

- Recommend monitoring in ICU postop.
- Respiratory failure and RV failure are the most common causes of death.
- Atrial tachyarrhythmias may contribute to or result from RV failure.
- VTE prophylaxis is paramount (particularly in pts with chronic pulm thromboemboli).

Anticipated Problems/Concerns

- Acute RV failure: Inotropic and vasopressor support (pulm vasodilators if pt has responsive PAH) and careful volume management. Acute PE may respond to careful volume loading, while RV failure from other causes generally responds best to diuresis.
- Hypercapnea/hypoxia: Increase pulm vascular resistance; treat underlying etiology (e.g., COPD, OSA, pulm edema).
- Atrial tachyarrhythmias (predominantly atrial fibrillation): May cause acute RV failure. Rhythm control is preferred in new onset AFib. Cardioversion in hemodynamically unstable pts. Avoid myocardial depressants (beta blockers, calcium channel blockers) in decompensating or unstable pts.
- Venous thromboembolism: Acute worsening of preexisting increased PVR, highly prevalent in pts with chronic pulm venous thromboemboli as well as PAH. VTE prophylaxis very important postop. Early, definitive treatment via thrombolytics or surgical intervention in hemodynamically unstable pts.

Purpura, Immune Thrombocytopenic

Evan G. Pivalizza | Olga Pawelek

Risk

- Rare (100:1 million)
- Children: Male > female
- Adults: Female > male (2–4:1).
- Pregnancy: 1:1000 deliveries; 5% of thrombocytopenia in pregnancy, especially if present in first trimester.

Perioperative Risks

- Hemorrhage (case reports put mortality for splenectomy at 1%, one-third of which is related to bleeding).
- Infection and thrombocytosis post-splenectomy
- Retrospective data from Taiwan point to a higher risk of postop mortality (OR 1.89), complications (1.47), increased length of hospital stay (1.73), and ICU admission (1.89). Preop blood/platelet transfusions are associated with increased risk.

Worry About

- Preop corticosteroids, immunosuppressive agents
- Splenectomy
- Hemorrhage (mucosal when platelet count is $<20{,}000 \times 10^3/mm^3$; severe risk [intracranial hemorrhage] with platelet count $<10{,}000 \times 10^3/mm^3$; suggestion that mortality is increased if platelet count is $<30{,}000 \times 10^3/mm^3$).

Overview

- Acute, intermittent, or chronic (12-mo) immune-mediated thrombocytopenia (accelerated destruction with appropriate megakaryocyte response). Recent appreciation of impaired plt production, leading to treatment to stimulate platelet growth. Dermal, mucosal, and CNS hemorrhage is most critical.
- Obstetric implications include risk of transient neonatal thrombocytopenia.

Etiology

- Antiplatelet IgG autoantibodies target mature platelets and megakaryocytes, leading to premature removal by spleen and RES. TMO produced in the liver as the principal regulator of megakaryocyte development and platelet production, is suboptimal in ITP pts.

Usual Treatment

- Decrease platelet destruction, although risks of immunosuppression and splenectomy are concerning.
- Corticosteroids: Begun at 1 mg/kg per d (30–60% response rate, up to 80% initially).
- IV immunoglobulin G (0.4–1 g/kg per d).
- Anti-D (if pt Rh-positive) is cheaper and easier than IV IgG.
- Splenectomy: Defer as long as possible in children. Now done laparoscopically (requires disruption of spleen into bag before extraction to prevent splenosis). In chronic disease, splenectomy is indicated if steroids cannot be tapered or response to therapy is poor. In acute disease, indicated for failed medical response and platelet transfusion.
- Second line: Rituximab, monoclonal anti-CD20 antibody, increasingly used to treat refractory ITP. Use is associated with infusion-related side effect, risk of progressive multifocal leukoencephalopathy and infections.
- New stimulatory agents mimic effect of TPO.
- Eltrombopag, a TPO receptor agonist approved (by the FDA) for adults (2008) and children >1 y of age (2015) with chronic ITP. Signal transduction different site than TMO receptor.
- Romiplostim, a TPO mimetic, binds directly to the receptor in the same manner as endogenous TPO. FDA-approved in 2008 (risk evaluation and mitigation strategies required).
- Platelets: Very short survival, may temporarily elevate pH count if there is a bleeding emergency.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway manipulation—potential hemorrhage	Oral bleeding		
CV	Vascular access			
HEME	Thrombocytopenia	Hemorrhage	Petechiae	Platelets $<20–50{,}000 \times 10^3/mm^3$, megakaryocytes, antiplatelet antibody
CNS	Hemorrhage in acute disease, trauma			Imaging if indicated
OB	Controversy predicting neonate at risk (10–15%) and mode of delivery			

Key References: Choi S, Brull R: Neuraxial techniques in obstetric and non-obstetric patients with common bleeding disorders, *Anesth Analg* 109(2):648–660, 2009; Kühne T, Imbach P: Eltrombopag: an update on the novel, non-peptide thrombopoietin receptor agonist for the treatment of immune thrombocytopenia, *Ann Hematol* 89(Suppl 1):67–74, 2010.

Perioperative Implications

Preoperative Preparation

- Consult with hematology. Acute ITP: Steroids, IV IgG ± anti-D to raise platelet count.
- Steroid supplement if already receiving steroids.
- Premedication: Avoid IM injections.
- Pneumococcal, meningococcal vaccine (plus *Haemophilus influenzae* in children) if for splenectomy.

Monitoring

- Routine.
- Protect pressure points and mucosal surfaces.

Airway

- Avoid nasal ET intubation; caution DLT (case report).
- Careful instrumentation, (especially with platelet count $<50{,}000 \times 10^3/mm^3$).

Induction

- Avoid hypertensive response to ET intubation (especially with platelet count $<10–20{,}000 \times 10^3/mm^3$) (posing risk to the CNS)

Platelets

- If required, transfuse after splenic pedicle ligation. Intraop monitoring of platelet function (e.g., thromboelastography) may be useful guide to replacement therapy (case reports).

Extubation

- As above: Care of mucous membranes and hemodynamic response.

Adjuvants

- Individual analysis of risk/benefit for neuraxial technique, especially in parturient pts. Authors recommend platelet count range $>50–100 \times 10^3/mm^3$ (European recommendation $>80{,}000 \times 10^3/mm^3$). Reports of point-of-care testing (e.g., thromboelastography) in decision making.

Postoperative Period

- Risks of thrombocytosis not as crucial as TTP

Anticipated Problems/Concerns

- Massive surgical hemorrhage
- CNS and airway hemorrhage

Purpura, Thrombotic Thrombocytopenic

Evan G. Pivalizza | Omonele O. Nwokolo

Risk

- TTP rare (1:1,000,000). Adult, pregnancy may be a predisposing factor. Survival 80% at 6 mo; 90% mortality if untreated.
- Periop risks
- Rarely reported in pregnancy or postsurgically (case reports point to cardiac/urologic complications). Refer pt for splenectomy if medical therapy fails. Risks include MAHA with variable neurologic deficits and renal dysfunction combined with thrombocytopenia.

Worry About

- Preop drugs, therapies (plasma exchange, steroids, rituximab)
- CNS/renal dysfunction
- Thrombocytopenia (although usual quantitative platelet transfusion triggers do not apply)

Overview

- Severe MAHA characterized by thrombocytopenia, variable multisystem organ involvement (particularly CNS and kidney); may be considered part of the spectrum of HUS. Differential in pregnancy from HELLP.

Etiology

- Low ADAMTS13 activity (<10%), a metalloprotease that cleaves multimers of von Willebrand factor, thus leading to increased intravascular platelet aggregation in high-shear environments.
- May be associated with ticlopidine or malignancy.
- Has been described after cardiac, vascular, and abdominal surgery.

Usual Treatment

- Parity of RCTs; combination of therapies
  - Plasmapheresis (exchange): Daily, more NB than plasma infusion (platelet-poor FFP) usually with rapid clinical response in days (failed Rx within 4–7 d)
  - Steroids: Adjuvant (methylprednisolone 10 mg/kg/d better than 1 mg/kg/d). Potentially suppress production of anti-ADAMTS13 autoantibodies.
  - Rituximab: Monoclonal Ab against CD20 Ag on B lymphocytes; used to treat refractory or relapsing TTP. Optimal dosing, timing, and side effects based on case series.
  - Splenectomy: For failed medical response, prevention of relapse (small series).
  - Avoid platelet transfusion.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Airway manipulation, potential hemorrhage			
CV	Rare conduction pathway involvement		Baseline MAP for perfusion CNS/kidney Vascular access	ECG
RESP	Rare infiltrates causing hypoxemia			CXR
RENAL	Proteinuria, hematuria, ARF less common than HUS			BUN, serum Cr, urine sediment
HEME	Thrombocytopenia	Hemorrhage	Petechiae Jaundice	PT, PTT, fibrinogen usually normal (differentiate from DIC). Fragmented RBCs (anemia); increased LDH, bilirubin, decreased haptoglobin
CNS	Fluctuating course	Spectrum—headache, seizures, coma		Lumbar puncture, EEG, neuroradiology studies
OB	May precipitate episode or relapse	Differentiate from HELLP/PIH (more CNS, less hepatic involvement, not improved postpartum)		

Key References: Sayani FA, Abrams CS: How I treat refractory TTP, *Blood* 125(25):3860–3867, 2015; Weinberg L, Chang J, Hayward P, et al.: Post-cardiac surgery TTP with digital ischemia, *Anaesth Intensive Care* 41(3):386–389, 2013; Pourrat O, Coudroy R, Pierre F: Differentiation between severe HELLP syndrome and thrombotic microangiopathy, TTP and other imitators, *Eur J Obstet Gybecol Reprod Biol* 189:68–72, 2015.

Perioperative Implications

Preoperative Preparation

- Steroid supplement if receiving.
- Premedication: Not IM; caution with CNS involvement.
- Pneumococcal, meningococcal (*Haemophilus influenzae* for children) if splenectomy is anticipated.

Monitoring

- Protect skin, mucous membranes (NIBP cuff, esophageal probe, pressure points)
- Central access is usually provided for plasma exchange. If this is required, avoid subclavian vein if possible (difficulty compressing hematoma).
- Theoretical risk of radial arterial line with thrombotic process.

Airway

- Avoid nasal ETT. Be careful with instrumentation, especially if platelet count $<50{,}000 \times 10^3/mm^3$.

Induction

- Avoid sympathetic intubation response (CNS disease spectrum), maintain MAP > CNS, renal autoregulatory thresholds (>50–60 mm Hg).

Maintenance

- Theoretical advantage of inhibitory effect volatile anesthetics on platelet aggregation

Fluids

- Do not transfuse platelet unless there is life-threatening thrombocytopenia: There are reports of deterioration due to further microthrombi.
- Bleeding managed with RBCs (>48 h old to avoid active platelets) and FFP (platelet-poor).

Extubation

- As above: Care of mucous membranes and hemodynamic response

Adjuvants

- Individual analysis of risk/benefit for neuraxial technique in thrombocytopenic pt (if in remission)

Postoperative Period

- Mobilize early: Precipitous increase in platelet count and viscosity with risk of thrombotic events.

Anticipated Problems/Concerns

- Hemorrhage if there is life-threatening thrombocytopenia (no platelet transfusion until then)
- Microthrombi with CNS dysfunction

Pyloric Stenosis

Inna Maranets

Risk

- Incidence: 1:300-1000 live births.
- Incidence is 3–5% higher among children of affected parents.
- More common in males.

Perioperative Risks

- Similar to other abd procedures in pts of same age.
- Some association with GU anomalies.
- Some pts have elevated unconjugated bilirubin related to decreased glucuronyl transferase activity; this returns to normal after correction of stenosis.

Worry About

- Full stomach. Recurrent emesis leads to dehydration, electrolyte imbalance, and alkalosis.
- Typically pts have hypochloremic, hyperkalemic metabolic alkalosis.
- Metabolic acidosis found in the most severe cases.

Overview

- Reduced size of gastric outlet impedes emptying of contents, which can cause abnormal nutrition, gastric distention, repeated vomiting, and dehydration.
- Onset of symptoms occurs at 3–6 wk of age.
- Usually surgically cured.

Etiology

- Almost exclusively genetic in infants
- Can be acquired in adults

Usual Treatment

- Normalize fluid/lyte status: This is not a surgical emergency.
- Surgical: Pyloromyotomy can usually be undertaken within 2–24 h of admission (unless fluid derangements are severe).
- Short procedure (<1 h): Open or laparoscopic.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GI	Gastric outlet obstruction	Nonbilious projectile emesis	Pyloric "olive" palpable in upper abdomen	Contrast study Abdominal US

Key References: Schapiro F, Litman RS: Pyloromyotomy. In Litman RS, editor: *Pediatric anesthesia practice*, New York, NY, 2007, Cambridge University Press, pp 173–175; Considine AA, Maranets I, Snegovskikh D, et al.: Induction and airway management for pyloromyotomy, *J Anesth Clinic Res* S3:003, 2011.

Perioperative Implications

Preoperative Preparation
- Correct fluid and acid-base deficits.
- Place orogastric tube to aspirate contents.
- Pyloric stenosis is not a surgical emergency.

Monitoring
- Routine

Airway
- Full stomach

Preinduction/Induction
- IV atropine 0.02 mg/kg; minimal dose 0.1 mg.
- Empty stomach with orogastric tube or suction cath.
- Consider awake intubation or IV RSI, especially if pt received barium contrast.
- Modified RSI with either propofol alone or propofol and nondepolarizing muscle relaxant; cricoid pressure and mask ventilation have been used successfully without increased incidence of complications.
- Hypoxemia is common during rapid-sequence induction; ventilate with cricoid pressure.
- In a properly resuscitated pt with recent loss of IV access, inhalational induction has been used successfully and can be considered a safe alternative.

Maintenance
- No technique is absolutely contraindicated by pyloric stenosis alone.
- Inhalational agent in O_2 and air or N_2O, short or intermediate-acting muscle relaxant.
- Avoid opioids.
- Local infiltration with bupivacaine or ropivacaine by surgeon.
- IV fluids should be warmed.
- Replacement fluids: LR 1–2 mL/kg per h.
- May consider using D_5 if the procedure lasts more than 1 h.

Extubation
- Potential of full stomach; suction stomach prior to extubation.
- Reverse NMB agent.
- Awake extubation
- Delayed awakening is common

Adjuvants
- Consider potential of associated liver and GU abnormality.

Postoperative Period
- Potential for central apnea and reactive hypoglycemia
- Pulse oximetry/apnea monitoring for the first 12–24 h
- Continue IV glucose until there is adequate PO intake.
- Pain score: 2–5, acetaminophen is usually sufficient; avoid opioids.

Anticipated Problems/Concerns
- Potential for full stomach.
- Need to correct fluid and/or electrolyte imbalances preop.
- Delayed awakening is common.

Q Fever

Thomas A. Russo | Paul R. Knight III

Risk
- Greatest after direct or indirect exposure to infected cattle, sheep, or goats; particularly at parturition
- Less from a variety of other animals, rarely from blood products
- Abattoir workers, veterinarians, and other animal workers at greatest risk
- Pts with immune impairment are at a higher risk (e.g., HIV, steroids)
- Mortality 2.4% overall; chronic infection ~16%.

Perioperative Risks
- Decreased respiratory reserve secondary to pneumonia
- Decreased myocardial reserve secondary to endocarditis
- Further increase in hepatocellular injury if there is liver involvement

Worry About
- Secondary respiratory complications
- Decreased myocardial performance and emboli with endocarditis
- Hepatic or neurologic involvement

Overview
- Acute infection: Asymptomatic (~50%) to moderate severity (2% hospitalized).
- Acute symptomatic disease presents as nonspecific febrile syndrome ± pneumonitis (~50%), hepatitis (80% or more), pericarditis and/or myocarditis (<5%), neurologic disease (<5%).
- Chronic disease occurs in <1% of infections, usually without fever.
- Chronic disease, primarily endocarditis (particularly abn or prosthetic valves) and occasionally bone.

Etiology
- *Coxiella burnetii*, the causative organism, is a fastidious obligate intracellular bacterium.
- The spore stage can withstand harsh environmental conditions for prolonged periods, facilitating indirect transmission.
- Highly infectious; transmitted (1–10 organisms) primarily by inhalation, from unpasteurized milk, or by a tick bite.
- Incubation period ~20 d (range, 3–40 d).
- Bacterium targets reticuloendothelial cells and develops into granuloma.

Usual Treatment
- Dx: Epidemiologic circumstance and serology (positive in 2–4 wk).
- Acute disease: Doxycycline or quinolones for 2–3 wk hastens resolution.
- Chronic disease: Doxycycline and rifampin for 1–3 y; with endocarditis, possible valve replacement.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Endocarditis Immune complex vasculitis Microthromboembolism	Rash, reduced exercise tolerance	Clubbing, rash, murmurs, petechiae	ECHO, ECG, culture negative with standard techniques serology, PCR
RESP	Atypical pneumonia, asymptomatic pneumonia, rapidly progressive pneumonia, interstitial pulm fibrosis	Pleuritic chest pain, cough, dyspnea	Consolidation, rales, pleural effusions	CXR, serology
GI	Acute hepatitis	N/V, fatigue, diarrhea, sweats and chills	Hepatomegaly or hepatosplenomegaly	SGOT, SGPT, bilirubin, granulomas on liver biopsy
HEME	Hyperglobulinemia, anemia, thrombocytosis/thrombocytopenia	Easy fatigue, bleeding tendency	Pallor; purpuric eruptions	Sedimentation rate, Hct/Hgb, plt count
OB	Immune complex vasculitis Q fever complications secondary to reactivation of infection during pregnancy	Spontaneous abortion more likely		Microscopic hematuria Isolation of *C. burnetii* from placenta
CNS	Meningoencephalitis Optic neuritis	Weakness, seizures, meningismus, blurred vision, headache	Focal deficits, sensory loss	Increased monocytes and protein in CSF; normal glucose
MS	Immune complex vasculitis, vertebral osteomyelitis	Myalgia	Point tenderness	X-ray

Key References: Marrie TJ: *Coxiella burnetii* (Q fever). In Mandell GL, Bennett JE, Dolin R, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 5, New York, NY, 2000, Churchill Livingstone, pp 2043–2050; Schaik EJ, Chen C, Mertens K, et al.: Molecular pathogenesis of the obligate intracellular bacterium *Coxiella burnetii*, *Nat Rev Microbiol* 11(8):561–573, 2013; Eldin C, Melenotte C, Mediannikov O, et al.: From Q fever to *Coxiella burnetii* infection: a paradigm change, *Clin Microbiol Rev* 30:115–190, 2016.

Perioperative Implications

Preoperative Preparation
- Continue or initiate antibiotic therapy and optimize any organ system dysfunction.
- Only emergency surgery should be performed.
- Assess respiratory and cardiac reserve and hepatic and neurologic status.
- Careful monitoring.
- Arterial line may be necessary if pneumonia present.
- Myocardial valvular disease secondary to chronic Q fever may require a PA line or other invasive hemodynamic monitors.
- Increased arterial line complications due to vasculitis (rare).

Airway
- None

Induction
- Pneumonia may cause rapid desaturation.
- Hypotension and CV instability if there is cardiac valvular injury.

Maintenance
- With acute hepatitis, avoid drugs that require hepatic metabolism or decrease blood flow to the liver.

Extubation
- Resp status and CV stability must be considered.

Adjuvants
- Depends on hepatic or renal impairment.

Postoperative Period
- Monitor respiratory and/or myocardial status carefully; ICU monitoring may be required.
- Liver enzymes should be followed if there is hepatic involvement.

Anticipated Problems/Concerns
- Pts who require emergency surgery and present with an acute infection might need extended antibiotic therapy to prevent persistent *C. burnetii* infection.

Raynaud Phenomenon

Veena Graff

Risk
- Prevelance: 3-5% of population (based on population-based surveys of various ethnicities)
- Five times more prominent in women than men; commonly diagnosed in second, third, and fourth decades of life.

Perioperative Risks
- Rare morbidity of ischemia, resulting in necrosis and gangrene

Worry About
- Associated systemic disorders
- Arterial thrombosis secondary to prolonged vasospasm and/or ischemic attacks, which can lead to ulcerations and/or gangrene in affected areas
- Hypothermia causing RP attacks (i.e., secondary to cold operating rooms, lack of pt warming, emotional stress)

Overview
- Primary RP, also known as Raynaud disease: No association with systemic diseases.
- Secondary RP: Systemic associations with connective tissue disorders (most common), drugs/toxins, endocrine disorders, hematologic disorders, or cancers.
- Abnormal sensitivity of small arteries and arterioles to vasoconstrictive stimuli.
- RP attacks typically triggered by cold and/or stress and often manifest in a bilateral symmetric pattern (commonly fingertips/toes).
- Triphasic color pattern in affected areas: Pallor due to vasoconstriction (white), followed by cyanosis (blue), followed by erythema and edema (red) due to vasodilation.

Etiology
- Etiology unclear; however, likely hypotheses include:
  - Loss of nerve fibers supplying the endothelium, which normally releases vasodilating chemicals such as nitric oxide, causing vasoconstriction
  - Hyperhomocysteinemia
  - Role of angiotensin II and serotonin in increasing endothelial smooth muscle proliferation

Usual Treatment
- Noninvasive preventive measures; avoid prolonged exposure to cold, dress warmly, and do not smoke.
- Pharmacotherapies: Calcium-channel antagonists and avoidance of vasoconstrictors.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Impaired joint mobility due to associated disorders such as scleroderma	Inability to open mouth due to limited TMJ mobility	Thorough airway assessment (neck ROM and mouth opening)	
RESP	Associated with primary pulm Htn	Chest discomfort Weakness	JVD Pulmonic ejection click	CXR, right cardiomegaly, dilated pulm artery ECG, right atrial enlargement
VASC	Small arterial occlusion	Often associated with numbness, tingling, and pain	Triphasic color pattern in affected areas: Pallor, then cyanosis, then erythema	

Key References: Wigley FM: Clinical practice. Raynaud's phenomenon, *N Engl J Med* 347(13):1001–1008, 2002; Liang YX, Gu MN, Wang SD, et al.: Perianesthesia management of Raynaud's phenomenon—a case report, *J Perianesth Nurs* 25(4):221–225, 2010.

Perioperative Implications

Preoperative Preparation
- Assess for coexisting systemic diseases.
- Potential for difficult airway; thorough airway assessment required (reduced TMJ mobility if associated with scleroderma).

Monitoring
- Standard ASA monitors.
- Can obtain ABG to assess oxygenation if unable to assess pulse oximeter readings.
- Assess risk/benefit ratio if considering arterial cannulation because of danger of arterial vasospasm.

Induction
- General or regional anesthetic options are acceptable.
- Balanced anesthetic with both types to avoid extreme fluctuations in BP.

Maintenance
- Avoid fluctuations in BP.
- Ensure pt warming.
- Use of tourniquet controversial.

Adjuvants
- Avoid vasoconstrictors if possible to avoid RP attacks.

Postoperative Period
- Ensure pt warming.
- Check pulses in all extremities.

Reflex Sympathetic Dystrophy (Complex Regional Pain Syndrome)

Arthur Kitt

Risk

- Incidence of 5.5:100,000 person years at risk (50,000 new cases per y in USA).
- Prevalence of 21:100,000 person years at risk.
- Female:male ratio is 2–4:1.
- Mean peak age is 37–50 y.
- Incidence of CRPS I is 1–2% after fractures, 12% after brain lesions; and 5% after MI.
- Incidence of CRPS II is 1–5% after injury to a peripheral nerve.

Perioperative Risks

- Increased pain flare postop if procedure is on affected extremity
- Increased tolerance and/or opioid requirements if managed with chronic opioids
- Increased incidence of comorbid anxiety and depression

Worry About

- Exacerbation or recurrence of CRPS with manipulation of affected extremity.
- Careful positioning of affected extremity.
- Interactions and/or end-organ effects of chronic pain medications.
- IV access and/or tourniquet placement on affected extremity may be intolerable because of pain.

Overview

- Spontaneous intractable burning pain; allodynia; hyperalgesia
- Edema, autonomic (vasomotor/sudomotor) abn, trophic signs
- Significant decrease in normal function of affected limb
- Symptoms not limited to the region of a single nerve (other causes ruled out)
- Pain disproportionate to inciting event
- Dx largely based on pt's Hx and clinical criteria such as the Budapest criteria
- No diagnostic "gold standard" test
- CRPS I (reflex sympathetic dystrophy): No clear evidence of nerve damage
- CRPS II (causalgia): Clear evidence of nerve damage with inciting event

Etiology

- Pathogenesis of CRPS unknown
- Classically associated with antecedent trauma, surgery, MI, stroke
- Probable involvement of peripheral, autonomic, and central nervous systems; myofascial dysfunction; altered psychological states
- Many proposed mechanisms:
  - Abnormal sympathetic outflow and/or adrenergic receptor sensitivity
  - Abnormal spinal and/or central neuronal sensitization
  - Abnormal and/or exaggerated inflammatory process
  - Neurogenic inflammation
  - Psychological and/or psychogenic factors
  - Genetic predilection with HLA-DR/DQ polymorphisms

Usual Treatment

- Early Dx and multidisciplinary treatment associated with best outcomes
- Physical therapy using desensitization and ROM exercises most important component of rehabilitation to achieve optimal functional restoration
- Psychological intervention, cognitive-behavioral therapy
- Typical first-line oral medications:
  - Antidepressants (SNRIs, TCAs)
  - Antiepileptics (gabapentin, pregabalin)
  - NSAIDs
- Chronic opioid therapy controversial
- Oral corticosteroids employed if inflammatory component is prominent
- Other adjuvant and second-line therapies:
  - NMDA antagonists (ketamine, memantine)
  - GABA agonists (intrathecal baclofen)
  - Bisphosphonates
  - Free radical scavengers (DMSO, NAC)
  - Alpha-2 agonists (epidural clonidine)
- Interventional therapies:
  - Sympathetic ganglion blockade
  - Chemical/surgical sympatholysis
  - Regional IV infusion therapy (lidocaine, reserpine, guanethidine)
  - Neurostimulation (SCS, TENS, deep brain stimulation)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Skin/hair/nail changes	Changes in limb appearance Increased/decreased hair growth	Thickened/thin skin Glossy, waxy skin Increased/decreased hair growth Thickened/brittle nails	Serial physical exams Comparative exam photos
MS	Muscle mass/strength change Stiffened joints Bone changes/osteoporosis	Subjective weakness Decreased ROM	Muscle atrophy Objective weakness Decreased active/passive ROM	 Three-phase bone scintigraphy Radiographs
PNS	Spontaneous pain Allodynia/hyperalgesia Motor changes	Spontaneous pain Pain to nonnoxious stimuli Exaggerated pain to noxious stimuli	Allodynia Mechanical/thermal hyperalgesia Tremor/dystonia	Quantitative sensory testing (thermal/ thermal/pain/ vibratory)
ANS	Vasomotor/sudomotor abnormalities	Hyperhidrosis/hypohidrosis Temp changes Swelling	Moist, clammy, cool skin Edema, skin color changes Skin temperature asymmetry of limbs	QSART Infrared thermometry/thermography Thermoregulatory sweat test

Key References: Stengel M, Binder A, Baron R: Update on the diagnosis and management of complex regional pain syndromes, *Adv Pain Manag* 1:96–104, 2007; Bussa M, Guttilla D, Lucia M, et al.: Complex regional pain syndrome type I: a comprehensive review, *Acta Anaesthesiol Scand* 59(6):685–697, 2015.

Perioperative Implications

Preoperative Preparations

- Preop PE noting location of pain symptoms as well as neurologic and/or MS deficits.
- Careful planning of pt positioning.
- Consider combined regional/GA for periop and postop pain control.
- Make a detailed plan for postop pain-control strategies.
- Wait until acute phase of CRPS has resolved.

Monitoring

- Standard ASA monitors.
- Avoid BP cuff, pulse oximetry, or other monitors on the affected extremity.

Induction

- Possible increased dosage of induction agent (for pts on chronic opioids).
- Consider regional blockade and/or catheter infusion.

Maintenance

- Possible increased anesthetic and periop opioid requirements (for patients on chronic opioids)
- Diligent assessment of affected limb position and temperature

Adjuvants

- Continuation of all neuropathic pain medications if possible.
- NMDA antagonist bolus and infusion (ketamine) and/or other neuropathic meds can possibly avoid central sensitization (windup).

Postoperative Period

- Continue regional anesthesia and/or analgesia postop if feasible.
- Resume preop pharmacologic regimen (home medications).
- Facilitate early mobilization.
- Consider pain medicine consultation if pt is admitted postop.

Acknowledgment

The author wishes to acknowledge the contribution to the previous edition of this chapter by Dr. David Bandola.

Renal Failure, Acute

Richard K. Patch III

Risk

- Incidence in USA: 1% of all hospital admissions (community-acquired); 5% of all general hospital pts (hospital-acquired); 10–30% of all ICU pts.
- Acute tubular necrosis (45%) is most common cause in hospitalized pts.
- Population with highest prevalence: Elderly (>65 y).
- Two most common definitions:
  - RIFLE criteria: Risk, injury, failure, loss, ESRD.
  - AKIN criteria: Stage 1, stage 2, stage 3.

Perioperative Risks

- Overall mortality of periop ARF: 60–90%
- Hyperkalemia (and arrhythmias), metabolic acidosis, acute pulm edema
- Aspiration
- Bleeding (plt dysfunction)

Worry About

- Metabolic acidosis and hyperkalemia (pH decrease of 0.1 causes K^+ increase of 0.5 mEq/L).
- Ventricular arrhythmias (may occur without warning).
- Encephalopathy (aspiration risk, increased sensitivity to all sedatives and anesthetics).
- GI symptoms and aspiration (N/V, bleeding, and encephalopathy).
- Coagulopathy (plt dysfunction) and surgical bleeding.
- Hemodynamic intolerance of hemodialysis; peritoneal dialysis compromises FRC.

Overview

- Elective surgery is contraindicated with new-onset ARF; procedures are urgent or emergency.
- Consider hemodialysis for severe hyperkalemia prior to nonemergent surgery.
- RA Regional anesthesia is relatively contraindicated (plt dysfunction, encephalopathy).
- Repetitive hemodynamic insults markedly impair renal recovery.
- Dialysis partially controls thrombocytopathy and enteropathy but does not decrease risk of sepsis and poor wound healing.
- Dopamine is not renally protective at low doses, and data are mixed about fenoldopam as a protective agent.

Etiology

- Prerenal disease: Hypovolemic states (acute hemorrhage, diarrhea, unreplenished insensible losses, heart failure, cirrhosis, distributive shock).
- Renal vascular disease: Microangiopathic hemolytic anemia, atheroemboli, compartment syndrome.
- Tubular and interstitial disease: ATN, acute interstitial nephritis, rhabdomyolysis, radiocontrast nephropathy, medications.
- Glomerular disease: Acute glomerulonephritis, vasculitis.
- Obstructive nephropathy.

Usual Treatment

- Treat underlying cause (e.g., shock, rhabdomyolysis).
- Medical therapy:
  - Fluid and electrolyte restriction, loop diuretics.
  - Hyperkalemia: Beta-adrenergic agonists, hyperventilation, bicarbonate, Ca^{2+}, insulin-glucose, sodium-polystyrene sultanate (kayexalate).
  - Kayexalate is relatively contraindicated in critically ill pts owing to colonic necrosis.
- Dialysis: IHD or CRRT.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Edema Coagulopathy	Epistaxis, GI bleeding	Airway edema Petechial hemorrhages	
CV	VTach, VFIB Pericardial effusion Hypertensive crisis	Syncope, cardiac arrest Dyspnea, pleuritic chest pain Headache, visual changes	Muffled heart sounds	ECG, serum K^+, Mg^{2+} ECG, CXR, TTE
RESP	Pulm edema	Dyspnea, orthopnea	Frothy sputum, crackles	CXR
GI	Reflux Ileus Serositis Ulceration, bleeding	Reflux Abdominal discomfort Acute abdomen Hematemesis, melena	Absent bowel sounds, tympany Tenderness, guarding Same	Esophagogram KUB series KUB, CT scan Stool guaiac, endoscopy
HEME	Plt dysfunction	Excessive bleeding	Petechial hemorrhages	
RENAL	AKI	Oliguria, anuria	Edema	Urinalysis, BUN, Cr, Cr clearance Renal US, scintigraphy
CNS	Encephalopathy	Confusion, disorientation, coma	Same plus asterixis	EEG CT scan
MS	Rhabdomyolysis	Crush injury, limb ischemia	"Red urine"	Urine myoglobin Serum CK

Key References: Ricci Z, Cruz DN, Ronco C: Classification and staging of acute kidney injury: beyond the RIFLE and AKIN criteria, *Nat Rev Nephrol* 7(4):201–208, 2011; Stafford-Smith, Raja A, Shaw AD: Evaluation of the patient with renal disease. In Longnecker DE, editor: *Anesthesiology*, ed 2, New York, 2012, The McGraw-Hill Companies, pp 166–179.

Perioperative Implications

Preoperative Preparation

- Dialysis to control fluid overload, hyperkalemia, metabolic acidosis, acute uremia.
- Consider metoclopramide, H_2 blocker, and rapid sequence induction to reduce reflux risk.
- Consider DDAVP 0.3 µg/kg to enhance Plt function (effective for 8–12 h).
- Regional techniques may be contraindicated by coagulopathy.

Monitoring

- Standard ASA monitoring.
- For large fluid shift operations with or without LV dysfunction, consider:
  - Arterial line ± CVP.
  - PA catheter or TEE.
  - Pulse pressure variation or stroke volume variation monitoring.

Airway

- Consider awake fiberoptic intubation with airway edema.
- Avoid nasal intubation (epistaxis).
- Treat as for full stomach: Head up, cricoid pressure.
- Succinylcholine is relatively contraindicated (avoid if K^+ concentration ≥5.0 mEq/L).

Preinduction/Induction

- Manage induction and/or replacement fluids as if renal function were normal (risk of hypovolemia).
- Anticipate enhanced pharmacodynamic effects of all sedative and/or anesthetic agents (encephalopathy).

Maintenance

- Restrict maintenance fluids; replace losses appropriately guided by hemodynamic monitoring.
- Euvolemia is key.
- Avoid morphine, meperidine, and pancuronium.
- Avoid nephrotoxic agents such as NSAIDs (ketorolac), antimicrobials (gentamicin), and ACEI/ARB
- Consider agents independent of renal elimination (volatile anesthetics, propofol, fentanyl, remifentanil, cisatracurium, esmolol, clevidipine).
- Increase minute ventilation to compensate for metabolic acidosis; sedative-hypnotic administration may lead to acidosis by eliminating compensatory resp alkalosis in spontaneously breathing pt
- Anticipate increased volume of distribution but decreased clearance of most drugs.
- Check ABGs and serum K^+

Extubation

- Anticipate delayed emergence, vomiting, aspiration.
- Treat as for full stomach.
- Neostigmine elimination is delayed in ARF.
- Consider a short period of postop mechanical ventilation if pt has intraop acidosis (will not be able to generate adequate spontaneous resp compensation).

Postoperative Period

- Careful assessment of CV and respiratory status; check ABG and serum K^+.
- Morphine and meperidine contain active metabolites that are renally excreted. Use with caution.
- May require IHD, CRRT, or sustained low efficiency dialysis for excess fluid, hyperkalemia, and/or acidosis in early postop period.

Anticipated Problems/Concerns

- Major concerns are always hyperkalemia, acidosis, and pulm edema.
- Hyperkalemic arrhythmias may occur without premonitory ECG signs.
- Rapid K^+ flux more ominous than stable high serum K^+.

Acknowledgment

The author would like to sincerely thank Dr. Robert Sladen for his work on this chapter in the previous edition.

Renal Failure, Chronic

Lee A. Fleisher | Donald S. Prough

Risk

- Incidence in USA and worldwide: >100 cases of ESRD per million population.
- Between NHANES of 1988–1994 and that of 2003–2006, the prevalence of CKD in people 60 y and older jumped from 18.8% to 24.5%.
- Racial prevalence: African Americans, ~200 cases per million; Hispanics, ~100 per million; Caucasians, ~50 per million.

Perioperative Risks

- Overall periop mortality of pts with ESRD: 4%.
- Overall periop morbidity of pts with ESRD: 50% (hyperkalemia, infections, hypotension/Htn, bleeding, dysrhythmias, clotted fistulas).
- In recent studies, adjusted HRs for death increased consistently as eGFR fell below 60.0mL/min per 1.73m^2 with a plateau and relative decrease in risk as eGFR fell below around 20mL/min per 1.73m^2.

Worry About

- Periop progression from CRI, not requiring dialysis, to dialysis-dependent ESRD.
- Hypovolemia and hypokalemia (especially if recently dialyzed)
- Hypervolemia, metabolic acidosis, and hyperkalemia (especially if not recently dialyzed)
- Autonomic dysfunction (excessive hypotensive responses)
- Exaggerated hypertensive responses to noxious stimuli
- Prolonged responses to renally excreted drugs and metabolites (e.g., vecuronium, pancuronium, narcotics)
- Impaired immune status
- Occult CAD

Overview

- Decreased excretory and other functions of kidneys related to long-standing disease; with dialysis, disease can persist for many years.
- Associated with multiple complications of failed renal excretory function, including volume overload, accumulation of products of catabolism (e.g., K^+ and hydrogen ions), platelet dysfunction, and side effects of dialytic therapy, including hypovolemia.
- Associated with complications of concurrent diseases (e.g., DM, Htn) with increased mortality for MI in those with versus without CRF
- Volume status and electrolyte balance related to how recent dialysis has been.

Etiology

- Htn (15% Hispanics; 20% Caucasians; 40% African Americans)
- DM (20% Caucasians; 30% African Americans; 37% Hispanics); represents 43.8% of all secondary cases
- Glomerulonephritis (12% African Americans; 22% Hispanics; 25% Caucasians)
- Other causes: Polycystic disease, collagen-vascular disease, pyelonephritis

Usual Treatment

- CRI: Fluid restriction, protein restriction, diuretics, antihypertensives
- Peritoneal dialysis or hemodialysis; continuous venovenous hemofiltration or continuous venovenous hemodialysis while hospitalized
- Renal transplantation (can be combined with pancreatic transplantation in diabetics)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CHF LVH Dysrhythmias	Exercise intolerance Htn Palpitations	Crackles; S_3, S_4 Pulse, auscultation	CXR ECG
GI	N/V, anorexia GI bleeding	N/V, anorexia Melena, rectal bleeding	Malnutrition	Positive occult blood
HEME	Plt dysfunction Anemia	Easy bruising Fatigability	Ecchymoses Pallor	Bleeding time Hgb
RENAL	Decreased concentrating ability (CRI)	Nocturia, frequency		Urinary osmolality BUN, Cr
CNS	Encephalopathy Autonomic dysfunction	Decreased mental acuity, disorientation Postural hypotension	Mental status Tilt-table test: Reduced BP, increased HR when tilted	
PNS	Peripheral neuropathy	Paresthesias, burning, itching of lower extremities	Excoriations	

Key References: Kalamas AG, Niemann CU: Patients with chronic kidney disease, *Med Clin North Am* 97(6):1109–1122, 2013; Prowle JR, Kam EP, Ahmad T, et al: Preoperative renal dysfunction and mortality after non-cardiac surgery, Br J Surge 103(10):1316–1325, 2016.

Perioperative Implications

Preoperative Preparation

- Assess adequacy of dialytic therapy, volume and acid-base status, Hgb conc, CV status, and serum K^+.
- If pt not dialysis-dependent, assess renal reserve and CV status.
- Consider issues of vascular access.

Monitoring

- Temp, ECG (rhythm, rate, hyperkalemia).
- Pulse oximeter, capnometer, peripheral nerve stimulator.
- Consider arterial catheter if pt is chronically hypertensive; consider PA catheter for high-risk surgery in pts with cardiac dysfunction.

Airway

- Gastroparesis precautions if pt is diabetic

Preinduction/Induction

- Reduce dose of thiopental.
- Higher doses of propofol required to achieve same level of BIS.
- Exaggerated response to benzodiazepines.
- Consider avoiding renally excreted NMBs (vecuronium, pancuronium).
- Use narcotics cautiously.
- If pt is not dialysis-dependent, there are theoretical concerns about sevoflurane, although they do not appear to be clinically relevant.
- Exaggerated BP swings with induction and intubation.
- Reduce dose of local anesthetics if metabolic acidosis is present or if sedatives will cause resp acidosis.

Maintenance

- Maintenance of an adequate renal perfusion pressure with fluids and inotropic agents may protect against acute kidney injury.
- Propofol infusions associated with faster eye opening.

Extubation

- Ensure adequate reversal of NMBs.
- Evaluate airway reflexes.

Adjuvants

- Avoid renally excreted NMBs.
- None of the pharmacologic interventions that have been used to prevent acute kidney injury have convincingly demonstrated a benefit during the periop period.

Postoperative Period

- Use dialysis if necessary.
- Monitor for frequent causes of postop morbidity (see above).

Anticipated Problems/Concerns

- Hyperkalemia: Treatment with $CaCl_2$, insulin/glucose, or $NaHCO_3$ may be necessary; intraop dialysis is occasionally required.
- Balancing intraop volume requirements with need for postop fluid removal.
- Exaggerated drug effects.

Rett Syndrome

Catherine R. Bachman | Lee A. Fleisher

Risk

- Occurs almost exclusively in females.
- Incidence is 0.4–0.7:10,000.

Perioperative Risks

- Abnormal control of ventilation, with periods of apnea and hyperventilation
- May have GE reflux
- Multiple orthopedic and motor movement disorders

Worry About

- Risk of periop apnea not known
- Risk of succinylcholine-induced hyperkalemia not known
- Aspiration due to GE reflux and swallowing disorder
- Cardiac: Prolonged QTc, abnormal autonomic regulation, increased incidence of sudden death
- Difficult intraop positioning because of spasticity and contractures

Overview

- Characterized by normal early growth and development followed by a slowing of development and then regression characterized by loss of purposeful use of the hands, distinctive hand movements, slowed brain and head growth, problems with walking, seizures, and intellectual disability
- Dx based on clinical characteristics with inclusion and exclusion criteria, mutations in *MECP2* gene
- Abnormal EEG; nonspecific changes
- Pathognomonic stereotyped hand movements, tortuous hand-wringing or other hand automatisms
- Seizures very common
- Respirations abnormal when awake; hyperventilation alternating with hypoventilation or apnea and hypoxemia
- Orthopedic and movement disorders such as scoliosis, spasticity, ataxia, loss of locomotion
- ANS dysfunction with increased sympathetic tone
- Cachexia

Etiology

- Mutations in the *MECP2* gene' mechanism not yet determined.
- MECP2 is needed for brain development and acts as one of the many biochemical switches in gene expression.
- Although genetic, most cases occur spontaneously.
- Dx made by Hx and clinical features (inclusion and exclusion criteria established).

Usual Treatment

- Supportive only; no specific therapy
- Aimed at improving quality of life, seizure control, nutrition, PT, possible surgery for orthopedic problems

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Nonspecific Spasticity may make airway difficult		Neck ROM Airway exam	Neck x-rays if indicated
CV	Possible prolonged QTc Peripheral vasomotor disturbances		Extremities cool Trophic changes	ECG
RESP	Abn control of ventilation when awake, with hyperventilation, apnea, cyanosis Lung changes due to scoliosis or aspiration	Apnea, cyanosis Scoliosis, aspiration	Observation Chest exam	O_2 saturation CXR
GI	GE reflux possible, swallowing difficulties, constipation Growth failure	GE reflux, feeding difficulties	Thin, small for age	Studies for GE reflux
CNS	Severe developmental delay Seizures Ataxia, loss of locomotion	Developmental level, seizure activity	Assessment of cognitive and movement disorders	EEG
MS	Hypotonia (early), spasticity (late), ataxia Secondary orthopedic manifestations: Scoliosis, joint contractures	Progress and extent of MS abnormality	Chest exam for scoliosis Limb and joint positions	X-rays

Key References: Acampa M, Guideri F: Cardiac disease and Rett syndrome, *Arch Dis Child* 91(5):440–443, 2006; Coleman P: Rett syndrome: anaesthesia management, *Paediatr Anaesth* 13(2):180, 2003.

Perioperative Implications

Preoperative Preparation

- As for any pt with developmental delay.
- Optimize respiratory status.
- Assess respiratory control.
- Minimize aspiration risk.

Monitoring

- Routine.
- More invasive depending on procedure.
- Consider brain function monitoring because of anesthetic sensitivity.

Airway

- Normal face.
- Spasticity may make positioning difficult.

Preinduction/Induction

- Risk of hyperkalemia following succinylcholine unknown
- Possible aspiration risk due to GE reflux

Maintenance

- Respiratory control abnormal; unknown if spontaneous ventilation under anesthesia associated with significant apnea
- Attention to body temp because of thin body habitus and peripheral vasomotor disturbances
- Can be excessively sensitive to both sedative drugs and volatile anesthetics

Extubation

- Possible aspiration risk.
- Assess respiratory control.

Postoperative Period

- Respiratory control abnormal.
  - Effect of anesthetic agents.
  - Duration of respiratory monitoring.
  - Effect of narcotics versus local anesthetics for pain control.
- Intense monitoring in postop period is essential as frequent desaturations in these pts may cause progressive cerebral damage.

Adjuvants

- None

Anticipated Problems/Concerns

- Respiration control abnormality is not well understood. Therefore effect of anesthetic agents intraop and postop on respiration is not known. Need for postop monitoring for apnea is unknown.

Reye Syndrome

Mary A. Keyes | Lee A. Fleisher

Risk

- Incidence prior to 1990: 0.3–0.6:100,000.
- From 1987 to 1993: 0.03-0.06:100,000; 2 cases/y have been reported since 1994.
- During early 1980s, an association between aspirin and Reye syndrome was recognized; thereafter, incidence declined dramatically. In 1986, a warning label on all aspirin-containing products was mandated in USA.

Perioperative Risks

- Surgery (all but life-or-death emergencies) contraindicated during Reye syndrome.
- Following recovery, LFTs must be repeated.

Worry About

- Unrecognized inborn errors of metabolism that produce Reye-like syndromes, such as fatty-acid oxidation defects, carnitine deficiency, and amino and organic acidopathies
- Recurrent liver dysfunction
- Permanent neurologic sequelae

Overview

- An acute, noninflammatory encephalopathy with hepatic dysfunction predominantly in children; typically starts several days after a viral illness, usually influenza or varicella.
- Encephalopathy heralded by protracted severe vomiting, with abnormal behavior and combativeness that may progress to coma.
- Dx is made by unexplained encephalopathy with one or more of following: Serum transaminases elevated to at least 3 times normal, blood ammonia levels at least 3 times normal, or hepatic microvesicular fatty infiltration on liver biopsy. There should be no other reasonable explanation for the cerebral or hepatic abnormalities.
- The CDC use a classification for progressive disease severity of stages 1–6. Mortality has decreased from 50% to 20% as a result of recognition of early phases and aggressive treatment.
- Prognosis depends on severity and duration of cerebral dysfunction. Severe disease can lead to subtle neuropsychological defects.

Etiology

- Abnormal reaction to viral illness modified by exogenous toxin in a susceptible host.
- Most frequently linked to influenza A and B and varicella. The exogenous toxin is aspirin in most cases. Salicylates were detectable in >80% of cases.

Usual Treatment

- Early recognition of mild cases and maintenance of fluid, lyte, acid-base, urine output and glucose balance.
- ET intubation may be required to ensure airway protection and control of ventilation to reduce ICP.
- Fluids restricted in pts with cerebral edema; ICP monitoring helps to improve cerebral perfusion pressure and manage ICP.
- Mannitol to induce cerebral dehydration and barbiturates to decrease cerebral metabolic demand.
- Coagulopathies treated with vitamin K and/or FFP.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GI	Hepatic dysfunction	Severe vomiting	Hepatomegaly	Hepatic transaminases, ammonia levels Liver biopsy PT, PTT
CNS	Delirium Combative behavior Seizures Lethargy Coma	Alteration in mental status	No focal signs	CT scan ICP monitor

Key References: Goetz CG: Aminoacidopathies and organic acidopathies, mitochondrial enzyme defects, and other metabolic errors. In Goetz C, editor: *Textbook of clinical neurology*, ed 3, Philadelphia, PA, 2007, Saunders; Tasker RC: Update on pediatric neurocritical care, *Paediatr Anaesth* 24(7):717–723, 2014.

Perioperative Implications

- Surgery should not be undertaken except in life-or-death emergencies.

Adjuvants

- Ondansetron to decrease vomiting.
- Treat seizures with phenytoin.
- Correct hyperammonemia with sodium phenyl-acetate/sodium benzoate.

Anticipated Problems/Concerns

- Hepatic dysfunction
- Neurologic sequelae
- Underlying inborn errors of metabolism, particularly in children under 5 y

Rheumatic Fever (Acute) and Rheumatic Heart Disease

Mark S. Weiss | Victoria M. Bedell | Roger A. Moore

Risk

- Common illness among children and young adults.
- Primary chronic sequelae is RHD.
- Worldwide estimate is over 15 million cases of RHD, with 282,000 new cases and 233,000 deaths annually.
- Up to 1% of all school-age children in Africa, Asia, Latin America, and the eastern Mediterranean show signs of the disease.

Perioperative Risks

- In ARF with acute cardiac manifestations (including first-degree heart block and pericarditis), medications and equipment for maintaining heart rhythm and function during anesthesia should be available.
- An actively febrile pt's surgery should be delayed unless it is urgent or emergent.
- The approach to anesthesia in RHD must be tailored to the pt's specific physiologic parameters. Control of the pt's hemodynamic profile to optimize cardiovascular stability will depend on which valves are damaged and the extent of the myocardial compromise, either from RHD or from secondary cardiovascular effects due to chronic valvular disease.
- In the presence of valvular disease, prophylactic antibiotics should be given to prevent bacterial endocarditis.
- Periop assessment of cardiac status, including direct and indirect effects of chronic valvular disease on cardiac function, must be performed prior to surgery. Pts may be clinically asymptomatic for 20 y after developing RHD owing to compensatory alterations in cardiac structure and function. Knowledge of the cardiac compensatory changes in heart function is essential.

Worry About

- If valvular damage is present, maintain tight control of cardiac rate and rhythm, pulmonary and systemic vascular resistance, and intravascular fluid volume.
- If pulm hypertensive crisis occurs, hyperventilate and increase inspired O_2 to 100%.

Overview

- ARF is primarily due to a pharyngeal infection with *Streptococcus pyogenes* or group A beta hemolytic streptococcus, which is a common cause of throat infections in children. If left untreated, the child can develop ARF, which is an inflammatory response occurring 2–3 wk after the initial infection.
- RHD is an autoimmune reaction with cardiac tissue, resulting in permanent deformities of heart valves or chordae tendineae.
- Scarring leads to valvular stenosis, classically in the mitral valve followed by the aortic valve. However, all cardiac valvular defects can occur.
- Joint pain and carditis with valve damage are the major clinical manifestations of ARF. Carditis can occur in up to 80% of people with ARF, leading to mitral or aortic valvular disease. About half of those affected will develop chronic RHD. Death from ARF is not common, but chronic rheumatic heart disease can lead to morbidity from arrhythmias, endocarditis, and stroke.

Usual Treatment

- ARF is easily treated with penicillin if initiated within 9 d of onset of pharyngitis; this will prevent the development of chronic manifestations, such as carditis. Corticosteroids can be used in the acute inflammatory stage. Bed rest for several wk is required, followed by gentle ambulation. Diuretics and vasodilators are given for severe carditis as well as furosemide for mild to moderate CHF. ACE inhibitors are given for severe aortic regurgitation. Serial ECHO will determine cardiac dimensions and function. Valve repair surgery should be delayed until after the acute inflammatory stage.
- Chorea: Treatment is supportive, including psychosocial support.
- Arthritis and arthralgias: NSAIDs may mask signs of acute rheumatic fever. By clinical consensus, paracetamol is preferred. After Dx has been made, naproxen twice daily is the drug of choice.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	First-degree heart block, pericarditis, myocarditis and valvulitis. Criteria: Major: Migratory polyarthritis, carditis, Sydenham chorea, erythema marginatum, and subcutaneous nodules Minor: Arthralgias, fever, elevated serum acute-phase reactants, and first degree heart block	Dyspnea Palpitations Chest pain	Cardiac murmur Chest pain CHF, edema, orthopnea, DOE	ECHO Cardiac cath ECG (first-degree block)
RESP	Pulm edema	DOE Orthopnea Paroxysmal nocturnal dyspnea Hemoptysis	Tachypnea Rales Wheezing	CXR
GI	Hepatomegaly from right heart failure		Enlarged liver	LFTs
RENAL	Fluid retention		Edema	Serum lytes
CNS	Embolic stroke	Sudden unilateral neurologic deficits TIA	Focal, unilateral neurologic deficits	CT or MRI of the head TEE Carotid US

Key References: Seckeler MD, Hoke TR: The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease, *Clin Epidemiol* 3:67–84, 2011; Moore RA, Martin DE: Anesthetic management for the treatment of valvular heart disease. In Hensley FA, Martin DE, Gravlee GP, editors: *A practical approach to cardiac anesthesia,* ed 3, Philadelphia, 2003, Lippincott Williams & Wilkins.

Perioperative Implications

Preoperative Preparation

- A determination of the specific cardiac lesions need to be made so that the ideal hemodynamic profile can be decided upon. Choice of anesthetic approaches and drugs will be largely determined by the desired hemodynamic profile.
- Note that with aortic stenosis, there is a need to keep a lower heart rate and a higher SVR. These are critical hemodynamic considerations and require special attention.
- Assess fluid status. If pt is dehydrated, liberal IV fluids should be provided preop, since with all lesions preload should be maintained. If fluid overload exists, concern for the development of CHF may direct treatment by fluid restriction and diuresis.
- If a decrease in PVR is desirable hemodynamically, avoid premedication causing hypoventilation.
- It is rare that a single valvular heart defect exists in RHD. The most common combined valvular defect is mitral stenosis with mitral regurgitation.

Monitoring

- Depending on the severity of the cardiac disease and the extent of surgery, have a low threshold for invasive monitoring. Consider arterial cath and CVP cath.
- Use caution when placing a pulm artery cath. Excessive force when placing the cath may rupture the pulm artery due to the combination of long-standing pulm Htn and thin pulm arterial walls.
- TEE is helpful for assessment of worsening valvular regurgitation and left ventricular dysfunction.

Airway

- In deciding between deep sedation and general anesthesia with a controlled airway, worsening pulm Htn with hypercapnia should be considered.
- If a difficult airway is anticipated, the initial intubation attempt should be aided by video or fiberoptic laryngoscopy.

Induction

- With mitral and aortic stenosis, tachycardia must be controlled upon induction and emergence from anesthesia.
- Induction agents should be chosen to minimize cardiovascular changes that would adversely affect the optimal hemodynamic profile.
- A potent alpha-adrenergic agonist such as phenylephrine should be on hand.

Maintenance

- Adequate fluids should be given to maintain adequate preload, but care should be taken to avoid fluid overload and the resultant CHF.
- Positive-pressure hyperventilation is an adjunct for decreasing PVR.
- Avoid long-acting narcotics that might depress ventilation postop.
- Use high FIO_2.
- Avoid hypothermia.

Extubation

- Do not attempt deep or early extubation.
- Prior to extubation, it is important to assess the adequacy of ventilation by measuring inspiratory pressure and ensuring adequate tidal volumes.

Postoperative Period

- Close monitoring of ventilation and pulse oximetry.
- Active warming.
- Be prepared for immediate reintubation.

Adjuvants

- Pulm vasodilators may be indicated for pts with severe pulm Htn. Nitric oxide, prostacyclin, and milrinone are all possible adjuvants, but use of these medications should be balanced with their effects on the hemodynamic profile, such as falls in SVR, before instituting treatment.

Rheumatoid Arthritis

Nathan Kudrick | Pedro Orozco | Lee A. Fleisher

Risk

- Internationally the prevalence of RA is believed to range from 0.4% to 1.3%.
- In 2005, an estimated 1.5 million (0.6%) of USA adults >18 y had RA.
- Male-female ratio: 1:2.

Perioperative Risks

- Risk of neurologic injury is increased due to possible occult damage to the cervical spine.
- Associated cardiac disease may be present but not clinically apparent.
- Pulm complications arise secondary to possible pulm fibrosis and restrictive lung disease.

Worry About

- Visualization of glottis and tracheal intubation may be difficult due to rheumatoid-associated damage to the cervical spine.
- Former successful ET intubation does not reliably eliminate existing airway abnormalities.
- Occult coronary vascular disease, pericardial effusion, pericardial thickening, rheumatoid nodules in the cardiac conduction pathway, valvular fibrosis.
- Iatrogenic injury to the cervical spinal cord during laryngoscopy and tracheal intubation.
- Chronic corticosteroid use may necessitate intraop steroid administration.
- Mental health conditions.

Overview

- Chronic systemic inflammatory disease involving diffuse joints and organ systems.
- The natural history of RA varies considerably with at least three possible disease courses:
  - Monocyclic: Have only one episode that ends within 2–5 y of initial diagnosis. This may result from early diagnosis or aggressive treatment.
  - Polycyclic: The level of disease activity fluctuates over the course of the condition.
  - Progressive: RA continues to increase in severity and does not go away.
- Systemic effects include pericardial effusion, tamponade, pleural effusion, pulm fibrosis, anemia, keratoconjunctivitis, and renal failure.

Etiology

- Autoimmune disorder triggered by an antigen in genetically predisposed persons.
- Clinical variability may stem from differences in triggering antigens and immune response.
- Pathology: Synovial cellular hyperplasia, synovial infiltration by lymphocytes, plasma cells, and fibroblasts leading to degeneration of cartilage and articular surfaces.

Treatment

- Aspirin and NSAIDs: Ibuprofen, indomethacin, naproxen, piroxicam, sulindac, and tolmetin
- Nonbiologic DMARDs: Methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, azathioprine, cyclosporine, penicillamine, and gold
- Biologic agents, sometimes called biologic DMARDs: Etanercept, adalimumab, infliximab, certolizumab pegol, and golimumab

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Edematous mucosa Arthritis of larynx	Epistaxis Hx of voice change	Friable mucosa Voice, airway exam	Direct laryngoscopy
CV	LV dysfunction Aortitis Pericarditis	Dyspnea Orthopnea Reduced exercise Reduced exercise Dyspnea	S_3 Rales Diastolic murmur (A1) Distant heart sounds Friction rub	ECG Stress ECG ECHO ECHO ECHO
RESP	Fibrosis	Dyspnea	Dry rales	CXR, PFTs
GI	Peptic ulcer	Epigastric pain, N/V		
RENAL	Renal dysfunction	Drug induced		Cr
CNS	Spinal cord compression Neurologic dysfunction	Neck pain Numbness	Sensory deficits Motor deficits ROM of neck	Radiography
MS	Arthritis	Joint pain	Swelling Pain with motion Restricted motion	Radiography

Key References: Lisowska B, Rutkowska-Sak L, Maldyk P, et al.: Anaesthesiological problems in patients with rheumatoid arthritis undergoing orthopaedic surgeries, *Clin Rheumatol* 27(5):553–556, 2008; Samanta R, Shoukrey K, Griffiths R: Rheumatoid arthritis and anaesthesia, *Anaesthesia* 66(12):1146–1159, 2011.

Perioperative Implications

Preoperative Evaluation

- Thorough airway evaluation is a priority. If atlantoaxial instability exists, flexion of the neck can compress the spinal cord. Radiating pain to the occiput may be an indication of cervical cord involvement. Imaging—such as x-ray, CT, or MRI—may be indicated if the amount of cervical involvement is not known.
- Cardiopulmonary status needs to be evaluated. If severe restrictive lung disease is suspected, preop pulm function tests may be indicated. Anticipation of postop ventilatory support should be considered.
- Must have adequate knowledge of the pt's current medications. Stress-dose corticosteroid supplementation may be indicated for pts being treated chronically with these drugs. Anti-inflammatory medications, aspirin, and other rheumatoid drugs can interfere with platelet function, clotting, and formation of RBCs.
- Joint mobility and restriction should be assessed to determine appropriate intraop positioning.

Monitoring

- Standard monitors
- Further invasive monitoring depending on pt's disease state and the anticipated procedure

Airway

- Presence of atlantoaxial instability involvement assessed. Cervical collar placement to minimize movement during direct laryngoscopy considered. Awake fiberoptic laryngoscopy may be best method.
- TMJ disease can limit mouth opening and ability to perform direct laryngoscopy adequately.
- Cricoarytenoid involvement can decrease size of the glottic inlet and necessitate use of a smaller ETT.

Preinduction/Induction

- Preinduction and induction agents/techniques dependent on pt's specific associated comorbidities.

Maintenance

- CV effects from induction agents and volatile anesthetics potentially more pronounced; risks of hemodynamic instability, cardiac conduction abnormalities, and myocardial ischemia increased.
- Pulm disease may be associated with restrictive changes leading to decreased lung volumes and vital capacity, V/Q mismatch, and poor arterial saturation.
- Hematologic abn such as anemia can be evident intraop.
- Appropriate extremity positioning; padding and manipulation assessed throughout procedure

Extubation

- Post-extubation laryngeal obstruction secondary to edema and erythema possible from cricoarytenoid involvement.
- With severe restrictive lung disease, postop ventilatory support is anticipated.

Adjuvants

- Regional and neuraxial techniques can be utilized assuming no significant thoracic, lumbar, and sacral spine involvement as well as normal coagulation studies

Anticipated Problems/Concerns

- Tracheal intubation difficulties secondary to cervical spine and TMJ involvement
- Intraop CV instability and restrictive pulm disease issues
- Associated side effects of current drug therapy (e.g., anticoagulation, anemia, poor wound healing).
- Multiorgan system involvement
- Intraop positioning concerns secondary to advanced joint involvement and decreased ROM
- Potential need for postop ventilatory support

Riley-Day Syndrome (Familial Dysautonomia, Hereditary and Sensory Autonomic Neuropathy Type III)

Elvedin Luković | H. Thomas Lee

Risk

- Incidence: 1:3700 live births among American and Israeli Jews.
- Since original description in 1949, more than 600 pts have been identified and registered with the Dysautonomia Center at New York University.

Perioperative Risks

- Prior to 1960 there was a 50% probability of death before age 5 y; currently a newborn with FD has 50% probability of reaching age 40 y, although many require multiple surgical interventions.
- Mortality is primarily due to pulmonary complications (26%, decreasing with aggressive treatment of aspirations). Some deaths are unexplained (38%, possibly due to unopposed vagal stimulation or sleep abnormality). Others are due to sepsis (11%), bradycardia/CHB, hyponatremia, or renal failure.

Worry About

- Labile blood pressures exacerbated by physical and/or emotional stress
- Dysrhythmias, especially bradycardia, which can lead to asystole/CHB
- Compromised respiratory function at baseline due to chronic aspirations and severe thoracic kyphosis/scoliosis
- Hyponatremic seizures secondary to hypertensive vomiting, which is associated with excessive secretion of vasopressin and water retention
- Advancing renal failure due to progressive denervation of renal arteries, leading to poor regulation of RBF during paroxysmal hypertensive and hypotensive episodes

Overview

- FD is characterized by poor development and poor survival of autonomic and sensory neurons; motor neurons are typically spared; intelligence is usually normal.
- Signs and symptoms of FD are usually apparent at birth and tend to progress with age.
- Diagnosis is based on documentation of mutation(s) in the *IKBKAP* gene. There is high suspicion for disease if five cardinal criteria are present: Absence of overflow emotional tears (after age 7 mo), absent

lingual fungiform papillae, depressed patellar reflexes, lack of an axon flare following intradermal histamine, documentation of Ashkenazi Jewish extraction.

- Affected individuals are hypersensitive to sympathomimetic and parasympathomimetic drugs (due to upregulation of adrenergic and cholinergic receptors) but have decreased endogenous catecholamine levels at baseline.
- During physical and emotional stress, plasma epinephrine, NE, and DA are relatively elevated and precipitate dysautonomic crises: intractable emesis, diaphoresis, tachycardia, Htn, and personality changes.
- Additionally there is a decreased response to temperature and somatic pain (palms, soles of feet, neck, and genital areas are spared). Visceral pain perception is normal or heightened.
- Pts also experience orthostatic and paroxysmal Htn (due to failure of the afferent baroreflex), arrhythmias/CHB, prolonged QT interval, erythematous skin rash, central sleep apnea/disordered sleeping, altered response to hypoxia and hypercarbia (due to malfunctioning chemoreceptors), dry-eye optic neuropathy with retinal injury, decreased blink rate, ocular anesthesia and corneal damage, oropharyngeal incoordination, GI dysfunction and bleeding, progressive glomerulosclerosis, hypotonia (in infants) and gait ataxia (in adults), and spinal deformities.
- Fixed Htn can develop chronically, secondary to advancing renal failure.
- Hyponatremic seizures may occur with hypertensive vomiting, excessive sweating, and poor fluid/salt intake. 10% of pts have a seizure disorder.

Etiology

- Autosomal recessive disease with complete penetrance, but variable expression.
- Relatively low carrier frequency (1:3000) in non-Jewish individuals; significantly higher carrier frequency (~1:30) among people of Ashkenazi/Eastern European Jewish ancestry.
- Single noncoding mutation (base pair 6 change from T to C on chromosome 9q31) in the *IKBKAP* gene leads to expression of truncated IKAP (IκB kinase–associated protein), responsible for >99% of all cases of FD.
- IKAP is believed to regulate gene transcription and expression during neuronal development and myelination in embryogenesis.

Usual Treatment

- Treatment is supportive and preventative.
- Careful hydration (pts tend to become dehydrated easily because of excessive sweating and drooling, fever associated with aspiration pneumonia, and vomiting).
- Gastrostomy and fundoplication allow improved nutrition and reduction of pneumonia.
- Pulmonary hygiene by bronchodilation, postural drainage, suction of tracheal secretions.
- Noninvasive positive-pressure ventilation during sleep because of tendency to hypoventilate. Make sure that mask fits properly to avoid corneal damage.
- Dysautonomic crisis is treated with centrally acting agents such as BZDs and clonidine; these must be used cautiously as they can precipitate hypotension and respiratory depression.
- Hypertensive vomiting can also be treated with carbidopa.
- Hyponatremic seizures are treated with slow correction of serum sodium.
- Blood pressure: Htn is treated with fluids, fludrocortisone (may exacerbate Htn and renal disease) and midodrine; Htn is treated with BZDs, α_2 agonists, CCBs, and positional changes, such as sleeping with head of the bed raised 20–40 degrees.
- Asymptomatic Htn is not treated because it is usually transient.
- Treatment with artificial tears, tarsorrhaphy, corneal surgery.
- Anemia of chronic disease is treated with erythropoietin.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Decreased somatic pain and temperature perception	Hx of injuries or self-injurious behavior	Assess extremities/back for injury/skin breakdown Assess for self-injurious behavior	
	Hypotonia (infants) Broad-based, ataxic gait (adults)	Delayed motor developmental milestones	Positive Romberg test, decreased vibrational sense and joint position	
	Catecholamine surge	Personality changes during dysautonomic crises, psychiatric disorders may also be present		
	Seizure disorder (10% of pts)			EEG
	Central sleep apnea	NIPPV	Baseline oxygen saturation	Polysomnography
HEENT	Altered sweet sensation		Absence of fungiform papillae on tongue	
	Reduced tear volume, corneal anesthesia, reduced blink rate, incomplete lid closure during sleep	Eye dryness, use of artificial tears, absence of overflow tears with emotional crying	Ocular injury/ulcers, infection, optic neuropathy, retinal detachment	
CV	BP lability (supine Htn, orthostatic hypotension, dysautonomic crises) due to dysfunction of baroreceptors and hypersensitivity to catecholamines	BP variation throughout the day, frequency of dysautonomic crises Nocturia may indicate Htn episodes during sleep	BP supine/standing	Ambulatory BP monitoring
	Dysrhythmias (bradycardia/CHB) Prolonged QT Conduction abnormalities	Syncope, DOE, poor exercise tolerance		ECG Holter monitoring, PPM placement/interrogation, BMP
	LVH/CHF	DOE, poor exercise tolerance	JVD, edema, rales, cardiomegaly, murmurs	CXR, TTE/TEE
GI	Incoordinated swallowing Excessive salivation GI dysmotility GI bleeding Emesis	Feeding and drinking difficulty, daily vomiting, recurrent aspiration, severe dysphagia and GERD	FTT, drooling Assess intravascular fluid status (decreased skin turgor/dry mucous membranes)	BMP Proper hydration
RESP	Chronic aspiration leading to recurrent infections, atelectasis, bronchiectasis Restrictive lung disease due to kyphosis/scoliosis	Difficulty breathing, DOE Last pneumonia episode SOB, increased work of breathing	Auscultation Assess for signs and symptoms of current infection (febrile response may be severely altered)	CXR PFTs
	Dysfunction of chemoreceptors	Hypoxia can induce hypotension and bradycardia leading to syncope	Baseline SpO_2/PaO_2/$PaCO_2$	ABG
RENAL	Glomerulosclerosis Anemia of chronic disease	UO, AKI on CKD, ESRD		BMP CBC
ENDO	Hyponatremia	History of emesis, poor fluid intake, excessive diaphoresis in hot weather, fevers		BMP
MS	Decreased DTRs			
	Spinal deformities (kyphosis/scoliosis)			

Perioperative Implications

Preoperative Preparation

- Stabilize vascular bed by hydration (NS/LR) prior to induction of anesthesia.
- Obtain ABG to correct, if able, pH and electrolyte (Na^+, K^+) abnormalities.
- Anxiolysis (pharmacologic or presence of parent in OR for children) to prevent dysautonomic crisis.
- Vent gastrostomy.

Monitoring

- Consider arterial BP for intraop and postop management. FD pts have lower resting PaO_2/SpO_2 and higher $PaCO_2$. Most pts have compromised pulm function and Hx of sleep apnea. Their BP is variable and extreme hypotension tends to occur with induction of anesthesia, especially if pt was not prehydrated.
- Consider central access with CVP monitoring in surgical procedures with significant hemodynamic shifts, as FD pts are more susceptible to extreme BP swings associated with intravascular volume.
- Consider TEE/CO monitoring for assessment of cardiac function and as guidance for rational fluid management.
- Consider placing defibrillation/external pacing pads.
- Maintain normothermia as temperature regulation is affected at baseline.

Airway

- Sialorrhea: consider glycopyrrolate/atropine prior to induction (carefully titrate, as pts are sensitive to cholinergic and adrenergic agents).

Induction

- Ensure eye lubrication and protection, as corneal epithelium is extremely prone to injury.
- Propofol has been used with preop hydration. Consider ketamine ± propofol when unable to prehydrate. Ketamine may exacerbate oral secretions.
- Both depolarizing and nondepolarizing neuromuscular blockers have been used successfully.
- Consider rapid sequence induction with cricoid pressure even in pts with Nissen fundoplication (studies have shown that 15% of pts had malfunctioning fundoplication after 5 y).

Maintenance

- Maintain normocapnia to decrease BP lability.
- Inhalational agents can be used, but consider adding opioid/dexmedetomidine infusion or TIVA to smooth out BP variation and minimize PONV.
- Consider EEG-based depth-of-anesthesia monitoring to help minimize exposure to anesthetics.

Extubation

- Titrate analgesics carefully. Consider alternatives to opioids (NSAIDs, IV acetaminophen, dexmedetomidine infusion).
- If able, use nonanticholinergic reversal of NMB, as pt are hypersensitive to cholinergic/adrenergic agents.
- Return of spontaneous breathing may be delayed due to chemoreceptor dysfunction ($PaCO_2$ is not a trigger for the brain stem to initiate spontaneous breathing).
- Due to a blunted ventilatory response to hypoxia, pts may experience hypercapnic-induced Htn. Apnea is associated with severe desaturation and hypotension.
- Gentle suction (as to not precipitate dysautonomic crisis) is important as pts are at increased risk for aspiration pneumonia.
- Prior to extubation, it is important to ensure that airway reflexes have returned, but conservative extubation criteria could create anxiety and precipitate dysautonomic crisis. Consider coating ETT with lidocaine jelly prior to intubation.

Adjuvants

- Consider regional anesthesia either alone or with GA for intraop and postop pain control.
- Successful use of epidural anesthesia has been reported (and is the preferred analgesic for labor and cesarean delivery). Spinal anesthesia should probably be avoided as it would likely precipitate severe and refractory hypotension due to sympathectomy.
- MAC sedation has also been safely administered in ambulatory settings with midazolam and propofol.

Postoperative Period

- Care must be taken in providing supplemental oxygen, as it may accentuate eye dryness and increase the risk of epithelial breakdown.
- Although somatic pain sensation is diminished, visceral pain sensation is intact. Pain must be well controlled so as to avoid precipitating dysautonomic crisis.
- Respiratory status should be carefully monitored in PACU/ICU, especially if respiratory depressants are administered (e.g., opioids for pain control, BZDs for dysautonomic crises).
- NIPPV may ameliorate respiratory depression and prevent respiratory failure and reintubation. However, properly fitted masks must be used to avoid eye injury.
- Pulm hygiene should be instituted, as most pt have chronic lung disease secondary to repeated aspirations.
- Manage dysautonomic crises with diazepam (first-line drug) or clonidine (second-line drug); may also use hydralazine and labetalol if Htn is refractory to initial treatments.
- Elevate head of bed to 30 degrees and encourage early sitting to avoid supine Htn.
- Treat hypotension with fluids/blood products and fludrocortisone.

Anticipated Problems/Concerns

- Dysfunction of chemoreceptors leads to altered response to hypoxia and hypercapnia. Low PaO_2 does not stimulate tachypnea and can cause syncope, as hypoxia induces both hypotension and bradycardia.
- Presence of spinal deformities may make neuraxial anesthesia more technically challenging.
- PONV precautions should be employed.
- Increased sensitivity to exogenous adrenergic and cholinergic agents; minimal doses may produce exaggerated responses.
- Avoid drugs that prolong QT interval.
- Pts may be on chronic BZDs and may have developed tolerance and dependence.

Rocky Mountain Spotted Fever

Sinisa Markovic | Paul R. Knight III

Risk

- Incidence in USA: In most states, most commonly in the southeastern and south central states, there are ~250-2200 cases per y.
- Exposure to tick-infested terrain or dogs.
- Severe infection; very young (<4 y), males and those with G6PD deficiency are at risk for death.
- Mortality is 23% when untreated, 0.3–4.0% even with early treatment (within first 5 d).
- Mortality increases with delay in Dx, older age (>60 y), male sex, very young age (<4 y), in blacks, chronic alcohol abuse, and those with G6PD deficiency.

Perioperative Risks

- Increased mortality secondary to CV instability and noncardiogenic pulm edema
- Increased risk of organ injury due to compounded insults
- Increased bleeding tendency

Worry About

- Severe intravascular volume depletion leading to shock
- Lyte disturbances
- Cardiac arrhythmias
- Microvascular hemorrhage
- Consumptive coagulopathy
- Intraop respiratory and renal failure

Overview

- Uncommon but severe; pathophysiology primarily due to endothelial cell prostaglandins, resulting in increased vascular permeability, edema, hypovolemia, and ischemia.
- Initial symptoms appear in 1–3 d: Nonspecific, mimicking a viral syndrome with fever, headache, malaise, myalgias, arthralgias, and nausea; specific symptoms appear in 2–14 d, most in 5–7 d, mostly in the spring and summer months; pts generally have a known or possible tick bite.
- Rash appears in most pts in 3–5 d, after onset of fever, initially maculopapular and progressing to petechiae; usually starts on the ankles and wrists, then palms and soles; finally spreads to the body and face; rash absent in 10–12%
- Disease progression (more likely with delay in treatment) results in multiorgan involvement: Noncardiac pulm edema, encephalitis, myocarditis, hepatitis, bleeding (secondary to thrombocytopenia and direct vessel damage), and acute renal failure.

Etiology

- *Rickettsia rickettsii* is transmitted via the saliva of ticks after 6–10 h of attachment and feeding or by exposure to infected tick hemolymph during the removal of ticks.
- Incubation period ~7 d (2–14 d).
- Obligatory intracellular bacterium that replicates in vascular endothelial cells, causing direct cell injury with loss of vascular integrity.

Usual Treatment

- Dx is difficult, made primarily from clinical and epidemiologic (potential tick exposure) evidence and serologic testing or biopsy of skin lesion to confirm.
- Doxycycline, chloramphenicol (for pregnant women in the first two trimesters of pregnancy or severe adverse reaction to doxycycline); therapy within first 5 d is important (mortality 6.5 vs. 22.9).
- Correct hypovolemia, coagulation defects, thrombocytopenia; provide intensive, supportive care for various organ system failures.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Extensive microvascular leak, interstitial myocarditis	Rash, swelling	Rash, edema, arrhythmias	ECG, CXR, lytes, BP
RESP	Noncardiac pulm edema, interstitial pneumonitis	Reduced exercise tolerance, dyspnea, cough	Rales by auscultation	CXR, spirometry
GI	Gastroenteritis; liver, spleen, and pancreatic microvascular hemorrhage and edema	N/V, abdominal pain, diarrhea	Abdominal tenderness Hepatosplenomegaly	SGOT, bilirubin
HEME	Thrombocytopenia, anemia	Easy bleeding, malaise	Rash	Hct/Hgb, plts/PT, PTT, BUN
RENAL	Microvascular hemorrhage and edema, interstitial nephritis, prerenal azotemia	Lumbar pain		Cr, lytes
CNS	Meningoencephalitis	Focal defects, deafness, confusion, meningismus, photophobia, seizures		CSF: Checking WBCs and protein
MS	Microvascular hemorrhage, edema	Myalgia, arthralgia	Reduced ROM	

Key References: Walker DH, Blanton LS: *Rickettsia rickettsia* and other spotted fever group rickettsiae (Rocky Mountain spotted fever and other spotted fevers). In Bennett JE, Dolin R, Blaser MJ, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases,* ed 8, Philadelphia, PA, 2014, Elsevier, pp 188, 2198–2205.e4; Walker DH: Rocky Mountain spotted fever: a disease in need of microbiological concern, *Clin Microbiol Rev* 2(3):227–240, 1989.

Perioperative Implications

Preoperative Preparation

- Antibiotic therapy and correction of underlying organ system dysfunction
- Surgery only for emergency
- Assess volume, respiratory, and renal status

Monitoring

- Consider PA cath, arterial line, UO.
- Intraop ABGs and lytes.
- Platelets and other coagulation variables.

Airway

- Severe edema of oropharynx and increasing bleeding tendency can lead to difficult intubation.

Induction

- Hypovolemia can cause hypotension.
- Microvascular leak in lung can cause rapid desaturation.
- Increased cardiac arrhythmias.

Maintenance

- Owing to CV instability, volume status is key.
- Possibility of respiratory failure and constant volume resuscitation should be anticipated in selecting an anesthetic technique.

Extubation

- Oropharyngeal edema and increased bleeding tendency may make reintubation very difficult.

Adjuvants

- Vasoactive drugs used in acute resuscitation should be readily available.
- Lidocaine for treatment of cardiac arrhythmias.

Postoperative Period

- Intravascular volume shifts; coagulation defects, respiratory failure, CV instability, renal failure

Anticipated Problems/Concerns

- Owing to the possibility of multisystem failure, prolonged postop management in the ICU may be required.
- Because early treatment with antibiotics is curative and highly successful in preventing complications, a high index of suspicion (e.g., after tick exposure in endemic areas) is needed.

Rubella and Congenital Rubella Syndrome

Ramchandra Vinayak Shidhaye

Risk

- A rubella epidemic in USA in 1964–1965 resulted in 12.5 million cases of rubella infection and about 20,000 newborns with CRS.
- The number of reported cases of rubella in USA remains low, with a median of 11 cases annually in 2005–2011 because of vaccination.
- The overall burden of CRS is still high in developing countries. There were 66 cases reported in Bangladesh, 26 in Romania, 16 in Nepal, 10 in Zambia, 9 in Japan, and 4 in Sri Lanka in 2014.
- Incidence of cardiac defects in CRS with eye involvement could be as high as 95%. Most common cardiac anomaly in CRS is PDA.

Perioperative Risks

- CRS is a constellation of multisystem abnormalities
- Such pts may require cardiac surgery like congenital cardiac septal defect correction and/or other noncardiac surgery like cleft lip/cleft palate repair and a variety of eye procedures under anesthesia. Cataract extraction is an urgent vision saving procedure, so complete optimization (correction of cardiac defects, adequate weight gain) of neonate may not be possible.

Worry About

- Unexpected difficult intubation in various upper airway anomalies like subglottic stenosis, shortened trachea, and short glottis carinal length associated with many congenital syndromes.
- Hypothermia.
- Hypoglycemia: Exogenous sodium, water and glucose should be provided periop, as they have low GFR and are more prone for hypoglycemia.
- Balance of PVR and SVR.
- Drug metabolism may be deranged because of associated liver abnormalities and hypothyroidism.
- IE prophylaxis is essential, as the turbulent flow produced by the high velocity systolic jet in pulm artery stenosis increases the potential for development of endocarditis.

Overview

- Rubella is a viral illness characterized by a mild, maculopapular rash. The rubella rash occurs in 50–80% of rubella-infected persons and is sometimes misdiagnosed as measles or scarlet fever.
- Rubella is contagious disease which spreads in droplets. The respiratory secretion, cataractous lens is one of the most infectious materials hence warrants universal precaution.
- CRS is an illness resulting from rubella virus infection during pregnancy. When rubella infection occurs during early pregnancy, serious consequences—such as miscarriages, stillbirths, and a constellation of severe birth defects in infants—can result. The risk of congenital infection and defects is highest during the first 12 wk of gestation and decreases after the 12th week of gestation, with defects rare after the 20th wk of gestation.
- Common congenital defects of CRS include cataracts; congenital heart disease, including PDA, coarctation of aorta, VSD, ASD, and pulm artery stenosis; hearing impairment and developmental delay; brain damage (microcephaly, mental retardation, meningoencephalitis); hepatosplenomegaly; thrombocytopenia; and neonatal jaundice. Other manifestations are type I diabetes mellitus, growth retardation, transient hemolytic anemia, metaphyseal "celery stalking" changes in long bones, transient pneumonitis, transient generalized lymphadenopathy, cryptorchidism, inguinal hernia, and dermal erythropoiesis ("blueberry muffin syndrome"). Infants with CRS usually present with more than one sign or symptom consistent with congenital rubella infection. However, infants may present with a single defect. Hearing impairment is the most common single defect.

Etiology

- Rubella is a viral illness caused by a togavirus of the genus *Rubivirus*, which is most closely related to group A arboviruses, such as eastern and western equine encephalitis viruses.
- It is an enveloped RNA virus with a single antigenic type that does not cross-react with other members of the togavirus group.
- Rubella virus is relatively unstable and is inactivated by lipid solvents, trypsin, formalin, ultraviolet light, low pH, heat, and amantadine.

- Rubella is transmitted through direct or droplet contact from nasopharyngeal secretions and has an average incubation period of 17 d (range: 12–23 d). Persons with rubella are most infectious when rash is erupting, but they can shed the virus from 7 d before to 7 d after rash onset. CRS develops in an infant as a result of maternal infection in first trimester and subsequent fetal infection with rubella virus (German measles). Because infants can shed the virus for prolonged periods (up to 1 y of age or longer), infants with CRS should be considered infectious until they are at least 1 y old or until two cultures of clinical specimens obtained 1 mo apart after the infant is >3 mo of age are negative for rubella virus.

Usual Treatment

- Treatment is supportive. No specific antiviral agent for rubella is currently available.
- Corrective surgeries are typical for other congenital defects.

Assessment Points

System	Effects	Assessment by Hx	PE	Test
HEENT	Cleft lip/cleft palate Various upper airway anomalies like subglottic stenosis, shortened trachea, and short glottis carinal length	Difficult feeding and poor nutrition	Difficult intubation	Airway assessment
CV	Congenital heart disease, including PDA, coarctation of aorta, VSD, ASD, and pulm artery stenosis; severe PHT	Dyspnea Cyanosis	Tachypnea Rales, rhonchi, wheezing Cyanosis Delayed milestones	ECG CXR 2D ECHO with color Doppler
RESP	Transient pneumonitis	Cough Dyspnea	Poor ventilation, cyanosis Cough, rales, rhonchi, wheezing	CXR
CNS	Brain damage Microcephaly, meningoencephalitis Sensorineural hearing loss	Mental retardation Hearing impairment	Mental retardation Behavioral and language disturbances Hearing impairment	
GI	Associated liver abnormalities Cryptorchidism, inguinal hernia	Neonatal jaundice Hepatosplenomegaly	Deranged drug metabolism	US LFTs
ENDO	Hypothyroidism Type I diabetes mellitus	Growth retardation	Deranged drug metabolism Growth retardation	Thyroid function tests Blood sugar
EYE	Microphthalmia, pigmentary retinopathy, congenital cataract	Affected vision		Ophthalmoscopy
MS	Long bones infection		Metaphyseal "celery stalking" changes in long bones	X-ray long bones
DERM	Blueberry muffin syndrome	Dermal erythropoiesis	Widespread maculopapular lesions of reddish-blue or magenta color Transient hemolytic anemia, thrombocytopenic purpura, transient generalized lymphadenopathy	Skin biopsy Hematologic investigations

Key References: Hariharan U, Garg R, Nagpal VK, et al.: Combined cardiac and noncardiac surgery in an infant with congenital rubella syndrome: an anesthetic challenge, *Paediatr Anaesth* 21(11):1168–1169, 2011; Gaur P, Harde M, Gujjar P, et al.: Unique anaesthesia problems encountered in congenital rubella syndrome, *Int J Adv Case Rep* 2(11):686–688, 2015.

Perioperative Implications

- Children with CRS require thorough evaluation of associated systemic abnormalities and great vigilance in the periop period.
- Anesthetic goals for pulm artery stenosis include maintenance of a normal or slightly low heart rate, augmentation of preload, and avoidance of factors that increase PVR. For ASD and PDA, maintenance of heart rate with increase in the preload and PVR along with decrease SVR reduces the flow across the defect.
- Anesthetic goals in pts with PS, ASD, and PDA are contrary to each other, but when both these defects are present together, a careful balanced technique has to be maintained to ensure hemodynamic stability as well as to ensure tissue needs are adequately met.
- Anesthetic drugs should be cautiously used due to associated liver abnormalities and hypothyroidism.
- Analgesic management should include avoiding drugs having effect on platelets, as these pts are prone to thrombocytopenia.
- De-airing of IV lines is also an important consideration.
- Combined procedures require change of position intraop, and care should be taken during positioning because of the association of bone abnormalities.
- Concerns related to ductal ligation including effects on blood pressure need to be monitored during the surgical procedure. During the ductal ligation, injury to recurrent laryngeal nerve or accidental ligation of the vessels like pulmonary aorta may occur.

Preoperative Preparation

- Cardiac status should be optimized prior to noncardiac surgery, which may involve performing cardiac surgery.
- Children should be adequately premedicated to allay separation anxiety and crying which can lead to tachycardia and hypertension.
- IE prophylaxis can be taken care of with cefotaxime 50 mg/kg and amikacin 2 mg/kg in 1 dose prior to surgery.
- Defibrillator and emergency drugs are to be kept ready and arrangements to be made for emergency cardiac surgery in view of difficult resuscitation in these children.

Monitoring

- Routine monitoring.
- Invasive monitoring with pulm artery cath may be required. Central venous cath may not reflect exact left ventricular status due to presence of PS.
- Transesophageal echocardiography can be more useful than CVP monitoring for evaluation of ventricular filling and function.
- An intra-aortic balloon pump may be kept ready for protection against myocardial ischemia.

Airway

- CRS may cause difficulty in airway maintenance and unexpected difficult intubation.

Induction

- IV induction with titrated doses of thiopentone to avoid exposure to higher concentrations of halothane, which would depress the myocardium.
- High dose of narcotics should be avoided; may cause postop respiratory depression, which may alter the PVR.
- Adequate amount of thiopentone sodium and fentanyl helps achieve deeper planes of anesthesia to suppress all presser responses and smooth intubation.

Maintenance

- Nitrous oxide should be avoided due to its adverse effects on pulm circulation. Air and oxygen with sevoflurane may be used, maintaining the adequate depth of anesthesia to decrease PVR. Vecuronium can be used for muscle relaxation and respiratory support is to be given targeting $ETCO_2$ in range of 35–40 mm Hg with low tidal volume without PEEP.
- Inj milrinone, a potent pulm vasodilator without marked decrease in systemic vasodilatation, can be used as inotrope if required. IV fluids are to be carefully titrated to avoid cardiac overload.

Extubation

- Extubation is preferably done in deeper planes to avoid acute arterial and pulm Htn.

Postoperative Period

- Children should be pain free in postop room, with stable hemodynamic monitors.

Anticipated Problems/Concerns

- Proper understanding of the hemodynamic effects of the previously mentioned congenital heart diseases and vigilance regarding their anesthetic implications enables us to manage such pts successfully.

Saethre-Chotzen Syndrome

Ankur Sharma | Varuna Vyas

Risk

- Incidence: 1:25,000–50,000 live births.

Perioperative Risks

- Difficult airway.
- Seizures.
- Oculocardiac reflex.
- The severity of cardiac lesion may affect the hemodynamic stability of the pt during anesthesia.

Overview

- A type of acro-cephalo-syndactyly syndrome, characterized by premature fusion of the coronal sutures, facial dysmorphism, syndactyly, skeletal deformity, and congenital heart malformations.
- Named after two physicians who independently reported it in the early 1930s—Haakon Saethre, a Norwegian psychiatrist, and F. Chotzen, a German psychiatrist.
- It may lead to brachycephaly and plagiocephaly, late closure of fontanels, and raised ICP, eventually provoking seizures.
- Midfacial hypoplasia leads to small maxilla and relative mandibular prognathia, as well as high arched palate.
- These pts can have a beaked nose; deviated nasal septum; narrow palate; cleft palate; super numerary teeth; small, low-set, unusually shaped ears; and enamel hypoplasia.
- Facial appearance tends to improve with age throughout childhood.
- It may involve multiple organs. The predominating involved systems are the cardiac system, the skeletal system, as well as the sensory and motor systems.
- Less common signs and symptoms include congenital heart defects (ASD, VSD, pulm stenosis, PDA, TOF), renal anomalies, cryptorchidism, and anorectal malformations.

Worry About

- Ruling out increased ICP is important, either by using CT scan or fundus examination.
- High arched palates make placement of the tube difficult, because of limited lateral space availability.
- Facial features can lead to difficulty in bag and mask ventilation, intubation, and LMA insertion.
- Vertebral fusion is progressive and hence may present at a more advanced stage, leading to cervical instability.

Etiology

- Autosomal dominant inherited syndrome.
- Results from a mutation of the TWIST1 gene on chromosome 7, which plays a key role in the early development of the skull, face, and limbs.
- Early fusion of the coronal or lambdoidal suture.

Usual Treatment

- These pts can present with multiple surgical and medical complaints.
- Most of them will undergo surgery and anesthesia, at least once in their lifetime, for correction of craniofacial, orthopedic, ophthalmic, or cardiac lesions, apart from incidental surgical conditions.

Assessment Points

System	Assessment by Hx, PE	Anesthetic Concerns and Management	Test
HEENT	Progressive cervical spine fusion, cleft palate, high arch palate Midfacial hypoplasia, small maxilla, relative mandibular prognathia asymmetry, flat-looking face due to underdeveloped cheekbones, deviated nasal septum, narrow palate, cleft palate, super numerary teeth, and enamel hypoplasia Eye: Shallow orbits with orbital asymmetry, orbital hypertelorism, ptosis, strabismus, blepharophimosis, down-slanting palpebral fissures, sparse eyebrows medially, epicanthal folds, optic atrophy, and corneal opacity Ear: Small, low-set, unusually shaped ears, sensorineural hearing loss	Limited neck extension, difficult intubation, cervical spine instability Difficulty in bag and mask ventilation, difficulty in oral and nasal intubation Increased incidence of OCR and postop N/V during eye surgery. Difficulty in communication with child	X-ray, CT scan X-ray, CT scan
MS	Short stature, cutaneous syndactyly, small distal phalanges, clinodactyly of fifth finger, digitalization of thumb, limited elbow extension, contracture of elbow and knee Short clavicles	Difficulty in positioning on OT table, difficult IV access Placement of subclavian venous catheter more difficult	
NEURO	Brachycephaly, plagiocephaly, late closure of fontanelles, ossification defects, hyperostosis of skull	Increase in ICP, seizure disorders.	CT scan
CV	ASD, VSD, pulm stenosis, PDA, TOF	Anesthetic implications as per the cardiac lesion	ECHO, cardiac cath
OTHER	Renal anomalies, cryptorchidism, anorectal malformations	Deranged renal parameters, lyte imbalance	Cr, BUN

Key References: Niemann-Seyde SC, Eber SW, Zoll B: Saethre-Chotzen syndrome (ACS III) in four generations, *Clin Genet* 40(4):271–276, 1991; Netke M, Carver E: Saethre-Chotzen syndrome and anesthesia, *Paediatr Anaesth* 18(11):1128, 2008.

Perioperative Implications

Preoperative Preparation

- Genetic counseling.
- Detailed airway examination using indirect laryngoscopy is recommended prior to anesthesia, whenever possible, to prepare airway management and map any upper airway deformity.
- Cervical instability can be seen on standard neck x-ray.
- If child is taking anticonvulsants, continue on the day of surgery.
- Excessive sedative premedications should be avoided.

Monitoring

- Routine.
- Cutaneous syndactyly may cause difficult IV access.
- Precautions to prevent cervical spine movement during airway management at the time of induction and recovery from anesthesia.
- Meticulous positioning and padding of pressure points should be done during surgery.
- Short clavicles may make the placement of subclavian venous catheter more difficult if indicated.

Airway

- Plan for airway management (a supra-glottic device for short duration surgery and, if required, fiberoptic guided intubation of the trachea).

Induction (General Anesthesia)

- Inhalational induction

Maintenance

- Hypoventilation should be avoided because it may exacerbate preexisting elevated ICP.
- These pts may have shallow orbits with orbital asymmetry. It may predispose to exacerbated OCRs during extra-ocular muscles handling.
- Interaction between neuromuscular blockers and anticonvulsants.

Postoperative Period

- Postop seizures
- Postop N/V during eye surgery
- Difficulty in communication with child

Anticipated Problems/Concerns

- Difficult intubation and cervical instability
- Seizure on induction or emergence

Sarcoidosis

Andrew D. Rosenberg

Risk

- Risk varies; ≤1–80:100,000, with highest incidence in Sweden; in USA, occurs in 30/100,000.
- Presents in pts ages 20–40 y in USA.
- More common in African Americans than whites in USA.
- Females at greater risk than males.

Perioperative Risks

- Severity depends on degree of airway, lung, cardiac, and CNS involvement.

Worry About

- Airway granulomas distorting and obstructing anatomy risking obstruction with sedation and making intubation potentially difficult
- Degree of lung involvement and pulm fibrosis
- Cardiac involvement, heart block, arrhythmia, and CHF
- CNS involvement

Overview

- Multisystem granulomatous disorder with widespread noncaseating epithelioid cell granulomas.
- Lung most frequently affected organ.
- Airway abnormality secondary to granulomas.
- Local organ distortion can result in symptoms.
- In mononuclear inflammatory cells, T-helper cells + mononuclear phagocytes lead to the formation of granulomas.

Etiology

- Unknown disease due to exaggerated cellular immune response involving mononuclear phagocytes and T lymphocytes

Usual Treatment

- Steroids: Oral prednisone (inhaled steroids not shown to be consistently effective)
- NSAIDs: Salicylates
- Chloroquine or hydroxychloroquine for mucocutaneous sarcoidosis
- If steroids ineffective, methotrexate or immunosuppressive agents

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Involvement of nares, polyps with distorted anatomy; larynx granulomas, epiglottis, arytenoid involvement	Dyspnea Breathing difficulty	Nasal stuffiness, wheezing, hoarseness, stridor Can see vocal cord palsy or paralysis	Laryngoscopy
CV	Heart block or arrhythmia Cor pulmonale secondary to RV enlargement	Palpitations	Arrhythmia Rales	ECG
RESP	Pulm granulomas, airway obstruction Bilateral hilar lymphadenopathy (eggshell calcifications of hilar nodes); pulm fibrosis; interstitial disease	Dyspnea Wheezing, cough	Dry rales Wheezes	CXR PFTs (decreased vital and diffusing capacities) ABG CT if airway obstruction considered an issue
GI	Liver involvement			Increased LFTs, increased alkaline phosphatase
ENDO	DI	Thirst		
RENAL	Increased Ca^{2+} resorption leading to nephrocalcinosis and other renal issues			BUN/Cr
CNS	Nerve involvement DI	Space-occupying lesions Seizures Psychiatric examination	Focal nerve deficits	

Key References: Sanders D, Rowland R, Howell T: Sarcoidosis and anaesthesia, *BJA Education* 16(5):173–177, 2015; Iannuzzi MC, Rybicki BA, Teirstein AS: Sarcoidosis, *N Engl J Med* 357(21):2153–2165, 2007.

Perioperative Implications

Preoperative Preparation

- Adequate steroid coverage.
- For pulm and airway, determine if airway obstruction exists and degree of pulm involvement. Evaluate for Hx of SOB and dyspnea. Obtain CXR and consider PFTs and preop ABG based on symptoms and Hx. If airway obstruction is suspected, obtain CT to better define issues.

Airway

- Distortion or obstruction secondary to granulomas
- Hypoxia secondary to lung disease

Monitoring

- Observe for heart block.
- Arrhythmia.

Anticipated Problems/Concerns

- Airway problems secondary to distorted anatomy
- Pulm problems secondary to lung involvement

Sarcoma

Onur Demirci

Risk

- Malignant bone tumors. Incidence is 1:100,000; 3000 new cases/y in USA, with bimodal age distribution (first peak during adolescence, second peak in older adulthood).
- Soft tissue sarcomas: Incidence is 1:100,000 for ages <20 y and 7:100,000 for ages ≥20 y; 12,000 new cases/y in USA; mean age at diagnosis is 58 y.
- Prevalence equal in both genders and all races except Ewing sarcoma (high Caucasian predominance).
- Overall: 15% of cancers in children age <20 y.

Perioperative Risks

- Morbidity and mortality related to surgical procedure.
- Metastatic vital organ involvement, especially lungs and liver.
- Mass effect, direct compression of organs and vascular structures.

Worry About

- Adriamycin-induced cardiotoxicity (global LV hypokinesis)
- Mitomycin-induced acute pulm toxicity, pulm fibrosis, ARDS with increased FiO_2
- Immunosuppression, hemorrhagic cystitis, renal failure induced by chemotherapeutic agents

Overview

- Heterogeneous group of malignant tumors of connective tissue derived from the embryonic mesoderm.
- Two most common sarcoma forms: Malignant bone tumors and soft tissue sarcomas.
- Malignant bone tumors such as osteosarcomas and Ewing sarcomas can be found throughout bones and cartilage.
- Soft tissue sarcomas often arise from muscles, joints, fat, nerves, deep skin tissues, and blood vessels.
- Can spread aggressively by local invasion and early hematogenous spread, especially to lungs.

Etiology

- Genetic factors, high-dose radiation, carcinogens (dibenzanthracene, methylcholanthrene), and some viral infections (Moloney sarcoma virus, human herpes virus 8) may predispose pts to sarcoma.
- von Recklinghausen's disease: 10–12% develop neurofibrosarcomas.
- Li-Fraumeni syndrome: Strong association with sarcomas.
- Retinoblastoma survivors have much higher incidence of osteosarcomas.
- Paget's disease: 0.9% develop osteosarcoma.
- Kaposi sarcoma strongly associated with human herpes virus 8 in immunocompromised pts.

Usual Treatment

- Neoadjuvant chemotherapy with antineoplastic agents
- Wide surgical resection
- Radiation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Atrial myxoma (ball-valve effect)	Sx of CHF, pulm edema	Rales S_3	CXR ECHO CT angio
	Vena cava obstruction	RV failure, CV collapse	Possible caput medusae, venous engorgement, edema	
	SVC syndrome	Head swelling, airway edema, increased ICP	Venous congestion of head and neck	CT angio
RESP	Pulm embolus	Dyspnea		PE protocol CT
GI	Gastroparesis Bowel obstruction Hepatic metastases Sarcoma of ampulla of Vater	Early satiety Vomiting Obstructive jaundice Hepatic dysfunction	Abdominal distention Jaundice	X-ray of abdomen EGD, bilirubin levels
HEME	Hypercoagulable Pancytopenia due to chemotherapy Anemia due to GI hemorrhage	Opportunistic infections Bruising, bleeding	Gross rectal bleeding	PT/PTT Leukocyte and plt counts CBC Stool guaiac
RENAL	Compression of ureters by retroperitoneal tumor	Sx renal failure		BUN/Cr Renal US or CT
CNS	CN compression	Various symptoms Dysphagia Loss of sensation, motor function	Neurologic exam	EMG Head CT
MS	Bone sarcomas Limb loss	Hypercalcemia	Chvostek's sign	Blood Ca^{2+}

Key References: Burningham Z, Hashibe M, Spector L, et al.: The epidemiology of sarcoma, *Clin Sarcoma Res* 2(1):14, 2012; Makela J, Kiviniemi H, Laitinen S: Prognostic factors predicting survival in the treatment of retroperitoneal sarcoma, *Eur J Surg Oncol* 26(6):552–555, 2000.

Perioperative Implications

Preoperative Preparation
- Use aspiration precautions for pts with gastroparesis, including prokinetics and NG decompression.
- Assess end-organ impairment (especially heart and lungs) secondary to chemotherapeutic agents.

Monitoring
- Use arterial line and CVP or PA cath for resection of large tumors.

Airway
- Risk of aspiration with large abdominal mass or brainstem compression.
- Possibility of difficult airway with SVC syndrome.

Induction
- Hemodynamic instability with cardiac involvement or caval compression.

Maintenance
- Potential blood loss

Extubation
- Awake if at risk for aspiration due to GI or CNS involvement.

Adjuvants
- Altered pharmacokinetics with hepatic or renal involvement.

Postoperative Period
- Pulm embolism, coagulopathy

Anticipated Problems/Concerns
- Adverse effects of chemotherapeutic agents
- Respiratory compromise due to pulm metastases
- Mass effect and/or organ compression and functional impairment
- Effects of prolonged anesthesia
- In prolonged abdominal cases, hypothermia, complications of massive transfusion

Scheie Syndrome (Mucopolysaccharidosis Type IS)

Arun K. Gupta

Risk
- Incidence: 1:500,000
- Inherited as autosomal recessive

Perioperative Risks
- Difficult intubation
- Positioning difficulty
- Cardiac problems

Worry About
- Macroglossia leading to difficult intubation
- Valvular heart disease, cardiomyopathy
- Stiff joints
- Spastic paresis
- Poor IV access

Overview
- Described by American ophthalmologist Harold Glendon Scheie in 1962.
- Mildest form of mucopolysaccharidosis type (1) and a rare lysosomal storage disease.
- Pts are of normal height and do not show intellectual deficiency.
- Corneal clouding and glaucoma.
- Coarse facial features.
- Normal life expectancy, stiff joints, and aortic regurgitation.

Etiology
- Caused by mutations in genes that control production of enzyme alpha-L-iduronidase (IDUA).
- The gene known as IDUA causes deficiency of enzymes and results in buildup of undigested mucopolysaccharidesin the cells.
- Diagnosis occurs by elevated GAG in urine and demonstration of IDUA deficiency in leukocytes.

Usual Treatment
- Enzyme replacement
- Hematopoietic stem cell transplant
- Bone marrow transplant and cord blood transplant

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult airway anticipation Coarse facial features Small chin, corneal clouding	Pain	Neck ROM	Neck x-ray Neck US
CV	Aortic regurgitation Cardiomyopathy Difficult IV access	Poor exercise tolerance Angina Hx		ECG, CXR, ECHO
RESP	Restrictive lung disease Obstructive sleep apnea			PFT, sleep studies
GI	Hepatosplenomegaly Umbilical hernia, inguinal hernia			
CNS	Many have normal intelligence Cervical cord compression Hydrocephalus leads to increased ICP, deafness			CT/MRI
MS	Stiff joints Carpal tunnel syndrome Spondylolisthesis	Joint mobility	Decreased ROM of joints	

Key References: Clarke LA, Heppner J: Mucopolysaccharidosis Type I. October 31, 2002 [Updated July 21, 2011]. In Pagon RA, Adam MP, Ardinger HH, et al. editors: *GeneReviews®*, Seattle, WA, 1993–2015, University of Washington. <http://www.ncbi.nlm.nih.gov/books/NBK1162/> (Accessed 06.06.16); Nakayama H, Arita H, Hanaoka K: Anesthesia in a patient with Scheie syndrome, *Masui* 43(9):1385–1388, 1994.

Perioperative Implications

Preoperative Preparation
- Anticipate upper airway obstruction.
- Excessive secretions (need for antisialagogue).
- Antibiotic prophylaxis for valvular heart disease.

Monitoring
- Routine

Airway
- Abnormal airway and short chin predispose to difficult airway.
- Large tongue and secretions leads to airway problems.
- Small size of ETT needed.
- Fiberoptic bronchoscopy.
- Use LMA and other supraglottic devices.

Induction
- IV access before induction
- Proper positioning with padding
- Spontaneous breathing

Maintenance
- Avoid myocardial ischemia.

Extubation
- Pt should be fully conscious, with intact airway reflexes.

Adjuvants
- Local anesthetics infiltration and regional anesthesia where needed

Postoperative Period
- Delayed emergence
- Pneumonia, bronchospasm, and laryngospasm apnea

Anticipated Problems/Concerns
- Management of difficult airway
- Cardiopulmonary problems common

Schizophrenia

Alan David Kaye | Christopher J. Cullom

Risk
- Most common psychotic disorder with a lifetime worldwide prevalence of 1%
- Increased risk of suicide (5–10%)

Perioperative Risks
- Marked by deterioration of function and self-care
- Exacerbation of psychosis with abrupt discontinuation of medications

Worry About
- Pt being uncooperative, combative, or catatonic.
- Increased morbidity and mortality due to poorly controlled coexisting systemic disease and increased incidence of alcohol and substance abuse.
- Drug interactions and side effects:
  - Cardiogenic side effects include hypotension, tachycardia, prolonged QT interval, VFIB, and torsades-de-pointes.
  - EPS include muscle rigidity and laryngospasm.
  - Use of metoclopramide may worsen schizophrenic symptoms.

Overview
- Schizophrenia is a psychiatric disorder that may be characterized by thought disorders, hallucinations, and fixed false beliefs.
- Antipsychotic medications are the mainstay treatment for schizophrenia.
- Antipsychotics have anticholinergic effects (dry mouth, blurry vision, urinary retention, constipation, tachycardia), histamine antagonism (sedation), and α1 antagonism (orthostatic hypotension).
- First-generation antipsychotics have strong dopamine antagonism leading to EPS, such as tardive dyskinesia.
- Second-generation or atypical antipsychotics have serotonin antagonism and less dopamine antagonism leading to less EPS.
- EPS can be treated with anticholinergics such as benztropine 2 mg or diphenhydramine 50–100 mg.
- NMS is a rare but potentially fatal syndrome occurring after an increase in dosage of antipsychotic medications or abrupt D/C of dopamine agonist. The syndrome is marked by muscle rigidity, hyperthermia, altered consciousness, and autonomic instability. It is clinically similar to malignant hyperthermia and may be related to dopamine blockade.
- Autonomic instability presents as labile blood pressure, tachycardia, diaphoresis, incontinence, and flushing.
- Treatment of NMS includes hydration and cooling measures, IV dantrolene, and dopamine agonists such as bromocriptine.
  - Bromocriptine reduces mortality by 50% and is only available orally; thus NGT may be required.
  - Dantrolene is a skeletal muscle relaxant and will reduce heat production.
  - Benzodiazepines may also be used to alleviate catatonic symptoms.
- Avoid dopamine antagonists, such as metoclopramide, if NMS is suspected.

Etiology
- Functional hyperactivity of dopamine transmission may play a role.
- Genetic and environmental factors are unclear and controversial.

Usual Treatment
- Antipsychotic medications
- Psychotherapy
- ECT

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	QT, PR prolongation Torsades de pointe MI Postural hypotension Tachycardia	Dizziness Palpitations	Orthostatic hypotension Arrhythmia	ECG
RESP	Significant increased incidence of smoking		SOB, wheezing	
GI	Paralytic ileus (postop) Liver dysfunction due to meds			Abdominal x-ray LFTs
HEME	Agranulocytosis due to meds			CBC
ENDO	DM due to meds Hyperlipidemia due to meds			Blood glucose Lipid profile test
NEURO	Sedation EPS 1. Tardive dyskinesia 2. Akathisia 3. Dystonia 4. Parkinsonism		Somnolence 1. Choreoathetoid movements of head, limbs, trunk 2. Subjective discomfort causing agitation and restlessness 3. Slow sustained bodily contractions 4. Catatonia, rigidity, akinesia	
GENERAL	NMS	Antipsychotic use (usually increase in dose) or abrupt discontinuation	Hyperthermia, rigidity, autonomic instability, cardiac arrhythmia	WBC, body temperature monitoring, CK, UA (myoglobinuria)

Key References: Kudoh A: Perioperative management for chronic schizophrenic patients, *Anesth Analg* 101(6):1867–1872, 2005; Sukhminder B: Psychiatric diseases: need for an increased awareness among anesthesiologists, *J Anesthesiol Clin Pharmacol* 27(4):440–446, 2011.

Perioperative Implications

Preoperative Preparation
- Hx may be unreliable or unattainable.
- Continue antipsychotic medications preop.

Monitoring
- Routine

Airway
- Routine considerations

Preinduction/Induction
- No specific technique clearly superior

Maintenance
- Hypotension.
- Tachycardia, arrhythmia.
- Increased risk of thermodysregulation and hypothermia. Monitor temp and warm/cool pt appropriately.

Extubation
- Usual criteria

Postoperative Period
- Decreased reports of pain
- Increased incidence of severe postop ileus
- Increased risk of postop confusion
- Increased postop mortality

Regional Anesthesia
- While controversial, epidural analgesia may decrease incidence of postop ileus.

Anticipated Problems/Concerns
- Cardiac arrhythmia
- Hemodynamic instability and hypotension
- Hypothermia
- Potential for neurolytic malignant syndrome
- Disruption of the hypothalamic pituitary adrenal axis
- Medication side effects, including cardiac and extrapyramidal

Scimitar Syndrome

Piedad Cecilia Echeverry Marín

Risk
- Occurs in 1 to 3–5:100.000 live births. The incidence could be higher because of asymptomatic cases in adult population.

Perioperative Risks
- Significant risk of pulm Htn, respiratory failure, and cardiac failure in the periop period.

Worry About
- Intraop pulm Htn crisis, severe bleeding with hypovolemia, worsening left to right shunt, and in critical cases, reverse shunt right to left with acute cardiac failure and cardiac arrest.

Overview
- Disease characterized by cardiopulmonary anomalies as partial or total anomalous pulmonary venous return connection of the right lung to the inferior caval vein, leading a left to right shunt.
- Associated with other anomalies such as hypoplastic right lung, anomalous systemic arterial supply to the right lung with or without pulmonary sequestration, pulm Htn, dextroposition of the heart, heart failure, and atrial septal defect (with ostium secundum being the most frequent).

Etiology
- Etiology is unknown, but in some pts, the anomalous pulmonary venous return has been coded genetically in the chromosome 4q12.

Usual Treatment
- Depends on hemodynamic state and symptoms of the disease. The adult presentation usually is asymptomatic, and the diagnosis is made by incidental findings.
- In children, clinical presentations are diverse. Symptoms in neonatal pts are severe and are associated with significant mortality due to severe respiratory insufficiency, cardiac failure, and pulm infections.
- When the L-to-R shunt and pulm Htn are significant, surgical correction is necessary to repair the anomalous venous return, ligation of collateral arteries, or lung segmentectomy.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Cardiac failure signs Anomalous pulmonary venous return, dextroposition of the heart	Poor breast feeding tolerance, poor physical activity tolerance, delay in growth and neurodevelopment	Jugular ingurgitation, hepatomegaly, low weight, heart murmurs at right side	ECHO, ECG Cardiac MRI
RESP	Hypoplastic right lung, recurrent infections, respiratory failure, pulm sequestration	Poor exercise tolerance, abnormal breathing, irritability, feeding inability, fever	Signs of respiratory distress, nasal flaring, decreased breath sounds at right side, hoarseness or wheezing if there is associated lung infection	CXR, ABG
IMMUNE	Chronic hypoperfusion Increased risk of infections	Recurrent respiratory symptoms, low weight	Fever, tachycardia, abnormal bronchial secretions	CBC
HEME	Chronic anemia Coagulation system is usually normal preop	Pallor, weakness, poor exercise tolerance	Tachycardia, pale skin, irritability	Hgb, Hct, blood type, and reserve blood components
GI	Prolonged fasting	Poor breast feeding tolerance, dehydration signs, low urine output	Lyte imbalance	Lytes
CNS	Neurodevelopmental delay	Psychomotor retardation, poor language development	Delay for crawling and walking	None

Key References: Orphanet. Scimitar syndrome. <http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=185>, 2009 (Accessed 06.06.16); Rajaii-Khorasani A, Kahrom M, Mottaghi H, et al.: Scimitar syndrome: report of a case and its surgical management, *Ann Saudi Med* 29(1):50–52, 2009; Luna AM, Gonzalez G, Echeverry PC: Scimitar syndrome and anesthetic implications, *Rev Col Anest* 43(3):245-249, 2015.

Perioperative Implications

Preoperative Preparation

- Anxiolytics like midazolam could help reduce anxiety but are contraindicated if pt is hemodynamically unstable or there are symptoms of cardiac failure.
- Avoid hypoxemia, pain, anxiety, dehydration, hypovolemia, severe anemia, and hypoxia. (FiO_2 higher than 35% because it raises L-to-R shunt.)

Monitoring

- Basic monitoring of ECG, noninvasive blood pressure, end tidal carbon dioxide, and temperature
- Pulse oximetry preductal and postductal (in neonates) and airway pressure
- Major surgery requires arterial line, venous central cath (to measure CVP and to instill inotropic drugs), urine output, and arterial blood samples.

Airway

- Tracheal intubation is essential.
- In cases of pneumonectomy, selective intubation and one lung ventilation could be useful but is not mandatory.

Induction

- Avoid hypotension during induction. Induction with inhalant agents takes longer than normal because of L-to-R shunt.

Maintenance

- Maintain cardiovascular stability, replace blood loss, correct lyte imbalance, and avoid acidosis, hypothermia, hypercarbia, hypovolemia, and severe anemia (Hb <7).
- Ventilation controlled by pressure is the best option with gentle airway pressure: low volumes (<8 mL/kg) and plateau pressure <30 cm H_2O.

Extubation

- Awake extubation if cardiovascular conditions, ventilation, and oxygenation are normal.

Adjuvants and Postoperative Period

- CXR to check central venous line position and to evaluate postop lung images.
- Although regional anesthesia is not contraindicated, be careful with epidural/caudal cath if pt will need postop anticoagulation.
- Pediatric intensive care should be available; ensure excellent pain management.

Anticipated Problems/Concerns

- Prolonged fasting is associated with hypovolemia and cardiovascular instability. Check fasting time and correct lyte imbalance.
- Respiratory signs of ventilatory failure require tracheal intubation and stabilization before surgery and suspect pulmonary infection that requires antibiotic use.

Scleroderma

Lee A. Fleisher

Risk

- Incidence: 9:1,000,000 per y.
- Prevalence: 300,000 Americans have scleroderma.
- Male:female ratio is 1:4; highest in young African-American women.
- More severe in Native Americans and African Americans.
- 10-y survival is 55–60%; presence of pulm Htn is a major prognostic predictor.

Perioperative Risks

- Severe hypotension secondary to hypovolemia
- Hypoxia secondary to pulm Htn and restrictive disease
- Failed intubation

Worry About

- GI reflux
- Obliterative vasculopathy leading to pulm Htn
- Restrictive lung disease
- Renal crises
- Intraop hypothermia-induced vasospasm

Overview

- Scleroderma, or systemic sclerosis, is a chronic connective tissue disease generally classified as one of the autoimmune rheumatic diseases.
- Targets skin, lungs, heart, GI system, kidneys, and MS system.
- Onset generally occurs between 25–55 y.
- Three features: Tissue fibrosis, vasculopathy of small blood vessels, autoimmune response.
- Two major classifications: Limited and diffuse cutaneous scleroderma.
- May have overlap syndromes with other rheumatic diseases.

Etiology

- Autoimmunity, genetics, hormones, and environmental factors may all play a role.
- Autoantibodies: Antitopoisomerase in diffuse forms, anticentromere in limited form.
- Twin studies suggest a limited genetic role.

Usual Treatment

- Treatment begins during early inflammatory stage, and strategies are target-organ specific, including antifibrinolytic agents, antiinflammatory drugs, immunosuppressive therapy, and vascular drugs.
- Treatment of symptoms including pain and reflux.
- Skin thickening can be treated with numerous experimental drugs or interventions (including D-penicillamine, interferon-gamma, mycophenolate mofetil, cyclophosphamide, photopheresis, allogeneic bone marrow transplantation).
- Surgical treatments include amputation and lung transplantation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Cutaneous fibrosis		Masked facies Small oral aperture Atrophy of gums Hyperpigmentation	
CV	Pericardial disease Myocardial fibrosis Conduction abn	DOE CHF Arrhythmia Syncope	Rales	ECHO ECG, Holter
RESP	Fibrosing alveolitis Obliterative vasculopathy Pulm Htn	Dyspnea Nonproductive cough		CXR PFT Bronchoalveolar lavage ECHO
GI	Esophageal fibrosis/colonic dysmotility	Difficulty chewing Dysphagia Bloating Diarrhea	Weight loss	UGI/endoscopy
RENAL	Intrinsic renal vessel disease		Malignant Htn	Proteinuria Hematuria BUN or Cr
DERM	Cutaneous fibrosis		Fibrosis of limbs Sweating Atrophy and contractures Telangiectasis	
MS	Raynaud disease	Excessive cold sensitivity Pain	Cyanosis of digits	

Key References: Roberts JG, Sabar R, Gianoli JA, Kaye AD: Progressive systemic sclerosis: clinical manifestations and anesthetic considerations, *J Clin Anesth* 14(6):474–477, 2002; Dempsey ZS, Rowell S, McRobert R: The role of regional and neuroaxial anesthesia in patients with systemic sclerosis, *Local Reg Anesth* 4:47–56, 2011.

Perioperative Implications

Preoperative Preparation

- PPIs to reduce gastric acid.
- Consider metoclopramide for early disease; less effective for late disease.

Monitoring

- Invasive arterial monitoring relatively contraindicated in pts with Raynaud disease because of risk of digit ischemia, but ABG may be indicated.
- BP may be difficult because of reduced forearm blood flow.
- Consider PA cath in presence of pulm Htn.
- Skin temp may be significantly lower (1.5° C) than core temperature.

Anesthetic Technique

- RA may be preferable considering pulm problems, although it may be technically difficult.
- Regional technique may be associated with prolonged block in the presence of epinephrine because of severe vasoconstriction.
- Vasomotor instability may be seen.

Airway

- Pt may have severe decrease in oral aperture
- Consider awake FOB intubation.
- May require nasal intubation.

Preinduction/Induction

- Pt may be hypovolemic due to vasoconstriction.
- Consider volume expansion.
- May initially observe Htn, followed by vasodilation and hypotension.

Maintenance

- Usually requires mechanical ventilation because of restrictive lung disease.
- Intraop hypoxemia may develop secondary to pulm Htn.

Extubation

- Postop ventilation if significant pulm compromise.
- Pain control important to pulm status.

Anticipated Problems/Concerns

- Difficult airway
- Hypoxemia
- Hypotension

Scoliosis and Kyphosis

Chris C. Lee | Marie A. Theard

Risk

- Scoliosis is a lateral and rotational deformity of the spine that, when measured by x-ray, has a Cobb angle of >10 degrees. The incidence of this spine deformity is 1–4%.
- Most cases of scoliosis are idiopathic (70% of cases) with the infantile (<3 y) and juvenile (3–8 y) onset associated with higher morbidity and mortality than if developed later during adolescence (9–18 y). The F:M ratio for adolescent idiopathic scoliosis is 4:1, with severe curves occurring predominantly in females.
- Congenital scoliosis (1:1000 live births) in children is associated with bony abnormalities and GU malformations, or neural tube defects (meningomyelocele, spina bifida, syringomyelia). Failure of segmentation versus formation of part or all the vertebral body leads to development of this disease, with environmental influences like maternal alcohol abuse, IDDM, vitamin deficiencies, and hypoxia contributing to this defect.
- Neuromuscular scoliosis may be neuropathic (cerebral palsy and poliomyelitis) or myopathic (Duchenne muscular dystrophy).
- Other types of scoliosis include that found in neurofibromatosis type I (1:3000), Marfan syndrome, and osteogenesis imperfect.
- Kyphosis, a convex curvature of the spine (typically thoracic) usually occurs in older pts and is due to trauma (most common), degenerative disc disease, muscle weakness, inflammatory disease, postural changes or genetic. Congenital kyphosis, like congenital scoliosis, is caused by a failure of segmentation versus formation of part or all of the vertebral body.
- Scheuermann disease, with a prevalence of 8.3%, is the most common cause of juvenile kyphosis, defined by a Cobb angle ≥45. Males are more commonly affected. Mechanical factors and trauma have a role in the pathogenesis.

Overview

- Dx: The Cobb method is used to measure the severity of the curvature. A parallel line is drawn to the superior border of the caudal most vertebral body, which tilts to the concavity of the curve. A second line is then drawn parallel to the inferior border of the cephalad most vertebral body that tilts to the concavity of the curve. Perpendicular lines are drawn from these two lines, and the angle made by the intersection is measured as the Cobb angle.
- If left untreated, progression of this disease will lead to severe respiratory compromise (pts with curves >100 degrees).

Usual Treatment

- The treatment goal is prevention of curve progression and correction of the deformity.
- Observation or bracing techniques are used for skeletally mature with mild curves (<40–45 degrees).

For Cobb angles >55–60 degrees in the skeletally mature, spinal fusion with instrumentation of rods, pedicle screws, and/or laminar hooks are placed surgically to correct the deformity. Bone graft is applied to the fused area. Treatment between 45–55 degrees is not clear; however, most would recommend surgery once the Cobb angle reaches 50 degrees.

- Surgery may be approached posteriorly or via a combined anterior/posterior approach. The procedure may be staged to decrease morbidity and mortality. The anterior approach requires a thoraco-abdominal incision and retroperitoneal dissection. One lung ventilation may be needed for anterior exposure.

Assessment Points

System	Effect	Assessment by History	PE	Test
HEENT	Potential for difficult airway management	Prior difficult intubations, neck movement restrictions, glossal hypertrophy or aspiration risk secondary to DMD	Airway and neck exam	Cervical lateral spine, CT scan
HEME	Coagulation disorders	History of easy bruising or bleeding disorders		CBC, PT, PTT, platelet function, cross match, CMP
CV	Pulm Htn, cardiomyopathy secondary to underlying muscular dystrophies or mediastinal distortion	Functional status by exercise tolerance		ECG, ECHO, pulm arterial pressure
RESP	Restrictive pulm defect, severity of functional impairment related to curve severity	Functional status by exercise tolerance		CXR, ABG, spirometry, PFT with bronchodilator reversibility
GI	Poor nutrition	Feeding difficulty		Albumin, serum protein

Key References: Raw DA, Beattie JK, Hunter JM: Anesthesia for spinal surgery in adults, *Br J Anaesth* 91(6):886–904, 2003; Agabegi S, Kazemi N, Sturm P, et al.: Natural history of adolescent idiopathic scoliosis in skeletally mature patients: a critical review, *J Am Acad Orthop Surg* 23(12):714–723, 2015.

Perioperative Implications

Preoperative Preparation

- Respiratory dysfunction: Decreased chest wall compliance causing a restrictive pulm defect leads to chronic hypoxemia. Preop pulm function tests demonstrating VC <40% indicate the need for postop ventilation.
- CV dysfunction: Cor pulmonale may develop from chronic hypoxia and pulm Htn. An ECHO will help determine the degree of pulm Htn.
- Airway: Pre-existing arthritis in the cervical spine may necessitate an awake fiberoptic intubation or video laryngoscopy.
- Be aware of preop neurologic deficits.
- Consider administration of antifibrinolytics for surgery due to the significant risk of blood loss related to number of levels fused and length of surgery, and coagulopathy.

Preinduction/Induction/Maintenance

- Bronchodilators and pulm toilet may help to optimize the pt's respiratory status.
- Consider preop evaluation by the pain service for pain control.
- Induction with propofol or awake fiberoptic intubation.
- The use of succinylcholine should be avoided in pts with muscular dystrophies due to the risk of hyperkalemia causing cardiac arrest. Nondepolarizing muscle relaxants should be used sparingly due to the need for MEP and TCeMEP.
- Although IV induction agents can cause a slight reduction in amplitude and increased latency of cortical SSEPs, recording of SSEP or TCeMEP is still reliable.
- Maintenance of stable anesthetic depth is necessary to provide effective monitoring of SSEPs or MEPs. SSEPs and MEPs are mostly resistant to IV anesthetics. In the case of propofol, there is a decrease in SSEPs; however, rapid recovery after termination makes this an acceptable anesthetic for spine surgery. In the case of volatile anesthetics, it is recommended that low doses be used (<1 MAC), as higher doses cause a dose-dependent decrease in amplitude and increase in latency of SSEPs and MEPs. Nitrous oxide can also cause a decrease in amplitude of SSEPs, with less of an effect on MEPs. Hypothermia may also decrease the amplitude of SSEPs. Ketamine and etomidate may augment the amplitude of SSEP. Opioids have little effect on monitoring.
- For SSEP monitoring, an anesthetic technique with less than 0.5 MAC volatile anesthetic plus a propofol infusion with moderate/high dose opioid works well for these cases. For MEP monitoring, remifentanil/fentanyl combined with a propofol infusion is preferred. Ketamine and dexmedetomidine are also acceptable choices.

Monitoring

- Scoliosis correction is associated with major blood loss. Pts should be equipped with large-bore IV access and consideration given to strategies for reducing the need for blood transfusion (i.e., antifibrinolytic agents, preop erythropoietin, cell saver, preop autologous donation, intraop hemodilution).
- ASA standard monitors.
- Continuous blood pressure monitoring with an arterial line/CVP cath.
- SSEPs, MEPs and EMG, TCeMEP.
- BIS monitor to help asses anesthetic depth.
- Estimate blood loss from suction canister, cell-saver device, and sponges.
- Urinary cath.
- Consider O_2 sat pulse oximetry on big toes during anterior exposure of the lower lumbar spine to assess amount of iliac artery compression.

General Anesthesia

- Positioning for posterior fusion is prone with the abdomen free and in reverse Trendelenburg to reduce venous pressures at the surgical site and bleeding. Special care should be taken to ensure peripheral nerves are padded to prevent compression neuropathies, and eyes should be protected to avoid corneal abrasions. The potential for visual loss, though rare, is real; pts should be counseled preop regarding this risk.
- Thoracic approaches may require a lateral position with a double-lumen ETT for one lung ventilation. DLT position should be verified by fiberoptic bronchoscopy.
- Wake-up test allows intraop testing of the lower limb for motor function, allowing early detection of neurologic injury after instrumentation. The pt awakens from anesthesia and completes motor tasks on command. Wake-up test carries the risk of unintentional extubation or IV access loss if the pt becomes agitated.

Postoperative Period

- Postop ventilation may be necessary for some pts: Pts with neuromuscular disorders, severe restrictive pulm disease, congenital cardiac abnormalities, right heart failure, obesity and OSA, prolonged surgical procedure, pts who have a thoracotomy, and significant blood loss.
- Pain management requires a multimodal technique, including spinal/systemic opioids, local anesthetics, and NSAIDs.
- Ileus can be minimized with utilization of a multimodal pain management regimen.
- Fluid management with UO monitoring and replacement of blood loss is necessary.
- Pulm toilet and ambulation is beneficial to help decrease respiratory complications.

Anticipated Problems/Concerns

- Pulm compromise
- Corneal abrasions/vision loss (posterior ischemic optic neuropathy)
- Neurologic injury due to direct contusion by instrumentation, decreased spinal cord blood flow, distraction injury of the spinal cord, and epidural hematoma
- Vascular injuries/PE
- Superior mesenteric syndrome/acute kidney failure

Seizures, Absence (Petit Mal)

Melissa Brockerville | Lashmi Venkatraghavan

Risk

- Incidence of absence seizures in USA is 1.9–8 cases per 100,000 population.
- Seizures are most common in children aged 4–14 y but rare in adults.

Perioperative Risks

- Risk of transition of absence seizures into tonic-clonic seizures or SE is low but still possible.
- Seizure induced sequelae, including physical injuries, tachycardia, hypertension, hypoxia, metabolic acidosis, pulm aspiration, elevated ICP, and cerebral edema.

Worry About

- Seizure induction with periop drugs and hyperventilation can occur, especially with sevoflurane induction.
- Altered pharmacokinetics and dynamics with anticonvulsants: Resistance to neuromuscular blockers and opioids with chronic therapy
- Maintain serum anticonvulsant levels.

Overview

- Absence seizures are a common seizure disorder of childhood; up to two-thirds of pts are girls.
- Age of onset has bimodal distribution, with the first peak at 6–7 y (childhood) and the second around 12 y (juvenile).
- International League against Epilepsy classification of absence seizures:
  - Absence seizures: Typical or atypical.
  - Absence with special features: Includes myoclonic absence and eyelid myoclonia.
- Typical absence seizures are brief absence (5–20 sec), with impairment of consciousness and an abrupt onset/offset, often accompanied by one or more mild motor manifestations: staring, behavioral arrest, eyelid fluttering, or hand/face automatisms.
- Atypical seizures have a less rapid onset/offset with more motor features and prolonged seizures.
- Hyperventilation and bright flickering lights are common triggers for absence seizures, except for atypical absence seizures, which often occur during drowsiness.
- Attacks may be few or occur >100 times per d.
- Accidental injuries are rare.
- Minimal postictal sequelae occurs: EEG and consciousness return immediately.
- SE may occur: Convulsive and nonconvulsive SE are possible
- Remission rate for childhood absence epilepsy is 80%; juvenile myoclonic epilepsy carries a high risk of generalized tonic-clonic seizures.

Etiology

- Strong genetic predisposition in otherwise normal children.
- A mutation in the GABA (A) receptor gene was found in some pts with childhood absence epilepsy.
- Structural lesions in adults.

Usual Treatment

- ESM or VPA are first-line drugs. If there is a high risk of generalized tonic clonic seizures, VPA should be used.
- LTG is an alternative agent. Often a combination treatment may be needed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEME	Agranulocytosis (ESM, VPA) Thrombocytopenia (VPA) Pancytopenia (ESM)			CBC with plt count
RESP	Hyperventilation may induce seizure			
GI	Hepatotoxicity (ESM, VPA) GI upset (VPA)	GI Sx		Liver enzymes
CNS	EEG typically normal between seizures Normal development is rule			EEG
ENDO	Insulin resistance and metabolic syndrome (VPA) Subclinical hypothyroidism (VPA)			Blood sugar TSH
MS	Mild myoclonic movements		Movements	

Key References: Barakat A, Mallory S: Anaesthesia and childhood epilepsy, *Contin Educ Anaesth Crit Care Pain* 11:93–98, 2011; Tenney JR, Glauser TA: The current state of absence epilepsy: can we have your attention? *Epilepsy Curr* 13(3): 135–140, 2013.

Perioperative Implications

Preoperative Preparation

- Continue anticonvulsants on the day of surgery.
- Determine characteristics of typical seizures and frequency, compliance with anticonvulsants therapy.
- Ensure therapeutic anticonvulsant levels.
- Avoid triggers (e.g., bright flashing lights, hyperventilation, crying).

Monitoring

- Routine
- Depth of anesthesia monitors

Airway

- No issues

Induction (General Anesthesia)

- Standard induction drugs provide anticonvulsant action.
- Sevoflurane induction in conjunction with hypocapnia can produce epileptiform spikes and seizure activity in children.
- Avoid etomidate and ketamine; these lower seizure threshold.

Maintenance

- Normocarbia unless otherwise indicated
- Interaction between NMBs and anticonvulsants

Extubation

- Delayed emergence could be because of sedation from periop anticonvulsant use and nonconvulsive SE.

Regional Anesthesia

- Check coagulation profile; use lowest effective LA dose.
- Avoid transarterial injections.

Postoperative Period

- Anticonvulsants should be restarted as soon as possible.
- Adequate pain management is important to avoid stress-induced hyperventilation.

Anticipated Problems/Concerns

- Major periop morbidity is rare.
- Transition of absence seizures into tonic-clonic seizures or SE is the major concern, which would modify the periop risk.

Seizures, Epileptic

R. Alexander Schlichter | Guy Kositratna | W. Andrew Kofke

Risk

- Incidence of epilepsy estimated to be 0.5–2.3%.
- 30–40% of pts with epilepsy will develop intractable seizures (>1/mo refractory to two or more medications).
- Approx 400,000 people in USA have medically uncontrolled epilepsy.

Perioperative Risks

- Epilepsy has causality with a variety of syndromes throughout multiple systems.
- Various psychiatric disorders are assoc with epilepsy (e.g., migraines, depression, psychosis), and antiepileptic drugs are associated with mood, behavior, or cognition disturbances.
- 2 cases per 1000 pt-years result in sudden death associated with epilepsy.
- Many antiepileptic drugs induce hepatic enzymes (p450) or inhibitors which may affect blood levels of drugs such as warfarin, tricyclic antidepressants, statins, chemotherapeutic agents, and antivirals. Specific to anesthesia are NDMRs.

Worry About

- Different anesthetic effects on seizure threshold.
- Antiepileptic drug therapy-induced resistance to NDMRs and opioids.
- Anticonvulsant-induced blood dyscrasia (carbamazepine and others), hepatitis (valproate and others), Stevens-Johnson syndrome, toxic epidermal necrolysis (lamotrigine and others; 10× greater risk for carbamazepine with Chinese ancestry), and hyponatremia (oxcarbazepine).
- Rapid IV administration of IV phenytoin can cause profound hypotension.
- Acidosis in pts following a ketogenic diet as part of an anticonvulsant regimen.

Overview

- Epilepsy can lead to significant reduction in pt ADLs.
- Cognitive decline can be worsened by organic damage from refractory epilepsy, side effects of an anticonvulsant regimen, and increased social isolation from societal misunderstanding of the disease.
- Newer AEDs are generally well tolerated, but most still have significant side effects.
- Seizures are categorized as partial (simple, complex, or with generalization), generalized (convulsive or nonconvulsive), absence, nonepileptic (pseudoseizures), or unclassified. Up to 56% of comatose neurologic ICU pts have seizure activity.

Etiology

- Congenital often associated with other syndromes such as tuberous sclerosis, neurofibromatosis, multiple endocrine adenomatosis, and Jervell-Lange-Nielsen syndrome.
- Acquired associated with traumatic brain injury, stroke, brain tumor, Alzheimer, or idiopathic causes.

Usual Treatment

- Antiepileptic drugs, as monotherapy or in combination, include phenytoin, barbiturates, benzodiazepines, carbamazepine, and newer agents such as levetiracetam, lamotrigine, topiramate, oxcarbazepine, and many others.
- 13% of epileptic pts are thought to be candidates for epilepsy surgery, but only about 1% actually undergo surgery.
- Surgical techniques include temporal lobectomy (sometimes with epileptic foci mapping performed awake or asleep), deep brain stimulators, or fiberoptic laser ablation.
- A ketogenic diet is a nonpharmacologic approach to epileptic management.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Gingival hyperplasia	Phenytoin use		
CV	Cardiac tumors with tuberous sclerosis Increased incidence of sudden death with epilepsy (anesthetic implications unknown) Hypotension	Tuberous sclerosis Phenytoin use	Murmur possible	ECHO
RESP	Pulm involvement with neurofibromatosis; lipoid pneumonia	Neurofibromatosis Ketogenic diet	Cor pulmonale Pneumonia	CXR ECG Chest CT
GI	Anticonvulsant-induced hepatitis	Anticonvulsant use (except levetiracetam)	Jaundice, tender RUQ	LFTs if symptomatic
ENDO	Hyponatremia, hypothyroid, acidosis	Carbamazepine use (rare); ketogenic diet		Na^+ Plasma glucose, ketones
CNS	Tolerance to opioids, psychiatric disturbances, depression	Anticonvulsant use Organic brain disease		Assess effects of preop sedatives
MS	Tolerance to NDMRs	Anticonvulsant use		TOF monitoring in the OR

Key References: Kofke WA: Anesthetic management of the patient with epilepsy or prior seizures, *Curr Opin Anaesthesiol* 23(3):391–399, 2010; Kang HC, Chung DE, Kim DW, et al.: Early and late-onset complications of the ketogenic diet for intractable epilepsy, *Epilepsia* 46(2):272–279, 2005.

Perioperative Implications

Preoperative Preparation

- History and physical exam, including neuropsychiatric status.
- Determine antiepileptic drug Hx and review potential drug interactions.
- Obtain drug levels (phenytoin) if possible.
- Assess for signs of concurrent disease, such as murmur suggestive of myocardial tumor (tuberous sclerosis) or stigmata of neurofibromatosis.
- Lytes (Na+), plasma glucose, and ketones.

Monitoring

- For seizure surgery, EEG may be placed intraop.
- Epileptic mapping can be performed while pt is awake or asleep.

Airway

- Routine considerations

Preinduction/Induction for Epilepsy Surgery

- GA propofol or barbiturates (if available), etomidate are all acceptable. Avoid ketamine or nitrous-narcotic.
- For conscious analgesia craniotomy: Position determined by protection of pressure points. O_2 delivered by nasal prongs or facemask with capnography. Have airway adjuncts (nasal airway, LMA, ETT) immediately available. Analgesia/sedation administered using short acting opioid (remifentanil, alfentanil), propofol, and dexmedetomidine. Scalp block and local infiltration at frame pinning sites before surgical incision.

Maintenance

- Inhale anesthetic at less than 1 MAC, TIVA, or a balanced anesthetic are appropriate for GA.
- If the surgeon wishes to induce a seizure during intraop EEG monitoring, low dose propofol and inhalational less than 1 MAC are acceptable. To facilitate seizures, methohexital, etomidate, alfentanil, and remifentanil have been used.
- For conscious sedation, continued titration of sedation/analgesia during painful parts of procedure.
- Consider "asleep-awake-asleep" anesthetic plan with appropriate airway management during "asleep" portions of the surgery.

Extubation

- NMB agents and narcotics may not last as long as expected, with unanticipated coughing as procedure comes to close. Low dose IV lidocaine can suppress coughing. Consider remifentanil infusion until out of surgical frame.

Adjuvants

- Muscle relaxants: Enzymatic induction can lead to fast metabolism. Consider titrating an infusion to a desired train of four.
- Opioids tolerance with antiepileptic drug therapy.
- Recovery or withdrawal from anticonvulsant anesthetics can precipitate seizures.
- Antiepileptic drug levels can be significantly affected by anesthetics, changes in body physiology, ketogenic diet, and prolonged NPO status.

Postoperative Period

- Blood levels of antiepileptic drugs can be unpredictable. Be ready to redose additional anticonvulsants.
- Monitor serum glucose.
- Numerous case reports of postop seizures with a variety of anesthetics suggest ongoing concern for this possibility.

Anticipated Problems/Concerns

- Blood levels of antiepileptic drugs can be significantly affected by anesthetics, changes in physiology, and prolonged NPO status; may also affect non-AED drug levels as a result.
- Opioid tolerance may result in increased need for pain medication.
- Be prepared to treat postop seizures with additional anticonvulsants, benzodiazepines, barbiturates, or propofol.

Seizures, Intractable

René Tempelhoff

Risk

- Incidence in USA: 600,000 people with epilepsy have uncontrolled seizures.
- Racial predominance: None.

Perioperative Risks

- Sudden death
- Status epilepticus
- Seizure-mediated cardiac dysrhythmias

Worry About

- Liver toxicity from anticonvulsants (on the decline with the new drug generation)
- Periop trauma from convulsions
- Sudden death
- Status epilepticus postop
- Altered pharmacologic responses due to chronic drug therapy

Overview

- Neurologic disease associated with birth, congenital malformation, trauma, CNS pathology, idiopathic.
- Periop risks for acquired seizure disorder are increased, but some epilepsy and/or congenital malformations carry their own anesthetic risks.
- Check type of seizures, clinical manifestations, duration, and frequency.
- Anticonvulsant therapy and side effects (liver function, level of consciousness).

Etiology

- Congenital (e.g., tuberous sclerosis and/or infantile seizure)
- Idiopathic
- CNS pathology: Trauma, tumor, hemorrhage

Usual Treatment

- Anticonvulsant and diet.
- Surgery for ablation of foci.
- GA is regarded as a last resort for seizures unresponsive to sedative-hypnotics and resulting in decrease in consciousness or significant (<7.28) metabolic acidosis.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Tongue biting/swallowing		Airway assessment	
CV	Cardiac dysrhythmias	Syncope Tachycardia		ECG ECHO Holter monitor
RESP	Hyperventilation due to metabolic acidosis			ABG
GI	Altered liver function Anticonvulsant toxicity Tuberous sclerosis		Jaundice	LFTs Anticonvulsant levels
ENDO	Associated multiple endocrine adenomatosis			Glucose Ca^{2+}, thyroid function tests
RENAL	Renal dysfunction Tuberous sclerosis			Cr
CNS	Psychiatric problems CNS pathology			
MS	Occult trauma from seizures		Check joints, bones Examine tongue	

Key Reference: Kofke WA, Tempelhoff R, Dasheiff RM: Anesthesia for epileptic patients and epileptic surgery. In *Anesthesia and neurosurgery*, ed 3, St. Louis, MO, 1994, Mosby, pp 495–520.

Perioperative Implications

Preoperative Preparation

- Usual anticonvulsant regimen

Monitoring

- Routine monitors.
- $ETCO_2$: Increase in CO_2 production could be an indirect sign of seizure.
- Consider EEG monitoring.

Induction

- Have propofol and/or benzodiazepines available to treat possible seizures.
- Significantly higher requirement for nondepolarizing muscle relaxants and narcotics.

Maintenance

- Avoid proconvulsants (ketamine, etomidate, enflurane, and probably sevoflurane).
- Continue scheduled anticonvulsants.
- GA is sometimes used as treatment for status epilepticus.

Extubation

- To be delayed in case of doubt or situation such as:
  - High $ETCO_2$ despite adequate ventilation (can be a sign of active seizure).
  - Pt nonresponsive.
  - Obvious convulsions.
- Consider adding anticonvulsant (benzodiazepines) and ordering EEG.

Adjuvants

- See specific anticonvulsant used.

Postoperative Period

- Watch $ETCO_2$ as patient awakens since high production may indicate seizure activity.
- Resume anticonvulsants.
- Treat seizures ad libitum.

Anticipated Problems/Concerns

- Seizures on induction and awakening are treated with first-line benzodiazepine Rx (e.g., lorazepam load) rather than long-acting anticonvulsants. The latter (e.g., phenytoin, keppra ± levetiracetam) to be used after the seizure has been controlled.
- Evolution to status epilepticus: GA.
- Sudden death (ventricular arrhythmias).

Seizures, Tonic-Clonic (Grand Mal)

Veena Sheshadri | Lashmi Venkatraghavan

Risk

- Incidence in USA: 500,000–1,000,000 with recurrent tonic-clonic seizures.
- 10–20 million at risk to have one tonic-clonic seizure secondary to alcohol withdrawal, febrile convulsions (in children), CNS pathology, and/or metabolic disturbances.
- Prevalence of epilepsy is 0.5–1% of the population.

Perioperative Risks

- Seizures:
  - Periop seizures: Incidence is 3.1:10,000 pts; incidence related to LA toxicity is 120:10,000; in pts with known seizures undergoing RA, frequency is 5.8%.
  - SE
- Seizure-induced sequelae:
  - Physical injuries
  - Tachycardia, hypertension, hypoxia, metabolic acidosis
  - Pulmonary aspiration
  - Elevated ICP, cerebral edema, postictal paralysis (Todd paralysis)

Worry About

- Seizure induction with periop drugs: Local anesthetics, sevoflurane, etomidate, ketamine.

- Altered pharmacokinetics and dynamics with anticonvulsants: Resistance to neuromuscular blockers and opioids with chronic therapy.
- Routine preop monitoring of serum anticonvulsant levels is indicated only in pts with poor seizure control or those who are critically ill.
- Caution with intraop IV phenytoin or fosphenytoin (hypotension, rate of 50 and 150 µg/min, respectively).
- Delayed emergence.

Overview

- Periop seizures: First episode or with known seizure disorder.
- Often self-limiting, trauma to head or extremities is common if precautions are not taken (padded hospital bed). May progress to SE, a life-threatening condition requiring rapid and emergent intervention to terminate attack before cerebral damage results (30–60 min). Subtherapeutic anticonvulsant serum levels and alcohol withdrawal most commonly provoke SE.
- During seizures and postictally, airway reflexes are typically preserved; intubation is not indicated unless aspiration is strongly suspected.
- Postictally, enhancement of a previous neurologic motor deficit is common (Todd paralysis) for hours after seizure.

Etiology

- Idiopathic; Leading cause (30%).
- Acquired: Secondary to congenital syndromes, perinatal asphyxia, developmental disorders, trauma, CNS infection, cerebrovascular disease, intracranial tumor, drug withdrawal (commonly alcohol), metabolic (glucose, Na^+, Ca^{2+}, Mg^{2+}), renal or hepatic failure.
- Periop factors that might precipitate seizure in a pt with a known seizure disorder include NPO status, noncompliance with anticonvulsants, sleep deprivation, fatigue, stress, surgical pain, adverse drug reactions, and interactions between anticonvulsants and anesthetic agents.

Usual Treatment

- For one seizure, no therapy required. Check serum anticonvulsant levels if there is a Hx of epilepsy.
- Rule out hypoxia, STAT determination of serum glucose, electrolytes, and serum Ca^{2+}.
- Treatment includes IV benzodiazepines like lorazepam 0.1–0.2 mg/kg, midazolam 0.2 mg/kg, diazepam 0.15–0.2 mg/kg. Alternatively, thiopental 1–2 mg/kg, propofol 1 mg/kg. To prevent recurrence, load with phenytoin/fosphenytoin, or levetiracetam.
- IV levetiracetam often used in intraop settings owing to lack of hemodynamic disturbance and limited drug-drug interactions.
- Refractory seizures: Consider midazolam, thiopental 2–3 mg/kg, propofol 1–2 mg/kg boluses followed by infusion. May require ventilator assistance. IV magnesium and inhalational agents (isoflurane) are other options.
- EEG required if neurologic status does not return to baseline after 10 min following seizure.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Gingival hyperplasia (phenytoin) Seizure-induced oral trauma		Oral exam	
CV	Drug-induced SIADH (carbamazepine) Hypoglycemia, hypocalcemia, Thrombocytopenia, bone marrow suppression (several drugs)			CBC, lytes
RESP	Hypoxia Aspiration pneumonia	Need for supplemental O_2 SOB, fever	Auscultation	ABGs, O_2 sat CXR, sputum culture
GI	Poor absorption of anticonvulsant Drug-induced increase of hepatic P450 Drug-induced transaminase elevation	Low serum levels Increase dosage requirement of various drugs		Drug levels
CNS	Postictal somnolence Nonconvulsive SE Possible multiple CNS abnormalities	 Developmental Hx	Disturbed sensorium Delayed emergence Cognitive, motor deficits	 EEG
MS	Seizure-induced focal injury			

Key References: Brophy GM, Bell R, Claassen J, et al.: Guidelines for the evaluation and management of status epilepticus, *Neurocrit Care* 17(1):3–23, 2012; Perks A, Cheema S, Mohanraj R: Anaesthesia and epilepsy, *Br J Anaesth* 108(4):562–571, 2012.

Perioperative Implications

Preoperative Preparation

- Continue anticonvulsants on the day of surgery. Confirm availability of parenteral preparations.
- Ensure therapeutic anticonvulsant levels.
- Avoid triggers.
- Provide protection from injury should seizure occur.

Monitoring

- Routine
- Depth of anesthesia monitors
- EEG if poor emergence is observed

Airway

- Evaluate for past seizure-induced oral trauma.
- Gingival hyperplasia (phenytoin).

Induction (General Anesthesia)

- Standard induction drugs provide anticonvulsant action.
- Benzodiazepines are a useful adjunct.
- Sevoflurane induction in conjunction with hypocapnia can produce epileptiform spikes and seizure activity, especially in children.
- Avoid etomidate and ketamine; they lower the seizure threshold.

Maintenance

- Interaction between NMBs and anticonvulsants.
- CV changes may indicate seizures.

Extubation

- Delayed emergence could be due to sedation from periop anticonvulsant use, postictal state, and nonconvulsive SE.

Regional Anesthesia

- Check coagulation profile
- In pts predisposed to seizures, use lowest effective LA dose.
- Avoid transarterial injections.

Postoperative Period

- Postop seizures should be differentiated from conditions mimicking seizures (e.g., postop shivering, myoclonic and dystonic reactions, psychogenic nonepileptic seizures).
- Anticonvulsants should be restarted as soon as possible.
- Avoid meperidine for analgesia or postop shivering.
- EEG if level of arousal not as expected.

Anticipated Problems/Concerns

- Seizure on induction or emergence (risk of injury and aspiration).
- Intraop seizure with consequent delayed emergence.
- Subclinical or convulsive SE.

Sepsis, Severe Sepsis, and Septic Shock

Justin D. Ramos | Peter M. Schulman

Risk

- Incidence of sepsis within USA: Approximately 1 million per year and increasing. Severe sepsis and septic shock are associated with high morbidity and mortality, and septic shock is the most common cause of death among critically ill pts in noncoronary ICUs.
- Although in-hospital mortality rates are very high, they have been declining. With prompt and appropriate treatment, approximate mortality from septic shock is 20–30%.
- Increased prevalence with advanced age, male gender, nonwhite ethnic origin, comorbid diseases (COPD, cancer, chronic renal and liver disease, DM).

Perioperative Risks

- Hemodynamic and respiratory instability
- Thrombocytopenia and DIC
- End-organ ischemia and worsening multisystem organ dysfunction

Worry About

- Rapid hemodynamic deterioration following induction of anesthesia secondary to limited physiologic reserve
- Blunted response to vasopressors and inotropes
- Early and appropriate initiation of antibiotics
- Multidrug-resistant bacteria (in up to 25% of cases of severe sepsis and septic shock)
- Multisystem organ failure (mortality increases with each successive organ failure)

Overview

- Syndrome is a continuum from sepsis to severe sepsis to septic shock, resulting in worsening inflammation and widespread tissue injury, ultimately leading to multisystem organ dysfunction.
  - SIRS: Dx based on alterations in temperature, HR, RR, and WBC count; should prompt evaluation for sepsis.
  - Sepsis: Infection (documented or suspected) and its systemic manifestations.
  - Sepsis-induced hypotension: SBP <90 mm Hg, MAP <70 mm Hg, or SBP decrease >40 mm Hg in adults (or less than two standard deviations below normal).
  - Severe sepsis: Sepsis plus sepsis-induced tissue hypoperfusion or organ dysfunction.
  - Septic shock: Severe sepsis plus hemodynamic instability (hypotension not reversible with fluid resuscitation).
- Prompt diagnosis and appropriate treatment are critical for survival (highest chance of survival occurs when therapies are initiated within 6 h of recognition, and preferably sooner).
- Signs and symptoms of septic shock are nonspecific; presentation is based on initial source of infection.

Etiology

- Environmental factors (exposure to infecting pathogen) plus possible genetic predisposition result in abnormal immune, coagulation, and inflammatory responses.
- Gram-positive bacteria (MRSA, VRE, *Streptococcus*) have become the most common causative pathogens. Other causative pathogens are gram-negative bacilli (*Escherichia coli*, *Pseudomonas*), and fungi (*Candida*).
- Most common site of infection is the respiratory tract (pneumonia). Other common sites are the genitourinary system, abdominal organs, skin and soft tissue, devices (central lines), CNS, and heart (endocarditis).
- Also consider noninfectious causes of SIRS (burns, acute pancreatitis, trauma, thromboembolism, surgery).

Usual Treatment

- Speed and appropriateness of treatment affects outcome.
- General approach is triad of broad-spectrum antimicrobial therapy (ideally within 1 h of Dx), hemodynamic resuscitation to maintain adequate perfusion pressure and optimize O_2 balance, and source control.
- Key considerations:
  - Obtain blood cultures prior to initiation of broad-spectrum antibiotics.
  - Imaging studies if warranted to confirm potential source of infection.
  - Initial fluid resuscitation with crystalloid (30 mL/kg) for hypotension or hyperlactemia.
  - Vasopressors to maintain MAP ≥65 for hypotension not responsive to initial fluid resuscitation.
  - Target normal lactate (remeasure within 6 h if initially elevated).
  - Repeat clinical examination to reassess volume status and tissue perfusion. Consider other methods to assess fluid responsiveness and tissue perfusion, including cardiac ultrasound, CVP, $SCVO_2$, passive leg raise, and additional fluid challenge.
- Other considerations:
  - Fluid resuscitation with crystalloid is preferred. Albumin may be considered if significant amounts of crystalloid are required, but hydroxyethyl starches should be avoided.
  - Restrictive approach to blood transfusion (target transfusion trigger of 7 g/dL). A higher transfusion threshold may be appropriate in the setting of acute coronary syndrome, acute hemorrhage, or tissue hypoperfusion.
  - Lung protective ventilation strategy with PEEP if pt is mechanically ventilated.
  - Daily reassessment of antibiotic therapy to narrow coverage when appropriate.
  - Stress-dose steroids (200 mg/d via hydrocortisone infusion) only for refractory septic shock (BP not responsive to fluid and vasopressor therapy) for up to 7 d or until vasopressors are no longer needed.
  - First-choice vasopressor is norepinephrine.
  - Addition of low-dose vasopressin infusion (0.03 U/min) to augment MAP or reduce norepinephrine dose in refractory septic shock.
  - Recommended target blood glucose range 110–180.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Altered mental status	Level of consciousness, delirium	Somnolent, obtunded, confused	CT of the head if there is a focal deficit
CV	Vasodilation, hypovolemia, acidosis, hypercontractility or hypocontractility, circulatory failure	Signs of end-organ hypoperfusion	Tachycardia, hypotension, wide pulse pressure, warm (or cold) extremities, low SVR, high or low CI, low SVO_2	Invasive hemodynamic monitoring, ECHO
PULM	Hypoxemia, hyperventilation, respiratory failure	Tachypnea, dyspnea	Use of accessory muscles, rapid shallow breathing, cyanosis	CXR, ABG
RENAL	Oliguria, acute kidney injury, ATN	UO	Signs of hypovolemia, rising, Cr, BUN	UO, Cr, BUN, urine lytes, UA
ID	Infection	Fever, chills, rigors	Hyperthermia or hypothermia	WBC with differential, cultures, radiographic imaging
HEME	Hemolysis, thrombocytopenia, DIC		Bleeding	CBC, D-dimer, INR, PTT, fibrinogen

Key References: Dellinger RP, Levy MM, Rhodes A, et al.: Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012, *Crit Care Med* 41(2):580–637, 2013; Mouncey PR, Osborn TM, Power S, et al.: Trial of early, goal-directed resuscitation for septic shock, *N Engl J Med* 372(14):1301–1311, 2015.

Perioperative Implications

Preoperative Preparation

- Septic pts are often extremely unstable and have limited physiologic reserve.
- Surgery should be postponed until sepsis is treated unless underlying cause requires surgical intervention (source control).
- If surgery is urgent, consider whether pt's condition may be optimized before proceeding to the OR.

Intraoperative

- Goal for induction is hemodynamic stability.
- Invasive monitoring is generally indicated.
- Inotropes and vasopressors should be readily available.
- Target goal: Directed resuscitation to MAP >65, CVP 8–12, adequate UO, normal pH, normal lactate, SVO_2 >70.
- Consider steroids for refractory shock.
- Consider need for pt to remain intubated postprocedure.

Postoperative Period

- Need for ICU care and possible prolonged mechanical ventilation

Anticipated Problems/Concerns

- Hemodynamic and respiratory instability
- Worsening metabolic acidosis, low central or mixed venous O_2 sat
- Altered coagulation/DIC
- Multisystem organ dysfunction
- Prolonged ICU stay
- High morbidity and mortality

Shy-Drager Disease

Saumil J. Patel | Prakash A. Patel

Risk

- More common in men than in women.
- Symptoms begin in fifth-seventh decades of life.

Perioperative Risks

- Autonomic dysfunction with CV collapse due to decreased sympathetic outflow and abnormal parasympathetic homeostatic mechanisms
- Aspiration risk

Worry About

- Orthostatic hypotension and intraop fluctuations in BP, particularly during induction.
- Response to sympathomimetic drugs is unpredictable and may be exaggerated owing to denervation hypersensitivity.
- Little or no HR or BP response to indirect sympathomimetic agents (i.e., ephedrine, methamphetamine) or anticholinergic medications (i.e., atropine).
- Hyperresponsiveness of BP to hyperventilation/hypoventilation (hypercapnia/hypocapnia).
- Loss of baroreceptive response leads to hyperresponsiveness to volume status and sudden changes in blood volume.
- Cannot use sweating, tachycardia, or BP as indicators of anesthesia depth.
- Positive-pressure ventilation can decrease venous return and cause dramatic hypotension without associated change in HR.
- Up to 50% of pts will have supine hypertension.
- Liver blood flow can be dependent on posture, so hepatically cleared drugs' plasma levels can be highly dependent on posture.
- Lyte abnormalities: Hypokalemia and hypomagnesemia when treated with fludrocortisone.
- Central sleep apnea: Apneic syndromes due to impaired central regulation of respiration.
- Obstructive sleep apnea: Found in advanced stages.
- Vocal cord paralysis due to laryngeal muscle dysfunction: Found in advanced stages.
- Impaired GI motility increased the risk of aspiration as well as postop ileus.
- Faulty thermoregulatory systems: Hyperthermia-induced hypotension, lack of peripheral vasoconstriction to cold environment, can lead to hypothermia and hypotension.

Overview

- Irreversible, rapidly progressive, and fatal disease causing death usually within 10 y of onset due to postsyncopal cerebral ischemia.
- Primary neurodegenerative disease with primary autonomic failure. Parkinsonism-plus syndrome; however, Shy-Drager involves loss of vascular reflexes. There is secondary autonomic failure in Parkinson disease.
- Clinical manifestations: Orthostatic hypotension, supine hypertension, parkinsonian symptoms, urinary and bowel dysfunction, impaired potency and libido, decreased sweating.
- Autopsies showed diffuse involvement of the CNS and peripheral autonomic nervous system as well as corticobulbar and corticospinal tracts, basal ganglia, and cerebellum.
- Difficult to treat the parkinsonian symptoms, as dopaminergic drugs may exacerbate orthostatic hypotension.

Etiology

- Unknown

Usual Treatment

- Goals of treatment: Reduce venous pooling, increase peripheral vascular resistance, increase plasma volume.
- Nonpharmacologic: Symptomatic relief of orthostatic hypotension with postural change, liberal salt intake, graded elastic stockings, postural training with head of bed elevated during sleep.
- Pharmacologic: Fludrocortisone (mineralocorticoid, started preop); midodrine (peripheral α-adrenergic agonist); pyridostigmine (cholinesterase inhibitor, may increase BP); octreotide (splanchnic vasoconstriction elevates SVR); atomoxetine (inhibits reuptake of norepinephrine); sympathomimetics (ephedrine/methamphetamine effective only in early stages); prostaglandin inhibitors (indomethacin, ibuprofen); MAO inhibitors; tyramine.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vocal cord paralysis	Obstruction; apnea episodes; stridor, particularly during sleep	Midline position of the cords after induction	Direct laryngoscopy, fiberoptic nasopharyngoscopy
	Obstructive sleep apnea	STOP-BANG OSA risk questionnaire	Neck circumference	Polysomnography
CV	Orthostatic hypotension	Syncope; dizziness, visual changes related to position	BP changes related to position	Tilt table test, Valsalva maneuver testing, cold pressor test, sympathetic and parasympathetic "stress" testing
	Fixed HR			Palpation, ECG
RESP	Irregular breathing			Auscultation, visualization
GI	Gastroparesis Fecal incontinence, diarrhea, constipation, sodium loss	Early satiety, dysphagia, GERD	Loss of rectal sphincter tone	Gastric emptying study Lytes/BMP
GU	Urinary incontinence Atonic bladder Sexual dysfunction	Nocturia; stress/overflow incontinence Sexual impotence		
CNS	Parkinsonian symptoms Anhidrosis Heat intolerance		Cogwheel rigidity Shuffling gait Anisocoria Horner syndrome	Sudomotor testing for anhidrosis
MS	Osteoporosis and aseptic necrosis (may be assoc with autonomic dysfunction)		Muscle atrophy Fasciculations	

Key References: Bevan DR: Shy-Drager syndrome. A review and a description of the anaesthetic management, *Anaesthesia* 34(9):866–873, 1979; Mustafa HI, Fessel JP, Barwise J, et al.: Dysautonomia: perioperative implications, *Anesthesiology* 116(1):205–215, 2012.

Perioperative Implications

Preoperative Preparation

- Reduce venous pooling, increase PVR, and increase plasma volume.
- Oral fludrocortisone can be started up to 2 wk preop.

Monitoring

- Arterial and central venous cath to guide fluid replacement and use of vasopressors
- Temperature: Avoid hypothermia/hyperthermia.

Airway

- Vocal cord paralysis and dysautonomia with gastroparesis may make awake intubation or rapid sequence intubation with cricoid pressure more desirable.

Preinduction/Induction

- Avoid drugs that would cause decrease in cardiac output, HR, or SVR as profound hypotension may occur due to decreased sympathetic outflow.
- Regional anesthesia can be used if indicated for procedure.
- Consider steroid supplementation if pt is on fludrocortisone preop.

Maintenance

- Positive-pressure ventilation and pneumoperitoneum during laparoscopic surgery may decrease venous return and exaggerate hypotension.
- Use direct-acting sympathomimetic drugs in small doses titrated to effect. Pt may have an exaggerated response due to denervation hypersensitivity. Vasopressin has been used successfully in cases in which hypotension was not responsive to other sympathomimetics.
- Atropine may not increase the HR owing to parasympathetic deficiency.
- Rapid blood loss or rapid fluid administration can precipitate exaggerated changes in BP.
- Maintain normothermia.

Extubation

- Ensure pt can protect airway.

Postoperative Period

- Continue invasive BP monitoring if necessary.
- Monitor volume status, respiratory mechanics, and temp closely.
- Abnormal lytes can affect BP and response to medications.
- Restart home dysautonomia medications as soon as possible postop.

Anticipated Problems/Concerns

- Autonomic dysfunction with CV collapse
- Aspiration risk

Acknowledgment

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Sick Sinus Syndrome

Pranav R. Shah | Erin A. Sullivan

Risk

- Highest incidence occurs in pts >60 y.
- Common in pts who have had congenital heart defect repair surgery.
- Sinus node dysfunction is a common indication for pacemaker implantation.

Perioperative Risks

- Syncope, symptomatic bradycardia, and asystole.

Worry About

- Sinus bradycardia can be poorly responsive to atropine and require a pacer intraop.
- Termination of a tachy-brady event where an atrial tachycardia occurs can lead to a prolonged bradycardia or asystole.
- A tachy-brady event can lead to demand myocardial ischemia and can precipitate heart failure in pts with related comorbidities.

Overview

- A significant portion of elderly pts with SSS frequently have other cardiac comorbidities, such as CAD.
- SSS includes several ECG abnormalities: Noniatrogenic persistent spontaneous sinus bradycardia that is inappropriate for physiologic circumstance, sinus arrest or exit block, or alterations of paroxysmal atrial tachyarrhythmia (often fibrillation or flutter) and period of bradycardia—tachy-brady syndrome.
- Class I indications for pacemaker insertion in SSS include SND with documented symptomatic bradycardia, or sinus pauses; SND as a result of essential long-term therapy; or SND with symptoms of chronotropic incompetence.
- A large portion of pts with chronotropic incompetence (defined as the inability to achieve 80% of age predicted HR during physiologic stimulus) also have SND.

Etiology

- Causes are numerous and not clearly defined.
- In the elderly, likely due to fibrosis of SA node and hypersensitivity to autonomic changes.
- In adults with congenital heart disease (especially with ASD repair, or extensive atrial reconstruction), likely due to surgical (direct or inflammatory) trauma to the SA node.

Usual Treatment

- When SSS remains undiagnosed until an episode of bradycardia in the OR, administer atropine (0.5 mg–3 mg IVP) and epinephrine (10 µg IVP with rapid up-titration based on HR), along with pacing (external or transvenous). Pts with SSS often have a poor response to atropine.
- When SSS is diagnosed preop (i.e., ECG changes with symptoms), suggest a pacemaker (often DDD or AAI). A pacemaker does not control tachyarrhythmia, but instead it allows antiarrhythmic therapy for tachycardia by pacing during bradycardia caused by the therapy.
- Anticoagulation with warfarin is used if continuous ECG monitor detects paroxysms of atrial tachyarrhythmia, since this subset of pts has an increased thromboembolic risk.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Low cardiac output Tachy-brady event	Syncope, presyncope, lightheadedness, decreased exercise capacity, dyspnea on exertion, fatigue, confusion, memory loss, CVA (especially in elderly) Palpitation, angina, CHF symptoms	Bradycardia, tachycardia	ECG Continuous ECG monitor with symptom diary
RENAL	Accentuate SSS			Potassium (hypokalemia)

Key References: Semelka M, Gera J, Usman S: Sick sinus syndrome: a review, *Am Fam Physician* 87(10):691–696, 2013; Staikou C, Chondrogiannis K, Mani A: Perioperative management of hereditary arrhythmogenic syndromes, *Br J Anaesth* 108(5):730–744, 2012.

Perioperative Implications

Preinduction/Induction

- Factors that alter autonomic balance to favor a parasympathetic state can produce sinus bradycardia: Eye surgery, increased ICP, severe hypoxia, and cervical/mediastinal tumors.
- Optimize extrinsic factors that can decrease heart rate: hypoxia, hypothermia, ICH, and hypothyroidism.
- Volatile anesthetics, propofol, and vecuronium all decrease sinus node activity in a dose-dependent fashion. Consider using NMBA with vagolytic properties (e.g., rocuronium).
- Standard monitors (pulse oximetry, ECG).
- In pt population that is dependent on atrial systole for sufficient cardiac output (such as those with ischemic cardiomyopathy, aortic stenosis, or diastolic dysfunction), an atrial tachyarrhythmia (as part of the tachy-brady phenomenon) can lead to hypotension.
- Consider placing transcutaneous pacing pads on pt prior to induction, or placing a central venous introducer in preparation for a transvenous pacing wire if needed.
- In cases of asystole or bradycardia, attempt therapeutic medications: Atropine 0.5–1 mg IV q 3–5 min up to 0.04 mg/kg (max 3 mg), or ephedrine 5–5 mg IV bolus, or infusions of dopamine 5–20 µg/kg per min IV, or epinephrine 2–10 µg/min IV, or isoproterenol 2–10 µg/min. Electrical pacing is most likely to succeed.
- If an episode of tachycardia occurs in pt with pacemaker, use normal agents for control of arrhythmia, as the pacemaker should rescue bradycardia. If no pacemaker, use short acting agents for rate control such as esmolol.

Regional Anesthesia

- Case reports demonstrate that SSS may manifest from several types of blocks, including a regional block that produces sympathectomy, stellate ganglion blockade, thoracic epidural, and spinal anesthesia.
- Standard monitoring is recommended.
- If history is strongly suggestive of SSS, consider having pacing pads in the room.

Postoperative Period

- If SSS manifests in a pt without pacemaker intraop, consult cardiology to further evaluate for permanent pacemaker placement.

Anticipated Problems/Concerns

- An episode of atrial tachyarrhythmia that terminates in asystole or significant bradycardia.
- Atrial tachyarrhythmia in a susceptible population (aortic stenosis, diastolic dysfunction) may itself compromise cardiac output.
- Symptomatic sinus bradycardia may not respond robustly (or at all) to atropine. It may need a pacing if a second agent (isoproterenol, epinephrine, ephedrine, or dopamine) does not work.

Sickle Cell Disease

Michael E. Nemergut

Risk

- Affects persons with African, Greek, Turkish, Italian, Arab, Latin American, and Indian ancestry.
- Incidence in USA: Most common disease identified through state-mandated screening, occurring in 1:2647 births; varies by race, occurring in 1:396 African-American births and 1:36,000 Hispanic births.
- Early mortality: Varies by type of disease. In one longitudinal study of pts with sickle cell anemia (i.e., Hgb SS homozygous), median age of death was 42 y in men and 48 y in women; for those with Hgb SC disease, median age of death was 60 and 68 y in men and women, respectively.
- In children, mortality has been decreasing, with rates (deaths per 100 pt-years) of 0.67, 0.37, and 0.15 for years 1983–1990, 1991–1999, and 2000–2007, respectively.

Perioperative Risks

- Complication rate varies by disease severity and surgical risk category, reported to be as high as a 39% overall complication rate and 1.1% 30-day mortality.
- Complications include anemia, stroke, acute chest syndrome, myonecrosis, heart failure, MI, hepatic or splenic sequestration, retinal hemorrhage, hematuria, renal failure, seizure, wound infection, UTI, and unexplained death.

Worry About

- Degree of preop anemia
- Surgical risk category
- Preexisting end-organ dysfunction including CNS, heart, lung, kidney, and immunologic disorders
- Precipitation of vaso-occlusive crisis (by dehydration, stasis, hypoxia, hypothermia, acidemia, pain) and subsequent end-organ ischemia
- Risk of acute or delayed transfusion reactions due to preexisting alloimmunization

Overview

- Broad group of disorders involving pts with sickle cell anemia (Hgb SS homozygous) as well as compound heterozygous pts having one Hgb S allele with another, different hemoglobinopathy allele including Hgb C, Hgb β-thalassemia, Hgb D, and Hgb O Arab.
- Lifelong cause of vaso-occlusive episodes inducing end-organ ischemia and pain.
- In adults, renal insufficiency, leukocytosis, and the severity of hemolytic anemia have been reported to be major risk factors for mortality.
- In children, dactylitis in infancy, Hgb concentration <7 g/dL, and leukocytosis without infection have been reported to predict adverse outcomes, including stroke, recurrent acute chest syndrome, and death.
- End-organ damage due to vaso-occlusion causes morbidity and mortality. Key conditions are pregnancy, heart failure, MI, CVA, acute chest syndrome, sequestration crisis, and severe anemia.
- Sickle Hgb causes a rightward shift (P50 = 31 mm Hg) of oxyhemoglobin dissociation curve, favoring deoxygenated Hgb.
- Hgb S permits deoxygenated Hgb molecules to polymerize into rigid insoluble intraerythrocytic fibers, resulting in sickled erythrocytes.
- Sickled erythrocytes are unable to traverse the microvasculature, leading to tissue ischemia and end-organ damage.

Etiology

- Single amino-acid substitution on β-chain of Hgb at position 6 (Glu → Val).
- Sickled erythrocytes have a shortened life span, leading to chronic hemolysis and anemia.

Usual Treatment

- Vaccines against pneumococcus, *Haemophilus influenzae* type b, and seasonal influenza.
- Prophylactic penicillin therapy.
- Supportive care for vaso-occlusive crisis
- Simple and exchange transfusions; treatment of iron overload.
- Hydroxyurea reduces the incidence of painful crises, acute chest syndrome, hospital admissions, and transfusion requirements.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Hypoxemia due to sleep apnea	Snoring or sleep apnea Hx	Tonsillar hypertrophy	Sleep study
CV	MI; LV and RV dysfunction; CHF Pulmonary hypertension	Angina Sx; poor exercise tolerance; dyspnea	Displaced PMI S_3, S_4	ECG, exercise ECG; ECHO, Hct
RESP	Acute chest syndrome; lung and rib infarction; pneumonia	Previous acute chest syndrome; dyspnea Chest pain	Chest pain; rales; crackles	CXR
GI	Gallstones; sickle girdle syndrome (mesenteric ischemia); hepatic sequestration crisis	RUQ pain; abdominal pain	Jaundice; RUQ tenderness; pallor	RUQ US
HEME	Sickle pain crisis; asplenia or splenic sequestration crisis; anemia; infection	Pain in affected areas; fatigue; sepsis	Pallor; splenic enlargement; flank tenderness; fever	Hgb, Hct, WBC, reticulocyte count, culture data
RENAL	Renal failure and insufficiency	Hematuria; hemodialysis Hx		UA, BUN, serum Cr
OB	Preterm labor and delivery; perinatal mortality; placenta previa; abruptio placentae	Vaginal bleeding		US
CNS	Stroke; intracranial hemorrhage; pneumococcal meningitis; retinopathy and hyphema; seizure	Previous CNS Sx (weakness, TIA, or neurologic dysfunction); headache; vomiting or altered mental status	Focal deficits, stupor or coma; nuchal rigidity	Head CT, EEG, MRI
MS	Leg ulcers; myonecrosis; myofibrosis; dactylitis; shoulder or hip avascular necrosis; osteomyelitis	Pain in affected areas	ROM; skin changes; fever	WBC, UA, x-ray; culture data

Key References: O'Meara M, Davies G: Anaesthesia for patients with sickle cell disease (and other haemoglobinopathis), *Anaesth Intensive Care Med* 14:54–56, 2013; Howard J, Malfroy M, Llewelyn C, et al.: The transfusion alternatives preoperatively in sickle cell disease (TAPS) study: a randomised, controlled, multicentre clinical trial, *Lancet* 381(9870):930–938, 2013.

Perioperative Implications

Preoperative Preparation

- Aggressive exchange transfusion to obtain an Hgb SS <30% demonstrates no benefit over simple transfusions to obtain a Hgb of 10 g/dL with Hgb AA erythrocytes using extended matched transfusions (minor group E, K, C, Fya).
- In Hgb SS and Hgb Sβ0-thal pts undergoing low-medium risk surgery, pts with preop simple transfusions to a target Hgb of 10 g/dL within 10 d prior to surgery had decreased periop complications compared with pts who were not transfused.
- Alkalinization confers no benefit.
- Autotransfusion: Predonated units do not have established efficacy.
- Peripheral venous access may be difficult, and central venous catheters may be required.
- Standard NPO times should be used; ensure adequate hydration by encouraging intake of clear fluids up to 2 h prior to surgery unless clinically contraindicated in which case IV hydration should be considered.

Monitoring

- Routine

Airway

- None

Induction

- If premedication is indicated, avoid oversedation, which may induce hypoxemia and hypercarbia that promotes sickling.
- Retrobulbar blocks appear safe.
- No differences in morbidity or mortality shown among various anesthetic agents or between regional and GA techniques.

Maintenance

- Cardiopulmonary bypass imposes challenges secondary to mechanical hemolysis, inflammation, hypothermia, hemostasis, and platelet activation; while rare, successful case series have been described in adults and children.
- Maintain euvolemia; replace volume loss with warmed, isotonic fluids; maintain normothermia; tourniquet use is relatively contraindicated but described in small case series.

Extubation

- Respiratory depression at emergence may induce hypoxemia/hypercarbia that may promote atelectasis and vaso-occlusion.

Postoperative Period

- Adequate IV hydration until oral fluids are tolerated; early mobilization and incentive spirometry; supplemental O_2 therapy to keep saturation >96%; access pain regularly and provide analgesia; consider multimodal analgesic techniques, particularly in opioid-tolerant pts.

Anticipated Problems/Concerns

- Blood transfusions carry higher risk for acute and delayed transfusion reactions due to alloimmunization.
- Avoid hypoxemia, hypovolemia, acidemia, hypothermia, hypertonicity, or stasis.

Sickle Cell Trait

Michael F. Roizen

Risk

- Incidence in USA: 3 million; 350 million in world
- Race with highest prevalence: African Americans

Perioperative Risks

- Increased risk of complications following CABG.
- Periop mortality rate in published cases of SA trait is 0.8%.
- Some increased risk of CVA and pulm infection but not well quantified.

Worry About

- Increased risk of vasoocclusive phenomenon with hypoxia and stress.
- Sudden death with stresses such as vigorous exercise make one worry because recovery from surgery may be considered a similar stress as vigorous exercise.

Overview

- Is not a disease
- Is not a cause of abnormalities in blood count
- Does not produce vaso-occlusive symptoms under physiologic conditions; painful crisis not a hallmark or concomitant of condition
- Does not adversely affect individual's life expectancy
- Dx established by Hgb electrophoresis
- See also Sickle Cell Disease

Etiology

- Heterozygous, in which individual has one beta S and beta A globin gene (SA disease); Sickle Thal is one beta S and one beta C (SC disease)

Usual Treatment

- None except iron supplementation (debated)

Assessment Points

System	Effect	Assessment by Hx	Test
RESP	Pulm embolism		
HEME	Hgb level usually 13–15 g/dL	Hx SOB: Poor exercise tolerance 10–40% of Hgb S; same cells as Hgb A	Hgb
GU	Painless hematuria and bacteriuria; pyelonephritis (especially with pregnancy) RO polycystic kidney disease		UA (culture if prosthesis planned)
CNS	Stroke	Migraine headache	

Key References: Djaiani GN, Cheng DC, Carroll JA, et al.: Fast track cardiac anesthesia in patients with sickle cell abnormalities, *Anesth Analg* 89(3):598–603, 1999; Tsaras G, Owusu-Ansah A, Boateng FO, et al.: Complications associated with sickle cell trait: a brief narrative review, *Am J Med* 122(6):507–512, 2009; Ingle SS, Ubale P: Anesthetic management of a patient with sickle cell disease for common bile duct exploration, *J Anaesthesiol Clin Pharmacol* 27(4):547–549, 2011.

Perioperative Implications

Preoperative Preparation

- Warm room.
- Consider prehydration.

Monitoring

- Temperature

Airway

- Occasionally distorted anatomy secondary to extramedullary erythropoiesis.
- Sinusitis possible.
- Prehydrate liberally if CV status will tolerate.

Induction

- Routine

Maintenance

- Keep warm.
- Keep vasodilated.
- Keep without stasis.
- High O_2 content.

Extubation

- Keep warm.

Adjuvants

- Vary if hepatic or renal insufficiency exists.

Postoperative Period

- Aggressively prevent pain, hypovolemia, and hypothermia.

Anticipated Problems/Concerns

- Stroke and/or pulm emboli or infection have been reported after CPB; 5 of 546 pts in literature of sickle trait disease died periop.

Silicosis

Alexander A. Vitin | Karen B. Domino

Risk

- Silicosis is irreversible fibronodular lung disease caused by inhalation of dust containing crystalline silica (alpha-quartz or silicon dioxide) during occupational exposure.
- Currently, >1,000,000 workers are exposed, with 200–300 deaths/y; protection devices decrease incidence.
- Mostly >65 y of age
- Incidence higher in males than females.
- No racial predilection.

Perioperative Risks

- Hypoxemia, CO_2 retention with chronic respiratory acidosis, bronchospasm, pneumothorax, atelectasis, mycobacterium (30-fold increased risk for TB) and fungal infection, bacterial pneumonia, chronic bronchitis exacerbation
- Periop respiratory failure, especially following thoracic and upper-abdominal surgery
- Pulm Htn; cor pulmonale
- Renal insufficiency (tubular nephropathy)
- Steroid-induced diabetes (in cases of chronic steroid treatment)

Worry About

- In cases of associated scleroderma and/or rheumatoid arthritis, possible difficult intubation
- Bronchospasm and chronic bronchitis exacerbation
- Respiratory failure
- Cor pulmonale

Overview

- Silicosis-pulmonary fibrosis commonly occurs after 4–5 (acute, very rare), 5–10 (accelerated), or >10 y (chronic) of occupational exposure.
- In advanced stage, both obstructive (graduate loss of FEV_1, FVC and decrease of FEV_1/FVC ratio) and restrictive ventilatory defects, as well as decreases in diffusing capacity, are common; exertional dyspnea is the predominant symptom.
- CO_2 retention, pulm Htn, or cor pulmonale late in the course.
- Associated TB, lung cancer, connective tissue diseases (scleroderma, rheumatoid arthritis, Sjögren's syndrome), nephritic syndrome, and renal failure.

Etiology

- Prolonged occupational exposure may occur from mining, stone cutting, sandblasting, abrasive industries, granite quarrying, packing silica flour; this causes dose- and time-related development of pulmonary fibrosis.
- Alveolar macrophages engulf inhaled free silica particles and enter lymphatics and interstitial tissue. The macrophages cause release of cytokines (tumor necrosis factor-α, IL-1), tumor growth factor-β, and oxidants, stimulating parenchymal inflammation, collagen synthesis, and ultimately fibrosis.
- Initial lesions are silicotic nodule mostly located near the respiratory bronchiole. The nodule is composed of refractile particles of silica surrounded by whorled collagen in concentric layers, with macrophages, lymphocytes, and fibroblasts in the periphery. Emphysematous blebs surround the silicotic nodule, especially in the subpleural area. Bleb and bulla formation, and airways and vascular bed distortion by these nodules complicate advanced disease.

Usual Treatment

- Discontinue occupational exposure.
- In cases of silicoproteinosis, the whole lung lavage, with double-lumen tube intubation, may be indicated; rarely, lung transplantation.
- In some cases, oral corticosteroids.
- Empiric use of bronchodilators and inhaled corticosteroids for obstruction.
- If symptomatic/hemodynamically significant, pulm Htn treatment may include sildenafil; endothelin receptor antagonists (bosentan); high-dose calcium channel blockers, such as diltiazem, amlodipine, and in selected cases, verapamil. Epoprostenol infusions are rarely indicated.
- Prophylaxis for complicating infections (pneumococcal and influenza vaccines, TB treatment).
- Smoking discontinuation.
- No cure so far.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm Htn Cor pulmonale	Dyspnea Exercise tolerance Leg swelling	S_3 Peripheral edema Distended neck veins	ECG CXR TTE
RESP	Pulm fibrosis Bulla/bleb formation	Cough Sputum production Dyspnea Exercise tolerance	Rales, rhonchi, Wheezing Cyanosis Use of accessory respiratory muscles RR	CXR ABG PFTs Inspiratory force Diffusing capacity Lung biopsy/lavage fluid microscopy
GI/ENDO	Weight loss Hyperglycemia (in chronic steroid treatment)			Body weight monitoring Blood glucose
MS	Generalized weakness			
RENAL	Renal insufficiency		Hypertension Peripheral edema Oliguria	Serum creatinine, BUN, potassium Creatinine clearance
IMMUNE	Hilar adenopathy (eggshell calcification) Increased susceptibility to infection, especially pulm	Cough Fever Sputum production		CXR Sputum culture and sensitivity

Key References: Rose C: Silicosis. In King TE Jr, Hollingsworth H, editors: *UpToDate*, Waltham, MA. www.uptodate.com/contents/silicosis. (Accessed 09.06.16); Stafford M, Cappa A, Weyant M, et al.: Treatment of acute silicoproteinosis by whole-lung lavage, *Semin Cardiothorac Vasc Anesth* 17(2):152–159, 2013.

Perioperative Implications

Preoperative Preparation

- Lung condition optimization: Treat bronchospasm (if present), bronchitis, and other pulmonary infections; possible lung lavage.
- Consider steroids (short course).
- Stop smoking at least 24 h before surgery.

Monitoring

- Preop and postop: Consider repetitive ABGs, lung mechanics (RR, TV, MV, FVC, NIF, etc.).
- Intraop: Arterial line; CVP is controversial. Consider PA catheter if pulm Htn is present and/or significant fluid shifts are expected.

Pre-induction/Induction

- Caution with IV agents that depress ventilation and regional techniques that affect accessory muscles of respiration (e.g., high epidural and interscalene blocks).
- Maintain adequate preload, and optimize cardiac output. Avoid hypoxemia, hypercapnia, and acidosis (both respiratory and metabolic), as these may increase PA pressures and worsen cor pulmonale.

Airway

- In case of difficult airways, consider techniques with spontaneous respiration preservation (e.g., awake FOI).

Maintenance

- Consider pressure-controlled mode of ventilation, for poor lung compliance may require increased airway pressures to reach the adequate TV. Observe for spontaneous pneumothorax, especially in severe disease.
- Optimize volume status, while avoiding crystalloids overload; rather, use colloids. If possible, minimize blood products use to avoid lung injury.
- Avoid hypotension. Treatment may include low doses of vasopressin, which decreases PA pressures while maintain systemic BP, rather than norepinephrine, which increases PAP and promotes acidosis; phenylephrine, while safe at low rates (0.2–0.6 mcg/kg/min), may exacerbate pulm Htn in higher rates.
- For severe metabolic acidosis treatment, consider THAM solution. Bicarbonate should be avoided because of excessive CO_2 production and hypernatremia.
- Consider use of remifentanil. Caution with long-acting opioids.
- For muscle relaxation, short-acting agents titrated to effect may be preferred.
- Any of inhalational agents are adequate options.

Extubation

- Consider temporary postop mechanical ventilation, especially for upper abdominal and thoracic surgery, until stringent criteria are met.

Postoperative Period

- Pain management is critical for adequate respiration and to avoid worsening pulm Htn.

Adjuvants

- Bronchodilators, supplemental O_2, incentive spirometry may improve ability to wean.

Anticipated Problems/Concerns

- Increased risk of respiratory failure and complications, especially after upper abdominal and thoracic surgery.
- Pts with pulm Htn with or without cor pulmonale are at increased risk of cardiac complications.

Single (Including Common) Ventricle

Jamie McElrath Schwartz | Sinead Nyhan | Laeben Lester

Risk

- HLHS is the most common SV congenital cardiac malformation.
- HLHS accounts for 7.5% of newborns with CHD.
- Male predominance for HLHS.

Perioperative Risks

- Paradoxical emboli.
- Complications of chronic hypoxemia: Hyperviscosity, decreased coagulation factors and platelets
- Surgical shunts (narrowing of vessels anastomosed, obstructed shunts)
- Hypovolemia-induced poor pulm blood flow or shunt occlusion.
- Additional risks specific to anatomy and planned procedure.

Worry About

- Effect of changes in PVR, SVR, and cardiac function on blood flow, cardiac output, and O_2 saturation.
- Diastolic pressure and coronary perfusion.
- AV valve regurgitation.
- Systolic and diastolic dysfunction.
- Associated anomalies.
- Increasingly common to care for CHD and SV pts having noncardiac surgery who may be at various stages in the palliation repair process and may have comorbidities including protein losing enteropathies, plastic bronchitis, ventricular dysfunction, and arrhythmias.

Overview

- A wide variety of lesions are usually associated with atresia of the ipsilateral AV or semilunar valve resulting in SV physiology:
  - TA is the prototypic single left ventricle (see Tricuspid Atresia).
  - HLHS with mitral and aortic stenosis/atresia is the prototypic single right ventricle.
- Other anatomies include unbalanced AV canal, some double inlet or double outlet ventricles, and some heterotaxies.
- Initial lesion requires mixing of systemic and pulm venous return at ASD or VSD level. The SV output is divided between pulm and systemic circulations.
- SV anatomy may be associated with hypoplasia of a great vessel (pulm artery or aorta) and prior to initial palliation; systemic or pulm blood flow may be dependent on ductus arteriosus patency.
- Balance of blood flow in each Qp:Qs is governed by the relative resistance to flow as determined by both anatomic and vascular resistance considerations.
- Goal throughout all stages is to balance the Qp:Qs at 1:1.
  - With complete mixing, Qp:Qs at 1:1 results in sat of 75–80% at FiO_2 0.21.
- FiO_2, CO_2, and pH management can be used to manipulate the Qp:Qs.
- Qp:Qs > > 1 results in pulm overcirculation/pulm vascular congestion and potentially hypoperfusion to end organs.
- Qp:Qs < < 1 results in hypoxemia.

Etiology

- Incompletely understood and likely multifactorial. Has been associated with several genes (connexin protein 43, lesion at 11q23.3, cardiac homeobox transcription factor NKX2) and chromosomal abnormalities (Jacobsen syndrome, Turner syndrome, trisomy 18, trisomy 13).

Usual Treatment

- Series of palliative procedures with the goal of creating reliable systemic and pulm blood flow.
- Stage a connection of systemic venous return directly to pulm artery, dedicating the SV to systemic circulation.
- First, stable blood flow to systemic and pulm circulations are established and balanced.
  - For TA, a BT shunt is placed.
  - For HLHS, a stage I Norwood procedure is performed.
- For other SV lesions, BT shunt or PA banding as dictated by anatomy.
- Complete intracardiac mixing of blood is imperative.
- Stage I Norwood:
  - A neoaorta is created from hypoplastic aortic arch and native PA tissue, connecting the SV to systemic circulation.
  - A BT shunt provides pulm blood flow, connecting branch of neoaorta to ipsilateral pulm artery.
  - An atrial septectomy is performed to ensure complete intracardiac mixing of systemic and pulm venous blood.
- At completion of the stage I Norwood, the SV provides cardiac output to the systemic circulation via the neoaorta and the pulm circulation via the BT shunt.
- The second stage is the first of two procedures to direct systemic venous return to the pulm artery.
  - The SVC is connected to the ipsilateral PA, which remains connected to the PA confluence.
  - This procedure is referred to as a cavopulmonary connection, Bidirectional Glenn or hemi-Fontan, and is commonly performed around 6 mo of age.
  - Low PVR is necessary to promote pulm blood flow, which is passive.
- The final stage, Fontan completion, is typically done 18 mo-5 y.
  - The IVC blood is directed to the ipsilateral PA, either intracardiac via lateral tunnel or extracardiac via graft.
  - This effectively separates the circulations and reduces volume workload on SV; systemic venous return now flows passively to the PA without interposed pumping chamber.
  - A small fenestration from the IVC-PA conduit to the atrium is sometimes created. The fenestration ensures preload to the systemic circulation even when PA pressures fluctuate, maintaining cardiac output but at the expense of decreased O_2 sat via right-left shunt.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CHF	Dyspnea, tachypnea, feeding difficulties	S_3, rales, wheeze, enlarged liver, metabolic acidosis	CXR, pulse oximetry, ABG ECHO
	Hypoxia Arrhythmia	Dyspnea, tachypnea, feeding difficulties cyanosis	Cyanosis	CXR, pulse oximetry, ABG ECG
HEME	Polycythemia	See above	See above	Hgb, Hct

Key References: Barron DJ, Kilby MD, Davies B, et al.: Hypoplastic left heart syndrome, *Lancet* 374(9689):551–564, 2009; Yuki K Casta A, Uezono S: Anesthetic management of noncardiac surgery for patients with single ventricle physiology, *J Anesth* 25(2):247–256, 2011.

Perioperative Implications

Preoperative Preparation

- Depending on the stage of the palliative process (Norwood stage I, Glenn/hemi-Fontan, completion Fontan), optimize hemodynamics.
- Cardiac catheterization is typically performed prior to Glenn/hemi-Fontan to measure PVR and coil any collateral venous vessels.
- Higher O_2 sat can decrease O_2 delivery to the tissues by facilitating overcirculation to the lungs, particularly when pulm blood flow is via BT shunt.

Monitoring

- Arterial BP.
- CVP monitoring via IJ is controversial due to SVC thrombosis risk and implications for subsequent staging, which requires patency of these vessels.
- Consider TEE.

Preinduction/Induction

- Dependent on exact anatomy and stage of palliation.
- Induction technique should consider impact of PVR and SVR changes on myocardial, systemic, and pulm blood flow.

Airway

- ET intubation and PPV.
- Minimize intrathoracic pressures where possible to encourage pulm blood flow.

Maintenance

- IV or inhalational agents are acceptable.
- Body temperature as dictated by potential use of cardiopulmonary bypass.

Extubation

- Following stage I Norwood, pt requires mechanical ventilation for >2 d.
- Early extubation is recommended to facilitate pulm blood flow after stage II (Glenn or hemi-Fontan) or the completion Fontan. High intrathoracic pressure from PPV impedes venous flow to the pulm circulation, while negative intrathoracic pressure (spontaneous respiration) enhances flow.

Anticipated Problems/Concerns

- Overcirculation.
- Hypoxemia.
- New anatomy postprocedure will necessitate a reassessment of desired PVR and SVR to optimize flow to both circulations.
- Postop low cardiac output syndrome.

Sleep Apnea, Central and Mixed

Michael F. Roizen | Andreas M. Ostermeier

Risk

- Incidence USA is 3–12% of middle-aged adults (which has increased fourfold in last 15 y, presumably due to increase in obesity). The M:F ratio is 2–2.5:1; obstructive or mixed.
- Risk increases with male sex, upper middle age (55–64 y), obesity, and Hx of snoring with impaired daytime performance.
- In elderly, risk is 2× higher for African Americans.

Perioperative Risks

- Increased risk of central and mixed (central and obstructive) apnea. In mixed SAS, obstructive apnea component can mask central apnea.
- Risk for respiratory depression also in intubated, tracheotomized, and awake pts.
- Increased risk with sedative-hypnotic narcotics, postop with any form of pain relief.

Worry About

- See medical records for previous problems.
- Look for related medical disorders (e.g., cor pulmonale, cardiac arrhythmias, erythrocytosis, disordered cognition, daytime somnolence).
- Apnea possible even several h postop, especially after epidural anesthesia.
- When administering O_2, think of possible dependence of ventilation on hypoxic drive.

Overview

- Central sleep apnea implies failure of respiratory rhythmogenesis. In SAS pts, at least 30 periods of apnea, defined as cessation of airflow for ≥10 sec, are found during normal nocturnal sleep.
- Obstructive sleep apnea relates to a failed or inadequate respiratory activation of upper airway muscles, resulting in lack of airflow.
- In central apnea, hypoventilation persists despite relief of obstruction.
- Central apnea is unaccompanied by any respiratory effort, in contrast to obstructive sleep apnea.
- Related to central alveolar hypoventilation syndrome, also known as Ondine curse.

Etiology

- Central: Familial basis is evident in some cases; possible relation to neurologic disorders (e.g., encephalitis in childhood, damaged respiratory centers, autonomic neuropathy in diabetes)

- Mixed: Has obstructive component. Upper airway narrowing superimposed on coexistent abnormality of neurologic control or function of upper airway muscle tone or ventilatory control.
- Associated with obesity and nasal obstruction (polyps, rhinitis, deviated septum, acromegaly, hypothyroidism, Htn).

Usual Treatment

- CPAP or BiPAP; bring to hospital and OR/PACU.
- Tracheotomy and mechanical vent at night.
- Diaphragmatic pacing, especially at night.
- Surgery to remove obstruction
- For central/mixed apnea, additional medical treatment with protriptyline, progesterone.
- For mixed apnea, weight loss and physical aids.
- Avoid narcotics, benzodiazepines, and alcohol.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Obstructive apnea	Snoring, partner gives Hx of pt's awakening at night with grunts	Visualization of uvula and tonsillar pillars	
CV	Htn	Dyspnea at rest, DOE Poor exercise tolerance, angina	Cardiomegaly S_3/S_4 murmur	ECG, ECHO
RESP	Right-sided heart dysfunction, snoring, respiratory dysfunction, DOE	Awakening at night with grunts	Venous engorgement Rapid respiratory rate Cardiomegaly	SaO_2 supine ECG, CXR, ABG, Hct Polysomnogram, home sleep study
GI	Hepatic dysfunction Full stomach T2DM	Jaundice, bleeding disorders, ascites, heartburn, hiatus hernia, polydipsia, polyuria	Hepatomegaly, ascites, spider nevi, jaundice	LFTs, PT, PTT Fasting glucose
ENDO	Obesity Hypothyroidism Acromegaly		Mental function reflexes BMI	Free T_4 estimate TSH, GH levels
HEME	Polycythemia		Plethora, clubbing, cyanosis	O_2 sat, Hct
CNS	Disturbed sleep, impaired daytime performance, morning headache, memory problems, irritability	Daytime sleepiness, complaints of disrupted sleep Ask for encephalitis, autonomic neuropathy, brainstem damage		Polysomnogram, home sleep study

Key References: Ostermeier AM, Roizen MF, Hautkappe M, et al.: Three sudden postoperative arrests associated with epidural opioids in patients with sleep apnea, *Anesth Analg* 85(2):452–460, 1997; Somers VK, White DP, Amin R, et al.: Sleep apnea and cardiovascular disease: an American Heart Association/American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research, *Circulation* 118(10):1080–1111, 2008; American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea: Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea, *Anesthesiology* 120(2):268–286, 2014.

Perioperative Implications

Preoperative Preparation

- Take sleep Hx, if possible, from bed partner.
- If a question of sleep apnea, use home sleep apnea tests (helmet or wrist; several distinct types now exist) as a screen. Sleep lab unnecessary for this screen. If positive, refer to sleep lab preop.
- Avoid preop sedation with benzodiazepines and narcotics.
- Examine airway carefully.
- Consider metoclopramide 10 mg, cimetidine 300 mg PO the night before and IV preop.
- Assess myocardial and volume status.
- Initiate CPAP or BiPAP therapy over periop period, and in recovery room.

Monitoring

- Routine; consider arterial line.
- UO, possible CVP or PA catheter, if volume status likely to be significantly altered.

Airway

- Airway control necessary if prominent central component and sedation mandatory.
- Awake, sitting, fiberoptic intubation may be indicated if difficulty anticipated.

Induction

- Pt may need to remain semisitting if SaO_2 drops when supine. Preoxygenation should be complete throughout lungs.

Maintenance

- Oxygenation may deteriorate with upper abdominal surgery or increased intraabdominal pressure.
- Consider the use of short-acting substances (e.g., propofol, remifentanil).
- Minimize postop sedation.

Extubation

- Extubate as soon as pt maintains normocapnia and responds to command.
- Consider close monitoring after extubation.

Adjuvants

- Initial dose of induction agent and narcotics calculated on a mg/kg basis, and muscle relaxants calculated on estimated lean body mass.
- Subsequent doses of sedatives, hypnotics, relaxants, and narcotics calculated on estimated lean body mass.
- RA if physically possible and if pt can use accessory muscles to help with breathing.

Postoperative Period

- Pain control with opioids only when NSAIDs and/or RA is contraindicated and/or insufficient, as (sudden) complete pain relief may increase risk of respiratory arrest.
- Some think epidural or narcotics are indicated, and others think these are relatively contraindicated.
- Extended respiratory monitoring.
- Stabilize ABG to adequate levels.
- Pain control necessary; PCA acceptable in sleep apnea, but not in continuous mode.
- Consider DVT prophylaxis if pt is overweight.

Anticipated Problems/Concerns

- Respiratory insufficiency and pneumonia postop; use devices and/or CPAP in immediate and long-term preop and postop periods.
- Postop thromboembolic phenomena.
- If problems occur, inform pt before discharge with written instructions, especially for further anesthetic interventions.

Sleep Apnea, Obstructive

Michael F. Roizen | Charles Ahere | Claude Brunson

Risk

- Incidence in USA is 3–15% of the whole population (increased fourfold in last 15 y, presumably due to increase in obesity).
- M:F ratio: 2.5:1.
- Race with highest prevalence: Unknown.

Perioperative Risks

- Increased risk of pulm Htn, RV failure, and systemic Htn.
- Some pts may be polycythemic and have an increased risk of CVA.
- Complications associated with obesity and craniofacial and upper airway soft tissue abnormality.
- Increased risk in supine position of sudden arrest postop.

Worry About

- Airway obstruction with sedating drugs; need for awake, sitting intubation without sedation if obstruction occurs when supine.
- Increased sensitivity to sedating drugs.
- Difficult airway management; mask ventilation and intubation.
- Aspiration risk in the morbidly obese.
- Postop airway obstruction or resp depression.
- Nasal obstruction from NG tubes (e.g., may lead to resp compromise).
- Have pt bring CPAP or other apparatus with them to hospital and to OR/PACU.

Overview

- Apnea refers to cessation of airflow at the mouth for >10 sec.
- Sleep apnea refers to repetitive episodes of upper airway occlusion during sleep, often with O_2 sat to 85% and nearly always associated with loud snoring. Episodes of apnea often terminate with a snort or gasp.
- Upper airway obstruction from relaxation of muscles of oropharynx.
- Frequent periods of apnea lead to hypoxia and hypercarbia, which could lead to cor pulmonale.
- Polycythemia may result from chronic hypoxia.
- Nocturnal cardiac arrhythmias are common.
- Monitor depth and quality of sleep along with cardiopulmonary variables in those with severe symptoms.
- Another name is Pickwickian syndrome, associated with morbid obesity (see also Morbid Obesity).

Etiology

- Cessation of airflow due to complete obstruction of upper airway.
- Narrowing due to enlarged tonsils, adenoids, uvula, low soft palate, or craniofacial abn superimposed on coexistent abn of upper airway muscle tone and/or neurologic control.
- Obesity exacerbates upper airway obstruction.
- Structural abnormality such as tonsillar hypertrophy, enlarged tongue, and micrognathia may contribute to airway obstruction.

Usual Treatment

- Weight loss in overweight pts
- Tobacco cessation
- Avoidance of alcohol and sedatives before sleep; avoidance of sleep deprivation
- Nasal CPAP; BiPAP
- Physical aids such as devices to detect and prevent snoring; keep pt off back while sleeping (e.g., tennis ball sewn on nightshirt)
- Nasopharyngeal or oropharyngeal airway and oral appliance therapy.
- Uvulopalatopharyngoplasty
- Tracheotomy in extreme cases
- Electrophrenic pacing for central sleep apnea

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Obstructive apnea	Snoring, partner gives Hx of pt's awakening with grunts at night	Visualization of uvula and tonsillar pillars	
CV	Htn	Dyspnea at rest and on exertion Poor exercise tolerance	Rapid resp rate Increased BP, cardiomegaly	ECG, ECHO
RESP	Right-sided heart dysfunction Restrictive dysfunction	Snoring, partner gives Hx of pt's awakening with grunts at night DOE	Venous engorgement, rales, S_3 and S_4, cardiomegaly	Pulse oximetry on room air while supine ECG, CXR, ABG, Hct, polysomnogram, overnight sleep study
GI	Hepatic dysfunction Full stomach T2DM	Angina Jaundice, bleeding disorders, ascites Heartburn, hiatus hernia Polydipsia, polyuria	Hepatomegaly, ascites, spider angiomas, jaundice	LFTs, PT, PTT Fasting glucose
ENDO	Obesity Hypothyroidism Acromegaly		Mental function Reflexes BMI	Free T_4 estimate TSH level, GH level
HEME	Polycythemia		Plethoric clubbing, cyanosis	Hypoxemia Hct
CNS	Disturbed sleep Memory problems Irritability	Daytime sleepiness Complaints of disrupted sleep		Polysomnogram Overnight sleep study

Key References: Fletcher EC, Proctor M, Yu J, et al.: Pulmonary edema develops after recurrent obstructive apneas, *Am J Respir Crit Care Med* 160(5 Pt 1):1688–1696, 1999; American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea: Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea, *Anesthesiology* 120(2):268–286, 2014.

Perioperative Implications

Preoperative Preparation

- Avoid sedatives.
- Assess CV status.
- Histamine H_2 blockers, metoclopramide, and antacids for morbidly obese pts.
- Have pt bring CPAP, BiPAP, or other apparatus with them to hospital and to OR/PACU.

Monitoring

- Routine.
- Volume status if RV dysfunction present.
- Consider arterial cath if BP cuff does not fit or takes too long to inflate.

Airway

- Airway obstruction with induction; see HEENT in the Assessment Points table.
- Awake intubation in those with potentially difficult airway.
- Consider elevating shoulders on bolsters.

Induction

- Airway obstruction
- Exacerbation of pulm Htn by hypoxemia and hypercarbia

Maintenance

- Volume status may change precipitously with position change.
- Oxygenation may deteriorate with upper abdominal surgery or increased abdominal pressure.

Extubation

- Only when pt is fully awake.
- Airway obstruction from residual anesthetics.
- Avoid opioids and sedatives.
- Monitor for airway obstruction and apnea.

Adjuvants

- Very sensitive to CNS-depressant drugs.
- CPAP, BiPAP, or other apparatus for use in PACU and hospital or home recovery periods.

Anticipated Problems/Concerns

- Airway obstruction at induction and after extubation.
- 13% risk of periop complications, especially of pneumonia; avoid by minimal sedation, appropriate pain control, and early ambulation.
- Worsening pulm Htn and right-sided heart failure.
- Aspiration risk in the morbidly obese.
- Postop thromboembolism; consider routine 162 mg of aspirin beginning preop, or other methods to prevent DVT.
- Poor motivation resulting in poor ambulation. Avoid by intensive preop teaching and postop coaching.

Smallpox

Ray Munroe | Lee A. Fleisher

Risk

- Declared eradicated worldwide in 1980.
- Two repositories hold the variola virus: VECTOR in Koltsovo, Novosibirsk, Russia, and the CDC in Atlanta, Georgia, USA.
- Potential agent of bioterrorism.
- Vaccinations are not administered to the general public.
  - In 2007, ACAM2000, the newest version of vaccine made of vaccinia virus, became part of the USA stockpile of smallpox vaccines.

Perioperative Risks

- Hemodynamic compromise from dehydration and/or sepsis

Worry About

- Facility and provider contamination

Overview

- Virus enters respiratory tract, migrates into pulmonary lymph nodes, and spreads into the bloodstream.
- Incubation period is 7–17 d; at this point, not contagious.
- Prodromal phase is 2–3 d. Abrupt, severe headache, backache, and fever; possibly contagious.
- Rash develops, increases, and lasts for weeks; this is contagious:
  - Mucous membrane enanthemas, then skin lesions.
  - Centrifugal spread.
  - Starts on extremities and spreads to trunk.
  - Deep-seated, firm, round pustules, leading to rupture and necrosis. leading to scabs.
  - Lesions all in same stage of development.
- Contagious until resolution of scabs.
- Approximate 30% mortality; death primarily from sepsis.
- Must be distinguished from chicken pox (varicella):
  - No prodrome.
  - Lesions centripetal spread.
  - Start on trunk.
  - Superficial vesicles.
  - Lesions in different stages.

Etiology

- Caused by *Orthopoxvirus variola*
- Human vector only
- Transmission via prolonged, inhalational contact with infected bodily fluid or contaminated material

Usual Treatment

- No direct treatment.
- Early stage: Vaccination
- All stages: Supportive (hydration, nutrition).
- Treat secondary infections.
- Prevent further viral contraction: Use respiratory and contact precautions, pt isolation, negative pressure room, and quarantine exposed persons.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Oral/mucosal enanthemas Rash Corneal ulceration (rare)	Centrifugal lesion spread Ocular pain	Pox lesions: Vesicular or pustular	CBC, differential, virus titer, PCR Ophthalmology exam
RESP	Respiratory viral infection Bacterial pneumonia	Often asymptomatic		Virus titer Sputum smear for Guarnieri bodies CXR, CBC
CV	None			
GI	Occasionally abdominal pain and/or diarrhea with prodrome			
CNS	Constitutional symptoms Encephalitis	Sudden onset, severe headache, backache, malaise	Temp >38.1° C Delirious	CBC, differential
HEME	Disseminated intravascular hemolysis	Mucosal bleeding	Epistaxis, gastrointestinal bleeding, hemoptysis, subconjunctival and/or gum bleeding	CBC, peripheral smear, D-dimer, PT, aPTT, fibrinogen
METAB	Dehydration Malnutrition	Poor oral intake	Dry mucus membranes, tenting skin, subcutaneous fluid accumulation, massive skin desquamation	Electrolytes, Ca^{2+}, Mg^{2+}, albumin, prealbumin

Key References: Breman JG, Henderson DA: Diagnosis and management of smallpox, *N Engl J Med* 346(17):1300–1308, 2002; Schumacher J, Runte J, Brinker A, et al.: Respiratory protection during high-fidelity simulated resuscitation of casualties contaminated with chemical warfare agents, *Anaesthesia* 63(6):593–598, 2008; Neligan P: Smallpox. In Fleisher LA, editor: *Anesthesia and uncommon disease*, ed 6, Philadelphia, PA, 2012, Saunders, pp 392–393.

Perioperative Implications

Preoperative Preparation

- Anesthesiologists would be among the first responders to those affected by a biologic terrorist attack.
- Pt resuscitation and any airway management would need to be administered with special attention to provider respiratory protection, including contact precautions and wearing a N95 mask.
- Vaccinate providers as indicated by CDC guidelines.

Monitoring

- Consider arterial line or CVP catheter as indicated.

Airway

- Caution with provider exposure to airway secretions
- Gentle manipulation of airway if friable oral lesions are present

Preinduction/Induction

- Pt likely to be extremely dehydrated; hydrate before induction and/or gentle induction.

Maintenance

- Manage as appropriate for surgical procedure.
- Adequate hydration; continue TPN if being nutritionally supported.
- Dispose of all used materials in appropriate biohazard containers.

Extubation

- Avoid excessive coughing to minimize viral particulate spread.

Postoperative Period

- Continue medical support.
- Diligence in washing hands and returning of soiled scrubs by personnel.

Anticipated Problems/Concerns

- Strict infection control needs to be continued.
- Follow CDC recommendations if provider exposed.

Spasmodic Torticollis

Todd A. Bromberg | Richard Boortz-Marx | Lee A. Fleisher

Risk

- Estimated prevalence of 9 cases per 100,000.
- ST, also known as cervical dystonia, is the most common form of focal dystonia.
- Peak incidence is in the fifth decade.
- Two times more common in females.
- 80% of cases are sporadic or primary.
- 20% of cases are secondary to an underlying brain lesion or trauma.

Perioperative Risks

- Dysphagia
- Aspiration
- Consider comorbid neurologic problems such as seizures, cranial nerve palsies, hemiplegia, and so forth.

Worry About
- Difficult pt positioning secondary to sustained muscle contractions
- Difficult intubation as a result of poor extension of the cervical spine and diminished mouth opening

Overview
- ST is defined as twisting of the neck caused by involuntary muscle contractions.
- Idiopathic ST is a slowly progressive disease that manifests between the third and fifth decades. Idiopathic ST is likely caused by abn of the basal ganglia circuitry.
- Dystonia typically progresses over 3–5 y before it plateaus.
- Pain occurs in 75% of pts and contributes to disease disability.
- If ST occurs acutely, it is necessary to rule out causes related to trauma, medications (metoclopramide, haldol, phenothiazines), intracranial abnormalities (tumors, AVMs, hemorrhages), and neck pathology (retropharyngeal abscess).
- The sternocleidomastoid and trapezius muscles are most commonly involved, but extracervical dystonia may occur in 20% of pts.
- Jerking of the head and head tremors are common features.
- Head positioning determines the type of torticollis:
  - Rotational torticollis: Rotation of the head around the long axis of the neck.
  - Anterocollis: Head tilts forward with neck flexion.
  - Retrocollis: Head tilts backward with neck extension.
  - Laterocollis: Head tilts to one side with the ear pulled toward the shoulder.

Etiology
- A genetic component probably contributes to the development of ST since it is a familial pattern.
- Trauma, medications, and intracranial pathology can cause focal dystonic reactions such as torticollis.

Usual Treatment
- Chemical denervation with botulinum toxin is the mainstay of therapy. Botulinum toxin is injected into overactive muscles in the neck that are responsible for the dystonia. It usually takes a week to take effect and lasts up to 3 mo before a repeat injection must be given.
- Pharmacologic therapy with anticholinergics, benzodiazepines, Parkinson medications, and baclofen are used as adjuncts to botulinum toxin.
- Surgical options include mechanical denervation of affected muscles, deep brain stimulation, and intrathecal baclofen if spasticity is prominent.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT	Head deviation	Twisting, pulling sensation	Hypertrophic SCM and trapezius
RESP	Restrictive lung disease	Dyspnea	
GI	GERD	Food regurgitation; pain after meals	
CNS	Diplopia Difficulty with transfers Aspiration risk	Vision deficits Coughing with food Use of walker, cane, wheelchair	Abnormal eye movements. facial droop, depressed gag, tremor, spasticity of muscles, weakness

Key References: Mac TB, Girard F, McKenty S, et al.: A difficult airway is not more prevalent in patients suffering from spasmodic torticollis: a case series, *Can J Anaesth* 51(3):250–253, 2004; Patel S, Martino D: Cervical dystonia: from pathophysiology to pharmacotherapy, *Behav Neurol* 26(4):275–282, 2013.

Perioperative Implications
Preinduction/Induction/Maintenance
- Routine considerations.
- Consider the use of nondepolarizing muscle relaxants.
- NMB may have no effect on muscle contractures, which are permanently shortened muscles that result from structural muscle changes.
- Anticipate the use of fiberoptic intubation.

Preoperative Considerations
- Consider preop injections of Botox at least 1 wk prior to anesthesia.
- It is imperative to evaluate the range of cervical spine extension, maximal mouth opening, and integrity of the temporomandibular joint.

Monitoring
- Routine

General Anesthesia
- Propofol is likely to be safe with all dystonias.
- GA with thiopental, succinylcholine, atracurium, isoflurane, and fentanyl is thought to be safe in spasmodic torticollis.

Regional Anesthesia
- Limited reports but thought to be safe
- Postop period
- Risk of aspiration

Anticipated Problems/Concerns
- Anticipate difficult intubation secondary to fixed head turning from muscle contractures that do not respond to muscle relaxants.
- Be aware of cervical spine pathology that may result from prolonged torticollis.
- Neurologic conditions such as cranial nerve dysfunction and seizure disorders may accompany secondary ST caused by an underlying intracranial lesion.
- ST can cause head tremors, which should not be confused with hyperkinetic movement disorders.

Spinal Cord Injury

Janelle B. Snoddy | Lee A. Fleisher

Risk
- In USA, trauma is the number one cause.
- Approx 10,000–12,000 cases per y.
- Males (80%) primarily affected.
- Motor vehicle collisions, falls, violence (GSW), sports-related injuries, hematoma, and transverse myelitis most common.

Perioperative Risks
- Hypotension, particularly in acute injury resulting in neurogenic shock and concurrent hypovolemia
- Autonomic instability, which may result in severe cardiopulmonary compromise.

Worry About
- Autonomic dysreflexia (T6 or above, but as low as T12 in some; usually seen 1–6 mo after injury)
- Hypoventilation leading to acute respiratory compromise and chronic infections
- Irregular thermoregulation

Overview
- Injury to the spinal cord at level of the cervical or thoracic vertebrae resulting in loss of underlying sympathetic stimulation, unopposed vagal tone, and sensory and motor deficits.
- Cervical spine and thoracolumbar junction (T11–L2) most susceptible to injury.
- Lower lumbar regions also susceptible to injury, although they do not usually result in neurologic injury.
- Neurologic injuries rare from sacral or coccygeal fractures.
- Acute (<3 wk): Neurogenic shock, urinary/fecal retention, vagal predominance, and hyperesthesia.
- Chronic (>6 mo) injury: Hyperreflexia and spasticity.
- Upregulation of Ach receptors from immobilization results in increased resistance to NDMBs and increased potassium release with succinylcholine.

Etiology
- Direct mechanical injury usually from traumatic insult leading to hemorrhage, edema, and ultimately spinal cord ischemia.
- Release of inflammatory mediators and membrane-destabilizing enzymes leading to disruption of electrophysiologic pathways and tissue degeneration.
- Complete lesions result in total loss of sensory and motor function below level of injury.
- Incomplete lesions result in maintenance of some function below primary level of injury and some degree of recovery.
- Above T1 = quadriplegia, below T2 = paraplegia, usually.

Usual Treatment

- Assessment of pt via advanced trauma life support protocol with focus on spinal stabilization and immobilization on board and/or cervical collar to prevent further injury.
- Consider timely surgical intervention if appropriate; injury is typically irreversible after 48 h.
- Maintain adequate spinal cord perfusion via adequate fluid resuscitation and vasopressors, if needed.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Neurologic deficits, autonomic dysreflexia, altered mental status, neurogenic shock, spinal shock	Weakness, headache, hyperhidrosis	Thorough neuro exam	Review imaging
HEENT	Cervical cord injury, inability to tolerate secretions	Pain, choking, drooling, weakness	Neurologic exam, c-collar/halo vest	Early intubation with in-line stabilization, CT scan
RESP	PE, hypoventilation, pulm edema	SOB, tachypnea, hemoptysis	Decreased chest rise/ breath sounds, use of accessory respiratory muscles	CXR, ABG, PFTs
CV	Hypotension, conduction abnormalities, low baseline BP	Dizziness, nausea, fatigue	Orthostasis	ECG, invasive BP monitoring
GI	GI atony, GI bleeding/stress ulcer, ileus	Nausea, heartburn, melena, abdominal pain	Abdominal TTP, bloody stool, absent bowel sounds	NGT, GI prophylaxis
RENAL	Frequent UTI, renal dysfunction, lyte disturbance, priapism	Dysuria, hematuria	Urinary cath (often suprapubic)	BMP
HEME	Anemia, hypercoagulability	Dizziness, easy bleeding/bruising, h/o blood clot	Visible purpura, bruises, swollen/ tender limb(s)	VTE prophylaxis CBC, coagulation, US if warranted
MS	Bone fractures, decubitus ulcers, skeletal muscle spasticity/contractures	Chronic muscle spasms, areas of skin breakdown	Thorough MS exam	Imaging if necessary

Key References: Stevens RD, Bhardwaj A, Kirsch JR, et al.: Critical care and perioperative management in traumatic spinal cord injury, *J Neurosurg Anesthesiol* 15(3):215–229, 2003; Oropello JM, Mistry N, Ullman JS: Spinal injuries. In Hall JB, Schmidt GA, Kress JP, editors: *Principles of critical care,* ed 4, New York, 2015, McGraw-Hill.

Perioperative Implications

Preoperative Preparation

- Perform thorough neurologic examination.
- Ensure adequate volume resuscitation.
- Strongly consider RA if appropriate.

Monitoring

- Standard ASA monitors.
- May consider invasive hemodynamic monitoring, including arterial line and CVP if instability anticipated.
- Monitor temp closely, as hypothermia/hyperthermia may occur.

Airway

- Consider advanced airway techniques (i.e., fiberoptic intubation/video laryngoscopy) if neck extension is limited due to cervical injury or c-collar/ halo vest.

Preinduction/Induction

- Rapid sequence intubation, particularly in acute spinal cord injury, due to high risk of respiratory compromise, gastric atony/dilation, and aspiration.
- Be sure pt is adequately anesthetized prior to endotracheal intubation to avoid autonomic dysreflexia.
- Avoid significant hypotension.
- Pt may have increased resistance to NDMBs.
- Avoid succinylcholine, as it may result in severe bradycardia and hyperkalemia.
- Atropine should be administered if succinylcholine must be used.

Maintenance

- Keep MAP >80 mm Hg when possible for adequate perfusion to spinal cord.
- Maintain adequate analgesia to avoid autonomic dysreflexia.
- Have short-acting vasopressors and antihypertensives readily available.

Extubation

- Use caution.
- Depending on level lesion, and risk respiratory muscle paresis and/or paralysis, long-term mechanical ventilation may be indicated.

Adjuvants

- Consider body warmer and/or warmed IV fluids.
- Careful padding of pressure points/decubitus ulcers.
- NGT for decompression, given risk of gastric atony.

Postoperative Period

- Due to increased risk of hypoxia, pt should receive continuous supplemental oxygen and pulse oximetry monitoring, aggressive pulmonary toilet.
- Low threshold for reintubation, particularly in higher lesions.
- Increased risk of visceral pain, phantom pain, and muscle spasms.

Anticipated Problems/Concerns

- Autonomic dysreflexia; if left untreated, can lead to myocardial ischemia and potentially cardiac arrest.
- Make it a priority to minimize inciting factors.
- Pts are at increased risk of developing VTEs, which may lead to pulm embolism.
- Pt should be on VTE prophylaxis and GI ulcer prophylaxis if there is no contraindication.

Spinal Muscular Atrophy

Karim El Harchaoui

Risk

- Incidence: 7.8 -10:100,000 live births.
- Estimated panethnic disease frequency: ~1:11,000.

Perioperative Risks

- Airway: Intubation can be difficult.
- Pts may need postop respiratory support.
- Anesthetic risk varies significantly between the different types of SMA.

Worry About

- Pts may display increased sensitivity and prolonged effect of neuromuscular blockers.
- Postop respiratory depression could be catastrophic.
- Concomitant pulmonary disease and bulbar dysfunction.
- Gastroesophageal reflux.
- Prolonged effects of nondepolarizing neuromuscular blockers (even after reversal).
- Neuromuscular monitoring can be unreliable.

Overview

- SMA is an autosomal recessive neuromuscular disease.
- The disorder leads to degeneration of the anterior horn cells of the spinal cord, which causes muscle weakness.
- The rate of progression varies between pts and is classified in four categories:
  - SMA I (Werdnig-Hoffman disease): Onset of symptoms before 6 mo of age
  - SMA II (Dubowitz type): Onset between 6 and 18 mo
  - SMA III (Kugelberg Welander disease): Present later in childhood
  - SMA IV (adult type): Onset during middle or late age
- Prognosis for long-term survival depends on the type and ranges from neonatal death to onset of weak muscles in adulthood.
- Respiratory failure is the major cause of mortality.
- Scoliosis and chest wall muscle weakness may predispose to pulmonary dysfunction.
- Normal intellectual and emotional capacity.

Etiology

- Autosomal recessive inheritance can occur with deletions or mutations in the survivor motor neuron genes located on chr5q13.
- The loss of full-length SMN protein leads to degeneration of anterior spinal motor neurons and, in severe cases, degeneration of brainstem nuclei.
- Degeneration of spinal anterior neurons and brainstem nuclei correspond to a range of clinical characteristics, including global hypotonia, pulmonary insufficiency, and autonomic and bulbar dysfunction.

Usual Treatment

- There is no cure for SMA.
- Supportive treatment as required, including physiotherapy and orthopedic intervention, to prevent contractures and maximize respiratory function.
- Low threshold for antibiotic use during acute illnesses due to the risk of pneumonia.

Classification of Spinal Muscular Atrophy

Type	Age at Onset	Highest Motor Milestone Achieved	Lifespan Without Treatment	Symptoms	Affected Organ
Type I Werdnig-Hoffman disease	Birth–6 mo	Never sits unsupported	<2 y	Progressive muscle weakness, respiratory failure, hypotonia, reduced bulbar function	Muscular: Respiratory
Type II Dubowitz disease	6–12 mo	Sits independently, never stands or walks	70% reach adulthood	Progressive onset of proximal limb weakness in infancy Legs > arms Scoliosis Joint contractures	Muscular: Kyphoscoliosis Joint contractures
Type III Kugelberg-Welander disease	>18 mo	Stands and walks	Normal lifespan	Onset of proximal weakness during childhood Legs > arms Scoliosis Increased risk of fractures	Muscular: Joint problems
Type IV Adult SMA	>5 y to mostly >30 y	Normal	Normal	Onset of proximal leg weakness in adulthood	Muscular

Key References: Islander G: Anesthesia and spinal muscle atrophy, *Paediatr Anaesth* 23(9):804–816, 2013; Darras BT: Spinal muscular atrophies, *Pediatr Clin North Am* 62(3):743–766, 2015.

Perioperative Implications

Preoperative Preparation

- Preop pulm evaluation and pulm function testing.
- Evaluate intubation conditions.
- Start air-stacking techniques preop.
- Make a preop and postop plan. Pt may require postop ventilator support.

Monitoring

- When nondepolarizing muscle relaxants are used, the effect should be monitored carefully both clinically and with a monitor of neuromuscular transmission and muscular contraction.
- Consider ABG.

Airway

- Difficult intubation can occur due to limited mobility of the cervical spine and reduced mouth opening.
- Pt may present with artificial ventilation (NIV).
- Awake fiberoptic intubation could be the technique for intubation in pts with restricted neck movements.

Preinduction/Induction

- No specific anesthetic drug is recommended.
- Laryngeal mask may be appropriate in superficial surgery.
- Peripheral neural blockade may be useful.
- Avoid succinylcholine due to the risk of inducing rhabdomyolysis and hyperkalemia.
- Nondepolarizing muscle relaxants are suitable but should be titrated carefully since sensitivity to these drugs appears to vary.
- Approach when choosing anesthetic techniques and agents:
  - Minimize modifications of chest wall dynamics due to residual muscle relaxants effect or high level of neural axis blockade.
  - Avoid excessive depression of central respiratory drive.

Maintenance

- Both TIVA and inhalation agents may be used.
- Pts with SMA are not at increased risk for malignant hyperthermia.
- Short-acting opioids are suitable for intraop use.
- Continuous infusion of local anesthetic solutions via peripheral nerve block cath should be considered as safer alternatives to systemic opioids.
- Wound infiltration anesthesia is recommended whenever possible.

Extubation

- Muscle strength must be evaluated before extubation, not only with train-of-four stimulation but also clinically.
- Reverse neuromuscular blockade with sugammadex.

Postoperative Period

- Pts with SMA I need postop ventilator support.
- Some pts with SMA II and III will require respiratory support during acute illness or in advanced disease; NIV for bridging from intubation to spontaneous breathing.
- Use oxygen with caution because too much oxygen can mask hypoventilation due to muscle weakness.
- Postop pain management must be individualized and multimodal. Acetaminophen and ibuprofen are useful.

Anticipated Problems/Concerns

- Opioid-induced respiratory depression is dangerous in SMA pts with weak muscles. Careful monitoring is mandatory.
- The major concern related to the response from anesthesia is prolonged impairment of neuromuscular function and suppression of central respiratory drive, which can compromise the limited pulm reserve leading to acute respiratory failure.
- Neuraxial anesthesia can be difficult or unreliable due to altered spine anatomy (severe scoliosis).

Stevens-Johnson Syndrome

Lauren M. Nakazawa | Lee A. Fleisher

Risk

- Incidence of SJS and TEN, a more severe variant of SJS, is 2–7 cases per million per y.
- Incidence around 100 times higher in the HIV-positive population.
- More common in women.
- Affects all age groups.

Perioperative Risks

- High risk for infection
- Hypovolemia
- Cutaneous, mucosal, and ocular injury
- Respiratory failure requiring mechanical ventilation in around 25% of pts

Worry About

- Sepsis and septic shock
- Fluid and lyte imbalances
- Development of multiorgan failure
- Disease recurrence if culprit drug is readministered

Overview

- Severe cutaneous reaction with epidermal necrosis and detachment in conjunction with mucosal and conjunctival involvement.
- SJS and TEN fall along a disease continuum. SJS is less severe, involving <10% total BSA. TEN involves >30% BSA, and SJS-TEN overlap involves 10–30%.
- Clinical presentation:
  - Prodrome: Fever, flu-like symptoms (malaise, myalgia, arthralgia), skin pain/tenderness, oral pain, photophobia, and conjunctival burning can be early signs of mucosal involvement.
  - Cutaneous lesions: Diffuse erythema or erythematous macules starting on trunk and face and developing central necrosis and bullae formation with eventual sloughing off of epidermis and exposed dermis.
  - Mucosal involvement in 90% of pts.

- Mortality from SJS is around 5–10% and increases to 30% or more for TEN.
- Mortality primarily from sepsis, respiratory failure, and multiorgan dysfunction.
  - Prognosis worse with advanced age and greater BSA involvement.
  - Prognostic scoring system, called SCORTEN, can estimate pt survival.

Etiology

- Leading causes of disease are medications, followed by infections
- Medications most commonly implicated include allopurinol, anticonvulsants (lamotrigine, phenytoin, carbamazepine, phenobarbital), sulfonamide antibiotics, and oxicam NSAIDs.
- Reactions to medications occur in early treatment, typically occurring within the first 2 mo of initiation.
- Infectious etiologies: *Mycoplasma pneumoniae*, cytomegalovirus.
- Pathogenesis not completely understood; keratinocyte apoptosis attributed to cytotoxic T cells and natural killer cells through release of cytokines and cytotoxic proteins (granulysin, Fas-ligand, perforin, TNF-alpha).

Usual Treatment

- Depending on severity of disease and pt comorbidities, consider transfer to burn unit or ICU.
- If medication is suspected trigger of disease, attempt to identify and discontinue culprit drug.
- Similar to pts with major burns, treatment mainly consists of supportive care:
  - Wound care and eye care.
  - Pain management.
  - Fluid resuscitation, thermoregulation, and correction of electrolyte imbalances.
  - Nutritional support.
  - Monitoring for and treatment of superinfections.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Conjunctivitis, corneal ulceration Stomatitis, mucositis, pharyngeal erosions	Eye pain, photophobia Oral pain, odynophagia, impaired oral intake	Purulent discharge, corneal ulceration Oral/mucosal friability	Obtain baseline ophthalmologic exam
RESP	Erosions of trachea and bronchi Respiratory failure (pulm edema, pneumonia, infiltrates)	Dyspnea, cough, hemoptysis, hypoxemia	Tachypnea, pulm. consolidation, rales	CXR, CT scan ABG, bronchoscopy
CV	Hypovolemia Sepsis and septic shock	Dizziness, decreased urine output Lethargy, confusion	Tachycardia, hypotension, oliguria Fever	BP, CBC/BMP, lactate, ECG Blood culture—bacteremia (especially with *Staphylococcus aureus, Pseudomonas aeruginosa*)
GU	Urethritis Genital erosions	Difficulty voiding, dysuria Genital pain	Urinary retention Vulvar/vaginal bullae	Bladder scan, UA/culture Early gynecologic exam
HEME	Anemia Leukocytosis	Fatigue	Pallor, tachycardia Fever	CBC, differential Blood culture, CXR, urine culture, thorough dermatologic exam
METAB	Electrolyte abnormalities Insulin resistance Hypoalbuminemia			CMP Albumin

Key References: Rabito SF, Sultana S, Konefal TS, et al: Anesthetic management of toxic epidermal necrolysis: report of three adult cases, *J Clin Anesth* 13(2):133–137, 2001; Saeed H, Mantagos IS, Chodosh J: Complications of Stevens-Johnson syndrome beyond the eye and skin, *Burns* 42(1):20–27, 2016.

Perioperative Implications

Preoperative Preparation

- Correct preexisting electrolyte imbalances.
- Ensure adequate fluid resuscitation, as increased water loss from exfoliated skin can occur.
- Anticipate challenges with vascular access.
- Aim to minimize further cutaneous injury by placing soft foam or gel padding on OR table.
- Maintenance of normothermia is a challenge; transport pts to and from the OR with warm blankets and increase ambient OR temperature.

Airway

- Minimize upper airway instrumentation.
- Use extreme caution with friable oral and pharyngeal mucosal surfaces.
- Avoid nasal airway.

Preinduction/Induction

- Lubricate face and face mask prior to preoxygenation, and apply face mask with gentle pressure.
- Skin trauma can occur from tape, blood pressure cuffs, tourniquets, and adhesives (ECG leads, securing IV catheters).
- Use soft padding under blood pressure cuffs, nonadhesive pulse oximeters, and limit use of tape to secure IV or intra-arterial catheters. (Consider suturing in place or using gauze wrap.)
- Administer prophylactic antibiotics appropriate to surgical procedure; routine systemic antibiotic therapy not recommended in SJS or TEN unless there is evidence of superinfection.
- Similar to burn injured pts, SJS/TEN pts at risk for hyperkalemia if given succinylcholine.
- Meticulous ocular care and lubrication with eye drops or ointments.
- Anticipate difficulty securing and stabilizing endotracheal tube.

Maintenance

- Maintain normothermia; pts prone to heat loss from epidermal loss.
- Minimize conductive, convective, and evaporative heat loss by maintaining warm OR temp, using warming blankets, fluid warmers, and wrapping extremities with thermal insulation.
- Respiratory mucosal sloughing leading to tracheal or bronchial obstruction can occur and be life threatening; consider fiberoptic scope in the OR to aspirate bronchial casts and assess airway involvement.
- Monitor for adequate fluid resuscitation.

Extubation

- Use care with oropharyngeal suctioning to avoid further mucosal damage.
- Decision to extubate or not should be based on degree of airway involvement and intraop course.

Postoperative Period

- Increased susceptibility to infection
- Pain management

Anticipated Problems/Concerns

- Morbidity is worse in pts with tracheal or bronchial epithelial involvement.
- For pts that survive, long-term sequelae are common and primarily involve the skin, eyes, oral cavity, and teeth. Pulm complications occur, in addition to genital and urinary symptoms in female pts.

Sturge-Weber Syndrome

Puneet Khanna | Renu Sinha

Risk

- Incidence: 1 in 5000.
- Prevalence: No racial or sex prediction; sporadically occurring neurocutaneous syndrome.

Perioperative Risks

- Increased risk of seizures, neurologic deficits, bleeding due to presence of angiomas involving the oral cavity, vascular abnormality, and congenital cardiac malformations.

Worry About

- Seizures, mental retardation, neurologic deficits, headache
- Congenital glaucoma, retinal detachment
- Difficult airway
- Intracerebral angiomas

Overview

- Described by Sturge (1879) and Weber (1929).
- Also known as encephalotrigeminal angiomatosis.
- Involves a triad of (1) vascular malformation (port wine stain); (2) leptomeningeal angioma; and (3) vascular malformation of the eye.
- Facial, extrafacial, and bilateral port wine stain, along with hypertrophy of the facial soft tissue and facial bone:

- Obstructive sleep apnea.
- Difficult mask ventilation and laryngoscopy.
- Seizure:
  - The earlier the onset, the poorer the prognosis.
  - May need multiple antiepileptic drugs.
  - Treatment of dehydration/fever/infection.
- Mental retardation leads to anxiety, agitation.
- Hemiparesis, hemianopsia, hemiplegia.
- Status-like episodes.

Etiology

- Unknown. Suggested etiology includes
  - Failure of primitive cephalic venous plexus to regress during first trimester of pregnancy
  - Failure of superficial cortical veins to develop
  - Thrombosis of veins leading to vascular steal phenomena
  - Deficiency of sympathetic insertion of vessel

Usual Treatment

- Anticonvulsants.
- Control of IOP.
- Antiplatelet therapy.
- Surgery for ocular diseases, epilepsy control, angiomas.
- Require anesthesia for examination, investigations, and surgery.

Assessment Points

System	Effect	History	PE	Test
CNS	Headache (migraine like) Stroke like episodes (hemiparesis) Hemianopsia	Seizures (focal/generalized) Mental retardation		CT scan MRI X-ray: Tram-track calcification
EYE	Choroidal/episclera/conjunctival hemangioma Iris heterochromia Retinal pigment degeneration Retinal degeneration Buphthalmos Optic disc coloboma		Glaucoma Cataract	IOP monitoring Fundoscopy
CV	Septal defects, valvular stenosis and malposition of great vessels			ECG, ECHO
HEENT	Difficult mask ventilation and laryngoscopy	Hypertrophy of the soft tissue and bone	Facial and airway hemangiomas	
ANGIOMATOUS		Pituitary, thymus, lung, thyroid, testis, spleen, and lymph nodes		

Key References: Khanna P, Ray BR, Govindrajan SR, et al: Anesthetic management of pediatric patients with Sturge-Weber syndrome: our experience and a review of the literature, *J Anesth* 29(6):857–861, 2015; Thomas-Sohl KA, Vaslow DF, Maria BL: Sturge-Weber syndrome: a review, *Pediatr Neurol* 30(5):303–310, 2004.

Perioperative Implications

Preoperative Preparation

- Anticonvulsants in pts with convulsions.
- Assess airway and vascular malformation.
- Establish rapport with mentally retarded pts to decrease anxiety.
- Maintain adequate hydration.
- Benzodiazepines premedication.

Monitoring

- Intraop: Intracerebral bleed, convulsion
- ECG, respiration, NIBP, $ETCO_2$, SpO_2, BIS, EEG

Airway

- Hypertrophy of soft tissue and bone
- Facial and airway hemangioma
- Decreased intraoral space/high arched palate
- Difficult mask ventilation and laryngoscopy
- Bleeding during airway manipulation
- Difficult supraglottic placement
- Better option: Videolaryngoscopes

Anesthesia

- Based on history, examination, investigation, and type of surgery.
- Adults: Regional anesthesia:
  - Avoid systemic complications.
  - Modification of antiplatelet therapy before block.
- Children: General anesthesia

Induction

- Inhalational:
  - Use of sevoflurane is controversial for cortical epileptical activities. No persistent neurologic sequelae have been described.
  - Halothane can be used.
- For IV induction, both thiopentone and propofol can be used.

Maintenance

- O_2, N_2O or air, isoflurane or desflurane.
- Vecuronium or atracurium for muscle relaxation.
- Avoid succinylcholine (increases IOP/ICP).
- Analgesia: Fentanyl and NSAIDs.
- Avoid hypercarbia and light plane of anesthesia (increases IOP/ICP).
- Avoid hypoxia, hypoglycemia, hypotension, and hypothermia (to prevent seizure).

Extubation

- Prevent extubation response (increased risk of intracranial bleed, IOP, ICP).

Adjuvants

- Topical anesthesia, local anesthetic infiltration, and nerve blocks.

Postoperative Period

- Continue antiepileptic drugs.
- Maintain hydration.
- O_2 supplementation.

Anticipated Problems/Concerns

- Mental retardation, neurologic deficit, convulsion, facial and airway hemangiomas, and difficult airway (arrange difficult intubation cart)
- CNS hemangiomas: Increased chances of intracranial bleed, postop convulsion, and neurologic deficit (control BP)

Subclavian Steal Syndrome

Dolores B. Njoku | Natalia Hnatiuk

Risk

- Uncommon entity with a variably reported clinical significance
- Male:female ratio: 2:1

Perioperative Risks

- Stroke from a plaque originating from vertebral artery system
- Stroke from a plaque originating from subclavian artery

Worry About

- Worsening neurologic symptoms
- Upper limb ischemia

Overview

- Retrograde blood flow from vertebral artery to distal subclavian secondary to proximal ipsilateral subclavian or innominate artery stenosis or occlusion occurs when the pressure at the subclavian end of the vertebral artery drops below the basilar artery pressure.
- Presence of other extracranial arterial disease is a prerequisite to development of symptoms.
- Criteria for diagnosis (must be symptomatic):
  - Cerebral ischemia causing neurologic symptoms associated with ipsilateral arm exercise.
  - Decreased BP or arm claudication in ipsilateral arm secondary to occlusion or stenosis of subclavian artery proximal to vertebral artery.
- Ratio of left-sided to right-sided SSP is 3:1. The left subclavian artery at increased risk for atherosclerosis secondary to more acute angle of takeoff and turbulent flow.

- Symptoms may be obscured by concomitant carotid insufficiency.
- Spontaneous resolution of vertebrobasilar symptoms may be related to the establishment of extracranial collaterals to the subclavian circulation.

Etiology

- Most common atherosclerosis.
- Other causes include Takayasu's arteritis, tumor, history of aortic stenting/grafting for aneurysm, and previous surgery, as well as trauma.
- Rare causes include congenital atresia of first portion of left subclavian, hypoplastic arch with severe coarctation, or stenosis of left subclavian at old suture site of a coarctation repair, as well as Blalock-Taussig shunts.

Usual Treatment

- Surgical:
  - Common carotid to subclavian artery bypass graft
  - Subclavian-to-subclavian artery bypass graft
  - Axillary-to-axillary artery bypass graft
- Nonsurgical: Percutaneous transluminal angioplasty and stent placement

Assessment Points

System	Assessment by Hx	PE	Test
CV	Claudication	Bruit	Difference in brachial systolic BP of at least 20 mm Hg Diminished pulse in ipsilateral arm Bruit at base of neck or supraclavicular area on affected side (proximal subclavian artery) Reactive hyperemia: Temporary cuff inflation causes peripheral vasodilation distal to cuff, when released results in increased demand leading to neurologic symptoms Color Doppler ultrasound: Ipsilateral vertebral artery flow reversal with a parvus tardus waveform in the ipsilateral subclavian artery confirms the diagnosis of SSP Vascular structures well demonstrated by contrast-enhanced MRA Flow reversal well demonstrated by flow-encoded MRI
CNS	Vertigo Rarely cortical visual disturbances, ataxia, syncope, dysarthria		Retrograde cath Angiogram Transcranial Doppler
MS	Paresis/paresthesias		See CV

Key References: Wood RJ, Walmsley AJ: Subclavian artery stenosis and blood pressure control, *Anaesthesia* 61(4):409–410, 2006; Potter BJ, Pinto DS: Subclavian steal syndrome, *Circulation* 129(22):2320–2323, 2014.

Perioperative Implications

Preoperative Preparation

- Bilateral upper extremity BP in pts undergoing surgery is characterized by large variations in hemodynamic status or in pts with previous internal mammary-coronary bypass grafts.
- Neurologic evaluation prior to surgery.

Monitoring

- Consider arterial cath, since BP maintenance may be essential for cerebral perfusion.
- Consider CVP monitoring and/or PA cath if contributing factors in pt.

Maintenance

- Consider maintaining arterial BP and heart rate near preop levels to facilitate cerebral perfusion.

Extubation

- None

Postoperative Period

- Neurologic evaluation at end of surgery.

Anticipated Problems/Concerns

- Pts with internal mammary grafts may experience a similar syndrome of coronary-subclavian steal. There is a gradient in systolic brachial blood pressure of 60 mm Hg. In such situations, myocardial ischemia that is refractory to medical management may occur.

Subphrenic Abscess

Betsy Ellen Soifer | Lee A. Fleisher

Risk

- Prior abdominal surgery, either open or laparoscopic
- Blunt or penetrating trauma
- GI perforation (malignancy, appendicitis, diverticulitis)
- Inflammatory bowel disease
- Immunocompromised pt

Perioperative Risks

- Developing sepsis

Worry About

- Respiratory compromise (pleural effusion, atelectasis, V/Q mismatching, ARDS)
  - Preop ileus/bowel obstruction; aspiration risk
  - Sepsis, including septic shock and associated renal failure and/or coagulopathy
  - Increased capillary permeability (hypovolemia)
  - High-output cardiac failure/LV dysfunction
- Lyte and acid-base disturbances

Overview

- Classic findings include fever, leukocytosis, and abdominal pain.
- Associated findings include atelectasis, pleural effusions, elevated diaphragm, ipsilateral shoulder pain, and/or hiccups secondary to diaphragmatic irritation.
- May be right- or left-sided, or both; above or below the liver or spleen.
- Fistulas may form to any abdominal or thoracic organ, including pericardium or bronchi.
- Disease severity ranges from mild to moribund.

Etiology

- Primary: Associated with perforated viscus such as duodenal ulcer, diverticulitis, appendicitis, primary liver abscess, immunocompromised state. (Pathogens include *Escherichia coli*, *Enterococcus* spp, *Bacteroides fragilis*, *Clostridium* spp and are often polymicrobial.)
- Secondary: Following surgical intervention, critical illness, or blunt abd trauma. (Pathogens include *Candida* spp, *Enterococcus* spp, *Enterobacter* spp, *Staphylococcus epidermidis*, *E. coli* and are often polymicrobial with anaerobic bacteria outnumbering or equal to aerobic bacteria in all but postbiliary surgeries.)

Usual Treatment

- Broad-spectrum antibiotics ± antifungals. Narrow coverage after cultures obtained based on culture and sensitivity.
- Percutaneous or surgical abscess drainage (80–90% successful resolution).
- Supportive therapy: Appropriate monitoring, nutrition, oxygenation, hydration, vasopressors, as indicated using the surviving sepsis recommendations.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Early: Hyperdynamic state, high cardiac output assoc with low SVR Late: Septic shock, low output assoc with high SVR, LV dysfunction		Tachycardia Bounding pulses Warm, ruborous skin Tachycardia Diminished pulses Cool integument Peripheral cyanosis	ECG CVP *Or* PA cath ECHO
RESP	Atelectasis, elevated diaphragm, pleural effusion, abdominal distention, pain, or ARDS Decreased diaphragm excursion	Dyspnea Ipsilateral shoulder pain	Tachypnea Cyanosis Decreased or abnormal breath sounds, dullness to percussion	CXR, fluoroscopy ABG CT scan
HEME	Anemia due to suppressed marrow Coagulopathy associated with sepsis	Fatigue	Pallor Oozing around old incisions or IV sites Petechiae Ecchymoses	Hgb, Hct Plt count PT/APTT Fibrinogen, FSPs, D-dimer Thromboelastogram
GU	Decreased perfusion due to hypovolemia or sepsis	Decreased UO		BUN, Cr Lytes Acid-base balance
CNS	Mental status changes associated with sepsis		Range from mild confusion to coma	Must exclude other possible causes (e.g., CVA, CNS infection)

Key References: Singer M, Deutschman CS, Seymour CW, et al.: The third international consensus definitions for sepsis and septic shock (Sepsis-3), *JAMA* 315(8):801–810, 2016; Royal College of Anaesthetists: The first patient report of the national emergency laparotomy audit. Available at <www.nela.org.uk/reports>; 2015 (Accessed 11.07.16).

Perioperative Implications

Preoperative Preparation

- Appropriate broad-spectrum antibiotics.
- Restore intravascular volume.
- Optimize respiratory function: PEEP, bronchodilators, rarely thoracentesis.
- NG tube for ileus and/or obstruction.
- Tenuous CV status may require central venous access for monitoring/access or vasopressor and/or inotrope infusion.
- Assess coagulation status.

Monitoring

- Tailor to severity of illness.

Airway

- Rapid-sequence induction or awake fiberoptic intubation (aspiration risk)

Preinduction/Induction

- Titrate agents to severity of disease

Extubation

- Tenuous pulm status and/or septic deterioration may require prolonged mechanical ventilation.

Postoperative Period

- NPO until intestinal function returns.
- Analgesia important for adequate respiratory function.
- Monitor for postinterventional complications (transient sepsis, organ injury, hemorrhage, pneumothorax, peritonitis, wound dehiscence).

Anticipated Problems/Concerns

- Drainage will need to be prolonged (often greater than 10 d).
- Recurrent abscess formation or sepsis (57% in high-risk pts).
- At risk for MODS (respiratory/ARDS, renal, hepatic, GI bleed).
- High mortality rate (23–50%) in the presence of multiple organ dysfunction.
- Periop pneumonia/empyema/pleural effusion.
- Fistula formation.

Substance Abuse Disorder (Perioperative)

Lewis Fry | Robert A. Fry

Risk

- Incidence in USA (2013 estimation): 24.6 million (9.4% population)
- Marijuana 7.5%, heroin 0.27%, cocaine 0.6%, prescription drugs 2.5%, alcohol (heavy drinkers) 6.5%, tobacco products 25.2%
- Associations: Males, trauma, gunshot wounds, MVAs, falls, mental illness

Perioperative Risks

- Difficult airway and IV access
- Hemodynamic instability, autonomic dysfunction
- Opioid tolerance, achieving adequate analgesia, hyperalgesia/pain intolerance
- Systemic/blood borne infections (HIV, hepatitis B and C, TB, septic arthritis)
- Malnutrition, coagulopathy

Worry About

- Withdrawal (prevention and treatment)
- Pain management
- Acute psychosis (hallucinations, aggression, anxiety)
- Multiagent abuse, drug interactions, smoking, and drug-related lung disease
- Obstetrics: Lack of prenatal care, IUGR, 4× increased incidence of abdominal delivery, abruptio placenta, fetal abnormalities, drug effects that may mimic preeclampsia

Overview

- Chronic condition characterized by (1) impaired control of use, (2) social impairment, (3) risky use of substance, and (4) pharmacologic effects (tolerance, withdrawal)
- Physiologic and pathologic changes specific to drug class

Etiology

- Biopsychosocial disease: Possible genetic predisposition, susceptible premorbid personality types

Usual Treatment

- Team-oriented multimodal approach: Detoxification, psychiatric assessment, pharmacotherapy. Drug-specific pharmacotherapy may include naltrexone, slow-release morphine, buprenorphine, methadone, suboxone, disulfiram, acamprosate.
- Support group or special treatment facility; compliance 30–60%.

Assessment Points

System	Effect	Assessment by Hx	PE	Tests
GENERAL	Poor general health (malnutrition, poor dentition) hypothermia/hyperthermia withdrawal	Drugs and alcohol	Temperature, trauma, tracking Diaphoresis, tremors, N/V	Blood, urine toxicology screens
HEENT	Miosis (opioids), mydriasis (stimulants)		Pupils	
CV	Sympathetic stimulation, arrhythmias, ischemia/MI (cocaine, amphetamines), cardiomyopathy (opioids, ETOH, cocaine), aortic dissection (cocaine, amphetamines), endocarditis (IVDU)	Palpitations, SOB on exertion, chest pain	BP/HR, murmur, SVR, long QT	ECG ECHO Troponins
RESP	Bronchoconstriction, pulmonary Htn, interstitial fibrosis, pneumonia, pulmonary hemorrhage (cocaine), resp depression (heroin, opiates, PCP)/stimulation (amphetamines, LSD), emphysema (tobacco/marijuana)	SOB on exertion, hemoptysis	RR, O_2 sats, air entry, wheeze	CXR if indicated
GI	Cirrhosis (ETOH), salivation (PCP)	Anorexia, N/V, bleeding	Hepatomegaly, ascites	LFTs
RENAL	Retention (marijuana), ARF, ESRF (cocaine, amphetamines), hyponatremia (MDMA)		Oliguria Anuria (rhabdomyolysis)	Urea and lytes, CK and Cr Urine myoglobin
ENDO/METAB	Serotonin syndrome (cocaine, amphetamines, buprenorphine, LSD)		BP, temp, tremors, diaphoresis, confusion, seizures	
CNS	Altered mental state SAH, CVA (cocaine)	Anxiety, hyperactivity, euphoria. Aggression, hallucinations	Neuro exam, MSE	CT, MRI
PNS	Peripheral neuropathy (ETOH)	Altered sensation	Neuro exam	
OB	IUGR, preterm labor, placental abruption	Exposure, abdominal pain, bleeding	Vaginal bleeding	US

Key References: Lüscher C: Drugs of abuse. In: Katzung BG, Trevor AJ, editors, *Basic and clinical pharmacology,* ed 13, New York, 2015, McGraw-Hill; Bryson EO, Frost EAM, editors: *Perioperative addiction: clinical management of the addicted patient,* New York, 2012, Springer.

Perioperative Implications

Preoperative Preparation

- D&A Hx: CAGE-AID questionnaire, drugs abused, duration, frequency, route of administration
- Consideration of drug and toxicology screening (has limitations)
- Addiction specialist consultation recommended
- Acutely intoxicated: Delay of treatment wherever possible due to hemodynamic instability
- Chronic use: Management of pharmacotherapy, including opiate-replacement therapy as appropriate and prevention of withdrawal

Monitoring

- Standard ASA monitors; consider invasive monitoring for cardiovascular instability or end-organ dysfunction.

Airway

- Consider rapid-sequence induction in intoxication.
- Nasal septal/soft palate necrosis; drug-associated pulmonary disease (see Assessment Points table).

Preinduction/Induction

- Consider premedication: benzodiazepines, dexmedetomidine, or beta-blockers.
- Propofol (no specific contraindications); relative contraindications: Cocaine: etomidate, succinylcholine, ketamine. PCP & LSD: Ketamine. Marijuana: Barbiturates

Maintenance

- Autonomic dysfunction common; anticipate hemodynamic instability, myocardial ischemia, arrhythmias, myocardial depression, diminished or exaggerated responses to vasopressors.
- Consider decreased MAC (chronic opioid, cocaine, amphetamine use) and increased MAC (stimulant intoxication).

Postoperative Period

- Depressed airway reflexes and respiratory depression; postop apnea monitoring (recommended).
- Anticipate agitation, confusion, hallucinations, withdrawal, seizures, delayed return of motor function, fever, and hemodynamic instability.
- Withdrawal management (e.g., lorazepam, haloperidol, clonidine).
- Pain management: Consideration of alternative multimodal analgesia, including alternative routes, local anesthetics, regional blocks, nonsteroidals, ketamine, alpha blockers, and gabapentin; may require opiate doses 2-3× more than in opiate-naïve pts.
- In pts drinking >4 drinks/d, 2–3× increased risk for postop complications.

Supratentorial Brain Tumors

Tod B. Sloan | Antoun Koht

Risk

- Highest incidence age is 3–12 y and 55–65 y.
- Account for 80% of adult CNS tumors; incidence of primary tumor is ~15–20:100,000 per y.
- Account for one-third of childhood CNS tumors.

Perioperative Risks

- Increased ICP: Headache, seizures, neurologic deficit/dementia, visual and hearing changes, focal neurologic changes (hemiparesis, numbness, ataxia), and/or visual deficits if pituitary tumor present
- Endocrinopathy, fluid, and electrolyte imbalance

Worry About

- AEDs: Dilantin, keppra, tegretol. Adequate levels needed to avoid postop seizures.
- Raised ICP and brain edema: May lead to herniation (transtentorial [dilate ipsilateral] pupil), subfalcine (leg weakness), tonsillar (neck stiffness, spasticity, extensor-plantar response), and upward transtentorial (small pupils, extensor rigidity).
- Dexamethasone Rx may lead to hyperglycemia.
- Hyperglycemia may cause more retractor-induced ischemic injury to adjacent brain tissues.
- Endocrinopathy, particularly diabetes insipidus, if near pituitary.

Overview

- Portion of brain superior to tentorium cerebella.
- 13,000 deaths per y; third leading cause of death in pts 15–34 y of age.
- Brain edema surrounding malignant tumors causes initial Sx; often improve initially after corticosteroids.
- Seizures due to local neuronal irritation; 30–70% incidence related to tumor type.
- Obstructive hydrocephalus if the tumor is near third ventricle or foramen of Monro.

Etiology

- In adults, 85% of primary tumors occur in anterior two-thirds of cortex (most benign): glioma (45–50%), medulloblastoma, ependymoma, low-grade lymphoma (children: astrocytoma, medulloblastoma). 15% are meningiomas. Common presentation age is 55–65 y (1% of all cancers).
- Many supratentorial tumors are metastases (20–30%): Melanoma, breast cancer, small-cell lung, non-Hodgkin's lymphoma, colon, renal, nasal/throat. 50% have multiple metastases (25% of all pts with cancer have brain metastases), usually located at white-gray border.

- Associated Dx includes neurofibromatosis and von Hippel-Lindau syndrome.
- Brain tumors rarely metastasize outside the brain.
- Pediatric (uncommon >age 2) <1 y present when large (pliable skull, glioma 50%; (astrocytoma). Most are low-grade and deep midline; others are ependymoma, medulloblastoma, and PNET (primitive neuroectodermal tumors).

Usual Treatment

- Dexamethasone for initial Sx (reduce vasogenic edema).
- Usually surgery with almost all tumors for diagnostic biopsy/resection/debulking.
- Surgical techniques; neuronavigation, neuroendoscopy, ultrasound, fluorescence-guided resection, intraop MRI, and IC Green.
- Radioactive implants, antibodies against tumor-specific antigens, or radiosensitizing agents may be used.
- Radiation/Gamma Knife (common with metastasis) and chemotherapy.
- Children may need anesthesia for Gamma Knife. Linear accelerator, and proton-beam treatments.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Cartilaginous overgrowth in acromegaly Skin: Melanoma with metastases		Acromegalic features third nerve palsy, papilledema, vision changes, hearing changes, macrocrania, bulging fontanel (infant)	Lateral neck x-ray
CV	Age effect: CHF, ASCVD, chemotherapy cardiomyopathy, including ICP	DOE, edema, angina	Gallop, rales, jugular distention, Htn, bradycardia	CXR, ECG, ECHO
RESP	COPD: Primary lung tumor with cerebral metastases	Dyspnea, cough, sputum	Signs of COPD, altered breathing pattern	FEV_1, FVC (if indicated)ABG CXR
RENAL/GI	Dehydration, SIADH, colon, renal tumor with metastases	Mannitol, diuretics, decreased intake, vomiting (especially children)	Dry mucous membranes	Urine SG, sodium, Cr
ENDO	Iatrogenic Cushing syndrome due to decadron, infertility	Improved level of consciousness with decadron	Cushingoid appearance	Glucose levels
HEME	Anemia, paraneoplastic syndrome, increased thromboembolism	Occult GI bleeding caused by primary tumor	Pale conjunctiva, positive occult fecal blood	Hct, Hgb, T&C
CNS	Seizures (50% as presenting symptom), somnolence, hydrocephalus	Headache, confusion, ataxia, neck stiffness	Altered consciousness, personality changes, memory loss, speech changes	MRI, CT, note peritumoral edema, loss ventricles, basilar cisterns, midline shift
PNS	Hemiparesis	Clumsiness	Weakness, numbness, hemiparesis, tingling, spasticity, or rigidity	Nerve conduction velocity

Key References: Rahimi E, Manninen PH: Routine craniotomy for supratentorial masses. In Mongan P, Soriano S, Sloan T, editors: *A practical approach to neuroanesthesia,* Philadelphia, 2013, Wolters Kluwer, pp 37–52; McClain CD, Soriano SG: Anesthesia for intracranial surgery in infants and children, *Curr Opin Anaesthesiol* 27(5):465–469, 2014.

Perioperative Implications

Preoperative Preparation

- Neurologic exam: LOC, pupil size, reactivity.
- Evaluation: Is pt a candidate for awake stereotaxic surgery.?
- Focal neurologic symptoms; new weakness within 1 y (avoid succinylcholine)
- Is there elevated ICP to start with? (headache, N/V, loss of vision, or diplopia)
- Delayed gastric emptying or N/V with increased ICP.
- Dexamethasone: May lower ICP initially, but ICP may increase with small change in physiology.
- Temporal lobe lesion with impending herniation.
- Imaging studies; massive peritumor edema with shift of midline.
- Seizure behavior; AED adequate; beware postop seizure.
- Assess volume status (dehydration).
- Implants affecting MEP or MRI.
- Paraneoplastic syndromes, hypercoagulopathy.

Monitoring

- Consider arterial line: BP control, frequent ABGs, glucose; avoid dec PaO_2.
- Monitor CPP (MAP–ICP), BP transducer at ear level, Foley.
- $ETCO_2$ as rough guide only; rely on $PaCO_2$ and avoid including CO_2
- ICP: Zero at ear level, for postop use
- If lumbar CSF drains are used, connect to transducer, leave closed until head open and surgeon ready, then drain slowly as needed by surgeon.
- Optimize hyperventilation (25–30 mm Hg $PaCO_2$), mannitol, 3% hypertonic saline Rx.
- Diagnostic if pt is slow to awaken from anesthetic.
- NMB: Increased receptor density in paretic extremities gives false twitch data. Use nonparetic arm/leg.
- ECoG used if surgery to treat seizure disorder or brain mapping.
- Positioning occipital and pineal tumors: Mild head up; if sitting, then monitor for air embolism (precordial Doppler, CVP, etc).

Airway

- Cushingoid facies may result in difficult mask ventilation.
- Acromegaly causes laryngeal compromise by cartilaginous overgrowth. Anticipate difficult intubation; may require smaller endotracheal tube. Consider lateral neck x-ray for airway abn, such as enlarged epiglottis, narrowed cricoid ring.
- Stereotactic frame may inhibit laryngoscopy (may need LMA).

Preinduction/Induction

- Induction with agents that act to decrease cerebral blood flow (avoid ketamine).
- Opioids prn to avoid hemodynamic responses during induction, pinning, and incision.
- Avoid increased BP with intubation/head pins.
- Avoid brain swelling due to venous outflow occlusion: Do not permit overflexion or excessive rotation of neck.
- Eye protection from prep solution and pressure while face covered by drapes, instruments.
- Use soft bite block, and check tongue and lips (especially with MEP).
- Local anesthesia for reduced bleeding of incision.

Maintenance

- Goal is normovolemia, normotension, normonatremic fluids; replace diuresis if needed.
- Avoid hyperglycemia, hypo-osmolality (<290 mOsm/kg).
- Low intrathoracic pressure (reduced cerebral venous pressure).
- Monitor $PaCO_2$, esp with COPD.
- Mannitol at 0.5–1 g/kg per surgeon (but occasionally hypertonic saline).
- No painful structures below dura: Implement minimal anesthetic requirement with brain manipulation, low-dose inhalation agent, and/or propofol infusion.
- Avoid N_2O, use inhalational agent <1 MAC, <½ MAC if SSEP, ECoG, or MEP. Implement TIVA if EP signals are poor.
- Consider high dose short-acting opioids.
- Avoid NMB during MEP or EMG monitoring.
- Maintain good cerebral perfusion but not Htn.
- Antibiotics; redose at appropriate interval.

Extubation

- Extubate in head up position to dec bleeding.
- Awake: Implement normocarbia, early neurologic assessment (risk of coughing, straining, possible hematoma formation, with risk of increasing postop Htn).
- Deep: Avoid coughing; may be Htn (transient $PaCO_2$ about 50 mm Hg until pt awakens and use deep extubation only if there is no brain edema during craniotomy and no anticipated airway problems).
- Htn on awakening. Consider prophylactic beta blockers/antihypertensives.
- Consider postop intubation/ventilation with preop poor mental status.

Adjuvants

- Decadron, mannitol, and Lasix.
- Profound paralysis: May minimize need for inhalation agents.
- For muscle relaxants, expect nondepolarizing NMB will be shorter acting with most AED (except keppra).
- Expect hemodynamic effects from epinephrine in local infiltrated into scalp incision site.
- Antiemetics (differentiate PONV vs. increased ICP).
- Vasoactive compounds.
- Consider first-line Htn treatment with labetalol.
- Consider cerebral vasodilators: Hydralazine, sodium nitroprusside if severe Htn.

Anticipated Problems/Concerns

- Intraop brain swelling (head up, decreased CO_2, including venous drainage, decreased inhaled anesthesia, propofol/barbiturates, dexamethasone, correct hypoxemia)
- Air embolism with tumors near dural sinuses and sitting position
- Intracranial bleeding (dural sinuses, vascular tumors)

- Postop, including ICP due to loss autoregulation
- Delayed awakening, especially with depressed consciousness preop
- Postexcision brain swelling; seizures
- Postop arterial Htn/bleeding
- Postop endocrine problems, diabetes insipidus

Awake Craniotomy

- Awake craniotomy with mapping to remove tumors near motor strip or speech centers
- Good communication
- Controlled sedation, short-acting medications, and LMA for lost airway
- Scalp blocks, one side, bilateral, long-acting medication, pins sites, specific scalp nerves, ring block, and possible high doses
- Methods: Awake, sedated/awake/sedated, asleep/awake/sedated
- Mapping: Speech, reading, counting, motor, observed movements or EMG, sensory

Complications

- Seizures, cold irrigation, short-acting medications
- Vomiting, hypoxemia, respiratory depression
- Air embolism
- Nose itching, dry mouth, and urinary urgency (males)

Supraventricular Tachycardia (Tachyarrhythmias)

Gina Whitney | Lee A. Fleisher

Risk

- SVT is associated with advancing age and significant cardiac and pulm disease.
- PSVT is associated with WPW, congenital heart disease, and mitral valve prolapse. It is more common in younger pts. The mechanism is reentrant in nature.
- AAT may be automatic, triggered, or reentrant. It is seen more commonly in children and those with a Hx of prior atrial surgery. It is rare in adults, although it can be associated with digitalis toxicity and hypokalemia.
- MAT is seen in adult pts with critical illness or advanced pulm disease.

Perioperative Risks

- Myocardial ischemia associated with tachycardia and resulting coronary insufficiency.
- Circulatory compromise.
- Increased risk of atrial thrombus.
- Chronic sustained tachycardia can result in irreversible cardiomyopathy.

Worry About

- Lyte and acid-base balance (K^+, Mg, alkalosis)
- Digitalis toxicity

Overview

- Tachycardia (HR >100 in adults) with origin above the bundle of His in sinus node, atrial, or junctional tissue. It may be reentrant, automatic, or triggered in origin.
- SVT may be paroxysmal (PSVT) or gradual in onset (sinus tachycardia, atrial tachycardia, or multiform atrial tachycardia). Tachycardia mechanisms vary (reentrant vs. triggered and automatic); treatment varies accordingly.
- PSVT is a reentrant arrhythmia usually seen more commonly in children. The reentrant circuit usually involves an accessory conducting pathway and the AV node.
- AAT is more commonly seen in the pediatric population owing to the enhanced automaticity seen in children.

Etiology

- PSVT is due to reentry, which generally involves the AV node and an accessory pathway. Accessory pathways are relatively common in children. It is also assoc with WPW and LGL.
- AAT is much more common in children and thought to stem from areas of enhanced automaticity of sites, which are usually found at the mouth of either atrial appendage, the orifices of the pulm veins, or the crista terminalis.

Usual Treatment

- PSVT: Drugs, which alter the refractoriness of tissue within the reentrant circuit, may terminate tachycardia. Adenosine delivered by IV push is commonly used to terminate tachycardias. Other agents that may be used include procainamide, propafenone, amiodarone, sotalol, esmolol, and verapamil.
- PSVT may also be terminated by cardioversion or rapid atrial pacing; includes placement of a pacemaker.
- AAT may be treated using amiodarone, sotalol, flecainide, or beta blockers.
- MAT may be managed using beta blockers or calcium-channel blockers to slow the ventricular rate and improve cardiac function. Underlying cardiopulmonary disease must be addressed as well.
- Consider cath ablation in recurrent symptomatic conditions.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmia	Palpitations, presyncope or syncope, angina, dyspnea Failure to thrive (pediatrics)	Regular (PSVT, AAT) or irregular pulse (MAT)	ECG, Holter, EP study
	LV function Ischemia	CHF, exercise intolerance Angina	Signs of CHF (S_3, rales, edema, wheezing) Diaphoresis	CXR, ECHO Angiogram Scintigram
RESP	CHF, COPD	Dyspnea, orthopnea, cough	S_3, rales, wheezing	CXR, PFTs
GI	Hypoperfusion	Abdominal discomfort, diarrhea		
RENAL	Hypoperfusion	Oliguria, polyuria	UO	BUN/Cr, FENa

Key References: Thompson A, Balser JR: Perioperative cardiac arrhythmias, *Br J Anaesth* 93(1):86–94, 2004; Price A, Santucci P: Electrophysiology procedures: weighing the factors affecting choice of anesthesia, *Semin Cardiothorac Vasc Anesth* 17(3):203–211, 2013; Page RL, Joglar JA, Caldwell MA, et al: 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, *Circulation* 133(14):e506–e574, 2016.

Perioperative Implications

Preoperative Preparation

- PSVT: Adenosine, esmolol, and amiodarone should be available.
- AAT: Check and optimize electrolyte (K^+, Mg) and acid-base status. Rule out digitalis toxicity.
- MAT: Optimize status of various organ systems including cardiac, pulm, renal, and metabolic.
- Check pacemaker function.

Monitoring

- ECG, ST-segment analysis.
- Ability to monitor pacemaker if appropriate.
- Consider arterial pressure or PAC monitoring depending on anticipated case and pt status.

Induction

- In the setting of LV dysfunction or cardiomyopathy, aim for hemodynamically stable induction.
- AAT and MAT: Use caution with medications or situations that increase pt's heart rate (ketamine, pancuronium, desflurane, beta agonists, light anesthesia).

Maintenance

- Volatile agents with the possible exception of desflurane are not thought to increase the incidence of PSVT, AAT, or MAT.
- Prophylactic beta blockade may be useful intraop if the pt is able to tolerate it.

Extubation

- Avoid excessive sympathetic stimulation around the time of extubation because this increases the incidence of tachyarrhythmias. Strategies aimed at mitigating airway stimulation and hyperdynamic circulation are helpful in this regard.

Adjuvants

- Avoid use of beta agonists and histamine-releasing drugs if at all possible

Postoperative Period

- Ensure adequate sedation and pain control.
- Use of beta blockers as tolerated will reduce incidence of MAT and AAT postop.
- Optimize cardiopulmonary and metabolic status.

Anticipated Problems/Concerns

- PSVT: Be prepared to treat atrial fibrillation/flutter with rapid ventricular rate or ventricular fibrillation with cardioversion and/or defibrillation, particularly in pts with WPW or LGL.
- Cardioversion of AAT or MAT may result in life-threatening arrhythmias.

Swallowing Disorders

Matthias Eikermann | Danuza Nunn

Risk

- Neuromuscular disorder or mechanical obstruction can cause difficulty in swallowing (dysphagia).
- Dysphagia can be classified into distinct types: Oropharyngeal dysphagia due to malfunction of the tongue, pharynx, larynx and/or upper esophageal sphincter and esophageal dysphagia due to malfunction of the esophagus.
- Dysphagia is often a symptom of a systemic disease (impaired consciousness, sarcopenia, dyspnea).
- Effects of dysphagia can go undetected until more serious medical complications—such as respiratory disorders, sepsis, and/or profound weakness and cachexia—are identified.
- According to AHRQ, approximately 300,000–600,000 people each year are affected by dysphagia and around 51,000 of these cases stem from neurologic disorders other than stroke.
- Aspiration pneumonia is one of the leading causes of death among the elderly.
- Not all pts with swallowing disorders will develop an aspiration pneumonia but the majority are at risk for dehydration and malnourishment.

Perioperative Risks

- Subclinical dysphagia often becomes symptomatic periop with increased volume of airway secretions; effects of sedatives, opioids, and neuromuscular blocking agents; and inflammation.
- Increased risk of aspiration when consciousness is impaired (decreased sensorium, impaired breathing-swallowing coordination).

Worry About

- Impaired breathing-swallowing interplay in pts with dyspnea and impaired mental status.
- Full stomach/impaired gastric emptying.
- Mask ventilation: Gastric inflation may increase the risk of life-threatening regurgitation and pulm aspiration.
- Underlying malnourishment/frailty/sarcopenia: Poor periop outcome.
- Risk of extubation failure: Deconditioned pt (weakness, anemia, renal failure).
- Aspiration in pts with severe muscle weakness.

Overview

- Dysphagia is defined as any difficulty that can affect the swallowing mechanism or safe transference of food, liquid, and secretions anywhere through and along the digestive tract.
- Only 40– 60% of institutionalized elderly have overt signs and symptoms of oropharyngeal dysphagia.
- About 50% of hospitalized pts with recurrent respiratory failure leading to reintubation have swallowing disorders and silent aspiration.
- Oropharyngeal dysphagia in the hospitalized elderly is an indicator of poor prognosis for pts with pneumonia; however, this is dependent on their functional capacity prehospitalization and any functional decline that occurs during hospitalization.
- Pts with overt signs or symptoms of aspiration often have poor functional status, a higher prevalence of neurologic comorbidities, and greater exposure to paralytics or sedative drugs that might affect level of consciousness, swallow efficiency, and coordination.
- Adequate screening methods to identify pts at risk for aspiration help to prevent adverse outcomes (aspiration, inadequate hydration, poor nutrition).
- Muscle weakness is an independent predictor of aspiration in critically ill pts.
- Complete evaluation of swallowing disorders to diagnose and treat dysphagia and determine aspiration risk requires a multidisciplinary team and is not limited to bedside clinical evaluation. It might include a combination of instrumental tests such as FEES, VSS, and/or BaS.
- Hospitals that implement a swallowing screening do have a lower rate of aspiration pneumonia, reduced rate of readmission, decreased length of stay, increased staff and patient satisfaction, and reduced admission cost.
- An aspiration risk screening tool can be used in pts who are considered to be at risk for swallowing disorders.
- Evaluation:
  - Clinical bedside evaluation: Aims to determine risk and presence and severity of swallowing disorder and aspiration risk. It includes reviewing history and identifying risk factors for swallowing disorders, observing pt's level of arousal and alertness, oral sensory motor evaluation, observation for any signs or motor speech or voice abnormalities, observation of food and liquid administration, and saliva management.
  - FEES: Allows structural laryngeal evaluation and functional evaluation of swallowing efficiency and safety. Assessment of aspiration before, during, and after swallowing. During the moment of swallow is the view is obliterated, so microaspiration might go undetected.
  - Video swallowing study: Considered the gold standard. Allows functional evaluation of swallowing efficiency and safety from oral cavity to stomach. Uses barium in different consistencies. Not only detects prandial aspiration but also determines the cause, and all efforts are made to eliminate aspiration and improve efficiency of swallowing during examination. Requires hemodynamic stability and travel off the floor and involves radiation exposure.
  - BaS: Evaluates esophageal function and clearance. Might detect aspiration but does not eliminate and or seek to understand causes of aspiration aside from esophageal retroflow or reflux. Larger volumes of barium are ingested, and pts may be prone during procedure if they are unable to stand up. Pts at risk for prandial aspiration are not considered safe to participate on a BaS.
  - Swallow screening: Pass/fail procedure to determine overt risk of aspiration, safety to feed, and likelihood of need for further swallow assessment. There are many tools available but few have been validated. The Massachusetts General Hospital Swallow Screening test is a two-step exam:
    - Part 1: The pt is essentially assessed for readiness. The screener looks at wakefulness, breathing, posture, and cleanliness of the mouth. If any of these items are missing, the patient fails, is kept NPO, and rescreening is performed as appropriate.
    - Part 2: This includes the five elements most sensitive to determining risk of aspiration. Four of the elements have a 1-point value (tongue movement, volitional cough, vocal quality, and pharyngeal sensation). Note that pharyngeal sensation must be intact on both sides to receive a score of 1. The ability to swallow water without a cough, throat clear, wet or congested quality of voice, or shortness of breath is assigned 2 points because this is the best indicator of aspiration risk.
    - A score of 5 or 6 is needed to pass. A score of 4 or less results in a fail. If at any time during the screening there is concern for aspiration, the pt fails based on clinical judgment.
    - This screening instrument requires appropriate training to assure valid and reliable assessment. It was created to detect aspiration and has been validated on neurologic population. For more information and training, go to https://www2.massgeneral.org/stopstroke/swallowScreen.
    - Pts with known history of dysphagia or medical diagnosis that frequently causes swallowing disorders (stroke, head and neck cancer, neuromuscular disorder) who have signs or symptoms of dysphagia (coughing/choking) or aspiration (recurrent pneumonias, recurrent fever of unknown cause) should be referred to a bedside clinical swallow evaluation to determine need of further instrumental evaluation.

Etiology

- Leading causes of dysphagia include stroke, neurodegenerative diseases, brain tumors, and traumatic head or cervical spine injuries.
- Other common mechanisms of dysphagia include local cancer of head, neck, and esophagus; respiratory diseases (acute hypoxia and/or hypercarbia); congenital structural defects (cleft palate, tracheoesophageal fistula, laryngeal cleft, esophageal atresia); frailty; sarcopenia; and poor nutritional status.
- Airway devices: Large tracheal cannulas and nasogastric tubes, cervical collars.

Usual Treatment

- Aspiration prevention: Rapid sequence induction; 30 degrees elevated body position; conscious use/reversal of sedatives, opioids, and neuromuscular blocking agents; screening for high aspiration risk prior to oral feeding
- Implementation of preventive and compensatory measurements such diet texture and consistency; modifications to improve the safety and efficiency of swallowing and prevent further malnourishment, dehydration, or recurrent respiratory infections due to aspiration pneumonia.
- Implementation of swallowing maneuvers by changing head posture to change the direction and control of bolus flow.
- Neuromuscular swallowing exercises (head lift, tongue pressing, Mendelsohn maneuver)
- Oral hygiene.
- Implementation of airway clearance techniques to reduce effects of aspiration.

Assessment Points

Systems	Effects	Assessment by Hx	PE	Test
HEENT	Aspiration	Coughing, choking, speech and voice changes	Oral motor sensory exam, saliva management, food and liquid administration	Clinical bedside swallow exam, VSS, or FEES
CV	Dehydration	Skin, orthostatic vital signs	UO	
RESP	Pneumonia	Cough, sputum production	Fever	CXR, clinical bedside swallow exam, video swallow exam
GI	Dysphagia	Recurrent pneumonia, weight loss Heartburn, food impaction, regurgitation of food, odynophagia	Hoarseness (reflux), frequent throat clearing, laryngeal exam for signs of laryngo-esophageal reflux	Swallow screening, BaS, endoscopy, esophageal manometry, pH monitoring
CNS	Cranial nerves dysfunction and mental status changes	Hoarseness, motor speech, voice changes, decreased arousal	Oral motor sensory exam, level of arousal	Swallow screen
MS	Sarcopenia,cachexia	Weight loss, fatigue	Proximal muscle strength	VSS, FEES

Key References: Mirzakhani H, Williams J-N, Mello J, et al.: Muscle weakness predicts pharyngeal dysfunction and symptomatic aspiration in long-term ventilated patients, *Anesthesiology* 119(2):389–397, 2013; D'Angelo OM, Diaz-Gil D, Nunn D, et al.: Anesthesia and increased hypercarbic drive impair the coordination between breathing and swallowing, *Anesthesiology* 121(6):1175–1183, 2014.

Perioperative Implications

Preoperative Preparation

- Consider performing an aspiration risk screening tool or more comprehensive swallowing evaluation if there are any concerns for dysphagia, as detailed in the Assessment Points table.

Monitoring

- Assess dyspnea and desaturation.
- Closely monitor ventilatory drive (hypercapnia decreases hypopharyngeal pressure) because of increased risk of pathologic swallowing (swallowing on inhalation).

Airway

- Consider upper body elevation to decrease aspiration risk.

Induction

- Anesthesia disrupts the physiologic coordination between breathing and swallowing.
- Gentle (or absence of) mask ventilation helps avoid gastric insufflation.

Maintenance

- Ensure airway is clear of secretions due to the decreased frequency of swallowing.

Extubation

- Goal is an awake pt with no residual paralysis, as this will affect swallowing stability and ability to protect airway.
- Closely monitor ventilatory drive because hypercapnia increases the incidence of pathologic swallows

Adjuvants

- Consider clinical bedside evaluation after extubation if pt failed swallowing screening.

Postoperative Period

- Monitor changes in pulm function closely.
- Ensure ability to maintain enteral nutrition.
- Monitor for changes in mental status to ensure swallow stability across time.

Anticipated Problems/Concerns

- Residual paralysis and sedation
- Inability to manage own secretions

Syndrome of Inappropriate Antidiuretic Hormone Secretion

Sara Nikravan | Albert T. Cheung

Risk

- Elderly pts
- Nursing home residents
- Planned major operations, especially neurosurgical procedures
- Pts receiving exogenous hormone therapy, especially desmopressin
- CNS disorders including psychiatric diseases
- Cancer, especially small-cell lung cancer
- Lung disease

Perioperative Risks

- Hyponatremia
- Cerebral edema causing altered mentation, seizures, and coma
- Acute water intoxication and fluid overload

Worry About

- Other causes of hyponatremia, such as heart failure, liver failure, renal failure, or pseudohyponatremia (e.g., hyperglycemia) (see Hyponatremia).
- Acuity and magnitude of hyponatremia influences the risk of CNS complications.
- Osmotic demyelination syndrome is caused by rapid correction of hyponatremia.

Overview

- Hyponatremia is the most common electrolyte disorder in hospitalized pts (affects 15%), and SIADH is the most frequent cause of hyponatremia, but other causes of hyponatremia should be excluded before making a Dx of SIADH.
- Normally, increased serum osmolarity, hypovolemia, or hypotension triggers thirst and ADH release. ADH increases aquaporin-2 channels on the luminal surface of the distal tubules and collecting duct and acts to promote free water reabsorption. Thirst, free water intake, or hypotonic fluid administration combined with ADH-induced free water retention causes hyponatremia.
- Dx of SIADH: Symptoms include serum osmolarity less than 275 mOsm/L, urine osmolarity >100 mOsm/L, urine sodium >40 mEq/L, euvolemia, normal thyroid and adrenal function, and absence of diuretic therapy.
- SIADH can be classified as follows: Type A is unregulated secretion of ADH, type B is elevated basal secretion, type C is reset osmostat, and type D is undetectable ADH.

Etiology

- Malignant diseases causing ectopic ADH secretion: Lung cancer (especially small-cell and mesothelioma), brain tumors, cancer of the duodenum, pancreas, head and neck, GU tract, lymphoma, and sarcomas.
- Pulm disorders: Infections, asthma, cystic fibrosis.
- CNS disorders: Infection, masses, head trauma, intracranial bleed, MS, Guillain-Barré syndrome, Shy-Drager syndrome, delirium tremens, and acute intermittent porphyria.
- Immune compromised states like HIV with associated pulm infections or malignancies.
- Drugs include, but are not limited to, chlorpropamide, carbamazepine, cyclophosphamide, SSRIs, TCAs, clofibrate, nicotine, NSAIDs, antipsychotics, narcotics, arginine vasopressin analogues (DDAVP, oxytocin, and vasopressin).
- Major surgery: Pain, stress, general anesthesia, PPV, neurosurgery.
- SIADH may be hereditary, with a mutation of gene for renal vasopressin-2 receptor and a mutation for gene affecting osmolarity sensing in the hypothalamus.

Usual Treatment

- The decision to treat depends on acuity and severity of hyponatremia or the presence of symptoms.
- Treat underlying causes for SIADH when possible.
- Water should be restricted to 500–1000 mL per day for asymptomatic or chronic SIADH.
- Normal saline (0.9%, 154 mEq/L) infusion and furosemide (20 mg) for hyponatremia of unknown duration or moderate CNS symptoms. The goal is to increase Na^+ by 8–10 mEq/L in first 24 h. Measure Na^+ every 4 h.
- Hypertonic saline (3%, 513 mEq/L) at 1–2 mL/kg per h infusion and furosemide (20 mg) for acute hyponatremia associated with coma or seizures. The goal is to increase Na^+ by 2 mEq/L per h until symptoms improve. Measure Na^+ every 2 h.
- Demeclocycline 300–600 mg PO bid to diminish responsiveness of collecting tubule to ADH for persistent hyponatremia unresponsive to other therapy.
- Vasopressin-receptor antagonist such as conivaptan (20–40 mg IV qd) or tolvaptan (15–60 mg PO qd) as an adjunct to increase free water clearance and Na^+.
- Urea, 15-30 mg tid or qid to enhance water excretion in chronic SIADH.
- Infusion rate (mL/hr) = $[TBW \times (Na_{target} - Na_{current})/(Na_{infusion})] \times (1000\ mL/L) \times (1/t)$, where TBW = total body water (0.6 × body weight); Na_{target} = target Na^+; Nacurrent = current Na+; Nainfusion = Na+ of saline infusion; t = time to achieve target Na+ in h.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Cerebral edema	Headache, confusion, coma, seizures, difficulty concentrating, lethargy	Decerebrate posturing, altered level of consciousness	CT (brain) MRI (brain) EEG
GI	Increased free water intake	N/V, anorexia		
RENAL	Free water retention	Concentrated urine	No edema	Serum Na^+ <130 mEq/L, serum Osm <275 mOsm/L, urine Osm >100 mOsm/L, urine Na^+ >40 mEq/L
NM	Fatigue, lethargy	Muscle cramps, falls	Motor weakness	

Key References: Ellison DH, Berl T: Clinical practice. The syndrome of inappropriate antidiuresis, *N Engl J Med* 356(20):2064–2072, 2007; Cornforth BM: SIADH following laparoscopic cholecystectomy, *Can J Anaesth* 45(3):223–225, 1998.

Perioperative Implications

Preoperative Preparation

- Medical evaluation for duration and other causes of hyponatremia.
- Neurologic assessment for symptomatic hyponatremia.

Monitoring

- Periop measurement of serum Na^+
- CVP or pulm artery cath if necessary to maintain euvolemia

Induction

- Avoid drugs that may potentiate SIADH.

Maintenance

- Hyponatremia reduces MAC.
- Avoid hypotonic IV fluids.

Extubation

- Symptomatic hyponatremia may contribute to delayed emergence from anesthesia.
- Hyponatremia can cause obtundation and diminished ability to protect the airway.

Adjuvants

- Normal saline (0.9%, 154 mEq/L) and furosemide to maintain euvolemia and normal Na^+.

Postoperative Period

- Free water restriction, and avoid hypotonic fluids.
- Monitor serum Na^+.
- Assess for CNS signs of hyponatremia: Lethargy, confusion, and seizures.

Anticipated Problems/Concerns

- Major surgery causes increased ADH release.
- Acute symptomatic postop hyponatremia is a medical emergency.
- The practice of using hypotonic maintenance fluids in pediatrics is controversial.
- Most reported cases of ODS were assoc with rapid correction of hyponatremia at rates over 12 mEq/L per day but may occur at slower rates of correction.

Syndrome X

James A. Ramsey | Lee A. Fleisher

Risk

- True incidence unknown
- Postmenopausal or posthysterectomy women most often at risk
- Common cause of chest pain in women with angiographically normal coronary arteries
- Linked to adverse cardiovascular outcomes and a poor quality of life
- No diagnostic test

Perioperative Risks

- Acute withdrawal of sex hormone replacement can potentially lead to symptoms.
- Preop angina can delay procedures.

Worry About

- Discontinuation of medications (HRT) can precipitate symptoms

Overview

- Characterized by angina with or without ST-segment changes, with or without reversible perfusion defects on stress test, and with normal coronary arteriograms.
- Poorly understood multifactoral etiology makes specific treatment difficult.
- Some studies have found an increased risk of other vasospastic disorders in pts with cardiac syndrome X, such as migraine and Raynaud phenomenon.
- A multimodal approach to reducing oxidative stress and improving endothelial function may be beneficial.

Etiology

- Etiology unproved but thought to be due to endothelial dysfunction, ± vasospasm and abnormal cardiac nociception, with systemic inflammation (increased CRP) playing a role.
- Bioavailability of NO plays a role.
- Acute withdrawal of estrogen appears to be a more significant factor than chronic withdrawal.

Usual Treatment

- Treatment includes lifestyle modification, antianginal, antiatherosclerotic, and antiischemic medications.
- Nonpharmacologic options include cognitive behavioral therapy, enhanced external counterpulsation, neurostimulation, and stellate ganglionectomy.
- Estrogen patch has been found to significantly improve exercise tolerance and alleviate chest pain.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Angina (chest pain) Inflammation	Hx of exertional angina Hx of evaluations leading to catheterization Hx of hormone replacement therapy		Normal coronary angiogram in presence of chest pain Elevated CRP

Key References: Lim TK, Choy AJ, Khan F, et al.: Therapeutic development in cardiac syndrome X: a need to target the underlying pathophysiology, *Cardiovasc Ther* 27(1):49–58, 2009; Agrawal S, Mehta PK, Bairey Merz CN: Cardiac syndrome X: update, *Heart Fail Clin* 12(1):141–156, 2016.

Perioperative Implications

Preoperative Preparation

- Estrogens are withdrawn owing to the threat of procoagulant activity. Pts with this syndrome may experience significant angina upon such withdrawal.
- Distinguish chest pain due to this syndrome from chest pain due to coronary insufficiency from other causes.
- Continue preop medications with appropriate thromboembolic prophylaxis.

Monitoring

- ST-segment analysis, usual ASA monitors
- Invasive as appropriate for procedure

Preinduction/Induction

- Contingent upon type of surgery; may consider maintaining usual medications with use of beta-blockers as appropriate.
- No data as to preferred anesthetic technique or agents.

Anticipated Problems/Concerns

- Angina preop or periop in a pt with known clear coronary arteries.
- Continuation of HRT can increase coagulability.
- Continuation of beta-blockers and CCBs can lead to expected use of vasopressors.

Systemic Lupus Erythematosus

Erez Ben-Menachem

Risk

- Prevalence: 1:2500 in Northern Europeans and 1:500 in African American population.
- Female:male ratio: 9:1.
- Peak age of onset is between 16-40 y; 20% of SLE pts present prior to age 16 y.

Perioperative Risks

- Increased lupus activity is associated with surgery and stress.
- Infections can initiate lupus or cause a relapse.

Worry About

- CV: Htn, CAD, pericarditis, Libman-Sacks endocarditis with mitral insufficiency, myocarditis, pulmonary
- Pulm: Restrictive lung disease with decreased diffusion capacity
- Renal: Lupus nephritis and renal insufficiency
- Endo: Adrenal insufficiency secondary to chronic corticosteroid use
- Heme: Increased risk of thromboembolism in pts with antiphospholipid antibodies or severe nephrotic syndrome; thrombocytopenia and anemia
- Neurologic: Peripheral neuropathy, delirium, and stroke due to thromboembolism
- Neonatal lupus syndrome: Fetal heart block from maternal autoantibodies that cross placenta

Overview

- Autoantibody-mediated tissue damage results in multisystem organ damage.
- Biopsy demonstrates inflammation, deposition of autoantibodies, and complement in skin and kidneys.
- 15-y survival with lupus is 80%.
- Procainamide, hydralazine, quinidine, clonidine, enalapril, isoniazid, or captopril may cause drug-induced lupus variant.
- Mechanism of increased lupus activity with surgery is unclear but may be related to release of antigens into the bloodstream that bind to circulating antinuclear antibodies to form immune complexes.

Etiology

- Abnormal handling and clearance of cellular debris may lead to autoimmunity against nuclear particles with a high prevalence of specific autoantibodies; ANA, anti-dsDNA, anti-Smith, antiphospholipid.
- A genetic contribution (major histocompatibility complex gene) is important in increasing susceptibility to lupus.
- Ultraviolet radiation is the strongest environmental factor linked to lupus exacerbations.

Usual Treatment

- Lack of specific therapy for SLE.
- Most pts should receive antimalarials (hydroxychloroquine or chloroquine).
- NSAIDs for musculoskeletal symptoms and serositis.
- Immunosuppressive medications, including glucocorticoids, azathioprine, cyclophosphamide, methotrexate, and mycophenolate; belimumab; and monoclonal antibody therapy for treatment resistant disease.
- Smoking cessation; smoking is associated with higher disease activity.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, increased CAD, pericarditis, endocarditis, myocarditis, CHF, conduction blocks, pulm Htn	Chest pain Palpitations Dyspnea	Murmur Pericardial friction rub Peripheral edema	ECG ECHO CXR
RESP	Restrictive lung disease, alveolar hemorrhage, pleural effusion, pulm edema	Pleuritic chest pain Hemoptysis Cough Dyspnea	Pleural rub Cyanosis Decreased lung volume Rales, crackles	CXR PFTs ABG
GI	Gastritis/PUD secondary to medications, lupoid hepatitis, SLE vasculitis resulting in colitis, pancreatitis, and bowel ischemia	N/V Abdominal pain Ileus	Hepatomegaly Splenomegaly Jaundice	LFTs PT/PTT/INR
HEME	Thrombocytopenia, leukopenia, anemia, thromboembolism (lupus "anticoagulant" prolongs aPTT in vitro, but pts have prothrombotic tendency)	Bruising Thrombosis	Lymphadenopathy Splenomegaly	CBC/plts PTT aPL antibodies
RENAL	Glomerulonephritis, nephrotic syndrome, renal insufficiency, renal failure	Fever, hematuria Polyuria Oliguria	Costophrenic tenderness Edema	Urinalysis BUN, Cr, TP, albumin Renal US or scan
CNS	Peripheral neuropathy, stroke, psychosis, fatigue, seizures	Numbness Hemiparesis Paranoid states Hyperirritability	Psychosis Nystagmus, ptosis, diplopia Aphasia	EMG/NCS MRI CT scan EEG
MS/ DERM	Vasculitis and ulceration Arthritis, myalgias, myositis, Raynaud phenomenon	Photosensitivity Ecchymosis or purpura Joint pain or immobility	Malar or butterfly rash Perioral ulcerations	X-ray ANA

Key References: Rahman A, Isenberg DA: Systemic lupus erythematosus, *N Engl J Med* 358(9):929–939, 2008; Ben-Menachem E: Systemic lupus erythematosus: a review for anesthesiologists, *Anesth Analg* 111(3):665–676, 2010.

Perioperative Implications

Preoperative Preparation

- Consider hydrocortisone 50-100 mg IV prior to induction if pt is on chronic steroid therapy.
- Antibiotic prophylaxis if valvular disease is present.

Monitoring

- Caution with arterial line in pts with Raynaud phenomenon.
- Consider PA cath for pulm Htn or CHF.
- Consider Foley cath and CVP/PA cath for fluid titration if renal involvement.

Airway

- Occasionally reduced TMJ, ROM, subglottic stenosis, or cricoarytenoid arthritis manifesting as hoarseness, stridor, or airway obstruction; consider fiberoptic intubation.

Preinduction/Induction

- Consider stress dose corticosteroid therapy.

Maintenance

- No specific agents indicated or contraindicated; consider myocardial function.
- Regional acceptable if no coagulopathy.
- Avoid renally excreted drugs and renal toxins if renal insufficiency is present.
- Cyclophosphamide inhibits plasma cholinesterase and may cause prolonged response to succinylcholine.
- Careful pt positioning if peripheral neuropathies or osteoporosis is present.
- Appropriate thromboprophylaxis.

Adjuvants

- Corticosteroids, supplemental O_2, and careful titration of fluids with renal involvement

Extubation/Postoperative Period

- Reassess respiratory, renal, and CV status prior to extubation.

Anticipated Problems/Concerns

- Adrenal insufficiency from chronic steroid suppression
- Postop infections and pulm complications
- Postextubation laryngeal edema or stridor
- CAD, CHF and arrhythmias
- Renal insufficiency and volume status
- CNS dysfunction, seizures, neuropathy
- Thrombocytopenia, anemia, and thromboembolism
- Lupoid hepatitis

Takayasu Disease

Adrian P. Jennings | Caroline M. Cardy

Risk

- Worldwide incidence: 2.6 cases per million per y.
- Race with highest prevalence: Asian.
- Females 8–9 times more likely to be affected than males.

Perioperative Risks

- Severe uncontrolled Htn leading to end-organ dysfunction
- Stenosis of major blood vessels affecting regional circulation
- Difficulties in monitoring BP.
- Long-term corticosteroids.

Worry About

- Multiple occlusions of peripheral arteries, CHF, stroke, cardiac valve dysfunction, hypertensive episodes, intracranial hemorrhage, and iatrogenic adrenal suppression

Overview

- A rare systemic inflammatory large-vessel vasculitis primarily affecting the aorta and its main branches
- Initial "inflammatory phase" characterized by systemic illness with malaise, fever, weight loss, and fatigue
- Secondary "pulseless phase" characterized by vascular insufficiency from intimal narrowing of the vessels manifesting as arm or leg claudication, renal artery stenosis causing Htn, and neurologic manifestations due to decreased blood flow to the brain

Etiology

- Unknown; some evidence to support a genetic predisposition.
- Cell-mediated immune mechanisms are of primary importance.
- Panarteritic inflammatory infiltrates cause marked thickening of the affected artery. Segmental and patchy granulomatous inflammation leads to arterial stenosis, thrombosis, and aneurysms.
- Initial vascular lesions frequently occur in the left subclavian artery, with other branches and the aorta becoming affected as the disease progresses.

Usual Treatment

- Two components:
  - Controlling inflammatory process: Corticosteroids are the mainstay of therapy. Additional cytotoxic agents may be required to achieve remission and steroid taper.
  - Controlling Htn: Antihypertensive agents. Aggressive therapy is necessary to prevent complications. Low-dose aspirin may have therapeutic effect.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Uncontrolled Htn Aortic regurgitation Ischemic heart disease CHF Stenosis, thrombosis, or aneurysms of systemic and pulm vessels	Poor exercise tolerance, arm or leg claudication, angina, CHF symptoms, syncope, headaches, Hx of CVA	Chest exam for signs of CHF Absence of peripheral pulses BP with difference >10 mm Hg between the arms Arterial bruit Raynaud syndrome	LVH on ECG ECHO Angiography/MRA
RESP	Pulm Htn Ventilation-perfusion mismatch	Dyspnea		CXR ABG
RENAL	Renal artery stenosis		Uncontrolled BP Renal bruit	BUN/Cr Doppler US
ENDO	Cushingoid	Long term steroid use	Features of Cushing	Check blood sugar
CNS	CVA, intracranial hemorrhage, syncope, retinopathy	Headache Amaurosis fugax Stroke/TIA Seizures	Ophthalmic exam Carotid bruit Focal neurologic deficits	Angiography/MRA/CT
HEME	Anemia	Fatigue		FBS

Key References: Kathirvel S, Chavan S, Arya VK, et al: Anesthetic management of patients with Takayasu's arteritis: a case series and review, *Anesth Analg* 93(1):60–65, 2001; Keser G, Direskeneli H, Aksu K: Management of Takayasu arteritis: a systematic review, *Rheumatology* 53(5):793–801, 2014.

Perioperative Management

Preoperative Preparation

- Assess myocardial and volume status.
- Assess peripheral pulses.
- BP control.

Technique

- General anesthesia involving endotracheal intubation/extubation and inadequate depth may result in considerable BP fluctuation and may precipitate cerebral hemorrhage, rupture of aneurysms, and cardiac dysfunction.
- Regional techniques avoid the need for cerebral monitoring, although they may be associated with hypotension. Anticoagulation precludes. Epidural and spinal used successfully for cesarean section.

Monitoring

- Measure BP proximal to areas of arteritis. When weak or absent peripheral pulses, pulse oximetry, automatic NIBP, and Doppler flow signals can be used to record blood pressure.
- Avoid invasive BP due to increased risk of vessel damage. Femoral may be preferred site.
- Consider cerebral monitoring if asleep and compromised carotid blood flow (e.g., transcranial Doppler, EEG, cerebral oximetry).
- ECG and urine output to assess adequacy of coronary and renal blood flow.

Airway

- Hyperextension of head during laryngoscopy may compromise cerebral blood flow.

Induction

- Avoid a hypertensive crisis during tracheal intubation. Regional anesthesia should proceed with cautious neuraxial dosing to minimize hypotension.

Maintenance

- Maintain BP, avoid tachycardia, and maintain peripheral perfusion. Avoid excessive hyperventilation due to effect on CBF.

Extubation

- Aim for prompt awakening to allow prompt evaluation of mental status.

Adjuvants

- If risk of adrenal suppression from long term steroids, consider need for supplemental periop dosing.
- Consider periop antibiotics if immunosuppressed.

Postoperative Period

- Continue CV, CNS, and renal monitoring. Control BP. Consider ICU/PACU overnight.
- Risk of infection and sepsis due to immunosuppression.

Tetanus

Kirk Lalwani

Risk

- A major public health problem in the developing world, but improving; responsible for 200,000–300,000 deaths/y in 2000 and only 60,000 in 2013, and the vast majority were neonatal deaths.
- Incidence in USA: 0.16 cases/million population (1998–2000).
- Highest incidence in USA is among the elderly (>60 y), persons of Hispanic ethnicity, older adults with diabetes, and parenteral drug users.

Perioperative Risks

- Difficult airway or intubation in the presence of masseter spasm, neck rigidity, or opisthotonus
- Autonomic instability with sudden fluctuations in BP, arrhythmias, cardiac failure, and cardiac arrest

Worry About

- Spasms of the laryngeal and respiratory muscles can be life-threatening as a result of airway obstruction or chest wall rigidity respectively, and may mandate urgent ET intubation.

- Respiratory failure may require NM paralysis in addition to sedation for effective PPV in the presence of severe spasms.
- Autonomic instability: Tachycardia, bradycardia, Htn, hypotension, arrhythmias, cardiac failure, and repeated cardiac arrest.
- Pneumonia, sepsis, myoglobinuria, pulm embolism, bony fractures, and hyperthermia.

Overview

- Infection of penetrating wounds or devitalized tissue with spores of anaerobic gram-positive bacillus *Clostridium tetani*; enters the CNS via peripheral nerves and spreads via retrograde intraneuronal transport to disable inhibitory pathways in the spinal cord and brain (glycine and GABA).
- CNS disinhibition characteristically begins with spasms of the masseter muscles ("risus sardonicus," lockjaw) and progresses to involve rest of the body, including spasms of respiratory muscles ("respiratory convulsions") that cause glottic spasm, airway obstruction, hypoxia, and respiratory failure.
- Autonomic instability is a hallmark of the disease and may cause fatal cardiac arrest.
- Initial injury may be insignificant or unnoticed by the pt.
- Neonatal tetanus typically presents 6–8 d after birth with trismus and inability to feed.
- Tetanus may follow surgery (usually intraabdominal or on contaminated tissues), burns, gangrene, dog bites, chronic infection, parenteral drug use, dental infection, abortion, and childbirth.

Etiology

- Infection of penetrating wound or devitalized tissue by spores of anaerobic, gram-positive bacillus *Clostridium tetani*; they proliferate and produce a potent exotoxin, tetanospasmin.
- Tetanospasmin is taken up by motor nerve endings and spreads to other neurons in skeletal muscle, the spinal cord, and brain, where it principally inactivates inhibitory interneurons in glycinergic and gamma-aminobutyric acid pathways.

Usual Treatment

- Neutralize circulating toxin with IV human antitetanus globulin.
- Eradication of the organism by wound care, surgical debridement, and antimicrobial therapy.
- High-dose metronidazole or penicillin G (erythromycin if penicillin allergy) therapy IV for 10 d is effective at eradicating spores and bacilli.
- Control muscle spasms by sedation, other muscle relaxants, and NM paralysis.
- Magnesium may control spasms and autonomic disturbances in mild cases, but has no beneficial effect on mortality compared to diazepam, which is considered the standard of treatment.
- Supportive therapy, including ventilatory support, treatment of autonomic instability, nutritional support, prophylaxis of DVT, and prevention of nosocomial infection, particularly ventilator-associated pneumonia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Laryngospasm and glottic obstruction	Dyspnea, noisy breathing	Stridor, retractions of accessory muscles, limitation of mouth opening and ROM of neck	
CNS	Generalized or localized muscle rigidity and spasms	Dysphagia, drooling, spasms	Opisthotonus, trismus, "risus sardonicus," onset of spasms with minimal stimuli, bony fractures	
CV	Cardiac failure, myocarditis, arrhythmias, Htn, hypotension, cardiac arrest	SOB, palpitations	Episodic fluctuations in BP, heart rate; arrhythmias, signs of cardiac failure	ECG, ECHO
RESP	Hypoventilation, apnea, respiratory failure, pneumonia	Dyspnea	Hypoventilation, limited chest excursions, decreased breath sounds, rhonchi, cyanosis	ABG, CXR
RENAL	Rhabdomyolysis	Pink or red urine	Hematuria	US, serum CK

Key References: Rodrigo C, Fernando D, Rajapakse S: Pharmacological management of tetanus: an evidence-based review, *Crit Care* 18(2):217, 2014; Rodrigo C, Samarakoon L, Fernando SD, et al: A meta-analysis of magnesium for tetanus. *Anaesthesia* 67(12):1370–1374, 2012.

Perioperative Implications

Preinduction/Induction/Maintenance

- Adequate sedation with benzodiazepines to control spasms; muscle relaxants may be necessary.
- Minimize environmental stimuli.
- Difficult airway or intubation: Consider fiberoptic intubation.
- Avoid pancuronium and desflurane (sympathetic stimulation).
- Resistance to multiple nondepolarizing agents has been described.

Monitoring

- ECG for dysrhythmias
- Echocardiography (CV decompensation)
- Arterial line for continuous BP measurement and arterial blood gas measurement
- NM monitoring with nerve stimulator

General Anesthesia

- Magnesium sulfate may be useful in controlling spasms, decreasing autonomic instability, and decreasing the requirements for sedative drugs.
- Watch for S-T segment and T-wave changes that may indicate toxic myocarditis.
- Hypotension and bradycardia may be indicative of brainstem involvement and a poor prognosis.
- Elective tracheostomy recommended for long-term ventilator support and pulm toilet.
- Consider pulm embolism in the event of sudden decompensation during anesthesia.
- Maintain alkaline diuresis in the event of myoglobinuria.

Regional Anesthesia

- Consider adding epidural anesthesia for autonomic hyperreactivity.

Postoperative Period

- Endotracheal intubation or tracheostomy is needed for assisted ventilation on ICU with sedation and NMBs.
- Benzodiazepines, magnesium sulfate, opioids, clonidine, and intrathecal baclofen may help control spasms; magnesium also decreases autonomic instability and the need for sedation.
- Nutritional support via enteral or parenteral feeding.
- DVT prophylaxis to prevent pulm embolism.

Anticipated Problems/Concerns

- Sudden CV instability or cardiac arrest may occur.
- Propranolol, labetalol, and phentolamine are assoc with increased risk of cardiac arrest.
- Mortality in US averages about 10%, rising to 50% in pts >60 y of age.
- Abnormal neurologic findings may persist for up to 2 y following recovery.

Tetralogy of Fallot

Sarah Deverman

Risk

- Occurs in 4-5:10,000 live births (1:2,000–2,500)
- Most common cyanotic CHD (10% of all CHDs)
- Occurs equally in males and females

Perioperative Risks

- If unrepaired, tet spells can lead to RVH, RV failure, and death (50% in first year of life).
- Mortality after TOF repair: 5–8% in first 2 y postrepair (if uncomplicated anatomy).
- Increased mortality if coexisting PA hypoplasia, atresia, or major AP collaterals.

Worry About

- Increased R-to-L shunt from decreased SVR or increased PVR
- Crying and agitation leading to tet spell leading to more hypoxemia, hypercarbia, acidosis
- Air bubbles in IV tubing
- Polycythemia and assoc thrombocytopenia
- RV failure after inadequate or late repair
- Arrhythmias following repair

Overview

- Anatomy:
  - RVOT obstruction: Infundibular narrowing, pulm stenosis, PA hypoplasia, pulm atresia.
  - VSD: Large, unrestrictive.
  - Overriding aorta.
  - RV hypertrophy.

- 5–12% have anomalous origin of LAD from RCA and cross the RVOT inferiorly. Must confirm prior to OR.
- 25% have right aortic arch.
- Severity of symptoms correlates with degree of RVOT obstruction, as this determines the degree of R-to-L shunting.
  - RVOT obstruction has fixed components (degree of infundibular obstruction, size of pulm valve annulus, size of PA) and dynamic components (infundibular muscle bundle spasm, PVR, SVR).
- Fixed factors determine amount of chronic cyanosis.
- Dynamic factors determine tet spells.
- Pink tets have minimal amount of PS.
- Avoid hypoxia, acidosis, high airway pressures, excitement, and agitation.
- Dx by ECHO, cardiac cath, and/or MRI.
- Associated with chromosome 22 deletions and diGeorge syndrome, VACTERL, CHARGE, and velocardiofacial syndrome.

Usual Treatment

- Primary repair: Usually done at 3–12 mo
- If not immediately operable (low birth weight, prematurity, other disease processes), palliative shunts to increase pulm blood flow (Blalock-Taussig shunt, aortopulmonary shunts)
- Beta-blockers to decrease infundibular spasm and spelling
- Treatment for tet spell:
  - 100% O_2 (pulm vasodilator)
  - Sedation (morphine/fentanyl)
  - Increased SVR (squatting, phenylephrine)
  - Propranolol (decreased contractility of infundibulum; decreased RVOTO)
  - Bicarbonate to correct metabolic acidosis

Assessment Points

System	Effect	Assessment by Hx	Test
GENERAL		FTT, clubbing	Growth charts
CHEST	RVH	Signs of right heart failure	CXR with boot-shaped heart
CV	See Overview	Frequency and severity of tet spells	ECHO, cath, MRI ECG-RVH, RA
HEME	Polycythemia from chronic hypoxemia Plt count may be low from polycythemia	Chronic cyanosis	Hct, plt count

Key References: Doyle T, Kavanaugh-McHugh A: Pathophysiology, clinical features, and diagnosis of tetralogy of Fallot. In Connolly HM, Triedman JK, Armsby C, editors, Waltham, MA, *UpToDate*, 2016. www.uptodate.com/contents/pathophysiology-clinical-features-and-diagnosis-of-tetralogy-of-fallot. (Accessed 13.06.16.); Schmitz ML: Anesthesia for right-sided obstructive lesions. Tetralogy of Fallot. In Andropoulos DB, editor: *Anesthesia of congenital heart disease*, ed 2, Hoboken, NJ, 2010, Wiley-Blackwell, pp 427–432.

Perioperative Implications

Preoperative Preparation

- Heavy premedication to avoid agitation, crying

Monitoring

- Standard monitors plus radial arterial line, CVP, and TEE

Airway

- Standard oral or nasal intubation

Preinduction/Induction

- Mask induction with sevoflurane and oxygen. Ketamine (1–2 mg/kg) with fentanyl (10 mcg/kg) and rocuronium (1 mg/kg) if IV present. AVOID decrease in SVR.

Maintenance

- Phenylephrine appropriately drawn up and diluted.
- Avoid increase in PVR and decrease in SVR.

Extubation

- Pts are taken to the ICU monitored and intubated.

Anticipated Problems/Concerns

- Intraop tet spells
- Arrhythmias

Thalassemia

Sohail Bampoe | Michelle R. Cole

Risk

- Over 60,000 children are born annually with severe beta-thalassemia.
- Global regions that are primarily affected include the Mediterranean, North Africa, and Southeast Asia, where alpha thalassemia is more common.
- Beta-trait carrier status has a global prevalence of approximately 1.5%.
- Over 200,000 pts are currently receiving treatment for thalassemias.
- In endemic areas with highest frequency, carrier status is present in as many as 1:7 individuals, and thalassemia major can occur in 1:158 live births.

Perioperative Risks

- Abnormal globin chains result in severe anemia (mild microcytic anemia in those with carrier status).
- CHF is the leading cause of death.
- End-organ effects of hemochromatosis from chronic iron therapy: Cardiomyopathy, cirrhosis, endocrinopathies (e.g., diabetes, hypopituitarism).
- Diabetes mellitus is common.
- Restrictive lung dysfunction and pulm Htn.
- Airway difficulties, including maxillofacial abnormality secondary to bone marrow expansion.
- Hypercoagulopathy in asplenic pts, and coagulopathy in pts with cirrhosis.
- Alloimmunization secondary to multiple blood transfusions. Obtaining appropriately cross-matched blood may require prolonged testing.

Worry About

- Difficult airway secondary to maxillary deformation in up to 19%
- Cardiac arrhythmias or HF
- Hypercoagulability
- Pulm Htn
- Immunocompromisation

Overview

- Thalassemia is a heterogeneous group of inherited microcytic anemias that result from a genetic mutation causing a defect in the synthesis of one or more globin chain subunits of the HbA, which is normally composed of $\alpha 2\beta 2$.
- Thalassemia is classified according to the genotype that correlates with clinical severity.
- Alpha thalassemia: Alpha globin gene deletion leads to a decrease in alpha chain production with a relative overproduction of beta chains. This leads to formation of β4 tetramers, which causes RBCs to be more rapidly removed leading to anemia.
- Alpha thalassemia silent carrier: One gene absent (aa/a-); healthy except occasional mild anemia.
- Alpha thalassemia trait: Two genes absent on the same or different chromosomes (a-/a- or aa/--); mild anemia.
- Alpha thalassemia intermedia (Hb H disease): inactivation of three genes (a-/--) leads to a spectrum for manifestations; mild to moderately severe anemia, splenomegaly, icterus, abnormal RBC indices; recurrent infections. Heinz bodies = beta chain tetramers. Hb H disease results in poor oxygen delivery to the tissues due its high affinity for oxygen.
- Alpha thalassemia major (Hb Barts): Complete deletion of all alpha chain genes resulting in the formation of Hb-Bart's, which has an exceptional affinity for oxygen resulting in extremely limited tissue oxygen delivery. Incompatible with life; hydrops fetalis unless intrauterine blood transfusions.
- Beta thalassemia: Decreased beta chain production relative to the alpha chain production as a result of mutation resulting in either absence (beta o) or decrease (beta+) in the production of beta globin. Alpha chains are in excess and precipitate leading to inadequate erythroid maturation and hemolysis. In most severe forms, this leads to splenomegaly, anemia, massive expansion of medullary and extramedullary erythropoietic tissue leading to skeletal growth, and metabolic abnormalities.
- Beta thalassemia is a silent carrier (beta/beta+); it shows no clinical symptoms except for low RBC counts.
- Beta thalassemia trait (beta/beta+) = beta thalassemia minor: Mild anemia, abn RBC indices, hypochromia, microcytosis.
- Beta thalassemia intermedia (beta/beta o, beta+/beta+, beta+/beta o): A compound heterozygous state; profound anemia, which periodically may require transfusion support and occasionally splenectomy.

- Beta thalassemia major (beta o/beta o) = Cooley's anemia, transfusion-dependent anemia, massive splenomegaly, bone deformities, growth retardation, and abnormal facies. As a result of chronic anemia and ineffective erythropoiesis, bone expansion and extramedullary erythropoiesis may develop in liver and spleen, and marrow space expansion at sites such as the cranium and paravertebral areas can lead to disfiguring bony changes. Deaths are usually secondary to cardiac manifestations, including cardiomyopathies and heart failure. The incidence of pulm Htn and lung fibrosis increase, leading to a restrictive pattern of lung dysfunction.

Etiology

- Genetic mutation associated with ancestry in areas endemic to malaria

Usual Treatment

- Alpha thalassemia carriers (aa/-a) and those with alpha thalassemia trait (a-/a- or --/aa) are usually asymptomatic and require no treatment.
- Alpha thalassemia intermedia (--/-a): folic acid, transfusions, and possible splenectomy for progressive anemia; avoidance of oxidant drugs.
- Beta thalassemia minor (beta/ beta+) usually does not require treatment.
- Beta thalassemia intermedia and major treatment is symptomatic and supportive.
  - Blood transfusion support with leukodepleted blood when Hb <7 g/dL; transfuse up to Hb 11–13 g/dL. Transfusions are usually required several times a week and can result in iron overload.
  - Iron chelation therapy; deferoxamine IV can cause renal toxicity. Deferasirox causes less toxicity.
  - Splenectomy usually needed around age 6–7 y or in adolescence when transfusion treatments required are at 1.5 times normal (e.g., >200 mL/kg/y).
  - Hematopoietic stem cell transplantation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Maxillary hypertrophy Orofacial malformations High arched palate	Prior difficulties with intubation	Airway evaluation	
CV	Cardiomyopathy Arrhythmias Pericarditis Heart failure	Exercise tolerance Palpitations	Dyspnea Dysrhythmias Murmurs	ECG, annual ECHO, CXR Holter
RESP	Restrictive lung disease Pulm Htn Lung fibrosis	Exercise tolerance	Fine inspiratory crackles	PFTs
HEME	Anemia Splenomegaly Alloimmunization	Exercise tolerance H/o splenectomy Blood transfusion reactions	Tachycardia Splenomegaly	CBC Type and screen
	Coagulopathy			Coagulation studies
HEPAT	Cirrhosis		Hepatomegaly	LFTs, coagulation studies, hepatitis serologies
ENDO	Diabetes mellitus	Recurrent infections Poor wound healing		Fasting glucose Glucose tolerance test
	Hypothyroidism	Cold intolerance Lethargy, depression Decreased metabolism		Thyroid function test
	Adrenal insufficiency			Cortisol determination

Key References: Higgs DR, Engel JD, Stamatoyannopoulos G: Thalassaemia. *Lancet* 379(9813):373–383, 2012; Staikou C, Stavroulaki E, Karmaniolou I: A narrative review of peri-operative management of patients with thalassaemia. *Anaesthesia* 69(5):494–510, 2014.

Perioperative Implications

- Thalassemia minor, in general, does not create anesthetic problems. In pts with thalassemia major, consideration has to be given to problems derived from the severity of the anemia itself and the associated cardiorespiratory complications, but also those related to transfusion therapy, and to bony malformations. Pts may present for major surgery, such as splenectomy.

Preinduction

- Detailed airway evaluation and planning.
- Cardiac function evaluation (including echocardiography).
- Pulm function evaluation.
- Hemoglobin level should be determined and preop transfusion considered.
- Cross-matched blood should be available (antibody matched, leukocyte reduced for frequently transfused children); high degree of alloimmunization in this population exists.
- Evaluation for endocrine dysfunction (e.g., DM, hypopituitarism, hypothyroidism) and adequacy of treatment.
- Hepatic function evaluation in light of risk of cirrhosis and iron or viral-induced damage.
- Coagulation studies.
- Presplenectomy antibiotics and immunizations (when appropriate).

Monitoring

- Consider the need for a Swan-Ganz cath and measurements of CI, CO, and mixed-venous oxygenation.
- Consider arterial cath and frequent hemoglobin, lactate, and blood gas analysis.
- Esophageal Doppler or transesophageal ECHO may contribute useful information.

Induction/Maintenance

- Preparation for possible difficult airway.
- Close attention to the positioning in light of demineralization, pathologic fractures, and scoliosis.
- Careful monitoring of CV function, including postsplenectomy Htn.
- Beware of the effects of laparoscopy on circulatory and respiratory function.
- Thromboembolism prophylaxis; SCD and/or pharmacotherapy when applicable.
- Consider cell salvage.
- Prophylactic antibiotics may be indicated.

General Anesthesia

- Facial abnormalities can present a difficult airway.
- Volatile concentrations should be kept low to avoid cardiac depression in those with high cardiac output states.
- Hypoxemia and acidosis will exacerbate pulm Htn.

Regional Anesthesia

- Osteoporosis, osteopenia, and scoliosis are common.
- Vertebral bodies maybe of reduced height as a result of osteoporosis; the segmental portion of conus medullaris may be lower than predicted.
- Extramedullary hematopoiesis is uncommon in the intraspinal location, but if symptoms of spinal compression are suspected, MRI should be performed prior to regional anesthesia.
- Consider epidural versus spinal in pts who need a regional anesthetic but have CV pathology.
- Evaluate closely coagulation studies prior to regional anesthesia.
- Thromboembolism prophylaxis, especially in postsplenectomy pts.
- Spinal and epidural techniques have been performed safely.

Postoperative Period

- Postop monitoring dependent on the preop status.
- Critical care admission may be necessary.
- Prophylaxis for thromboembolism (postsplenectomy pts in particular).

Anticipated Problems/Concerns

- Intubation difficulties
- CV instability secondary to severe chronic anemia, cardiomyopathy, and endocrinopathies
- Pulm insufficiency
- Coagulation abnormalities: Hypercoagulable or hypocoagulable
- Impaired drug metabolism secondary to cirrhosis
- Adrenal insufficiency complications
- Difficulty in obtaining cross-matched blood due to alloimmunization
- Postop infections

Thrombocytopenia

Aliaksei Pustavoitau | Nauder Faraday

Risk

- Commonly present in pts with systemic illness (e.g., sepsis), pathologic conditions of pregnancy, and in pts requiring extracorporeal circulation.
- Prognosis is determined by underlying illness, not absolute platelet count.
- HIT, a prothrombotic immune-mediated disorder, occurs in <5% of pts exposed to heparin.

Perioperative Risks

- Bleeding associated with invasive procedures.

Worry About

- Spontaneous bleeding when platelet count <10,000/μL
- Bleeding from nonneurologic invasive procedures when platelet count <50,000/μL
- Bleeding from neurologic and spinal procedures when platelet count <100,000/μL
- Excessive periop bleeding with resultant hypovolemia and hemodynamic instability
- Potential need for transfusion of blood and blood products
- Concurrent anemia and pancytopenia
- Underlying cause(s) of thrombocytopenia
- Risk of thrombosis in pts with HIT (~50%)

Overview

- Defined by <150,000 platelets/mL. Severe thrombocytopenia defined by <50,000 platelets/mL.
- High risk of bleeding if prior bleeding at similar platelet count.
- High risk of bleeding if presence of generalized petechiae, purpura, and bleeding from mucous membranes.
- Treatment of thrombocytopenia is guided by underlying illness.
- Initial diagnostic workup includes CBC and peripheral smear, with other tests based on clinical examination.
- Bleeding time does not correlate with the risk of surgical bleeding.
- Need for platelet transfusion is determined by severity of thrombocytopenia and invasiveness of procedure.

Etiology

- Increased platelet destruction and non-immune causes: Infection with or without DIC, pregnancy-related HELLP syndrome, and TTP.
- Increased platelet destruction and immune causes: Drug-induced (including HIT), ITP, rheumatologic disorders, post-transfusion purpura, neonatal immune thrombocytopenia, and HUS.
- Hypersplenism (e.g., due to portal hypertension or hematologic malignancy).
- Decreased platelet production: Bone marrow failure, chemotherapy and radiation therapy, ethanol, and liver failure.
- Dilution: Platelet count is maintained until intravascular replacement >1.5-2 blood volumes

Usual Treatment

- Treat underlying cause:
  - Discontinue offending drugs, treat infection, splenectomy.
  - If HIT confirmed by positive platelet factor 4 antibody test and serotonin release assay, then anticoagulate with direct thrombin inhibitor.
  - ITP is treated with steroids and high-dose IgG in severe cases.
  - TTP is treated with exchange transfusion and plasmapheresis.
- Platelet transfusion is performed up to a single apheresis unit or equivalent at a time.
- Effect of platelet transfusion: Each unit of transfused platelets should raise count by ~10,000 platelets/μL but increases risk of future thrombocytopenia from alloimmunization (occurs in 50% of pts transfused with platelets).
- Transfusion thresholds:
  - ≤10,000/μL: Prophylaxis of spontaneous bleeding.
  - <20,000/μL: Prophylaxis of elective central venous catheter placement.
  - <50,000/μL: Prophylaxis of elective lumbar puncture, neuraxial anesthesia/analgesia, and nonneuraxial surgery.
  - <100,000/μL: Treatment of active bleeding; prophylaxis of neuraxial surgery (intracranial or spinal).
- Pts undergoing cardiac surgery with cardiopulmonary bypass should not be routinely transfused with platelets in the absence of thrombocytopenia.
- Transfusion of platelets in a ratio of 1:1:1 unit with packed red blood cells and fresh frozen plasma improves hemostasis and reduces risk of death from exsanguination in trauma pts requiring massive transfusion.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mucosal hemorrhage		Petechiae, purpura and ecchymoses of skin, oral mucosa and conjunctivae	
NEURO	Intracranial hemorrhage	Change in mental status	Mental status (GCS), focal motor deficits	Head CT
CV	Hypovolemia, anemia, pericardial effusion	Lightheadedness, syncope, palpitations	Tachycardia, hypotension, orthostasis, pericardial friction rub, pulsus paradoxus	ECG, CXR, ECHO
RESP	Pulm hemorrhage	Cough, hemoptysis		CXR
GI	GI bleeding	Hematemesis, hematochezia, melena		Stool guaiac
RENAL	Prerenal or renal azotemia, glomerulonephritis with specific disease entities	Urine output		BUN, Cr, urinalysis

Key References: Kumar A, Mhaskar R, Grossman BJ, et al.: Platelet transfusion: a systematic review of the clinical evidence, *Transfusion* 55(5):1116–1127, 2015; Kaufman RM, Djulbegovic B, Gernsheimer T, et al.: Platelet transfusion: a clinical practice guideline from the AABB, *Ann Intern Med* 162(3):205–213, 2015.

Perioperative Implications

Preinduction/Induction/Maintenance

- Assess hematologic and hemodynamic presentation.
- Determine bleeding risk based on underlying pathology, physical exam, degree of thrombocytopenia, and proposed surgical procedure.
- Ensure blood products availability based on the risk assessment.
- Consider prophylactic platelet transfusion if platelet count <50,000/μL or if <100,000/μL and high-risk surgical procedure.
- Avoid use of hetastarch, which can cause platelet dysfunction.

General Anesthesia

- Caution with nasal procedures, including nasotracheal intubation, nasogastric intubation, and nasopharyngeal thermometer placement.

Monitoring

- Platelet count should be obtained when a history of bleeding is present; diagnosis of periop bleeding is unclear; screening for heparin-induced thrombocytopenia (5–14 d after heparin exposure).
- Viscoelastic tests of coagulation (e.g., thromboelastography, thromboelastometry) can help diagnose cause of periop bleeding and reduce blood product usage.

Regional Anesthesia

- Neuraxial techniques may be considered when platelet count is >50,000/mL.
- Similar considerations should be given to performing deep plexus or peripheral nerve blocks.

Anticipated Problems/Concerns

- Excessive bleeding with invasive procedures
- Requirements for transfusion of platelets and other blood products

Thyroid Neoplasms

Michael F.M. James

Risk

- Incidence in USA is 23,500 new thyroid cancer cases/y, but incidence is increasing.
- Account for approximately 1% of new cancer diagnoses each y.
- Hispanics, African Americans, lower rate; Caucasians, moderate rate; Japanese, Chinese, Hawaiian, Filipinos, higher rate.
- Overall incidence 3× higher in women than in men; peaks in third and fourth decades of life.

Perioperative Risks

- Large thyroid mass may produce airway compression, deviation, or vocal cord paralysis.
- Decreased BP, decreased HR, asystole with manipulation of carotid sinus.
- Postop complications: Phrenic nerve injury, pneumomediastinum, pneumothorax, tracheomalacia and tracheal collapse postextubation, hematoma or laryngeal edema leads to airway compromise; bilateral laryngeal nerve injury calls for tracheotomy; superior laryngeal nerve injury leads to aspiration.
- Accidental removal and/or injury of parathyroid glands causes decrease in Ca^{2+}.

Worry About

- Occult pheochromocytoma: Bilateral lobe medullary thyroid cancer is associated with MEN IIA and IIB.

Overview

- Four main types: Papillary (80–90%), follicular (5–15%), medullary (<5%), primary thyroid lymphoma (rare), and primary thyroid sarcomas (rare).
- Prognosis of well-differentiated papillary cancer is excellent, especially for age <40 y with small tumors.
- Prognosis worsens for large tumors with poorly differentiated, anaplastic histology.
- Age at Dx, tumor burden, gender, extra-thyroidal invasion, and distant metastases are important prognostic factors.
- Latest research defines subcellular and molecular prognostic factors through genetic studies.
- BRAF mutation is the most common mutation in papillary thyroid cancer and is associated with disease aggressiveness and resistance to radioiodine treatment.

Etiology

- Factors include previous radiation, dietary iodine deficiency, goitrogens (chemical or dietary), preexisting benign thyroid disease, and genetic factors (Gardner syndrome, Cowden disease).
- Association between primary thyroid cancer and increased incidence of subsequent breast cancer.

Usual Treatment

- Surgery initial therapy of choice.
- Lobectomy with or without isthmectomy, near-total, or total thyroidectomy as indicated.
- Radioiodine scanning and ablation commonly used after thyroidectomy in well-differentiated tumors.
- Radical debulking procedure (palliative) for large tumors invading airway and causing esophageal obstruction and bleeding.
- Recurrences usually treated with surgery.
- Combined chemotherapy and radiation therapy for poor prognosis cases.
- Doxorubicin: Most active single agent; medullary thyroid cancer responds poorly.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vocal cord dysfunction Tracheal obstruction	Dysphonia SOB, DOE Wheeze/stridor	Neck mass	Indirect laryngoscopy US of neck, fine needle biopsy CXR CT of neck
CV	Mediastinal mass	SOB, DOE Wheeze, may be asymptomatic	Facial swelling	CXR CT/MRI
RESP	Lung metastases Lower airway obstruction	SOB, DOE Wheeze, hemoptysis		CXR CT/MRI
GI	Esophageal obstruction Liver metastases	Dysphagia		LFTs
ENDO	MEN IIA/IIB pheochromocytoma	Htn, especially episodic Flushing Palpitations, episodic Sweating		CT/MRI 24-h urine epinephrine Increased epinephrine/norepinephrine
	Hyperthyroidism	Tachycardia, tremor, heat intolerance		Increased T_4^+ Increased TSH
	Hyperparathyroidism			Increased Ca^{2+} Increased PTH
	Ganglioneuromatosis	Colic Cramping Diarrhea Obstruction	Mucosal neuromas in tongue, subconjunctival areas, or GI tract Thickened lips Marfanoid features	Hypercalciuria provocative test for calcitonin release
MS	Bone metastases PTH-induced bone disease	Bone pain		Bone scan

Key References: Katoh H, Yamashita K, Enomoto T, et al.: Classification and general considerations of thyroid cancer, *Ann Clin Pathol* 3:1045–1054, 2015; Longbottom J, Macnab R: Thyroid disease and thyroid surgery, *Anaesth Intens Care Med* 15:458–464, 2014.

Perioperative Implications

Preoperative Preparation

- Assess thyroid gland and/or tumor size, metastases, and hormonal activity.
- Ensure euthyroid state prior to surgery (antithyroid agents and beta-blockers as indicated).
- Assess larynx and/or trachea compression.
- May need smaller or armored ETT to prevent kinking (check CT scan).
- Record description of voice preop; obtain indirect laryngeal assessment of cord function.
- Correct abnormal Ca^{2+} prior to surgery.
- Check serum calcitonin level if medullary cancer suspected; rule out pheochromocytoma.

Monitoring

- Routine

Airway

- Usually straightforward. Difficult airway associated with standard predictors, obesity, invasion of the tracheal, or pharyngeal structures by tumor.

Induction

- Direct or videolaryngoscopic intubation is more reliable than fiberoptic. If airway is considered to be a major hazard, pt may need to plan ECMO or femoro-femoral bypass in advance.

Maintenance

- No one agent or technique shown to be superior.
- CV instability may occur with manipulation of carotid sinus (rare).

Extubation

- May develop tracheomalacia (very rare).
- May require reintubation owing to hematoma. (Anticipate pharyngeal and laryngeal edema and serious difficulty in airway management.)

Postoperative Period

- Metabolic: Decreased Ca^{2+}, hypoparathyroidism
- Nonmetabolic: Unilateral or bilateral nerve injury, hemorrhage, airway obstruction

Adjuvants

- May be performed under local anesthesia with IV sedation in selected cases
- Antiemetics, including dexamethasone, effective in reducing postop N/V

Anticipated Problems/Concerns

- Pts with medullary thyroid cancer: Rule out occult pheochromocytoma.
- Thyroid tumor can invade larynx, trachea, pharynx, or esophagus.
- Preplanned airway management strategies, especially with invasive tumors.
- Possible hyperthyroidism/hypothyroidism.

Tracheoesophageal Fistula (Congenital)

Anthony M.-H. Ho | Melinda L. Fleming

Risk

- Incidence of EA + TEF: 1:3500.
- EA/TEF in twins is 2.6 times higher than in singletons.

Perioperative Risks

- Respiratory distress
- Stomach distention, rupture (1%) possible
- Dehydration and hypoglycemia

Worry About

- Respiratory status
- Congenital heart disease (23%): PDA, VSD, TOF, ASD, right-sided aortic arch
- Location of fistula (typically unknown)
- Fluid and metabolic status
- Prematurity
- Low birth weight (common)

Overview

- Association with vertebral abnormalities (17%), anal and/or duodenal atresia (12%), cardiovascular anomalies (23%), tracheoesophageal fistula, esophageal atresia, renal (16%) and/or radial anomalies, and limb defects (10%) (VACTERL association).
- Respiratory compromise is possible from aspiration pneumonitis, tracheomalacia (usually present but clinically significant in 10–20% of cases), gastric distention, prematurity, and congenital heart disease.
- Gross classification: (A) EA without TEF (8%); (B) proximal TEF with distal EA (3%); (C) distal TEF with proximal EA (85%); (D) proximal and distal TEF (<1%); (E) TEF without EA or "H"-type TEF (4%). Gross type A is the only type without TEF and the attending risk of aspiration but the most likely to have associated anomalies (up to 65%).
- Preop echocardiography is useful for identifying cardiac anomalies and the presence right aortic arch (2.5–5%); if present, left-sided approach is required.
- In Gross C TEF, the fistula may be below the carina (11%) or within 1 cm proximal to the carina (22%), making the classic recommendation of positioning the ET tip between the carina and the fistula impossible or difficult. If margin between ET tip and carina is low, inadvertent endobronchial intubation of the compressed right lung may occur due to tube migration, and inadvertent ventilation of the fistula can occur due to tube migration. Repositioning of ET may lead to inadvertent endobronchial or fistula intubation.
- Most Gross C type do not have a long esophageal gap.
- Some fistula openings may be ≥3 mm with increased risk of stomach insufflation and inadvertent fistula intubation.
- Having the ET bevel facing posteriorly reduces the risk of inadvertent intubation in the beginning and subsequent ET position adjustments, if required.
- Avoiding high positive pressure ventilation reduces stomach insufflation.
- The fistula subtends an angle not unlike those of the mainstem bronchi, not orthogonally as illustrated in many textbooks. This makes it plausible on the one hand to accidentally intubate with the ET, but makes it easy to insert a balloon-tipped Fogarty cath (Plan A, discussed later).

Etiology

- Genetic syndromes associated with EA/TEF include all full trisomies (Down syndrome, Edwards syndrome, Patau syndrome), single gene disorders (CHARGE syndrome, Feingold syndrome, Opitz syndrome, and Fanconi anemia).
- Environmental factors implicated include maternal exposure to methimazole, exogenous sex hormones, alcohol, tobacco, diethylstilbestrol, infectious diseases, advanced maternal age, and working in agriculture or horticulture.
- An adriamycin-induced EA/TEF rat model facilitates embryologic study of the disease.

Usual Treatment

- Prevention of aspiration (NPO, continuous suctioning of esophageal pouch, elevation of head).
- Urgent surgery but 24–48 h for optimization with antibiotics and fluids is acceptable. Emergent if positive pressure ventilation is required with progressive distention of stomach; consider placement of a blocker in the fistula in NICU if stomach distention is a problem.
- Primary surgical correction via right posterolateral extrapleural thoracotomy below the tip of the scapula.
- Alternatively, use right thoracoscopic approach with thoracoscope inserted just caudad to the right scapula tip through which CO_2 is insufflated at a rate of 0.5 L/min to a pressure of 6 mm Hg into the right pleural cavity to collapse the right lung gradually.
- Extrapleural approach does not lead to empyema or mediastinitis if anastomosis leak occurs (up to 20%) but only an esophagocutaneous fistula.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	PDA, VSD, ASD, right-sided aortic arch	Cyanosis, tachypnea, respiratory distress	Murmur, cyanosis, enlarged liver, hypotension, bounding pulses	CXR, ECHO
RESP	Pneumonia, tracheomalacia, prematurity	Respiratory distress	Decreased breath sounds, tachypnea, cyanosis	CXR, ABG, bronchoscopy
GI	Gastric distention, anal and duodenal atresia	Enlarged abdomen, respiratory distress	Enlarged and tympanic abdomen	CXR, KUB series
RENAL	Dysplastic/dysfunction	UO	Palpation for kidneys	Abdominal US

Key References: Ho AMH, Dion JM, Wong J: Airway and ventilatory management options in congenital tracheoesophageal fistula repair, *J Cardiothorac Vasc Anesth* 30(2):515–520, 2016; Pinheiro PF, Simões e Silva AC, Pereira RM: Current knowledge on esophageal atresia, *World J Gastroenterol* 18(28):3662–3672, 2012.

Perioperative Implications

Preoperative Preparation

- NPO
- Placement of an orogastric cath into esophageal pouch for low continuous suction of secretions.
- Elevation of the head of the bed to minimize reflux.
- Consider antireflux and antacid medications.
- IV fluids and glucose.
- If intubation is needed in NICU, consider intubating the fistula with a blocker first.

Monitoring

- Arterial line is usually not required.
- Preductal (right upper limb) and postductal (lower limbs) oximetry.
- Left chest stethoscope for right-sided approach and vice versa.

Airway

- Plan A: Insert 3-Fr balloon-tipped Fogarty-type cath prior to ET. Immediate fiberoscopy via ET to ascertain location of fistula. If fistula is too distal to block by the ET, intubate the fistula with balloon cath. The surgeon is informed of the presence of a blocker in fistula, and the blocker is withdrawn prior to ligation.
- Plan B: Position the ET tip between the fistula and carina. This is the plan of choice if fiberoscopy after ET placement confirms the ET tip near carina and fistula is not in view. If carina-fistula distance is very small, or fistula is at or below carina, consider switching to Plan A.
- Plan C: If Plan B is impossible and Plan A is not in place, ventilate with the lowest pressure possible. There is significant risk of stomach insufflation; emergency decompressive gastrostomy may be required in rare situations.
- Plan D: Intubate the left mainstem bronchus with the ET (with bevel facing right and ET slightly concave to left, 92% chance it will go into the left mainstem).
- Choose an ET without Murphy eye to reduce exposure of fistula to positive airway pressure during surgery and in NICU.
- Cuffed versus uncuffed ET (without Murphy eye) based on individual preference.
- Intubate with bevel facing posteriorly to reduce chance of inadvertent fistula intubation.
- Subglottic stenosis may be present.

Induction

- Maintain spontaneous ventilation; minimal positive pressure ventilation if necessary.
- Topicalization of airway with lidocaine prior to balloon cath and ET placements.

Maintenance

- Pt in left lateral (thoracotomy) or left semi-prone position (thoracoscopic approach).
- Adjustment of ET depth quite difficult during surgery because of impeded access to airway.
- Positive pressure ventilation necessary once the right lung space is entered.
- Intraop O_2 desaturation is common. Most commonly this is due to right lung compression and/or mediastinal retraction by surgeon; temporary resumption of two-lung ventilation or easing of retraction may be necessary. Communication with surgeons is crucial. Other causes include inadvertent right mainstem intubation; ventilation of or inadvertent migration of ET into fistula; ET obstruction due to kinking, secretions, or blood; severe cardiovascular compromise; or bleeding while accessing the fistula, which is deep to the azygos vein.
- Intraop low or disappearance of $ETCO_2$ is common. Causes include migration of the ET tip into the right mainstem bronchus or fistula, cardiovascular compromise, or ET blockage. A left lung stethoscope helps monitor for inadvertent loss of ventilation to the left lung.
- In severely hypoxic and hypercarbic cases, use high frequency ventilation.
- Dopamine infusion may be required to maintain blood pressure.

Extubation

- Respiratory distress after surgery is common due to pain, tracheomalacia, prematurity, and aspiration prior to fistula ligation.

- High positive airway pressure from mask or ET ventilation puts stress on the fistula stump. ET tip distal to fistula (if possible) and use of ET without Murphy eye reduces such stress.
- Consider sedating and paralyzing the infant for several days as laryngoscopy puts stress on the esophageal anastomosis; intubation risks inadvertent intubation of the fistula stump.
- Surgeons may request placement of a trans-anastomotic tube via the mouth.
- Discuss with surgeon, including the degree of anastomotic tension.

Adjuvants

- Fiberoptic bronchoscopy to position the ET and fistula blocker (if deployed) and to ascertain the location of the fistula. Rarely, more than one fistula may be present.
- Have dopamine drawn and hooked up.
- May consider having NO and standby drugs for reducing pulm Htn.
- Emergency gastrostomy rarely indicated but could be lifesaving.
- High-frequency ventilator.

Postoperative Period

- Sedate and paralyze for several days unless all favorable conditions are present for early extubation and chance of requiring re-intubation is very low.
- Postop elective ventilation may protect against the development of leak in primary repair.
- Keep neck flexed to reduce tension on the esophagus.
- Respiratory distress after extubation poses a dilemma. Consider the possibility of inadequate pain control, tracheomalacia, pneumonia, and prematurity as causes. Pain may be a concern even after several days, especially with a chest drain in situ, and during handling, a neuraxial block (e.g., caudal entry thoracic epidural) may help avoid respiratory distress and the need for reintubation. Be wary of dynamic airway closure caused by tracheomalacia during rigorous crying. Caudal morphine may provide both analgesia and sedation. Fentanyl/adjunct analgesia infusion is an alternative but finding that sweet spot can be challenging.
- Antibiotics for 48–72 h or longer as required.
- Avoid tracheal and esophageal suctioning (transanastomosis cath is in place).
- A contrast study prior to oral feeding may be performed at 7–10 d postop.
- Minor leaks may heal spontaneously.
- Major leak requires surgical repair.

Anticipated Problems/Concerns

- ET not in ideal location, especially with pt movement and surgical manipulation. Correction by sliding the ET proximally and distally has associated risks (noted previously).
- Stomach insufflation.
- Respiratory distress.
- Cardiovascular anomalies which may affect hemodynamics and respiratory parameters.
- Low birth weight.
- Risk of prematurity.
- TEF recurrence (3–14%).
- A history of EA/TEF repair is associated with gastroesophageal reflux (50%).
- Tracheomalacia (an obstruction that exceeds 50% of the anteroposterior diameter of the trachea during inhalation) is found in 60% of children between 2–3 y.
- Respiratory symptoms during the first 5 y of life (>66% of cases), during adolescence (40%), and during adulthood (10%).

Transfusion-Related Acute Lung Injury

Tarang Safi | Sheela Pai Cole

Risk

- Can occur in any pt receiving blood or blood products, including platelets, plasma, cryoprecipitate, and rarely, IVIG.
- Overall incidence probably <1%; increasing awareness of the syndrome has resulted in improved recognition.
- Use of leukodepleted blood has decreased the incidence of packed red cell-related lung injury.

Perioperative Risks

- Noncardiogenic pulm edema, usually within 6 h of transfusion.
- Mortality reported as 5–10%.

Worry About

- O_2 toxicity
- Barotrauma or volutrauma secondary to PPV
- May be confused with transfusion-associated circulatory overload (TACO)

Overview

- Classic presentation is acute development of resp compromise indistinguishable from ARDS.
- Symptoms usually begin within 1–2 h after transfusion and may be manifested by 2–6 h.
- Severe hypoxemia and bilateral infiltrates are always present, while hypotension, fever, and pink frothy sputum may be present in some.
- Dx is clinical and one of exclusion.

Etiology

- Classically, has been attributed to the presence of leukocyte antibodies in the plasma of multiparous donors directed against recipient WBCs.
- Alternatively, may be effect of biologically active lipids in stored cellular blood components.
- Pulm edema arises from capillary injury rather than volume overload.

Usual Treatment

- Supportive care: Ventilation, if required, or supplemental O_2. There are no clear indications for steroids. Generally resolves within 1–4 d with appropriate care and no supervening complications.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Pulm edema		S_3, S_4	PA cath, ECHO
RESP	Pulm edema	Recent transfusion	Rales, hypoxemia	CXR: Bilateral infiltrates, SpO_2
HEME	Leukoagglutination			Agglutination of recipient leukocytes by donor plasma; contact blood collection agency

Key References: Triulzi DJ: Transfusion-related acute lung injury: current concepts for the clinician, *Anesth Analg* 108(3):770–776, 2009; Silliman CC, Ambruso DR, Boshkov LK: Transfusion-related acute lung injury, *Blood* 105(6):2266–2273, 2005.

Perioperative Implications

Preoperative Preparation

- Acute respiratory compromise may occur within 6 h of a transfusion, usually with FFP. Unlike RBCs, FFP is not leukodepleted; the presence of WBC in FFP is associated with an inflammatory response similar to that for large volumes of plt transfusion.
- Usually related to massive transfusion, although on occasion may happen after a single unit transfusion.

Monitoring

- PA cath may aid in the exclusion of cardiac etiology (i.e., normal wedge pressure).
- Beta-natriuretic peptide level may be checked to differentiate TRALI from TACO.

Postoperative Period

- Most pts require ventilatory support for several d.
- Ventilator management may be appropriate for ARDS.

Anticipated Problems/Concerns

- O_2 toxicity and barotraumas
- Hemodynamic instability

Transposition of the Great Arteries

Gregory J. Latham

Risk

- Incidence: 2.7-3.2:10,000 live births
- Relatively common; represents >5% of all congenital cardiac malformations
- One of the most common causes of newborn cyanosis
- Male predominance of 2.25-fold increased risk
- Relatively low risk (12%) of coexisting syndromes/noncardiac malformations

Perioperative Risks

- Newborn: Hypoxemia, acidemia, low cardiac output syndrome, and death.
- Risk of inadequate mixing of pulm and systemic circulations to allow oxygen uptake and delivery.
- Closure of ductus arteriosus can be fatal.
- Myocardial ischemia secondary to increased myocardial workload, aortic hypotension, and severe hypoxemia.

Worry About

- Adequate mixing of pulm and systemic circulations
- Adequate cardiac output, aortic root diastolic pressure, systemic perfusion, and systemic oxygenation
- Adequate, but not excessive, pulm blood flow
- Rapid changes in PVR in first 72 h of life and impact on adequate flow in pulm and systemic circulation
- Embolic stroke in setting of shunt-dependent physiology

Overview

- Aorta arises from RV, and pulm artery arises from LV, resulting in futile cycle of blood flow in two parallel circulations; saturated blood continuously cycles through lungs, and desaturated blood continuously cycles through body.
- Adequate mixing (shunting) between these two parallel circulations is required to prevent imminent death.
- Intracardiac and extracardiac mixing of parallel circulations may occur at ductus arteriosus, PFO, and/or VSD.
- Three primary subgroups of TGA:
  - TGA with intact ventricular septum (70% incidence) usually present with poor circulatory mixing and profound hypoxemia and acidemia.
  - TGA with ventricular septal defect (25% incidence) usually present with adequate mixing and short-term cardiopulmonary stability but may have severe pulm overcirculation and systemic hypotension.
  - TGA with ventricular septal defect and left ventricular outflow tract obstruction (5–10% incidence) usually present with poor pulm flow and severe hypoxemia and acidemia.

Etiology

- Embryologically, TGA results from abnormal rotation and septation of the truncus arteriosus, resulting in ventriculoarterial discordance.
- No known fetal environmental risk factors for TGA.

Usual Treatment

- Surgical correction is required for survival; medical management is crucial prior to surgery.
- Preop medical management:
  - Ensure adequate mixing as needed: prostaglandin E_1 for ductal patency and/or balloon atrial septostomy for atrial mixing.
  - Supplemental oxygen, ventilation, and/or paralysis as needed in setting of severe hypoxemia and acidemia.
  - Inotropic support as needed for support of systemic blood pressure.
- Surgical options, typically within first wk of life:
  - The arterial switch operation (ASO) is fully corrective and the procedure of choice for most neonates. Aorta and pulm artery are transected and transposed to location above proper ventricles. The ASO has a 97% 30-day survival rate.
  - Surgical banding of the pulm artery may be required for those unable to tolerate early complete repair.
  - The Rastelli, Nikaidoh, or REV procedure may be required for TGA with ventricular septal defect and left ventricular outflow tract obstruction.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Hypoxemia/acidemia	Dyspnea, tachypnea, poor feeding	Cyanosis	CXR, ECHO, pulse oximetry, NIRS, ABG
	CHF	Dyspnea, tachypnea, poor feeding	Lung auscultation	CXR, ECHO, pulse oximetry, ABG
	Apnea	Receiving PGE_1		
CV	RV (systemic ventricle) failure, ischemia, hypotension	Nonvigorous, shock	Cool, mottled, cap refill	ECHO, ECG, NIRS, ABG
	Inadequate mixing of systemic and pulm circulations leads to hypoxemia/acidemia	See above	See above	ECHO
CNS	Cerebral stroke/intracranial hemorrhage	Irritability, hypotonia, seizure	Hypotonia, neurologic signs (rare)	US, CT, or MRI of head

Key References: Latham GJ, Joffe DC, Eisses MJ, et al.: Anesthetic considerations and management of transposition of the great arteries, *Semin Cardiothorac Vasc Anesth* 19(3):233–242, 2015; Warnes CA: Transposition of the great arteries, *Circulation* 114(24):2699–2709, 2006.

Perioperative Implications

Preoperative Preparation

- Optimize oxygenation; ventilation and paralysis or RBC transfusion may be required preop.
- Optimize systemic perfusion; inotropic support may be required preop.
- Order blood products and anticipate severe coagulopathy after neonatal hypothermic CPB.
- Review ECHO to understand complex shunt physiology that will dictate intraop management.
- Review electrolytes, complete blood count, coagulation labs, ECG, and CXR.

Monitoring

- Arterial line and central venous access are required if not already present.
- Adequate IV access for transfusion.
- Five-lead ECG, NIRS, core temperature, TEE, and preductal and postductal saturations.

Airway

- Oral or nasal endotracheal intubation.

Preinduction/Induction

- Induction technique should consider impact on SVR, PVR, cardiac output, and shunt physiology.
- IV induction with a combination of an opiate, muscle relaxant, and inhalational agent.
- Inotropic support as needed to maintain cardiac output.
- Short-term hyperoxygenation prior to intubation is acceptable; adjust FIO_2 down thereafter.

Maintenance

- High-dose opiate has advantage of reduced stress response, less coagulopathy, less transfusion requirements, and less postop morbidity in this age.
- SaO_2 of 75–80% is acceptable and may not improve significantly with increased FiO_2.
- Cool pt in preparation for CPB; surround head in ice if using deep hypothermic circulatory arrest.
- Utilize TEE findings to guide therapy in setting of cardiopulmonary instability.
- Manage CPB per institutional protocol.
- Provide inotropic support prior to separation from CPB; observe ECG and TEE for signs of coronary ischemia.
- Prepare for extensive coagulopathy post-CPB and transfuse as indicated.

Extubation

- Postop ventilation is required; extubation is not recommended.

Postoperative Period

- Be vigilant for signs of coronary insufficiency/ischemia due to mechanical kinking of coronary arteries during translocation.
- Continue inotropic support in anticipation of late-onset low cardiac output syndrome from myocardial edema and imperfect protection on CPB.
- Depending on surgical procedure, postop arrhythmias may occur.

Anticipated Problems/Concerns

- After CPB, the LV is now handling the systemic rather than pulm circulation; this increased pressure load can lead to LV failure.
- Postop low cardiac output syndrome.
- Ischemia and arrhythmias.

Transverse Myelitis

Gyaninder P. Singh | Barkha Bindu

Risk

- Incidence: 1–8 cases per million per y.
- Age distribution: Bimodal peaks between ages of 10–19 y and 30–39 y.

Perioperative Risks

- Data scarce
- Autonomic disturbances (hypertension, hypotension, arrhythmias)
- Delayed gastric empting
- Anesthetic induced worsening unclear; causative role described

Worry About

- Risk of aspiration due to gastroparesis
- Autonomic dysfunction:
  - Acute: Spinal shock (hypotension)
  - Chronic: Autonomic dysreflexia (hypertension, bradycardia)
- Potential worsening of neurologic symptoms
- Hyperkalemia from succinylcholine
- Prolonged NM blockade
- Effects of steroid and immunomodulation therapy in pts on prolonged treatment

Overview

- Inflammatory demyelination disorder of spinal cord characterized by acute or subacute motor, sensory, and autonomic dysfunction.
- Motor paralysis/paresis, sensory (pain, numbness, paresthesia), and autonomic (bowel bladder/ sexual) dysfunction.
- Symptoms onset over h to d; stabilize over 2–3 wk, followed by resolution.
- May be preceded by nonspecific febrile illness or immunization within 1 mo.
- CSF pleocytosis, elevated IgG index, and MRI gadolinium enhancement.
- Cord enlargement and focal increase in signal intensity in T2-weighted MRI.
- Recovery with minimal sequelae in one-third of pts, moderate disability in one-third, and severe disability in one-third.
- Interleukin-6 level in CSF is highly predictive of disability and may predict recurrence.
- Rapid progression, spinal shock, back pain, and EMG evidence of muscle denervation, and 14-3-3 protein in CSF predict poor prognosis.

Etiology

- Idiopathic
- Disease associated:
  - Infectious: CNS infection (viral, bacterial, parasitic)
  - Noninfectious: Connective tissue disease (SLE, Sjögren, sarcoidosis, Behcet), demyelinating disease (MS, NMO), post vaccination

Usual Treatment

- High-dose steroids (methylprednisolone, dexamethasone) and immunoglobulin antibodies
- Plasma exchange: Possibly effective in pts not responding to steroids; good response with early treatment (<20 d of symptom onset), male sex, and clinically incomplete lesion.
- Immunosuppressants (mitoxantrone, rituximab, azathioprine, cyclophosphamide)
- Combination therapy with axonoprotective agents (erythropoietin, neurotrophin-3, neuroimmunophilin ligands)
- Other modalities of treatment: Stem cell transplantation and CSF filtration
- Nonpharmacologic management: Occupational and physical therapies, neural prostheses under trial
- Recurrent TM: Chronic immunomodulatory therapy
- Chronic pain: Spinal cord stimulation

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Eyes (in MS, NMO)	Pain in eye, loss in clear vision	Decreased visual acuity, Visual field defects	Ophthalmoscopy Visual EPs
CV	Acute: Decreased BP, tachycardia or bradycardia Chronic: Increased BP, bradycardia	Syncope Headache, flushing, sweating	BP changes Flushed skin above the lesion Blanched skin below the lesion	Test for autonomic dysfunction Remove stimuli below lesion
RESP	Neurogenic respiratory failure (in upper cervical cord lesion) Pulm embolism	Dyspnea, Respiratory distress	Tachypnea, cyanosis, altered consciousness DVT, Homans sign	ABG analysis CXR V/Q scan
GI	Gastric atony Bowel dysfunction	Hiccups, N/V, dyspepsia, early satiety Constipation or bowel incontinences	Percussion (tympanic note)	
CNS	Brain demyelination (in MS) Spinal cord inflammation and demyelination	Depression Encephalitis Sensory, motor, autonomic dysfunction	Mental status changes Sensory loss, reduced or absent motor power, flaccidity or spasticity, diminished or exaggerated tendon reflexes	MRI (brain) MRI (spine) LP
RENAL	Bladder atony (acute) Bladder spasticity (chronic)	Retention Increased frequency	Palpation, percussion (dull note)	Urine analysis, US, residual urine volumes

Key References: Scott TF, Frohman EM, De Seze J, et al.: Evidence-based guideline: clinical evaluation and treatment of transverse myelitis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology, *Neurology* 77(24):2128–2134, 2011; Balakrishnan IM, Yadav N, Singh GP, et al: Anaesthetic considerations in patients with transverse myelitis, *S Afr J Anaesth Analg* 19:323–324, 2013.

Perioperative Implications

Preoperative Preparation

- Document motor function and sensory and autonomic dysfunction.
- Relieve gastric ileus, treat as full stomach, aspiration prophylaxis.
- Adequate hydration.
- Concomitant steroid therapy and necessity of stress doses should be considered.

Anesthesia Technique

- GA (preferred) or epidural. TM has been reported following all anesthetic techniques.
- Spinal with caution, due to possible toxicity with usual doses; usually avoided.

Monitoring

- Standard monitoring and neuromuscular monitoring.
- Consider invasive monitoring if indicated (hemodynamic instability).

Airway

- RSI; avoid succinylcholine (hyperkalemia).

Induction

- IV or inhalational anesthetic agents.
- May exhibit hypotension; administer fluid to maintain adequate CO.

Maintenance

- Maintain intravascular volume status.
- Avoid NMB agents or use NM monitoring.

Extubation

- After return of airway reflexes. NM blocking action may be prolonged.

Adjuvants

- Sugammadex for reversal of prolonged neuromuscular blockade.
- Severe hypertension and bradycardia reported with dexmedetomidine.

Anticipated Problems/Concerns

- Gastroparesis
- Hemodynamic variability
- Variable response to NMBs
- Postop respiratory depression due to prolonged NM blocking action
- Potential worsening of neurologic functions

Treacher Collins Syndrome

Arlyne K. Thung | Inna Maranets

Risk

- Incidence of 1:25,000–50,000 live births.

Perioperative Risks

- Difficult airway management

Worry About

- Difficult mask ventilation and intubation
- Acute airway obstruction
- Hx of obstructive sleep apnea and cor pulmonale

Overview

- Also known as mandibulofacial dysostosis and Franceschetti-Zwahlen-Klein syndrome.
- Clinical features include various degrees of mandibular hypoplasia, high arched or cleft palate, malar hypoplasia, ophthalmic abn (downward slant of palpebral fissures, lower lid coloboma, partial to total absence of lower eyelashes, visual loss), microtia, atresia of external ear canal, and middle ear hypoplasia.
- Choanal atresia may be present.
- Conductive hearing loss due to ear abn is universal with varying degrees of severity.
- Normal intelligence.
- Airway compromise may occur due to maxillary hypoplasia (narrow nasal passages resulting in choanal stenosis or atresia) and mandibular hypoplasia (tongue base is retropositioned thereby obstructing oropharyngeal and hypopharyngeal spaces).
- Limited oropharyngeal and hypopharyngeal space may lead to obstructive sleep apnea, pulm Htn, and in severe cases, cor pulmonale.
- Affected newborns and infants often have feeding difficulties.
- May have congenital heart disease.

Etiology

- Abnormal bilateral first and second branchial arch development due to mutation in TCOF1 (78–93%) and POLR1C or POLR1D genes (8%).
- When inherited, shows autosomal dominance with variable penetrance and expression.
- TCOF1 mutation results in a deficiency of neural crest cells leading to failed development of cartilage, bone, and connective tissues, particularly in the head and neck region.

Usual Treatment

- Prenatal detection of micrognathia and dysmorphic facial features on fetal US may prompt genetic testing and counseling if TCS is suspected.
- Evaluate airway and assess swallowing and feeding difficulties at birth. Some pts require ET intubation in delivery room.
- Severe airway compromise and feeding issues may require tracheostomy and gastrostomy tube placement. Mandibular distraction procedures can be used to relieve airway obstruction and facilitate tracheal decannulation or avoid tracheostomy.
- Evaluate and correct any hearing and visual impairment. Early use of hearing aids (bone conduction) allows for proper development of speech. Surgery for bone anchored hearing aids placement may improve the quality of sound transmission.
- Oral-motor physical and speech therapy for speech clarity.
- Detailed assessment and imaging to determine the extent of craniofacial involvement during the first year of life. Repeated imaging may be needed prior to reconstructive procedures.
- Staged zygomatic, orbital, maxillomandibular, and nasal reconstruction.
- Surgical repair for cleft palate and choanal atresia.
- Staged external ear reconstruction. Very few TCS pts are candidates for external ear canalplasty to restore hearing.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Limited airway	Stridor, dyspnea, snoring, obstructive sleep apnea	Micrognathia, retrognathia, limited pharyngeal area	Facial X-rays, CT scan, nasal fiberoptic endoscopy
	Hearing loss	Hearing difficulties	External/middle ear atresia	Hearing evaluation
CV	Cor pulmonale Pulm Htn	Easy fatigability	S_3, hepatomegaly Increased jugular venous pulsations Heart murmur	ECG: Right axis deviation P waves in II, IIIa, VF ECHO/cardiac cath
GI	Difficulty feeding GERD, especially in pts with tracheostomy	Difficulty swallowing, chewing, poor PO intake Frequent regurgitation, discomfort after meals	Poor weight gain	Videofluoroscopic swallowing study Upper endoscopy
RESP	Obstructive sleep apnea	Loud snoring, intermittent complete obstruction, frequent arousal, daytime hypersomnolence or hyperactivity		Polysomnography

Key Reference: Plomp RG, van Lieshout MJ, Joosten KF, et al: Treacher Collins syndrome: a systematic review of evidence-based treatment and recommendations. *Plast Reconstr Surg* 137(1):191–204, 2016; Posnick JC, Tiwana PS, Costello BJ: Treacher Collins syndrome: comprehensive evaluation and treatment, *Oral Maxillofac Surg Clin North Am* 16(4):503–523, 2004.

Perioperative Implications

Preoperative Preparation

- Thorough airway assessment and review of previous anesthetics.
- Review of pertinent labs, studies, and imaging.
- Medical Hx, inquiring about obstructive sleep apnea or cor pulmonale.
- Antisialagogues for airway preparation.
- Antibiotic prophylaxis for pts with congenital heart disease as needed.

Monitoring

- Standard monitors.
- Invasive monitoring for lengthy reconstructive procedures with anticipated blood loss.

Airway

- Assume difficult intubation and prepare anesthetic plan in a case-by-case situation (ease of intubation with previous anesthetics may not guarantee ease of intubation with current anesthetic).
- Back up airway devices with fiberoptic bronchoscope, video laryngoscope, and surgical airway preparation. LMA may be bulky due to a small hypopharynx, particularly in younger pts.

Preinduction/Induction

- Avoid sedatives if Hx of severe OSA is present.
- Inhaled sevoflurane induction with maintenance of spontaneous ventilation during laryngoscopy.

Maintenance

- Avoid excessive opioids to minimize risk of postop respiratory depression.

Extubation

- Strict extubation criteria.
- Airway devices and staff support in case pt requires reintubation.

Postoperative Period

- Acute airway obstruction.
- Consider steroids, racemic epinephrine to decrease airway swelling.

Anticipated Problems/Concerns

- Obstructive sleep apnea, pulm Htn, and cor pulmonale
- Difficult airway

Tricuspid Atresia

Jimmy Windsor

Risk

- Uncommon; occurs in 0.056:1000 live births.

Perioperative Risks

- Hypoxia caused by limited pulm blood flow.
- Reliable systemic and pulm blood flow in these pts depends on existence of an unobstructed atrial level right to left shunt, an unobstructed left to right ventricular septal defect, and intact pulm artery.
- There is obligatory mixing of systemic venous blood return to the heart from the vena cavas (lower O_2 sat) and blood return to the heart from the pulm veins (higher O_2 sat).

Worry About

- Inadequate ability of systemic venous and pulm venous blood to mix caused by restrictive atrial septal defect (rare additional problem, but vital).
- Inadequate pulm blood flow caused by restrictive ventricular septal defect, pulm artery stenosis, pulm subvalvular obstruction, or pulm atresia.
- Less common is that the pt that presents with too much pulm blood flow and CHF (completely unobstructed pulm blood flow).

Overview

- Defined by the lack of a connection between the right atrium and hypoplastic (could be practically nonexistent) right ventricle.
- The tricuspid valve may be completely absent, or there may be a rudimentary valve-like structure on the floor of the right atrium that is not patent.
- Basically, there are three major types:
  - Tricuspid atresia with normally related pulm artery and aorta (70–80%). There are three subtypes:
    - Ia Tricuspid atresia with normally related great vessels, pulm atresia, and no ventricular septal defect (pulm blood flow completely dependent on the maintenance of a patent ductus arteriosus in the immediate period after birth)
    - Ib Tricuspid atresia with normally related great vessels, hypoplasia of the pulm artery, and a small ventricular septal defect
    - Ic Tricuspid atresia with normally related great vessels, no hypoplasia of the pulm artery, and a large ventricular septal defect
  - Tricuspid atresia with transposition of the great arteries (pulm artery arising from the left ventricle and the aorta arising from the hypoplastic right ventricle—20–30%). There are three subtypes:
    - IIa tricuspid atresia with transposed great arteries, atresia of the pulm artery arising from the left ventricle, and a ventricular septal defect allowing systemic blood flow to occur through the aorta arising from the hypoplastic right ventricle (pulm blood flow completely dependent on the maintenance of a patent ductus arteriosus in the neonatal period)
    - IIb tricuspid atresia with transposed great arteries, hypoplasia of the pulm artery arising from the left ventricle and a ventricular septal defect
    - IIc tricuspid atresia with transposed great arteries, no hypoplasia of the pulm artery, and a ventricular septal defect
  - Tricuspid atresia with congenitally corrected transposition of the great arteries. The pt can have varying degrees of pulm, subpulmonary, or subaortic stenosis. Also, can be assoc with other lesions like atrioventricular septal defect.

Etiology

- Cause is unknown.
- Although specific genetic causes of the malformation have not been determined in humans, data indicate that the FOG2 gene may be involved in the process.

Usual Treatment

- Two phases of treatment: The first stage is geared to allow the pt to survive the immediate postnatal period. The goals of treatment being to provide adequate but not a plethora of pulm blood flow and sufficient systematic blood flow. Ideally unity would be achieved in blood flow to the pulm and systemic vasculature. Another goal is attain satisfactory mixing of the relatively desaturated blood from the venous return and fully saturated blood from the pulm venous return.
- Limited pulm blood flow makes the pt temporarily dependent on Prostin (PGE_1) to maintain the patency of the ductus arteriosus. This is followed by the creation of a modified Blalock-Taussig-Thomas shunt to create a reliable source of pulm blood flow in the stage prior to the superior caval pulm shunt (Bidirectional Glenn procedure).
- Rarely, if the atrial level communication is limited, then adequate mixing of blood return from the vena cavae and the pulm veins is impeded. An atrial balloon septostomy may be required.
- Rarely, if pulm blood flow is unrestricted, then a surgical banding of the pulm artery may be needed.
- Long-term palliation of these pts involves two more operations intended to separate the blood returning to the heart via the vena cavas (with lower O_2 sat) from the blood returning to the heart via the pulm veins (with higher O_2 sat). This will mimic normal series physiology. A pathway is first created directly from the superior vena cava in the right pulm artery (bidirectional Glenn procedure). Then a pathway is created from the inferior vena cava to the right pulm artery (Fontan procedure).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV/RESP	More common, limited pulm blood flow causing hypoxia and possibly resp acidosis	Possibly requiring intubation or supplemental O_2	Cyanosis, holosystolic murmur, possible thrill	SpO_2 ABG ECHO
	Rare, over-circulation of pulm vessels causing unacceptably high PO_2	Signs of poor systemic arterial blood flow like metabolic acidosis, necrotizing enterocolitis, poor wt gain	Tachypnea, tachycardia, hepatomegaly	CXR SpO_2 ABG
CNS	Stroke due to single ventricle physiology	Pt may have received a balloon septostomy	Varying levels of consciousness Varying degrees of hemiplegia	CT MRI

Key References: Brown ML, DiNardo JA, Odegard KC: Patients with single ventricle physiology undergoing noncardiac surgery are at high risk for adverse events, *Paediatr Anaesth* 25(8):846–851, 2015; Holtby HM: Anesthetic considerations for neonates undergoing modified Blalock-Taussig shunt and variations, *Paediatr Anaesth* 24(1):114–119, 2014.

Perioperative Implications

Preoperative Preparation

- Maintain PGE_1 preop if needed.
- Have drugs and blood products available to maintain acceptable BP, preload, and contractility to maintain pulm blood flow in ductal or systemic to pulm shunt–dependent pt.

Monitoring

- In addition to routine monitors, implement continuous arterial and central venous pressure monitoring for procedure to create systemic arterial to pulm arterial shunt is recommended.
- If available, monitoring of central venous saturation (SvO_2) is also recommended.

Airway

- Keep the pt intubated postop after systemic arterial to pulm shunt creation. This is usually the period when the Prostin is weaned off, and the transition is made to pulm flow being purely maintained by the newly created shunt.

Preinduction/induction

- Maintain adequate afterload, preload, contractility, heart rate, and heart rhythm.
- Careful titration of benzodiazepines and narcotics help maintain hemodynamic goals.

Maintenance

- Maintain preload and a hemoglobin level of approximately 13.5–15 g/dL. This will maintain adequate tissue O_2 delivery.
- Maintain adequate sedation to prevent rises in PVR.
- This anesthetic involves a careful balance of resistances (PVR and SVR).

Adjuvants

- Heparin, usually 100 units/kg (more may be necessary), to maintain an activated clotting time of at least 200 sec during the creation of the surgical shunt. May require redosing, over the length of the procedure. Remeasure ACT every 20–30 min.
- Inotropes to maintain adequate contractility and SVR.

Anticipated Problems/Concerns

- Thorough understanding of parallel physiology and maintenance of equal pulm arterial and systemic arterial blood flow from a single ventricle is required.

Trigeminal Neuralgia (Tic Douloureux)

L. Jane Easdown

Risk

- Has an incidence of 12–27:100,000/y.
- More common in women and pts >50 y.
- 1–5% of pts with MS have TN, and 2–4% of pts with TN have tumors or vascular malformations in the posterior fossa. There is an association with Charcot-Marie-Tooth disease.

Perioperative Risks

- Evaluate comorbidities with pts with MS, tumors.
- Liver enzyme induction with use of antiepileptic drugs.
- Difficulties with mastication might lead to nutritional deficits.
- Bradyarrhythmias with percutaneous balloon compression.

Worry About

- Severe bradycardia/asystole with manipulation of the fifth nerve in the posterior fossa or with balloon compression
- Oversedation and management of the airway in RFA procedures
- Postop exacerbation of MS

Overview

- TN is a facial pain syndrome characterized by recurrent episodes of intense pain over the distribution of the fifth cranial nerve, more commonly the V2 and V3 divisions. Diagnosis is made by pain distribution and quality. Characteristic pain is severe in intensity, shooting or stabbing, lasts seconds to minutes, and is often precipitated by light touch or cold air. Pt may have bouts over weeks or months, with some spontaneous remissions up to 6 mo. Usually the bouts become more frequent and the pain more sustained. Pts with MS rarely have remissions.
- Imaging techniques such as MRI and MRA are used to evaluate nerve decompression, and to rule out MS and tumors.
- Neurologic exam is normal in most pts, with the exception of a minimal amount of sensory loss over the affected area.

Etiology

- Idiopathic: >90% of cases are idiopathic with evidence of focal demyelination of trigeminal sensory fibers within the nerve root or within the brainstem. Compression by an aberrant artery or vein results in close apposition of axons and absence of intervening glial processes. This favors ectopic impulses and ephaptic conduction to adjacent fibers. In the area of the trigeminal nerve entry zone, demyelination would lead to ephaptic conduction between fibers for light touch and those for pain explaining the sensitivity of trigger zones.
- Symptomatic: These pts have less classical features of TN. Primary demyelinating disorders such as MS will lead to demyelination and plaque formation in the root entry zone, but they may also have nerve compression by a vascular structure. Rarer presentations would include compression by tumor, infiltration by tumor or amyloid, small infarcts, or angioma in the brainstem.

Usual Treatment

- Pharmacologic: The mainstay of treatment is anticonvulsant/antiepilepsy drugs. Initial response in over 70% of pt occurs with carbamazepine (Tegretol) or oxcarbazepine (Trileptal). Polypharmacy with other medications is common: baclofen, gabapentin, lamotrigine, and pimozide. Pain or inability to tolerate these medications limits their use.
- Procedural:
  - RFA: Under sedation and fluoroscopic control, a radiofrequency electrode is advanced into the foramen ovale, and the pt is awakened to describe the location of the paresthesia. The lesion is made in cycles of 45–90 sec at temps 60–90° C. Glycerol, ethanol, and cryotherapy have been used to create a nerve lesion by this approach. Injections of local anesthesia and also botulinum toxin have been reported efficacious. Percutaneous balloon compression of the nerve in the foramen ovale for 1–6 min has been employed under general anesthesia.
  - MVD: The posterior fossa is approached through a suboccipital craniotomy. The fifth nerve is identified and a surgical felt is interposed to protect the nerve from the artery or vein. This procedure is performed under general anesthesia. Endoscopic MVD has been reported. Outcome: 70–80% pain free for >10 y.
  - Stereotactic radiosurgery: The trigeminal nerve root at the pons is targeted with a "Gamma knife" radiosurgery. There is delayed onset of pain control. Few centers offer this treatment and long-term outcomes are yet unknown. May be performed with sedation.
  - Neuromodulation: Deep brain stimulation and motor cortex stimulation; these new procedures might have value for pts refractory to current therapies.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Cranial nerve involvement, sensory loss	Pain Hx and distribution	Full neurologic exam	MRI, MRA

Key References: Montano N, Conforti G, Di Bonaventura R, et al.: Advances in diagnosis and treatment of trigeminal neuralgia, *Ther Clin Risk Manag* 11:289–299, 2015; Rath GP, Dash HH, Prabhakar H, et al: Cardiorespiratory arrest during trigeminal rhizolysis, *Anaesthesia* 62(9):971–972, 2007.

Perioperative Implications

Preinduction/Induction/Maintenance

- If the procedure calls for pt assistance in identifying the area for ablation, then minimal sedation is used, especially longer-acting benzodiazepines.
- NPO status must be observed.
- Pts with MS require a detailed neurologic examination.
- Pts on anticonvulsant/antiepilepsy medications will be less responsive to induction agents and metabolize liver metabolized agents more quickly.
- Must take special care to avoid trigger zones when placing mask and nasal prongs.

Monitoring

- For MAC or GA for ablation procedures, usual ASA monitors.
- For posterior fossa craniotomy, ASA monitors, invasive arterial and venous lines, and precordial Doppler for venous air embolism detection, depending on the position of the pt.
- Consider the means to pace the heart: transesophageal pacemaker and transthoracic noninvasive pacer (Zoll pads).

General Anesthesia

- All usual considerations for posterior fossa craniotomy, including pt positioning, detection of air embolism, brainstem, and cranial nerve manipulation resulting in bradycardia, asystole, tachyarrhythmias, and Htn or hypotension.
- Avoid succinylcholine in MS pts with extensive motor involvement.
- Expect rapid metabolism of opioids, nondepolarizing muscle relaxants in pts managed with anticonvulsants medications (cytochrome P-450).
- Surgeons may monitor BAERS for eighth nerve function.
- Arousal and extubation will require careful management of BP, HR.
- If manipulation of lower cranial nerves has occurred, the pt may not be able to protect the airway and delayed extubation may be planned.
- Surgeons will expect the pt to respond to commands before leaving the OR.

Regional Anesthesia/Monitored Anesthesia Care

- Judicious use of sedation required such that level can be increased during painful lesioning, but the pt can be aroused for consultation. Agents used include remifentanil, fentanyl, methohexital, propofol, and dexmedetomidine.
- Use nasal prongs, careful assessment of patent airway, oxygenation, and ventilation, especially in the elderly and obese.
- Head and airway may be at a distance from the anesthesiologist.
- Placing the radiofrequency electrode may be very painful; may need to convert to GA.

Postoperative Period

- Outpatient surgery is possible with RFA.
- Posterior fossa craniotomy postop care will require a monitored unit for overnight neuro vital signs.

Anticipated Problems/Concerns

- Surgical problems: Infarct, hemorrhage, cranial nerve paralysis, masseter muscle weakness, eighth nerve injury, CSF leak, and dysaesthesia
- Anesthesia problems
- For GA: Positioning problems, including skin, joints, nerve compression, and eye injuries in prone/lateral position
- For MAC care: Oversedation and loss of airway

Truncus Arteriosus

Manchula Navaratnam | Chandra Ramamoorthy

Risk

- Uncommon congenital heart defect; <3% of all congenital heart defects
- No gender predilection

Perioperative Risks

- CHF.
- Volatile agents may depress myocardial contractility and lower SVR.
- Inadvertent hyperventilation resulting in reduced PVR, excess PBF, and worsening CHF.
- Infective endocarditis.
- Risks of CPB.

Worry About

- Difficult intubation due to assoc with velocardiofacial syndrome (e.g., DiGeorge)
- Air embolus (VSD almost always present)
- Hyperoxia and hyperventilation resulting in pulm overcirculation
- CV collapse at induction due to diastolic runoff and assoc truncal regurgitation with resulting coronary steal and myocardial ischemia.
- Hypocalcemia due to parathyroid hormone dysfunction.

Overview

- There is a single great artery arising from heart, supplying the systemic, pulm, and coronary circulations.
- VSD almost always present; ASD present in two-thirds of pts.
- Abnormal truncal valve; 50% are regurgitant.
- Anomalies of coronary artery and aortic arch may be present.
- Pulm circulation arises directly from systemic circulation.
- Dominant physiology is a L-to-R shunt driven by the relatively lower resistance of the pulm vascular bed.
- Runoff from systemic circuit into the PA during diastole may compromise myocardial perfusion.
- Primary goal is to balance PVR and SVR so that Qp:Qs is close to unity.
- Pulm vascular obstructive disease due to excessive pulm blood flow develops early.
- Repair preferably done in early neonatal period before onset of pulm Htn.
- Uniformly fatal without surgical correction (50% of pts die by 1 mo and 80% within 1 y).
- Approx 30% have a deletion of 22Q11, resulting in phenotypic variants such as DiGeorge and Sphrintzen syndromes.

Etiology

- Conotruncal defect.
- Embryonic truncus arteriosus fails to separate into a pulm and aortic trunk.
- Partial or complete absence of conotruncal septum.
- A single arterial trunk arises from both ventricles.
- Classified into four types.
- Maternal diabetes mellitus predisposes to conotruncal abn.

Usual Treatment

- Medical therapy is temporizing (digoxin, loop diuretics, inotropes) to treat CHF and usually only to optimize status before surgery. Surgery should not be delayed for an extended period of time.
- Surgical repair in the neonatal period is the definitive treatment. On hypothermic CPB, the pulm trunk is separated from the truncal artery. The VSD is closed. A conduit from the RV to the PA (Rastelli) is placed to provide for pulm blood flow. The PFO is left open.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Difficult laryngoscopy and intubation		Small mandible, small mouth	
CV	CHF—truncal valve regurgitation Pulm Htn	Difficulty feeding Sweating during feeds FTT	Cyanosis with or without a single S_2 Murmur—systolic or diastolic	Pulse oximetry, ECG, ECHO, cardiac cath±
RESP	CHF, excessive pulm blood flow	Difficulty breathing	Tachypnea with retractions	CXR (increased pulm markings, cardiomegaly)
ENDO	Parathyroid hypoplasia	Seizures, tetany		Serum ionized Ca^{2+}, parathyroid hormone level
IMMUNE	Cellular immunodeficiency	Recurrent infections Chronic diarrhea	70% of 22q11 pts are immunosuppressed.	CBC, T-cell function
MS	Dysmorphic facies		Hypertelorism, low-set ears	

Key References: Jonas RA: Truncus arteriosus. In *Comprehensive surgical management of congenital heart disease,* ed 2, Boca Raton, FL, 2014, CRC Press, pp 571–584; Walker SG: Anesthesia for left to right shunt lesions. In Andropoulos DB, Stayer S, Mossad EB, et al. editors: *Anesthesia for congenital heart disease,* ed 3, Hoboken, NJ, 2015, Wiley, pp 486–489.

Perioperative Implications

Perioperative Preparation

- Treat CHF.
- If intubated, transport and ventilate pt with the FIO_2 at 21%, aiming for an SpO_2 of 75–80%, and appropriate hypoventilation to maintain the $PaCO_2$ at 45–50 mm Hg and pH at 7.25–7.35.
- Avoid hyperventilation and hyperoxia, which will lower PVR, increase PBF, and possibly compromise systemic and coronary perfusion.
- Check serum electrolytes, Ca^{2+}, and Hct.

Airway

- High index of suspicion for a difficult airway, with appropriate precautions if velocardiofacial syndrome present.
- Maintain FIO_2 at 21% but possibly give a few breaths at 100% just prior to intubation.
- Once pt is intubated, return FIO_2 to 21% and avoid hyperventilation.

Preinduction/Induction

- Meticulous air bubble exclusion
- Preop antibiotics.
- Consider inotropic support (e.g., dopamine at 3–5 µg/kg/min) if MAP is low prior to induction.
- Obtain a baseline ECG prior to induction. Monitor for myocardial ischemia (best detected with ECG leads II and V) due to PA runoff.
- Volume infusion is unlikely to increase diastolic BP unless the pt is significantly volume depleted. Consider a 1–2 µg/kg bolus of phenylephrine for low MAP.
- Pts are usually ventricular volume overloaded, and aggressive volume resuscitation will further elevate ventricular end-diastolic pressure, compromising subendocardial perfusion.
- Balance PVR and SVR so that Qp:Qs approaches unity. Key: Maintain SVR; keep SpO_2 below 90%.
- Surgeon must be in the OR prior to induction and prepared for sternotomy.
- For persistent hypotension and rapid sternotomy, snare the branch PAs to elevate MAP and reduce pulm overcirculation.

Monitoring

- Intra-arterial cath and CVP. May have in situ umbilical arterial and/or venous lines.
- TEE is valuable to assess truncal valve function, VSD patch leak, ventricular function, and PA pressure.
- Intraop LA line placement for postop management of preload.
- NIRS monitoring is standard, especially during low-flow selective cerebral perfusion or DHCA.

Maintenance

- Usually with fentanyl infusion 2–4 µg/kg/h.
- Inotropic drugs commonly used to facilitate weaning from CPB incl dopamine (3–5 µg/kg/min), milrinone (0.5–0.75 µg/kg/min) and low-dose epinephrine (0.03–0.05 µg/kg/min), calcium chloride (20–30 mg/kg/h).
- Inhaled NO should be available in the OR for the post-CPB period, as there is a high risk of pulm vasoreactivity.

Extubation

- Postop ventilation is usually required for at least 24 h, as pulm hypertensive crisis may occur. Not suitable for fast-tracking.

Postoperative Period

- Poor RV function (right ventriculotomy and Rastelli conduit placement): maintain appropriate inotropic support, afterload reduction, and adequate preload for RV. Mechanical ventilation with minimal mean airway pressure.
- LV dysfunction (circulatory arrest, long bypass time, myocardial ischemia, truncal valve abn).
- Increased PVR and pulm Htn (low CO and low SaO_2) responds to hyperventilation, metabolic alkalosis, vasodilators (milrinone, PGE_1, NO), sedation (analgesia, paralysis).
- If PA pressures are high, residual VSD and RV outflow tract obstruction must be excluded in addition to treating pulm Htn.
- R-to-L shunting across PFO facilitates systemic cardiac output at the expense of SaO_2 in the face of RV dysfunction and elevated PA pressures.
- AV block requiring temporary pacemaker.
- Bleeding.
- Cardiac tamponade.

Anticipated Problems/Concerns

- CHF
- Truncal valve regurgitation and/or stenosis
- Pulm Htn
- Infective endocarditis

Tuberculosis

Muhammad B. Rafique

Risk

- Incidence in USA in 2014 was 2.96 cases per 100,000 persons; worldwide, incidence is over 9 million cases per year. There were 1.5 million TB-related deaths worldwide in 2014.
- Incidence in USA has been decreasing every year since 1992.
- Risk is higher among homeless, elderly, Asian, and Latin American immigrants, minorities, and prisoners. Also, immunosuppression (e.g., HIV infection, transplant recipients, chronic renal insufficiency) increases TB risk.
- TB is still a leading cause of death among HIV-infected pts.

Perioperative Risks

- Risk to the pt and to medical personnel.
- Pt risk depends on extent of pulm disease, organ system involvement, and overall health status.
- Elective surgery is best delayed until pt is either noninfectious or free of TB.

Worry About

- Overall health status of the pt, infectiousness of the pt, cross-contamination through anesthesia machine and other nondisposable equipment
- Effects of anti-TB drugs on organ systems (e.g., liver damage, hearing loss, neuritis, nephrotoxicity)

Overview

- TB is caused by *Mycobacterium tuberculosis*.
- Pulmonary TB is the most common form of infection in humans; intestine, spine and bones, kidneys, and meninges can also be affected.
- TB left untreated can be fatal.

Etiology

- TB is transmitted by droplet nuclei produced by coughing, sneezing, or talking (causative bacilli can remain airborne for hours).
- TB does not spread by casual contact (e.g., shaking hands, sharing food or drink, or disposing of bed linens).
- Primary infection can be the reason for up to one-third of newly diagnosed TB cases.

Usual Treatment

- Initial phase (2 mo) of treatment comprises a four-drug regimen taken orally (i.e., isoniazid, rifampin, pyrazinamide, and ethambutol), followed by continuation phase (4 mo) with a two-drug regimen taken orally (i.e., isoniazid and rifampin).
- Four-drug regimen is recommended for 6 mo in drug-resistant cases.
- HIV/AIDS pts may need a longer duration of therapy (9–12 mo).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL		Night sweats, weight loss	Fever	Tuberculin skin test and in vitro T-cell release of IFN-gamma assay
RESP	Hilar or mediastinal lymphadenopathy, apical infiltrate or necrosis.	Cough and hemoptysis	None or inspiratory rales in affected area	CXR, sputum culture
CV	Pericardial effusion, constrictive pericarditis	SOB	Signs of tamponade, muffled heart sounds	ECG, ECHO
CNS	TB meningitis	Listlessness, headache, seizures, coma	Altered mental status, cranial nerve abnormality	LP, CSF analysis
GI	Peritonitis, enteritis	Abdominal pain, obstruction	Palpable mass, ascites	Endoscopy and biopsy, ascitic fluid analysis/culture
GU	Chronic cystitis, epididymitis, hydronephrosis, female genital tract disease	Late appearance of pyuria, hematuria	May have thickened epididymis	Cystoscopy
MS	Weight-bearing joints (e.g., spine, hip, knee)	Pain, kyphosis	Spinal tenderness	X-ray, CT, bone biopsy

Key References: Centers for Disease Control and Prevention (CDC): Tuberculosis. <www.cdc.gov/tb>. (Accessed 13.06.16); Shaikh SI, Sudhindra GB: Tuberculosis and anaesthesia, *Indian J Appl Res* (4)2:15–17, 2014.

Perioperative Implications

Preoperative Preparation

- Evaluate for toxicity due to anti-TB therapy: CBC, ALT, AST, serum bilirubin levels, visual symptoms, and peripheral neuropathy. For extensive pulmonary TB, consider PFTs.
- Care team must wear properly fitted N95 masks.
- Schedule TB/suspected TB cases at the end of d to maximize time for clearing and minimize spread. A comprehensive discussion and planning among the team members (surgery team, anesthesia team, and support staff) is necessary.
- Use an OR that has an anteroom; otherwise keep the doors closed, minimize traffic, and use additional air cleaning.
- Use disposable equipment and add a bacterial filter (0.3 µm) to the expiratory limb or at the Y-connection of the anesthesia circuit.
- After use, stop all gas flow through the anesthesia machine for at least 1 h to avoid cross- contamination. If machine contamination is suspected, formaldehyde gas can be used to sterilize it.

Monitoring

- Standard ASA monitors
- Depending on comorbidities and type of surgery, invasive monitoring should be considered case by case.

Postoperative Period

- Postop recovery in an AII room (AII room—an isolation room with single occupancy, negative pressure in the room, airflow at 6–12 ACH or equivalent; remember that mycobacterial bacilli can remain airborne for hours).
- If AII room is not available, air-cleaning technologies (e.g., HEPA filtration, UVGI) can be used.

Ulcerative Colitis, Chronic

Patrick J. Forte | Kathleen E. Barrett

Risk

- Incidence in USA and Northern countries of 35-100:100,000; incidence of 11:100,000/y with 2- to 4-fold increased frequency in Jewish populations.
- Mortality highest in early years of disease, or with prolonged disease due to risk of colon cancer; two peaks for age of onset: 15–30 y and 60–80 y.
- Male:female ratio is 1:1; smokers:nonsmokers, 0.4:1; former smokers:nonsmokers, 1.7:1. Up to 20% of pts have a positive family Hx.

Perioperative Risks

- Inflammatory mediators activate the coagulation cascade in local blood vessels.
- Increased interleukin-17 level is being investigated as having a cause or effect connection between IBD and inhalational anesthetics.
- Chronic steroid use can cause adrenal insufficiency and delayed wound healing.

Worry About

- Diarrhea causing metabolic acidosis, hypokalemia, lyte abnormalities, intravascular volume depletion
- Defects in bleeding or clotting due to activation of coagulation cascade
- Bowel distention precluding use of nitrous oxide and increasing risk of perforation.
- Extracolonic manifestations: Primary sclerosing cholangitis and/or cirrhosis of the liver: choose appropriate anesthetics, analgesics, and NMBs. Ankylosing spondylitis: Limited cervical ROM, restrictive pulm mechanics.

Overview

- Indications for surgery include toxic megacolon, colonic perforation, massive hemorrhage, obstruction, and cancer prevention or resection. If pt is presenting for surgery, disease is in progressive stage and operation can be urgent/emergent in nature.
- Pts may have steroid dependence, hypovolemia, electrolyte imbalance, malnutrition, hypoalbuminemia, anemia, bleeding.
- Sulfasalazine is the mainstay of treatment for all stages of disease. Side effects include blood

dyscrasias, aplastic anemia, hemolytic anemia, hepatitis, pancreatitis, nephrotoxicity, hypersensitivity pneumonitis, and impaired folate absorption.

Etiology

- Unknown.
- Genetics, exogenous factors, host factors, and specific environmental factors are all hypothesized to play a role.

Usual Treatment

- Mild: Sulfasalazine or other 5-ASAs
- Moderate: 5-ASA + glucocorticoid oral and enema, electrolyte repletion, parenteral nutrition
- Severe: 5-ASA, glucocorticoid enema, glucocorticoid PO or IV
- Fulminant: Glucocorticoid IV, cyclosporine IV, azathioprine PO, 6-mercaptopurine PO; TNF-alpha inhibitors or "biologics": Infliximab IV, adalimumab IV, golimumab IV, vedolizumab IV.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia		Tachycardia, hypotension, orthostatic vital signs, delayed capillary refill	BUN/Cr
HEME	Anemia, thrombocytosis	Passing fresh blood	Pallor	CBC
RENAL	Metabolic acidosis, electrolyte abn		Tachypnea, oliguria	Lytes, BUN/Cr, ABG
RESP	Restrictive pulm mechanics (if ankylosing spondylitis) Hypersensitivity pneumonitis from 5-ASA	SOB, DOE	Cyanosis, SpO_2	CXR, PFTs
GI	Diarrhea, bowel obstruction/perforation Hepatic steatosis, PSC/cirrhosis	Diarrhea, no bowel movements	Abdominal pain only present with toxic colitis Hepatomegaly	Lytes Abdominal x-ray Abdominal CT

Key References: Kasper B, Fauci H, Longo J: *Harrison's principles of internal medicine,* ed 16, vol II. New York, NY, 2005, McGraw-Hill, pp 1776–1788; Yuksel I, Uflaz B, Erarslan E, et al.: Ulcerative colitis after anesthesia with desflurane and sevoflurane, *Inflamm Bowel Dis* 17(7):E76, 2011.

Perioperative Implications

Preinduction/Induction/Maintenance

- Fluids, lytes, volume repletion
- Stress-dose steroids if needed
- Special attention to airway if ankylosing spondylitis
- Careful choice of anesthetics if hepatic or renal dysfunction
- Aggressive volume replacement

Monitoring

- Standard monitoring.
- Monitor urine output.
- Consider arterial line if there are lyte abnormalities.
- Consider CVP if hypovolemic or anticipating large fluid shifts.

General Anesthesia

- Consider renal function for opioid dosing.
- Consider renal and biliary function for NMB dosing.
- Monitor ventilator settings carefully in the presence of restrictive pulm mechanics or toxic megacolon.
- Beware of nitrous oxide owing to risk of perforation.

Regional Anesthesia

- Caution with local anesthetic esters; may decrease effects of sulfasalazine

Postoperative Period

- Maintain normothermia for wound healing and coagulation.
- Early parenteral nutrition.

Anticipated Problems/Concerns

- Complicated operations with adhesions, obstructions, perforation risk
- Large intraop fluid requirement
- Need for stress-dose steroids
- Correction of lyte abnormalities
- Risk of hemorrhage

Upper Respiratory Infections

Selina Read | Lee A. Fleisher

Risk

- Most adults will suffer 1 URI per year; this incidence jumps to approximately 6 episodes per year in the pediatric population. Approximately 95% of the infections have a viral etiology.
- URIs are generally self-limiting; however, airway hyperreactivity may persist for several wk.
- Adults are less likely to have URIs due to larger airways enabling them to compensate with edema and increased secretions.
- Those with underlying disease, especially diseases afflicting the airways, are more likely to have complications following anesthesia when confounded with URI.

Perioperative Risks

- Complications include laryngospasm, bronchospasm, atelectasis, coughing, airway obstruction, hypoxia, stridor, and breath holding.
- A pt with a fever, purulent rhinitis, or productive cough should have elective surgery canceled.

Worry About

- Lung-specific: Bronchospasm, desaturation, apnea, and atelectasis
- Cancelation of surgery and prolonged hospital stay

Overview

- To cancel or not to cancel has been the dilemma of many anesthesiologists when confronted with a pt scheduled for elective surgery who has recently had or currently has an URI.
- Several studies have linked URIs to possible morbidity; however, none have linked them to increased mortality.
- Retrospective studies: Children with a recent URI were at higher risk for laryngospasm, bronchospasm, and stridor. Such children had a 2–7 times greater incidence of resp complications. The complication risk increased to 11-fold if the trachea was intubated.
- Prospective studies: Children who developed laryngospasm were twice as likely to have a URI.

Etiology

- Affect the airway by making them especially susceptible to touch or chemical irritation, such as airway management and inhalational anesthetics.
- It is postulated that viruses release neuraminidases that damage the M2 muscarinic receptors, increasing acetylcholine released at NM junctions and setting off vagally mediated bronchoconstriction.
- Viruses also cause the release of chemical mediators—such as bradykinin, prostaglandins, and histamine—that contribute to bronchospasm.
- URIs increase airway secretions, thus intensifying intraop atelectasis, decreasing diffusion capacities, and increasing closing volumes.

Usual Treatment

- If a pt scheduled for elective surgery has a fever, purulent rhinitis, or productive cough, the case is best postponed.
- Laryngospasm treated with PPV or small-dose muscle relaxation.
- Bronchospasm treated by deepening the anesthetic and administering IV bronchodilators or inhaled beta agonists.
- Hypoxemia treated with supplemental O_2.
- Atelectasis can be decreased with incentive spirometry or sigh breaths intraop.
- Increased secretions can be managed by frequent suctioning.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia due to infection	Assess for possible CHD, which can complicate the picture	Auscultation: BP, HR	
RESP	Increased secretions, bronchospasm	Quantify cough, secretions	Auscultation: Wheezes, rhonchi	CXR ABG in severe cases
RENAL	Dehydration	Poor intake and UO	Skin turgor, sunken fontanelles	BMP

Key References: Tait A, Malviya S: Anesthesia for the child with an upper respiratory tract infection: still a dilemma? *Anesth Anal* 100(1):59–65, 2005; Becke K: Anesthesia in children with a cold, *Curr Opin Anaesthesiol* 25(3):333–339, 2012.

Perioperative Implications

Preinduction/Induction/Maintenance

- Evaluate whether symptoms are severe or due to an infectious etiology. Examples are copious secretions and fever. If so, consider postponing.
- Minimize secretions by deep suctioning after pt is deeply anesthetized.
- Avoid airway stimulation if possible; consider using an LMA or bag masking.
- If bronchospasm is encountered, an IV line will be needed to provide adequate hydration and potential medications.
- Optimization of resp status is of utmost importance. Preop inhalational therapy with salbutamol should be considered.

Monitoring

- Standard ASA monitors absolutely necessary: Heart rhythm, pulse oximeter, and BP.
- Have ABG monitoring available.

General Anesthesia

- Depending on the procedure, this may be the best option to allow for deep anesthesia during stimuli, helping to prevent bronchospasm.
- Try to avoid endotracheal intubation. Consider an LMA.
- The agent used for induction can have an effect on the chance of bronchoconstriction: Propofol and sevoflurane are best, thiopental and desflurane are worst.

Regional Anesthesia

- Useful as an adjunctive anesthetic. May be preferred over GA.

Postoperative Period

- Almost all of the complications cited as possible reasons to cancel surgery can easily be treated by an experienced and diligent anesthesiologist along with proper monitoring and a rapid response in the recovery room.
- Must monitor HR and pulse oximetry.

Anticipated Problems/Concerns

- Must have all airway equipment available, such as ETTs and LMAs.
- Have rescue medications available, especially beta agonists, and the ability to administer them in a variety of ways.

Urinary Lithiasis

Suchin R. Wadhwani | Lee A. Fleisher

Risk

- Annual incidence of stone disease is 16.4 per 10,000.
- Lifetime prevalence is 1–15%, although this varies with age, gender, race, and geography.
- Men are affected 2-3 times more often than women, but this varies with race.
- Racially, prevalence highest among Caucasians, followed by Hispanics, Asians, and African Americans.
- Peak incidence in fourth-sixth decades of life.
- Increased risk of recurrence after first stone.

Perioperative Risks

- Morbidity and mortality very low if stone is not obstructing ureter; however, relative morbidity increases with obstructing ureteral stone in setting of UTI, especially if signs of systemic inflammatory response.

Worry About

- Urosepsis, possibly septic shock, if surgical procedure is performed in presence of UTI, especially with an obstructing ureteral stone.
- Decreased renal function from partial or complete renal obstruction.
- Perinephric hematoma if kidney is punctured by lithotripter during stone breakdown.
- Pregnancy testing of women of childbearing age because of ESWL. Lithotripsy is contraindicated during pregnancy, although ureteroscopy and lithotripsy of stone under direct visualization is only relatively contraindicated and is often necessary if the stone obstructs drainage to the bladder, especially given excessive urine production during pregnancy.

Overview

- An obstructing ureteral stone with signs of infection (tachycardia, hypotension, toxic appearance) is considered a urologic emergency, as the infected/obstructed urine constitutes an abscess.
- Stones are classified as containing calcium: Calcium oxalate (60%), hydroxyapatite (20%), or brushite (2%); or noncalcium: Uric acid (7%), struvite (7%), cystine (1–3%), and other minor contributors.
- Calculi <4 mm in diameter usually pass with conservative management (hydration, NSAIDs, tamsulosin)
- Approximately 20% of stones cause severe enough symptoms to require surgical removal.

Etiology

- Intrinsic factors: Renal tubular acidosis, cystinuria, primary hyperparathyroidism, gout, Lesch-Nyhan syndrome, Dent disease, Bartter syndrome, hypercalciuria, sarcoidosis
- Extrinsic factors: Hot, dry climates resulting in increased perspiration and thus hyperconcentrated urine (southeastern and southwestern regions of USA); poor hydration resulting in low UO; diet rich in calcium, animal fat (uric acid), or leafy vegetables (oxalate); immobility (e.g., sedentary occupations); obesity or metabolic syndrome; UTI with urease-producing bacteria

Usual Treatment

- Trial of passage with hydration, NSAIDs (toradol) for symptomatic pain relief and alpha-1a antagonist (tamsulosin/flomax) to relax smooth muscle of ureter/urethra
- If surgical intervention necessary (20%), choice based on stone size and location:
  - ESWL
  - Flexible ureteroscopy and holmium laser lithotripsy
  - Percutaneous nephrolithotomy
  - Retroperitoneal laparoscopy

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Increased heart rate or BP secondary to pain or urosepsis		Tachycardia Htn	
RESP	Grunting respiration during renal colic		Normal chest exam	
GI	Abdominal pain	N/V Moving irritation in abdomen	Tenderness to deep palpation of abdomen. radiation of pain to ipsilateral groin	
RENAL	Renal colic with very severe pain localizing to the affected flank; pain may radiate to groin or abdomen	Sudden onset of flank pain	Flank tenderness to palpation over affected kidney	UA (hematuria), BUN/Cr, Noncontrast CT scan (gold standard), KUB plain film, IVP

Key References: Pearle M: Urinary lithiasis: etiology, epidemiology, and pathogenesis. In Wein AJ, Kavoussi LR, Partin AW, et al., editors: *Campbell-Walsh urology*, ed 11, Philadelphia, PA, 2016, Elsevier, pp 1170–1199; Cheney FW, Domino KB, Caplan RA, et al.: Nerve injury associated with anesthesia: a closed claims analysis, *Anesthesiology* 90(4):1062–1069, 1999.

Perioperative Implications

Preoperative Preparation

- If obese, acid aspiration prophylaxis and airway evaluation.
- If signs of urosepsis, assess hydration status and peripheral perfusion.

Monitoring

- Routine.
- Temperature monitoring during immersion lithotripsy is essential because water temperature may produce hyperthermia or hypothermia.
- Shock waves synchronized to ECG in ESWL to avoid dysrhythmias prior to initiation of shock.

Preinduction

- Adequate padding to avoid nerve damage

Induction

- Sedation may be adequate for lithotripsy and minor ureteroscopy procedures. GA as well as spinal or continuous lumbar epidural with T8-level epidural are all acceptable depending on type of procedure, comorbid conditions, and pt preference.
- An LMA is appropriate for urolithiasis of the lower tract; an ETT may be necessary for the removal of an upper-tract stone so as to fully control ventilation and thus excursion of the kidney during lithotripsy procedures.

Maintenance

- Central blood volume may increase.
- Pt may become hypotensive secondary to urosepsis or warm irrigant causing decreased SVR.
- Vital capacity may decrease and work of breathing increase.
- Pleural effusion or hydropneumothorax may occur during percutaneous renal procedures.

Adjuvants

- Visualization of stone may require iodine-containing contrast material.
- Anticholinergic agents (glycopyrrolate) are occasionally given to shorten lithotripsy treatments; however, tachycardia can occur, resulting in myocardial ischemia in high-risk pts.
- Most pts receive prophylactic antibiotics prior to urinary tract procedures.

Anticipated Problems/Concerns

- Peroneal nerve compression from lithotomy position
- Allergic reactions in 5% receiving IV contrast media
- Steinstrasse, or ureteral obstruction by fragmented calculi, may cause ureteral colic following lithotripsy.
- Htn may occur following lithotripsy.
- Septic complications occur in 1% of pts after lithotripsy, specifically in those with signs of infection and obstructing ureteral stones.
- Ureteral injury occurs in 9% of ureteroscopy procedures, with 1.6% requiring further surgical intervention.
- Bladder perforation may present as shoulder pain, unexplained Htn, or tachycardia in the PACU.

Urticaria, Cold

Christina Iliadis | Lee A. Fleisher

Risk

- Higher incidence found in regions with colder climate
- Prevalent in all races and genders; most commonly seen between ages 10–40 y

Perioperative Risks

- Can develop urticaria and/or angioedema with skin cooling and rewarming
- Systemic shock-like reactions can occur with whole-body cold exposure (e.g., swimming)

Worry About

- Exposing patients to cold stimulus (e.g., cold room, cold IV or irrigation fluids, cold instruments or devices against the skin)

Overview

- A subdivision of chronic inducible urticaria (when symptoms last >6 wk)
- Accounts for 3–5% of all physical urticarias (urticaria caused by physical stimuli)
- Characterized by appearance of urticaria and/or angioedema after cold exposure
- Urticaria, which presents as pruritic, superficial erythematous papules or plaques that are blanchable, and angioedema, involving swelling of the deeper dermis, which usually affects face/lips/extremities and tends to be painful
- Disease course usually lasting from 5–9 y but may resolve after several months
- Symptoms occurring within min after exposure to cold stimulus (cold air/fluids)
- Disease: acquired (most common) or familial (rare hereditary disorder)
- Acquired: Primary or secondary to an underlying disease process, such as malignancy, cryoglobulinemia, or infection (e.g., HIV, infectious mononucleosis).
- After treatment of underlying disease (e.g., treatment with antibiotics): secondary cold urticaria may resolve
- Dx: Made with cold stimulation test (ice cube to volar surface of forearm)
- If + stimulation test, threshold testing to determine severity of disease
- Threshold testing: performed with a computer-aided thermoelectric Peltier device

Etiology

- Primary cold urticaria appears related to skin mast cells sensitization to cold by a serum factor, and is very likely autoantibodies mediated (functional anti-IgE antibodies have been described in pts with ACU).
- Sensitized skin mast cells release histamine and other proinflammatory mediators upon interaction with cold stimulus.
- Cryoglobulins cause activation in secondary cold urticaria.

Usual Treatment

- Nonsedating second-generation H_1 antihistamines are standard treatment, successful at delaying and preventing occurrences (up to 4× the standard dose). Cyproheptadine is not used as commonly as in the past because of its sedating and anticholinergic effects.
- Omalizumab, an anti-IgE monoclonal antibody, has been shown effective in resistant chronic urticaria, including cold urticaria.
- Emergent treatment consists of steroids, H_1 blockers, and epinephrine, especially if airway compromise is evident.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
DERM	Urticaria or angioedema Flushing, erythema, pruritus	Cold reactions	Wheals (hives) Nonpitting edema	Cold stimulation test Threshold testing
RESP	Bronchospasm Dyspnea	Swelling on cold exposure	Breath sounds Wheezing and hypoxemia	Auscultation, SpO_2, ABG
CV (systemic Rx)	Tachycardia, hypotension Dizziness	Syncope after aquatic activities	Headache and weakness Loss of consciousness	ECG, NIBP
HEENT	Laryngeal edema, oropharyngeal edema	Dysphagia after cold drinks/food	Tongue/lip or facial edema	Fiberoptic exam of airway if compromise suspected

Key References: Abajian M, Schoepke N, Altrichter S, et al.: Physical urticarias and cholinergic urticaria. *Immunol Allergy Clin North Am* 34(1):73–88, 2014; Trevisonno J, Balram B, Netchiporouk E, et al.: Physical urticaria: review on classification, triggers and management with special focus on prevalence including a meta-analysis. *Postgrad Med* 127(6):565–570, 2015.

Perioperative Implications

Preoperative Preparation

- Use antihistamines (H_1 and H_2) and steroid prophylaxis in pts with known disease, especially if cold challenge is expected during surgery (e.g., CPB).
- Avoid medications that provoke histamine release (e.g., morphine, atracurium).
- Warm the OR, table, IV fluids, and all medications before injection.

Monitoring

- Monitor skin temp, examine skin for urticaria, and use standard monitors (ECG, SpO_2, NIBP).

Airway

- Have emergency airway equipment if suspected angioedema (fiber optic, video laryngoscope)

Induction

- All IV meds must be warmed before injection; avoid histamine-releasing medications.

Maintenance
- Warm IV and irrigation fluids; keep room and the pt warm.
- Monitor for signs of anaphylaxis: tachycardia, hypotension, and/or bronchospasm.

Extubation
- If concern for angioedema with airway involvement exists, evaluate the airway before extubation with a FOB or video laryngoscope; can perform cuff-leak test.

Postoperative Period
- Monitor for possible delayed urticarial reactions (atypical cold urticaria).

Anticipated Problems/Concerns
- Laryngeal/oropharyngeal angioedema may compromise the airway, which can make intubation and securing the airway challenging.
- Localized areas of urticaria and/or angioedema are usually benign, but serious widespread edema can compromise the airway or lead to systemic shock.
- Maintaining core body temperature can also be challenging due to redistribution while under general anesthesia and radiant heat loss to the environment.

Uterine Rupture

Benjamin T. Cobb | John Kissko III

Risk
- Incidence varies; 1:1500 women for all pregnancies; 1:8400 for unscarred uteri.
- Incidence of rupture with prior uterine scar (i.e., cesarean, myomectomy) ranges from 0.5–2% in developed countries.
- Maternal mortality is between 0.1–1% of cases.
- Risk factors: Uterine scar (e.g., prior classical cesarean, prior low transverse cesarean, previous uterine myomectomy), congenital uterine anomalies, multiparity (especially previous cesarean deliveries), fetal macrosomia, uterine instrumentation, uterine trauma, rapid progression of labor, polyhydramnios, abnormal placentation (e.g., accreta, percreta), placenta previa, pharmacologic induction, or augmentation of labor

Perioperative Risks
- Potentially catastrophic for pt and fetus. Maternal morbidity is ~0.1% and includes hemorrhage, shock, and hysterectomy. If the fetus is delivered within 10–37 min of diagnosis, fetal morbidity is improved but still includes hypoxemia and/or acidosis, depressed Apgar scores, and a neonatal ICU admission.
- Dx is difficult and usually delayed owing to nonspecific symptoms. Physicians should have a low threshold for diagnosing pts with risk factors given the increased maternal morbidity and mortality over time.
- Hemodynamically stable pts can become unstable quickly.

Worry About
- Massive hemorrhage in the pregnant pt
- Fetal morbidity due to hypoperfusion and hypoxemia or anoxia
- Amniotic fluid embolism and DIC

Overview
- Because of a breach in the myometrium, which is often secondary to separation of a previous cesarean scar, uterine rupture can occur antepartum, intrapartum, or postpartum. At term, the lower uterine segment contains mostly connective tissue and little placental tissue. Therefore ruptures of the lower uterine segment can be asymptomatic and not result in maternal and/or fetal compromise. However, ruptures of the upper uterine segment where placental tissue is involved can lead to massive bleeding, with resultant need for emergent cesarean delivery and/or laparotomy.
- Vaginal delivery is preferred over cesarean delivery as there is less maternal blood loss and maternal morbidity.
- The American Congress of Obstetricians and Gynecologists (ACOG) advocates for a trial of labor after cesarean (TOLAC) in pts with a previous low transverse uterine scar. TOLAC is discouraged by ACOG in pts being induced with prostaglandins or with a history of a classical cesarean because the risk of rupturing is greatly increased. Additionally, TOLAC is discouraged in hospitals where emergency cesarean delivery cannot be performed within 20–30 min.
- Uterine rupture is usually a clinical Dx since there is often not enough time for ultrasound, CT, or MRI.
- Diagnosis: Prolonged late decelerations, recurrent variable decelerations, and fetal bradycardia are the most common presenting symptoms (87%). Other symptoms include diminished uterine contractility; reduced baseline uterine pressure; abdominal, lower back, or shoulder pain; halting or retracting of the presenting fetal part; vaginal hemorrhage; and hypotension or shock. Abdominal pain remains a reliable sign even in the presence of a labor epidural, as a low-dose local anesthetic is typically used.

Etiology
- Separation of the scar from a previous uterine surgery, often during TOLAC, is technically "uterine dehiscence," but as they have similar presentations, they are considered together here.
- Rupture of myomectomy scar (highest incidence of rupture).
- Weak or stretched uterine muscles due to grand multiparity, polyhydramnios, multiple gestations, abnormal placentation, fibroids.
- Rapid labor or prolonged labor with pharmacologic augmentation.
- Traumatic rupture.

Usual Treatment
- When a uterine rupture occurs antepartum or during labor, urgent or emergent laparotomy with cesarean delivery and uterine repair (or possibly even hysterectomy) is the only treatment. Urgency is determined by the speed of diagnosis and maternal and fetal stability. Once rupture is diagnosed, the cesarean should begin within 20–30 min.
- If rupture is diagnosed incidentally postpartum, the pt may undergo close observation without surgery.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia, hypotension, shock		BP, HR, orthostasis	
RESP	Discomfort with breathing due to diaphragmatic irritation	Shortness of breath	Tachypnea, labored breathing	
GU	Vaginal bleeding	Abdominal pain, shoulder pain, absence of contractions	Abdominal tenderness, presenting fetal parts	Hgb/Hct
HEME	DIC		Widespread bleeding especially at the IV site	Platelets, TEG, coagulation factors
FETUS	Category 2 or 3 fetal distress			FHR monitor

Key References: Nahum GG: Uterine rupture in pregnancy, *Medscape* <http://reference.medscape.com/article/275854-overview#showall>, 2016 (Accessed 15.03.16); Rossi AC, Prefumo F: Pregnancy outcomes of induced labor in women with previous cesarean section: a systematic review and meta-analysis, *Arch Gynecol Obstet* 291(2):273–280, 2015.

Perioperative Implications

Preoperative Preparation
- In TOLAC, monitor fetal heart rate tracing continuously.
- Strongly consider placing at least two 18-gauge IV lines for high-risk pts in labor.
- Identify high-risk pts for early epidural placement to confirm adequate anesthesia.
- Continuous epidural during labor can be advantageous in that it can be dosed for surgical anesthesia if a repeat cesarean is indicated. Use a combination of low-dose local anesthetic and opioid to reduce the likelihood of an instrumented delivery or mask the pain symptoms of uterine rupture.
- If an epidural is not present when uterine rupture is diagnosed or time for dosing is inadequate, GA may be necessary for an emergent repeat cesarean.
- Consider the following for the anesthetic management of suspected or confirmed uterine rupture:
  - Two large-bore IV lines.
  - Typed and cross-matched blood products.
  - Arterial line.
  - Large-bore central line if peripheral access is poor.
  - Fluid warmer.
  - Quick access to laboratory values (point-of-care blood gas analyzer).

Monitoring
- ASA monitors; consider invasive monitoring of BP and CVP.

Induction/Airway
- If pt is grossly unstable and does not have an epidural, GA will likely be needed.
- Reexamine the airway, as this can change through labor; consider video laryngoscopy.
- Rapid sequence induction.
- If pt is severely hypovolemic, consider blood transfusion with a hemodynamic-sparing induction technique.

Maintenance
- If pt is hemodynamically stable, may consider neuraxial anesthesia.
- For general anesthesia, 100% FIO_2 with volatile anesthetic at 0.5 MAC or less (to minimize uterine relaxation) plus nitrous oxide throughout the procedure as maternal BP tolerates. If an arterial line is present, can use PO_2) from ABG to measure oxygenation while using nitrous oxide to minimize the volatile agent.
- Restore blood volume to keep Hgb >7–8 g/dL and BP stable.
- If pt is stable after delivery, consider midazolam and titrating opioids.
- Fetus may require intensive resuscitation; have neonatologist present.

Extubation
- Standard extubation criteria: Pt awake, full return of neuromuscular function, hemodynamically stable, no continuous bleeding, baseline acid/base and electrolyte status

Postoperative Period
- Consider admission to ICU.
- EBL may be 3000–6000 mL, so follow the trend of CBC and coagulation factors q2h for at least 8 h.
- Consider IV PCA or postop epidural if coagulation status is normal.

Anticipated Problems/Concerns
- Consider other more common causes of antepartum hemorrhage (e.g., placenta previa, placental abruption).
- Pregnant pts who hemorrhage can develop DIC quickly. Monitor coagulation factors and platelets.
- Symptoms of uterine rupture may be vague or misleading. Obstetricians and anesthesiologists must possess a high index of suspicion to diagnose uterine rupture in a timely fashion.
- Rupture of classic cesarean scar or previous upper uterine surgery scar is much more likely to result in severe hemorrhage.

Varicella-Zoster Virus

Lee A. Fleisher

Risk
- Prevalence: <10% of adults seronegative
- Usually contracted during childhood.

Perioperative Risks
- Minimal additional risk to pts unless immunocompromised.
- Risk of infection for caregivers.

Worry About
- Encephalitis in immunocompromised pt
- Potential nosocomial transmission
- Acyclovir-induced nephrotoxicity
- Transmission to pregnant woman

Overview
- Viral cause of varicella (chickenpox) and herpes zoster (shingles).
- Caused by both nosocomial transmission and direct contact.
- Development of herpes zoster is common in immunocompromised pts and may be a forerunner of AIDS.
- Zoster is a reactivated form of varicella from neural ganglion cells and can be associated with severe pain.
- May lead to congenital abn if contracted during first trimester of pregnancy.

Etiology
- Herpes group of viruses

Usual Treatment
- Varicella immune globulin.
- Vaccine is available but controversial.
- Antiviral medications decrease the duration of symptoms and the likelihood of postherpetic neuralgia, especially when initiated within 2 d of the onset of rash.
- Most common treatment is acyclovir; valacyclovir, penciclovir, and famciclovir are also available.
- Corticosteroid use is controversial for postherpetic neuralgia in pts with herpes zoster; controlled-release oxycodone was superior to placebo in the early period of pain.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Pneumonia	Dyspnea	Rhonchi	CXR
HEME	Thrombocytopenic purpura	Bleeding		Plts
DERM	Rash		Erythematous macules, papules, vesicles	
RENAL	Acyclovir nephrotoxicity			Cr
CNS	Encephalitis Optic neuritis; transverse myelitis	MS changes Vision changes		CT scan
PNS	Zoster shingles		Shingles in single dermatome Multiple dermatomes in immunocompromised	
IMMUNE	Associated with AIDS			HIV tests; CD4 titer

Key References: Christo PJ, Hobelmann G, Maine DN: Post-herpetic neuralgia in older adults: evidence-based approaches to clinical management, *Drugs Aging* 24(1):1–19, 2007; Philip A, Thakur R: Post herpetic neuralgia, *J Palliat Med* 14(6):765–773, 2011.

Perioperative Implications

Preoperative Preparation
- Consider isolation precautions.

Monitoring
- Routine

Airway
- Routine

Induction/Maintenance
- Routine
- Pts may require modification of periop pain management regimen if treatment for postherpetic neuralgia.

Extubation
- Routine

Anticipated Problems/Concerns
- Multiple dermatomes may indicate immunocompromised individual.
- Avoid exposing pregnant individuals to virus.

Ventricular Fibrillation

Sheela Pai Cole

Risk

- VFIB/VTach: Most frequent rhythm in sudden cardiac arrest and the most frequent cause of death in pts with coronary disease.
- Risk of VF complicating an acute MI: 4–7%; has remained unchanged for several years.
- 1-y mortality in survivors of near sudden death: 20–30% if nonresponsive to antiarrhythmics (20–50% of survivors).

Perioperative Risks

- Primary VFIB associated with acute infarction may not affect prognosis if treated promptly with defibrillation.
- Secondary VFIB (preceded by pump failure or hypotension) associated with 75–80% mortality during hospitalization

Worry About

- Hypoxemia, hypercarbia, hyperkalemia or hypokalemia, ischemia, hypomagnesemia, digitalis toxicity, acid–base abnormalities, and coronary graft failure
- Antiarrhythmic drug levels
- Availability of defibrillator, myocardial ischemia, and early revascularization

Overview

- Asynchronous, chaotic contractions of ventricles with no organized ventricular depolarization and therefore no QRS complexes and no cardiac output.
- Coarse VFIB indicates recent onset and is readily correctable with prompt defibrillation.
- Fine VFIB (coarse asystole) indicates delay since collapse; successful resuscitation is more difficult.

Etiology

- Usually ischemic; often associated with an LV aneurysm
- Idiopathic cardiomyopathy
- Coronary spasm or graft failure, especially in the immediate postop period
- Hypothermia
- Long-QT syndrome is associated with VTach, especially torsades de pointes (one type of polymorphic VTach; other types are not associated with long-QT).

Usual Treatment

- Definitive emergency Rx is always electrical defibrillation: External—either manual or automatic (AEDs)—or internal (ICD may be implanted).
- Time to defibrillation is a major determinant of survival, with chances of success reduced by 10% each minute.
- Early bystander CPR and early defibrillation with return of spontaneous circulation has been associated with decreased mortality.
- Vasopressors such as epinephrine and vasopressin are indicated after three successive countershocks fail to terminate VFIB. Vasopressors improve coronary and cerebral perfusion pressures; increased coronary perfusion pressure is assoc with increased likelihood of return of spontaneous circulation.
- Vasopressin may have fewer side effects than epinephrine while being equally or more effective, particularly in acidotic pts. Vasopressin's longer duration of action (10–20 min) has led to the recommendation of a single, one-time dose for VFIB.
- Amiodarone is the only antiarrhythmic associated with improved resuscitation rates from VFIB; it is recommended after three successive shocks, an IV vasopressor (epinephrine or vasopressin), and a subsequent fourth shock are unsuccessful in restoring a perfusing rhythm.
- Prospective trials of lidocaine and bretylium in VFIB pts have shown no benefit regarding outcome. However, based on historical use and the lack of side effects, lidocaine is considered an alternative to amiodarone in VFIB, especially in the setting of amiodarone toxicity.
- Owing to inconsistent availability, side effects, and lack of confirmed benefit, bretylium is no longer recommended for VFIB.
- Evidence supporting procainamide use in VFIB is limited. Although the need for slow infusion makes it less than ideal, it may be an alternative when amiodarone is contraindicated.
- Magnesium may be beneficial in torsades de pointes (polymorphic VTach associated with long-QT), but routine use does not improve outcome.

Assessment Points

System	Effect
HEENT	Right radical neck dissection assoc with increasing QT interval
CV	No effective cardiac output
RESP	Apnea should be anticipated
CNS	Glucose administration may worsen CNS outcome

Key Reference: ECC Committee, Subcommittees and Task Forces of the American Heart Association: 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, *Circulation* 112(Suppl 24):IV1–IV203, 2005.

Perioperative Implications

Preoperative Preparation

- Antiarrhythmic drug levels in optimal therapeutic range
- If for EPS, ablation, or ICD, antiarrhythmic drugs may be held on the day of procedure with ECG monitoring.
- Avoid anticholinergic premedication or sympathetic stimulation.
- For pts with prolonged QT syndrome, consider β-blockers or prophylactic left stellate ganglion block.

Monitoring

- Consider ECG and pulse oximetry en route to OR.
- Consider arterial cath for procedures involving greater than minimal risk, especially during ablative procedures in the cath lab.

Airway

- Apnea expected with acute VFIB; oxygenation should be supported with 100% O_2 and bag mask ventilation. Once successful ventilation established, interruption of CPR for a definitive airway is not recommended.
- Airway secured with ETT if three successive countershocks fail to restore perfusing rhythm.

Induction

- Avoid ketamine; intubate after adequate depth of anesthesia.

Maintenance

- Suppress sympathetic responses to stimulation.

Extubation

- Suppress sympathetic stimulation; extubate when spontaneous ventilation with oropharyngeal reflexes has been restored.
- Reversal of NMBs acceptable.
- Regional: Serum levels of local anesthetics given epidurally may affect intraop defibrillation threshold testing during ICD placement.
- Defibrillator should be available with sterile defibrillator paddles on the surgical field; pharmacologic therapy required for dysrhythmia conversion/maintenance and for treating Htn and tachycardia, which frequently follow defibrillation; bradycardia may require pacing.

Postoperative Period

- Cardiac monitoring; resumption of preop antiarrhythmics, maintaining adequate oxygenation and ventilation
- Avoid lyte abnormalities and treat promptly if they appear.
- Postdefibrillation pain score: 1–3 from chest wall and psychic disturbances.
- Psychiatric counseling if pt is disturbed by shock or has "out of body" experience.

Anticipated Problems/Concerns

- PA cath insertion may induce VT or VFIB in dysrhythmia-prone pts; if PA cath necessary, consider central venous placement with advancement after ventricular dysrhythmia procedure has been completed. If PA cath is essential, consider placement of defibrillation pads prior to placement of the cath.
- In pts with long-QT syndrome, avoid drugs that prolong the QT interval (class Ia antiarrhythmic drugs such as quinidine and procainamide).
- Psychic disturbances from defibrillation in aware state.

Ventricular Preexcitation Syndrome

Nathalie Stevenson | Peter M. Odor

Risk

- Not all patients are symptomatic or have a prior diagnosis; 1–3% of diagnoses are made following ECG in previously asymptomatic individuals.
- WPW syndrome affects 0.1–0.3% of the population, is more prevalent in males, and is characterized by symptomatic arrhythmias and an ECG showing a short PR interval (<120 ms) with a widened QRS (>100 ms) and often, but not always, δ waves, representing fusion of early and late depolarization via the accessory pathway and AV node. Abnormal conduction occurs via a bundle-of-Kent accessory pathway between atria and ventricles. Risk of SCD is estimated to be 0.25% per annum in WPW syndrome.
- LGL syndrome affects 0.5% of adults, is more prevalent in women, and reflects abnormal conduction through the James bundle (atria to bundle of His). Characterized by a short PR interval, normal QRS, and no δ waves, it manifests through reentrant type PSVT or atrial fibrillation/flutter. No studies have shown an increased risk of SCD in LGL.
- The Mahaim type is a rarer form of preexcitation, caused by Aps in the right ventricle, called Mahaim fibers. It is characterized by a normal PR interval, long QRS, and δ waves and may trigger episodes of SVT.

Perioperative Risks

- General or regional anesthesia may unmask ventricular preexcitation syndromes.
- Asymptomatic individuals with a WPW ECG pattern may present no added risk. Symptomatic individuals with WPW syndrome are prone to PSVT (up to 75%), or less commonly to atrial fibrillation (15–30%) and flutter (5%); rapid ventricular rates may occasionally deteriorate to VT or VF.
- There is a danger of misrecognition of WPW ECG patterns for BBB (wide QRS); myocardial infarction (negative δ waves simulating pathologic Q waves); other tachyarrhythmias (including VT). All prompt inappropriate treatment.
- Drugs used to suppress AV conduction (to slow the ventricular rate in treatment of atrial fibrillation/flutter) may dangerously accelerate the rate in WPW.

Worry About

- Periop nausea, gagging, hypothermia, pneumoperitoneum, and pregnancy can all accentuate conduction via abnormal APs. Hyperadrenergic states, overstimulation (including laryngoscopy), and other interactions can also provoke or aggravate tachyarrhythmias.
- High spinal anesthesia may block sympathetic cardiac accelerator nerves and suppress normal AV conduction. Alongside relative parasympathetic predominance, this may further facilitate conduction by the APs, resulting in preexcitation and tachyarrhythmias.
- Cholinergic medications, such as suxamethonium and reversal agents, along with other AV-nodal blocking drugs (diltiazem, digoxin) may enhance conduction via APs, worsening tachyarrhythmias.
- Potential of WPW-related PSVT to deteriorate into atrial fibrillation or flutter, with danger of extremely rapid ventricular rates and ensuing VT and VF.

Overview

- The presence of a short PR interval, often with a δ wave, reflects the underlying early depolarization of ventricles and defines preexcitation syndrome.
- The extent of preexcitation may change depending upon the conduction characteristics of the abnormal AP, AV node, and autonomic tone. The majority of pathways allow dual conduction, both anterograde (i.e., atrial to ventricular) and retrograde (i.e., ventricular to atrial). Retrograde-only conduction occurs in 15% and anterograde only is rare.
- Pts with a ventricular preexcitation syndrome have an abnormal AP that bypasses the AV node to electrically connect atria and ventricle. The majority of these APs generate fast action potentials due to rapid sodium current influx, resulting in faster conduction of electrical impulses to the ventricle than the slower calcium current–dependent AV nodal route. This electrochemical distinction means that the onset of ventricular activation occurs *earlier* than if impulses had conducted through the AV node; hence preexcitation. Additionally, at faster atrial rates, progressive prolongation of AV nodal conduction is also bypassed, meaning that atrial tachycardias may deteriorate into VF.
- A range of arrhythmias may occur in preexcitation syndromes, from SVTs (more common) to life-threatening ventricular arrhythmias (less common).
- OAVRTs are due to abnormal circuits, in which anterograde conduction occurs via the AV node and retrograde conduction via the AP. Since the normal AV pathway is used for ventricular depolarization, QRS complexes are narrow and no δ waves are present. This accounts for most tachyarrhythmias in WPW syndrome (70%).
- Antidromic tachycardias derive from anterograde ventricular activation via an AP, with retrograde current reentering atria via the AV nodal route. Wide QRS and δ waves are present on the ECG.
- The first episode of PSVT in many pts appears before the age of 20 y, rarely in middle age, and infrequently after age 50. The frequency of episodes of PSVT increases with age in WPW syndrome.

Etiology

- APs are congenital in origin, and preexcitation syndromes may be hereditary.
- Associated with congenital cardiac defects (most commonly tricuspid value lesions) and acquired cardiac defects (e.g., cardiomyopathy, idiopathic hypertrophic subaortic stenosis, asymmetric septal hypertrophy).

Usual Treatment

- Long-term therapy in recurrent symptomatic tachyarrhythmias is through the delivery of electrical or radiofrequency impulses to the AP using catheter ablation. Success rate is about 90–95%.
- Pharmacologic prophylaxis is reserved for pts in whom catheter ablation has failed. Agents that prolong refractoriness in APs are recommended, such as disopyramide, procainamide, and flecainide.
- In the acute setting with a hemodynamically unstable pt, the treatment of choice is synchronized DC electrical cardioversion (50–200 J). The minimum effective energy should be used initially and energy subsequently titrated to minimize potential injury to the myocardium.
- The most common tachyarrhythmia in pts with preexcitation is a regular, narrow-complex tachycardia due to an OAVRT. These tachycardias respond well to treatments that momentarily block transmission through the AV node. In stable pts, vagal maneuvers may be attempted, followed by rapid administration of adenosine (unless contraindicated). Second-line agents include calcium channel blockers such as verapamil. An external cardioverter-defibrillator should be immediately available, as adenosine can increase risk of atrial fibrillation with preexcitation, and calcium channel blockers can precipitate reduced cardiac output in those who have structural heart disease.
- If a regular, broad complex tachyarrhythmia occurs in a pt with preexcitation, it should be considered as ventricular in origin as it is often difficult to determine the difference between ventricular origin and an OAVRT with bundle branch block, for example. Drugs that block the AV node (adenosine, calcium-channel blockers, beta blockers, digoxin) must *not* be used as they could precipitate VF and cardiac arrest. AP-blocking drugs such as procainamide and flecainide (class 1a) are recommended first-line treatment in the stable pt. Amiodarone slows AV node conduction as well as AP conduction and should be used with caution.
- If the pt presents with a tachyarrhythmia that is irregularly irregular, this is likely due to the different degrees of fusion at the ventricular level, as AV and AP conduction coexists. Preference should be to block the AP conduction (e.g., procainamide) with amiodarone as the second line.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmia LV function	Palpitations, dizziness, syncope, angina, chest pain, sometimes asymptomatic Weakness, exercise intolerance, CHF	Monitor BP; variable S_1-pulse amplitude; fast regular, irregular, and/or weak pulse	12-lead ECG, Holter ECG, cardiac EP study, ECHO, possible further study

Key References: Blomström-Lundqvist C, Scheinman MM, Aliot EM, et al.: ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias—executive summary: a report of the American college of cardiology/American heart association task force on practice guidelines and the European society of cardiology committee for practice guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias), *Circulation* 108(15):1871–1909, 2003; Bengali R, Wellens H, Jiang Y: Perioperative management of the Wolff-Parkinson-White syndrome, *J Cardiothorac Vasc Anesth* 28(5):1375–1386, 2014.

Perioperative Implications

Preoperative Preparation

- Take a thorough cardiac history to elucidate symptoms in keeping with existence of preexcitation, such as palpitations, syncope, dyspnea, angina, or dizziness. A 12-lead ECG can identify preexcitatory syndrome patterns, but these may not always be apparent.
- If pt is symptomatic, a cardiology consultation should be sought. This may involve exercise testing and Holter monitoring to determine the AP anterograde refractor period. If the pt is symptomatic, he or she will almost always be offered catheter ablation therapy.
- Pts on prophylactic medications must continue these and have them on the day of surgery, with minimal delay to taking them postop.
- Pts may benefit from RA where appropriate to avoid sympathetic stimulation, stress, and tachycardia.

Monitoring

- Ventricular preexcitation does not mandate use of invasive BP monitoring, central venous access, or placement of defibrillator pads. The anesthetist must consider the ability to urgently access the chest or arms while the pt is under the drapes or in the prone position.

Induction
- A smooth induction with the use of anxiolytics should be implemented in pts who may hyperventilate secondary to stress. A deep plane of anesthesia must be balanced with the effects of agents such as propofol, which can cause hypotension and compensatory tachycardia.
- Aim to obtund the effects of laryngoscopy by using a supraglottic airway device such as a laryngeal mask airway where appropriate.
- Adequate preloading should be considered to avoid the use of sympathomimetics for BP, and sympathomimetics should be used cautiously.

Maintenance
- The volatile agent halothane can precipitate conduction via APs and should be avoided.
- Avoid agents that can precipitate tachycardia, such as ketamine and pancuronium.

Extubation
- Avoid neostigmine, which induces vagal tone, causing slowing of the AV node and preference for conduction down AP. Avoid atropine and glycopyrrolate, which can induce tachycardia.

Adjuvants
- For control of postop N/V, avoid metoclopramide and cyclizine, which can induce tachycardia.

Postoperative Period
- Adequate pain control is essential and use of regional anesthesia may be beneficial.

Anticipated Problems/Concerns
- SVT or VF in those known to have preexcitation with or without symptoms throughout the periop period.
- Vigilance is required in interpreting the ECG of a tachyarrhythmia to avoid incorrect drug selection.

Ventricular Septal Defect (Congenital)

Menachem M. Weiner | Alexander J.C. Mittnacht | David L. Reich

Risk
- Incidence: About 2–6:1000 live births.
- May be isolated or part of several complex malformations such as TOF.

Perioperative Risks
- Mortality higher in older children; elevated PVR (>7 Wood units); surgery may be complicated by complete heart block.

Worry About
- Worsening of L-to-R shunt with hyperventilation and increased FIO_2
- Paradoxical embolization
- Hypothermia
- Post–CPB pulm Htn and RV failure

Overview
- Small defects asymptomatic, present with murmur, and usually close spontaneously.
- Larger unobstructed defects result in CHF symptoms, poor weight gain, and URIs beginning at 3–12 wk of age, as decreases in PVR cause increase in L-to-R shunting.
- Untreated large L-to-R shunting may result in fixed pulm Htn (Eisenmenger syndrome) in some pts.

Indications/Usual Treatment
- Some 75% of small defects close spontaneously. Small, unrepaired defects do not require antibiotic prophylaxis.
- Medical therapy for symptoms of CHF includes digoxin, ACE inhibitors, and furosemide.
- Surgery is indicated when CHF not amenable to medical treatment or if there is FTT.
- Surgical repair contraindicated if PVR >10 Woods units unless reactive to selective pulm vasodilators.
- Transcatheter closure is often used for muscular defects, which can be difficult to access surgically.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Low forward cardiac output due to L-to-R shunt Pulm Htn due to excessive flow	CHF symptoms, FTT Age of pt	Loud holosystolic murmur and thrill Cyanosis	Auscultation, ECHO, cardiac cath
RESP	Congestion/edema due to L-to-R shunt	Frequent URIs	Rhonchi	CXR
HEME	Anemia in massive L-to-R shunt; polycythemia in R-to-L shunt	Pallor or cyanosis	Paleness or plethora	Hct
MS	Chronic hypoxemia due to late reversal of shunt flow (Eisenmenger syndrome)	Cyanosis	Clubbing of digits	Pulse oximetry

Key References: Penny DJ, Vick GW 3rd: Ventricular septal defect, *Lancet* 377(9771):1103–1112, 2011; Scully BB, Morales DL, Zafar F, et al.: Current expectations for surgical repair of isolated ventricular septal defects, *Ann Thorac Surg* 89:544–549, discussion 550–551, 2010.

Perioperative Implications

Preoperative Preparation
- Digoxin and furosemide until day of surgery; ACE inhibitors controversial, but vasoplegic syndrome following CPB less common in pediatric pts.
- May not be possible to delay operation until pt is free of upper resp symptoms.

Anesthesia
- Limit FIO_2 to minimum necessary prior to CPB to restrict excessive pulm blood flow.
- Maintain normal to slightly high $PaCO_2$ to restrict excessive pulm blood flow.
- Pts typically receive inhalational anesthesia for induction; if peripheral IV in place, IV drugs can be administered alternatively.
- Avoid N_2O to prevent sequelae of paradoxical air embolization.

Monitoring
- Indwelling arterial catheter for invasive monitoring in all pts.
- Central venous access and pressure monitoring in most pts undergoing surgery with CPB.
- Standard ASA monitoring, including pulse oximetry, ECG, capnometry, multiple-site temp monitoring.
- TEE

Induction/Maintenance
- Mask induction with sevoflurane in most cases; IV drugs if peripheral IV in situ; IM induction possible for uncooperative pts.
- High-dose opioid anesthesia technique rarely used.

Surgical Stages
- Pre-CPB:
  - Low FIO_2, normal to high $Paco_2$.
  - Avoid hemodilution with large amounts of crystalloid and/or colloid prior to CPB.
- CPB:
  - After pt's Hct has been obtained in the OR, dilutional Hct including CPB prime is calculated. If calculated Hct is less than 25%, consider priming of CPB with whole blood or reconstituted whole blood (PRBC and FFP).
  - Inhalational anesthetic administration via CPB or continuous IV drug administration is recommended to allow for fast-tracking in most pts presenting for VSD repair.
- Post-CPB:
  - Rule out residual shunting by TEE.
  - Maintain Hct >25% to 30%.

Postoperative Period
- Most pts presenting for VSD repair can be extubated at end of surgery.
- Consider mechanical ventilation and sedation in the immediate postop period in pts prone to pulm hypertensive crises (e.g., Down syndrome).
- Infective endocarditis prophylaxis for 6 mo; if residual defect is present, should be continued indefinitely.

Anticipated Problems/Concerns
- Imbalance in pulm to systemic blood flow ratio:
  - Excessive pulm blood flow results in high arterial saturation but with diminished tissue perfusion and metabolic acidosis.
  - Diminished pulm blood flow results in good tissue perfusion but with cyanosis and potential injury due to hypoxia.
- Postop ventricular dysfunction more likely with ventriculotomy.
- Pulm Htn and/or right heart failure.
- Coagulopathy, particularly in very small children.

Ventricular Septal Rupture (Defect), Postmyocardial Infarction

Menachem M. Weiner | Gregory W. Fischer | David L. Reich

Risk

- Historically seen in 1–3% of MIs prior to era of acute revascularization.
- Incidence is 0.2% in current era of acute percutaneous intervention.
- Most occur within 1 wk of MI; 20–30% occur in first 24 h post-MI.
- Rarely occurs >2 wk post-MI.
- Medical management alone results in a mortality >90%.

Perioperative Risks

- Accounts for 5% of MI-related deaths,
- Without surgical therapy, survival is less than 10% at 1 mo.
- Surgical short-term survival 40–81%.
- Increased mortality seen in the setting of urgent repair (due to tissue fragility), posterior VSD, preop dialysis, mitral regurgitation, and redo cardiac surgery.
- Improvements in surgical techniques have enabled earlier surgery prior to hemodynamic deterioration, with associated increase in survival.
- Percutaneous device closure with GA and TEE has similar mortality.

Worry About

- Associated papillary muscle rupture
- Poor systemic perfusion and end-organ dysfunction
- Pulm congestion with massive L-to-R shunt

Overview

- Sudden onset of holosystolic murmur with thrill and hemodynamic deterioration (hypotension and pulm congestion).
- Despite advances in periop management, expect increased morbidity and mortality.
- Expect a complicated postop course with prolonged ICU stay.

Usual Treatment

- Repair of new VSD with hemodynamic deterioration using pericardial or prosthetic patch material.
- Support preop with inotropic agents/intra-aortic balloon counterpulsation.
- Percutaneous device closure as an alternative to surgery.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Low forward cardiac output due to massive L-to-R shunt	Sudden onset of hypotension and shock	Loud holosystolic murmur and thrill	ECHO, cardiac cath
RESP	Congestion/edema	Respiratory distress	Rales	CXR
RENAL/HEPATIC	Dysfunction due to cardiogenic shock	Anuria		ABGs, Foley cath

Key References: Arnaoutakis GJ, Zhao Y, George TJ, et al.: Surgical repair of ventricular septal defect after myocardial infarction: outcomes from the Society of Thoracic Surgeons National Database, *Ann Thorac Surg* 94(2):436–443, 2012; Jeppsson A, Liden H, Johnsson P, et al.: Surgical repair of post infarction ventricular septal defects: A national experience, *Eur J Cardiothorac Surg* 27:216–221, 2005.

Perioperative Implications

Preoperative Preparation

- Consider elective tracheal intubation and PEEP.
- Support cardiac output using inotropic agents.
- Lower resistance to forward cardiac output using afterload reduction, including intra-aortic balloon counterpulsation.
- Obtain coronary angiogram. Concurrent revascularization can potentially improve outcome, although recent studies have not found this.

Anesthetic Technique

- High-dose opioid/muscle relaxant technique common
- Prior to CPB, use minimal FIO_2 and PEEP (maximizes PVR) to decrease L-to-R shunt across VSD.

Monitoring

- Intra-arterial line.
- Most use PA cath owing to pulm Htn and for shunt quantitation; step up saturation between right atrium and PA to measure degree of shunting.
- Thermodilution cardiac output may be falsely elevated.
- TEE to define anatomy, diagnose assoc papillary muscle rupture, monitor ventricular function (including stroke volume), and assess adequacy of surgical repair.

Airway

- High airway pressures and frequent suctioning in the setting of pulm edema.

Induction

- High-dose opioid technique to maintain hemodynamic stability. Avoid vasodilation assoc with volatile anesthetics.

Maintenance

- If pt is hypertensive, titrate low doses of volatile agent or benzodiazepines.

Surgical Stages

- Pre-CPB:
  - Median sternotomy with aortic and biatrial cannulation.
  - Vein or internal mammary artery harvest may be required for concomitant myocardial revascularization.
  - Lowest FIO_2 consistent with adequate oxygenation.
- CPB:
  - Maintain Hct using hemofiltration and transfusion.
- Post-CPB:
  - Inotropic support almost universally required for LV failure.
  - RV failure common.
  - Assess ventricular repair using TEE or right atrial-to-pulm O_2 sat ratio.
  - FIO_2: 1.00 to minimize PVR.
  - May require ventricular assist devices.
  - Rule out residual shunting by TEE.
  - Emergent surgery is associated with residual shunt.
- Blood loss/volume concerns:
  - Antifibrinolytic therapy (beginning pre-CPB).
  - Transfuse coagulation factors based on results obtained from point-of-care testing (TEG, platelet function analyzers).

Postoperative Considerations

- Postop renal/hepatic/neurologic dysfunction
- Postop LV, RV, or biventricular failure

Anticipated Problems/Concerns

- Cardiogenic shock with MODS
- Prolonged ventilatory dependency and ICU stay
- Course not dramatically improved with percutaneous device closure

Ventricular Tachyarrhythmias

John O.R. Whittle | Sanjoy Saha

Risk

- VTach/VFIB are uncommon but potentially fatal dysrhythmias requiring urgent diagnosis and management.
- Risk increases with age owing to the higher incidence of structural and ischemic heart disease and cardiac failure.
- Primary cause of sudden death and accounts for 75–80% of sudden cardiac death. Incidence in USA is about 300,000/y and similar in other developed nations.
- Males at greater risk (46% vs. 34%).
- Pts under 30 with HOCM, myocarditis, RV dysplasia, or long-QT syndrome are at higher risk for VTach/VFIB.

Perioperative Risks

- Cardiac and vascular surgery (up to 50% incidence) does not influence late mortality if LV function is preserved.
- Low cardiac output after CABG (requiring pressors) predicts life-threatening VTach/VFIB within 72 h postop.
- Cardiac ischemia.
- Uncorrected electrolyte and/or acid-base disturbances, hypoxia, hypercarbia, hypothermia.
- Use of class 1 and 3 antiarrhythmics, sympathomimetics, QT-prolonging drugs.
- Placement of central venous catheters.

Worry About

- Electrolyte imbalance (particularly hypokalemia and hypomagnesemia), acid-base disturbances, hypoxia, hypotension, fluid overload, ongoing myocardial ischemia, and metabolic disturbances.
- Use of IV epinephrine and other catecholamines/sympathomimetics.
- Drugs that prolong QT (organophosphates, antipsychotics, tricyclics) may precipitate PVT, particularly in Brugada and other long-QT syndromes.
- Poor cardiac function.
- Modulation of neuroendocrine stress responses.

- R-on-T phenomenon.
- Chest pain, SOB, palpitations, presyncope, altered mental status.

Overview

- VTach is caused by high-frequency electrical depolarization from a ventricular myocardial focus and is characterized by a widened QRS (>0.12 sec), high rate (>120 bpm) and variable morphology (MVT or PVT) and duration (sustained vs. nonsustained).
- Atrioventricular dissociation may be present, where p waves may be seen with or without capture/fusion beats. This implies VTach rather than SVT with aberrant conduction.
- MVT has a single QRS morphology and can evolve into PVT. Often reentrant etiology post-MI.
- Torsade de pointes: Atypical PVT with beat-to-beat variation, prolonged QT, changing/twisting QRS axis around baseline.
- VFIB: Nonperfusing broad complexes (fast, chaotic, irregular, and disorganized).
- Ventricular ectopic beats can sometimes precede VTach.

Etiology

- Structural and ischemic heart disease (MI, CAD, CHF, valvular disease, cardiomyopathies, myocarditis).
- VEs are provoked by dental procedures and anal stretch, particularly in combination with halothane, raised CO_2, and light anesthesia.
- TdP: Severe nonuniform delay in repolarization (QT prolongation). Familial, idiopathic, or acquired secondary to hypokalemia, hypocalcemia, hypomagnesemia.
- QT-prolonging drugs include class 1 and 3 antiarrhythmics, antihistamines, TCAs, lithium, antipsychotics, certain analgesics, ondansetron, and droperidol (see http://www.sads.org.uk/drugs-to-avoid/).
- Short-QT syndrome
- MVT/PVT secondary to excessive endogenous or exogenous catecholamines (stress, exercise, cocaine, etc.).
- Brugada syndrome: RBB-like conduction and ST-segment elevation in precordial leads without prolonged QT or structural heart disease (heritable).
- VFIB: Recent MI, ischemic heart disease, hypokalemia/hyperkalemia, excessive catecholamine levels (endogenous or exogenous), myocardial irritation (e.g., from CVC guidewire or mechanical ventilation).
- Hypoxia, hypothermia, hypercarbia, hypokalemia, hypomagnesemia, acidosis, thromboembolism, tamponade, tension pneumothorax.

Usual Treatment

- Assess vital signs (ABCs).
- Depends on stability of patient. Unstable (systolic BP <90 mm Hg, HR >150 bpm, heart failure, evidence of myocardial ischemia) with pulse then synchronized DC cardioversion. Pulseless VTach equals cardiac arrest, so ALS/ ACLS protocols are needed (CPR, DC cardioversion, epinephrine/vasopressin).
- VFIB is not associated with palpable cardiac output and should be treated with CPR or ALS/ACLS protocols.
- In either VFIB or pulseless VTach in the cardiac cath lab or immediately after cardiac surgery, three consecutive "stacked" shocks may be used.
- Hemodynamically stable MVT/PVT: Amiodarone 300 mg IV over 1 h via central access (or large-bore peripheral access; risk of extravasation) followed by 900 mg over 24 h. Alternative drugs include lidocaine (100 mg bolus, 4 mg/min for 30 min, 2 mg/min for 2 h, 1 mg/min for 4 h) or sotalol 100 mg/procainamide 100 mg. Consider adenosine if there has been earlier SVT with aberrant conduction. Electrical cardioversion as above.
- Correct electrolyte and acid-base disturbances (including magnesium), hypoxia, hypovolemia, hypothermia, and hypercarbia. Look for and treat tension pneumothorax, cardiac tamponade, and thromboembolic causes.
- TdP $MgSO_4$ 1–2 g over 1–2 min, replete K+, consider atropine, isoprenol, asynchronous DC countershocks (avoid epinephrine as it may precipitate VFIB).
- If all fails, then cardiology for overdrive pacing.
- Review medications and remove possible precipitants.
- Chronic VTach: ICD, RF ablation of aberrant pathways, regular antidysrhythmic medications. Stellate ganglion blockade has been used in long-QT syndrome.
- VEs may be treated with beta blockade. If slow, they could be ventricular escape beats calling for anticholinergics (e.g., atropine/glycopyrrolate) or >30 sec (VTach).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Ischemia, MI, decreased cerebral perfusion, decreased cardiac output	Angina, palpitations, anxiety, lightheadedness, syncope	Pallor, diaphoresis, heart murmur, tachycardia, JVD, cannon a waves, displaced PMI, S_3 gallop	12-lead ECG, TTE, TEE, Holter monitor, cardiac CT and cardiac MRI, cardiac cath (right or left heart), cardiac enzymes
RESP	Increased pulm venous pressure, pulm edema secondary to HF	Dyspnea, tachypnea, sleep apnea	Wheezing, course breath sounds, crackles	CXR, CT chest, PFTs, ABG

Key References: Thompson A, Balser JR: Perioperative cardiac arrhythmias, *Br J Anaesth* 93(1):86–94, 2004; Roberts-Thompson K, Lau D, Sanders P: The diagnosis and management of ventricular arrhythmias, *Nat Rev Cardiol* 8:311–321, 2011.

Perioperative Implications

Preinduction/Induction/Maintenance

- Pt history of VFIB/VTach, CAD, CHF. Is cardiac disease optimized medically?
- Congenital/acquired long-QT syndrome; avoid and/or stop causative drugs.
- Minimize sympathetic stress response; adequate depth of anesthesia/analgesia; avoid sympathomimetics/sensitizers; be careful with catecholaminergics.
- Ask: Is there a problem with the anesthetic? Modify depth of anesthesia, look for drug interactions or error.
- Ask: Is there a problem with the surgery? Avoid anal stretch, ocular traction, peritoneal traction. Care with Moffats solution in ENT surgery. Air or fat embolism? Unexpected blood loss? Mediastinal manipulation?
- Ensure that acid-base, lytes, hypoxia/hypercarbia are assessed and treated

Monitoring

- Routine monitoring including ST-segment trending and recording.
- Arterial +/– cardiac output monitoring for pts with a history of cardiac disease, history of VTach, or undergoing high-risk procedures.

General Anesthesia

- Unclear evidence on usage of volatile anesthetic agents in long-QT syndrome; both prolongation and shortening have been reported. Consider use of TIVA in at-risk population. Halothane in particular is implicated in ventricular dysrhythmias.
- Care with CVC placement: Check position if there are new ventricular arrhythmias.

Regional Anesthesia

- Meticulous avoidance of intravascular injection
- Avoid hypoperfusion secondary to vasodilatation

Postoperative Period

- Adequate analgesia
- Further workup including echocardiography, 12-lead ECG, and cardiology consult.
- Consider increased care environment and ongoing antiarrhythmic therapy.

Ventricular Tachycardia

Arvind Rajagopal | Kenneth J. Tuman

Risk

- Structural heart disease (most commonly a chronic phase of MI); predictor of sudden cardiac death after MI.
- Most common cause of mortality with CHF.
- Cardiomyopathies, both hypertrophic and dilated, are assoc with VTach.
- Seen in genetic syndromes such as long QT syndrome, Brugada syndrome, and arrhythmogenic right ventricular dysplasia.

Perioperative Risks

- Endogenous or exogenous catecholamines trigger VTach in susceptible pts.
- Central venous, pulm artery cath and intubation can trigger VTach.
- Hyperventilation may decrease serum K^+.
- Precipitation of polymorphic VTach with agents that alter QT interval.

Worry About

- Decreased vital organ perfusion related to low cardiac output
- Possible effect of antiarrhythmics on cardiac and pulm function
- Periop ventricular dysfunction and/or ischemia
- Progression of VTach to VFIB
- Reduction of left ventricular function due to IV antiarrhythmic

Overview

- Defined as 3 or more consecutive ventricular beats (usually at a rate >100 bpm).
- Sustained VTach persists for >30 sec or requires an intervention for termination.
- VTach storm is 3 or more separate episodes of sustained VTach within 24 h requiring intervention.
- Nonsustained VTach is ≤6 consecutive beats terminating spontaneously within 30 sec.
- Possible signs of VTach include a wide QRS (>140 ms), presence of fusion beat, AV dissociation, and LBBB morphology.
- Must rule out SVT with aberrant conduction or preexisting bundle branch block.
- Torsades de pointes refers to VTach characterized by polymorphic QRS complexes that undulate in a regular fashion about baseline. Often associated with prolonged QT interval.

Etiology

- CAD: Acute myocardial ischemia or MI or old MI with left ventricular scar or aneurysm
- Cardiomyopathies, especially with ventricular dilation/enlargement
- Myocarditis
- Mechanical irritation (cath)
- Metabolic (hypokalemia, hypomagnesemia)
- Hypertrophic cardiomyopathy or mitral valve prolapse may present with VTach.
- Acquired polymorphic VTach (torsades) may result from electrolyte imbalances (K^+, Mg^{2+}) or drugs that prolong repolarization (phenothiazines, tricyclic antidepressants, class Ia antiarrhythmics, erythromycin, pentamidine, terfenadine, astemizole).
- Congenital QT prolongation may be assoc with left-sided cardiac sympathetic dominance.
- Rare association with right radical neck dissection.

Usual Treatment

- Removal or manipulation of intracardiac cath if pt hemodynamically stable.
- Chronic PO therapy: Ia: quinidine, procainamide, disopyramide; Ib: mexiletine, tocainide; Ic: propafenone; II: beta-blockers; III: amiodarone, sotalol.
- IV therapy includes amiodarone, procainamide, phenytoin, lidocaine, and bretylium (less commonly quinidine) as well as Mg^{2+} and/or K^+ when necessary. Amiodarone is superior to other agents.
- Digoxin antibodies for digitalis-induced VTach.
- Class I antiarrhythmics are generally contraindicated in presence of polymorphic VTach (torsades de pointes).
- Electrical cardioversion for VTach with hemodynamic instability.
- Nonpharmacologic management includes ablative techniques, myocardial revascularization, implantable cardioverter-defibrillators (recommended for recurrent VTach and structural heart disease with poor ventricular function), and left ventricular assist devices.
- IABP may be used to improve myocardial perfusion and hemodynamics.
- Treatment of torsades includes withdrawal of offending agent, correction of electrolyte abn (K^+, Mg^{2+}), and/or electrical defibrillation to terminate episode. Accelerating HR with isoproterenol or cardiac pacing may terminate rhythm. Empirical Mg^{2+} treatment may be lifesaving.
- Treatment of congenital QT prolongation, including beta-blockade to blunt sympathetic activity, Mg^{2+}, and/or left cervicothoracic sympathectomy.
- Treatment of VTach storm has involved sympathetic blockade with a thoracic epidural or a stellate ganglion block.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Myocardial ischemia Hypotension Cardiac arrest	Angina/anginal equivalent (syncope, SOB, palpitations, and exercise intolerance) CHF	Cardiomegaly, JVD Cannon A waves; S_3, S_4	ECG, CXR Electrophysiologic studies Ambulatory ECG
RESP	Pulm edema Amiodarone effects (fibrosis)	SOB	Rales (wet or dry)	CXR, PFTs (A-a)O_2 gradient
CNS	Syncope	Dizziness or LOC		

Key References: Amar D: Strategies for perioperative arrhythmias. *Best Pract Res Clin Anaesthesiol* 18(4):565–577, 2004; Mittnacht AJ, Dukkipati S, Mahajan A: Ventricular tachycardia ablation: a comprehensive review for anesthesiologists. *Anesth Analg* 120(4):737–748, 2015.

Perioperative Implications

Preoperative Preparation

- Ascertain etiology of VTach and associated problems.
- Evaluate for Hx of palpitations, SOB, VTach, dizziness, syncope, chest pain.
- Evaluate ECG for morphology of PVCs, QT interval, underlying BBB (important for Dx and therapy of wide complex tachycardia).
- Review electrophysiologic studies to determine optimal treatment of VTach.
- Assess K^+ and Mg^{2+} levels and digoxin level if indicated.
- Pulm and thyroid function tests may be indicated for chronic amiodarone therapy.
- Continue PO antiarrhythmic therapy.
- Have defibrillator immediately available (nearby) whenever inserting central venous cath.
- May need to have AICD deactivated for surgery to prevent firing with electrocautery use.

Monitoring

- ECG for ischemia or QT prolongation.
- Consider invasive hemodynamic monitor if suspicion of serious concomitant cardiac disease and major anesthetic/surgical intervention.

Anesthetic Considerations for VTach Ablation

- Typically occurs in non–operating room settings with limited support.
- The type of anesthetic may impact ability to induce VTach, especially catecholamine sensitive VTach. Sedation is preferred for shorter procedures.
- Paralysis may need to be avoided for phrenic nerve monitoring during procedure.
- Prolonged complex ablation procedures in pts with structural heart disease often are associated with significant volume expansion, electrolyte disturbances, lactate accumulation, and acute exacerbation of heart failure.

Induction/Maintenance

- Avoid myocardial ischemia (maintain O_2 supply and minimize O_2 demand).
- Minimize surgical stimulus response and subsequent catecholamine release.
- Avoid sympathomimetics, which may aggravate ventricular dysrhythmias.
- Avoid hypokalemia and excessive hyperventilation.

Postoperative Period

- Consider continuous arrhythmia monitoring.
- Continue parenteral antiarrhythmics until able to resume PO.
- Treat Mg^{2+} and K^+ deficits (common postop, especially after major surgical procedures).

Vitamin B_{12}/Folate Deficiency

Sharmil S. Gohil | Onyi Onuoha

Risk

- 5–10% of adults over the age of 65 have vitamin B_{12} or folate deficiency.
- Vitamin B_{12} (cobalamin) deficiency is associated with a strict vegan diet, pernicious anemia, gastrectomy procedures, exposure to nitrous oxide, HIV infection, *H. pylori* infection, certain medications, and ileal resections.
- Folate deficiency is associated with chronic alcoholism and malnutrition.

Perioperative Risks

- Intraop:
  - Increased risk of vitamin B_{12} deficiency after the exposure to nitrous oxide anesthesia due to the irreversible inhibition of vitamin B_{12} activity.
  - Homocysteine levels can be elevated after the use of nitrous oxide. The risk of coronary artery and cerebrovascular complications are increased in patients with high total plasma homocysteine levels.
- Postop:
  - Increased risk of postop MI.
  - Risk of neurologic symptoms including peripheral neuropathy, paresthesias, and subacute combined degeneration of spinal cord following nitrous oxide anesthesia.

Worry About

- Limited oxygen carrying capacity due to megaloblastic anemia caused by vitamin B_{12} and folate deficiency.

- Delayed onset of hematologic and neurologic abnormalities seen after nitrous oxide exposure; several wk may elapse before symptoms develop.

Overview

- Vitamin B_{12} and folate have interdependent and essential roles in DNA synthesis.
- Vitamin B_{12} is needed for
  - Synthesis of methionine from homocysteine via methionine synthase.
  - Conversion of methylmalonyl coenzyme A to succinyl coenzyme A via methylmalonyl-CoA mutase.
  - Development and myelination of the CNS and its maintenance.
- Folate has multiple metabolic roles including purine synthesis and amino acid metabolism.
- Deficiencies of vitamin B_{12} and folate lead to increased serum homocysteine levels, which is associated with cardiovascular disease.

Etiology

- Vitamin B_{12} deficiency is normally associated with inadequate absorption from the GI tract, as seen with
  - Pernicious anemia due to antibodies to gastric cells and the lack of intrinsic factor.
  - Gastrectomy and gastritis causing decreased gastric acid and the inability to liberate cobalamin from food.
  - Intestinal disorders and resections leading to malabsorption.
  - Medications such as proton pump inhibitors and H_2 receptor antagonists, which decrease gastric acid secretion and lead to an inability to liberate cobalamin from food.
- Folate deficiency is commonly associated with poor nutrition, alcoholism, goat's milk, and medications such as methotrexate and phenytoin.

Usual Treatment

- Daily oral supplements of folate and/or weekly IM injections of vitamin B_{12}. Vitamin B_{12} can also be given orally, sublingually, or via a nasal spray/gel; however, due to erratic absorption, these therapies should be considered after levels have normalized with parental vitamin B_{12} first.
- Folate treatment alone in individuals who are vitamin B_{12} deficient may produce partial hematologic remission but can result in irreversible neurologic symptoms. Therefore, if emergent therapy is indicated without a diagnosis, both folate and vitamin B_{12} should be supplemented simultaneously.
- Deficiencies associated with nitrous oxide exposure have been successfully treated with IM injections of vitamin B_{12}, IV administration of folinic acid, and oral methionine.

Assessment Points

System	Effect	Test
HEENT	Glossitis and painful tongue (infrequent)	
CV	Angina and DOE secondary to anemia Coronary artery disease secondary to increased homocysteine levels	ECG
GI	Anorexia, diarrhea	Schilling test for malabsorption of vitamin B_{12}
HEME	Megaloblastic anemia Thrombosis	Serum levels of vitamin B_{12} and folate. RBC folate considered better indicator of tissue folate levels than serum folate. ↑ Urinary levels of methylmalonic acid in vitamin B_{12} deficiency. Hematologic variables may be normal or abnormal. Anemia, increased mean corpuscular volume Increased serum levels of plasma homocysteine Hypersegmented neutrophils may be present Marked hyperhomocysteinemia
GU	Impotence	
CNS	Subacute combined degeneration of spinal cord Gait ataxia Romberg sign, memory deficits, psychosis	
PNS	Diminished vibratory sense, proprioception, and sensation; paresthesias, loss of deep tendon reflexes	

Key References: Badner NH, Freeman D, Spence JD: Preoperative oral B vitamins prevent nitrous oxide-induced postoperative plasma homocysteine increases. *Anesth Analg* 93(6):1507–1510, 2001; Nagele P, Zeugswetter B, Wiener C, et al: Influence of methylenetetrahydrofolate reductase gene polymorphisms on homocysteine concentrations after nitrous oxide anesthesia. *Anesthesiology* 109(1):36–43, 2008.

Perioperative Implications

Preoperative Preparation

- If elective procedure, postpone to correct vitamin deficiencies and hematologic and/or neurologic abnormalities.
- Preop vitamin therapy has been shown to prevent an increase in homocysteine levels after nitrous oxide anesthesia.

Monitoring

- Myocardial ischemia may occur with anemia and is associated with increased homocysteine levels.
- Basic monitoring should include measuring ECG (lead II and V5) for ischemia, pulse rate, pulse oximetry, and BP by noninvasive method. Consider direct intra-arterial BP monitoring in unstable pts.

Induction/Airway

- Large and painful tongue may be present. Hence, with the need for general anesthesia:
  - Tongue swelling may complicate optimal mask ventilation and intubation. An oral airway should be immediately available.
  - With the anticipation of a difficult intubation, consider the use of airway adjuncts (e.g., video laryngoscopy) or an awake/anesthetized fiberoptic endotracheal tube placement. A difficult airway cart should always be in close proximity.

Maintenance

- Avoid nitrous oxide if pt is known to be vitamin B_{12}/folate deficient and has hematologic and/or neurologic abnormalities.

Adjuvants

- Regional: Documentation of preexisting neurologic deficits is required before proceeding with regional anesthesia.

Postoperative Period

- Worsening of hematologic and neurologic abnormalities may not occur until several wk after nitrous oxide exposure.
- Monitor for postop myocardial infarction.

Anticipated Problems/Concerns

- Anemia may result in impaired oxygenation of tissues and be associated with myocardial ischemia.
- CNS and PNS symptoms may exist.
- Nitrous oxide may exacerbate preexisting hematologic/neurologic symptoms associated with vitamin B_{12} and/or folate deficiency.

Vitamin D Deficiency

Nancy C. Wilkes

Risk

- High prevalence of deficiency (much more than previously recognized).
- At risk: Dietary insufficiency, breastfed infants, inadequate sun exposure, elderly, nursing home residents, institutionalized, dark skinned individuals, obese, post gastric bypass, IBD.
- Genetically predisposed: Rickets, osteomalacia.

Worry About

- Hypocalcemia; vitamin D promotes calcium absorption in the gut and aids in maintenance of calcium and phosphorus levels. Without vitamin D, only 10–15% of dietary calcium and approx 60% of phosphorous is absorbed. Low total body magnesium is also likely.
- Calcitriol influences muscle function, CV homeostasis, and immune response.
- Deficiency associated with Htn, MI, CHF, and calcific aortic stenosis.
- Ample evidence to connect adequacy to risk and/or severity of certain cancers (colorectal, prostate, breast, leukemia) and autoimmune diseases (RA, MS, type 1 DM).
- Chronic vitamin D deficiency may lead to impaired mineralization of cervical spine (increased incidence of abn neck mobility). Pediatric pts with deformed chest wall may experience lowered FRC and increased incidence of respiratory infections.

Overview/Pharmacology

- Fat soluble vitamin and biologically inert. Amount obtained through food sources is minimal compared to that from sun exposure.
- There are two main forms. Vitamin D_3 (cholecalciferol) is synthesized in the skin by exposure to ultraviolet (UVB) radiation. Vitamin D_2 (ergocalciferol) is obtained through irradiation of ergosterol in plants and subsequent dietary intake.
- Intake involves two hydroxylations. Vitamins D_2 and D_3 are hydroxylated in the liver to 25 vitamin D (calcidiol), the major circulating form. Further hydroxylation in the kidney produces the active metabolite 1,25 vitamin D (calcitriol). Calcitriol is the physiologically active form.
- Involved in functioning of hemopoietic cells, skin cells, cancer cells of various origins, islet cells of the pancreas, immune response, as well as CV function (via serum Ca^{2+}).

Etiology

- Inadequate sun exposure, dietary insufficiency.
- There are two types of vitamin D-dependent rickets: Type I: Inherited autosomal recessive trait (defect in the 25OH-D_3 conversion into calciferol [true vitamin D]); type II: Autosomal dominant disorder, where single amino acid change in vitamin D receptor results in nonfunctional state.
- Osteomalacia is a metabolic disease with inadequate and/or delayed mineralization of osteoids in mature bone.

Usual Treatment

- Now recognized as an essential supplement for most adults, especially ages >50.
- Dose: Ages 1–70 recommendation, 600 IU/d in normal children/adults. Ages 71 and greater, 800 IU/d.
- Occurs in few food sources in nature. Fatty fish and fish liver oils are best source. Other sources in USA diet are from fortified foods such as milk, breakfast cereals, yogurt, and orange juice.
- Toxicity: Margin of safety is large. Prolonged intake of doses >40,000 IU/d promotes bone demineralization, leads to hypercalcemia, and enhances CV calcification.
- Prescribed for rickets, osteomalacia.
- Vitamin D insufficiency: Vitamin D 800–2000 IU/d + elemental calcium 1200 mg/d.
- Vitamin D deficiency: Elemental calcium 1200 mg/d plus ergocalciferol 50,000 IU/wk for 8–12 wk, then 2000 IU/d vitamin D_3.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS	Impaired mineralization Increased arthritis due to bone spur formation Osteomalacia Osteoporosis	Bone pain, fracture Joint pain Weak antigravity muscles	Dry, scaly skin Brittle nails Coarse hair Neck immobility Osteoarthritis	Bone density X-ray
CV	CHD CHF Irregular heart beat Orthostatic hypotension Htn Cardiac hypertrophy Vascular calcification Stroke	Angina Dyspnea Palpitations Fatigue	Auscultation	ECG BP Stress test Cardiac ECHO
CNS/PNS	NM irritability	Muscle stiffness, rigidity Numbness, paresthesias Muscle cramps Persistent, nonspecific musculoskeletal pain	Seizure, tetany	Calcium levels PTH (if severe)

Key References: Stechschulte S, Kirsner R, Federman D: Vitamin D: Bone and beyond, rationale and recommendations for supplementation. *Am J Med* 122(9):793–802, 2009; Akhtar S: Diseases of the endocrine system. In Fleisher LA editor: *Anesthesia and uncommon diseases,* ed 6, Philadelphia, PA, 2012, Elsevier, pp 406–408.

Perioperative Implications

Preoperative Preparation

- Both PTH and vit D_3 (calcitriol) work to keep the level of ionized Ca^{2+} within tight range (±0.1 mg/dL).
- Periop considerations are related to:
  - Level of ionized Ca^{2+} (regulation of muscle contraction)
  - Neurotransmitter release
  - Blood coagulation

Monitoring

- ECG changes: Compare to previous tracing. Prolonged QT interval (adjusted to R-R interval; 2:1 intraventricular heart block).
- Easy availability of blood sample for immediate serum calcium assessment (art catheter vs. vein stick).

Maintenance

- $ETCO_2$: Avoid hyperventilation (alkalosis shifts ionized Ca^{2+} into the cells). Acute hypocalcemia increases chance of tetany.
- Monitor/replete calcium, phosphate, and magnesium.

Extubation

- Laryngeal spasm on extubation in fully awake pt is also likely. Predictor may be distal extremity paresthesia.

Management

- Acute treatment (laryngospasm, seizure, tetany): Initial IV bolus 10–20 mL 10% calcium gluconate over 10 min followed by infusion over 6–24 h if needed.
- Monitor calcium, magnesium, phosphate, potassium, and creatinine.

Anticipated Problems/Concerns

- Chronic anticonvulsant Rx (phenobarbital/phenytoin) may lead to hypocalcemia (decreased Ca^{2+} absorption from the intestine) and diminished vitamin D biosynthesis in the liver.
- Vitamin D serum concentration is decreased when PTH is decreased (may occur with thiazide medications).
- Deficiency can be a result of deficient production of vitamin D in the skin, lack of dietary intake, impaired vitamin D activation, or resistance to the biological effects of calcitriol.
- Disorders of small bowel, hepatobiliary system, and pancreas (bile salt deficiency, pancreas insufficiency, poor intestinal absorption of fat-soluble vitamins [A, D, K, E]) may cause maldigestion and/or malabsorption.
- Liver disease can impact CRI/ESRD (GFR <25% of nml), with moderate to severe impairment of renal phase synthesis of vitamin D with reduction of serum albumin.
- Uremia, CRF, and nephritic syndrome suppress vitamin D action on gut.
- Nephrotic syndrome causes vitamin D deficiency related to chronic proteinuria (loss of circulating 25 vitamin D_3–binding globulin). Symptoms present are 2° hyperparathyroidism, low serum Ca^{2+}, osteomalacia.
- Vitamin D_3 (1,25 dihydroxycholecalciferol) directly facilitates Ca^{2+}, Mg^{2+}, and $(PO_4)^{3-}$ uptake by intestinal mucosa, their transport through intestinal cells and efflux.

Vitamin K Deficiency

Megan K. Werntz | Jeffrey R. Kirsch

Risk

- Vitamin K deficiency bleeding (VKDB) from abnormal factors II, VII, IX, and X.
- Controversy exists regarding whether vitamin K deficiency leads to osteoporosis, abnormal cartilage calcification, and possible arterial calcification resulting in CV disease.

Perioperative Risks

- Minor or massive hemorrhage unrecognized as VKDB
- Long-bone fractures during positioning the anesthetized pt (particularly in women)

Worry About

- Underlying risk factors demonstrating unexplained coagulopathy.
- Intracranial hemorrhage in infants (30–60% infants with VKDB) and other occult bleeding sites such as retroperitoneal hemorrhage (more commonly in infants).
- Avoid IM dosing of vitamin K if bleeding is present.
- Anaphylaxis with IV vitamin K replacement (extremely rare).

Overview

- Vitamin K is cofactor for a carboxylase enzyme in the liver, which is essential for normal function of factors II, VII, IV, X and proteins C, S, and Z.
- Coagulopathy manifests as prolonged PT and INR (normal or prolonged aPTT) with normal fibrinogen and factor 5 (both lowered in liver disease and DIC).
- Fat-soluble vitamin K is absorbed in the small bowel and colon and synthesized in gut by bacteria.
- Poor oral intake alone is not sufficient to cause vitamin K deficiency.
- Prevalence is extremely rare in adults with adequate nutrition. Prevalence is as high as 30% in pts with chronic GI disorders. It is more frequent in infancy with classic VKDB occurring in 0–1.5% despite routine prophylaxis.

Etiology

- Inadequate nutrition (often combined with antibiotic therapy)
- Malabsorption diseases (IBD, celiac, short bowel syndrome)
- Total parenteral nutrition
- Parenchymal liver diseases (vitamin K supplementation will not likely correct coagulopathy)
- Biliary diseases
- Drugs (coumadin, salicylates, rifampin, antibiotics, sulfa drugs)
- Hemorrhagic disease of newborn or VKDB
  - Early stage (<24 h): Drugs taken by mother during pregnancy and low placental vitamin K transfer
  - Classic (d 1–7): Inadequate formula intake or breastfeeding only
  - Late (wk to 6 mo): Breastfeeding only or malabsorption disease (most often cholestatic)

Usual Treatment

- Vitamin K can be administered orally, intramuscularly, or through IV, with both route and dosage depending on urgency and degree of coagulopathy.
- Massive bleeding should be treated promptly with FFP, prothrombin complex concentrate (PCC), anti-inhibitor coagulant complex (FEIBA NF), or factor VIIa along with IV administration of vitamin K (most sources recommend an adult dose of 10 mg IV and rarely more than 50 mg in first 6 h).
- Labs for PT, INR, aPTT, fibrinogen, and platelet count should be obtained in urgent situations to determine the etiology of bleeding.
- When vitamin K is administered through an IV, normalization of INR should be noted as soon as 30–120 min and no longer than 12 h. If no correction is noted or there is no improvement in bleeding within 24 h, an alternative etiology other than vitamin K deficiency must be suspected, such as liver dysfunction or DIC.
- In nonurgent settings of prolonged INR without bleeding, other tests available include serum vitamin K level or abnormal prothrombin level (most specific).
- Definitive diagnosis of vitamin K deficiency is made by correction of coagulopathy with vitamin K administration.
- For all routes of administration of vitamin K, sufficient serum vitamin K levels are present within 24 h to reverse coagulopathy in most cases.
- Consider vitamin K therapy in the setting of supratherapeutic warfarin:
  - In the setting of supratherapeutic warfarin therapy and no evidence of bleeding, if INR >9.0 omit next 1–2 warfarin doses and administer 2.5–5 mg oral vitamin K. Oral vitamin K should produce substantial reduction in INR within 24–48 h of administration.
  - For pts with an INR between 5–10 and no evidence of bleeding, provider should hold next warfarin dose and may or may not consider vitamin K administration, oral dose 1–2.5 mg.
  - For pts on warfarin therapy with serious bleeding, administration of 5–10 mg vitamin K IV (over 20–60 min) is appropriate without waiting for lab tests. IV vitamin K should be administered slowly to minimize risk of potential anaphylactic reaction.
  - For life-threatening bleeding in supratherapeutic warfarin pts, at any elevation of INR, or in warfarin-treated pts undergoing emergency surgery, provider should consider PCC, FFP, and/or possibly FEIBA NF. Four-factor prothrombin complex concentrate, or nonactivated PCC (Kcentra), contains the coagulation factors low in warfarin-treated pts including II, VII, IX, and X. PCC, unactivated, rather than FFP, is the recommended therapy by the American College of Chest Physicians. FFP may be considered if PCC is not available or pt is already requiring massive transfusion. Other antifibrinolytic agents may also be considered in this pt population, including tranexamic acid or epsilon-aminocaproic acid or DDAVP for suspected platelet dysfunction. Recombinant activated factor VII is not the recommended therapy for warfarin-associated bleeding, as it does not provide the other affected factors II, IX, and X.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEME	Insufficient hemostasis, mucosal bleeding, acute or chronic anemia	Bleeding diathesis	Easy bruising, epistaxis, ICH (infants), retroperitoneal bleeding (infants)	Coagulation profile includes PT/INR, aPTT, fibrinogen, Hct, plts
GI/RENAL	Mucosal bleeding, inadequate production of clotting factors, inadequate absorption of vitamins	Inadequate nutrition, parenchymal liver disease, cholestatic disease, malabsorption, bleeding diathesis	Hematuria, GI bleeding, weight loss, jaundice, pale stools, dark urine	Urinalysis, endoscopy
GYN	Mucosal bleeding	Bleeding diathesis	Vaginal bleeding	
METAB/ OTHER		Antibiotic therapy, coumadin, other drugs		

Key Reference: Merli GJ, Fink J: Vitamin K and thrombosis, *Vitam Horm* 78:265–279, 2008; Mansour J, Graf K, Lafferty P: Bleeding disorders in orthopedic surgery, *Orthopedics* 35:1053–1062, 2012.

Perioperative Implications

Preinduction/Induction/Maintenance

- Suspect vitamin K deficiency in pts with underlying risk factors and unexplained anemia, bruising/bleeding, or prolonged PT/INR.
- Providers should have low threshold to correct unexplained prolonged PT/INR with vitamin K supplementation periop. With no signs of bleeding or easy bruising, a 1-mg IV dose of vitamin K is reasonable.
- If VKDB is present, PRBCs and FFP should be available and IV vitamin K should be given concomitantly to promote synthesis of clotting factors. Prothrombin concentrate, though less readily available, is more effective than FFP due to higher concentrations of factors II, VII, IX, and X.
- Large-bore (16 gauge or larger in adults) IV access should be established prior to surgery to allow rapid volume resuscitation in the event of significant hemorrhage.

Monitoring

- Anesthetic monitors recommended depend on degree of coagulopathy and signs of bleeding. Consider Foley catheter and CVP to monitor for volume status, and invasive arterial pressure monitoring to assess beat-to-beat BP during hemorrhage.

General Anesthesia

- Significant coagulopathy can result in easy bleeding with venipuncture, surgical incision, line placement, and airway instrumentation.

Regional Anesthesia

- Prolonged PT and INR precludes neuraxial anesthetic secondary to risk of hematoma and subsequent neurologic injury.
- There is also risk of neuraxial hematoma in the setting of normal preop coagulation parameters in pts who develop vitamin K deficiency in periop period.
- Prolonged PT and INR may result in hematoma formation during plexus anesthesia.

Postoperative Period

- Common setting for unrecognized vitamin K deficient coagulopathy, given inadequate oral intake and aggressive antibiotic therapy.

Anticipated Problems/Concerns

- Oral vitamin K is often ineffective therapy in pts with GI disease or cholestatic disease.
- IV vitamin K should be administered in a diluent such as 0.9% isotonic sodium chloride and administered at a rate no faster than 1 mg/min to reduce the risk of an adverse reaction.
- FFP will only temporize VKDB unless a supplemental source of vitamin K is provided.
- Prolonged PT/INR related to liver disease often will not correct with vitamin K supplementation.

Von Hippel-Lindau Disease

David Hallsworth

Risk

- Rare; approximate incidence is 1:36,000.
- Usually occurs in young adults with complex multiple manifestations.

Perioperative Risks

- Pts with cerebral hemangioblastoma have a 23% incidence of VHLD; assess other systems carefully.

Worry About

- Space-occupying central nervous tumors (retinal and cerebellar hemangioblastomas in 60% of pts).
- Pheochromocytoma (7–20% pts) may be undiagnosed.
- Pregnancy and childbirth may dramatically change disease progression and symptom expression; multidisciplinary involvement essential.

Overview

- VHLD is a complex multisystem disorder, and pts frequently require anesthesia for surgical treatment of tumors and embolizations.
- Most common causes of death are renal cell carcinoma or complications from cerebral hemangioblastomas.

Etiology

- Autosomal dominant with variable expression, due to mutation of a tumor suppressor gene on chromosome 3p25–p26.
- The most common lesions are hemangioblastomas (benign vascular tumors) involving the retina, cerebellum, brainstem, spinal cord, adrenal glands, and kidneys. VHLD is also associated with pheochromocytoma, renal and pancreatic tumors, endolymphatic sac tumors of the middle ear, and papillary tumors of the broad ligament and epididymis.
- Type I pts are less likely to develop pheochromocytoma than type II.

Usual Treatment

- Surveillance and surgical management of tumors with or without radiotherapy.
- Manage active tumors and/or complications of treatment (e.g., pheochromocytoma, diabetes, steroid insufficiency, renal insufficiency).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Retinal hemangioblastomas Glaucoma Hearing loss	Visual loss, blindness	Ocular microscope and pressure testing	Fluorescein angiography
CV	Erythrocytosis	History of venous thromboembolism		Full blood count
RESP	Cystic lung tumor	Chest pain, hemoptysis		CXR, CT
GI	Pancreatic cysts	Abdominal discomfort		US/CT
RENAL	Renal tumors and/or previous nephrectomy			Blood lytes and renal function tests Renal US/CT
ENDO	Pheochromocytoma Adrenal insufficiency due to adrenal resection Diabetes (due to previous pituitary surgery)		Complications of diabetes BP	Urinary catecholamines Plasma metanephrines/normetanephrines, adrenal imaging
CNS	Cerebellar hemangioblastoma Spinal cord hemangioblastoma	Headache, nausea, visual disturbance, motor and sensory deficit	Neurologic examination Ocular signs of raised ICP	CT brain MRI spine
PNS	Nerve root lesions are very rare			
MS	Limb weakness due to CNS tumors		Neurologic examination	

Key References: Plon SE, Jonasch E: Clinical features, diagnosis, and management of von Hippel-Lindau disease. In *UpToDate*, Atkins MB, Firth HV, Perrone RD, et al, editors: *UpToDate*, Waltham, MA (Accessed June 20, 2016); Hallsworth D, Thompson J, Wilkinson D, et al: Intracranial pressure monitoring and caesarean section in a patient with von Hippel-Lindau disease and symptomatic cerebellar hemangioblastomas. *Int J Obstet Anesth* 24(1):73–77, 2015.

Perioperative Implications

Monitoring

- Full invasive monitoring if pheochromocytoma is present or suspected.
- Consider ICP pressure monitoring if pt is symptomatic.

Induction

- Spinal and epidural anesthesia are relatively contraindicated if CNS/spinal tumors are present; discuss with neurosurgeons.

Maintenance

- TIVA has theoretical advantages on cerebral circulation and ICP if cerebral tumors present.

Adjuvants

- Intraop control of blood sugar

Postoperative Period

- May require HDU if complex comorbidity

Anticipated Problems/Concerns

- Surgery for one problem often complicated by other manifestations of the disease

Von Willebrand Disease

Thomas M. McLoughlin Jr.

Risk

- Most common inherited bleeding disorder.
- >1 million people within USA; 1% carry the gene (severe disease 1:10,000-1,000,000).
- No race/gender with highest prevalence.

Perioperative Risks

- Significant risk of bleeding if untreated
- Increased risk if hepatic dysfunction present

Worry About

- Excessive periop hemorrhage
- Concurrent antiplatelet agents or NSAIDs contributing to bleeding
- Adverse reactions to desmopressin therapy (seizures due to hyponatremia, hypotension, anaphylaxis)

Overview

- Coagulopathy is characterized by quantitative/qualitative alterations in vWF. vWF acts as a bridge between plts and vascular subendothelium and stabilizes Factor VIII to prolong its circulating half-life.
- Presents as defect in primary hemostasis—mucocutaneous hemorrhage.
- Marked by highly variable severity; family Hx is very helpful in predicting severity.
- Diagnosed by prolonged aPTT, Factor VIII antigen and activity levels, vWF antigen, and Ristocetin aggregation studies. Many disease subtypes can be further classified by band pattern of radiolabeled vWF after gel electrophoresis (multimeric analysis).
- Type I: Quantitative decrease in vWF of all sizes (most common, 70–80% of cases). Type II: Quantitative/qualitative alterations primarily in largest molecular weight vWF multimers; many subtypes exist (20–30% of cases). Type IIB: May be accompanied by thrombocytopenia. Type III: Marked by severe quantitative reductions or absence of vWF (rare, secondary to homozygous inheritance).

Etiology

- Autosomal dominant trait; variable penetrance and expression lead to unpredictable clinical severity; most severe disease occurs in homozygotes.
- Acquired disorder (von Willebrand syndrome) can be associated with autoimmune disease, neoplasm, myeloproliferative or lymphoproliferative disorders, hypothyroidism, or circulatory destruction of large vWF multimers through shear stress (valvular or vascular stenoses, extracorporeal circulatory devices).

Usual Treatment

- Disease subtype must be determined prior to therapy.
- DDAVP, 0.3 μg/kg IV, stimulates release of endothelial vWF; variably effective in types I and II disease; first-line treatment in acquired von Willebrand syndrome (possible accelerated clearance in these pts, however).
- Intranasal desmopressin is used, but response is more variable.
- Desmopressin contraindicated in type IIB.
- Pasteurized pooled factor VIII concentrates that preserve vWF (Humate-P) and solvent detergent heat-treated pooled concentrates (Alphanate) are mainstays of therapy.
- Recombinant vWFs are not currently available in USA; agents are in Phase III trial in 2015.
- Cryoprecipitate is best alternative if concentrates are unavailable.
- Antifibrinolytics often useful adjuncts.

Assessment Points

System	Effect	Assessment by Hx	Test
HEENT	Mucocutaneous bleeding	Epistaxis	
GI	GI bleeding	Melena, hematochezia	Stool guaiac
HEPAT	Requirement for transfusion therapy	Random donor exposures	LFTs, hepatitis panel
HEME	Coagulopathy, principal defect in primary hemostasis	Easy bruising, menorrhagia, epistaxis, patient or family experience during prior surgery or hemostatic challenge (e.g., dental extraction) vital to assessing periop risk, given variable severity of disease among individuals	PT, PTT, plt count often normal; plt function assay; quantitative vWF antigen; ristocetin cofactor activity; multimeric analysis

Key References: Mensah PK, Gooding R: Surgery in patients with inherited bleeding disorders, *Anaesthesia* 70(Suppl 1):S112–S120, 2015; Stone ME, Mazzeffi M, Derham J, Korshin A: Current management of von Willebrand disease and von Willebrand syndrome, *Curr Opin Anesthesiol* 27(3):353–358, 2014.

Perioperative Implications

Preoperative Preparation

- Collaborate with consultant hematologist and blood bank.
- Desmopressin 1 h preop in all but IIB subtype.
- Antifibrinolytics for dental procedures.

Monitoring

- Bleeding time/vWF activity periodically in prolonged procedures; $T_{1/2}$ of administered vWF is about 8–12 h.
- Target vWF factor levels:
  - Major surgery: 100 IU/dL vWF preop, trough levels 50 IU/dL through POD 7–10
  - Minor surgery: 50 IU/dL vWF preop, trough levels 30 IU/dL through POD 3–5
  - Dental extractions: 60 IU/dL pre-procedure (single level)
  - Peripartum: 50–80 IU/dL predelivery, trough levels 30 IU/dL through postdelivery d 3–5
  - Avoid levels of 200 IU/dL or greater to reduce periop thrombosis risk

Airway

- Laryngoscopy can lead to tissue trauma.
- Nasotracheal route best avoided.

Induction

- No specific recommendations

Maintenance

- Meticulous surgical hemostasis.

Extubation

- Avoid coughing if possible; gentle orotracheal suction best performed under direct vision.

Adjuvants

- Consider RA with caution; no epidural hematoma from neuraxial technique has been reported when diagnosis of vWD known in advance.
- Repeat desmopressin doses likely to be less effective than initial; reaccumulation of endothelial stores takes time.

Anticipated Problems/Concerns

- Excessive intraop and postop blood loss
- Increased likelihood of infectious bloodborne disease

Waldenström Macroglobulinemia

Amy C. Robertson

Risk

- Rare hematologic neoplasm (accounts for 1–2% of hematologic malignancies).
- In USA, age-adjusted incidence of 5.7 per million among males and 2.7 per million among females. Median age at diagnosis is 73 y.
- Racial preponderance: Whites >African Americans (4.1 vs. 1.8 million).
- 10-y survival rate is 66%.
- Factors associated with worse prognosis: age >65 y, hemoglobin <11.5 g/dL, platelet count <100,000, B_2-microglobulin >3 mg/L, and monoclonal IgM >7 g/dL.

Perioperative Risks

- Consequences of hyperviscosity
- Anemia and coagulopathy

Worry About

- Anemia
- Coagulopathy
- Hyperviscosity
- Hypervolemia
- Hepatomegaly (20%)
- Splenomegaly (15%)
- Lymphadenopathy (15%)
- Peripheral neuropathy: Most common neurologic complication; may be seen in up to half of all pts.
- Primary systemic amyloidosis is a rare complication.

Overview

- Uncommon lymphoplasmacytic lymphoma associated with monoclonal IgM protein.
- Diagnosis: Presence of IgM monoclonal protein is associated with >10% clonal lymphoplasmacytic cells in bone marrow.
- Symptoms attributable to tumor infiltration and/or excessive IgM production.

- Most common presenting symptom is fatigue related to anemia.
- Anemia can be caused by combination of factors: Decrease in red cell survival, impaired erythropoiesis, hemolysis, plasma volume expansion, and blood loss from GI tract.
- Potentially severe adverse neurologic, hematologic, and CV problems periop.
- Anesthetic concerns similar to those in multiple myeloma, except that hypercalcemia and bone lesions are rare; renal failure and proteinuria less common.

Etiology

- Familial clustering: First-degree relatives of pts with WM have a 20-fold increased risk of WM.
- L265P mutation in myeloid differentiation primary response 88 gene (*MYD88*) is detectable in more than 90% of pts.
- Role of environmental factors remains to be clarified.

Usual Treatment

- Alkylating agents (chlorambucil, cyclophosphamide), purine analogues (cladribine, fludarabine), monoclonal antibody (rituximab), and dexamethasone
- Stem cell transplantation
- Plasma exchange to treat hyperviscosity symptoms

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hyperviscosity (high output cardiac failure, valvular dysfunction, MI)	Angina Dyspnea Fatigue	Venous thrombosis Fluid overload	Serum viscosity >4 g/dL
RESP	Pulm involvement	Dyspnea	Hypoxia	CXR (pleural effusion, diffuse pulm infiltrates)
HEME	Coagulopathy (multifactorial)	Episodic epistaxis, mucosal and gum bleeding		Coagulation studies
	Anemia (multifactorial)	Fatigue	Pallor	CBC (normocytic, normochromic anemia)
	Cryoglobulinemia	Cold intolerance Raynaud syndrome Arthralgia	Purpura	Cryoglobulin assay
	Lymph node involvement		Lymphadenopathy	
RENAL	Glomerulonephritis	Dehydration Uremic symptoms		BUN/Cr UA (proteinuria)
CNS	Leukoencephalopathy Abn cerebrovascular permeability (hyperviscosity)	Headaches Blurred vision	Mental status changes Retinal hemorrhage, papilledema	
PNS	Demyelinating peripheral neuropathy		Symmetric, distal sensorimotor neuropathy, ataxic gait	
GI	Organomegaly secondary to IgM infiltration		Hepatomegaly Splenomegaly	

Key References: Gertz MA: Waldenström macroglobulinemia: 2015 update on diagnosis, risk stratification, and management, *Am J Hematol* 90(4):347–354, 2015; Leff J, Shore-Lesserson L, Fischer GW: Hematologic diseases. In Fleisher LA, editor: *Anesthesia and uncommon diseases,* ed 6, Philadelphia, PA, 2012, Elsevier, pp 350–358.

Perioperative Implications

Preinduction/Induction/Maintenance

- Consider plasmapheresis and transfusion.
- All drugs: Theoretical unpredictable pharmacokinetics due to alterations of relative proportions of globulins in blood and expanded plasma volume.
- Judicious fluid management.

Monitoring

- Normothermia to prevent cryoglobulin precipitation.

General Anesthesia

- Macroglossia if amyloidosis (rare).

Regional Anesthesia

- Relative contraindication in presence of peripheral neuropathy.

Postoperative Period

- Transient postop paresis due to disease rather than anesthetic management.

Anticipated Problems/Concerns

- Hyperviscosity symptoms (<15% of pts; rare in pts with IgM concentration <4 g/dL):
  - Symptoms are due primarily to shear forces of excessive IgM that rupture venous channels.
  - Capillary blood flow impaired, leading to decreased O_2 delivery through microcirculation and tissue ischemia.
  - Epistaxis, gingival bleeding, and visual changes due to retinal hemorrhage are common presenting manifestations.
  - Severe cases of hyperviscosity syndrome may be associated with confusion, dementia, stroke, and coma.
  - CV manifestations secondary to expanded plasma volume include angina, high output cardiac failure, valvular dysfunction, or MI.
  - Plasma exchange is the fastest, most effective method to reduce plasma viscosity. Should be considered a temporizing measure until systemic therapy reduces IgM protein concentration.
- Anemia:
  - Hgb value may be artificially reduced by 2 g/dL secondary to increased plasma volume.
  - Transfusion may precipitate CHF or hyperviscosity syndrome (by increasing serum viscosity) and potentially decrease O_2 delivery.
  - Consider plasmapheresis before transfusion.
- Coagulopathy
- Cryoglobulinemia (5% risk):
  - Precipitation of cryoglobulins at cold blood temp triggers complement activation, which results in immune complex vasculitis and ischemia.
  - Raynaud syndrome, arthralgia, purpura, peripheral neuropathy, hepatic dysfunction, and renal failure may develop.

Wegener Granulomatosis (Granulomatosis With Polyangiitis)

Christopher J. Cullom | Alan David Kaye

Risk

- Prevalence of 3:100,000 persons affected
- More common in the white race; however, no gender affinity
- Respiratory failure
- Upper airway compromise
- Cardiovascular instability
- Acute renal failure
- Peripheral neuropathy
- Bleeding disorder

Perioperative Risks

- Medication toxicity, side effects, and interactions
- Systemic involvement, primarily respiratory, cardiovascular, and renal systems
- Airway compromise

Overview

- Systemic vasculitis of small, medium, and occasionally large arteries
- Characterized by necrotizing granulomatosis of upper and lower respiratory tracts in addition to glomerulonephritis

Etiology

- Autoimmune disorder of unknown etiology.
- Type II hypersensitivity reaction.
- May involve lack of alpha-1 antitrypsin.
- Antineutrophilic cytoplasmic antibodies are involved.
- Symptoms include
  - Upper airway involvement in 95% of pts, including paranasal sinus drainage and nasal mucosa ulceration.
  - Subglottic stenosis present in 9–16% of pts.
  - Pulm involvement manifests as cavitating granulomatous lesions.
  - Pulm arterial/venous vasculitis creates V/Q mismatch and pulm shunting.
  - Lower resp tract findings also may be present including cough, dyspnea, and hemoptysis.
  - CXR may reveal alveolar opacities, diffuse hazy opacities, nodules, and pleural opacities.
  - 77% of pts manifest with renal failure.
  - Eye involvement in 52% of pts including conjunctivitis, scleritis, keratitis, uveitis, and episcleritis.
  - Skin symptoms include papules, vesicles, purpura, ulcers, and nodules occurring in 40% of pts.
  - Nonspecific symptoms include night sweats, malaise, fatigue, arthralgias, anorexia, and weight loss.
- Diagnosis:
  - Biopsy of nasopharyngeal lesion preferred, showing necrotizing granulomatous vasculitis
  - Biopsy of kidney or lung showing segmental necrotizing glomerulonephritis with no immunoglobulin deposition
  - Elevated ESR, leukocytosis, normocytic anemia, and thrombocytosis

Usual Treatment

- Cyclophosphamide combined with oral glucocorticoid.
- Complete remission may take 1–2 y.
- 90% of pts achieve improvement, and 75% have remission.
- 50% of pts in remission have relapse.
- Morbidity from disease includes renal insufficiency, hearing loss, tracheal stenosis, and saddle nose deformity.
- Drug considerations:
  - Glucocorticoid side effects include diabetes, cataracts, osteoporosis, and Cushingoid features.
  - Cyclophosphamide side effects include cystitis, bladder cancer, myelodysplasia, and infertility.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	MI PVD	H/o ischemic heart disease		ECG
RESP	Destructive lesions of epiglottis, pharynx, or larynx V/Q mismatch and pulm shunting, destructive lesions pulm parenchyma		SOB, cough, hemoptysis, pleuritic CP, upper airway ulcerations	PFTs, CXR, ABG
RENAL	Glomerular destruction and tubular atrophy	Caution with drugs dependent on renal excretion		Renal function panel, renal biopsy, urinalysis
HEME	Bleeding propensity	CH/o cyclophosphamide or methotrexate treatment	Petechiae, bleeding gums	CBC, clotting studies
OPHTH	Vision loss, keratitis, scleritis, conjunctivitis, uveitis		Ophthalmic exam	Visual acuity test
ENT	Nasal mucosal ulceration or obstruction	Nasal discharge or drainage, epistaxis, hyposmia, epiphora	Upper airway exam	Nasal biopsy
NEURO	Peripheral neuropathy		Peripheral neuro sensory exam	
DERM	Ulceration distal arms/legs			Skin biopsy

Key References: Rookard P, Hechtman J, Baluch AR, et al.: Wegener's granulomatosis, *Middle East J Anaesthesiol* 20(1):21–29, 2009; Kahn AM, Elahi F, Hashmi SR, et al.: Wegener's granulomatosis: a rare, chronic, and multisystem disease, *Surgeon* 4(1):45–52, 2006.

Perioperative Implications

Preoperative Preparation

- Upper airway assessment to identify ulcerations or obstructing lesions, CXR, and PFTs.
- Screen for symptoms including cough, dyspnea, hemoptysis, or pleuritic chest pain.
- Consider RA when possible, but be aware that pts may have peripheral neuropathy and coagulation disorders that may add risk to the procedure.

Intraoperative Considerations

- Upper airway considerations should include careful physical inspection using laryngoscopy for ulcers of the palate, pharynx, or epiglottis. Care should be taken during intubation to avoid bleeding or displacement of brittle tissue. May consider regional anesthesia to avoid airway manipulation.
- Respiratory considerations include increased dead space and V-Q mismatch due to pulmonary artery and vein vasculitis. Bronchial obstruction and destruction may occur; thus frequent suctioning may be required. Monitoring of ABG ensures adequate oxygenation.
- Cardiovascular considerations include increased risk of MI due to not only peripheral but also coronary vasculitis as well. Avoid situations of increased preload, afterload, heart rate, or coronary spasm.
- Pts on corticosteroid therapy should be given 100 mg hydrocortisone prior to surgery to avoid Addisonian hypotensive crisis.
- Renal considerations include avoidance of anesthetics that require renal excretion such as morphine, meperidine, diazepam, midazolam, vecuronium, pancuronium, and nitroprusside.
- Cyclophosphamide inhibits pseudocholinesterase, which prolongs the activity of succinylcholine, thus warranting consideration when determining paralytic drug choice.

Postoperative Period

- Close observation of the upper airway following extubation should be performed, as edematous granulation tissue from intubation is possible.

Wilms Tumor

Peter J. Davis

Risk

- Most common malignant renal tumor in childhood.
- Accounts for 6% of all childhood malignancies.
- 5-7.8 cases per million children <15 y old in the USA.
- Prevalence: Males equal to females.
- Peak age is 1–3 y.
- 5% bilateral.
- Relapse-free survival rate at 2 y: 90%.
- Pts with favorable staging have an 80–90% chance of cure. Pts with metastasis have 50% long-term survival.
- Overexpression of HER-2 oncoprotein is a good predictor of survival.
- Along with hepatoblastoma, more common in Beckwith-Wiedemann syndrome.

Perioperative Risks

- Increased intraabdominal pressure
- Immunocompromised
- Tumor extension into renal vein, IVC, and heart
- Some treated with chemotherapy prior to surgery
- Associated Htn
- Acquired Von Willebrand syndrome, 10%

Worry About

- Anomalies:
  - Aniridia 1%, hemihypertrophy 2%
  - Neurofibromatosis
  - Beckwith-Wiedemann syndrome
  - GU abnormalities, horseshoe-shaped kidney, cryptorchidism, gonadal dysgenesis, hypospadias, duplication of collecting systems
- Metastatic disease: Lymph nodes, lung, liver, brain

Overview

- Most common abdominal tumor of childhood; prognosis related to staging.
- Because of the location of the tumor, blood loss can be significant.
- Tumor is also associated with other congenital abnormalities, which may affect anesthetic and/or surgical management.
- Tumor extension into IVC and heart carries increased morbidity and mortality.

Etiology

- Embryonal neoplasm
- No consistent chromosome abn, although abnormalities in chromosomes 1 and 11 are common.
- Three genes associated with Wilms:
  - 11p13 interstitial deletion associated with Wilms-aniridia-growth retardation
  - 11p15.5 deletion associated with Beckwith-Wiedemann syndrome
  - Third locus not determined to be associated with familial Wilms

Usual Treatment

- Chemotherapy (with vincristine, actinomycin D, and adriamycin).
- Radiotherapy.
- Surgical removal of tumor: If tumor bilateral, surgery has focused on nephron-sparing procedures. (Procedure including biopsy followed by chemotherapy and delayed definitive resection.)
- Open or laparoscopic procedure.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Beckwith-Wiedemann syndrome	Obstructive airway secondary to large tongue	Direct exam	Blood glucose levels
CV	Htn Tumor extension into heart	Asymptomatic	Htn	ECG CT abdomen US renal vein/IVC Cardiac ECHO
RESP	Resp compromise	Abdominal distentions Metastatic disease Tumor embolization	Increased RR Hypoxemia	Pulse oximetry CT abdomen US renal vein/IVC Possible cardiac ECHO
GI	Gastric reflux	Increased intraop pressure Hx of reflux	Abdominal distention	Review CT scan
HEME	Von Willebrand syndrome	Unusual bleeding		Bleeding time Ristocetin platelet aggregation

Key References: Whyte SD, Mark Ansermino J: Anesthetic considerations in the management of Wilms' tumor, *Paediatr Anaesth* 16(5):504–513, 2006; Green DM: The evolution of treatment for Wilms tumor, *J Pediatr Surg* 48(1):14–19, 2013.

Perioperative Implications

Preoperative Preparation

- Htn-controlled.
- R/O renal vein and/or IVC tumor involvement.
- Evaluate for bleeding disorder.
- Evaluate cardiovascular function if prior chemotherapy Rx.

Monitoring

- Arterial cath may be indicated.
- CVP cath may be needed. especially if IVC and tumor extend mid-heart.
- For preexisting hematuria, Foley cath can aid in fluid balance.
- IV catheters above diaphragm; large-bore cath preferable.
- $ETCO_2$ to rule out air and/or tumor embolus.

Airway

- May be a problem if Beckwith-Wiedemann syndrome is present.

Preinduction/Induction

- Age-appropriate use of sedation.
- Rapid-sequence if increased intraabdominal pressure.
- Regional anesthesia; epidural or paravertebral block for postop pain.
- Preexisting chemotherapy may have cardiac depressant effect.
- IV access above diaphragm.

Maintenance

- Requires a prolonged procedure.
- Avoid N_2O.
- Maintain temperature.
- Increased third space fluid requirements.
- Procedure may be associated with large blood loss.
- Pulm function may be compromised, secondary to metastasis and/or tumor embolization, abdominal distention, and/or surgical traction.

Extubation

- Expected if temp maintained and pt hemodynamically stable.

Postoperative Period

- Administer pain control:
  - Multimodal anesthetic
  - RA (epidural or paravertebral)
- Third space fluid requirements.
- Htn may still be present.

Anticipated Problems/Concerns

- Risk of tumor and/or air embolus: If tumor extends into renal vein, IVC may have to be cross-clamped, the IVC opened, and the tumor removed.
- Intraop blood loss can be extensive.
- Periop implications.

Wilson Disease

Cobin D. Soelberg

Risk

- Incidence: 1:30,000.
- Slightly more common among Eastern European Jewish populations.
- Children and young adults tend to present with nonspecific GI symptoms.
- Adults tend to present with neurologic symptoms.

Perioperative Risks

- Increased risk of liver failure, kidney failure, and cardiac complications.
- 6–12% of all pts require liver transplantation.

Overview

- Presentation can vary widely. Hepatic symptoms tend to present prior to neurologic symptoms.
- Often nonspecific symptoms such as abdominal pain, nausea, and vomiting may occur. Rarely presents with acute liver failure.
- More commonly presents with elevated transaminases, hepatomegaly or hepatosplenomegaly, or mild jaundice.
- Can be diagnosed by presence of Kayser-Fleischer rings and low serum ceruloplasmin levels. In the absence of Kayser-Fleischer rings, diagnosis is more difficult, relying on free copper and liver copper concentrations.

Etiology

- Autosomal recessive.
- In the liver, copper is not passed to ceruloplasmin and so the liver has an excess of copper. Once this excess exceeds the ability of the liver to hold it, it is released in its free form into the blood. It then accumulates in tissues and causes damage.
- Copper balance is regulated through excretion of bile.
- Copper accummulation leads to hepatic cirrhosis
- Lenticular degeneration.

Usual Treatment

- D-penicillamine, an oral chelating agent
- Trientine in pts with adverse reactions to penicillamine
- Liver transplantation in rare cases of fulminant liver failure

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Tremor, muscular rigidity, dysarthria, apraxia	Medication history, difficulty ambulating, talking	Focused neuro exam looking for strength/rigidity	
CV	Early: LV thickening, SVTs Late: Hyperdynamic state—high CO, low SVR	SOB, chest pressure/flutter	Auscultate, pronounced LLSB	ECG; TTE if indicated by clinical symptoms
RESP	Pulm shunting 2/2 high portal pressures Hepatopulmonary syndrome in severe cases	SOB, hypoxia	Auscultate	CXR, PFTs
HEME	Anemia, thrombocytopenia	Decreased Hct	Signs of bruising, petechiae	CBC, PT/INR
GI	Esophageal varices, ascites, hepatomegaly/splenomegaly	Upper GI bleeding, paracentesis, abdominal fullness	Abdominal pain, hepatomegaly, splenomegaly	Lytes, liver enzymes
RENAL	Renal failure, can be acute or chronic	Oliguria	Decrease in UOP	Lytes; rarely need kidney biopsy

Key References: Baykal M, Karapolat S: Anesthetic management of a pediatric patient with Wilson's disease. *J Clin Med Res* 2(2):99–101, 2010; Vaja R, McNicol L, et al: Anaesthesia for patients with liver disease. *Contin Edu Anaesth Crit Care Pain* 10(1):15–19, 2010.

Perioperative Implications

Monitoring

- Standard ASA monitors.
- Recommend arterial line and central line in fulminant liver disease.
- Also consider TEE or PA catheter.

Induction

- Decreased doses of hypnotic agents 2/2 cardiac function and neurologic disease.
- Vecuronium/rocuronium have prolonged elimination.
- Cisatracurium does not rely on hepatic metabolism.

Maintenance

- Isoflurane, sevoflurane, and desflurane undergo minimal hepatic metabolism.
- Morphine metabolism can be delayed 2/2 decreased hepatic blood flow, and its active metabolite, morphine-6-glucuronide, will accumulate 2/2 renal failure.

Postoperative Period

- Rare concerns for respiratory failure 2/2 ascites.
- Avoid dopaminergic drugs (i.e., droperidol, metoclopramide).

Anticipated Problems/Concerns

- Remember: Anything you would be concerned about for ESLD can be seen in Wilson disease.
- Assess neurologic and cardiac status. Let the severity of symptoms guide your periop plan.

Wolff-Parkinson-White Syndrome

Sara K. Davis | Jeffrey R. Kirsch

Risk

- WPW pattern (asymptomatic) prevalence: 0.15–0.25% in the general population and 0.55% in pts with a primary relative with WPW; autosomal dominant trait.
- WPW syndrome (ECG pattern and arrhythmia) prevalence is 0.005% to 0.07% in the general population and approximately 2% out of pts with WPW. It is often first presented in ages 20–40 y.

Overview

- Definition: WPW syndrome is a preexcitation syndrome. Ventricular depolarization occurs in part via an AP from the atrium (bundle of Kent) bypassing the AV-His Purkinje conduction system.
- The AP allows for antegrade or retrograde conduction which is faster than the AV node resulting in a shortened PR interval (<0.12 sec). The impulse then spreads through the muscle fibers until it joins the regular conduction system resulting in a slurred upstroke and widening of the QRS complex on the ECG.
- PSVT results from a reentrant circuit involving the AV node and AP. The QRS complex during PSVT matches the usual QRS morphology when conduction is antegrade through the AV system and retrograde through the AP (i.e., orthodromic). 5–10% of the time, conduction through the AP is antegrade (i.e., antidromic in the reentrant circuit), producing a wide QRS complex. This rhythm may be confused with VTach.
- AFIB and/or AFLT is more common in pts with WPW. Usually, AFIB is precipitated by an episode of PSVT. Rapid (≥300 bpm) ventricular rates may occur in pts with APs with short refractory periods. These pts are at risk for developing Vfib and hemodynamic collapse.
- Other heart abnormalities (e.g., Ebstein's anomaly) are often commonly (7–20%) associated with WPW.

Perioperative Risks

- AVRT (80% of pts WPW syndrome): Rapid HR impairs LV filling, leading to hemodynamic instability and/or myocardial ischemia.
- AFIB (15–35%); increasing incidence with age. A major concern is rapid ventricular response due to antegrade conduction over AP.
- Atrial flutter (5%).
- VFIB/sudden death (0–0.4%): Out of rapid ventricular response due to antegrade conduction over AP in AFIB/AVRT.

Usual Therapy

- With severe hemodynamic compromise, synchronized DC cardioversion (50–100 J).
- AVRT and/or narrow complex tachycardia: Apply vagal maneuvers or IV adenosine (6–12 mg IV). A small incidence of induction of AFIB with adenosine therapy for PSVT in WPW has been described.
- AFIB: Agents that reduce the accessory bundle refractory period (digoxin, Ca^{2+}-channel blockers, beta-blockers, and adenosine) increase the risk of causing VFIB and hemodynamic collapse in pts with WPW and AFIB and should therefore be avoided.
- Broad complex tachycardia (i.e., antidromic AVRT) should be treated with IV procainamide or amiodarone.

Assessment Points

ECG Criteria	P Wave and PR Interval	QRS	Comments
Classic (type A)	Shortened PR interval, typically <0.12 s (left-sided bypass track)	Slurred upstroke (delta wave), widened QRS complex	The faster the AP conduction, the more prominent the delta wave and the wider the QRS
Atypical (type B)	Shortened PR interval (right-sided bypass track)	Q waves (inverted delta wave) in V1	May be confused with MI
Concertina effect	Periodically progressive shortening of the PR interval, with the P wave disappearing in QRS	The shorter the PR interval, the more pronounced is the delta wave (wider QRS)	This is the result from a periodically increased conduction via the AP
Intermittent WPW	May be mistaken for frequent ventricular premature beats, if it persists for several beats may be held for accelerated idioventricular rhythm		

Key References: Wheeler DW, Sayeed RA, Ritchie AJ: Unsuspected Wolff-Parkinson-White syndrome causing arrhythmias after cardiac surgery, *J Cardiothorac Vasc Anesth* 16(3):354–356, 2002; Bengali R, Wellens HJ, Jiang Y: Perioperative management of the Wolff-Parkinson-White syndrome, *J Cardiothorac Vasc Anesth* 28:1375-1386, 2014.

Perioperative Implications

Preoperative Preparation

- If preexcitation on ECG or Hx of WPW, consider cardiology evaluation.
- If symptomatic, consider electrophysiologic study and catheter ablation.
- Continue all preop cardiac and anti-arrhythmic medications.

Monitoring

- ECG for detection of periop PSVT or AFIB.
- Consider arterial line and CVP catheter if LV dysfunction or valve disease, as these pts have a high dependence on preload and atrial kick.
- For emergency surgery, consider placement of defibrillator pads prior to induction.

Maintenance

- Consider RA techniques to avoid sympathetic stimulation.
- Avoid laryngoscopy and non-depolarizing muscle relaxants if possible to avoid reversal agents and neostigmine, which can facilitate transmission via an accessory pathway. Use LMAs when indicated.
- Avoid light planes of anesthesia, anxiety, hypovolemia, hypothermia, hyperventilation, which can all increase sympathetic tone that may decrease the refractory period and therefore accelerate the conduction in the AP and AV node. This may facilitate the precipitation of AVRNT, AFIB, and/or VFIB.
- Volatile anesthetics and IV induction agents such as propofol and benzodiazepines seem to have no influence on the conduction system and are safe to use. Sevoflurane and isoflurane as well as medications that enhance vagal tone (e.g., opioids, dexmedetomidine) actually decrease conduction via the AP and are safe to use as well.
- Limit the use of vagolytic agents (e.g., glycopyrrolate, atropine) and ketamine.
- Use α-1 agonists (phenylephrine) instead of ephedrine to avoid positive chronotropy and arrhythmias.

Postoperative Period

- Implement pain management to avoid catecholamine excess.
- If the delta wave appears in periop period, rule out myocardial infarction (decreased AV conduction second to ischemia facilitating increasing AP conduction).

Anticipated Problems/Concerns

- AV nodal blockers (digoxin, Ca^{2+}-channel blockers, adenosine, and beta-blockers) may shorten refractoriness in the AP and thereby provoke VFIB in WPW pts with AFIB.
- Hemodynamic collapse may occur when verapamil or beta-blockers are used in the treatment of antidromic (wide-complex) PSVT in pts with WPW that is mistaken for VTach.

ACE Inhibitors

Thai T. Nguyen | Lee A. Fleisher

Uses

- Treatment of essential Htn, CHF, and mitral regurgitation.
- Numerous studies show that ACE-I use improves symptoms and quality of life, as well as reduces mortality rate in elderly with heart failure and decreased LVEF.
- Decreases mortality after myocardial infarction.
- Safe and effective treatment of Htn in diabetics; strong evidence that ACE-I delays the progression of diabetic renal disease.

Perioperative Risks

- Severe and prolonged hypotension in pts undergoing general anesthesia
- May increase insulin sensitivity and hypoglycemia in diabetics
- Conflicting evidence regarding risk of AKI

Worry About

- Decreased GFR and not recommended in pts with renal artery stenosis.
- Life-threatening angioedema involves the swelling of head, neck, and tongue.
- Hyperkalemia because of decreased production of aldosterone.
- Fetal anomalies and fetal and neonatal death.

Overview/Pharmacology/Dose

- A recent systematic review did not find evidence to support that periop ACEIs or ARBs can prevent mortality, morbidity, and complications (hypotension, periop cerebrovascular complications, and cardiac surgery–related renal failure).
- Captopril is available in oral dose and very effective in treating Htn.
- Enalapril has to be converted by esterase in liver to the active metabolite enalaprilat.
- Both captopril and enalapril are renally excreted and should be reduced in pt with renal dysfunction.
- Lisinopril is absorbed as the active form and offered as once-daily dosing.

Characteristic	Captopril	Enalapril	Lisinopril	Benazepril	Fosinopril	Quinapril	Ramipril
Elimination	Renal	Renal	Renal	Renal	50% renal 50% hepatic	61% renal 37% hepatic	Renal
Onset of hypotensive action (h)	0.25	1	1	1	1	1	1–2
Peak hypotensive effects (h)	1–1.5	4–6	6	2–4	2–6	2	3–6
Duration of hypotensive effects (h)	Dose related	24 (18–30)	24 (18–30)	24	24	24	>24 (24–60)
Dose (mg)	25–150, max 450	5–40, max 40	10–40, max 80	20–80, max 80	10–40, max 80	10–80, max 80	2.5–20, max 20

Drug Class

- Affects the renin-angiotensin system by blocking the conversion of angiotensin I to the active angiotensin II and delaying bradykinin breakdown and associated prostaglandins.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Angioedema Bronchospasm	Swelling of face, neck, tongue Dyspnea	Difficulty speaking, swallowing Wheezing	Airway exam
CV	Hypotension	Assess CV response to Rx		
GU	Renal failure Hyperkalemia	Orthopnea, dyspnea	Edema	BUN, Cr, lytes
HEME	Leukopenia, agranulocytosis	Fever	CBC with diff	

Key References: Zou Z, Yuan HB, Yang B, et al.: Perioperative angiotensin-converting enzyme inhibitors or angiotensin II type 1 receptor blockers for preventing mortality and morbidity in adults, *Cochrane Database Syst Rev* (1):CD009210, 2016; Mets B: To stop or not? *Anesth Analg* 120(6):1413–1419, 2015.

Drug Interactions

Preoperative Period

- Assess for evidence of renal insufficiency.
- Monitor for hyperkalemia.
- ACE-I can be continued until the day of surgery because of the potential benefits in reducing mortality and morbidity, but many hold the day of surgery. This issue is controversial.

Induction/Maintenance

- Consider reducing the ACE-I dose so that hypotension can be avoided.
- Severe and refractory hypotension can be resistant to vasopressors such as phenylephrine, ephedrine, and norepinephrine.
- Vasopressin and analogs can be useful to restore BP.
- Use of succinylcholine with elevated K^+ may be associated with cardiac arrhythmia.

Adjuvant/Regional Anesthesia/Reversal

- Hypotensive episodes may be associated with spinal and epidural anesthesia.

Postoperative Period

- Monitor for hypotension.

Acetaminophen

William J. Fawcett

Uses

- Minor analgesic for acute and chronic pain.
- First-line agent in WHO analgesia treatment ladder.
- First-line agent in treatment of pain in pregnancy and compatible with breastfeeding.
- Commonly administered in combination with codeine phosphate (e.g., paracetamol 500-mg and codeine 8-mg or paracetamol 500-mg and codeine 30-mg tablets).
- Commonly used as multimodal analgesic with an opioid-sparing effect.

Risk

- Well tolerated in normal therapeutic doses.
- Overdose associated with hepatotoxicity and nephrotoxicity.
- Unlike NSAIDs, negligible clinical antiinflammatory and antiplatelet effects.

Overview/Pharmacology

- Rapidly absorbed in GI tract, mostly in the small intestine.
- Rectal bioavailability is variable (30–70%).
- IV preparation has been associated with flushing, tachycardia, and hypotension.
- Half-life 1.25–3 h, peak plasma concentration 30–60 min
- 20% is protein-bound.
- Serum therapeutic levels 10–30 μg/mL.
- Analgesic effect lasts for approximately 6 h.
- 25% of dose undergoes first-pass effect in the liver; this is reduced with larger doses as liver's enzymatic capacity is overwhelmed.
- 90% is metabolized by conjugation in the liver via mainly by glucuronidation conjugation (and to a lesser extent sulfate conjugation), forming nontoxic metabolites (saturated at doses >150 mg/kg) and renally excreted (90–100% is recovered in urine within 24 h). Less than 5% is excreted unchanged in the urine.
- 10% undergoes oxidative metabolism via cytochrome P450 isoenzymes CYP2E1, CYP1A2, CYP3A4, and CYP2D6 to form the potentially hepatotoxic and nephrotoxic metabolite N-acetyl-p-benzoquinoneimine NAPQI. This metabolite is readily detoxified by glutathione.

- High levels of NAPQI (e.g., in overdose, cytochrome P450 system induction, low glutathione levels) results in NAPQI forming covalent bonds to hepatocyte cysteinyl-sulfhydryl groups. The loss of glutathione leads to increased formation of reactive oxygen and nitrogen species, causing mitochondrial permeability transition with loss of membrane potential and ultimately failure to synthesize ATP, leading to hepatic necrosis.

Drug Class/Mechanism of Action/ Usual Dose

- Mechanism of action remains unclear.
- COX isoenzymes (which produce prostaglandins and other eicosanoids) are pivotal in treating pain and inflammation. Peripheral COX-1 (constitutive) and COX-2 (inducible) isoenzymes are inhibited by a variety of peripherally acting NSAIDs, but paracetamol has little or no effect here.
- A central mechanism of action likely due to
  - COX-2 inhibition.
  - Cannabinoid receptor agonism.
  - Indirect augmentation of descending serotoninergic pathways.
  - Transient potential receptor (TPR) channel activity. The metabolite NAPQI causes spinal-level analgesia by activating the transient receptor potential ankyrin-1 (TRPA1) receptor.
  - Other suggested mechanisms include inhibition of L-arginine-NO-pathway (preventing NO synthesis) and activation of another TPR, the transient receptor potential vanilloid-1 (TRPV1) receptor. Inhibition of a COX-3 receptor is no longer accepted as a significant mechanism.

Available in oral, rectal, and parenteral preparations.

- Maximum dose 4 g q24h; dosage, 1 g q4–6h.
- Adjust dose for renal impairment. If estimated GFR is <30 mL/min per 1.73 m^2, increase dose interval to 6 h.
- If body weight is <50 kg, adjust dose to a maximum of 60 mg/kg/d.

Assessment Points

System	Effect	Assessment by Hx	Test
CNS	Encephalopathy, antipyretic effects, analgesia (following overdose)	Coma	GCS, CT/MRI (cerebral edema)
GI	Hepatic dysfunction (following overdose)	N/V, anorexia, sequelae of liver failure	Transaminases, INR, bilirubin, hypoglycemia
RENAL	Renal dysfunction, acute tubular necrosis (following overdose)	Oliguria	BMP, Cr, UA
METAB	Metabolic acidosis (following overdose)		Lactate, ABG
DERM	Stevens-Johnson syndrome Toxic epidermal necrolysis		Full blood count, C-reactive protein
HEME	Thrombocytopenia Leukopenia Neutropenia		FBC
RESP	Bronchoconstriction	Labored breathing, wheeze	Increased peak/plateau airway pressure, auscultation

Key References: Sharma CV, Mehta V: Paracetamol: mechanisms and updates, *CEACCP* 14(4):153-158, 2015; http://www.evidence.nhs.uk/formulary/bnf/current/4-central-nervous-system/47-analgesics/471-non-opioid-analgesics-and-compound-analgesic-preparations/paracetamol (Accessed February 15, 2017).

Suspected Toxicity and Treatment

- Overdose accounts for nearly 50% of acute liver failure in USA and UK.
- Can occur with 150 mg/kg taken in <1 h.
- Rare with doses <75 mg/kg.
- Half of acetaminophen overdoses leading to hospitalization were unintentional.
- Nephrotoxicity occurred in only 1–2% of pts with acetaminophen overdose.
- If toxicity is suspected, do not delay giving N-acetylcysteine (NAC). Proposed mechanisms of action for antidote include increasing glutathione stores and conjugation to NAPQI, antioxidant effects, antiinflammatory effects, and increases in NO resulting in microvascular perfusion.
- Serum acetaminophen concentration and treatment plotted according to normograms (e.g., Rumack-Matthew).
- Serum concentrations unreliable at <4 h; uncertain prognostic accuracy at >15 h.

Symptoms

- Phase I (0–24 h): Asymptomatic, anorexia, N/V, malaise, subclinical rise in serum transaminases
- Phase II (18–72 h): Right-upper-quadrant abdominal pain, anorexia, N/V, increased transaminases levels
- Phase III (72–96 h): Centrolobular hepatic necrosis, jaundice, coagulopathy, hepatic encephalopathy, renal failure, fulminant hepatitis, death
- Phase IV (96 h–3 wk): Complete resolution of symptoms and organ failure

Treatment

- Gastric decontamination: Within 4 h of ingestion (charcoal 1g/kg PO)
- NAC administration IV (150 mg/kg over 60 min, then 50 mg/kg over 4 h, then 100 mg/kg over 16 h). Sometimes the oral route is used (140 mg/kg, then 70 mg/kg for 72 h).
- Side effects of IV NAC: Anaphylactoid reactions; oral NAC, N/V.
- Supportive measures.

Perioperative Implications

- Ensure pts have not been self-medicating with acetaminophen prior to admission.
- Loading dose often administered in pediatric pts is 20–30 mg/kg, but do not exceed 75 mg/kg or 4 g in 24 h.
- Need to know dose 24 h prior to any acetaminophen administration.
- Care required in pts with reduced liver capacity (e.g., preexisting liver impairment, following liver resection).
- Increased periop morbidity in pts with abnormal liver function tests.

Drug Interactions

- CYP inducers: Barbiturates, buproprion, caffeine, carbamazepine, charcoal-broiled food, cruciferous vegetables, dihydralazine, isoniazid, phenytoin, primidone, rifampin, ritonavir, sulfinpyrazone, ethanol, isoniazid.
- Warfarin, NSAIDs: Coagulopathic effects may be potentiated by acetaminophen.
- Potential antinociceptive effect by 5-HT_3 receptor antagonists.

Alkylating Agents

Raymond D. Sroka | Mark J. Lema

Uses

- Bone marrow transplants
- Breast and bladder cancers
- Lymphomas and leukemias
- Cancers of the lung, pancreas, and brain
- Ovarian and testicular cancers
- Multiple myeloma
- Sarcomas and melanomas

Perioperative Risks

- Increased risk of infection
- Aspiration (subsequent to N/V)
- Prolonged succinylcholine action (CTX, thiotepa)
- Fluid retention (HN_2)
- Prolonged bleeding (thrombocytopenia)

Worry About

- Extravasation if given by IV infusion

Overview/Pharmacology

- First chemotherapy agents (1940s)
- First used in chemical weapons during World War I
- Structurally diverse compounds
- Generate reactive, electron-deficient intermediates
- Covalently bind to DNA bases, especially guanine, often during mitosis
- Disrupt DNA replication and transcription
- Side effects (acute) 1–3 wk after therapy
- High incidence of cytotoxicity to normal, rapidly dividing cells:
  - Bone marrow suppression
  - GI distress
  - Sterility
  - Increased risk of secondary malignancies (leukemia)
  - Alopecia
- End-organ toxicities:
  - CNS
  - Hepatic
  - Pulm
  - Renal

Drug Effects

Class	Name	Abbrev	Special Indication	Adverse Effects
Nitrogen Mustards				
Mechlorethamine	Mustargen	HN_2	LM	N/V, phlebitis, hyperuricemia, potent vesicant
Cyclophosphamide	Cytoxan	CTX	LM, Brt, Bl, Lu, Ov	Decreases pseudo-ChE; myocardial toxicity, hemorrhagic cystitis
Ifosfamide	Ifex		LM, Ov, Te, Sa	Hemorrhagic cystitis, N/V, CNS toxicity, metabolic acidosis
L-Phenylalanine	Alkeran (melphalan)	L-PAM	MM	Mild N/V
Chlorambucil	Leukeran	CLR	CLL, LM	N/V, seizures
Ethyleneamines				
Triethylene-thiophosphoramide	Thiotepa	T-TEPA	BMT	Can lower pseudo-ChE, prolongs succinylcholine action
Alkyl Sulfonates				
Busulfan	Myleran	MYL	CML	Pulm toxicity, N/V, seizures, mucositis, hyperbilirubinemia
Nitrosoureas				
Chloroethyl-cyclohexyl-nitrosourea	Lomustine	CCNU	LM, Brn	N/V, hepatic toxicity, pulm toxicity, renal toxicity
Bis-chloroethyl-nitrosourea	Carmustine	BCNU	LM, Brn	N/V, phlebitis, pulm toxicity
Streptozocin	Zanosar	STZ	Pa	N/V, dose-related renal toxicity
Triazenes				
Dimethyltriazenoimidazole carboxamide	Dacarbazine	DTIC	HD, Sa, Me	N/V, anaphylaxis, phlebitis, hepatotoxicity

Bl, bladder; *BMT*, bone marrow transplant; *Brn*, brain; *Brt*, breast; *CLL*, *CML*, leukemias; *HD*, Hodgkin disease; *LM*, lymphoma; *Lu*, lung; *Me*, melanoma; *MM*, multiple myeloma; *Ov*, ovarian; *Pa*, pancreatic; *Sa*, sarcoma; *Te*, testicular.

Key References: Cytotoxic agents. In Brunton LL, Chabner BA, Knollmann BC *Goodman & Gilman's the pharmacological basis of therapeutics*, ed 12, New York, 2011, McGraw-Hill; Huettemann E, Sakka SG: Anaesthesia and anti-cancer chemotherapeutic drugs. *Curr Opin Anaesthesiol* 18:307–314, 2005.

Perioperative Implications

Preoperative Preparation
- Full-stomach precautions.
- Risk of infection secondary to leukopenia.
- Adequate hydration to prevent additional nephrotoxicity.
- Check CBC due to myelosuppression.
- Consider PFTs (busulfan, cyclophosphamide).
- Consider ECHO or MUGA (if concern for cyclophosphamide-induced pericarditis/myocarditis).

Intraoperative Considerations
- Risk of aspiration during induction.
- Prolonged bleeding.
- Consider RBC transfusion.
- Maintain UO.
- Reduced dose of succinylcholine (CTX, thiotepa).

Postoperative Period
- Risk of N/V (most agents).
- Continued fluid hydration.
- Monitor for cardiac or pulm dysfunction.
- Monitor renal and hepatic function.

Alpha$_1$ Antagonists

Patrick F. Wouters

Uses
- First-line drug treatment for male lower urinary tract symptoms
- Treatment of primary hypertension (not as first-line therapy)
- Preop treatment of pheochromocytoma
- Emerging role in treatment of autonomic dysreflexia
- Occasionally used in treatment of Raynaud phenomenon
- Less commonly used in congenital heart surgery to reduce SVR and correct systemic-to-pulmonary blood flow ratio
- Less commonly used to achieve controlled hypotension intraop
- Being explored as a potential treatment of posttraumatic stress disorder

Perioperative Risks
- Intraop hypotension with attenuated response to the effect of alpha$_1$-agonist therapy
- Intraop floppy iris syndrome: Inhibition of iris dilator muscle contraction and tendency of iris to protrude through surgical incision

Worry About
- Orthostatic hypotension, syncope (less with α_{1A}-selective blockers; more when combined with antihypertensive medication
- Reflex tachycardia (less with selective alpha$_1$ blockers)
- Volume expansion of interstitium and plasma (secondary hyperaldosteronism)
- Priapism, urinary incontinence
- Other adverse events: Asthenia, nasal congestion, headache, dizziness

Overview/Pharmacology
- Also known as α_1-adrenoceptor antagonists (α_1-blockers)
- Mechanism of action: reversible competitive antagonism of postsynaptic alpha$_1$-adrenergic receptors
- Primarily active in tissues that sustain high levels of alpha-adrenergic sympathetic tone (resistance arteries, capacitance veins, urinary bladder outflow tract)
- Effect proportional to baseline sympathetic tone
- Nonselective (alpha$_1$ and alpha$_2$) adrenergic blockers: Phenoxybenzamine (irreversible) and phentolamine
- Selective alpha$_1$-adrenergic blockers: Prazosin (highest affinity), doxazosin, terazosin, silodosin, tamsulosin, bunazosin, alfuzosin
- Mixed alpha$_1$ and beta-adrenergic blocker: Labetalol
- Mixed alpha$_1$-adrenergic and 5-HT1A blocker: Urapidil

Usual Dose
- Treatment of hypertension: Prazosin 1–20 mg 2–3x/d; terazosin 1–20 mg 1–2x/d; doxazosin 1–16 mg 1x/d
- Treatment of benign prostatic hypertrophy: Alfuzosin 5 mg 1–2x/d; silodosin 4–8 mg 1x/d; tamsulosin 0.4 mg 1x/d; terazosin 1–10 mg 1x/d

Toxicity
- Safety unknown during pregnancy; many pass through breast milk
- No safety studies in children

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension Tachycardia	Dizziness, headache	BP, HR	
HEENT	Nasal congestion			
RENAL	Volume expansion		Edema	Ionogram: Na/K

Key References: Grimm RH Jr, Flack JM: Alpha 1 adrenoreceptor antagonists, *J Clin Hypertens (Greenwich)* 13(9):654–657, 2011; Oelke M, Gericke A, Michel MC: Cardiovascular and ocular safety of alpha1-adrenoceptor antagonists in the treatment of male lower urinary tract symptoms, *Expert Opin Drug Saf* 13(9):1187–1197, 2014.

Perioperative Implications

Preoperative Preparation
- Unknown effects in pediatric and pregnant pts.
- Continue until surgery.
- Less responsive to $alpha_1$ agonists.

Monitoring
- Routine; invasive BP for pheochromocytoma surgery

Regional Anesthesia
- Potential for exaggerated hypotensive effect with neuraxial anesthesia

Emergence/Extubation
- No known complications to date

Postoperative Period
- Continue to assess volume status and closely monitor BP.

Alpha$_2$ Adrenergic Agonists

Corey Amlong | Robert Sanders

Uses (Off-Label Uses Included)
- Treatment of hypertensive states (clonidine, guanfacine, guanabenz, alpha methyldopa).
- Sedation of mechanically ventilated pts (dexmedetomidine).
- Adjunct agent in general anesthesia (dexmedetomidine, clonidine, tizanidine).
- Sedation for awake intubation and other minor procedures (dexmedetomidine).
- Management of alcohol, nicotine, benzodiazepine, and cocaine withdrawal symptoms via reduction in cardiosympathetic stimulation. Also used for symptom management during naloxone therapy (dexmedetomidine, clonidine).
- Additive in central neuraxial and peripheral nerve blockade with efficacy possibly from systemic spread (dexmedetomidine, clonidine).
- Reduction in intraocular pressure via decreased aqueous humor secretion (brimonidine, apraclonidine).
- Reduction in postop shivering (clonidine, dexmedetomidine)
- Treatment of myofascial pain, spasticity, and rigidity (tizanidine)
- Treatment of ADHD and impulsivity in children and young adults (clonidine, guanfacine).

Perioperative Risks
- Acute Htn after initiation of use mediated by postsynaptic $alpha_{2B}$-mediated vasoconstriction
- Hypotension and bradycardia mediated by central postsynaptic $alpha_{2A}$ decreases in peripheral sympathetic outflow and peripheral presynaptic $alpha_{2A/2C}$ inhibition of NE/EPI release
- CV collapse in hypovolemic states or other pts dependent on sympathetic tone or SVR for maintenance of BP (e.g., trauma pts, aortic stenosis).

Worry About
- Rebound Htn (>24 h after dexmedetomidine infusion) or any interruption of clonidine (especially after 18 h or in pts taking >1.2 mg daily).
- Xerostomia (may be beneficial in awake intubation).
- Increased half time ("context sensitivity") with prolonged infusions of dexmedetomidine: Half-time of 4 min after a 10-min infusion grows to 250 min after an 8-h infusion.

Overview/Pharmacology
- Dexmedetomidine: This imidazole derivative is highly $alpha_2$-specific (1620/1 $alpha_2$/$alpha_1$ activity), with wide-ranging effects. It binds to postsynaptic $alpha_{2A}$ receptors on inhibitory neurons of the CNS (predominantly in the locus ceruleus), resulting in a unique brand of sedation that simulates natural sleep and preserves respiratory drive. Disinhibition and agitation are observed relatively rarely because sedation is unrelated to the GABA receptor. Agonism at presynaptic peripheral sympathetic nerve terminals inhibits NE release. Central $alpha_{2A}$ postsynaptic agonism leads to inhibition of peripheral sympathetic outflow; agonism at $alpha_{2C}$ autoreceptors in the adrenal medulla leads to inhibition as well. The net result is a reduction in arterial tone, venomotor tone, stroke volume, and heart rate.
- Signal transduction occurs via coupling to G-protein effector systems. Activation of Gi leads to decreases in adenylyl cyclase activity (with resultant reductions in protein kinase activity) as well as increases in hyperpolarizing K^+ currents. Decreases in N-type and L-type Ca^{+2} currents are also seen and may in part be coupled to the activation of Go.
- Amnesia is not reliably seen with $alpha_2$ agonists; however, analgesia is a proven benefit and may occur owing to effects at multiple sites. Direct presynaptic and postsynaptic $alpha_2$ agonism in the substantia gelatinosa may diminish substance P and glutamate release (presynaptic heteroreceptor agonism) and directly inhibit second-order neurons (postsynaptic agonism). Thus ascending nociceptive afferent flow is reduced (in a manner that has minimal cross tolerance with opioids). Supraspinal modulation of ascending input may also occur in the CNS itself.
- Clonidine: This imidazole derivative is less specific for $alpha_2$ receptors (220/1 $alpha_2$/$alpha_1$ activity). Effects on the vascular system are more pronounced than those of dexmedetomidine, whereas its sedative effects are less significant. Nonetheless clonidine has been used to reduce anesthetic requirements in people undergoing general anesthesia and has been successful as an additive in central neuraxial and peripheral nerve blockade in both extending the duration and enhancing the quality of sensory neural blockade while avoiding side effects seen with neuraxial opioids used for the same purpose.
- Dexmedetomidine undergoes extensive hepatic metabolism whereas clonidine is approx 50% hepatically metabolized and 50% excreted unchanged in urine.

Drug Class/Mechanism of Action/Usual Dose
- $Alpha_2$ adrenergic agonists have varying specificity for the different $alpha_2$ receptors.
- Dexmedetomidine: This imidazole derivative is given by IV infusion. An ampule of 200 µg/2 mL is diluted in 48 mL saline with resulting concentration 4 µg/mL. A loading dose of 1 µg/kg is given over 10–15 min followed by an infusion of 0.2–0.7 µg/kg per hour. Loading doses may be given over longer periods (20–30 min) in pts undergoing awake FOI so that response and airway patency may be continually evaluated. Cardiovascular side effects are generally rare and dose-dependent. Rates may need to be reduced in infusions over 24 hr as half-life increases markedly with prolonged infusion. Elimination half-life 2–3 h. The drug's effect can be reversed with atipamezole.
- Clonidine: This imidazoline derivative is given in dosages of 100–300 µg orally 1–4 times daily or via a transdermal patch. Its elimination half-life of 6–10 h limits its utility as sedative.
- Tizanidine: This imidazoline derivative is an antispasmodic used in the treatment of cerebral and spinal spasticity. It has also been used as a premedication adjunct to general anesthesia. It is supplied in 2-, 4-, and 6-mg tablets or capsules; dosing regimens vary by indication.
- Guanfacine and guanabenz: These phenylguanidine derivatives have relatively long half-lives (12–24 h and 4–6 h, respectively). They are functional antihypertensives and are rarely utilized currently.
- Alpha methyldopa: This drug is given in divided doses of 1– 2 g daily. It acts via its central $alpha_2$ agonist metabolite alpha methylnorepinephrine and may cause a positive Coombs test or hemolytic anemia. It has a safe historic record for use as an antihypertensive in pregnancy.
- Brimonidine and apraclonidine: These ophthalmologic agents are used topically in the treatment of glaucoma.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Increased SVR (with initiation) Decreased SVR Decreased inotropy Decreased chronotropy	Headache, palpitations, dizziness, diaphoresis, abdominal pain	Pulse, BP, skin temperature and turgor	ECG PA cath TEE
RESP	Usually minimally reduced Minute ventilation and preserved CO_2 Responsivity		Hypopnea, apnea, cyanosis	Spirometry Pulse oximetry Capnogram
CNS	Sedation Amnesia Analgesia Reduced CBF	Ramsay sedation scale Recall Pain	Somnolence	BIS Blood glucose
OTHER	Xerostomia/antisialagogue Plt aggregation Lipolysis inhibition Insulin secretion inhibition	Dry mouth/nasal decongestion		

Key References: Carollo DS, Nossaman BD, Ramadhyani U: Dexmedetomidine: a review of clinical applications, *Curr Opin Anaesthesiol* 21(4)457–461, 2008; Giovannitti JA Jr, Thoms SM, Crawford JJ: Alpha-2 adrenergic receptor agonists: a review of current clinical applications, *Anesth Prog* 62(1):31–39, 2015.

Perioperative Implications

Preoperative Preparation

- Pts who do not take their dose of clonidine on the morning of surgery commonly develop rebound hypertension. Pts on clonidine often take it for refractory Htn; labile BP should be anticipated. Baroreceptor sensitivity is generally preserved.
- Clonidine has shown some effectiveness for myocardial protection in CV surgery and can be considered in pts who would benefit from but have a contraindication to periop beta blockade.
- When $alpha_2$ agonists are used for sedation during awake FOI, consider adding low-dose (30–70 μg/kg) midazolam if definitive amnesia is desired.
- Concomitant use of inhibitors of cytochrome P450 enzymes (i.e., cimetidine, some fluoroquinolones, verapamil) may lead to increased serum levels of clonidine and tizanidine.

Induction/Maintenance

- Slow, controlled induction is preferred when not contraindicated. Decreases in SVR and inotropy may be exaggerated in pts receiving $alpha_2$ agonists.
- Pts on clonidine and dexmedetomidine can have significant reductions in MAC requirements (30–50% in some studies but wide ranges seen). Titration to hemodynamic variables or BIS may be useful.

Postoperative Period

- Pts already taking clonidine should continue it to avoid rebound Htn.
- Rebound Htn is unlikely with dexmedetomidine infusions of <24 h duration.
- Dexmedetomidine infusion has been used in the immediate postop setting to reduce narcotic requirements in certain populations where narcotic use is undesirable (e.g., morbidly obese).

Anticipated Problems/Concerns

- Treatment of hypotension and dysrhythmias such as symptomatic bradycardia and AV block may become necessary. Treatment of hypotensive bradycardia with anticholinergics alone (esp. in those in whom coronary perfusion is SVR-dependent) may precipitate myocardial ischemia in pts with low SVR (altered supply/demand ratio).

Acknowledgment

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Amphetamines

Luis R. Sauceda-Cerda | Jeffrey R. Kirsch

Uses

- Attention deficit hyperactivity disorder
- Weight loss
- Narcolepsy
- Recreational

Perioperative Risks

- Possible increased requirement for volatile anesthetic with acute use
- Possible decreased requirement for volatile anesthetic with chronic use (CNS depression)
- Catecholamine depletion with chronic use
- Increases in temperature with acute intoxication
- Increases in blood pressure and heart rate with acute intoxication
- Altered mentation, dysphoria, and euphoria with acute intoxication
- Acute intoxication can mimic preeclampsia or eclampsia in parturient pt

Worry About

- Severe Htn, palpitations, confusion, dizziness, and vasomotor disturbances especially in pts with ischemic heart disease, Htn, rhabdomyolysis, and hyperthyroidism

Overview/Pharmacology

- Consumed enterally, inhaled (i.e., smoked), snorted, or administered IV
- Psychoactive substance with CNS stimulation and mood-altering properties; several amphetamine derivatives used for illicit purposes (i.e., meth, Ecstasy).
- Consumption of amphetamine-producing plants occurs in some geographical areas (i.e., East Africa).
- Endogenous (i.e., beta-phenethylamine) amines may have amphetamine-like effects
  - Found in trace quantities in the peripheral nervous system and CNS.
  - Metabolized rapidly by monoamine oxidase.
- Elimination half-life ranges between 6–12 h (renal and hepatic clearance); urine alkalization prolongs half-life, so abusers may ingest HCO_3 to prolong half-life.
- Cardiotoxic manifestations include stress cardiomyopathy, MI, and arrhythmias.

Drug Class/Mechanism of Action/Usual Dose

- Amphetamine
- Complicated mechanism of action likely involves
  - Downregulation of monoamine transporters at synaptic cleft
  - Competitive inhibition of monoamine reuptake at synaptic cleft
  - Stimulation of monoamines at nerve terminals
- Dose variable depending on indication

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Increases BP, CO, HR, SVR, arrhythmias	Recent/chronic use	Vital signs	ECG
RESP	Respiratory stimulation	Recent/chronic use	Pulm exam	ABG
CNS	Increased alertness, electrical activity Overdose: Anxiety, psychoses, seizures	Recent/chronic use	CNS exam	EEG
METAB	Renal failure, lactic acidosis Dehydration	Recent/chronic use	Vital signs, PE	ABG, lytes
OTHER	Mydriasis, diaphoresis, hyperthermia, decreased GI motility	Recent/chronic use	Vital signs, PE	

Key References: Johnston RR, Way WL, Miller RD: Alteration of anesthetic requirement by amphetamine, *Anesthesiology* 36(4):357–363, 1972; Carvalho M, Carmo H, Costa VM, et al.: Toxicity of amphetamines: an update, *Arch Toxicol* 86(8):1167–1231, 2012.

Perioperative Implications

Preoperative Concerns

- Cancel case (when appropriate) if acute intoxication is suspected; urine drug screen may be appropriate when suspected.
- Catecholamine drip (i.e., norepinephrine) may be needed in chronic users.
- Ensure that any other psychotropic or analgesic medications are taken on the morning of surgery.

Induction/Maintenance

- Volatile anesthetic requirements may be affected in acute versus chronic users; increased in the acute setting and decreased with chronic users.
- Hypotension
  - Rule out cardiotoxic manifestations if acute use is suspected.
  - Ephedrine likely less effective in chronic amphetamine users.
  - Catecholamine infusion should be readily available.
- Hypertension
  - Rule out cardiotoxic manifestations if acute use suspected.
  - Deepen anesthesia and treat pain when appropriate.
  - Calcium channel blockers and/or beta blockers when appropriate.

Postoperative Period

- Regional anesthetics if consent obtained preop.
- Nonopioid medications (i.e., acetaminophen) where appropriate.
- If hypotension persists, rule out myocardial complications.

Adjuvants/Regional Anesthesia

- Multimodal analgesia
- RA and/or monitored anesthetic care

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Angiotensin II Receptor Blocking Drugs

Davide Cattano

Uses

- AT1–receptor antagonists, or sartans, are a group of pharmaceuticals that modulate the renin-angiotensin-aldosterone system. Their main use is in hypertension, diabetic nephropathy, and CHF.

Perioperative Risks

- ARBs do not inhibit ACE; they do not cause an increase in bradykinin, which contributes to the vasodilation produced by ACE inhibitors and also some of the side effects of ACE inhibitors (cough and angioedema).
- Dementia: It has been found that pts with Alzheimer's disease or dementia are up to 50% less likely to have to be admitted to a nursing home or to die if they were taking an ARB.

Worry About

- Rebound Htn if drug is withdrawn acutely, especially with longer-acting agents.
- Refractory hypotension in pts undergoing general anesthesia. BP responds to vasopressin agonists.
- Questionable increased risk of MI with ARBs.

Overview/Pharmacology

- Renin-angiotensin cascade begins with the cleavage of angiotensin by renin, angiotensin I converted by ACE to angiotensin II, angiotensin II receptors activated by binding of angiotensin.
- Clinical effects of angiotensin II (e.g., vasoconstriction, sodium/water retention, renin suppression) are mediated by AT1.
- Blockade of AT1 receptors directly causes vasodilation, reduces secretion of vasopressin, and reduces production and secretion of aldosterone, among other actions—the combined effect of which is reduction of BP.
- Three important PD/PK factors: Pressor inhibition, AT1 affinity, biologic half-life (e.g., losartan 100 mg, 25–40%, 1000-fold, 6 h, or valsartan 80 mg, 30%, 20,000-fold, 6 h).
- Contraindicated in pregnancy

Mechanism of Action/Usual Dose

- The activated receptor, in turn, couples to Gq/11 and thus activates phospholipase C and increases the cytosolic Ca^{2+} concentrations, which in turn trigger cellular responses such as stimulation of protein kinase C. The activated receptor also inhibits adenylate cyclase and activates various tyrosine kinases.
- Available in once-daily dosing:
  - Candesartan (Atacand) 4–32 mg
  - Irbesartan (Avapro) 150–300 mg
  - Losartan (Cozaar) 50–100 mg
  - Telmisartan (Micardis) 40–80 mg
  - Valsartan (Diovan) 80–320 mg

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Lowers BP	Assess response to Rx	BP	Monitor BP, can also have tachycardia and bradycardia with lowering BP, careful when discontinuing
GI	Increase in LFTs Rare reversible hepatotoxicity reported			Watch for rebound Htn, change in LFTs
METAB	Hyperkalemia			K^+
DERM	Angioedema reported	Ask pts for clinical Hx		
HEME	Microcytic anemia			CBC
RENAL	Can cause ARF in pts with renal artery stenosis or diffuse infrarenal stenosis			BUN/Cr
CNS		Rare headache, dizziness, fatigue insomnia		

Key References: Li EC, Heran BS, Wright JM: Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension, *Cochr Database Syst Rev* 8:CD009096, 2014; Hajjar I, Brown L, Mack WJ, et al.: Impact of angiotensin receptor blockers on Alzheimer disease neuropathology in a large brain autopsy series, *Arch Neurol* 69(12):1632–1638, 2012.

Perioperative Risks

- Reduced responsiveness to vasopressor, potential risk of rebound Htn in withdrawal (potential risks in general/neurologic/vascular surgery).
- Potential risk of ARF in major bleeding and kidney ischemia.

Induction/Maintenance

- Watch for refractory hypotension, which requires treatment with a vasopressin agonist.

Adjuvants/Regional Anesthesia/Reversal

- No known interactions

Postoperative Period

- Resume preop drugs for BP control if no ARF
- Only available in "per os" forms

Anticipated Problems/Concerns

- Recommended preop withdrawal for 24–48 h

Antianxiety Medications

Ijeoma Nwachukwu | Lee A. Fleisher

Uses

- Preop anxiolysis, anterograde amnesia, IV sedation, IV induction of anesthesia, suppression of seizure activity, muscle relaxation

Perioperative Risks

- Sedation
- Respiratory depression
- Apnea
- Airway obstruction
- Delayed emergence
- Delirium

Worry About

- Potentiation of respiratory depression with opioids

Overview/Pharmacology

- Benzodiazepines (midazolam and diazepam) are the most commonly used antianxiety medications in the periop period.
- Benzodiazepines:
  - Highly lipid-soluble, allowing a rapid onset of action and quick termination of effects.
  - Antianxiety effect via activation of the GABA receptor by binding to the gamma subunit.
  - Metabolized in the liver by microsomal oxidation or glucuronide conjugation.
  - Effects can be reversed by flumazenil, a selective benzodiazepine antagonist.

Drug Class/Mechanism of Action/Usual Dose

- Benzodiazepines
- GABA activator
- Chronically taken for generalized anxiety, panic attacks, muscle spasms, phobias
- Acutely taken for periop anxiolysis, IV sedation, induction of general anesthesia, seizures
- Anxiolysis dose for midazolam is 1–2.5 mg IV q5 min or 0.07–0.08 mg/kg IM q30–60 min
- Alternatives: Other benzodiazepines (clonazepam, alprazolam), beta blockers (propranolol), tricyclic antidepressants (amitriptyline), SSRIs (duloxetine), anticonvulsants, propofol

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CNS	CNS depression, decreased cerebral metabolic rate, decreased cerebral blood flow, decreased seizure activity	Headache, anterograde amnesia		
CV	Decreased SVR, decreased systolic BP		Hypotension	ECG
RESP	Dose-dependent respiratory depression, decreased ventilatory response to CO_2	Drowsiness, sedation	Hypoventilation, apnea, hiccoughs, cough	ABG
GI	Decreased to increased N/V		Increased secretions	
DERM	Eruptions	Pain at IV injection site, pruritus, burning	Erythema Hives	
Toxicity				
CV	Cardiac arrhythmias including premature ventricular contraction, bradycardia, and tachycardia		Hypotension	ECG
RESP	Respiratory arrest, airway obstruction, laryngospasm, bronchospasm		Apnea, shallow respirations	ABG
DERM	Thrombophlebitis	Pruritus	Hives	
CNS	Unconsciousness, physical dependence, anterograde amnesia		Unresponsiveness, delirium, dysphoria	

Key References: Olkkola KT, Ahonen J: Midazolam and other benzodiazepines, *Handb Exp Pharmacol* 182:335–360, 2008; Eilers H: Intravenous anesthetics. In Miller RD, Pardo M editors: *Basics of anesthesia*, 6th ed. Philadelphia, 2011, Elsevier, pp 99–114.

Perioperative Implications

Preoperative Concerns

- Antianxiety medications have a synergistic effect with opioids and propofol and may potentiate respiratory depression, leading to airway obstruction or respiratory arrest.
- Effects of benzodiazepines can be prolonged in the elderly and in pts with severe liver disease.

Induction/Maintenance

- Benzodiazepines can be used for the induction of general anesthesia. A dose of 0.1–0.3 mg/kg of midazolam is sufficient to produce unconsciousness.
- When administered with other induction agents, benzodiazepines decrease the speed of induction and decrease minimal anesthetic concentration MAC requirements.

Reversal

- Effects of benzodiazepines can be reversed by flumazenil, a benzodiazepine antagonist.

Anticipated Problems/Concerns

- Flumazenil has a shorter half-life than benzodiazepines; hence medication should be redosed to avoid resedation.

Antipsychotics

Christopher J. Cullom | Alan David Kaye

Uses/Risk

- In a given year, 26.2% of Americans 18 y or older have some form of mental disorder.
- Schizophrenia has a community prevalence rate of 1%.
- Psychiatric disorders such as schizophrenia, bipolar disorder, major depression, and disorders with psychotic features are treated with this class of drugs.

Perioperative Risks

- Cardiovascular instability, including hypotension and arrhythmia
- Cardiomyopathy/myocarditis
- Extrapyramidal effects
- Drug-drug interaction
- Postop psychosis

Worry About

- Antipsychotics act as CNS depressants; thus anesthetic drugs need to be titrated carefully.
- Reports of hypotension and cardiopulmonary arrest with concomitant propranolol and haloperidol usage.
- Antipsychotics have selectivity for CYP2D6, which is metabolized by many beta blockers; thus coadministration may result in drug interactions.
- Clozapine, risperidone, chlorpromazine, haloperidol, olanzapine, thioridazine, and quetiapine linked with cardiomyopathy and myocarditis.
- Cardiovascular side effects: Hypotension, tachycardia, QT prolongation, and rarely VFIB.
- Extrapyramidal side effects: Dystonic reactions, tardive dyskinesia, and, importantly, laryngospasm, which is treated with anticholinergics.
- Most serious extrapyramidal reaction is neuroleptic malignant syndrome, which manifests as hyperthermia, muscle rigidity, autonomic instability, encephalopathy, and tachydysrhythmias.
  - Treat with dantrolene or bromocriptine.
  - Related to recent increased dose in antipsychotic or start of new medication.
- Hypothalamic dysfunction causing temperature dysregulation.
- Alters the endocrine system, including elevating prolactin and ADH and disrupting glucose regulation.

Overview/Pharmacology

- Schizophrenia is defined by disturbances in emotional, behavioral, and cognitive function.
- All antipsychotics block dopamine D2 receptors to some extent.
- Two classes of antipsychotics: Typical and atypical.
- Typical antipsychotics have predominantly antidopaminergic properties.
- Atypical antipsychotics have significantly greater 5-HT2A receptor than D2 receptor occupancy, as well as greater affinity for D1, D3, and D4 receptors than for D2 receptors.
- Atypical antipsychotics have less extrapyramidal adverse effects and little or no effect on prolactin levels.
- Atypical antipsychotics allow for fewer extrapyramidal side effects and have become the mainstays of treatment.
- Atypical antipsychotics appear to be more effective in treating negative symptoms of schizophrenia and treatment-resistant schizophrenia.
- Preop discontinuation of antipsychotics was common practice as it was thought to lower incidence of intraop hypotension; however, discontinuation causes periop psychosis.
- Recent studies have found that preop discontinuation did not significantly decrease the incidence of periop hypotension. Therefore the recommendation is to continue drug therapy throughout surgery.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension, tachycardia, QT interval prolongation, torsades de pointes, myocarditis, increased risk of MI	Palpitations, syncope	Heart sounds, BP, pulse	ECG, ECHO
ENDO	Amenorrhea, galactorrhea, abnormal temp regulation, increased prolactin, abnormal glucose Abnormal ADH and aldosterone	Cold intolerance		CMP, prolactin, LH, FSH, ADH, aldosterone
HEME	Agranulocytosis			CBC
GI	Paralytic ileus			Abdominal x-ray
NEURO	Psychosis Extrapyramidal side effects: 1. Tardive dyskinesia 2. Dystonic reactions 3. Akathisia 4. Parkinsonism		Choreoathetoid movements of head, limbs, trunk Slow sustained muscle contractions State of discomfort causing agitation and restlessness Tremor, bradykinesia, rigidity, postural instability	
GENERAL	Neuroleptic malignant syndrome	Increase of medication dosage or beginning new medication	Rigidity, autonomic instability, hyperthermia, arrhythmia	Increased WBC, Cr, and CK; myoglobinuria

Key References: Ellender R, Kaye AD, Kaye AM: Neuroleptic drugs. In Manchikanti L, Trescot A, Christo PJ, et al., editors: *Foundations of pain medicine and interventional pain management: A comprehensive review*, Paducah, KY, American Society of Interventional Pain Physicians, 2011, pp 553–558; Kaye AD, Liu H, Fox C, et al.: Psychiatric and behavioral disorders. In Fleisher LA, editor: *Anesthesia and uncommon diseases*, ed 6. Philadelphia, Elsevier, 2012, pp 444–461.

Perioperative Implications

Preoperative Preparation/Concerns

- History may be unreliable.
- Continue antipsychotic medications preop.
- Assess cardiac, hepatic enzymes, and WBC count.

Monitoring

- Routine
- Arrhythmia, hemodynamic changes
- Temperature

Airway

- Laryngospasm a possible side effect

Induction

- Hypotension after induction, particularly with chlorpromazine

Maintenance

- Drug-drug interactions, particularly with antihypertensive drugs.
- CV instability, arrhythmias.
- Thermoregulation; concern for hypothermia.
- Continue antipsychotics throughout surgery; total IV anesthesia with propofol, ketamine, and fentanyl can avoid many periop complications.

Extubation

- Usual criteria

Postoperative Period

- Postop confusion
- Postop ileus
- Decreased pain sensitivity

Anticipated Problems/Concerns

- Cardiovascular instability
- Cardiac arrhythmias
- Drug-drug interactions
- Hypothermia
- Neuroleptic malignant syndrome potential
- Drug side effects: Extrapyramidal, cardiac, and endocrine

Aspirin (Acetylsalicylic Acid)

Lee A. Fleisher

Uses

- People in USA consume 10,000–20,000 tons annually.
- Rx for mild and/or moderate pain, fever, arthritis, and prevention of MI.

Perioperative Risks

- Peptic ulcer disease
- Plt dysfunction
- Increased bleeding risk
- Stroke
- Interstitial nephritis
- Reye syndrome

Worry About

- Displacement of protein-bound drugs (e.g., warfarin, sulfonylureas, thiopental, methotrexate)
- Potentiation of anticoagulants.
- Thrombosis secondary to aspirin withdrawal.

Overview/Pharmacology

- Cyclooxygenase inhibition prevents platelet aggregation and vasoconstriction.
- Platelet inhibition irreversible for the life of the platelet.
- Aspirin
  - Is metabolized by the liver and excreted by the kidney
  - Mildly antagonizes antihypertensive medications (beta-blockers, vasodilators, diuretics)
  - Displaces protein-bound drugs, increasing their effects
- Not shown to decrease risk of periop cardiac events; some increased risk of bleeding in large-scale trials.

Drug Class/Mechanism of Action/ Usual Dose

- NSAID
- Cyclooxygenase inhibitor
- Chronically taken for:
  - MS pain (e.g., arthritis, neuralgia)
  - Prevention of CV events
  - Claudication
- Acutely taken for:
  - Acute, mild to moderate pain (e.g., headache, myalgia)
  - Fever
  - Dysmenorrhea
- Usual dose is 325–1000 mg q3–4h for acute illnesses and pain.
- 62.5–325 mg for platelet inhibitor effects.
- Alternatives include acetaminophen, other NSAIDs (ibuprofen, naproxen), steroids, opioids, gold, ticlopidine, dipyridamole, and pentoxifylline.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Hyperventilation, respiratory alkalosis		Tachypnea	ABG
GI	Gastritis PUD	Dyspepsia N/V, hematemesis, melena		Endoscopy Upper GI, x-rays, stool heme, Hgb
ENDO	Hyperglycemia, corticosteroid release			Glucose
HEME	Plt dysfunction	Bleeding, bruising	Hematomata, petechiae	Bleeding time
HEPAT	Hepatocellular damage	Nausea, anorexia	Hepatomegaly, jaundice	SGOT, SGPT, alk phos
Toxicity				
CV	Vasomotor paralysis		Hypotension	
RESP	Hypoventilation, respiratory acidosis		Hypopnea	ABG
DERM	Eruptions	Pruritus	Acneiform, erythematous, pruritic, eczematoid, or desquamative lesions	
RENAL	Renal failure due to analgesic nephropathy	Oliguria, anuria	Edema, rales	BUN/Cr, UA, CXR
CNS	Headache, tinnitus, drowsiness, dizziness, diminished vision and hearing		Sweating, confusion, convulsions, coma	
ACID-BASE	Metabolic acidosis			ABG

Key References: Wong SS, Irwin MG: Peri-operative cardiac protection for non-cardiac surgery, *Anaesthesia* 71(Suppl 1):29–39, 2016; Vela Vásquez RS, Peláez Romero R: Aspirin and spinal haematoma after neuraxial anaesthesia: myth or reality? *Br J Anaesth* 115(5):688–698, 2015.

Perioperative Implications

Preoperative Concerns

- D/C 1 wk prior to surgery for full reversal of plt inhibition (need only 1/7 of normally functioning platelets, so if no dilution effect expected, need only 48 h off low-dose ASA); may see hyperthrombotic state around 7–10 d, particularly in pts with coronary stents.
- Continue aspirin in pts with coronary stents unless contraindicated.
- May potentiate the effects of protein-bound drugs.

Induction/Maintenance

- Possible mildly exaggerated effects of thiopental

Adjuvants/Regional Anesthesia/Reversal

- May increase the risk of hemorrhagic complications of regional anesthesia. Aspirin does not contraindicate regional anesthesia, but those techniques with low potential for bleeding are preferable (e.g., spinal may be preferred over epidural).
- May increase the risk of hemorrhagic complications of invasive monitoring.

Special Considerations

- A potent inhibitor of plt aggregation that can seriously impair surgical hemostasis. Most surgeons request D/C of aspirin 1 wk prior to surgery. However, if CAD or other vascular occlusive disease will be left untreated, consult with surgeon, pt's primary physician, and pt about advisability of D/C aspirin.
- Risks of regional anesthesia and invasive monitoring may be increased.
- May displace protein-bound drugs (e.g., warfarin, sulfonylureas, thiopental, methotrexate), thus augmenting their effects.
- Associated with gastritis, PUD, GI bleeding, and increased risk for aspiration of gastric contents.
- Associated with Reye syndrome and contraindicated in febrile viral illness in children.

Benzodiazepines

Robert I. Cohen

Uses

- Prescribed for the treatment of anxiety
- Used for premedication and procedural (moderate and deep) sedation

Perioperative Risks

- High levels associated with hypnosis, unconsciousness, apnea/respiratory depression

Worry About

- Combination (synergy) with opioids and other CNS depressants may result in severe respiratory depression, apnea, hypotension.

Overview/Pharmacology

- Anxiolysis, sedation, hypnosis, muscle relaxation, anterograde amnesia, anticonvulsant
- Midazolam: Short-elimination half-life (2.5 h)
- Lorazepam: Intermediate-elimination half-life (15 h)
- Diazepam: Long-elimination half-life (30 h)
- Metabolized by hepatic microsomal oxidation and glucuronide conjugation.
- Active metabolites: Diazepam (P450-2C19 and 3A4) → nordazepam; (P450-3A4) → temazepam → oxazepam

- Midazolam:
  - IV: Peak effect in 2–4 min
  - IM: Peak effect in 30–60 min
- Lorazepam:
  - IV: Peak effect in 5–15 min, painful injection, thrombophlebitis
  - IM: Peak effect in 60–90 min
  - Oral: Peak effect in 2 h
- Diazepam:
  - IV: Peak effect in 1–2 min, painful injection, thrombophlebitis
  - IM: Painful, unpredictable absorption, do not use
  - Oral: Peak effect in 30–60 min, well absorbed; food, aluminum-containing antacids delay absorption
- No clear difference in speed of recovery from diazepam and midazolam drug effect after low dose for sedation in short procedures; differentially shorter clinical recovery times for midazolam after larger dose/prolonged administration.
- Lorazepam provides long duration (>4 h) of sedation and amnesia by any route of administration; do not use in benzodiazepine-naïve pts when rapid recovery from drug effect is desired.
- Prolonged use can lead to tolerance.

Drug Class/Mechanism of Action/Usual Dose

- Anxiolytic, sedative, hypnotic, antispasmodic, antiseizure (DEA Schedule IV).
- Potentiation of GABA–mediated neural inhibition (Ca^{2+} outflow leading to cell hyperpolarization).
- Safe use involves careful titration to the desired effect.
- Usual dosage for premedication and moderate (conscious) sedation
  - Midazolam
    - IV: 0.5–1 mg, repeated; maintenance infusion: 0.04–0.10 mg/kg per h
    - IM: 0.07 mg/kg
    - Oral: 15 mg (0.5 mg/kg in children up to 20 kg)
  - Lorazepam
    - IV: 0.25 mg, repeated
    - IM: 0.05 mg/kg, max 4 mg
    - Oral: 0.5–4 mg
  - Diazepam
    - IV: 1–2 mg, repeated
    - Oral: 5–10 mg

Drug Effects

System	Effect	PE	Test
CV	Decreased systemic vascular resistance and cardiac output	Arterial BP	
RESP	Central respiratory depression Apnea	Respiratory rate	Tidal volume Minute volume, capnography, oximetry
CNS	Anxiolysis Sedation Hypnosis Amnesia Anticonvulsant Decreased cerebral metabolic rate and cerebral blood flow	Slurred speech, drowsiness, ataxia Unresponsiveness	

Key References: Griffin CE, Kaye AM, Bueno FR, et al.: Benzodiazepine pharmacology and central nervous system–mediated effects, *Ochsner J* 13(2):214–223, 2013; Vuyk J, Sitsen E, Reekers M: Intravenous anesthetics. In Miller RD, Eriksson LI, Fleisher LA, et al., editors: *Miller's anesthesia*, ed 8. Philadelphia, 2015, Elsevier, pp 821–863.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- Elderly: Reduce dose up to fivefold (5–10% reduction per decade)
- Cimetidine, ranitidine (microsomal cytochrome P450 inhibitors), and liver cirrhosis decrease clearance; enhanced effect may be seen.
- Smoking and enzyme-inducing drugs increase diazepam clearance.
- Renal failure increases half-life of diazepam.
- Monitor ventilation.

Induction/Maintenance

- Synergistic interaction with anesthesia induction agents and opioids.
- In pts reporting intense pain, consider analgesic titration first before titrating anxiolytic.
- Provide education and instruction for postop care prior to administration of benzodiazepine.

Monitoring

- End-tidal CO_2

Airway

- May require support

Extubation

- Consider benzodiazepine reversal with flumazenil (prior to naloxone) after major surgery for intubated pts who are slow to emerge from general anesthesia, have return of spontaneous ventilation at a normal rate, and received benzodiazepine. Caveat: Increase intensity and duration of postop monitoring.

Regional Anesthesia

- May exacerbate respiratory depression during spinal anesthesia (mechanism unknown).

Postoperative Period

- Additional monitoring time and care required if benzodiazepine reversal agent (flumazenil) administered owing to unequal duration of active and reversal agent.
- Provide written postop education/instructions and/or offer prior to first administration of benzodiazepine, as amnestic effect may last several times the elimination half-life.

Anticipated Problems/Concerns

- Combination with opioids or other CNS depressants may result in severe respiratory depression, apnea, and hypotension.
- Large doses result in prolonged drowsiness and respiratory depression, especially in the elderly; reverse with flumazenil.
- Undesirable intensity/duration of amnesia for some pts.
- Amnesia is anterograde (retrograde amnesia can occur after head injury and ECT but not from administration of benzodiazepine).
- May not be safe to reverse with flumazenil in pts receiving chronic benzodiazepine, particularly as part of an antiseizure regimen.

Beta-Adrenergic Receptor Antagonists (Blockers)

Duminda N. Wijeysundera

Uses

- Available PO and IV.
- Prescribed long term for stable angina, systolic CHF, MI (secondary prevention), Htn, and AFIB (for control of heart rate). No longer considered first-line Rx for essential Htn, especially in elderly pts.
- Long-term Rx must be continued periop (Class I ACC/AHA recommendation).
- Risk-benefit balance of periop (prophylactic) beta-blocker Rx is unclear.
- Periop Rx prevents MI after surgery, but increases risks of CVA and hypotension.
- Periop Rx may be reasonable for selected pts with ischemia on cardiac stress testing or three or more risk factors on the Revised Cardiac Risk Index (Class IIb ACC/AHA recommendation).

Perioperative Risks

- Increases risks of hypotension, bradycardia, and CVA. Risks may be further elevated in the presence of anemia, nonselective beta-blockers, or short duration of preop medication (<5 d).
- Periop beta-blockade should be avoided in pts with CVD.
- Contraindicated in pts with asthma. Nonselective beta-blockers may precipitate bronchospasm in COPD with significant reversible airway obstruction.
- May worsen or precipitate CHF in pts with decreased LV function.

Worry About

- May cause hypotension and CVA, especially in the presence of anemia or nonselective beta-blockers.
- May worsen underlying systolic cardiac dysfunction.
- Can precipitate bronchospasm, especially with nonspecific beta-blockers and COPD with known reversible airway obstruction.

Overview/Pharmacology

- Competitive selective antagonists of beta adrenoreceptors. Binding to receptors is reversible.
- Beta-blockers with intrinsic sympathomimetic activity (e.g., acebutolol) are partial agonists of beta adrenoreceptors that activate the receptors to some extent.
- Partial antagonists cause smaller reductions in HR and CO than beta-blockers without intrinsic sympathomimetic activity.
- Some beta-blockers are also antagonists of alpha$_1$-adrenoreceptors (labetalol, carvedilol) or partial agonists of beta$_2$-adrenoreceptors (nebivolol).
- Selectivity for beta$_1$ adrenoreceptors varies among beta-blockers, with the most selective drugs being nebivolol, followed by bisoprolol, atenolol, and metoprolol.

Drug Class/Mechanism of Action/Usual Dose

- Beta-blockers block interfere with ability of catecholamines and other sympathomimetics to activate beta adrenoreceptors on heart and smooth muscle of airways or blood vessels.
- Chronic administration leads to upregulation of beta adrenoreceptors.
- Routes of clearance include hepatic (metoprolol, carvedilol, propranolol), renal (atenolol, acebutolol), mixed renal and hepatic (bisoprolol, nebivolol), or plasma hydrolysis (esmolol).
- Elimination half-life is specific to individual agents and depends on dose, protein binding, and route of administration (oral vs. IV).

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Decreased HR Decreased CO Decreased contractility Increased CVR Decreased myocardial O_2 consumption	Relief of angina Decreased BP Decreased HR	HR BP	ECG; cardiac stress test
RESP	Increased airway resistance (especially nonselective agents)	Increased wheezing Increased bronchospasm		FEV_1; FEV_1/FVC ratio Increased peak airway pressure
ENDO	Hyperglycemia Hypokalemia			Lab measurements of K^+ and glucose
CNS	Fatigue, lethargy, sleep disturbance, peripheral paresthesia			
OB	Beta-blockers cross placenta and can cause fetal bradycardia, hypotension, or hypoglycemia			

Key References: Frishman WH: β-Adrenergic blockade in cardiovascular disease, *J Cardiovasc Pharmacol Ther* 18(4):310–319, 2013; Wijeysundera DN, Duncan D, Nkonde-Price C, et al.: Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines, *Circulation* 130(24):2246–2264, 2014.

Perioperative Implications

Preoperative Concerns

- Long-term beta-blocker Rx must be continued periop (Class I ACC/AHA recommendation).
- May be reasonable for selected pts with ischemia on cardiac stress testing or three or more risk factors on the Revised Cardiac Risk Index (Class IIb ACC/AHA recommendation).
- Abrupt withdrawal results in excess SNS activity within 24–48 h and can lead to unstable coronary syndromes.

Induction/Maintenance

- Beta-blockers may potentiate myocardial depression associated with inhaled or IV anesthetics.

Adjuvants/Regional Anesthesia/Reversal

- Bradycardia can often be reversed with atropine, but life-threatening bradycardia may require a temporary pacemaker.
- Catecholamines (e.g., isoproterenol, dobutamine, epinephrine) can help reverse negative cardiac effects, but very high doses are typically needed. $CaCl_2$ (250–1000 mg in adults) or glucagon (1–5 mg in adults) administered IV can also help reverse myocardial depression.
- In severe overdoses where usual Rx has failed, hyperinsulinemic euglycemia (high-dose insulin with concurrent glucose infusion to maintain euglycemia) may help.

Anticipated Problems/Concerns

- Beta-blocker dose may require temporary adjustment after surgery to account for hemodynamic effects of fluid shifts, epidural analgesia, and other medications. Goal is to avoid hypotension.

Bisphosphonates

Silvia Duong | De Q.H. Tran

Uses

- Oral bisphosphonates:
  - Alendronate (Fosamax), risedronate (Actonel): Prevention and treatment of postmenopausal osteoporosis, prevention and treatment of glucocorticoid-induced osteoporosis, treatment of osteoporosis in men, and Paget disease of bone
  - Etidronate (Didronel): Prevention and treatment of postmenopausal osteoporosis and Paget disease of bone
  - Ibandronate (Boniva) administered PO and IV: Prevention and treatment of postmenopausal osteoporosis
- IV bisphosphonates:
  - Pamidronate (Aredia): Treatment of hypercalcemia of malignancy, osteolysis secondary to bone metastases in breast cancer, osteolytic lesions of multiple myeloma, and Paget disease of bone
  - Zoledronic acid (Zometa): Treatment of hypercalcemia of malignancy, osteolysis secondary to bone metastases in breast cancer, and osteolytic lesions of multiple myeloma
  - Zoledronic acid (Reclast): Prevention and treatment of postmenopausal osteoporosis, prevention and treatment of glucocorticoid-induced osteoporosis, treatment of osteoporosis in men, and Paget disease of bone

Perioperative Risks

- Use of bisphosphonates has been associated with osteonecrosis of the jaw (ONJ) in those undergoing dental surgery. The risk of ONJ is higher (1–12%) among cancer pts receiving higher doses of bisphosphonates. The risk is much lower (1:10,000-100,000) among those who are treated with oral bisphosphonate for osteoporosis.

Overview/Pharmacology

- Oral bisphosphonates are poorly absorbed; bioavailability is only 1–5%.
- After binding to bone surfaces and exerting their effects on osteoclasts, bisphosphonates are retained in the bone for months to years (biologic half-life up to 10 y). Bisphosphonates are gradually and slowly released with the process of bone turnover.
- Bisphosphonates are not metabolized.
- Bisphosphonates are excreted primarily by the kidneys; their elimination decreases linearly with decreased renal function. The use of bisphosphonate is not recommended in individuals with CrCl <30 mL/min.

Mechanism of Action

- Bisphosphonates are analogs of pyrophosphate that adsorb to the surface of bone hydroxyapatite. Bisphosphonates reduce the risk of bone fracture by suppressing osteoclastic bone resorption.
- By interfering with osteoclast-mediated bone resorption, bisphosphonates inhibit calcium release and are used in the management of hypercalcemia.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
ENDO	Hypocalcemia	Indication of bisphosphonate Calcium level should be normal before IV administration of bisphosphonate	Chvostek sign Trousseau sign	Serum calcium levels
GI	Heartburn Esophageal irritation Esophagitis Abdominal pain Diarrhea	For safe administration of oral bisphosphonates, pt must be able to remain upright for ≥30 min after administration		
RENAL	Renal clearance	Monitoring of renal function to ensure safe administration of bisphosphonate. The use of bisphosphonate is not recommended in pts with CrCl <30 mL/min		Serum Cr
MS	Osteonecrosis of jaw Atypical femur fractures			Radiography
OTHER	Flu-like symptoms with IV bisphosphonate (low-grade fever, myalgia, arthralgia)	Acute-phase reaction within 24–72 h of infusion		

Key References: Friedman PA: Agents affecting mineral ion homeostasis and bone turnover. In: Brunton LL, Chabner CA, Knollmann BC, editors: *Goodman & Gillman's the pharmacological basis of therapeutics*, ed 12, New York, 2011, McGraw-Hill, pp 1275–1306; Ruggiero SL, Dodson TB, Assael LA, et al.: American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of jaws—2009 update, *J Oral Maxillofac Surg* 67(5 Suppl):2–12, 2009.

Perioperative Implications

Preoperative Concerns

- Guidelines of the American Association of Oral and Maxillofacial Surgeons recommend holding oral bisphosphonates for 3 mo prior to elective dental surgery in pts who have been receiving them for ≥3 y or who are treated with corticosteroids. However, urgent surgery should not be delayed. The oral bisphosphonate should be restarted only when the bone has healed.

Induction/Maintenance

- No known drug interactions

Adjuvants/Regional Anesthesia/Reversal

- No known contraindications

Postoperative Concerns

- Bisphosphonates should be held in pts with postop renal complications.
- In the presence of bisphosphonate-related ONJ, risks and benefits of continuing IV bisphosphonate therapy in oncology pts should be determined in consultation with the treating oncologist, oral/maxillofacial surgeon, and pt.

Drug Interactions

- The absorption of oral bisphosphonates can be greatly decreased in the presence of food, beverages (other than plain water), calcium supplementation, and other drugs. Therefore oral bisphosphonates should be administered on an empty stomach at least 30 min–2 h prior to the ingestion of food, beverages, and other drugs.

Bleomycin

Carin Tauriello | Mark J. Lema

Uses

- Treatment of squamous cell carcinoma
- Treatment of melanomas and sarcomas
- Treatment of testicular carcinoma
- Treatment of Hodgkin and non-Hodgkin lymphoma
- Sclerosing agent for malignant pleural effusion

Perioperative Risks

- Adverse effects >10%.
- Acute febrile reactions (25 -50%).
- Dermatologic:
  - Skin thickening, diffuse scleroderma, onycholysis, pruritus.
  - 50% of pts develop erythema, rash, striae, indu hyperkeratosis, vesiculation, and peeling of the skin; predominantly seen on the palmar and plantar surfaces of the hands and feet.
  - Hyperpigmentation (50%), alopecia, nail bed changes.
  - Effects are usually dose-related and reversible with discontinuation.
- Gastrointestinal: Stomatitis and mucositis (30%), anorexia, weight loss.
- Adverse effects (1 -10%)
  - Miscellaneous: Anaphylactoid-like reactions and idiosyncratic reactions (1% in lymphoma pts).
- Adverse effects <1%
  - Angioedema, cerebrovascular accident, cerebral arteritis, hepatotoxicity, hypoxia, MI, Raynaud's phenomenon, renal toxicity, scleroderma-like skin changes, thrombotic microangiopathy, vomiting.
- Respiratory: Tachypnea, rales, acute or chronic interstitial pneumonitis, and pulm fibrosis (5 -10%).
  - Rapidly progressive interstitial pneumonitis known to occur after general anesthesia using O2 conc >30%, overhydrating pt; postop ARDS.
- FDA Black Box Warning:
  - Idiosyncratic reaction: A severe reaction similar to anaphylaxis has been reported in 1% of lymphoma pts treated with bleomycin. These reactions typically occur after the first or second dose.
  - Pulmonary fibrosis: Most severe toxicity of bleomycin, with risk increasing in elderly pts, those receiving >400 U total lifetime dose, and possibly smokers and pts receiving concurrent O_2 therapy.
  - Experienced physician: Should be administered under the supervision of a physician experienced in delivering chemotherapy.
- Contraindications: Hypersensitivity to bleomycin or any component of the formulation, severe pulm disease, pregnancy.

Worry About

- Sustained O_2 concentration >30%
- Liberal use of maintenance fluids/blood products
- Interstitial pneumonitis
- Postop acute respiratory distress syndrome

Overview/Pharmacology

- 1 U bleomycin = 1 mg activity of bleomycin.
- $T_{½}$ approximately 2 h, but Cr <35 mL/min raises $T_{½}$ exponentially.
- 70% is recovered in urine as active bleomycin.

Drug Class/Mechanism of Action

- Mixture of cytotoxic antibiotics isolated from *Streptomyces verticillus*.
- Cytotoxic action caused by inhibition of DNA synthesis.
- Usual dose: 0.25–0.5 U/kg weekly or twice weekly (10–20 U/m^2) to 400 U (total dose).
- Cause of pulm toxicity is unclear; thought possibly to be related to production of free radicals.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Raynaud phenomenon (rare)	Color changes in fingers	Observation	
RESP	Interstitial pneumonitis (10%) Pulm fibrosis (1%)	Dose (>250 U), age (>65 y) Previous lung disease	Dyspnea, fine rales and cough, fever	PFTs (decreased TLC, decreased VC)
GI	N/V			
HEME	Not associated with pancytopenia			
DERM	Mucocutaneous toxicity (50%)	1–3 wk after start of medication (dose 150–200 U)	Urticaria, hyperpigmentation, hyperkeratosis, alopecia	

Key References: Aakre BM, Efem RI, Wilson GA, et al.: Postoperative acute respiratory distress syndrome in patients with previous exposure to bleomycin, *Mayo Clin Proc* 89(2):181–189, 2014; Donat SM, Levy DA: Bleomycin associated pulmonary toxicity: is perioperative oxygen restriction necessary? *J Urol* 160(4):1347–1352, 1998.

Perioperative Implications

Preoperative Preparation/Concerns

- Assess bleomycin cumulative dose; there is a dose–toxicity relationship; toxicity increases dramatically with a cumulative dose>450 U.
- Assess age (>65 y).
- Assess previous Hx of lung disease and smoking.
- Ask about previous radiation to thorax.
- Consider PFTs, CXR, and ABG.

Perioperative Period

- Limit delivered O_2 to <30% if adequate for O_2 sat >89%. (Controversial: Conflicting evidence/case reports regarding association of higher FiO_2 with pulm morbidity.)
- Limit fluids and avoid fluid overload. Minimize blood transfusion.
- Consider monitoring of CVP.
- Consider arterial monitoring and sampling.
- Use upper limit alarm for percentage of O_2 delivery.

Postoperative Period

- Keep delivered O_2 to <30% if adequate for O_2 sat >89%.
- Limit fluids.
- Corticosteroid use for pulm toxicity is controversial.

Anticipated Problems/Concerns

- Cyclophosphamide and radiation Rx (thorax) potentiate pulm toxicity.
- Cisplatin potentiates renal insufficiency.
- Vinca alkaloids (vincristine, vinblastine, VP-16) potentiate Raynaud phenomenon.
- Mitomycin C exhibits similar properties to those of bleomycin but with milder effects.

Buprenorphine

Veena Graff

Uses

- Management of opioid addiction
- Management of chronic pain ("off-label" use for SL buprenorphine and buprenorphine TD patch)

Perioperative Risks

- Challenges in pain management throughout periop period
- Respiratory depression
- Can cause neonatal abstinence syndrome

Overview/Pharmacology

- High affinity on mu opioid receptors; slowly binds to and slowly dissociates from receptors; therefore buprenorphine has a long duration of action.
- Agonist effects increase in linear fashion with increasing dose, but a ceiling effect exists; therefore there is no further analgesic benefit beyond certain doses.
- 95% bound to plasma proteins.
- Poor oral bioavailability due to extensive first-pass metabolism; therefore most commonly used routes of administration are SL by TD, IV, and IM.
- Half-life: SL ~37 h, TD ~26 h, IV ~3 h
- Time to peak plasma concentrations: SL ~1–3 h, IM ~1 h, TD ~steady state achieved by 72 h.
- Buprenorphine concentration in CSF is approximately 15–25% of the plasma concentration.
- Metabolism: N-dealkylation via CYP3A4 to active metabolite, norbuprenorphine. Also by glucuronidation by uridine diphosphate glucuronosyltransferase isoenzymes to buprenorphine 3-beta-O-glucuronide.
- Clearance: Dependent on hepatic blood flow.
- Excretion: Mostly in feces; 10–30% eliminated in urine.

Drug Class/Mechanism of Action/Usual Dose

- An opioid with mixed agonist-antagonist activity
- Classified as a Schedule III controlled substance under the Controlled Substances Act.
- Partial agonist at Mu-opioid receptors, delta-opioid receptors, and opioid receptor–like receptors (ORL-1).
- Antagonist at kappa-opioid receptors.
- Can precipitate opioid withdrawal if pt has full agonists in bloodstream.
- Best time to start and how to start: When pt is having clear and objective withdrawal symptoms. Titrate dosage quickly in 2–4-mg increments with the goal of reaching an appropriate dose within 1–2 wk.
- SL: Maintenance dose between 4–24 mg daily; adjustments made in 2- to 4-mg increments. Combination of buprenorphine/naloxone maintenance dose between 4 mg/1 mg and 24 mg/6 mg daily.
- TD delivery system (patch): Buprenorphine patch dosages are available in 5, 7.5, 10, 15, and 20 µg/h every wk.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension; also possible tachycardia and Htn if opioid withdrawal is precipitated	Low BP: Light-headedness, dizziness. High BP: anxiety, jitteriness	VS, CV exam	ECG to rule out any other arrhythmias
RESP	Respiratory depression, apnea, hypercarbia, hypoventilation	Lethargy, slow, deep breaths	Lung exam	ABG to assess pH and $PaCO_2$
HEPAT	Hepatitis induced with preexisting liver disease	RUQ pain	Abdominal exam	ALT, AST, alk phos, total bilirubin
GI	N/V	N/V	Abdominal exam	
CNS	Mental status changes, dizziness, headache	Mini-mental status exam	Neuro, HEENT exam	
PSYCH	Abuse, diversion, addiction	Inappropriately using, selling	Psychological exam	Urine drug screen, pill counts

Key References: Lutfy K, Cowan A: Buprenorphine: a unique drug with complex pharmacology, *Curr Neuropharmacol* 2(4):395–402, 2004; Sen S, Arulkumar S, Cornett E, et al.: New pain management options for the surgical patient on methadone and buprenorphine. *Curr Pain Headache Rep* 20(3):16, 2016.

Perioperative Implications

Preoperative Concerns
- Periop pain management
- If pt is taking buprenorphine prior to surgery, higher doses of opioids required to manage pain.
- If pt stopped buprenorphine 72 h prior to surgery, opioid dosing may be more manageable.
- Can cause neonatal abstinence syndrome, so watch for acute opioid withdrawal.

Adjuvants/Regional Anesthesia/Reversal
- Utilize nonopioid adjuvants periop, such as neuropathic agents, anti inflammatories, IV acetaminophen, ketamine, and regional anesthetic options.
- Naloxone can be used to reverse buprenorphine, but because buprenorphine has a long duration of action, naloxone infusion is recommended.

Drug Interactions
- CYP3A4 inhibitors can increase concentration of buprenorphine.
- CYP3A4 inducers can decrease concentration of buprenorphine.
- Administering pure agonist opioids while pt is on buprenorphine may not provide effective analgesia.
- Avoid alcohol.

Calcium-Channel Blockers

W. Scott Beattie | Duminda N. Wijeysundera

Uses
- Prescribed to treat Htn, angina, supraventricular arrhythmias, cerebral vasospasm, and HCM.

Perioperative Risks
- CCBs are used chronically in a significant proportion of the surgical population. CCBs are utilized in the treatment of Htn, CAD, or supraventricular arrhythmias and syndromes associated with vascular spasm. CCBs are recommended in combination with ACE inhibitors for diabetic pts with Htn. This class of drug effectively decreases myocardial O_2 demand through its effects on AV conduction, inotropy, and vasodilatation of systemic and coronary vasculature. The dihydropyridine class of CCB given as a single agent has been associated with tachycardia.

Worry About
- Hypotension: A meta-analysis of both cardiac and noncardiac RCTs shows a 50% increase in the incidence of unplanned periop hypotension.
- Neither RCTs nor nonrandomized trials have demonstrated an increased incidence of CHF or the need for inotropic support.
- AV nodal block or asystole has not been demonstrated; however, there is increased utilization of temporary cardiac pacing after cardiac surgery. Bradycardia requiring treatment has been demonstrated in a frequency similar to beta blockers.
- In both cardiac and noncardiac surgery, beneficial effects have been demonstrated; acute withdrawal can precipitate acute coronary ischemia.
- One large nonrandomized study has associated dihydropyridines with increased mortality.
- Neither meta-analyses nor nonrandomized trials have demonstrated any hematologic effects.

Overview/Pharmacology
- Ca^{2+} channels: Functional pores in cardiac and smooth muscle cell membranes allow calcium to flow down an electrochemical gradient. Channels are also present in sarcoplasmic reticulum and mitochondria. Calcium is a primary generator of the cardiac action potential and intracellular events regulating muscular contraction.
- Calcium enters through voltage-dependent or receptor-operated channels. Most of the effects of calcium channel blockers are regulated by components of the L (long-lasting) type receptor.
- Amlodipine is the most widely prescribed calcium channel blocker; has a half-life of 30–50 hr and bioavailability of 60–90%; it is predominately metabolized to inactive metabolites and excreted in urine.
- Verapamil: 90% absorbed PO, 20-35% bioavailability, onset of action 2 h, peak effect of IV/PO 3-4 h, 85% eliminated by first-pass hepatic metabolism with elimination T½ 3-7 h; IV effects almost immediate.
- Diltiazem: 89–90% PO absorption,40–70% bioavailability, PO onset of action <15 min, peak effect 30 min, 60% metabolized by liver, remainder excreted by kidneys, $T_{½}$ 3.5–6.0 h.
- Bepridil: >90% absorption, >80% bioavailability, PO onset of action 2–3 h, peak effect within 8 h, hepatic elimination with $T_{½}$ 26–64 h.
- Hepatic disease may necessitate decreased dosing of verapamil and other CCBs.

Drug Class/Mechanism of Action
- Four classes of CCBs:
  - 1,4 dihydropyridine (e.g., amlodipine, nifedipine, nicardipine).
  - Phenylalkylamines (e.g., verapamil).
  - Benzothiazepines (e.g., diltiazem).
  - Diethylaminopropylamine ether (e.g., bepridil).
- Mechanisms of action: Amlodipine—blockade of a voltage-dependent L-type inactive Ca^{2+}-channel receptor that has recently undergone activation and cannot open; the other three classes bind to specific receptors within the L-type channels.
- The dose of a CCB (e.g., nicardipine, diltazem, verapamil) used periop should be titrated to effect.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Ischemic protection, myocardial depression, vasodilation, AV conduction slowing	Short-acting nifedipine should be avoided due to risk of reflex tachycardia	Hypotension, bradycardia	BP measurement, ECG, ECHO for ventricular contractility
CNS	Cerebral vasodilation and decreased vasospasm; there is no indication of increased stroke in clinical studies	Ongoing assessment of neurologic status in pts at risk for vasospasm	Changes in neurologic assessment	Cranial Doppler or angiogram
NEURO	Potentiation of NMB	Increased risk of aspiration if extubated with residual block	Prolonged block	Use of NMB monitor
ENDO	Nifedipine delays insulin release and decreases serum glucose in DM; diltiazem has no effect on insulin, glucagon, growth hormone, or cortisol levels	Better glucose control in DM pts on nifedipine	Blood glucose	

Key References: Wijeysundera DN, Beattie WS, Rao V, et al.: Calcium antagonists reduce cardiovascular complication after cardiac surgery: a meta analysis, *J Am Coll Cardiol* 41(9):1496–1505, 2003; Wijeysundera DN, Beattie WS: Calcium channel blockers for reducing cardiac morbidity after noncardiac surgery: a meta-analysis, *Anesth Analg* 97(3):634–641, 2003; Kertai MD, Westerhout CM, Varga KS, et al: Dihydropiridine calcium-channel blockers and perioperative mortality in aortic aneurysm surgery, *Br J Anaesth* 101(4):458–465, 2008.

Perioperative Implications

Preoperative Concerns
- There is little evidence to advocate for continuation or withdrawal of chronic CCBs periop.
- Careful assessment of baseline hemodynamic variables
- Drug interactions: Verapamil increases digoxin levels
- Drug interactions: Inhibition of CYP3A4 markedly increases bioavailability of some CCBs and increases the risk of an adverse drug reaction.

Monitoring
- Routine.
- Pacing capability if associated AV block or CHF.
- Arterial line if BP instability likely.

Airway
- No special concerns

Preinduction/Induction
- Assess hemodynamics and ECG before induction.

Maintenance
- Volatile anesthetics may potentiate vasoactive effects.
- Effects of CCBs can be antagonized by administration of calcium or other pressor agents.

Extubation
- There is a potential for incomplete reversal of NMBs owing to interaction with CCBs on the postsynaptic membrane and blockade of Ca^{2+} channels in skeletal muscle. Check TOF if using NMBs.

Anticipated Problems/Concerns
- Hypotension
- Bradycardia
- AV nodal block and the increased use of temporary pacemakers
- Potential for paradoxical aggravation of myocardial ischemia due reflex sympathetic stimulation and tachycardia

Capsaicin

Jason L. McKeown

Uses

- Topical analgesic treatment for diabetic polyneuropathy, postherpetic neuralgia, and other peripheral neuropathic pain; also for osteoarthritis, rheumatoid arthritis, and other painful disorders
- Spray used as nonlethal force by law enforcement

Perioperative Risks

- None reported.
- After exposure to aerosolized capsaicin (e.g., in a trauma pt restrained by police), airway irritability, coughing, and bronchospasm may occur.

Overview/Pharmacology

- Topical effects only since very poorly absorbed from the skin

Drug Class/Mechanism of Action/Usual Dose

- Analgesic; 8-methyl-N-vanillyl-noneamide, an agonist of temperature-sensitive TRPV1.
- Selective binding to afferent nociceptive C fibers in the skin causes neuronal excitation and the release of substance P.
- Repeated application to the skin depletes C fibers of substance P and calcitonin gene–related peptide, which subsequently reduces sensitivity to pain.
- Reversible degeneration of small nerve fibers in the epidermis occurs with long-term use.
- Various creams and patches are available over the counter in a wide range of strengths as low as 0.025%.
- 8% capsaicin patch is approved in Europe for treatment of peripheral neuropathic pain. In USA, it is approved only for postherpetic neuralgia. Treatment is given in a series of 30–60-min applications.

Drug Effects

System	Effect	Assessment by Hx	PE	Test
DERM (topical)	Burning sensation at site, possibly also redness	Hx of chronic pain	Thermal allodynia at site, or hypesthesia at site of application	
HEENT (topical or inhaled)	Lacrimation, blepharospasm	Accidental exposure of topical agent to the eye; exposure to aerosol in confrontation with law enforcement	Eye exam	
RESP (inhaled)	Extreme airway irritability, coughing and bronchospasm, possibly death with heavy exposure	Exposure to aerosol in confrontation with law enforcement or in industrial accident	Auscultation, pulse oximetry	

Key References: Burness CB, McCormack PL: Capsaicin 8% patch: a review in peripheral neuropathic pain, *Drugs* 76(1):123–134, 2016; Knotkova H, Pappagallo M, Szallasi A: Capsaicin (TRPVI agonist) therapy for pain relief, *Clin J Pain* 24(2):142–154, 2008.

Perioperative Implications

- None known

Drug Interactions

- None known

Anticipated Problems/Concerns

- Moderate efficacy in chronic pain syndromes that have an anatomically superficial and localized pain generator.
- Compliance is poor because of burning pain with application.
- Topical or regional anesthesia is necessary for application of high-dose 8% concentration.

Carbamazepine–Oxcarbazepine

Christophe Aveline

Uses

- Synthesized in 1953, introduced for trigeminal pain in 1962 and for epilepsy in 1965; approved by the USA FDA since 1976 for the following:
  - Epilepsy: Generalized tonic-clonic seizures, partial seizures with complex pathology (psychomotor, temporal), partial seizures with or without generalization, mixed generalized and partial seizures
  - Chronic pain: Pain associated to trigeminal and/or glossopharyngeal neuralgia
  - CNS disorders: Acute or mixed episodes associated with bipolar I disorder
  - Off-label uses: Central and diabetic neuropathic pain; postherpetic neuralgia, phantom limb pain, alcohol withdrawal, preventing relapse in pts with bipolar disorders having a resistance or intolerance to lithium, treatment of manic or hypomanic excitation states, schizophrenia
  - Oxcarbazepine (OXC): 10-keto derivative of carbamazepine (CMZ), FDA-approved since 2000 as adjunctive therapy for partial seizures in adults and children >4 y and as monotherapy in adults for partial seizures

Perioperative Risks/Worry About

- Pharmacologic: Clinically significant drug interactions
- CNS: Increased sedation, dizziness, and ataxia
- CV: Aggravation of Htn, hypotension, CAD, arrhythmias, and rarely AV block
- Laboratory: Higher incidence of hyponatremia, aplastic anemia, agranulocytosis, thrombopenia and leukopenia, as well as elevated LFTs and hypothyroidism

Overview/Pharmacology

- The main activated form is the carbamazepine-10, 11 epoxide after transformation by hepatic CYP3A4 and CYP2C8.
- Peak plasma concentrations: tablet 2–6 h after ingestion, suspension 1.5 h, extended release 26–96 h. Bioavailability 85–100%, no gender differences, highly lipophilic, protein binding 70–80%, apparent volume of distribution: 0.8–1.5 L/kg. CMZ crosses the placental barrier and passes into breast milk, where it is half as concentrated.
- Hepatic biotransformation 98%. $T_{½}$: 10–20 h after 1 dose, 4–12 h after repeated administration (transcriptional upregulation of its own metabolism occurring from day 5 and stabilized between 3–5 wk). SNP in CYP450, in microsomal epoxide hydrolase, in ABCB1 and ABCB2 and Na_V are involved in the variation of metabolism of CMZ.
- Mainly metabolized by the CYP3A4 and CYP2C8, others CYP-involved are CYP2B6, CYP3A5, EPHX, and UGT2B7.
  - Inhibitors of CMZ: Aprepitant, erythromycin, clarithromycin troleandomycin, verapamil, diltiazem, ketoconazole, fluconazole, itraconazole, voriconazole, acetazolamide, ticlid, nefazodone, valproate, fluvoxamine, fluoxetine, trazodone, olanzapine, loratadine, terfenadine, omeprazole, oxybutynin, dantrolene, and grapefruit juice
  - Inducers of CMZ: Glucocorticoids, rifampicin, cotrimoxazole, ritonavir, sertraline, felbamate, cisplatin, doxorubicin, phenytoin, phenobarbital, theophylline, and CMZ autoinduction
  - CMZ decreases the plasma concentration of valproic acid, lamotrigine, phenytoin, felbamate, tiagabine, ethosuximide, aripiprazole, lapatinib, itraconazole, tramadol, protease inhibitors, dicumarol, doxycycline, levothyroxine, tricyclic antidepressant, cyclosporine, felodipine, aminosteroid NDMB (pancuronium, vecuronium, rocuronium), and benzodiazepines (interactions compensated by the antiepileptic effect of the added molecule and inductor/inhibitor effects of added molecule). Gabapentin, pregabalin, and levetiracetam are not affected by CMZ. CMZ reduces ethinyl estradiol and progestagen concentrations on the order of 50%.
  - OXC: Prodrug converted into active metabolite (S-licarbazepine) in liver by reductase; apparent volume of distribution 49 L, low protein binding fixation (40%), T_{max} 3–13 h, $T_{1/2}$ 7–20 h (for the active compound); steady-state 2–3 d; fewer drug-drug interaction (reduced impact on CYP450 system, $CYP2C19^{2+}$, $CYP3A4/5^{+}$), decreased dihydropyridine calcium antagonist and oral contraceptive

Side Effects

- Neurologic:
  - Very common: Dizziness, ataxia, drowsiness, fatigue (particularly in elderly)
  - Common: Headache, diplopia, accommodation disorders
  - Uncommon: Tremor, dystonia, orofacial dyskinesias, nystagmus
  - Rare: Oculomotor disturbances, ataxia, speech disorders, agitation, convulsion, suicidal behavior
  - Very rare: Neuroleptic malignant syndrome, dysgeusia, aseptic meningitis
- Respiratory:
  - Rare, pulm hypersensitivity usually associated with eosinophilia and systemic syndrome

- CV:
  - Negative chronotropic and dromotropic effects (above upper therapeutic level), reduced rise and amplitude on the AP in Purkinje fibers in atrial and ventricular myocardial cells
  - Sinus bradycardia, sinoatrial block, and AV block. Hypotension, vasoplegia (poisoning), pulm embolism, CAD and CHF, lymphedema and adenopathy. Very rarely: myocarditis
- Hematologic:
  - Rare: Leukopenia, thrombocytopenia, pancytopenia, hypogammaglobulinemia. Eosinophilia (aromatic structure associated with DRESS), more frequent in the presence of *HLA-A*3101* allele in European, Japanese, and Chinese pts.
  - Very rarely: Pancytopenia, agranulocytosis, variegate porphyria, acute intermittent porphyria
- Dermatologic:
  - More common: Maculopapular rash, urticarial, erythema multiforme, and lupus
  - Rare: Toxic epidermal necrolysis and Stevens-Johnson syndrome (10 times higher in Thai or Han Chinese pts with the *HLA-B*1502* allele). Known sensitivity to one anticonvulsant may increase the risk of serious rash with another anticonvulsant.
- Metabolic:
  - Weight gain, hyponatremia (SIADH, alterations of renal tubular electrolytes transport, V2R-dependent and V2R-independent ways with increased permeability by AQP2 expression, and resetting of osmoreceptors associated to renal impairment)
  - Increased T_4 and free T_4, increased TSH (particularly in children)
- GI:
  - Very common: N/V, dry mouth
  - Uncommon: Diarrhea, constipation
  - Rare: Abdominal pain
  - Very rare: Glossitis, stomatitis, and pancreatitis
- GU: Rare: Azotemia, renal failure, increased BUN, acute urinary retention, oliguria, erectile dysfunction
- Other:
  - Very rare: Allergy, conjunctivitis, leg cramps, hearing loss or hyperacusis, tinnitus
  - OXC: 25–35% crossed-hypersensitivity reaction with CMZ; hyponatremia possible but less; SJS and epidermal necrolysis very rare

Contraindications

- High degree of atrioventricular block
- Known hypersensitivity to CMZ or to any of the excipients or to tricyclic antidepressants
- Previous bone marrow suppression
- Acute intermittent porphyria, variegate porphyria, porphyria cutanea tarda
- Coadministration with telaprevir, voriconazole, nefazodone, *Hypericum perforatum*, MAO inhibitors

Acute Toxicity

- Lowest lethal doses: 3.2 g in adults and 1.6–4 g in children
- Peak levels delayed up to 96 h after massive ingestion of controlled-release forms. Clinical signs: Ataxia, nystagmus, mydriasis, movement disorders and anticholinergic syndrome, seizures and coma, hypotension, respiratory depression; decreased natremia, kalemia, and glycemia. Use diazepam or phenobarbital for seizures. Conventional cardiovascular and respiratory life support, charcoal-HP through gastric lavage, hemodialysis or hemoperfusion (rarely).

Drug Class/Mechanism of Action/Usual Dose

- Iminostilbene derivative (5H-dibenzazepine-5-carboxamide) blocks the IV-S6 transmembrane segment of the Na_V, prolongs the inactivated state (in a use- and frequency-dependent manner), blocks Na currents faster and in a concentration-dependent manner during high-frequency depolarization. Domains IV-S6 mutations are described, which lowers the affinity and activity of various Na_V blockers such as CMZ.
- Antihyperalgesic: Decreases presynaptic voltage-gated Ca channels, decreased presynaptic and post-synaptic NMDA, AMPA- and kainite-mediated inward currents. Modulation of central and peripheral adenosine receptors, α2a and α2c adrenoreceptors and P2X4 receptors of astrocytes. CMZ enhances synaptic protein activity and dendritic outgrowth, decreased pro-apoptotic Bcl-2 in neural cells, downregulates the arachidonic acid signaling and cascade in cerebral neurons via the NMDA and dopamine D2 signals.
- Available only orally as normal, chewable, and extended-release tablets and suspension
- Usual dose:
  - Epilepsy disorders: Adults and teenagers >15 y: maximal daily dose <1200 mg/24 h; children 6–12 y: <1000 mg/24 h; children <6 y: <35 mg/kg per 24 h
  - Trigeminal pain: 400–800 mg/d (<1200 mg/d); relapse prevention (bipolar disorders): 400–800 mg/d; treatment of manic or hypomanic excitation states: 600–1200 mg/d
  - Blood level for seizures disorders: 4–12 μg/mL; for trigeminal neuralgia: 5–18 μg/mL
- OXC:
  - Prodrug, reduced into active metabolite 10-hydroxy CBZ (MHD), 80% of S and 20% of R enantiomers of licarbazepine (ratio 4:1), S-licarbazepine in the main active metabolite in the CNS
  - Reduced impact on CYP450 system ($CYP2C19^{2+}$, $CYP3A4/5^{+}$), lower incidence of agranulocytosis and bone marrow depression while having similar seizure control. Same recommendation as CMZ for *HLA B*1502* testing. HypoNa 2.8% (risk factors: old age, polytherapy, diuretic use).

Drug Effects

System	Effect	Assessment by Hx	PE	Test
CV	Heart failure AV/sinoatrial block	Dyspnea, pulm edema Palpitations, bradycardia	Auscultation	X-ray, ECHO, BNP ECG
CNS	Sedation, confusion	Concomitant AED	Clinical assessment	
METAB	Hyponatremia SIADH-like hypothyroidism	Edema, drowsiness Wt gain Weakness, constipation, hair loss	Oliguria	Decreased Na, decreased serum osmolality, increased U_{na}/U_{crea}, increased U_k/U_{crea}, increased U osmolarity Increased TSH, decreased T_3, decreased free T_4
HEME	Anemia/aplasia Thrombocytopenia	Pallor Petechiae, bleeding	Clinical assessment Clinical assessment	CBC CBC
RENAL	Renal insufficiency	Edema Dyspnea	Azotemia, Acute oliguria	Cr, GFR, BUN, ABG
RESP/ DERM	Pneumonitis SJS-TEN	Pulm hypersensitivity Bullous rash	Clinical assessment Clinical assessment	X-ray, ECHO, *HLA-A*3101* screening Skin biopsy, *HLA B*1502* screening

Key References: Richard A, Girard F, Girard DC, et al.: Cisatracurium-induced neuromuscular blockade is affected by chronic phenytoin or carbamazepine treatment in neurosurgical patients, *Anesth Analg* 100(2):538–544, 2005; Yang YC, Huang CS, Kuo CC: Lidocaine, carbamazepine, and imipramine have partially overlapping binding sites and additive inhibitory effect on neuronal Na^+ channels, *Anesthesiology* 113(1):160–174, 2010.

Perioperative Implications

Preoperative Concerns

- CMZ must be continued, taken early in the morning in preop period, withdrawal can be associated with seizure and periop hyperalgesia.
- Functional evaluation, safety, and effectiveness of CMZ; previous systemic syndrome; determination of all other treatment, particularly neurologic, psychiatric, and cardiovascular drugs.
- Genetic screening for *HLA-A*3101* in European, Japanese, and Chinese pts and for *HLA B*1502* in Thai or Han Chinese pts usually proposed prior initiation therapy.
- Check the last blood level of CMZ (4–18 μmol/mL), taking into account the equilibration period and auto-induction by CMZ at the beginning of treatment.
- ECG for arrhythmias, AV block including second- and third-degree block, ischemic changes.
- Check lab tests:
  - Leukocytes, plts
  - Liver enzymes
  - Natremia in case of major surgery when other hyponatremia-induced drugs are associated with CMZ, surgery needing osmotherapy
  - Glomerular filtration rate (CKD-epinephrine [EPI]), BUN
  - TSH

Induction/Maintenance

- Be vigilant for arrhythmias, arterial hypotension or hypotension, and cardiac ischemia when using cardiodepressive drugs concomitantly.
- Use of propofol or thiopental possible. Both inhibit GABA and Na channels. Low dose of ketamine (high $GABA_A$ receptors potentiation, anti-NMDA effects) not contraindicated. No data for continuous IV lidocaine and CMZ. Etomidate should be avoided in epileptic pts.

- All NDMBs must be monitored from induction of anesthesia to emergence. Loading doses are not affected but maintenance dosing needs monitoring. Decreased potency and duration of aminosteroid NDMBs (rocuronium, vecuronium, and pancuronium) by PK/PD interaction, an increase in hepatic metabolism/biliary excretion, upregulation of acetylcholine receptors, and clearance. No impact on onset of NDMBs. Mivacurium and atracurium not concerned. No association between epileptic status, CMZ, and laudanosine. Faster recovery of neuromuscular block and more rapid speed of infusion with cisatracurium.
- Decreased blood level of midazolam (CTP3A4 induction); reduction of propofol concentration (common metabolic pathway CYP3A4, CYP2C8, and CYP2B6)
- No impact on sufentanil (total clearance > hepatic clearance) and remifentanil (esterase-dependent metabolic pathway not affected by CYP450). Higher dose of fentanyl needed (strongly catalyzed by CYP3A4). Combine objective assessment of analgesia (pupillometry or ANI) to usual hemodynamic variations to improve effective dosage. Morphine can be used without specific modification. CMZ decreases morphine-3-glucuronide-induced enhancement of $Na_v1.7$, and the combination of CMZ-morphine reverses late tactile allodynia in a neuropathic model of pain. No increase of morphine-induced hypercapnia/hypoventilation.
- CMZ decreases bioavailability of paracetamol. Short-term prescription of paracetamol with daily dose <4 g/d; risk of hepatotoxicity among long-term user of paracetamol, <3 g/d in adult. Ibuprofen can displace CMZ protein binding in uremic pt.
- PNB with recommended dose and performed under US is safe in CMZ pts. Lidocaine blocks the residue in the S6 segment of domain IV of Na_v with a lesser interaction with the S4 segment of domains III and IV (voltage sensor). A common site of binding for local anesthetics and CMZ was defined in the S6 segment. Lidocaine and CMZ produces an additive interaction on Na^+ ion passage. CMZ can induce the metabolism of lidocaine (CYP3A4 and CYP1A2 pathway and a high hepatic clearance). Ropivacaine and levobupivacaine are hydrolyzed by CYP1A2 and less by CYP3A4. Beneficial effect of combined oral CMZ and repetitive peripheral nerve block in pts suffering from trigeminal neuralgia. Clinical signs associated with LAST can mimic some signs of a CMZ overdose. In cases of suspected LAST, check blood level of CMZ and LA, initiate basic and advanced life support and pharmacologic measures according guidelines. US required to reduce vascular puncture and to obtain analgesia with a reduced total dose of LA.
- Consider increased tendency to hyponatremia in urologic procedures or neurosurgery (preop use of hyperosmotic solutions)

Postoperative Period

- Keep in mind the possible hemodynamic effects (arrhythmias, arterial hypotension or hypotension, cardiac ischemia).
- Neuromuscular monitoring of NDMB in PACU to confirm complete recovery.
- Resume CMZ after surgery at preop dosage. Use caution when oral alimentation is not rapidly obtained or when hypovolemic status after major surgery. Plasma level of CMZ must be checked after resuming and side effects evaluated.
- Thromboprophylaxis for the postop period according guidelines (cumulative risk of surgery and treatment by CMZ).
- Oral hormonal contraceptives call for additional safety precautions.
- Watch for natremia in the postop period after major and/or urologic interventions, geriatric or noncommunicating pts, and when pts are taking diuretics.
- Arrhythmias and atrioventricular block associated with CMZ remain possible. ECG and blood tests (troponin, BNP) in case of cardiovascular instability or after major surgery in pts receiving beta-blockers, CCBs, antiarrhythmics, or antihypertensives.

Anticipated Problems/Concerns

- PK/PD of CMZ and impact on CYP450 system
- Blood level of CMZ, hyponatremia
- Use caution in geriatric pts (confusion)
- Monitoring of neuromuscular block required (particularly aminosteroid muscle relaxants)
- CV impact and thromboembolism risk
- Antihyperalgesic drug
- Additive interaction between CMZ and lidocaine

Chemotherapeutic Agents

Juan P. Cata | Marc A. Rozner

Risk

- Cancer is the second most common cause of death in USA. In 2016, about 1,685,210 pts will be diagnosed with cancer and 595,690 will die of it.
- More than two-thirds of all cancers are diagnosed in people 50 y of age or older. Prostate cancer is the most common among men, while breast cancer is the most frequent in women. In both genders, lung cancer is the leading cause of death due to cancer.

Uses

- Drugs or biological agents (interleukins and interferon) are commonly used to (1) stop cancer cells from proliferating, migrating, and invading and/or (2) facilitate their recognition by the immune system.
- Traditional chemotherapy agents, targeted chemotherapies, and immunotherapies are still front-line drugs for the treatment of solid and hematologic malignancies.
- Neoadjuvant (before surgery) chemotherapy (and possibly radiation) remains the treatment of choice for many solid cancers.

Perioperative Risks

- Intraop bleeding due to thrombocytopenia, postop infection, complications (leukopenias), blood transfusions (anemia).
- Cardiac insufficiency and fluid overload (due to cardiotoxic agents such as the anthracyclines). Pulm toxicities can lead to periop pulm edema.
- Acute kidney injury (nephrotoxic agents).
- Mononeuropathy (neurotoxic drugs). Bone demineralization (osteopenia) is a risk for fracture after inadequate pt positioning.

Classification According to Mechanism of Action

Class	Activity	Agents
Alkylating agents	Covalent binding to nucleic acids or proteins	Nitrogen mustards (cyclophosphamide, melphalan, chlorambucil) Aziridines (thiotepa and mitomycin C) Procarbazine, oxazaphosphorines (cyclophosphamide, ifosfamide) Alkyl alkane sulfonates (busulphan) Nitrosoureas (carmustine, bendamustine, lomustine) Tetrazines (dacarbazine, mitozolomide, temozolomide)
Antimetabolites	Competition with natural substrates for the active site	Pyrimidine analogues (fluorouracil, cytarabine, sapacitabine, gemcitabine) Purine analogues (6-mercaptopurine, thioguanine) Folic acid antagonists (methotrexate)
Spindle agents	(1) Vinca alkaloids: Binding to microtubules (assembly inhibition) (2) Taxanes: Binding to microtubules (assembly facilitation)	Vincristine, vinblastine Paclitaxel, docetaxel, abraxane Epothilones, discodermolide
Antibiotics	Alteration of function and synthesis of nucleic acids	Anthracyclines (derived from *Streptomyces*), most commonly doxorubicin, daunorubicin, and epirubicin (most generic names except mitoxantrone end with -rubicin), actinomycin D, bleomycin, mitomycin C, vosaroxin
Heavy metals	Platinum agents: Crosslink with DNA strands—inhibition of protein synthesis	Cisplatin, carboplatin, oxaliplatin
Topoisomerase inhibitors	Inhibition of DNA replication	Topoisomerase I inhibitors: Camptothecin, irinotecan, topotecan Topoisomerase II inhibitors: Epipodophyllotoxin derivatives, vosaroxin
Hormone receptors, antagonists, and hormonal agents	(1) Estrogen receptor antagonists (2) Aromatase inhibitors (block conversion of androgens to estrogens) (3) Androgen receptor antagonists (4) Gn-RH antagonist (5) LHRH agonists	(1) Tamoxifen (2) Anastrozole, letrozole, exemestane (3) Enzalutamide (4) Degarelix
Proteasome inhibitors		Bortezomib
Monoclonal antibodies and small-molecule inhibitors	Direct effects against receptors or signaling molecules	Anti-HER-2 antibody (trastuzumab), antiangiogenesis (bevacizumab, ramucirumab), anti-EFGR antibody (cetuximab), anti-bcr-abl antibody, anti-CD20 antibody (rituximab), anti-CD30 antibody (brentuximab), and anti-CD33 antibody (SGN-33, AMG-330) Tyrosine kinase inhibitors (gefitinib, erlotinib), PIK-1 inhibitors (volasertib), FLT3 inhibitor (sorafenib, midostaurin, quizartinib), JAK inhibitors (pacritinib), mTOR inhibitors (everolimus), aurora A kinase inhibitor (alisertib)
Histone deacetylase inhibitors CDK4-CDK6 inhibitors	(1) Selective of paninhibition of HDAC (2) Inhibition of DNA synthetic phase	Vorinostat, romidepsin, belinostat, mocetinostat, panobinostat Palbociclib, ribociclib, abemaciclib
Biological response modifiers		Interferon, interleukin 2 Anti-PD-1 antibodies (nivolumab, atezolizumab, pembrolizumab, pembrolizumab) CTLA-4 blocker (ipilimumab) Thalidomide, lenalidomide

Key References: Ai D, Banchs J, Owusu-Agyemang P, et al.: Chemotherapy-induced cardiovascular toxicity: beyond anthracyclines, *Minerva Anestesiol* 80(5):586–594, 2014; Sahai SK: Perioperative assessment of the cancer patient, *Best Pract Res Clin Anaesthesiol* 27(4):465–480, 2013.

Perioperative Implications

Preoperative Considerations

- Hematologic toxicities (anemia, neutropenia, and/or thrombocytopenia) are among the most common toxicities caused by chemotherapeutic agents. Mythramycin can cause significant bleeding disorders (thrombocytopenia plus depletion of factors II, V, VII, and X). Preop complete blood count is recommended to address the severity of anemia and thrombocytopenia. PT/INR and APTT should be indicated for pts who have received mythramycin before surgery. The administration of blood products is usually necessary in symptomatic pts and those at risk for spontaneous bleeding (<10,000 platelets/dL) or if regional anesthesia is being considered.
- Cardiovascular toxicities: Arterial Htn (ponatinib and VEGF inhibitors), pulm arterial Htn (dasatinib), CHF, acute vascular occlusive events (nilotinib), and increased risk of CAD and sudden death. QTc prolongation has been reported after the administration of targeted agents; therefore ECG is recommended in pts treated with drugs. Echocardiographic evaluation of pts who have been treated with anthracycline agents is recommended before and after treatment and unrelated to the need for surgery. B-type naturetic peptide measurement might be an adequate substitute (with omission of echocardiography with BNP <100 pg/mL) in an asymptomatic pt, although this issue has not been settled. Fluorouracil can cause coronary artery vasospasm during administration with symptoms, but whether or not these events represent true underlying CAD still remains in question. Nevertheless, a pt with a history of chest discomfort during 5FU administration should be evaluated by a cardiologist.
- Pulmonary toxicities such as unilateral or bilateral pleural effusions or parenchymal infiltrates are not unusual. Chest x-ray and drainage of effusions might be needed in symptomatic pts. Although supplemental oxygen therapy and possibly fluid administration can worsen the pulm toxicity associated with bleomycin, hypoxemia can be observed in pts treated with monoclonal antibodies, TKIs, and IL-2.
- Nephrotoxicities manifesting as mild proteinuria, nephrotic syndrome, interstitial nephritis, profound hypomagnesemia, and renal failure have been reported after drugs such as cisplatin (or any platin) and antivascular endothelial growth factors. Preop serum Cr concentrations and calculation of the GFR rate are necessary to identify the acute onset or worsening of chronic renal failure, which might require treatment before surgery.
- Electrolyte abnormalities and fluid retention usually manifest as fatigue, ECG abnormalities, wt gain, periorbital edema, and lower limb edema. Vincristine, vinblastine, melphalan, cyclophosphamide, cisplatin, and immunomodulator drugs (IL-2 and levamisole) can cause hyponatremia. All of the platins can induce a magnesium-wasting nephrotoxicity, although some reports categorize the risk to be cisplatin > carboplatin > oxaliplatin. Preop serum electrolyte determination and ECG evaluation might be indicated in symptomatic pts. Pleural or pericardial effusions and cerebral edema can be observed after treatment with TKIs. Echocardiographic evaluation and chest x-rays might be recommended to evaluate the magnitude and direct treatment of pts with symptomatic or large effusions. Tumor lysis syndrome (hyperkalemia, hyperphosphatemia, and metabolic acidosis) in pts with hematologic malignancies requiring surgery needs careful evaluation of the pt's hydration status and electrolyte imbalances.
- Gastrointestinal adverse events including nausea, vomiting, diarrhea, GER, and abdominal pain are commonly reported. Pancreatitis and elevation of liver enzymes should be considered in pts treated with targeted agents. Assessment of the severity of the GER is needed to initiate preop treatment with proton pump inhibitors or anti-H_2 histaminic drugs. In pts with liver transaminitis, the use of acetaminophen should be avoided.
- Neurologic toxicities include peripheral neuropathy (sensorineural and/or motor) and autonomic

dysfunction, especially after platin, vincristine, or vinblastine use. Posterior reversible leukoencephalopathy and stroke have been reported in pts treated with antiangiogenic agents. Cognitive impairment is commonly reported in women treated with tamoxifen.
- Endocrine adverse events, such as hyperglycemia in pts taking dexamethasone and abnormal thyroid function in those treated with targeted therapies, have been reported.
- Musculoskeletal symptoms include cramps, myalgia, bone pain, and arthralgias.
- Ophthalmologic complications such as blepharitis, keratitis, xerophthalmia, and corneal ulcerations have been reported in pts treated with targeted therapies. Nasolacrimal tear duct obstruction has been reported after paclitaxel, radioactive iodine administration, and external beam radiation to the head/neck area causing profound xerophthalmia.
- Dermatologic adverse events can range from mild skin rashes to panniculitis and Stevens-Johnsons syndrome. They can also result from graft-versus-host disease in pts who have undergone stem cell or bone marrow transplants. Mucositis and stomatitis are frequent with most chemotherapeutic agents as well as radiation to the head and neck. Wound healing can be affected after the use of bevacizumab.

Vascular Access
- Vascular fragility, venous sclerosing, and poor venous access are commonly seen in pts who have received multiple regimens of chemotherapy. The need for a peripheral inserted central venous catheter should be considered in the preop visit. Occasionally, preanesthesia placement of a central venous cath is required.

Airway
- Difficult ventilation or endotracheal intubation should be considered in pts receiving corticosteroids or who have undergone radiation to the head and neck. Pts with oral mucositis and thrombocytopenia are at risk for airway trauma and bleeding. Pts with ocular toxicities might be at risk for eye injuries during airway instrumentation.

Induction (General Anesthesia)
- Rapid sequence induction might be needed in pts with moderate to severe GER. Hyperkalemia should be considered in pts with renal failure or tumor lysis syndrome in whom rapid sequence induction is indicated. Careful titration of hypnotics such as propofol is recommended in pts who have received cardiotoxic agents. Pts with autonomic dysfunction (due to taxanes) can develop significant arterial hypotension during induction of general anesthesia. Prolonged muscle relaxation after succinylcholine can be seen in pts treated with cyclophosphamide (inhibition of pseudocholinesterase). Dehydration should be considered in pts with protracted vomiting and diarrhea; therefore intravascular volume replacement and careful induction of general anesthesia is warranted in these pts.

Maintenance (General Anesthesia)
- Careful titration of anesthetic agents, analgesics, and muscle relaxants is recommended in pts treated with procarbazine, thalidomide, and muscle-wasting chemotherapies such as vincristine. Pulm edema can occur after aggressive fluid resuscitation in pts treated with agents such as IL-2, cardiotoxic drugs, or bleomycin and can complicate assessment and replacement of the intravascular volume where indicated in pts treated with nephrotoxic agents.

Positioning
- Careful positioning should be considered in pts with mononeuropathies or polyneuropathies, alopecias, skin bruises, blisters, and osteopenias. Pts with ocular toxicities need proper care of the eye to diminish the risk of corneal abrasions.

Regional Anesthesia
- Thrombocytopenia (due to myelosuppressive drugs), coagulopathy (associated with Mythramycin), and the presence of mononeuropathy or polyneuropathy might contraindicate the use of regional anesthesia.

Postoperative Period
- NSAIDs and acetaminophen should be used carefully in pts treated with nephrotoxic (cisplatin) and hepatotoxic (mithramycin, L-asparaginase) agents and targeted therapies. Cognitive impairment should be taken into consideration in pts treated with tamoxifen.
- Monitoring of hemodynamics and fluid status can be complicated in pts who have received anthracyclines and targeted chemotherapeutic agents that can possibly induce myocardial dysfunction, especially under high workload stress, which cannot be predicted by coronary artery evaluation (such as an adenosine-nuclear perfusion test) where coronary workload reserve has been compromised but coronary anatomy remains intact. Drugs that affect alveolar vascular permeability (such as bleomycin) can also complicate postop hemodynamic management, especially in the face of profound periop blood loss with resuscitation.

Hyperthermic Intraoperative Chemotherapy
- Complex surgical procedure involving extensive peritoneal stripping, tumor debulking, multiple visceral resections, and the delivery of high-dose hyperthermic chemotherapy to the abdominal cavity. Adequate fluid resuscitation is needed, particularly when cisplatin (risk of nephrotoxicity) is used. The need for fluid status monitoring can persist well into the postoperative period.

Cilostazol

C. David Mazer | Niamh McAuliffe

Uses
- Phosphodiesterase inhibitor with antiplatelet aggregation and arteriolar vasodilator properties.
- Prescribed for intermittent claudication in pts with peripheral arterial disease.
- Lowers restenosis rates after peripheral endovascular procedures in Asian populations.
- Secondary prevention of cerebral infarction with less hemorrhagic conversion than aspirin in Asian populations.
- Use has been limited by tolerability due to high incidence of side effects.

Perioperative Risks
- Plt dysfunction
- Unknown effect on periop blood loss
- Drug interactions
- Tachycardia

Overview/Pharmacology
- 6-[4-(1-cyclohexyl-1*H*-tetrazol-5-yl) butoxy]-3,4-dihydro-2(1*H*)-quinolinone
- Pharmacodynamics:
  - Antiplatelet effect: Strong and specific reversible inhibitor of PDEIII, which increases cAMP in plts, smooth muscle, myocytes, and adipose tissue. This decreases thromboxane A2 production and inhibits plt, aggregation.
  - Reversible plt, inhibition, with duration of up to 12 h. Recovery of plt function 48–96 h after drug cessation with no rebound increase in plt aggregation.
  - Vasodilatation: It targets PDE3 in smooth muscle cells resulting in vessel relaxation.
  - Antiproliferative effect: Increased cAMP upregulates antioncogenes P53 and P21 and hepatocyte growth factor, which induces apoptosis in vascular smooth muscle and inhibits smooth muscle proliferation in vascular beds.
  - Anti atherosclerotic: Alters monocyte chemoattractant protein-1, which recruits monocytes to atherosclerotic lesions.
- Pharmacokinetics:
  - Absorption: Dose—100 mg twice daily to reduce stent restenosis in cardiac patients. Oral administration with peak plasma concentration at 2 h. Steady state is achieved within 4 d. Dietary fat increases absorption and max concentration with potential toxic effects, therefore administer 30 min before or 2 h after meals.
  - Distribution: Cilostazol is 95–98% protein-bound, predominantly to albumin.
  - Metabolism: Hepatic metabolism by cytochrome p450 pathway giving rise to potential drug interactions. Hepatic metabolism involves CYP3A4 (major), CYP1A2 (minor), CYP2C19 (major), and CYP2D6 (minor). There are two major metabolites, the dehydrometabolite is 4–7 times as active as a plt inhibitor and the 4′-trans-hydroxy metabolite is one fifth as active.
  - Excretion: Excretion is predominantly renal, with 74% of metabolites in urine. The elimination half-life is 11–13 h.
- Clinical:
  - Peripheral arterial disease: Approved by the USA FDA for treatment of intermittent claudication because of the drug's ability to decrease plt function and increase vasodilation. Modest improvement in initial claudication distance as compared with placebo (31.41 meters, 95% CI 22.38–40.45 meters). Indicated when lifestyle changes and other therapies have not provided adequate benefit. No evidence of mortality benefit. Has been shown to reduce restenosis and reocclusion rates after peripheral endovascular procedures. May result in lower in-stent stenosis rates after carotid artery stenting.
  - Cerebrovascular disease: Shown to be noninferior to aspirin in secondary stroke prevention in a large RCT in an Asian population, with fewer bleeding events compared with aspirin. May have a role in prevention of intracranial arterial stenosis.
  - Cardiac disease: No reduction in MACE or mortality. Has been associated with a reduction in in-stent restenosis after coronary stent placement in some pt populations. No significant increase in bleeding noted; however, caution advised when used with aspirin or clopidogrel. Genetic polymorphisms in CYP2C19 reduce effectiveness of clopidogrel; this does not seem to be the case with cilostazol, making it a potential option in cases of "clopidogrel resistance." Cilostazol is contraindicated in pts with CHF because of its mechanism of action as a phosphodiesterase enzyme III inhibitor; also contraindicated in pts with moderate to severe renal or hepatic dysfunction. Contraindicated in pts with

hemostatic disorders or active pathologic bleeding. Caution advised in pts with a recent ACS/PCI or history of severe tachyarrhythmia.
  - Plasma lipids: Has been shown to decrease triglycerides by 15% and increase HDL cholesterol by 10%
- Drug interactions:
  - Dose reduction: Required with medications metabolized by cytochrome p450 pathway. CYP3A4 and CYP2C19 inhibitors may increase cilostazol levels and require dose reduction to 50 mg (e.g., erythromycin, clarithromycin, ketoconazole, diltiazem, statins, cisapride, ergot, omeprazole).
  - Dose increase: Caution with CYP3A4 and CYP2C19 inducers such as statins, which may decrease cilostazol plasma concentration. Smoking (which induces CYP1A2) has been shown to decrease cilostazol plasma concentrations by 18%.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Increased HR and palpitations Decreased BP Increased HDL cholesterol Decreased TG Worsens class 3-4 CHF	Avoid if Hx of severe tachyarrhythmia, ACS, or PCI in last 6 mo, class III-IV heart failure	Two-flight walk, Signs of CHF.	ECG ECHO
PVS	Arteriolar vasodilatation	Walking distance	Peripheral pulses	Ankle-brachial pressure index
GI	GI upset	Diarrhea, bloating		
HEPAT	Metabolized by cytochrome P450 with active metabolites	Hepatic failure, nausea, anorexia	Jaundice	ALT, AST, albumin, bilirubin
RENAL	Renal excretion; mot removed by dialysis	Severe renal insufficiency		CrCl <25 mL/min
HEME	Plt dysfunction Agranulocytosis	Temp, sore throat Hx of hemostatic disorders	Evidence of thrombocytopenia	CBC No effect on PT, APTT, INR
CNS	Headaches, dizziness, vertigo			

Key References: Rogers KC, Oliphant CS, Finks SW: Clinical efficacy and safety of cilostazol: a critical review of the literature, *Drugs* 75(4):377–395, 2015; Gogarten W, Vandermeulen E, Van Aken H, et al.: Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology, *Eur J Anaesthesiol* 27(12):999–1015, 2010.

Perioperative Implications

Preoperative Concerns

- Discontinue 2–5 d before surgery depending on type and anticipated blood loss. Limited data available on risk of preop surgical bleeding and no standard guidelines available.
- Discontinue 2 d (>42 h according to European Society of Regional Anaesthesia guidelines) before neuraxial or regional anesthesia. Avoid indwelling cath while pt is taking cilostazol.
- Preop: CBC, ECG. No effect on INR/APTT.
- Emergency surgery: No reversal agent. Consider plt transfusion.
- Plt function assessment can be done using cytometry, aggregatory, or point-of-care P2Y12 assays. Thrombin generation does not appear to be affected by cilostazol; therefore no evidence that TEG/rotational thromboelastometry are suitable for monitoring.

Induction/Maintenance

- Positive inotrope and chronotope in pts prone to tachyarrhythmias.
- May cause hypotension due to arteriolar vasodilation.

Postoperative Period

- Restart regular dose 24 h postop.
- Wait at least 5 h after regional/neuraxial cath removal to restart dose.

Anticipated Problems/Concerns

- Inhibitor of plt aggregation with increased risk surrounding regional anesthesia and invasive monitoring
- Caution in pts with heart failure, tachyarrhythmias, hemostatic disorders, renal or hepatic dysfunction, or concomitant administration of CYP3A4 or CYP2C19 inhibitors
- Predominantly studied in Asian populations; more studies required to extrapolate findings to broader population

Cocaine

Zeev N. Kain | Navid Alem

Uses

- Cocaine (benzoylmethylecgonine) is a commonly abused stimulant drug isolated from leaves of the coca plant (*Erythroxylon coca*).
- Administered IV, to mucosa, "snorted," or smoked ("crack"); lipophilic and crosses BBB.
- Extremely addictive; 5 million Americans are regular users and 30 million have tried it at least once (2012 National Survey on Drug Use and Health).
- Drug that is most commonly associated with mortality.

Perioperative Risks

- Hemodynamic instability, increased sympathetic discharge
- Myocardial ischemia: supply/demand imbalance
  - Increased myocardial O_2 demand (increased HR, BP, and LV contractility)
  - Decreased myocardial O_2 supply (increased endothelin and decreased NO, resulting in coronary vasoconstriction)

Worry About

- CV: Htn, tachycardia, dysrhythmias, MI, cardiomyopathy, premature coronary atherosclerosis, LV hypertrophy, sudden cardiac death, aortic dissection
- Neurologic: Intracerebral bleed, seizures, euphoria, delusions, hallucinations, coma
- Pulmonary: Pneumomediastinum, cocaine-induced asthma, hypersensitivity pneumonitis, chronic cough, pulm edema, abnormal diffusing capacity, perforation of nasal septum
- OB: Placenta previa, abruptio placentae, premature labor, fetal distress or demise

Overview/Pharmacology

- Cocaine is an ester local anesthetic and sodium channel–blocking drug; it is a class I antiarrhythmic agent.
- Blocks presynaptic reuptake of norepinephrine, dopamine, and serotonin, resulting in activation of the SNS. Note: Does not release catecholamines.
- Accumulation of dopamine in the synaptic cleft may lead to acute euphoria, increased alertness, and out-of-body experiences.
- The USA FDA approves cocaine 4% topical solution as a local anesthetic to be used on mucous membranes. Cocaine is useful for ENT surgery and awake fiberoptic intubation (dosage not to exceed 1-3 mg/kg).

Etiology

- Cocaine abuse
- Iatrogenic: OD during ENT surgery; ER use (part of tetracaine, epinephrine, cocaine mix)

Usual Treatment

- Supportive
- Myocardial ischemia induced by cocaine should be treated initially with O_2, sublingual aspirin, and benzodiazepines. If there is ongoing myocardial ischemia, use of nitroglycerine, verapamil, or phentolamine to reverse cocaine-induced coronary vasoconstriction may be necessary.

- Consider urgent coronary angiography in clinical setting of acute chest pain with evidence of myocardial ischemia.
- Treat hyperthermia promptly as it increases cardiac demand.
- Beta-blockers may worsen coronary vasoconstriction (because unopposed alpha agonism remains) and should be used with great caution if pt presents with signs of ischemia or acute cocaine toxicity.
- In management of short-lived arrhythmias, drug treatment should be avoided if possible, as antiarrhythmic agents and cocaine may cause a synergistic depression of contractile function.
- For sustained hemodynamically tolerated SVT associated with AV nodal reentry, adenosine is safe and free of major side effects. If adenosine is unsuccessful, administration of an α-antagonist and a beta-blocker in combination is likely to be both safe and effective. No reliable information on the safety and efficacy of other antiarrhythmic drugs.
- Supraventricular or ventricular tachyarrhythmias associated with hemodynamic compromise require urgent DC cardioversion.
- Avoid use of reversal agents including flumazenil or naloxone, because these may further precipitate cardiac dysrhythmia and autonomic instability.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, MI, dysrhythmias, myocarditis, cardiomyopathy, aortic dissection, endocarditis, premature coronary atherosclerosis, prolonged QT	Exposure Chest pain Palpitations	BP/HR Murmur	ECG ECHO CK-MB, troponins I and T
RESP	Pneumomediastinum, bronchoconstriction, pneumothorax, diffuse alveolar hemorrhage, pulm edema	Exposure Hemoptysis SOB	Wheezing Rales	CXR
HEME	Thrombocytopenia, enhanced platelet aggregation promoting thrombus formation	Bleeding problems, vasoconstriction		Plts
OB	Preterm labor, premature rupture of membranes, abruptio placentae, spontaneous abortion, meconium-stained amniotic fluid	Exposure Uterine contractions Abdominal pain	Vaginal bleeding	US
GU	Rhabdomyolysis, ARF, ESRD	Exposure	Oliguria, anuria	K^+, Cr, CK, urine myoglobin
CNS	Subarachnoid hemorrhage, intracerebral bleed, seizures, CVA	Headache, N/V	Neurologic exam	CT scan

Key References: Hernandez M, Birnbach DJ, Van Zundert AA: Anesthetic management of the illicit-substance-using patient, *Curr Opin Anaesthesiol* 18(3):315–324, 2005; Dwarakanath S, Cook AM, Fahy BG: Perioperative care of the cocaine-dependent neurosurgical patient, *J Anesthesiol Clin Sci* 2:12, 2013.

Perioperative Implications

Preoperative Concerns

- Outside of trauma, likelihood of pt presenting to the OR with acute intoxication is low because of rapid metabolism.
- Some recommend at least 1 wk cocaine-free interval before elective surgery.
- Pts who have been chronically abusing cocaine are at risk for catecholamine-induced cardiomyopathy. Inquire about exercise tolerance, chest pain, and DOE.
- Hx of smoking, alcohol use, positive syphilis serology, and use of other illicit drugs should alert to possibility of cocaine abuse.
- Difficult IV access due to sclerosis of peripheral veins.
- Consider urine screen (reliable for only 14–60 h after use). Tests typically screen for benzoylecgonine.
- Be alert for polysubstance abuse; rare that only one substance is abused. Cocaine is often "cut" with amphetamines. Check blood alcohol, comprehensive drug screen.

Monitoring

- Routine.
- Consider arterial line if Hx of acute intoxication or recent exposure. Consider central access for difficult IV access or if significant hemodynamic lability requiring use of vasoactive agents.

Airway

- Intranasal cocaine can cause perforation of nasal septum, oropharyngeal ulcers, and chronic sinusitis.
- Notify ENT surgeons if pt is chronically hypertensive, on MAO-I or a TCA. Usage of cocaine will precipitate hemodynamic instability.

Preinduction/Induction

- Benzodiazepines are helpful to decrease HR and BP.
- Severe Htn may occur during direct laryngoscopy.
- Usage of succinylcholine in acutely intoxicated pt can be associated with prolonged paralysis as cocaine is also metabolized by plasma cholinesterase. Succinylcholine may also compete for plasma cholinesterase metabolism and prolong acute cocaine effects. Use with caution.
- Use ketamine with caution; potentiates CV toxicity of cocaine.
- Neuraxial anesthesia may be associated with more frequent episodes of hypotension. Correct hypovolemia/coagulopathies first. Hypotension may be ephedrine resistant and thus more responsive to phenylephrine.

Maintenance

- Myocardial ischemia can manifest as CV instability, ECG changes.
- With acute exposure, anesthetic requirements may be increased (increased MAC with acute intoxication, decreased MAC with chronic abuser not using periop)
- Increased catecholamine levels due to inadequate anesthesia; cocaine in blood may result in cardiac dysrhythmias.
- Long-term cocaine abuse may downregulate postsynaptic catecholamine receptors such that indirect vasoconstrictors (ephedrine) are not as effective as direct vasoconstrictors (phenylephrine).
- Despite having alpha-antagonist effects, nonselective beta antagonist effects of labetalol are much more potent, leaving it as a questionable choice for hemodynamic control.
- Temperature rise, sympathomimetic effects associated with cocaine can mimic malignant hyperthermia.

Extubation

- No special issues

Adjuvants

- Ester local anesthetics and succinylcholine, which undergo metabolism by plasma ChE, may compete with cocaine, resulting in decreased metabolism of both.
- Cocaine decreases seizure threshold and enhances convulsant effect of other local anesthetics.
- Dexmedetomidine may be useful as an adjuvant because it counteracts cocaine's sympathomimetic cardiovascular effects. Use with caution if hemodynamics have not been optimized.

Postoperative Period

- Myocardial ischemia
- Pain medication requirements for chronic abusers are same as for nonabusers.
- Consider poor home social environment; may call for vigilant work with case management for pt's posthospital transitions in care that optimize longitudinal recovery.

Colchicine

Rae Stewart | Karina Gritsenko

Uses

- Specifically indicated for treatment and relief of pain in acute attacks of gouty arthritis. Often effective in aborting an attack when taken at initial sign of discomfort.
- Not an analgesic and should not be used for other causes of pain.
- Recommended for prophylaxis of gouty attacks with regular use between attacks.
- Well documented use in familial Mediterranean fever.
- Also used in other conditions such as Bechet disease, pericarditis, atherosclerosis, osteoarthritis, and prophylaxis for postop atrial fibrillation.

Preoperative Risks

- Narrow therapeutic window and possibility of toxicities. In view of its potential side effects—including renal, hepatic, respiratory, and gastrointestinal side effects—dosage adjustments must also be considered, especially in cases of renal and hepatic impairment.
- In animals, has been shown to alter neuromuscular function, intensify gastrointestinal activity, increase sensitivity to central depressants, heighten response to sympathomimetic compounds, depress the respiratory center, constrict blood vessels, cause hypertension through central vasomotor stimulation, and lower body temperature.

- Volume of distribution and total body clearance of colchicine are significantly reduced in the elderly, which can lead to higher plasma concentrations and increased risk of toxicity.
- Onset of toxic effects occurs several hours after acute overdose, initially with nausea, vomiting, abdominal pain, and diarrhea leading to extensive vascular damage and shock, kidney injury, muscle weakness, ascending paralysis, delirium, and ultimately death due to respiratory arrest.

Overview/Pharmacology

- Lipid-soluble alkaloid prepared from *Colchicum autumnale*.
- Has a long terminal half-life of 20–40 h. Bioavailability from 24–88%. About 40% of colchicine binds to albumin in the bloodstream. Peak plasma levels occur 1 h after administration, with maximal anti-inflammatory effects occurring over 24-48 h, reaching their highest concentration within leukocytes.
- Primarily eliminated by hepatobiliary excretion. Renal excretion accounts for 10–20% of colchicine elimination in pts with normal renal function.
- Preferentially binds tubulin, cytochrome P3A4, and P-glycoprotein. It persists on tubulin for 20–40 h, preventing fusion of autophagic vacuoles within lysosomes in neuronal, marrow, and muscle cells, risking damage of these organs. CYP3A4 metabolizes colchicine to 2- and 3-demethylcolchicine in hepatocytes and enterocytes. P-glycoprotein, an ATPase efflux pump, extrudes colchicine from the GI tract to limit GI absorption.
- Because of CYP3A4 interactions, there is decreased metabolism of colchicine in pts taking clarithromycin, fluoxetine, paroxetine, nefazodone, protease inhibitors, tolbutamide, azole antifungals, cimetidine, and several nondihydropyridine calcium channel blockers. P-glycoprotein may interact with macrolides, protease inhibitors, chemotherapeutic agents, glucocorticoids, statins, and calcium channel blockers.

Drug Class/Mechanism of Action/Usual Dose

- Tricyclic alkaloid antiinflammatory agent used to treat acute attacks of gouty arthritis.
- Binds tubulins, blocking microtubule assembly and polymerization, arresting microtubule growth at low doses, and promoting depolymerization at higher doses.
- Antiinflammatory effects due to disruption of microtubules and downstream cellular functions of leukocytes. Inhibition of neutrophil chemotaxis, adhesion and mobilization, superoxide production, NALP3, and interleukin 1B processing and release.
- Lactic acid production is reduced; there is decreased uric acid deposition and a reduction in phagocytosis, leading to a decreased anti-inflammatory response.
- Its CV effects are via inhibition of intimal hyperplasia and VEGF expression
- For acute gout, ACR guidelines recommend a loading dose of 1.2 mg followed by 0.6 mg. In the treatment of osteoarthritis, 0.5 mg twice daily. In treatment of recurrent pericarditis 1-2 mg day 1 and maintenance 0.5–1.0 mg/day. For postpericardiotomy syndrome on POD3, 1 mg twice daily and for maintenance, 0.5 mg twice daily.
- Recommend reducing dose by up to 50% in pts >70 y.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Circulatory collapse	Within 7 d of ingestion	Vital signs	
RESP	Respiratory failure		Vital signs	ABG
GI	N/V diarrhea	Symptoms within 24 h of ingestion		LFTs
RENAL	Renal failure	Within 7 d of ingestion		BUN/Cr
MS	Rhabdomyolysis, muscle weakness	Within 7 d of ingestion; concomitant use with statins		Creatinine kinase, LDH
HEME	Blood dyscrasias, marrow failure	Within 7 d of ingestion		CBC
CNS	Delirium, ascending paralysis, convulsions	Within 7 d of ingestion	Mental status exam, neurologic assessment	EEG

Key References: Leung YY, Yao Hui LL, Kraus VB: Colchicine—update on mechanisms of action and therapeutic uses. *Semin Arthritis Rheum* 45(3):341–350, 2015; Ismaeil MS, Tkachenko I, Hickey RF, et al.: Colchicine inhibits isoflurane-induced preconditioning. *Anesthesiology* 91(6):1816–1822, 1999.

Perioperative Implications

Preoperative Concerns

- Surgery and even minor procedures can precipitate acute gouty arthropathy. Prophylaxis against attacks of gout in pt undergoing surgery can be initiated 3 d before and 3 d after surgery.
- Narrow therapeutic index can cause toxicities in the setting of renal impairment or drug interactions.
- Recommended that colchicine be held on the morning of surgery and resumed when pt is again able to tolerate oral medications.

Monitoring

- Standard ASA monitoring

Induction/Maintenance

- Colchicine has been shown to abolish the myocardial protective effect of pretreatment with isoflurane.
- Owing to alterations in neuromuscular function, colchicine may increase sensitivity to CNS depressants, heighten response to sympathomimetic compounds, and depress the respiratory center.
- To decrease risk of toxicity, adequate urine output must be maintained and renal impairment avoided.

Possible Drug Interactions

- Interactions with calcium channel blockers, glucocorticoids, macrolides, statins, cimetidine, clarithromycin, fluoxetine, paroxetine, nefazodone, azole antifungals, protease inhibitors, tolbutamide, and chemotherapeutic agents owing to metabolism with CYP3A4 and P-glycoprotein.

Anticipated Problems/Concerns

- Colchicine IV is not available in USA; therefore if pt should develop an acute flare of gout postop and be unable to tolerate oral medications, intra-articular or systemic steroids can be used.

Cromolyn Sodium

Gregory A. Wolff | Christopher Ciarallo | Lee A. Fleisher

Uses

- Approved by the FDA in 1973 as the first prophylactic nonsteroidal drug available for treatment of chronic asthma.
- Alternative initial maintenance therapy for mild persistent and moderate persistent asthma.
- Preventative only; not effective during acute episodes of bronchospasm.
- Beneficial for allergic-component and exercise-induced asthma.
- May be beneficial in allergic rhinitis and atopic ocular diseases.
- Oral formulations for the management of mastocytosis, ulcerative colitis, and food allergies.
- Leukotriene receptor antagonists have largely replaced cromolyn sodium as the non-corticosteroid treatment of choice in the treatment of asthma.

Overview/Pharmacology

- Inhibits antigen-induced degranulation of pulm mast cells, eosinophils, neutrophils, monocytes, and lymphocytes.
- Prevents release of histamine, leukotrienes, and other autacoids.
- Reverses and suppresses leukocyte activation.
- Inhibits cough reflex.
- Does not directly relax bronchial smooth muscle.
- No apparent steroid-sparing effects and considered inferior to inhaled corticosteroids on measures of lung function and morbidity in 2006 Cochrane Review.
- Administered by inhalation to treat asthma.
- 8–10% of inhaled dose reaches lung parenchyma and is readily absorbed.
- $T_{½}$: 80–90 min; peak plasma concentration within 15 min.
- Active drug excreted unchanged in urine (50%) and bile (50%).
- Can be taken prophylactically 15–20 min before exercise or exposure to known allergen to prevent bronchospasm.

Drug Class/Mechanism of Action

- Cromolyn sodium (disodium cromoglycate) is a derivative of 2-chromone–carboxylic acid.
- Direct mechanism of action in asthma is poorly defined.
  - One proposed explanation is decrease in accumulation of intracellular Ca^{2+} in sensitized mast cells.
  - Another possible mechanism is Cl^- channel blockade in antigen-sensitized pulm C-fibers.
- Effective in preventing degranulation of mast cells only if given prior to antigenic challenge.

Usual Dose

- Cromolyn sodium inhalation (Intal) via a special nebulizer (20 mg/2 mL) or metered spray (2 puffs [1 mg/puff] 3–4 times daily for asthma).
- 4% liquid nasal spray (Nasalcrom) given as 1 spray to each nostril 3–6 times daily for allergic rhinitis.
- 4% ophthalmic solution (Opticrom) given as 1–2 drops to each eye 4–6 times daily for atopic eye conditions.

Assessment Points

System	Effect	Assessment by Hx	Test
RESP	Inhibition of pulm mast cell degranulation; decreased release of histamine and leukotrienes; reverse or suppress leukocyte activation	Decreased episodes of exercise- or antigen-induced bronchospasm after chronic use	Decreased bronchial hyperactivity as measured by histamine or methacholine challenge

Key References: Undem BJ: Pharmacotherapy of asthma. In Brunton LL, Lazo JS, Parker KL, editors: *Goodman & Gilman's the pharmacological basis of therapeutics*, ed 11, New York, 2006, McGraw-Hill Medical, pp 717–736; Netzer NC, Küpper T, Voss HW, et al.: The actual role of sodium cromoglycate in the treatment of asthma—a critical review, *Sleep Breath* 16(4):1027–1023, 2012.

Perioperative Implications/Possible Drug Interactions

- Continue administration periop. Do not discontinue abruptly.
- Cromolyn sodium is of no benefit in treating an acute exacerbation of asthma.
- Adverse effects are infrequent:
  - Unpleasant taste (most common)
  - Direct irritation (e.g., wheezing, coughing)
  - Dizziness, nausea, rash
  - Urticaria, anaphylaxis (extremely rare)
- No significant drug-drug interactions with cromolyn sodium are known.
- Compatible in a nebulized solution with albuterol, levalbuterol, ipratropium, and budesonide.
- Pregnancy category B, with no known evidence of teratogenicity.

Dabigatran

Kelly Byrne | Antony Aho

Uses

- Stroke prevention in nonvalvular AFIB
- Thromboembolism prophylaxis after total hip and knee replacement
- Treatment and prevention of DVT and PE not related to surgery

Worry About

- Contraindicated in pts with creatinine clearance less than 30 mL/min.
- Use with other anticoagulants will increase the risk of bleeding and is not recommended.
- Use with strong inhibitors of p-glycoprotein (e.g., ketoconazole, itraconazole, cyclosporine) is contraindicated as they increase plasma concentrations of dabigatran.
- Use with mild inhibitors of p-glycoprotein (e.g., amiodarone, quinidine, verapamil) should proceed with caution.
- P-glycoprotein inducers (e.g., rifampicin) will reduce dabigatran plasma concentrations.
- Major hemorrhage occurs in roughly 3.5% and fatal hemorrhage in 0.07% of pts.
- Gastrointestinal upset has been reported in postmarketing surveillance.

Overview/Pharmacology

- Competitive direct thrombin inhibitor that is active after a single dose.
- Inhibits both free and clot-bound thrombin and thrombin-induced platelet aggregation.
- For oral administration, available in 75-, 110-, and 150-mg capsules.
- Doses vary by country, but an indicative dose regime would be as follows: Dosing for prevention of stroke is usually 150 mg 2 times daily; this may be reduced to 110 mg 2 times daily in pts with renal impairment. Dosing for DVT treatment is usually also 150 mg 2 times daily. For prophylaxis following hip or knee joint replacement the usual dose is 110 mg on day 1 followed by 220 mg once daily.
- Oral bioavailability is 3–7%. Not much altered when administered with food but will increase significantly if capsule is broken before oral administration.
- Peak plasma concentration is reached within 2 h
- Approximately 35% plasma protein binding with volume of distribution 50–70 L.
- 80% of dabigatran is renally excreted.
- Half-life is 12–17 h, which is prolonged by renal impairment.
- Not metabolized by and does not induce cytochrome P450.

Test	Effect of Dabigatran	Clinical Usefulness
INR	May be normal or elevated in the presence of therapeutic levels of dabigatran	Not useful
APTT	Usually elevated in presence of therapeutic levels of dabigatran (around 1.3 times normal at steady state)	High APTT in a pt on dabigatran indicates therapeutic levels of dabigatran. However, this lacks sensitivity and a normal result does not exclude therapeutic levels of dabigatran.
TCT	Elevated in presence of even small amounts of dabigatran	Very sensitive predictor of the presence of dabigatran. Can also be elevated by other drugs that effect thrombin (e.g., heparin).
TEG	Unpredictable effect of dabigatran	Not currently useful, but may improve with the use of novel activating agents (e.g., ecarin)
Ecarin clotting time	Sensitive to the presence of small amounts of dabigatran Plasma is diluted in a standard fashion and thrombin time is carried out to estimate dabigatran levels when calibrated against known levels of dabigatran	Not widely available; tends to be used mainly as research tool Shown to be accurate in measuring dabigatran levels but unclear as to how the level correlates with degree of anticoagulation (i.e., at what dabigatran level it is safe to proceed to surgery).

Key References: van RJ, Stangier J, Haertter S, et al.: Dabigatran etexilate—a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity, *Thromb Haemost* 103(6):1116–1127, 2010; von Heymann C, Rosenthal C, Kaufner L, et al.: Management of direct oral anticoagulants-associated bleeding in the trauma patient, *Curr Opin Anaesthesiol* 29(2):220–228, 2016.

Perioperative Implications

Preoperative Concerns

- Guidelines for stopping dabigatran vary between organizations and depend on pt's bleeding risk and renal function.
- In low-risk pts with normal renal function, stopping dabigatran 2 d prior to surgery should be adequate to allow clearance of most of the drug from the plasma.
- Where there is a high risk of bleeding or with renal impairment or where neuraxial anesthesia is being considered, dabigatran should be stopped at least 4 d prior to surgery.
- Clearance in pts with renal impairment or failure can be highly unpredictable and certain scenarios (e.g., cardiopulmonary bypass) can result in increased levels of dabigatran.
- A normal TCT indicates a return to pt's normal coagulation status.

Regional Anesthesia

- Neuraxial anesthesia is contraindicated in the presence of therapeutic levels of dabigatran. Any elevation of TCT during neuraxial anesthesia may indicate an increased risk of epidural hematoma. Current guidelines suggest stopping dabigatran 5–7 d prior to undertaking neuraxial block.
- Dabigatran can be instituted or restarted 6 h after removal of epidural cath or after a single-shot spinal anesthetic. Dabigatran should not be administered while an epidural cath is in place.
- Dabigatran will increase the risk of bleeding from all types of regional anesthesia. Peripheral nerve blockade is not absolutely contraindicated in the presence of therapeutic levels of dabigatran. The risk/benefit will depend on individual cases. Broadly speaking, however, shallower blocks that allow for compression of the block site if bleeding occurs will be safest.
- There is currently no evidence to support the safety or otherwise of continuing dabigatran during an eye block. Current manufacturers' guidelines are to cease therapy 2–5 d preop.

Reversal/Special Considerations

- Idarucizumab is a specific monoclonal antibody for reversal of dabigatran. It was approved by the FDA in October 2015. Phase 3 trials of its efficacy and safety are continuing.
- Some expert guidelines recommend use of either activated factor VIIIa (FEIBA) or activated factor VIIa to overcome the effect of dabigatran on the coagulation system. Neither of these treatments has been proven to work, although there is some theoretical benefit to their use. There are some supportive data from animal studies.
- Elective or semiacute surgery should be delayed by the time periods indicated by local guidelines, ensuring that the TCT has normalized prior to surgery.
- For acute surgery, idarucizumab, if available, should be administered. If not available, activated charcoal may help reduce absorption of a recently administered dose of dabigatran; otherwise hemodialysis can be useful in reducing plasma levels. Dabigatran plasma levels usually rebound 4–6 h after cessation of dialysis.
- Massive transfusion, dialysis to remove dabigatran, and use of activated clotting factors and prothrombin complex concentrates have been described in case reports, but with mixed success in achieving hemostasis.

Digitalis (Digoxin)

Abhijit S. Nair

Uses

- Treatment of CHF, atrial fibrillation, and flutter.
- Prevention of supraventricular arrhythmias following thoracotomy (controversial).
- Cardiac side effects: Arrhythmias and conduction disturbances.
- Noncardiac side effects: GI—anorexia, N/V, and abdominal pain; CNS—visual disturbances, headache, drowsiness, and confusion.

Perioperative Risks

- Recent systematic review and meta-analysis suggest that use of digoxin is associated with increased mortality risk, especially in pts with atrial fibrillation.
- Cardiac arrhythmia (toxicity) can be precipitated by hypokalemia, hypomagnesemia, hypoxia, hypercalcemia, hypernatremia, and renal failure.
- DC cardioversion can cause severe ventricular arrhythmias in pts with toxic levels.
- AV block (with co-administration of β-adrenergic, Ca^{2+}-channel blocking drugs).

Worry About

- Dosing has a narrow therapeutic index (0.8–2 ng/mL or 1.2–2 nmol/L).
- Avoid in pts with ventricular extrasystole or VT, as it may precipitate VF due to increased cardiac excitability.
- Hyperventilation can cause alkalosis leading to relative hypokalemia toxicity.
- Renal insufficiency (decreased digoxin clearance and need for dose alteration, not appreciably removed by dialysis).

Overview/Pharmacology

- A glycoside extracted from leaves of the foxglove (digitalis lanata), available in oral and IV preparations.
- Has positive inotropic effects, along with negative chronotropic and dromotropic properties.
- Acts by raising intracellular sodium and calcium concentration, along with lowering of potassium concentration due to sarcolemmal Na^+K^+ ATPase inhibition.
- Indirect effect enhances release of acetylcholine at the cardiac muscarinic receptors. This slows conduction and prolongs the refractory period in AV node and bundle of His.

Dosing/Pharmacokinetics

Drug	Onset	Initial Dose (mg)	Maintenance Dose (mg/d)
Digoxin: IV	5–30 min	0.5–1.0	0.25
PO	1–3 h	0.75–1.2	0.125–0.5
Digitoxin: PO	3–6 h	0.8–1.2	0.05–0.3

Excretion

- Digoxin: Renal, mostly unchanged; decreased dose for increased Cr, monitor renal functions (creatinine, potassium)
- Digitoxin: Hepatic degradation

Drug Interactions

- Diuretics: Decreased serum K^+, increased toxicity
- Plasma levels increased by quinidine, amiodarone, verapamil, captopril, erythromycin.
- Plasma levels decreased by antacids, phenytoin, metoclopramide, and cholestyramine.

Treatment for Toxicity

- Due to Na^+/K^+ ATPase inhibition, hyperkalemia may be a feature and should be corrected.
- Hypokalemia exacerbates toxicity and should be corrected.
- Severe bradycardia: Atropine or pacing preferred over catecholamines.
- Ventricular arrhythmias:,Treat with lidocaine or phenytoin.
- Digoxin specific Fab: Indicated for digoxin levels >10 mcg/L, life-threatening arrhythmias, or uncontrolled hyperkalemia, with hemodialysis required in refractory acidosis and hyperkalemia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT			Decreased JVD	
CV	Decreased HR, Increased CO Arrhythmia from toxicity	Decreased SOB, orthopnea Palpitations	Decreased HR rate, size Irregular pulse	CXR: Decreased heart size ECG: Any arrhythmia except AFIB
RESP	Decreased congestion	Decreased SOB, orthopnea	Decreased rales	CXR: Decreased pulm edema
GI	Anorexia from toxicity			Serum digoxin >2 ng/mL
CNS	Headache, confusion from toxicity			Serum digoxin >2 ng/mL
MS	Fatigue from toxicity -and confusion (brain often more affected than heart) can be cause of reversible cognitive dysfunction			Serum digoxin >2 ng/mL

Key References: Ouyang AJ, Lv YN, Zhong HL, et al.: Meta-analysis of digoxin use and risk of mortality in patients with atrial fibrillation, *Am J Cardiol* 115(7):901–906, 2015; Mittal MK, Chockalingam P, Chockalingam A: Contemporary indications and therapeutic implications for digoxin use, *Am J Ther* 18(4):280–287, 2011.

Perioperative Implications

Preoperative Concerns

- Do not discontinue digitalis preop. Withdrawal in heart failure pts may lead to recurrence of failure symptoms.
- When changing from oral to IV therapy, dosage should be reduced by 20–25%.
- Correct and maintain serum K^+, magnesium.
- Decreasing dose with increasing serum creatinine.
- Maintain a high index of suspicion for digoxin toxicity.

Dipyridamole

Sushila Murthy

Uses

- Rx as adjunctive therapy for prophylaxis of thromboembolism with cardiac valve replacement.
- Used for secondary stroke prevention (often combined with aspirin).
- Used in stress tests to evaluate for presence of coronary artery disease.

Perioperative Risks

- Headache
- Plt dysfunction
- Hemorrhage
- Exacerbation of angina pectoris

Worry About

- Potentiation of anticoagulants
- Thrombosis secondary to dipyridamole discontinuation

Overview/Pharmacology

- Reversibly impairs plt function by inhibiting the activity of adenosine deaminase and phosphodiesterase, which causes an accumulation of adenosine, adenine nucleotides, and cyclic AMP.
- May also cause vasodilation.
- Affects hepatic metabolism and fecal elimination.
- Elimination half-life is 10 h.

Drug Class/Mechanism of Action/Usual Dose

- Antiplatelet agent.
- Chronically taken for secondary stroke prevention or prophylaxis of thromboembolism with cardiac valve replacement.
- Used acutely in IV formulation for diagnosis of CAD.
- Usual doses:
  - Dipyridamole 75–100 mg PO q6h
  - Dipyridamole extended release 200 mg/aspirin 25 mg: 1 capsule q12h
  - Evaluation of coronary artery disease: 0.14 mg/kg/min IV for 4 min; max dose: 60 mg; aminophylline should be available for urgent/emergent reversal; dosing of 50–100 mg (range: 50–250 mg) IV push over 30–60 sec
- Alternatives: Aspirin, NSAIDs, thienopyridines (clopidogrel, prasugrel), and GPIIb/IIIa receptor antagonists.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Vasodilation of cerebral vessels	Headache		
CV	Vasodilation of coronary arteries (theoretical increased risk of ischemia)	Chest pain	Hypotension	ECG, stress test, or cath to assess for myocardial ischemia/infarction
HEME	Plt dysfunction	Bleeding, bruising	Hematoma, petechiae	Bleeding time
HEPAT	Serum enzyme elevations and possible hepatic dysfunction		Jaundice	AST, ALT, alk phos
GI	Gastritis, exacerbation of PUD	Abdominal pain, nausea, hematemesis, melena, diarrhea		

Key References: Diener HC, Darius H, Bertrand-Hardy JM, et al.: Cardiac safety in the European Stroke Prevention Study 2 (ESPS2), *Int J Clin Pract* 55(3):162–163, 2001; Breivik H, Bang U, Jalonen J, et al.: Nordic guidelines for neuraxial blocks in disturbed haemostasis from the Scandinavian Society of Anaesthesiology and Intensive Care Medicine, *Acta Anaesthesiol Scand* 54(1):16–41, 2010.

Perioperative Implications/Possible Drug Interactions

Perioperative Concerns

- Lack of data on the safety of dipyridamole if continued in the periop period. Must balance the risk of bleeding and risk of ischemic events. If discontinued, dipyridamole should be stopped at least 2 d before surgery. Combination aspirin and dipyridamole should be discontinued 7–10 d before surgery.

Adjuvants/Regional Anesthesia/Reversal

- Lack of data regarding regional anesthesia and dipyridamole. Current guidelines suggest that when used alone, there is no need to discontinue before neuraxial blockade.

Anticipated Problems/Concerns

- May diminish the therapeutic effect of acetylcholinesterase inhibitors.
- May enhance the effect of adenosine.
- Extended-release dipyridamole use for stroke prevention is not empirically associated with an increased risk of myocardial ischemia or infarction.

Diuretics

Christopher Giordano | Nikolaus Gravenstein

Uses

- Prescribed for pts with Htn, CHF, elevated ICP, edema, hemoglobinuria, low intraop UO, hyperkalemia, volume overload, and rhabdomyolysis.
- Mannitol may function as a renal preservative by free radical scavenging and toxin dilution.
- Fenoldopam is a selective dopamine-1 agonist. As a vasodilator, it lowers blood pressure and augments renal blood flow, which improves UO and glomerular filtration rate. It may also serve as a renal protectant. Usual dose begins at 0.03 μg/kg/min titrated to effect.
- HCTZ is used to treat hypercalcemia for kidney stones.

Perioperative Risks

- Hypokalemia
- Hypovolemia
- Low intraop UO
- Hyperkalemia with aldosterone antagonists
- Hypomagnesemia

Worry About

- Hypokalemia and hypovolemia.
- Low intraop UO if preop holds usual diuretics.
- Hypokalemia provoking and/or aggravating digitalis toxicity.
- Deafness with ECA and tinnitus with furosemide.
- End result of diuretic use is increased UO with net loss of H_2O and solutes, especially K^+ and Mg^{2+}.
- Onset of diuresis is within 10 min after IV administration.
- With the exception of an aldosterone antagonist and K^+-sparing diuretics, all others cause K^+ loss.
- Serum K^+ <3.5 mEq/L in 15% of pts and <3.0 mEq/L in up to 10% of diuretic-treated pts.
- Chronic diuretic-induced hypokalemia is less arrhythmogenic than acute, but serum K^+ <3.0 mEq/L is associated with a twofold greater incidence of ventricular arrhythmias than K^+ >3.0 mEq/L.
- Site-specific action associated with additional effect if diuretics from two classes used.
- Mannitol causing brief but appreciable hypervolemia risking CHF and ICP if bolused.
- Mannitol causing hypotension from high osmolar effect if given too rapidly.

Drug Class/Mechanism of Action/Usual Dose

- Diuretics belong to osmotic, carbonic anhydrase inhibition, benzothiadiazide, high-ceiling (loop), K^+-sparing, or aldosterone antagonist class of drugs, based on mechanism of action.
- Only osmotic and loop diuretics are used intraop.
- Osmotic diuretic: Mannitol—ascending loop, limits H_2O reabsorption; onset of action 5–15 min after IV dose: renal clearance
- Usual dose: Mannitol 0.25–2 g/kg (rapid bolus may precipitate hypotension)
- Loop diuretics: Ascending loop, limit NaCl reabsorption; onset of action 5 min after IV dose; $T_{½}$ 1–2 h; duration of action 3–6 h: renal clearance
- Usual IV dose for 70-kg person: Furosemide: 5–40 mg (0.1–1.0 mg/kg); ECA: 25–50 mg (0.5–1 mg/kg); bumetanide: 0.5–1 mg q 2–3 h; max 10 mg/d
- Furosemide PO to IV conversion 2:1

Drug Effects

System	Effect
HEENT	Transient (<24 h) deafness or vertigo may follow IV rapid bolus of ECA; less common after furosemide or bumetanide; rarely permanent. Tinnitus may follow furosemide.
CV	Transient increased in venous capacitance causes hypotension with rapid IV loop diuretic administration; acute transient increase in intravascular volume precedes diuresis with mannitol; vasodilation with fenoldopam.
ENDO	Hypokalemia, metabolic alkalosis
GU	Diuresis
CNS	Mannitol decreased ICP following transient increase; the latter may be mitigated by coadministration of furosemide.

Key References: Bebawy JF, Ramaiah VK, Zeeni C, et al.: The effect of furosemide on intravascular volume status and electrolytes in patients receiving mannitol: an intraoperative safety analysis, *J Neurosurg Anesthesiol* 25(1):51–54, 2013; Kheterpal S, Khodaparast O, Shanks A, et al.: Chronic angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery, *J Cardiothorac Vasc Anesth* 22(2):180–186, 2008.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- In chronic hypertensive pts treated with diuretics, a significant intravascular volume contraction may exist, making them more prone to hypotension following induction of anesthesia and any acute blood loss.
- Hypokalemia: Check serum K^+; consider enhanced digitalis toxicity.
- Hypomagnesemia is common in pts treated with loop or thiazide diuretics and predisposes them to ventricular arrhythmias. It should be suspected when hypokalemia is noted. Hypomagnesemia should be corrected prior to repleting K^+.
- Enhanced ototoxicity and nephrotoxicity of loop diuretics are associated with rapid administration of large IV doses and concurrent use of another nephrotoxic drug (e.g., aminoglycoside antibiotic, another loop diuretic, and some cephalosporins, especially cephaloridine).
- It is probably best to continue a chronic dose through the periop period, including day of surgery. (UO will decline if a diuretic not given on day of surgery.) No increase in hypotension will be seen if usual oral diuretics are given preop the day of surgery.

Induction/Maintenance

- Intraop loop diuretic use may significantly decrease serum K^+ level with diuresis.

Adjuvants

- Enhanced renal clearance of other drugs (e.g., neuromuscular-blocking agents) provoked by diuresis is not clinically problematic.

Anticipated Problems/Concerns

- Pts receiving diuretics preop should be considered volume contracted until proven otherwise.
- Hypokalemia associated with diuresis will be aggravated by hyperventilation, which further lowers serum K^+ an additional 0.5 mEq/L for each 10 mm Hg decrease in $PaCO_2$.
- Catecholamine β effect (endogenous and/or exogenous); also lowers serum K^+.
- Low intraop UO in a euvolemic pt if antidiuretic hormone/stress mediated will, in authors' experience, respond to very low dose (e.g., 2–5 mg furosemide) with increased UO.

Epsilon-Aminocaproic Acid (Amicar)

Frank W. Dupont

Uses

- EACA is a hemostatic agent used in the treatment of hyperfibrinolysis associated with excessive bleeding.
- Indications: Fibrinolytic bleeding associated with surgical complications following heart surgery (with or without CPB) and portacaval shunt; surgical hematuria (following prostatectomy and nephrectomy) or nonsurgical hematuria (accompanying polycystic or neoplastic diseases of the GU system); acute and life-threatening abruptio placentae; hepatic cirrhosis; neoplastic disease such as carcinoma of the prostate, lung, stomach, and cervix; hematologic disorders such as amegakaryocytic thrombocytopenia
- Methods of administration: IV solution, oral solution, tablets

Perioperative Risks

- Increased risk of developing thrombosis in pts, who are concurrently treated with factor IX complex or antiinhibitor coagulant complex

Worry About

- EACA should not be used when there is evidence of an active intravascular clotting process. When there is uncertainty as to whether the cause of bleeding is primary fibrinolysis or DIC, this distinction must almost certainly be made before administering EACA. EACA must not be used in the presence of DIC without concomitant heparin.

Overview/Pharmacology

- EACA is an inhibitor of fibrinolysis and enhances hemostasis when fibrinolysis contributes to bleeding.
- Renal excretion is the primary route of elimination: 65% is eliminated unchanged within 12 h; approximately 11% is metabolized; renal clearance is 116 mL/min; and terminal elimination half-life is approximately 2 h.

Drug Class/Mechanism of Action/Usual Dose

- EACA is an antifibrinolytic agent of the lysine analogue class.
- EACA inhibits fibrinolysis principally via inhibition of plasminogen activators and to lesser degree through antiplasmin activity.
- The optimal dosage in the setting of CPB is undefined, but the following is a commonly used regimen in adults: Initial loading dose is 5 g IV over 1 h, followed by a continuous infusion of 1 g/h; maximum recommended daily dose is 30 g.
- Plasma concentrations are increased in pts with severe renal dysfunction, but no quantitative recommendations for dosing adjustments are available.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Dizziness, confusion, delirium, headache, seizure		Neurologic exam	
CV	Hypotension, bradycardia		Vital signs	ECG
GI	N/V, diarrhea			Lytes
RENAL	Renal failure, urinary tract obstruction	Oliguria		BUN/Cr
HEME	Thrombosis	Potential causes for DIC	Evidence for paradox of simultaneous thrombosis and bleeding	CBC, PT/PTT, DIC profile
MS	Myopathy, rhabdomyolysis	Myalgia, malaise, fatigue	Muscle weakness	CPK

Key References: Franchini M, Mannucci PM: Adjunct agents for bleeding, *Curr Opin Hematol* 21(6):503–508, 2014; Ortmann E, Besser MW, Klein AA: Antifibrinolytic agents in current anaesthetic practice, *Br J Anaesth* 111(4):549–563, 2013.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- In the presence of hematuria originating in the upper urinary tract, EACA can cause intrarenal obstruction due to clot retention.

Drug Interaction

- EACA should not be administered to pts treated with factor IX complex or antiinhibitor coagulant complex unless the risk of thrombosis is outweighed by the potential benefit of EACA.

Induction/Maintenance

- Close hemodynamic monitoring of cardiac pts because of the risk of hypotension and sinus bradycardia, particularly with rapid IV administration and in hypovolemia.
- Monitor renal function in pts with renal dysfunction and consider dosage adjustments depending on clinical response and degree of renal function impairment.
- Consider transfusion of platelets, FFP, and cryoprecipitate in the presence of bleeding not caused by hyperfibrinolysis.

Postoperative Period

- Continue assessment of bleeding and monitoring of coagulation profiles after discontinuation of EACA therapy.

Anticipated Problems/Concerns

- EACA should not be administered without a definite diagnosis and/or lab finding indicative of hyperfibrinolysis (hyperplasminemia) because of the potential for thrombotic complications in pts with DIC and underlying hypercoagulable states.

Fluoxetine (Prozac)

Stephen J. Shepherd

Uses

- Fluoxetine, an SSRI, is one of the most commonly prescribed medications in USA.
- Prescribed for the treatment of depression, OCD, and bulimia nervosa.

Perioperative Risks

- May be associated with periop anxiety
- Drug interactions with beta-blockers, phenytoin, benzodiazepines, antipsychotics (may increase levels by inhibition of CYP2D6), tramadol, and codeine

Worry About

- Suicidal behavior, psychotic, or extrapyramidal reactions (rare).
- Serotonin syndrome with concomitant administration of MAO inhibitors, tricyclic antidepressants, antipsychotics, tramadol, or meperidine.
- Increased risk of abn bleeding, particularly if combined with vit K antagonists or NSAIDs.
- Potential for increased mortality in high-risk pts, although whether there is a causative association or observation is unknown.

Overview/Pharmacology

- Selective inhibitor of serotonin reuptake.
- Administered as racemic mixture of R- and S-enantiomers.
- S-enantiomer more potent than R-enantiomer.
- Active metabolites, R- and S-norfluoxetine, formed by demethylation.
- Eliminated mainly through oxidative metabolism and conjugation.
- Long elimination $T_{½}$: 1–10 d for fluoxetine, 3–20 d for norfluoxetine.
- Fluoxetine inhibits (and is probably metabolized by) liver cytochrome P450 enzymes CYP2D6 and possibly CYP3A4: May inhibit metabolism, increase levels of beta-blockers, benzodiazepines, antipsychotics; similarly may decrease conversion codeine to morphine.
- Serotonin promotes platelet activation and vasoconstriction following vascular injury. Platelets cannot synthesize more, hence SSRIs deplete intracellular levels and impair hemostasis; opinions differ as to clinical relevance of this.
- Difficult to establish relationship between plasma concentration of fluoxetine and its effect, probably because there are four active compounds (R- and S-fluoxetine and R- and S-norfluoxetine) that require separate measurement.
- Withdrawal may cause dizziness, GI upset, and confusion/delirium, particularly periop.

Drug Class/Mechanism of Action/Usual Dose

- Selective inhibitor of serotonin reuptake are taken chronically for moderate to severe depression, OCD, bulimia nervosa, PTSD, and hypersexuality (off label).
- Full antidepressant effect may be delayed until 4 wk of treatment or longer
- Initial dose PO: 20 mg/d.
- Maximal dose: 80 mg/d.
- Alternatives: Other antidepressant medications, psychotherapeutic intervention.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Bradycardia, dysrhythmia Slight BP increase	Rare	Pulse	ECG
CNS	Extrapyramidal symptoms (rare), mania (rare), serotonin syndrome (rare)	Headache, anxiety, tremor		CK
ENDO	SIADH secretion (rare)	Confusion with significant hyponatremia, seizures	GCS	Urine specific gravity Plasma and urinary sodium
GI	Nausea, weight loss			
MS	Serotonin syndrome (rare)	Arthritic complaints (infrequent), muscle rigidity		
HEME	Impaired hemostasis			May possibly be identified with plt function testing but no specific assay for SSRI effect available

Key References: Zahajszky J, Rosenbaum JF, Tollefson GD: Fluoxetine. In Schatzberg AF, Nemeroff CB, editors: *The American Psychiatric Publishing textbook of psychopharmacology,* ed 4, Washington DC, 2009, American Psychiatric Publishing, p 289; Peck T, Wong A, Norman E: Anaesthetic implications of psychoactive drugs, *Contin Educ Anaesth Crit Care Pain* 10:177–181, 2010.

Perioperative Implications/Possible Drug Interactions

- Headache, anxiety, and nausea are common symptoms.
- May inhibit cytochrome P450 enzymes and increase serum concentrations of other drugs (beta-blockers, phenytoin, benzodiazepines, antipsychotics, tramadol) and potentiate their effects.
- Inhibition of CYP2D6 reduces conversion of codeine to morphine and may result in inadequate analgesia.
- Do not give to pregnant pts without assessing risk/benefit ratio.

Anticipated Problems/Concerns

- Approximately 7% of Caucasians lack the cytochrome P450 (CYP2D6) that probably metabolizes fluoxetine; these individuals may develop higher serum concentrations of fluoxetine and be more prone to side effects.
- Serotonin syndrome—characterized by agitation, confusion, diaphoresis, and muscle rigidity—may develop in pts who receive a combination of fluoxetine and MAO inhibitors.

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The author wishes to acknowledge the contribution of Dr. Donald D. Koblin to the previous edition of this chapter.

Folic Acid

Karen E. Iles | David W. Miller

Uses

- Prevention of folic acid deficiency
- Treatment of megaloblastic anemia
- Experimental treatment for major depressive disorder
- Treatment of folic acid deficiency caused by anorexia, chronic use of oral contraceptive and some antiepileptic drugs, alcoholism, malabsorption diseases (e.g., sprue), bowel resection, and diverticulosis
- Reduces incidence of neural tube defects (spina bifida) and congenital heart defects in developing fetus
- Reduces homocysteine; may have cardiovascular benefits (no evidence of such from randomized trials, but much anecdotal evidence)

Perioperative Risks

- Chronic overdosage increases proliferation of cancer as demonstrated in epidemiologic studies and in vitro studies of breast cancer.
- Exposure to nitrous oxide disrupts folic acid metabolism; repeated exposure can cause deficiency.
- Supraphysiologic doses (>15 mg/d) may decrease seizure threshold in pts taking some antiepileptic medications.

Worry About

- Allergic reactions (rare); most in response to the parenteral form.
- Loss of appetite, nausea, lethargy, stomach pain, insomnia.
- Supraphysiologic doses (>15 mg/d) increase all symptoms listed above.
- May cause seizures (>15 mg/d); higher risk in epileptic pts.

Overview/Pharmacology

- Vitamin with close synergistic relationships with vitamin B_{12}, ascorbate, and zinc.
- Very little found as folic acid in nature; converted to tetrahydrofolate in vivo.
- Absorption most efficient in the duodenum and upper jejunum.
- Loss from the body is prevented by efficient enterohepatic recirculation.
- Some fecal excretion; very little excreted in the urine.
- Alcohol decreases blood levels by interfering with enterohepatic recirculation.
- Tetrahydrofolate accepts and denotes one carbon group in amino acid degradation and metabolic reactions.

Drug Class/Mechanism of Action/Usual Dose

- Vitamin.
- Accepts and denotes one carbon group in amino acid degradation and metabolism reactions (i.e., in the synthesis of glycine from serine).
- Critical for cell division because required for purine and thymidine synthesis
- Oral and parenteral forms.
- RDA is 400 μg/d for healthy individuals and 600 μg/d for pregnant women.
- Higher requirements for anemia, antifolate drug therapy, and so on; 1 mg 1–3 times daily PO or IM or IV.
- Given as a multivitamin containing vitamin B_{12} because it can mask vitamin B_{12} deficiency and accompanying neurologic damage.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Improves O_2 delivery	Better exercise tolerance		Hgb
GI	Improves cell division	Less diarrhea	Better hydration/absorption	
ENDO/ METAB	Improves nucleic acid/protein synthesis		Weight gain	Folate level
HEME	Improves RBC synthesis	Better exercise tolerance		Hgb

Key References: Kaushansky K, Kipps TJ: Hematopoietic agents: growth factors, minerals, and vitamins. In Brunton LL, Chabner BA, Knollmann BC, editors: *Goodman & Gilman's the pharmacological basis of therapeutics,* ed 12, New York, 2011, McGraw-Hill, pp 1067–1100; Goodman BP: Metabolic and toxic causes of myelopathy, *Continuum (Minneap Minn)* 21(1 Spinal Cord Disorders):84–99, 2015.

Perioperative Implications

Preoperative Concerns

- Deficiency may cause megaloblastic anemia especially in the setting of chronic alcohol intake and medications that inhibit dihydrofolate reductase (i.e., methotrexate, trimethoprim).
- Consider general nutritional status (i.e., if evidence of poor diet, folic acid deficiency likely).
- Consider specific underlying conditions (i.e., anorexia, alcoholism, malabsorption disorders).
- Continue periop supplementation as needed.

Induction/Maintenance

- Same as Preoperative Concerns.
- Avoid repeated use of N_2O.

Adjuvants/Regional Anesthesia/Reversal

- Same as Preoperative Concerns

Postoperative Period

- Same as Preoperative Concerns

Anticipated Problems/Concerns

- Rare allergic reactions, especially to parenteral formulation.
- Generally none in otherwise healthy pts.
- May counteract the antiepileptic effect of phenytoin, phenobarbital, and primidone at high doses (>15 mg/d), leading to seizures.
- Potential danger of mistreating pt with vitamin B_{12} deficiency with folic acid; may result in improvement of megaloblastic anemia, but neurologic deficits of vitamin B_{12} deficiency may progress and become irreversible.

Glucocorticoids

Amit Prabhakar | Alan David Kaye

Uses

- Used to treat a wide range of illnesses including but not limited to autoimmune disorders, postop nausea and vomiting, and chronic pain

Overview/Pharmacology

- Adrenal cortex produces and releases two different types of corticosteroids: Mineralocorticoids (maintain salt and fluid balance) and glucocorticoids (affect metabolism and inflammation).
- Glucocorticoids have significant, wide-ranging physiologic effects by binding to cell surface receptors and crossing cell membranes to modify genetic expression.
- Endogenous glucocorticoids include cortisol.
- Exogenous glucocorticoids include prednisone, prednisolone, triamcinolone, dexamethasone, and betamethasone.

Physiology

- Glucocorticoids play a pivotal role in normal body physiology and the stress response.
- Three major mechanisms control cortisol release:
  - Negative feedback via the HPA axis: ACTH from the anterior pituitary stimulates the secretion of cortisol from the adrenal cortex. Cortisol exerts a direct negative feedback effect on ACTH secretion.
  - Diurnal variation: Cortisol is secreted in pulses that follow a circadian rhythm dependent on pt's sleep-wake pattern. Cortisol levels are highest in the morning, upon awakening, and lowest in the evening.
- Stress: Physical (trauma, surgery, exercise), psychologic (pain, anxiety), or physiologic (nausea, fever) stress can override the negative feedback mechanisms and lead to a rapid increase of cortisol concentration.
- Metabolic effects:
  - Stimulation of gluconeogenesis by the liver, resulting in increased blood glucose
  - Mobilization of fatty acids from adipose tissue and enhanced fatty acid oxidation in cells
  - Decreased protein synthesis and catabolism of proteins in cells
- Anti-inflammatory activity: Potent anti-inflammatory activity via inhibition of phospholipase A2 and COX-2. Blunts production and cascade of inflammatory cytokines.
- Bone metabolism: Inhibit osteoblast function. Excess results in osteopenia and osteoporosis.
- Blood pressure: Affects the kidney and vasculature to increase blood pressure; increases sensitivity of vascular smooth muscle to catecholamines and angiotensin II.
- CNS: Plays a role in depression, euphoria, apathy, and lethargy.
- Fetal development: Maternal cortisol plays key role in the fetal production of pulmonary surfactant and in the expression of key hepatic enzymes.
- Other endocrine effects: Suppresses thyroid axis; inhibits GnRH, LH, and FSH.

Commonly Used Types

- Exogenous corticosteroids have varying degrees of potency, duration of action (DOA), and mineralocorticoid or glucocorticoid activity.
- Cortisol: Equal anti-inflammatory and mineralocorticoid activity; short DOA (<12 h)
- Cortisone: Equal anti-inflammatory and mineralocorticoid activity; short DOA
- Prednisone: Anti-inflammatory > mineralocorticoid activity; intermediate DOA (12–36 h)
- Prednisolone: Anti-inflammatory > mineralocorticoid activity; intermediate DOA (12–36 h)
- Triamcinolone: Anti-inflammatory only; no mineralocorticoid activity; intermediate DOA (12–36 h)
- Dexamethasone: Potent anti-inflammatory only; no mineralocorticoid activity; long DOA (>36 h)
- Betamethasone: Potent anti-inflammatory only; no mineralocorticoid activity; long DOA (>36 h)
- Fludrocortisone: Potent mineralocorticoid activity

Relative Potency of Commonly Utilized Agents

- Anti-inflammatory potency: Cortisol 1, triamcinolone (Aristocort) and 6-methylprednisolone (Depo-Medrol) 5, fludrocortisone 10, betamethasone (Celestone) 25
- Mineralocorticoid potency: Cortisol 1, fludrocortisone 10
- Equivalent dose, mg: Cortisol 20, triamcinolone (Aristocort) and 6-methylprednisolone (Depo-Medrol) 4, betamethasone (Celestone) 0.75

Pathology

- Adrenal overactivity
  - Cushing syndrome: Due to excess cortisol in the body.
  - Cushing disease: Due specifically to ACTH-producing pituitary adenoma. Hypercortisolemia manifests as obesity, thin extremities, hypertension, buffalo hump, easy bruising, abdominal striae, hypervolemia, hypokalemic metabolic acidosis, osteoporosis, osteopenia, moon facies, poor wound healing.
- Adrenal insufficiency:
  - AD: Primary adrenal insufficiency. Pts with AD usually lack both mineralocorticoid and glucocorticoid production. Symptoms include weakness, weight loss, postural hypotension, constipation, diarrhea, anorexia, hyperpigmentation, hypoglycemia, hyperkalemia, and hyponatremia. AD usually has an autoimmune etiology but can also be due to tuberculosis, cancer, or amyloidosis.
  - Secondary adrenal insufficiency: Lack of ACTH production from the anterior pituitary. Can be due to abrupt cessation of exogenous steroids or surgical removal of a pituitary adenoma.
  - Adrenal crisis: Sudden, severe worsening of adrenal insufficiency. Manifests as severe dehydration, vomiting, diarrhea, hypotension, convulsions, and/or loss of consciousness.
- Adverse effects of steroid supplementation:
  - Short term: Exacerbation of Htn, fluid retention, stress ulcers, psychologic disturbances, osteoporosis, delayed wound healing, increased susceptibility to infection, decreased glucose tolerance. Nonparticulate steroids are recommended over particulate steroids for epidural steroid injections due to risk of intravascularly mediated embolization.
  - Long term: Suppression of the HPA axis, hypokalemic metabolic acidosis, weight gain, redistribution of body fat, proximal skeletal muscle wasting
  - Fungal meningitis: Outbreak (753 total infections in 20 states, 2012–2013) and mortality (64 deaths over the same time period) related to steroid compounds manufactured at the New England Compounding Center, a compounding pharmacy that was neither licensed nor inspected by USA FDA for large-scale pharmaceutical manufacturing.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT			Dilated, reactive pupils
CV	Retention of sodium and free water	Palpitations Sweating Hyponatremia	Htn/hypotension Tachycardia Autonomic degeneration including: loss of R-R variability on ECG
RESP	No consistent changes	COPD, asthma	Tachypnea, apnea
GI	Abdominal pain, gastritis	IBD, GI ulcer	Abdominal discomfort, guarding
ENDO	Insulin resistance induced hyperglycemia	DM	Sensory deficits from neuropathy
CNS/MS	Euphoria, panic attacks Inhibit calcium absorption Anxiety, mood disorders Hallucinations Sleep disturbances	Cataracts Osteoporosis	Altered mental status Muscle weakness Pathologic fractures Tremors, delirium
DERM		Bruising	Skin changes

Key References: Ericson-Neilsen W, Kaye AD: Steroids: pharmacology, complications, and practice delivery issues, *Ochsner J* 14(2):203–207, 2014; Shaikh S, Verma H, Yadav N, et al.: Applications of steroid in clinical practice: a review, *ISRN Anesthesiol* 2012(7), 2012.

Perioperative Implications

- Special consideration of preop blood glucose and lytes
- Steroid supplementation is necessary in the periop setting if pts have a history of hypoadrenocorticism or suppression of the HPA axis due to a history of steroid intake.
- In presence of adrenal insufficiency, it is important to be hypervigilant to prevent precipitation of adrenal crisis secondary to surgical stress.
  - Preop management should include treatment of hyperkalemia, hyponatremia, and hypovolemia.
  - Stress dose of glucocorticoids (100 mg hydrocortisone phosphate IV) should also be given
  - Avoid medications that are inhibitors of cortisol synthesis. These include ketoconazole, aminoglutethimide, etomidate (selectively inhibits adrenal 11-beta hydroxylase).
- Cushing disease or syndrome:
  - Obese/morbidly obese pts: May present difficult airways; carefully assess Mallampati and TM distance.
  - Pituitary adenoma can result in increased ICP.
  - Use opiates to prevent sympathetic surge associated with intubation.
  - Avoid ketamine to prevent excessive sympathetic effects.
  - Etomidate may be used.

Gold (Auranofin, Aurothioglucose, Aurothiomalate)

Kevin Miller | Jonathan Gavrin

Uses

- Rheumatoid arthritis treatment for patients without sufficient response to initial treatment with NSAIDs, steroids, or other DMARDs.
- May have efficacy in pemphigus vulgaris, psoriatic arthritis, and palindromic rheumatism but lacks trials is and rarely used due to availability of other therapies.
- Availability of other DMARDs, such as biologic TNF inhibitors and methotrexate, has decreased the use of gold.

Perioperative Risks

- IM gold associated with higher dropout rates due to side effects when compared to other DMARDs (up to 19% in one study).
- Cutaneous reactions range from erythema and pruritus (30% of pts) to exfoliative dermatitis.
- Mucous membrane lesions (20% of pts), including stomatitis, pharyngitis, gastritis, and colitis.
- Dermal deposits and chrysiasis (gray-to-blue pigmentation of sun-exposed skin) are possible with large cumulative doses. Effect on transcutaneous Hgb saturation measurement is unknown. Some pts are noted to have corneal deposits.
- Allergic (5% of pts): Anaphylactoid and nitritoid reactions, with transient flushing, nausea, hypotension, dizziness, and diaphoresis (especially seen in pts also taking ACE inhibitors).
- GI (5% of pts): Diarrhea (common in pts taking the oral formulation auranofin), enterocolitis, jaundice and hepatic toxicity (from cholestasis), transaminitis, pancreatitis, and metallic taste.
- Renal: Proteinuria (10–15%, usually resolves with cessation of treatment), renal tubule deposition, acute renal failure, and nephrotic syndrome. Use caution in pts with decreased renal function due to delayed elimination.
- Pulmonary infiltrates and interstitial pulmonary disease are rare and usually resolve with cessation of treatment; difficult to differentiate from underlying RA pulm fibrosis.
- Hematologic: Thrombocytopenia (<5%, usually develops in first 6 mo, immune-mediated attack on bone marrow reverses with cessation of treatment), leukopenia (2%), eosinophilia, bone marrow suppression, rare progression to aplastic anemia. This can be avoided in pts given antimalarials, phenylbutazone, or oxyphenbutazone because of cumulative bone marrow suppression.
- Neurologic: Cranial nerve palsies, encephalitis, Guillain-Barré-like syndrome. Peripheral neuropathy (<1%—painful paresthesias progressing to asymmetric weakness, may be preceded by fever/rash; direct toxic effect vs. hypersensitivity reaction).
- Not usually administered to pregnant pts but limited published data are available.
- Use caution in the elderly (due to underlying renal insufficiency and bone-marrow suppression).

Overview/Pharmacology

- Consider IM (aurothioglucose, aurothiomalate) versus oral (auranofin) use. Monitor closely for side effects; oral administration has less common side effects but higher incidence of immunosuppression and rare side effects.
- Rapidly absorbed; peak serum concentrations after IM injection 2–4 h.
- Highly (~95%) albumin-bound and also binds to macroglobulins.
- Slow elimination, with half-life of single 50-mg dose IM approximately 7 d.
- Can be noted in tissues up to 20 y following the last dose.
- After IM full dose, blood levels return to normal in 40–80 d.
- Elimination: Majority occurs in renal (approximately 75%), with the remainder in feces.

Drug Class/Mechanism of Action/Usual Dose/Monitoring

- Anti-inflammatory DMARD.
- Free thiol group may contribute to reduction in oxidative stress.
- Gold compounds sequestered in phagocytic cells of reticuloendothelial system (liver, spleen, lymph nodes) and synovial membranes.
- Gold suppresses migration of monocytes and macrophages.
- Suppresses proinflammatory cytokines such as interleukins 1α, 1β and 6, TNF-α, as well as prostaglandin synthesis, C1 inhibition, lysosomal hydrolytic enzymes and elastase inhibition, and B-cell inhibition.
- Slows radiologic progression of RA.
- Initial dose of 10 mg, with 25 mg dose in a wk used to test for hypersensitivity.
- Subsequent doses totaling 50 mg per wk are given until 1 g reached. May not see clinical effect for up to 20 wk.
- Continuing therapy involves 50 mg IM every 2–6 wk.
- Monitor for anemia, leukopenia, and thrombocytopenia with regular blood testing and for proteinuria with urinalysis.
- Auranofin dosage initially should be 6 mg/d in divided doses; may be increased to 9 mg/d in divided doses after 6 mo.

Assessment Points

System	Effect	PE	Test
HEENT/ DERM	Erythema, pruritus, dermatitis, mucous membrane lesions		
MS	Evaluate for manifestations of RA (arthritis, c-spine involvement, TMJ)	ROM, decreased cervical range of motion and oral mouth opening	Lateral neck radiograph, neck CT, MRI
RESP	Inflammation, pulm infiltrates		CXR
GI	Diarrhea, jaundice, hepatitis		LFTs
GU	Proteinuria, nephrotic syndrome, renal failure		Renal function, pregnancy
CNS	Encephalitis, peripheral neuropathy, cranial nerve palsy	CNS exam	

Key References: Bykerk V: Nonimmunosuppressive disease-modifying antirheumatic drugs. In Hochberg MC, Silman AJ, Smolen JS, et al., editors: *Rheumatology,* ed 6, Philadelphia, 2015, Elsevier, pp 434–442; Cohen SA, Stabile MJ, Warfield CA: Pain in the extremities. In Warfield CA, Bajwa ZH, editors: *Principles and practice of pain medicine,* ed 2, New York, 2004, McGraw-Hill, pp 315–342.

Perioperative Implications/Possible Drug Interactions

- No interactions with anesthetic medications have been reported.

Anticipated Problems/Concerns

- Assess pts for musculoskeletal manifestations of RA including C-spine and TMJ involvement; may require additional equipment or planning for endotracheal intubation or may require additional care during positioning. Pts with cutaneous manifestations may have friable tissue, including mucous membranes.
- Review lab evaluation for side effects of treatment causing pulm, hepatic, or renal dysfunction or hematologic disorders.

Hormone Replacement Therapy

Aliya Ahmed | Robyne Irshad Khan

Uses

- Prevention or alleviation of moderate to severe menopausal signs and symptoms such as vasomotor effects, depressive mood changes, vaginal dryness, urogenital atrophy, osteoporosis, cardiovascular disease, and cognitive dysfunction
- Treatment of physiologic and physical manifestations of primary ovarian insufficiency

Perioperative Risks

- Increased risk of VTE due to increased generation of fibrin, reduction in plasma levels of protein S, resistance to activated protein C, and higher levels of C-reactive proteins
- May cause reduction in fibrinogen, decrease in level of plasminogen activator inhibitor-I, leading to enhancement of fibrinolytic potential and prolonged bleeding

Worry About

- Increased risk of VTE including DVT, PE, stroke, and MI with HRT
- Increased risk of fibrinolysis and prolonged bleeding with combination estrogen-progestin

Overview/Pharmacology

- HRT is a generic term for the use of estrogen therapy alone, the combination of estrogen and progesterone, or a chemical analogue called a progestin.
- Conjugated estrogens and synthetic progestins have been most commonly used in HRT.
- Estrogens: A group of 18-carbon steroid compounds that occur naturally in three major forms: estrone, estradiol, and estriol. All steroids contain four condensed rings, designated A to D. The phenolic A-ring is the principal structural feature responsible for selective high-affinity binding to the estrogen receptors. Like most steroid hormones, estrogens can diffuse readily across cell membranes. Once within a cell, they bind and activate estrogen receptors, which, in turn upregulate gene expression. Estrogen receptors are abundant throughout the body and can be found in the female reproductive tract, mammary glands, hypothalamus, endothelial cells, vascular smooth muscle, lung, brain, and bone.
- Progestins: A family of 21-carbon steroids that are synthetic derivatives of the 19-nortestosterone structure. Having effects similar to progesterone, progestins work by binding to an intracellular progesterone receptor. This results in transcriptional activation, causing endometrial proliferation, suppression of uterine contractility, mammary gland development, and thickening of endocervical gland secretions.
- Tibolone: A synthetic compound having mixed estrogenic, progestogenic, and androgenic activities; it is used as an alternative to conventional HRT.
- SERMs: These (e.g., raloxifene) act as estrogen agonist in some tissues while exerting antagonist effects in others.

Drug Class/Usual Dose

- Various formulations are available for oral, parenteral, transdermal, and topical administration. Current recommendation is to use the lowest dosage to control symptoms for the shortest period.
- The typical daily oral dose of conjugated estrogen is 0.625 mg; however, initial treatment should start at 0.3 mg/d, with dose adjustment based on clinical response. For transdermal estrogen, 17-beta estradiol patches of 25, 37.5, 50, 75, and 100 μg/d are available. Subcutaneous implants in doses of 20, 50, and 100 mg—in addition to vaginal gels, rings, and tablets—are also available.
- Progestin is typically given in a cyclic regimen (5–10 mg/d) or continuous regimen (2.5 mg/d). Better choice is a micronized progestin (Prometrium, for example) which does not oppose the effect of estradiol on arterial function. Progestin transdermal and intrauterine preparations are also used.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Retinal vascular thrombosis, increased corneal curvature, increased lacrimal secretion, dry-eye syndrome, headaches	Changes or loss of vision, contact lens intolerance, headache	Pale retina with cherry red macula, retinal hemorrhages	Ophthalmologic exam
CV	Fluid retention, Htn, improved lipoprotein profiles: increased HDL, decreased LDL	Swelling and weight gain, Htn	Edema	BP, lipid profile
GI	Pancreatitis	Abdominal pain, bloating, nausea	Epigastric pain	Amylase, lipase, alk phos
HEPAT	Cholestasis, gallstone formation	Abdominal pain, intolerance to fatty food	RUQ pain	RUQ US, LFTs
GU	Abnormal uterine bleeding, changes in cervical secretions, increase in fibroid size, vaginal candidiasis	Vaginal bleeding, vaginal discharge, vaginal itching/burning	Enlarged lobulated uterus, vaginal discharge	Gynecologic exam, gynecologic US, KOH prep test
HEME	Increased coagulation, increased fibrinolysis	DVT, PE, MI, CVA Prolonged bleeding	LE swelling, SOB, CP, neurologic deficits	PT/PTT, D-dimer, duplex US, CT angio fibrinogen, antithrombin III, Protein C
DERM	Melasma, rashes	Skin changes	Hyperpigmentation, acne	Dermatologic exam

Key References: Voican A, Francou B, Novac L, et al.: Pharmacology of hormone replacement therapy in menopause. In Gallelli L, editor: *Pharmacology*, Intech, 2012, pp 313–338. <http://www.intechopen.com/books/pharmacology>. (Accessed 28.06.16); Brighouse D: Hormone replacement therapy and anaesthesia, *Br J Anaesth* 86(5):709–716, 2001.

Perioperative Implications

Preoperative Concerns

- Increased risk for VTE. Pts undergoing procedures associated with moderate to high risk for VTE should stop hormone therapy 4 wk prior to surgery. Rigorous prophylaxis for DVT must be observed in the periop period.
- Risks associated with discontinuation of HRT are withdrawal bleeding, hot flashes, and other menopausal symptoms.

Induction/Maintenance

- Progestin metabolite allopregnanolone may affect the excitability of neurons through direct modulation of the GABA-A receptors, exerting hypnotic/sedative, anxiolytic, and anesthetic effects.
- Alterations in the activity of various cytochrome P450 CYP isozymes may require dose adjustment of hepatically cleared drugs in some pts.
- Activation of fibrinolytic pathways with combined estrogen-progestin replacement therapy may result in periop bleeding.

Postoperative Period

- Increased risk for VTE extends into the postop period. Vigilance for DVT, PE, stroke, and MI is required.

Anticipated Problems/Concerns

- Coagulopathy, especially an increased risk for VTE, remains a top concern for women using HRT.

Inhaled Bronchodilators

Michael Feduska

Uses

- Reversal of airflow limitation via relaxation of airway smooth muscle tissue
- Long-acting formulations used for chronic therapy and short-acting formulations for acute symptom relief.
- Diagnosis of COPD: FEV_1/FVC <0.70 after bronchodilator treatment.

Overview/Pharmacology

- Two classes: $Beta_2$ agonist and anticholinergic.
  - Inhalational administration decreases systemic effects, increases potency, and shortens time to onset.
  - MDI, DPI, or NEB routes.
  - Airway responsiveness is measured by improvement of FEV_1.
  - Combined use of $beta_2$ and anticholinergic is superior to either used as single therapy.
  - Often combined with an inhaled corticosteroid.
- $Beta_2$ agonist:
  - Short-acting (albuterol, levalbuterol, fenoterol, terbutaline): Onset within about 5 min; peak 30 min to 1 h; duration 4 to 6 h; levalbuterol 6 to 8 h
  - Long-acting: Duration 12 h (arformoterol, formoterol, olodaterol, salmeterol), 24 h (indacaterol)
- Anticholinergic:
  - Short-acting (ipratropium bromide, oxitropium): Onset 1 to 3 h; duration 6 to 8 h
  - Long-acting (tiotropium): Duration 24 h

Perioperative Risks

- $Beta_2$ agonist:
  - Sinus tachycardia, cardiac arrhythmias
  - Hypokalemia/hypomagnesemia
  - Paradoxical bronchospasm
- Anticholinergic:
  - Nausea
  - Acute angle glaucoma
  - Urinary retention
  - Tachycardia

Worry About

- Delivery can be compromised by poor technique or coordination.
- $Beta_2$: Concern for additive effect with other drug classes that cause QT prolongation, cardiac arrhythmias, hypokalemia (thiazide diuretics)
- Long-acting $beta_2$ agonist subject to tachyphylaxis, unlike short-acting type
- Beta-blocker: $Beta_1$–selective antihypertensive is ideal
- Anticholinergic additive adverse effects with other anticholinergic medications

Drug Class/Mechanism of Action/Usual Dose

- $Beta_2$ stimulation: G protein–coupled receptor increases cAMP formation, increasing Ca^{2+} influx via L-type Ca^{2+} channel, causing smooth muscle relaxation
- Anticholinergic: Acetylcholine muscarinic receptor (M1, M2, M3) blockade inhibits G-protein signaling, decreases cGMP formation, and prevents bronchoconstriction
  - Short-acting is M2-, M3-selective
  - Long-acting is M1-, M3-selective
- Delivered via MDI, DPI, or nebulizer
- Short-acting salbutamol (albuterol): 2.5 mg/3 mL 0.083%, 5 mg/mL NEB 0.5%, q4-6h prn
- Long-acting arformoterol: 15 µcg/NEB q12h; formoterol: 12 µg/cap DPI q12h; olodaterol: 2.5 µg/MDI q12h; salmeterol: 50 µg/DPI q12h; indacaterol: 75 µg/cap DPI q24h
- Short-acting: Ipratropium 0.5 mg/2.5 mL NEB or 17 µg/spray DPI q6–8h
- Long-acting tiotropium bromide: 18 µg/cap DPI, 1 cap q24h

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Xerostomia, acute angle glaucoma (A-ch)	Glaucoma, Hx of administration via face mask, contact with eyes	Eye pain, erythema	
CV	Tachycardia, arrhythmias ($beta_2$, A-ch)	Palpitations	HR	ECG
GI	Nausea, constipation (A-ch)			
RESP	Bronchodilation ($beta_2$, A-ch)	Dose frequency, Hx of exacerbation, Hx of intubation	Screening FET	Spirometry: (FEV_1, FEV_1/FVC)
METAB	Hypokalemia, hypomagnesemia ($beta_2$)	Concurrent use of potassium-wasting medications (thiazide diuretics)		K+
GU	Urinary retention (A-ch)	Increased risk with BPH		
CNS	Anxiety, headache, resting tremor			

Key References: Currie G, Lee DK, Lipworth B: ABC of chronic obstructive pulmonary disease. Pharmacologic management—oral treatment, *Br Med J* 332(7556):1497–1499, 2006; Woods BD, Sladen RN: Perioperative considerations for the patient with asthma and bronchospasm, *Br J Anaesth* 103(Suppl 1):i57–i65, 2009.

Perioperative Implications

Preoperative Concerns

- Elicit Hx of frequent exacerbations, hospitalization, intubation.
- Pretreatment with short-acting $beta_2$ agonist is beneficial.
- Include risk of hypokalemia with concurrent use of potassium-wasting medications (thiazide diuretics).
- Forced expiratory time: Listen over the trachea while the pt exhales forcefully. FET <6 sec indicates airflow limitation.

Induction/Maintenance

- Bronchospasm: Treat with short acting nebulizer or MDI $beta_2$ agonist (albuterol) via ETT
- Increased dosage (8–12 puffs) required due to ETT rainout

Anticipated Problems/Concerns

- Ventilation difficulties in pts with poorly controlled COPD or asthma.
- Bronchoconstriction can lead to severe bronchospasm, air trapping, V/Q mismatch, right heart strain.
- Precipitation of tachyarrhythmias with $beta_2$ agonist or anticholinergic inhalers.
- Systemic effects associated with hypokalemia.
- Rare risk of paradoxical bronchospasm with $beta_2$ agonist.

Insulin

Thomas Schricker | Hiroaki Sato

Uses

- Treatment of pts with insulin-dependent DM, hyperglycemia, DKA, and hyperkalemia

Overview/Pharmacology

- Produced by the beta cells of the pancreatic islets of Langerhans.
- Proteolytic cleavage of the connecting peptide from proinsulin produces the C-peptide and insulin (peptides A and B), which are released into the circulation in equimolar amounts.
- In healthy subjects insulin is secreted at a basal rate of 0.5–0.7 U/h.
- The administration of insulin inhibits its endogenous secretion.
- Insulin's principal target organs are skeletal muscle, adipose tissue, and liver.
- Glycemia is controlled via insulin receptor–mediated effects of insulin on glycogen synthesis, cellular glucose uptake, and gluconeogenesis.
- Stimulates the Na^+K^+-ATPase activity and thus lowers plasma potassium.
- The kidneys are primarily responsible for the clearance of exogenous insulin, while endogenously produced insulin is cleared also by the liver.
- Classified according to onset, peak, and duration of action.
- Can be given IV, IM, and SQ.

Pharmacokinetics of Different Types of Insulin (After SQ Administration)

	Rapid-Acting	Short-Acting	Intermediate-Acting	Long-Acting	Very Long–Acting
	Humalog Novolog Apidra	Regular Humulin R Novolin R	NPH N	Lantus Levemir	Tresiba
Onset	10–30 min	0.5–1 h	1–2 h	1–2 h	1–2 h
Peak (h)	0.5–1.5	2–4	4–12	No peak	No peak
Duration (h)	3–5	5–8	18	<24	>24

- Periop and during critical illness, only short-acting insulin is being used. IM administration results in more rapid time-action profile than SQ injection.
- Effect of IV insulin is also more rapid than that of SQ.
- Maximum effect of IV insulin reached after 20–30 min and can last 1 h.
- Insulin's serum half-life is 7 min.

Dosing

- Wrong insulin dosing ranks among the top five drug administration errors.
- Handwritten abbreviations such as "u" and "iu" are major causes for unintentional administration of 10 or 100 times the prescribed dose.
- Regular human insulin available in two concentrations: 100 U/mL (U-100) and 500 U/mL (U-500).
- When administered IV, only U-100 regular insulin concentration should be used.
- For dosing, insulin should be drawn up with a specific insulin syringe (dilute 100 U in 100 mL normal saline, 1 U = 1mL).
- Effective dose depends on the (often unpredictable) extent of pt's tissue insulin sensitivity and target blood glucose.
- Initial bolus doses to treat hyperglycemia range between 2 and 10 U.
- Continuous insulin infusions typically start at 1–2 U/h (in type 1 diabetic pts, 0.5–1 U/h) and frequently must be titrated to achieve target blood glucose.
- Blood glucose should be measured at least every 30 min.
- Note: Half-life of insulin is prolonged in pts with renal failure.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
METAB	Decreased blood glucose	Use of oral hypoglycemic agents Fasting Alcohol consumption Renal and hepatic impairment	Sweating Tachycardia convulsion tremor Coma	Blood glucose
	Hypokalemia	Mineralocorticoid excess (Cushing syndrome, primary aldosteronism, use of steroids) Diet or parenteral nutrition Use of diuretics	Arrhythmia Weakness Fatigue Polyuria	Serum/urine lytes ECG
	Hypophosphatemia			Serum phosphate
	Protein anabolism	Kwashiorkor Marasmus Cancer cachexia Chronic renal disease	Edema	Serum albumin Whole body nitrogen balance
	Decreased lipolysis			Serum free fatty acids Acid-base balance
CV	Vasodilation Increased skeletal, myocardial, cerebral blood flow Positive inotropic	Use of vasodilators		BP Cardiac output
HEM	Decreased plt aggregation Impact on fibrinolysis	MI Cerebrovascular accident Pulm embolism, DVT Pregnancy Cancer Genetic factors	Chest pain SOB 5 Ps: Pain, paralysis, pulselessness, pallor, paresthesia Neurologic deficit	CT MRI Doppler US BP ECG

Key References: Evans CH, Lee J, Ruhlman MK: Optimal glucose management in the perioperative period, *Surg Clin North Am* 95(2):337–354, 2015; Dhatariya K, Levy N, Kilvert A, et al.: NHS diabetes guideline for the perioperative management of the adult patient with diabetes, *Diabet Med* 29(4):420–433, 2012.

Perioperative Implications

Metabolic Risks

- Hypoglycemia:
  - Glycemia ≤55 mg/dL: Neurologic and adrenergic symptoms including sweating, shaking, anxiety, and tachycardia.
  - Glycemia ≤50 mg/dL: Severe impairment of CNS—for example, headache, fatigue, dizziness, inappropriate behavior (sometimes mistaken for inebriation), confusion, blurred vision, and eventually coma and death.
- Hyperglycemia: Glycemia ≥600 mg/dL: Osmotic diuresis, fever, vision loss, hallucinations, and coma.
- DKA: Typically affects fasting type 1 diabetic pts who stop insulin treatment. Diagnosis is based on increased serum and urinary ketones, signs of dehydration, DVT and pulm embolism, acidosis, and a Kussmaul breathing pattern.
- Hypophosphatemia.
- Hypokalemia.

Preoperative Concerns

- Poor preop glycemic control (HbA_{1c} >8.5%) may warrant referral to diabetes specialist.
- Traditionally, long-acting insulin discontinued 2–3 d before surgery; glucose levels are then stabilized by a combination of intermediate- and short-acting insulin.
- If glycemic control is well managed, may consider continuing long-acting insulin regimen until day of surgery.
- Prandial insulin should be withheld while fasting and blood glucose is measured prior to surgery in all diabetic pts.
- If capillary blood ketones are >300 mol/L or urinary ketones >3+, cancel surgery, follow DKA therapeutic guidelines, and contact a diabetes specialist.
- Symptomatic hyperglycemia >400 mg/dL may also justify delay of surgery.
- In type 1 diabetic pts, rapid-acting analogue insulin may be given SQ assuming that 1 U decreases blood glucose by 54 mg/dL.
- Type 2 diabetic pts may require up to 0.1 U/kg of SQ rapid-acting analogue insulin.
- Blood glucose should be measured 1 h later and, if necessary, IV insulin started.

Intraoperative Concerns

- Surgical trauma reduces tissue insulin sensitivity, resulting in hyperglycemia also in nondiabetic pts.
- Acute insulin resistance is aggravated in the presence of stressors such as cardiopulmonary bypass, use of catecholamines, hypothermia, and after long periods of preop fasting.
- Even moderate hyperglycemia contributes to morbidity and mortality after major surgery.
- Although the ideal level of glycemia with regard to surgical outcomes is unknown, most professional associations recommend a blood glucose level <200 mg/dL.
- From a metabolic perspective, anesthetic techniques seem preferable that allow early return to normal diet, mobilization, and usual pharmacologic diabetes management. Efferent neuraxial blockade has been demonstrated to attenuate the hyperglycemic response to surgery and facilitate recovery.
- Glycemia in anesthetized, unconscious pts must be monitored and hypoglycemia avoided.
- If blood glucose is <72 mg/dL, 100 mL of 20% glucose can be given IV.
- Type 1 diabetic pts receive insulin infusions continuously (at doses equivalent to the daily dose of long-acting insulin prescribed before surgery).

Postoperative Period

- Hyperglycemia can be managed by SQ or IV administration of insulin using so-called sliding scales. However, in the context of surgery and critical illness, traditional insulin sliding-scale protocols are often ineffective (i.e., fail to achieve the quality of glycemic control aimed for).

Latest Developments

- There is evidence to suggest that the quality of preop glycemic control as assessed by HbA_{1c} is associated with clinical outcomes.
- Insulin has been reported to improve memory function in cognitively impaired individuals.
- Therapeutic use of intranasal insulin in pts with Alzheimer disease is under investigation (phase 2 trials).
- Inhaled insulin (Afrezza) was approved by the FDA in 2014.

Leukotriene Antagonists

Kathryn C. Hall | Michael A. Hall | Lee A. Fleisher

Uses

- Include the leukotriene receptor antagonists montelukast, zafirlukast, and pranlukast (not available in USA) as well as the 5-lipoxygenase (5-LO) inhibitor zileuton. Montelukast is the most commonly used drug of this class in USA.
- Montelukast is a once-daily oral drug approved for the prevention of exercise-induced bronchospasm.
- Most commonly used as adjuvant anti-inflammatory agents in the treatment of chronic asthma in addition to inhaled corticosteroids.
- Mixed evidence exists for the use of leukotriene antagonists for other lung diseases, such as COPD, interstitial lung diseases, and obstructive sleep apnea.
- These drugs may have a possible benefit in various malignancies as well as pulmonary and systemic vascular diseases; studies are ongoing.

Perioperative Risks

- Small risk (1.9%) of hepatic dysfunction in pts on zileuton. LFTs are usually monitored in these pts.
- Small risk of increased INR in pts taking zileuton and warfarin.

Worry About

- Potentiation of effects of warfarin, theophylline, and propranolol with zileuton.
- Pts on any of these second-line asthma therapies may have more severe asthma at baseline and may be more prone to bronchoconstriction/bronchospasm in the periop period.

Overview/Pharmacology

- Antagonism of the effects of leukotrienes decreases bronchoconstriction and inflammation associated with asthma.
- Montelukast: 99% protein-bound; metabolized in liver by CYP3A4 and CYP2C9; predominantly excreted in bile.
- Zafirlukast: 99% protein-bound; metabolized in liver, mainly by CYP2C9; 90% excreted in bile, remainder in urine.
- Zileuton: Metabolized by P450 system in liver, can inhibit CYP1A2 activity; CYP1A2 inhibition can increase serum concentrations of theophylline, propranolol, and warfarin (only the R enantiomer, metabolism of which has less of an impact on the therapeutic effect of warfarin when compared with metabolism of the S enantiomer).

Drug Class/Mechanism of Action/Usual Dose

- Activated leukocytes express 5-LO, which catalyzes the conversion of arachidonic acid to leukotriene precursors and eventually activated leukotrienes.
- The cysteinyl leukotrienes (C_4, D_4, and E_4) bind to endothelial receptors such as cysteinyl leukotriene receptor 1 ($cysLT_1$) and activate a signaling cascade that results in bronchoconstriction, inflammation, endothelial permeability, and mucus secretion.
- Leukotriene antagonists either inhibit $cysLT_1$ (montelukast, zafirlukast, and pranlukast) or inhibit 5-LO (zileuton). Both result in decreased cysLT signaling, decreasing bronchoconstriction and other leukotriene effects.
- Usual doses:
  - Montelukast: 10 mg daily (5 mg daily for children)
  - Zafirlukast: 20 mg twice daily
  - Zileuton: 2400 mg daily in divided doses (600 mg 4 times daily of the immediate release or 1200 mg twice daily of the continuous-release formulation)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	Decreased bronchoconstriction Decreased mucous production	Improved symptoms of asthma Fewer asthma attacks	Decreased wheezing	PFTs
GI	Dyspepsia	GI discomfort		
CNS	Headache	Headache		
HEPAT (zileuton only)	Hepatocyte damage Inhibition of CYP1A2	Toxicity of coadministered theophylline, propranolol, or warfarin	Jaundice Other signs specific to which drug levels have been increased	LFTs Serum drug levels

Key References: Scott JP, Peters-Golden M: Antileukotriene agents for the treatment of lung disease, *Am J Respir Crit Care Med* 188(5):538–544, 2013; Watts K, Chavasse RJ: Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children, *Cochrane Database Syst Rev* (5):CD006100, 2012.

Perioperative Implications

Preoperative Concerns

- Pts on second-line therapy for asthma may have more severe asthma at baseline. A detailed asthma history should be taken; pretreatment with inhaled beta agonists may be beneficial.
- There is no evidence of a withdrawal syndrome or of a rebound of symptoms after short-term discontinuation of use.

Induction/Maintenance

- Low index of suspicion for the development of bronchospasm.
- Intermittent administration of inhaled beta agonists may be beneficial.
- No reported interactions between any of the leukotriene antagonists and commonly used anesthetic medications.

Regional Anesthesia

- No reported impact on the effectiveness or safety of regional anesthetic techniques

Anticipated Problems/Concerns

- Although there have been reports of mood change and suicidal ideation in pts treated with montelukast, a review of clinical trial data has not supported a link between this drug and these adverse effects.
- The vasculitis Churg-Strauss syndrome has been associated with the use of leukotriene antagonists in pts with asthma. However, whether this is a causative relationship or merely an unmasking of the vasculitis by the allowed reduction in corticosteroid dosing after initiation of antileukotriene therapy has yet to be definitively shown.

Lithium Carbonate (Lithobid)

Ira Padnos | Viet Nguyen | John A. Helmstetter | Alan David Kaye

Uses

- For treatment of manic episodes of bipolar disorder and some schizoaffective disorders.
- Approved for maintenance therapy to help prevent episodes of mania or depression.
- As an augmenting agent for antidepressants. Has also been used to treat aggression, PTSD, and conduct disorder in children.
- For hyperthyroidism (e.g., Graves disease) (may eventually lead to hypothyroidism).

Perioperative Risks

- Extremely narrow therapeutic level with desired serum levels of 0.4-1 mmol/L.
- Interaction with depolarizing and nondepolarizing muscle relaxants causes a prolonged response, specifically with pancuronium and succinylcholine.
- Decreased dose requirement for IV and inhalational anesthetics (reduced MAC).
- Elderly pts are especially at risk for toxicity. Problems include GI (e.g., nausea, vomiting, and diarrhea), neurologic (e.g., sluggish, ataxia, confusion, agitation, tremors), cardiac (e.g., prolonged QTc, bradycardia, arrhythmias), and somatic (e.g., fatigue, chills, rhinorrhea, myalgias) symptoms.

Pharmacokinetics/Pharmacodynamics

- At the cellular level, acts as imperfect substitute for Na^+; intracellular accumulation of lithium decreases phosphatidylinositides by interfering with hydrolysis of myoinositol-1-phosphate in the brain. Specific mechanism of action is unknown.
- Decreases availability of norepinephrine at the central adrenergic synaptic cleft because it increases reabsorption into storage granules. Also interferes with calcium depolarization–mediated release of norepinephrine and dopamine centrally.
- May also inhibit the ability of some hormones to activate adenylyl cyclase.
- Apparent volume of distribution of 0.6–1 L/kg with no plasma protein binding.
- Almost complete absorption from GI tract; peak levels reached 2–4 h after oral dose.

- Initial distribution in extracellular fluid, subsequent accumulation in tissues.
- Eliminated exclusively by renal excretion with a half-life of 20–27 h after a single dose. One-third to two-thirds of acute dose excreted in 6–12 h; 80% reabsorbed in the proximal convoluted tubules.
- Reabsorption is related to sodium balance. Na^+ depletion causes retention of lithium; increase lithium levels from thiazide diuretics, extracellular carbonic anhydrase, furosemide; Na^+ loading causes increased excretion of lithium.
- Lithium clearance is 20% of creatinine clearance; toxic at levels >1.5 mEq/L.

Drug Class/Usual Dose

- Lithium salt, alkali metal, monovalent cation; is minimally protein bound.
- Daily dose is individualized; regular monitoring of lithium levels required. Usual adult dose varies: 900-2400 mg/d in 3–4 divided doses or 900–1800 mg/d in 2 divided doses of sustained release formulation.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Therapeutic levels cause benign ST interval/T-wave changes Toxicity: Malignant arrhythmias, heart block, hypotension	Dose, intercurrent illness, drugs precipitating toxicity	CVS examination	ECG
ENDO	Enlarged tender thyroid; hypothyroidism rare	Neck pain, hypothyroid symptoms	Thyroid	FT_4E/TSH
GU	Nephrogenic DI	Polyuria, polydipsia		Urine/serum lytes/osmolality
CNS	Toxicity: Tremor, drowsiness, coma, convulsions Therapeutic: May cause drowsiness, slowing of EEG	Dose, concomitant therapy, illnesses	CNS exam	Lithium level
DERM	Dermatitis			

Key References: Huyse FJ, Touw DJ, Schijndel RS, et al.: Psychotropic drugs and the perioperative period: a proposal for a guideline in elective surgery, *Psychosomatics* 47(1):8–22, 2006; Fox C, Kaye AD, Liu H: Psychopharmacologic agents and psychiatric drug considerations. In Kaye AD, Kaye AM, Urman RD, editors: *Essentials of pharmacology for anesthesia, pain medicine, and critical care.* New York, 2015, Springer, pp 581–594.

Perioperative Implications

Preoperative Concerns

- Drugs that affect GFR or promote renal sodium wasting lead to increased lithium levels and risk of toxicity: Thiazide diuretics, eplerenone, furosemide, ACE inhibitors, carbamazepine, NSAIDs.
- Increased risk of neurotoxicity: Verapamil, diltiazem, metronidazole.
- Increased risk of serotonin syndrome with SSRIs, tramadol, meperidine, and other serotoninergic agents.

Induction/Maintenance

- Must be aware of signs of lithium toxicity, which include skeletal muscle weakness, ataxia, sedation, widening of the QRS complex.
- Generally believed to reduce requirement for inhaled and injected anesthesia (e.g., reduced MAC), most likely related to decreased release of neurotransmitters.
- Possibility of prolonged NM blocking effects.
- Delayed recovery from barbiturates reported in literature.

Anticipated Problems/Concerns

- Toxic levels can be decreased with osmotic diuretics (do not use HCTZ), administration of saline, or dialysis.
- Renal toxicity is common with chronic lithium therapy. Nephrogenic DI is the most common manifestation and occurs in up to 20% of pts taking lithium. Electrolyte and fluid balance is very important.
- Hypothyroidism is the most common endocrine disorder cause by chronic lithium therapy.
- Acute exposure can cause leukocytosis; chronic exposure may cause aplastic anemia.
- Severe CV collapse; arrhythmias, heart block possible with toxicity.
- No abrupt withdrawal effects are associated with discontinuation of lithium; therefore lithium should be held in the periop period unless there is a risk/benefit reason related to the pt's mental status.
- Contraindicated in pregnancy, with increased risk of cardiac anomalies (Ebstein anomaly). May be excreted in breast milk. Lithium should be avoided in the first trimester of pregnancy.
- Pts using lithium have serious drug-drug interactions and because of this qualify for at least an American Society of Anesthesiologist classification 3.

Magnesium Sulfate

Sara A. Skrlin

Uses

- Treatment of hypomagnesemia and magnesium deficiency in critically ill pts
- Treatment of torsade de pointes, atrial or ventricular arrhythmias, digoxin toxicity
- Prevention of seizures due to preeclampsia/eclampsia
- Decrease risk of cerebral palsy in the early preterm fetus
- Management of conditions with catecholamine excess (tetanus, pheochromocytoma, attenuation of stress response during laryngoscopy)
- Orally as cathartic or laxative
- Treatment of acute severe asthma exacerbation not responding to conventional approaches
- Adjuvant to other agents during general anesthesia to reduce the requirements of analgesics, muscle relaxants, and hypnotics
- Treatment of refractory hypokalemia

Perioperative Risks

- Hypotension via decrease in SVR, worse with rapid administration.
- Muscle weakness in pts with high levels of serum magnesium (>8 mEq/L^{-1}).
- Inadvertent use in pts with impaired renal function can lead to a state of hypermagnesemia.

Worry About

- Potentiation of nondepolarizing NMBs. NMB dose adjustment and monitoring train of four is necessary. Adverse effects on neuromuscular function may occur at lower concentrations in pts with neuromuscular disease (e.g., myasthenia gravis).
- Magnesium deficiency is highly undesirable in the periop period and in critical care owing to the increased risk of arrhythmias.
- Decreased responsiveness to vasopressors due to effect of magnesium on catecholamine reuptake and hypotension due to decreased SVR.

Overview/Pharmacology

- Magnesium is the fourth most common cation in the body and second most common intracellular cation after potassium.
- Physiologic antagonist of calcium and has a fundamental role as a cofactor in over 300 enzymatic reactions.
- Conversion: 1 g of magnesium sulfate is 4 mmoL, 8 mEq, or 98 mg of elemental magnesium.
- CVS: Reduces SVR in high doses. Prolongs SA-node conduction time and reduces the rate of SA-node impulse formation. Excess catecholamine–induced vasoconstriction, arrhythmogenic effects, and diastolic dysfunction are attenuated by magnesium.
- Antiepileptic properties and the action on the CNS are not well defined. Various postulations for neuroprotection include cerebral vasodilation, blood-brain barrier protection, and anticonvulsant actions.
- Potentiation of nondepolarizing blockade is due to its presynaptic action.
- Studies have shown it to be a physiologic and pharmacologic antagonist of NMDA receptors in the CNS.
- Kinetics: 30% protein-bound, 50% renal excretion, half-life 4 h, only 1–2% is extracellular.

Drug Class/Mechanism of Action/Usual Dose

- Key actions are calcium antagonism via calcium channels, regulation of energy transfer, membrane sealing, or stabilization. Presynaptically inhibits release of acetylcholine at the NM junction.
- Emergency treatment: IV 2 to 4 g (8–16 mmoL) initially over 20 min, followed by 10 g (40 mmoL) over next 5 h.
- It can be given by IM route, but this is very painful.
- Torsade de pointes: 1–2 g IV push over 5–20 min.
- Acute severe asthma: 2 g IV (single dose) over 20 min.
- Preeclampsia/eclampsia: 4–6 g IV over 15–20 min followed by 1–2 g/h. Therapeutic levels: 4–8 mEq/L. Clinical signs of toxicity include loss of reflexes and respiratory insufficiency.
- Decrease dose by 50% in pts with impaired renal function and monitor levels closely.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Vasodilatation, sympathetic blockade, inhibition of catecholamine release, decreased myocardial contractility, antiarrhythmic	Light-headedness, flushing or sensation of warmth if given in an awake pt	Bradycardia, low BP, poor peripheral and systemic perfusion due to vasodilation and low cardiac output	Check Mg^{2+} levels, ECG, CO_2 monitoring (noninvasive and invasive)
RESP	Respiratory depressant effect due to NMB Bronchodilator	Respiratory insufficiency Improvement in asthmatic pts	Hypoxia, hypoventilation, sedation, hypercapnia	Monitor levels, pulse oximetry, ABG, end-tidal CO_2
CNS	Antiepileptic, NMDA receptor blockade, potentiation of NMB	Cessation of convulsions Analgesic adjuvant Muscle weakness	Postictal phase Decreased deep tendon reflexes Improvement in analgesia	Monitor levels
MS	Weakness, increased sensitivity to non-depolarizing relaxants	Respiratory depression Heightened response to muscle relaxants	Weakness, lethargy, absent or reduced DTRs	Monitor DTRs, twitch monitoring
OB	Tocolytic	Arrests labor	Decreased uterine tone	Uterine activity

Key References: Herroeder S, Schönherr ME, De Hert SG, et al.: Magnesium—essentials for anesthesiologists, *Anesthesiology* 114(4):971–993, 2011; Dubé L, Granry J: The therapeutic use of magnesium in anesthesiology, intensive care and emergency medicine: a review, *Can J Anesth* 50(7):723–746, 2003.

Perioperative Implications

Preoperative Concerns

- Assess baseline respiratory and CV, muscle strength, electrolytes including Mg^{2+}, renal function, and ECG prior to any anesthetic.

Induction/Maintenance

- Dose of induction agent to be titrated as an exaggerated hemodynamic response and drop in BP can occur.
- Use of muscle relaxants to be avoided unless indicated. Consider decreasing the maintenance dose and monitoring TOF. Succinylcholine can be used safely.
- Volatile agents can compound the drop in SVR. MAC may be reduced by 20%.
- When central neuraxial blockade is used, careful titration of local anesthetics dose is needed.
- Vasopressors may be required to maintain adequate MAP and SVR if serum levels are high.

Adjuvants/Regional Anesthesia/Reversal

- Depresses the stress response to laryngoscopy, intraop BP control during surgery for pheochromocytoma, hypotensive anesthesia for surgeries requiring bloodless fields.
- Magnesium is a useful analgesic adjuvant (IV, RA) as a part of multimodal therapy.
- Calcium is used as an antidote to magnesium toxicity. However, it does not reverse the effects on the NM junction.

Postoperative Period

- Assess the reversal of NMB before extubation. Muscle weakness and respiratory insufficiency may warrant extended ventilatory support.
- Risk of pulm edema.

Anticipated Problems/Concerns

- Intensive monitoring required if magnesium infusion is continued postop.
- Postpartum hemorrhage due to tocolytic effect of magnesium (decreased uterine tone) if used in labor.
- Residual NMB and watch for respiratory failure.

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Marijuana

Luis R. Sauceda-Cerda | Jeffrey R. Kirsch

Uses

- Antiemetic
- Appetite stimulation
- Analgesia
- Recreational
- Epilepsy
- Glaucoma
- Mood disorders
- Spastic disorders

Perioperative Risks

- Cross-tolerance with barbiturates, opioids, benzodiazepines, and phenothiazines
- Tachycardia, vasodilation with hypotension, anxiety, dysphoria, hallucinations (acute use)
- Airway hyperreactivity from chronic smoking (carbon monoxide inhalation)
- Decreased efficacy of oral birth control medication
- Possible procoagulant effect in immunocompromised and certain other populations

Worry About

- Multiple drug consumption

Overview/Pharmacology

- Marijuana flower is commonly smoked, vaporized, or turned into edible products.
  - Absorption via inhalation is rapid and effects are felt within minutes.
  - Enteral administration is slower and effects are felt within 30–120 min.
- Sublingual and topical preparations of cannabinoids are also available.
- Over 60 different cannabinoids have been identified.
  - Primary psychoactive agent is δ-9 THC.
  - Cannabidiol has no hallucinogenic properties and is under investigation in the treatment of epilepsy, psychotic disorders, and other neuropsychiatric conditions.
- Endogenous cannabinoid system involved in analgesia, cognition, memory, locomotor activity, appetite, vomiting, and immune control.
  - Endogenous ligands include anandamide, 2-arachidonoylglycerol, palmitoylethanolamide.

Drug Class/Mechanism of Action/Usual Dose

- Cannabinoid.
- Two G protein–coupled cannabinoid receptors (CB_1 and CB_2) have been identified.
  - CB_1 receptors found widely in central and peripheral nervous systems: Hippocampus, cortex, olfactory areas, basal ganglia, cerebellum, spinal cord.
  - CB_2 receptors found peripherally and linked to immunity (i.e., spleen, macrophages)
  - Leads to inhibition of adenyl cyclase and decreased cAMP.
  - Neurons become hyperpolarized by activating Ca^{2+} and K^+ channels
- Cannabidiol antagonizes and activates a variety of noncannabinoid receptors; reduces psychoactivity of THC.
- Dosage varies depending on indication.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypotension Tachycardia (bradycardia with chronic use) Vasodilation Myocardial depression with higher doses Increased myocardial O_2 demand Increased cerebral blood flow (decreased with chronic use)	Recent exposure Duration and amount of use Use of other recreational drugs Tobacco/alcohol use	Vital signs Injected conjunctiva Reduced oculomotor tracking	Urine toxicology screen
RESP	Coughing Decreased O_2-carrying capacity secondary to CO_2 intake with inhalation Bronchial dilation Increased ventilation (decreased with larger doses) Bronchitis Decreased transport of secretions Squamous metaplasia Emphysema			
CNS	Euphoria/dysphoria Lethargy Impairment of coordination Changes in perception Decreased ability to perform complex thoughts or actions Decreased nausea Dizziness Hallucinations Panic reactions Ataxia/dysarthria Confusion Amnesia Anticonvulsant/proconvulsant Schizophreniform symptoms Poor judgment Increasing cognitive impairment with chronic use Depression			
OPHTH	Decreased IOP Possible rebound increase in IOP with cessation Poor oculomotor tracking			
IMMUNE	Decreased resistance to infection Impairment of macrophages			
GU	Urinary retention			
OB	Preterm labor IUGR VSD in fetus Delay in cognitive development			

Key References: Whiting PF, Wolff RF, Deshpande S, et al.: Cannabinoids for medical use—a systematic review and meta-analysis, *J Am Med Assoc* 313(24):2456–2473, 2015; Kumar RN, Chambers WA, Pertwee RG: Pharmacological actions and therapeutic uses of cannabis and cannabinoids. *Anaesthesia* 56(11):1059–1068, 2001.

Perioperative Implications

Preoperative Concerns

- Chronic use can lead to prolonged intoxication, lasting several days, secondary to storage in adipose tissue and reuptake of active metabolites in the gut.
- Pts may be sedated or have signs and symptoms of bronchitis and asthma.
- Marijuana may increase opioid effects on ventilation.

Induction/Maintenance

- May interact with medications that affect heart rate
- Reduces the MAC and may cause pronounced myocardial depression with potent inhaled anesthetics.
- Anesthesiologists should anticipate interactions with anticholinergics, barbiturates, and depressants.

Postoperative Period

- Increased postop agitation and confusion.
- Motor function and coordination may be reduced for a longer period than anticipated.
- Some pts may experience withdrawal. Signs include restlessness, irritation, agitation, nausea, and cramping.

Anticipated Problems/Concerns

- Increased risk of having respiratory complications during anesthesia.
- Periop agitation.
- Recent use may impair pt's ability to give consent. Chronic use may lead to difficulty following postop instructions.
- Interactions with the effects of chronotropic medications.
- Cannabinoids have prolonged action in older pts and those with liver disease.
- Anesthesiologists should encourage preop discontinuance of the drug for elective cases and consider delaying elective cases with recent use.

Acknowledgment

The authors would like to acknowledge the contributions of Drs. Joshua W. Sappenfield and Christopher T. Stephens to this chapter in the previous edition.

Metformin (Glucophage)

Ketan Dhatariya | Nicholas A. Levy

Uses

- Treatment of type 2 DM, particularly in overweight pts, when dietary management and exercise alone do not result in adequate glycemic control.
- A reduction of diabetic complications has been shown in overweight type 2 diabetic pts treated with metformin as first-line therapy after diet failure.

Side Effects

Very common: Nausea, vomiting, abdominal pain
Common: Taste disturbance
Very rare: Lactic acidosis

Perioperative Risks

- Hypoglycemia (rare)
- Metformin-associated lactic acidosis: The summary of product characteristics states that "Metformin hydrochloride should be discontinued 48 h before elective surgery under general, spinal or epidural anaesthesia. Therapy may be restarted no earlier than 48 h following surgery or resumption of oral nutrition and only if normal renal function has been established." This is

due to the fear of metformin-associated lactic acidosis. It is unproven whether metformin causes the lactic acidosis or whether it is the diabetes that causes it.

Pharmacokinetics/Pharmacodynamics

- Oral bioavailability 50–60%
- Absorbed from the small intestine
- Binding to plasma proteins is negligible
- Not metabolized
- Excreted unchanged in the urine
- Half-life is approx 6 h; however, antihyperglycemic effects last >24 h.

Drug Class/Mechanism of Action/Usual Dose

- Biguanide oral antihyperglycemic agent
- Decreases hepatic glucose production.
- Decreases intestinal absorption of glucose.
- Improves insulin sensitivity by increasing peripheral glucose uptake and utilization.
- Usually dosed 500-1000 mg twice daily.
- Maximum recommended daily dose is 2550 mg.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
ENDO	Hypoglycemia	Use of other oral antihyperglycemic, decreased intake by mouth, alcohol consumption Elderly, debilitated, or malnourished pts, and those with adrenal or pituitary insufficiency more susceptible	Irritability, seizures, bradycardia, hypotension, respiratory failure	Serum glucose (72 mg/dL [4.0 mmol/L])
METAB	Lactic acidosis	Presence of predisposing conditions: Disease states that increase production of lactic acid (CHF, hypoxic states, shock, septicemia) or decrease removal of lactic acid (severe liver disease, alcohol)	Nonspecific Hypotension and respiratory failure have been reported	Serum lactate, serum bicarbonate, ABG, metformin levels
GI	Diarrhea, N/V, flatulence, indigestion, abdominal discomfort			
CNS	Headache			
OTHER	Asthenia, megaloblastic anemia			

Key References: Dhatariya K, Levy N, Flanagan D, et al.; for the Joint British Diabetes Societies: Management of adults with diabetes undergoing surgery and elective procedures: improving standards. Revised March 2016. www.diabetologists-abcd.org.uk/JBDS/Surgical_guidelines_2015_full_FINAL_amended_Mar_2016.pdf (Accessed February 21, 2017); Holstein A, Stumvoll M: Contraindications can damage your health—is metformin a case in point? *Diabetologia* 48(12):2454–2459, 2005.

Perioperative Implications

Perioperative Use of Metformin

- Although the summary of product characteristics states that metformin should be discontinued in the periop period, it is recognized that this strategy will lead either to widespread periop hyperglycemia (with its ensuing complications) or increased use of periop insulin and its ensuing complications. Pragmatic advice from UK suggests that the drug can be continued in the periop period in the absence of preexisting renal dysfunction, prolonged starvation, and periop risk factors for AKI.

Preoperative Concerns

- Renal, hepatic, and cardiac function should be assessed preop.
- Length of starvation should be anticipated preop.
- If there is no appreciable risk of AKI, the surgical time is short, and anticipated resumption of normal eating and drinking is rapid, it may be possible to continue metformin in preassessed pts.
- If metformin is stopped, alternative periop hypoglycemic strategies must be employed.

Postoperative Implications

- Metformin should be withheld in pts at risk of AKI.
- Do not resume metformin until the pt is tolerating an oral diet.
- Alternative strategies for maintaining euglycemia must be utilized if metformin is withheld.

Monoamine Oxidase Inhibitors; Reversible Inhibitors of Monoamine Oxidase

Jacob Addison Thomas | Lee A. Fleisher

Uses

- MAOIs are a broad class of psychoactive medications that affect the metabolism of multiple neurotransmitters.
- MAOIs are indicated for many psychiatric conditions including but not limited to atypical depression, refractory depression, depression with prominent anxiety, low psychomotor activity, and severe phobias.
- Other indications include Parkinson disease, narcolepsy, and intractable headache.

Perioperative Risks

- Risks result from accumulation of physiologically active neurotransmitters because of decreased levels of MAO. Best understood as either serotonergic or catecholic.
- Hypertensive crises arise because of excess levels of tyramine from food or norepinephrine with vasoactive drugs. Manifests as dramatically increased sensitivity to adrenergic drugs, especially indirect-acting catecholamine agonists such as ephedrine.
- Serotonin syndrome (central serotonergic hyperactivity) arises because of impaired metabolism and dramatic increase in concentration of serotonin. In pts on chronic MAOI therapy this concentration rarely rises with administration of anesthetic medications with serotonergic effects including but not limited to fentanyl and methadone.

Worry About

- Side effects of chronic MAOI administration include orthostatic hypotension, agitation, tremor, seizures, muscle spasms, urinary retention, dysuria, paresthesias, hepatotoxicity, jaundice, sedation, vision changes, hallucinations, dryness of the mouth, and constipation.
- Hypertensive crises can occur after ingestion of tyramine-containing substances such as red wine, cheeses, liver, beer, chocolate, fava beans, avocados, and pickled herring. Tyramine causes significant catecholamine release, which can lead to headache, tachycardia, nausea, hypertension, dysrhythmias, and stroke. Similarly, anesthetic medications including ephedrine and norepinephrine can precipitate a tyramine crisis. Adrenergic alpha-antagonists such as phentolamine and prazosin are useful in the treatment of tyramine-induced Htn.
- Serotonin syndrome is a well-described poisoning event described in the literature as a rare but potentially fatal reaction occurring following increased synaptic levels of synaptic serotonin. The syndrome manifests as Htn, hyperthermia, muscle rigidity, and agitation; if untreated, toxicity will progress to respiratory depression, seizures, and coma. Serotonin syndrome can be precipitated by periop or intraop coadministration of serotonin releasing medications.

Overview/Pharmacology

- MAO is an endogenous mitochondrial enzyme that inactivates neurotransmitters by deamination.
- MAOIs block oxidative deamination of naturally occurring amines, which permits neurotransmitter accumulation and increased adrenoreceptor activation.
- The two MAO isoenzymes (types A and B) differ in their substrate selectivities.
- MAO A is selective for serotonin, dopamine, and norepinephrine.
- MAO B is selective for tyramine and phenylethylamine; ineffective as antidepressant.
- Nonselective (irreversible MAO A inhibitors) agents include phenelzine, isocarboxazid, and tranylcypromine.
- Nonselective agents may interfere with many other enzymes.
- Selective agents (reversible MAO A inhibitors) include moclobemide, broforamide, lazabemide, toloxatone, and cimoxatone. Notably, reversible MAO A inhibitors are much less susceptible to drug/diet interactions.
- MAO regeneration after irreversible inhibition usually occurs after several wk.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Orthostatic hypotension, Htn	Dizziness, vision changes	BP, HR	Orthostatic BP, HR
GI	Hepatotoxicity, constipation	Jaundice		LFTs
CNS	Agitation, seizures			EEG

Key Reference: Tjan J, Malhotra V: *Yao and Artusio's anesthesiology: problem-oriented patient management*, ed 6, Philadelphia, 2008, Lippincott Williams & Wilkins, pp 641–645.

Perioperative Implications

Preoperative Concerns
- Avoid coadministration of MAOIs and SSRIs within 6 wk to avoid serotonin syndrome.
- Check LFTs, because hepatotoxicity and/or hepatic enzyme inhibition may exaggerate depressant effects of opioids, benzodiazepines, barbiturates, antihistamines, and anticholinergics.
- Controversy persists regarding discontinuation prior to elective surgery. Previous recommendations were cessation 2–3 wk prior to surgery, but recent reviews show no increased periop adverse hemodynamic effects.
- Effective anxiolysis to avoid sympathetic hyperactivity.

Induction/Maintenance
- Consider arterial cannula for close monitoring of BP.
- Phenelzine can prolong the duration of succinylcholine by inhibiting pseudocholinesterase.
- Interaction with opioids, particularly phenylpiperidine opioids including meperidine, methadone and tramadol, can lead to serotonin syndrome.
- Fentanyl and fentanyl analogues have also been implicated in other case studies as contributing to the serotonin syndrome.
- Consider regional techniques to avoid opioids; morphine or hydromorphone is preferred if necessary. Make sure that local anesthetic preparations are epinephrine-free.
- N_2O and volatile agents are acceptable.
- Hyperactive response to vasopressors and sympathetic stimulation can occur; direct-acting vasopressors of short duration at a reduced dose are preferred (such as phenylephrine at a reduced dose).
- Avoid drugs that increase sympathetic activity, such as ketamine, pancuronium, cocaine, and epinephrine (in local anesthetics).

Postoperative Period
- Judicious opioid use if needed. Analgesia is important to prevent Htn; use appropriate therapy to avoid serotonin syndrome.
- Use adrenergic alpha or beta antagonists or direct-acting vasodilators for Htn and use short-acting direct alpha agonism at a reduced dose for likely hypotension.
- Discuss timing and dosing of MAOI resumption with psychiatric consultants.

Naltrexone

Chris J. Curatolo

Uses
- Reverse the effects of opioid-agonist overdose (although IV therapy is preferred).
- Prevent relapse in pts (including physicians) addicted to alcohol and/or opioids.
  - Oral route is most common and popular.
  - Newer formulations (e.g., Vivitrol [naltrexone for extended-release injectable suspension]) are once-monthly forms that release the drug over a long period so that pts (1) do not feel the effects of opioids if they try to abuse and (2) cannot stop taking naltrexone during the treatment window.
- Treatment of intrathecal opioid-induced pruritus and nausea.
- Included in the formulation of "tamper-resistant" extended-release opioids (e.g., morphine extended release + sequestered naltrexone) so as to discourage alteration (e.g., crushing) of these long-acting formulations.
- Rapid detoxification of opioid dependence (performed under general anesthesia).

Perioperative Risks
- May precipitate acute opioid withdrawal in pts with chronic opioid use.
- Pts on chronic naltrexone therapy may be more sensitive to dangerous side effects due to receptor upregulation and hypersensitivity.

Worry About
- Pts may be refractory to the effects of opioid agonists.

Overview/Pharmacology
- Antagonist at μ-, δ-, and κ-type opioid receptors (with strongest affinity for μ-receptor)
- Longer-acting ($T_{½}$ 4 h) than its IV counterpart naloxone ($T_{½}$ 0.5–1.5 h, but has an active metabolite, 6-beta-naltrexol, with a $T_{½}$ of 13 h).

Usual Dose
- 50 mg/d oral, with higher doses once tolerated.
- IM injection of 380 mg once monthly for extended-release preparations.
- Toxicity: Generally considered safe without major adverse effects in most pts.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Syncope	Syncopal episodes	Potential markers of trauma from syncopal episodes	None usually indicated
GI	Nausea/vomiting Loss of appetite	Dyspepsia Anorexia	Usually none Weight loss	None usually indicated Weight
HEPAT	Transaminitis (supratherapeutic doses)	Usually no symptoms	Usually none	AST/ALT
MS	Increased CPK activity	Minimal typically, but may include pain	Myalgias or arthralgias	Plasma CPK
ENDO	Augments endogenous release of cortisol and catecholamines	Minimal	Minimal	Plasma cortisol
CNS	Mild dysphoria	Mild depressive symptoms	Minimal	Mood disorder inventory

Key References: Kleber HD: Naltrexone, *J Subst Abuse Treat* 2(2):117–122, 1985; Bryson EO: The perioperative management of patients maintained on medications used to manage opioid addiction, *Curr Opin Anaesthesiol* 27(3):359–364, 2014.

Perioperative Implications

Preoperative Concerns
- Pts on oral naltrexone therapy should discontinue approximately 3–7 d prior to surgery since chronic naltrexone therapy makes it more difficult to control pain.
- Pts on newer, extended-release formulations (such as once-monthly injectable naltrexone) should be at the end of their 30-d dosing window when having elective surgery.
- Pts may have an altered response to opioid agonists and may be entirely refractory to their effects while simultaneously more sensitive to dangerous side effects due to receptor upregulation and hypersensitivity.

Monitoring
- Routine
- If used in the setting of rapid detoxification under general anesthesia, monitor for signs of sympathetic hyperstimulation (e.g., increased catecholamine release and subsequent cardiovascular stimulation).

Regional Anesthesia
- Naltrexone may reduce pruritus and N/V following intrathecal opioid administration, but may also reduce the analgesic duration of the intrathecal opioid.
- RA is the preferred periop analgesic modality in pts on naltrexone therapy who are unable to discontinue prior to surgery.

Emergence/Extubation
- No known complications to date

Postoperative Period
- Increased risk of relapse to alcohol or opioid abuse postop in pts who discontinued chronic naltrexone use prior to surgery.
- Difficult to treat periop pain due to opioid receptor blockade by naltrexone.
- Maximize use of regional anesthesia and nonopioid medications to control pain.

Nicotine Replacement Therapies

Susan M. Lee

Uses
- NRTs are USA FDA-approved devices that are effective in helping treat tobacco dependence, acting on nicotinic acetylcholine receptors to mimic or replace the effects of nicotine, the highly addictive chemical from tobacco products.
- NRTs are available OTC (e.g., gum, transdermal patch, sublingual lozenge/tablet) and by prescription (e.g., nasal spray, inhaler).
- NRTs provide only nicotine; they do not contain the carcinogens and toxic gases that are found in cigarette smoke.

Perioperative Risks
- Pts who smoke cigarettes are at increased risk of periop complications, including respiratory, cardiac, and wound-healing complications. Preop smoking cessation can reduce these risks, particularly when abstinent for at least 3–4 wk before surgery.
- NRT is effective for increasing smoking cessation in both periop and nonperiop settings.
- Nicotine via NRTs is safer than cigarette smoking, since exposure to toxic combustion products is averted. Starting NRT as early as possible preop is advised to increase the duration of preop cessation. There is no evidence that short-term cessation increases complications. Smoking cessation at any time periop may lead to long-term cessation.
- Some preclinical evidence that nicotine in higher doses than produced by NRT decreases viability of skin flaps. However, no human studies have shown increased risk of cardiovascular or wound-healing complications caused by NRT.

Worry About
- During MRI procedures, transdermal nicotine patches that have metallic components can cause cutaneous burns if a pt wears them during the scan.
- Nicotine gum or sublingual lozenges/tablets can cause hiccups, nausea, and heartburn; this could potentially increase aspiration risk for pts undergoing general anesthesia.
- NRTs can cause irritation to the skin or inside of the mouth.
- A fatal nicotine dose for adults is more than 60 mg. Individual cigarettes contain 1–3 mg of nicotine. Serious overdose with standard NRT dosages is unlikely, although concomitant smoking could place the user at risk. Increased skin blood flow with inhalation agents could increase absorption from skin depot or patch.
- Nicotine toxicity manifests as nausea, salivation, abd cramps, vertigo, mental confusion, difficulty breathing, increased heart rate, skeletal muscle weakness, and seizures.
- Nicotine withdrawal can create a negative emotional state, anxiety and irritability, perception of increased stress, difficulty concentrating, increased appetite, headache, and insomnia.

Overview/Pharmacology
- Nicotine from NRTs is absorbed from the skin, the resp tract, or buccal mucous membranes. These methods deliver nicotine to the bloodstream more slowly than smoking.
- Nicotine's half-life is approximately 2 h. It is metabolized primarily by the liver and eliminated by the kidneys and in breast milk. Cotinine, which can be a urinary marker of nicotine exposure, is the principle metabolite.
- Nicotine can cause the induction of liver microsomal enzymes, resulting in faster metabolism of some anesthetics, analgesics, and sedatives.

Drug Class/Mechanism of Action/Usual Dose
- Nicotine is a highly addictive alkaloid. It is a sympathomimetic drug that stimulates autonomic ganglia and acts as a central nicotinic cholinergic agonist, thereby facilitating neurotransmitter release (i.e., dopamine, norepinephrine, serotonin, glutamate, GABA).
- A typical pack-per-day smoker absorbs 20–40 mg/d. The dose of NRTs is variable: transdermal patches (5–22 mg/24 h); gum, lozenges, tablets (1–4 mg each); inhaler (cartridge contains 10 mg); nasal spray (0.5 mg/spray). A typical 8–10 wk course of transdermal NRT for a smoker of >10 cigarettes/d is 21 mg/d patch × 6 wk, 14 mg/d × 2 wk, 7 mg/d × 2 wk. For <10 cigarettes/d: 14 mg/d × 6 wk, 7 mg/d × 2 wk.
- There is evidence that combining a nicotine patch with a rapid delivery form of NRT (e.g. gum, lozenge, inhaler, spray) is more effective than using a single type of NRT.
- Nicotine can have unpredictable effects, initially acting as a stimulant and then as a depressant.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Increased HR, BP, cardiac contractility; coronary and peripheral vasoconstriction	Palpitations, chest pain	Cardiac exam, heart sounds	Vital signs
RESP	Increased ventilation (stim of aortic and carotid body chemoreceptors)	Increased respiratory rate	Respiratory exam, breath sounds	O_2 sat, respiratory rate
GI	Vomiting, diarrhea, heartburn, initial ↑ salivary secretions	Dyspepsia, nausea		
CNS	Stimulation	Initially tremor		
ENDO	Decreased insulin sensitivity; may aggravate or precipitate diabetes			Blood sugar; HbA_{1c}
IMMUNE	May be a tumor promoter through angiogenesis, increased cell proliferation, and decreased apoptosis			

Key References: Stead LF, Perera R, Bullen C, et al.: Nicotine replacement therapy for smoking cessation, *Cochrane Database Syst Rev* 11:CD000146, 2012; Nolan MB, Warner DO: Safety and efficacy of nicotine replacement therapy in the perioperative period: a narrative review, *Mayo Clin Proc* 90(11):1553–1561, 2015.

Perioperative Implications

Preoperative Concerns
- The longer the duration of preop abstinence from smoking, the better.
- Pts may experience anxiety, irritability, increased stress, and/or headache from nicotine withdrawal; consider maintenance of nicotine supplementation via transdermal patch in medically stable pts.
- Behavioral support (brief advice and referral for individual, group, or telephone counseling) should be offered along with NRT to further increase the odds of successful smoking cessation.

Induction/Maintenance
- Pts who are smokers or receiving NRTs may experience resistance to some anesthetic or analgesic agents as a result of increased metabolism from induced hepatic enzymes.
- Nicotine is a sympathomimetic agent and also has effects on autonomic ganglia. Smokers receiving nicotine patches preop have been observed to show exaggerated increases in heart rate after tracheal intubation. NRTs may have hemodynamic effects that may need to be addressed in the periop period.
- While NRTs are safe in medically stable pts, the data are limited for critically ill pts or in pts undergoing

cardiopulmonary bypass surgery. NRT has been successfully used in nonoperative pts after acute coronary syndrome.

Postoperative Period

- Smoking contributes to acute physiologic effects such as increased sympathetic tone, lung inflammation, and tissue hypoxia, as well as long-term pathophysiologic changes such as atherosclerosis and COPD, placing these pts at higher risk for postop complications.
- Nicotine withdrawal should be considered as a cause of postop agitation or anxiety.

Anticipated Problems/Concerns

- NRTs have proven to be both safe and effective in treating tobacco dependence in medically stable pts, even in those with smoking-related diseases. NRTs can be valuable tools to manage tobacco dependence in the periop period.
- Use of NRTs in the periop period is far preferable to continued smoking, per most experts in the field.

Acknowledgment

The author wishes to acknowledge the contribution of Dr. Esther Sung to this chapter in the previous edition.

Nitric Oxide, Inhaled

Warren M. Zapol

Uses

- Children: Acute or chronic pulm Htn associated with persistent pulmonary Htn of newborn (PPHN), meconium aspiration, CHD, and congenital diaphragmatic hernia
- Adults: Acute or pulm Htn associated with ARDS, pulm embolism, placement of a LVAD, and cardiac surgery

Perioperative Risks

- Methemoglobinemia (especially breathing >80 ppm NO)
- NO_2 and peroxynitrite formation

Worry About

- Methemoglobinemia; measure metHb, especially in infants, within 6 h and then every 24 h.
- Measure inhaled NO and NO_2 levels continuously.
- Do not give if high NO_2 levels (>2 ppm).
- Do not allow NO to stagnate in ventilator or breathing circuits; it slowly converts to toxic NO_2 gas.
- High inhaled NO levels may inhibit platelet aggregation.
- In severe heart failure, reducing PVR with NO may raise left atrial pressure.
- Rebound pulm Htn during acute NO withdrawal.

Overview/Pharmacology

- Inhaled NO activates guanylate cyclase in lung vessels and airways and increases levels of cGMP, causing selective pulm vasodilation.
- Very rapid and avid binding with RBCs. Hgb inactivates NO and thereby prevents systemic vasodilation.
- NO is metabolized to nitrate and excreted in urine.
- Supplied as stock gas of ≤1000 ppm by volume of NO in nitrogen or other inert gas.
- Inhaled NO is mixed with O_2-containing gas immediately before administration via intratracheal cath, ventilator, mask, or nasal prongs.

Drug Class/Mechanism of Action/Usual Dose

- NO is a free radical with a short $T_{½}$ in aqueous solutions (~17 sec)
- It combines with ferrous-heme ring of guanylate cyclase and thereby stimulates the conversion of GTP to cGMP; cGMP reduces intracellular Ca^{2+}, causing smooth muscle relaxation, and modulates other cell functions by regulating gene expression; cGMP is broken down by phosphodiesterases.
- Usual inhaled NO dose is 1-40 ppm by volume.

Assessment Points

System	Effect	PE	Test
RESP	Decreased PVR		Decreased PAP Increased CO
	Increased gas exchange	Skin color	Increased PaO_2 Increased SaO_2 Decreased $PacO_2$

Key References: Abman SH: Inhaled nitric oxide for the treatment of pulmonary arterial hypertension, *Handb Exp Pharmacol* 218:257–276, 2013; Rossaint R, Lewandowski K, Zapol WM: Our paper 20 years later: inhaled nitric oxide for the acute respiratory distress syndrome—discovery, current understanding, and focused targets of future applications, *Intensive Care Med* 40(11):1649–1658, 2014.

Perioperative Implications

Preoperative Concerns

- Check for heart failure; do not use in severe heart failure (e.g., PCWP >25 mm Hg) or with pulm venous disease (e.g., pulm vein stenosis, pulm venoocclusive disease). Use of inhaled NO in these settings can cause severe pulm edema with hypoxemia and decreased lung compliance. Some pts with mild left heart dysfunction (diastolic dysfunction) may also develop worsening pulm edema with iNO.

Monitoring

- Must monitor: Inhaled NO, NO_2 levels; metHb levels
- Consider monitoring: PA pressure; RV ECHO; ABGs, SpO_2

Induction/Maintenance

- For inhalation, 1–40 ppm in pts with ARDS (usual dose: 5–15 ppm). Initiate therapy with a higher dose (usually 40 ppm) in the setting of ARDS with moderate or severe pulm Htn and lower doses (5–10 ppm) to reduce intrapulmonary shunt (e.g., ARDS).
- In PPHN, begin therapy at 20 ppm and progressively reduce the dose to 5 ppm or less with improved oxygenation (e.g., FiO_2 <0.60) and PAP by ECHO. Inhaled NO therapy should not be initiated without first optimizing lung volume, ventilation, cardiac performance, and systemic BP.
- Ideal doses need better definition, but lower doses are most effective for improving oxygenation by matching ventilation and perfusion and higher doses to treat pulm Htn. Failure to respond in term infants with PPHN may reflect underlying lung developmental abnormality or structural (anatomic) heart disease.
- Give as little NO as possible to reduce oxidant burden of lung.

Adjuvants

- Phosphodiesterase inhibitors (e.g., sildenafil) increase sensitivity and duration of the dilatory effect of inhaled NO but must be used with caution as they can cause systemic hypotension.

Postoperative Period

- Slowly wean from NO over hours if possible watching for abrupt worsening of oxygenation or pulm Htn with the D/C of NO ("rebound" effect).

Anticipated Problems/Concerns

- Beware rapid D/C of iNO; reactive pulm vasoconstriction and hypoxemia leading to RHF may ensue. These effects may not be seen while doses are being reduced but can be dramatic with D/C of iNO therapy and can even occur after D/C low doses of NO.
- Do not allow NO stock tanks to deplete.
- Provide NO freshly mixed in O_2-containing gas for manual ventilation even when briefly disconnecting from ventilator for suctioning or moving pt.
- If iNO does not reverse hypoxemia despite mechanical ventilation with PEEP, high-frequency oscillatory ventilation, and so on, ECMO may be required.

Nitroglycerin

Lee A. Fleisher

Uses

- Therapy for pts with angina.
- CHF
- In MI, can reduce infarct size.
- Prinzmetal angina.
- Can be given as a patch, paste, or pill taken sublingually as needed.
- Uterine relaxation for retained placenta, although a systematic review did not demonstrate the efficacy of NTG used alone.
- May be beneficial in reducing postop morphine usage for pain management.

Perioperative Risks

- Development of hypotension
- Drug rash (rare)

Worry About

- Severe hypotension, especially with regional anesthesia

Overview/Pharmacology

- Used for both chronic treatment and acute management.
- Prophylactic NTG has not been shown to reduce the incidence of intraop MI.
- Tolerance to drug from prolonged IV infusion or continuous patch can occur.
- Metabolized by reductive hydrolysis in liver.
- Rapidity of onset and duration of action are directly related to method of administration.
  - Sublingual: Onset within 1–2 min, duration less than 1 h
  - Oral: Peak effect within 60–90 min, duration 3–6 h
  - Paste: Onset within 60 min, duration 4–8 h
  - Patch: Duration up to 24 h
- Prolonged use can lead to tolerance and reduced effectiveness.
- NTG paste and/or patch may be absorbed unevenly intraop.

Drug Class/Mechanism of Action/Usual Dose

- Organic nitrate
- Activates guanylate cyclase; increases levels of cGMP in smooth muscle and other tissues; increases NO.
- Usual dosage
  - Sublingual: 0.4 mg as needed
  - Paste: 1/2–1 inch
  - Isosorbide dinitrate (Isordil): 5–30 mg every 6 h
  - IV: 0.5–2 μg/kg per min
- Bolus for uterine relaxation (slow 50 μg; may repeat once with caution if RA is actively causing sympathectomy).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Vasodilation of veins moreso than arteries Redistribution of coronary blood flow	Relief of angina	BP	PCWP
RESP	Decreased pulm vascular resistance			PCWP
GU	Uterine (smooth muscle) relaxation			
CNS	Dilation of meningeal arterial vessels	Headache		

Key References: Zvara DA, Groban L, Rogers AT, et al.: Prophylactic nitroglycerin did not reduce myocardial ischemia during accelerated recovery management of coronary artery bypass graft surgery patients, *J Cardiothorac Vasc Anesth* 14(5):571–575, 2000; Abdel-Aleem H, Abdel-Aleem MA, Shaaban OM: Nitroglycerin for management of retained placenta, *Cochrane Database Syst Rev* (11):CD007708, 2015.

Perioperative Implications

Preoperative Concerns

- Assess volume status
- Consider monitoring
  - BP (arterial cath)
  - PA cath (may give useful information if nitroglycerin infusion is used)

Induction/Maintenance

- May interact with other induction agents to cause hypotension.
- Ideally should be given IV because of uneven absorption intraop (binding sites on tubing).
- Effective means of alleviating myocardial ischemia intraop.
- Has been used prophylactically as bolus during induction.
- Anesthetic agents may mimic beneficial effects of nitroglycerin.

Adjuvants/Regional Anesthesia/Reversal

- Agents that can result in hypotension may be exacerbated by NTG.

Postoperative Period

- Pts on chronic NTG may benefit from resumption of the drug.
- Can be given as patch or paste after pt has been rewarmed.

Anticipated Problems/Concerns

- Tolerance to NTG manifests by reduced hemodynamic effects, a function of dose and frequency of administration.
- Many inhalational agents and opiates have some of the hemodynamic effects of NTG (e.g., venodilation, reduced demand for oxygen).

Nonstatin Hypolipidemic Agents

Michael G. Irwin

Uses

- Primary indications include
  - Hyperlipidemia: Hydroxymethylglutaryl coenzyme-A (HMG-CoA) reductase inhibitors (statins) are the major hypolipidemic drugs. Nonstatin drugs are used in pts with side-effects or those not responding well to statin therapy. Evolocumab also has an indication specifically for the treatment of homozygous familial hypercholesterolemia.
  - Primary and secondary prevention of CV disease: CV benefits (reduction in myocardial infarction and stroke) in pts with hypercholesterolemia and mixed dyslipidemia.

Overview/Pharmacology

- Selective cholesterol absorption inhibitors: Ezetimibe
  - Inhibits cholesterol absorption from the small intestine by blocking a critical mediator of cholesterol absorption, the Niemann-Pick C1–like 1 (NPC1L1) protein on the GI tract's epithelial cells as well as in hepatocytes.
  - Metabolized in the liver and small intestine via glucuronide conjugation with subsequent renal and biliary excretion. Half-life around 22 h. No significant inhibitor or inducer effects on cytochrome P-450 isoenzymes. Significant medication interactions with cyclosporine and fibrates other than fenofibrate.
  - Common adverse drug reactions (≥1% of pts) include headache and/or diarrhea (steatorrhea). Infrequent adverse effects (0.1–1% of pts) include myalgia and/or raised liver function test (ALT/AST) results.
- Niacin (also known as vitamin B3, or nicotinic acid)
  - Decreases synthesis of apoB-containing lipoproteins via inhibition of DGAT2, a key enzyme for triglyceride synthesis, binding to HCAR2, thereby decreasing lipolysis and FFA flux to the liver for triglyceride synthesis and increased apoB catabolism. HDL levels are increased through direct and indirect pathways.
  - Common adverse effects are flushing, headache, pain, abd pain, diarrhea, dyspepsia, nausea, vomiting, rhinitis, pruritus, and rash. High doses may reduce blood pressure as a result of acute vasodilation. Cardiac arrhythmias, increased PT and decreased platelet count have been reported.
  - Contraindicated in active liver disease, persistent elevated serum transaminases, active peptic ulcer disease, or bleeding.
- Fibrates (fibric acid derivatives): Gemfibrozil, fenofibrate, clofibrate
  - Reduce insulin resistance when dyslipidemia is associated with other features of the metabolic syndrome
  - Activate peroxisome proliferator-activated receptors (PPARs). Mechanism of action: Induction of lipoprotein lipolysis; increased hepatic FA uptake and reduction of TG production; induction of the β-oxidation pathway, causing a decrease in FA synthesis; increased removal of LDL particles; increase in HDL production; inhibition of cholesterol 7 alpha hydroxylase

- Adverse effects include gallstones, dyspepsia, and myopathy. Combination with statins increases risk of rhabdomyolysis (less lipophilic statins are probably safer). Substrate of CYP3A4.
- Caution with active liver disease, liver function test abnormalities

- Bile acid sequestrants: Cholestyramine, colestipol, colesevelam HCl
  - Bind bile acids and sequester them from the enterohepatic circulation, which reduces the amount of LDL in the blood.
  - Not significantly absorbed from the gut. May bind drugs and fat-soluble vitamins (A, D, E, K) in the GI tract, preventing absorption; therefore should be administered several h apart from other drugs. No systemic side effects. GI tract effects include constipation, diarrhea, bloating, and flatulence.
- Lomitapide
  - Inhibits the microsomal triglyceride transfer protein (MTP or MTTP), which is necessary for VLDL assembly and secretion in the liver. Improves insulin sensitivity.
  - Adverse effects: Elevated aminotransferase levels and hepatic steatosis; nausea, flatulence, and diarrhea.
  - Extensively metabolized by CYP3A4 and a direct inhibitor of CYP3A4.
- Mipomersen
  - Antisense oligonucleotide that targets the messenger RNA for apolipoprotein B. Administered as a weekly injection for familial hypercholesterolemia.
  - Adverse effects: Injection-site reactions, flu-like symptoms, elevated ALT and hepatic steatosis. No drug-drug interactions have been identified.
- Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors: Evolocumab, alirocumab
  - Monoclonal antibodies that bind to and inhibit PCSK9 near the catalytic domain. PCSK9 binds to the LDL receptor so that it cannot remove LDL cholesterol from the blood. Inhibition allows more LDL receptors to be present on the surface of the liver and to remove more LDL-C from the blood. Therapeutic inhibition of HMG-CoA reductase by statins upregulates PCSK9, limiting the effectiveness of statins in lowering plasma LDL-C, so the indications are adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease who require additional lowering of LDL.
  - Administered subcutaneously every 15 or 30 d.
  - Adverse effects include irritation at the injection site, possible neurocognitive effects (memory loss, amnesia, forgetfulness, dementia, or disorientation), nasopharyngitis. No renal or hepatic adverse effects and no apparent drug interactions.

Drug Effects

Class	Side Effects	Perioperative Risks and Management
Selective cholesterol absorption inhibitors	Common: Headache, diarrhea Uncommon: Myalgia, raised ALT/AST	Not fully known Stop on day before surgery Resume with normal diet
Niacin	Common: Flushing, headache, pain, abdominal pain, diarrhea, dyspepsia, nausea, vomiting, rhinitis, pruritus and rash Hypotension (high doses) have been reported Uncommon: Cardiac arrhythmias, increased bleeding time	Increases histamine release May increase bleeding; caution with anticoagulants Safe with regional anesthesia Nicotine patches may worsen or increase risk of flushing Myopathy and rhabdomyolysis may be exacerbated by surgery and statins Stop 2 wk before surgery Resume when no bleeding risk
Fibrates	Common: Headache, diarrhea Uncommon: Myalgia, raised ALT/AST	Myopathy and rhabdomyolysis may be exacerbated by surgery and statins Stop on day of surgery Resume after mobilization
Bile acid sequestrants	Common: Constipation, diarrhea, bloating, and flatulence Bind fat-soluble drugs and vitamins	May prevent oral drug absorption Stop on day of surgery Resume with normal diet
Lomitapide	Common: Elevated AST/ALT, hepatic steatosis; nausea, flatulence, and diarrhea	May increase risk of liver damage No consensus on cessation; avoid in liver surgery
Mipomersen	Common: Injection-site reactions; Flu-like symptoms, elevated ALT and hepatic steatosis	May increase risk of liver damage No consensus on cessation; avoid in liver surgery
PCSK9 inhibitors	Common: Injection site reactions Uncommon: Possible neurocognitive effects, nasopharyngitis	Safe during surgery No need to withhold

Key References: Pang J, Chan DC, Watts GF: Critical review of non-statin treatments for dyslipoproteinemia, *Expert Rev Cardiovasc Ther* 12(3):359–371, 2014; Everett BM, Smith RJ, Hiatt WR: Reducing LDL with PCSK9 inhibitors—the clinical benefit of lipid drugs, *N Engl J Med* 373(17):1588–1591, 2015.

Perioperative Implications

Preoperative Concerns

- Ezetimibe should stopped before surgery (periop safety is not clear).
- Stop niacin or niacinamide at least 2 wk before surgery.
- Fibrates should be withheld on day of surgery.
- Bile sequestrants interfere with bowel absorption of multiple medications that may be required periop and should be withheld on the day of surgery.
- Currently no consensus on withholding lomitapide and mipomersen.

Intraoperative Concerns

- Niacin and niacinamide:
  - May exacerbate allergies by increasing histamine.
  - May increase bleeding and accentuate the effects of anticoagulants. Safe to use with regional anesthesia.
  - May exacerbate the effects of antihypertensive drugs.
  - Cardiac arrhythmias have been reported.
  - Use of nicotine patches may worsen or increase the risk of flushing.
- Niacin and fibrates can cause myopathy and rhabdomyolysis, which may be exacerbated by surgery. Risk is higher when these agents are used in combination with statins.
- Lomitapide and mipomersen may increase the risk of liver damage.
- PCSK9 inhibitors appear to be safe in surgery but few data are available.

Postoperative Period

- Niacin may be resumed when there is no risk of bleeding.
- Fibrates can be resumed after mobilization.
- Bile sequestrants can be resumed with normal diet.
- All these drugs apart from PCSK inhibitors should be withheld in seriously ill pts.

Nonsteroidal Anti-Inflammatory Drugs

Zoe S. Gan | Christopher R. Page

Uses

- Incidence in USA: 100 million prescriptions are written per year; 17 million Americans use NSAIDs daily.
- Have analgesic, anti-inflammatory, and antipyretic properties.
- NSAIDs are the first step in the analgesic ladder of WHO; typically considered drugs of choice for mild to moderate pain.
- Can be obtained OTC or by prescription for chronic somatic pain states (e.g., arthritis) and rheumatologic disorders.
- Are given IV, IM, IN (intranasal ketorolac), and PO postop as part of a multimodal treatment regimen for acute pain.
- Should be considered in an enhanced recovery protocol.

Worry About

- Plt dysfunction
- Renal insufficiency
- Drug interactions
- Allergic reactions
- Effect on bone growth
- Gastric/GI bleeding
- Possible increased risk of thrombotic/CV events with long-term use.

Overview/Pharmacology

- Most NSAIDs are weak acids (pK_a 3–5) of diverse chemical structure and half-lives.
- Well absorbed from the stomach and intestinal mucosa.
- Highly protein-bound (>95%), usually to albumin.
- Work by inhibiting cyclooxygenase, which is a key enzyme in the synthesis pathway of prostaglandins.
  - Lead to decreased prostaglandin synthesis, thus decreasing the inflammatory response as well as the sensitizing effect of prostaglandins on nociceptors (both central and peripheral).
- Two isoforms of the COX enzyme have been identified.
  - COX-1: Expressed constitutively in most cell types; has an essential role in functions such as gastric protection, plt aggregation, and renal function.
  - COX-2: Traditionally considered to be induced by tissue injury/inflammation, now known to be constitutively expressed in some tissues (e.g., brain and/or kidney).
- Undergo liver metabolism to inactive metabolites, which are then excreted by the kidney.
- Have a low abuse potential but also a ceiling analgesic effect.

Drug Class

- Traditional or nonselective NSAIDs are both COX-1 and COX-2 inhibitors.
  - All NSAIDs inhibit both COX-1 and COX-2, although with varying ratios of COX-1/COX-2 inhibition.
- Several different subclasses
  - Salicylate (aspirin, salsalate, diflunisal, and choline magnesium trisalicylate)
  - Propionic (ibuprofen, ketoprofen, naproxen, fenoprofen)
  - Indole (indomethacin, sulindac, tolmetin)
  - Fenamate (mefenamic, meclofenamate)
  - Mixed (piroxicam, ketorolac, diclofenac)
- Coxibs are selective COX-2 inhibitors with a minimal degree of COX-1 inhibition at clinical doses.
  - Only celecoxib is commercially available in USA.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, HF, thrombotic events	Worsening SOB	BP, edema, rales, chest pain	
RESP	Nasal polyps, rhinitis, dyspnea, bronchospasm, angioedema	In asthmatics	Wheezing	
HEPAT	Hepatitis	N/V, anorexia,	Jaundice	LFTs
GI	Gastropathy (can be asymptomatic), GI bleeding, esophageal disease, pancreatitis	Ulcers, heartburn		Stool heme, Hgb, upper endoscopy
HEME	Increased bleeding	Easy bruising/bleeding	Pallor	Bleeding time, Hgb
DERM	Urticaria, erythema multiforme, rash			
GU	Renal insufficiency, sodium/fluid retention, papillary necrosis, interstitial nephritis		BP, edema, weight changes	Increased K^+/BUN/Cr, decreased UO, biopsy,
CNS	Headache, aseptic meningitis, hearing disturbances	Cognitive dysfunction, somnolence, confusion		CSF

Key References: Patrignani P, Patrono C: Cyclooxygenase inhibitors: from pharmacology to clinical read-outs, *Biochim Biophys Acta* 1851(4):422–432, 2015; Pogatzki-Zahn E, Chandrasena C, Schug SA: Nonopioid analgesics for postoperative pain management, *Curr Opin Anaesthesiol* 27(5):513–519, 2014.

Perioperative Implications

Preoperative Concerns

- Preop nonselective NSAID use has been associated with increased intraop blood loss due to plt inhibition.
  - Unlike aspirin, NSAID plt inhibition is reversible; common practice is to hold the NSAID for a period of 5 half-lives before surgery (e.g., ibuprofen 1 d, naproxen 5 d).
  - Coxibs do not affect plt function and therefore do not need to be held.
- For pts on aspirin for a primary or secondary ACC/AHA guideline indication, it may be safe to continue aspirin in the case of a non–closed space procedure or nonprostate surgery.
- NSAIDs displace albumin-bound drugs (e.g., warfarin) and can potentiate their effects.

Regional Anesthesia

- According to the consensus guidelines of ASRA, NSAIDs do not significantly increase the risk for spinal hematoma in pts undergoing neuraxial anesthesia.
  - May increase risk if combined with other anticoagulant/antiplatelet medications or if there is coexisting coagulopathy.
- Use of NSAIDs alone should not interfere with the performance of neuraxial blocks or the timing of neuraxial catheter removal.

Intraoperative Concerns

- Intraop administration of NSAIDs has been shown to cause a slight increase in the need for reoperation in surgeries at high risk for postop bleeding (e.g., tonsillectomy/CABG surgery).
  - In deciding to administer an NSAID, consider the need for improved analgesia, pt's ability to achieve hemostasis, and the risk of postop bleeding inherent to the surgery.
- May exacerbate asthma, especially in pts with a Hx of NSAID-induced bronchospasm, angioedema, urticaria, or rhinitis.

Postoperative Period

- NSAIDs may not consistently reduce pain intensity but do reduce opioid requirements and subsequent side effects (e.g., N/V, sedation).
- NSAIDs can be resumed with cautious monitoring for GI bleeding/renal dysfunction; avoid resumption in seriously ill pts.
- Risk of adverse effect on renal function is the same for both nonselective NSAIDs and COX-2 inhibitors.
  - For pts with baseline normal renal function, transient reduction in renal function with acute postop NSAID administration is usually clinically insignificant (normal function restored 2–7 d after stopping NSAID treatment).
  - Use caution when initiating therapy in pts with preexisting heart/kidney disease, use of loop diuretics, or loss of blood volume >10%.
- May increase risk of anastomotic leakage following GI surgery
- Both nonselective NSAIDs and coxibs have been implicated in potentially inhibiting bone healing.
  - May be prudent to avoid in cases where bone formation is especially crucial (e.g., spinal fusion).
  - Especially short treatment may be safe; decision to use postop should be done in consultation with surgeon.

Anticipated Problems/Concerns

- Generally associated with chronic rather than acute use.
- All NSAIDs pose a risk of gastropathy; ulcers are typically asymptomatic before an episode of GI bleeding.

- Risk with coxibs is approximately 50–60% less than with nonselective NSAIDs but still present.
- Concurrent treatment with a PPI or misoprostol may further decrease risk.

- All NSAIDs may carry an increased risk of CV events, especially if used with aspirin (one NSAID may antagonize benefit of another) and with chronic use.
  - Significantly increased risk with COX-2s led to withdrawal from market of most coxibs; increased CV risk was later determined to be a class effect.
  - Periop use is generally safe in pts with low CV risk, but contraindicated in cardiac surgery pts.
  - For most pts, increased risk is small; a risk/benefit analysis should be undertaken before continuing long-term use.
- Can exacerbate and/or induce CHF in susceptible pts.
  - Risk is nearly equivalent to that of NSAID-induced gastropathy.
- Can lead to increases in BP, especially in pts with preexisting Htn.
- Use in pregnancy considered safe for short courses of therapy (<72 hr) and up to 32 wk of gestation.
  - Chronic use and use of aspirin generally contraindicated
  - Some concern for increased risk of miscarriage early in first trimester and premature closure of ductus arteriosus after 32 wk.

Nutritional Support

Alan David Kaye | Mark R. Jones | Rachel J. Kaye

Risk

- Up to 40% of pts may be undernourished on admission to hospital, and two-thirds of all pts lose weight during hospital stay. 60% of elderly pts are malnourished at discharge. More than 376,000 people depend on TPN per year in USA.

Perioperative Risks of Malnutrition

- Decreased respiratory, cardiac, and skeletal muscle mass and strength.
- Up to 50% of heart failure pts are malnourished.
- Decreased visceral protein mass, altered GI mucosal barrier.
- Altered humoral, cell-mediated immunity.
- Altered neutrophil function.
- Increased pulm, thromboembolic complications.
- Pts with protein-calorie malnutrition have increased risk for postop cardiac, noncardiac complications.
- Increased risk for nosocomial infections and decreased wound healing.
- Increased risk for multiple organ failure.
- Increased length of hospital stay.

Worry About

- Hypoglycemia or hyperglycemia, depending on additives to TPN.
- Decreased ability to secrete insulin in malnourished pts.
- Kidney dysfunction and failure prevalent in cases of severe malnutrition.
- Increased free fraction of certain protein-bound drugs with low albumin levels.
- Vitamin B_{12} and/or folate deficiency, leading to anemia.
- Higher rates of infection with TPN.
- Excess carbohydrate administration via TPN may lead to increased CO_2 production and increased difficulty in weaning from ventilatory support and hepatic steatosis.
- Excess fat administration via TPN may lead to hyperlipidemia, decreased immune function, and reduced reticuloendothelial function.

Overview

- NRI = 1.519 × serum albumin (g/L) + [0.417 × (current weight/usual weight) × 100]. (Malnutrition defined as NRI <100; severe malnutrition defined as NRI <83.5.)
- Preop nutritional support for 5–7 d may result in decrease in infectious complications in severely malnourished pts.
- TPN composition:
  - Fluid: 30 mL/kg/d, additional losses
  - Calories: 25–30 kcal/kg/d
  - Glucose: 3.0–5.0 g/kg/d
  - Fat: 1.0–1.5 g/kg/d
  - Protein: 1.5–2.0 g/kg/d
  - Additives:
    - Multivitamins in the form of balanced formula should be provided daily.
    - IV formula requires addition of vitamin K, 2 mg/d.
    - Trace elements should be given daily to pts with GFR >20 mL/d; magnesium: 15–20 mg/d; zinc: 15–40 mg/d. (Requirement for replacement is based on serum level.)
- Special formulas: Modified amino acid formula is more efficient in restoring positive nitrogen balance, decreasing ureagenesis, and increasing support of protein synthesis.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
MS	>10% loss of body weight over 6 mo	Renal Hx of renal, hepatic dysfunction Short gut	Muscle wasting Decreased triceps and skinfold thickness, decreased mid-arm circumference	Alb <2.5 g/dL Total lymphocyte count <1500 cells/mm^3

Key References: Fernández López MT, Fidalgo Baamil O, López Doldán C, et al.: Prevalence of malnutrition in not critically ill older inpatients, *Nutr Hosp* 31(6):2676–2684, 2015; Fessler TA: Trace elements in parenteral nutrition: a practical guide for dosage and monitoring for adult patients, *Nutr Clin Pract* 28(6):722–729, 2013.

Perioperative Implications

Monitoring

- Daily monitoring of wt, electrolytes, magnesium
- Weekly monitoring of zinc, liver function tests, PT/PTT
- Nutritional variable: Prealbumin and transferrin are better indicators of nutritional status due to their shorter half-life compared to albumin. Failure to improve or maintain adequate levels usually represents inadequate nutritional support, intercurrent systemic inflammatory response, or advanced organ failure.

Induction/Maintenance

- TPN is usually continued intraop.
- Monitor glucose.
- Malnutrition may predispose a pt to having a higher risk for pseudocholinesterase deficiency; use succinylcholine with caution.

Adjuvants

- For morbidly obese pts, use ideal weight for calculation of TPN requirement.
- For severely underweight pts, use half the difference between pt's ideal weight and actual weight.

Anticipated Problems/Concerns

- Caloric and glucose overload can result in hyperglycemia and hepatic dysfunction.
- Moderate and severe hypoglycemia occur frequently in critically ill pts assigned to intensive glucose control, and are both strongly associated with an increased risk of death.
- Fat overload can result in WBC dysfunction, infectious complication, and increased CO_2 production.

Oral Contraceptives

Tracey L. Stierer

Uses

- Prevention of pregnancy
- Treatment of the following:
  - Dysmenorrhea
  - Menorrhagia/iron-deficiency anemia
  - Acne
  - Endometriosis
  - Functional ovarian cyst
  - Hyperandrogenism and/or polycystic ovarian disease
  - Premenstrual syndrome and/or premenstrual dysphoric disorder
  - Perimenopausal vasomotor symptoms
  - Mittelschmerz

Perioperative Risks

- Hypercoagulability; increased risk of venous and arterial thrombosis when given without concomitant aspirin, especially in women with blood type A+.

Worry About

- Thromboembolic events; increased relative risk of 2.7 (without aspirin).
- Hyperkalemia (drospirenone and/or ethinyl estradiol).
- Treatment failure and/or pregnancy. "Typical user" failure rates reported as high as 9%. Preop beta-HCG assay may be indicated in sexually active pts.

Overview/Pharmacology

- Oral preparations of synthetic estrogen, progestin generally well absorbed
- Metabolized by the liver and excreted in urine and feces

Drug Class/Mechanism of Action/Usual Dose

- Estrogens:
  - Mestrol.
  - Ethinyl.
  - Estradiol.
- Progestins:
  - Norethindrone.
  - Norgestrel.
  - Norethindrone acetate.
  - Ethynodiol diacetate.
  - Levonorgestrel.
  - Norgestimate.
  - Desogestrel.
  - Drospirenone.
  - Prometrium.
- Combination estrogen and progestin drugs inhibit ovulation by negative feedback effect on the hypothalamus; altering normal pattern of gonadotropin secretion by the anterior pituitary; cervical mucus thickens and is unfavorable to sperm even if ovulation occurs. Classified as:
  - Monophasic: Same ratio of progestin and estrogen in each pill.
  - Biphasic: Two phases of altered progestin and estrogen ratio.
  - Triphasic: Progestin and estrogen ratio varied in three phases.
- Progestin-only agents act directly by inhibiting ovulation or creating thick cervical mucus impenetrable to sperm.
- First- and second-generation progestin-only drugs pose a lower risk of thromboembolism. Third-generation progestins carry a 6- to 9-fold increase of venous thromboembolism, similar to the risk during pregnancy if given without concomitant aspirin.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn Greatly increased risk of thromboembolic events Arrhythmia due to hyperkalemia Altered lipid/cholesterol profile	Hx of MI or CVA Hx of DVT/PE Palpitations	BP Deep venous exam	 Venous Doppler Serum K^+ Serum lipid cholesterol levels
GI	May exacerbate gallbladder disease	Hx of jaundice/cholestasis during pregnancy		Bilirubin level, US, ERCP
HEPAT	Increased incidence of hepatic adenoma and hepatocellular cancer			

Key References: Blanco-Molina A, Trujillo-Santos J, Tirado R, et al: Venous thromboembolism in women using hormonal contraceptives, *Thromb Haemost* 101(3):478–482, 2009; Chalhoub V, Edelman P, Staiti G, et al: Oral contraceptives and hormone replacement therapy: management of their thromboembolic risk in the perioperative period, *Ann Fr Anesth Reanim* 27(5):405–415, 2008.

Perioperative Implications

Preoperative Concerns

- Consider D/C of combination OCs and third-generation progestin-only OCs 1 mo prior to major surgery if administered without aspirin and adding barrier method or adding aspirin for surgery with anticipated prolonged period of immobilization.
- Must weigh OC cessation with the risk of unwanted pregnancy or termination. In addition, consider risk of anesthesia and surgery to pregnant woman and fetus, including possible teratogenicity and spontaneous abortion.

Induction/Maintenance

- Consider thromboprophylaxis on an individualized basis judged according to additional genetic and acquired risk factors.

Postoperative Period

- Surveillance for DVT and PE. Restart aspirin.
- Early mobilization; resume agents 2 wk after surgery or mobilization.

Oral Hypoglycemic Agents

Nicholas A. Levy | Ketan Dhatariya

Uses

- Oral hypoglycemic agents are used to manage type 2 diabetes mellitus.
- The term oral hypoglycemic agents is becoming obsolete and is being replaced by the term noninsulin glucose-lowering drugs because the glucagon-like peptide 1 analogues are injected.

Perioperative Risks

- Hypoglycemia (sulfonylureas and meglitinides)
- Ketoacidosis (sodium/glucose cotransporter 2 [SGLT-2] inhibitors)
- Metformin-associated lactic acidosis
- Delayed gastric emptying and potential for aspiration (glucagon-like peptide 1 [GLP 1]analogues and dipeptidyl peptidase IV [DPP-IV] inhibitors)

Overview/Pharmacology

- There are currently eight different classes of noninsulin glucose-lowering drugs that can be used to treat diabetes:
  - Sulfonylureas
  - Meglitinides
  - Intestinal alpha-glucosidase inhibitors
  - SGLT-2 inhibitors
  - Biguanides
  - Thiazolidinediones
  - GLP-1 analogues
  - The gliptins/DPP IV inhibitors

Mechanism of Action

- These drugs work via four broad mechanisms:
  - By increasing the release of endogenous insulin and causing an actual drop in blood glucose (the sulfonylureas and meglitinides)
  - By inhibiting GI absorption and renal reabsorption of glucose (intestinal alpha-glucosidase inhibitors and the SGLT-2 inhibitors)
  - By altering effector-site sensitivity to endogenous insulin and reducing gluconeogenesis/glycogenolysis or endogenous metabolism (metformin and the thiazolidinediones)
  - By acting on the incretin pathway (GLP-1 analogues and the DPP-IV inhibitors)

Drug Effects

Drug Class	Examples	Mechanism of Action	Adverse Effects	Contraindications	Perioperative Concerns	Perioperative Implications
Sulfonylureas	Glibenclamide Gliclazide Glipizide Tolbutamide Glimepiride	Binds to an ATP-sensitive channel on the cell membrane of pancreatic beta cells Resultant depolarization leads increased secretion of (pro)insulin	Hypoglycemia GI disturbances Blood disorders	Type 1 diabetes Hepatic impairment Severe renal impairment Ketoacidosis	Hypoglycemia Blood disorders	Omit during period of starvation
Meglitinides	Repaglinide Nateglinide	Binds to the ATP-dependent K+ channel on the cell membrane of pancreatic beta cells in a similar manner to sulfonylureas but have a weaker binding affinity Resultant depolarization leads to increased secretion of (pro)insulin	Hypoglycemia GI disturbances	Type 1 diabetes Hepatic impairment Severe renal impairment Pregnancy	Hypoglycemia	Omit during period of starvation
Alpha-glucosidase inhibitors	Acarbose Voglibose	Inhibits digestive enzymes needed to digest complex carbohydrates in the gut Less glucose is absorbed because carbohydrates are not broken down into absorbable glucose molecules	GI disturbances	IBS Predisposition to intestinal obstruction	GI disturbances	Omit during period of starvation
SGLT-2 inhibitors	Dapagliflozin Canagliflozin Empagliflozin	Prevents the kidneys from reabsorbing filtered glucose and thus promotes glucose loss	Increased risk of UTI Dysuria Dehydration and renal impairment Ketoacidosis	Ketoacidosis Renal impairment Pregnancy and breast feeding	Ketoacidosis Dehydration	Omit during period of starvation
Biguanides	Metformin	Decreases hyperglycemia primarily by suppressing hepatic gluconeogenesis Enhances peripheral glucose uptake Decreases absorption of glucose from the GI tract	GI disturbances Taste disturbance Lactic acidosis	Ketoacidosis Surgery	Metformin associated lactic acidosis	Generally omit However, may be continued if starvation is short and there is no risk of AKI
Thiazolidinediones	Pioglitazone	Increases the expression of insulin cell-surface receptors in the tissues Increases insulin sensitivity Is glucose-dependent; therefore the risk of hypoglycemia is low	Heart failure Bladder cancer (small risk) Bone fractures GI disturbance Anemia Macular edema	Heart failure Bladder cancer Hematuria	Heart failure Fluid retention	May be continued if periop period of starvation is short
Incretin mimetics/ GLP-1 analogues	Exenatide Liraglutide Lixisenatide Dulaglutide	Stimulates insulin release in response to food Reduces gluconeogenesis Reduces gastric emptying Promotes satiety (therefore reduces calorific intake)	Delayed gastric emptying	Ketoacidosis Severe GI disease	Delayed gastric emptying	May be continued Supraglottic airways may be contraindicated
The gliptins/DPP IV inhibitors	Sitagliptin Vildagliptin Saxagliptin Alogliptin Linagliptin	Inhibit breakdown of the naturally occurring incretins Prolongs action of naturally occurring incretins	GI disturbances Delayed gastric emptying Pancreatitis	Ketoacidosis	Delayed gastric emptying	May be continued Supraglottic airway may be contraindicated

Key References: Dhatariya K, Levy N, Flanagan D, et al.: Management of adults with diabetes undergoing surgery and elective procedures: improving standards. Joint British Diabetes Societies. Revised March 2016. http://www.diabetologists-abcd.org.uk/JBDS/Surgical_guidelines_2015_full_FINAL_amended_Mar_2016.pdf (Accessed February, 21 2017); Inzucchi SE, Bergenstal RM, Buse JB, et al.: Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 38(1):140–149, 2015.

Perioperative Implications

- Pts on glucose-lowering drugs must be assessed preop to determine suitability for continuation of drugs.
- Continued use is associated with severe metabolic disturbance and is class-specific.
- Continued use is associated with risk of PONV.
- Most of these drugs must be discontinued during the periop period.
- If these drugs are omitted during the periop period, alternative strategies must be implemented to maintain and ensure periop glycemic control.
- Renal function must be monitored and ensured.
- If omitted, these agents should be reintroduced only once normal diet has been resumed and adequate renal function is ensured.

$P2Y_{12}$ Receptor Blockers

Johanna Paterson | Michelle R. Cole

Uses

- $P2Y_{12}$ RBs used alone or in combination with ASA (DAPT).
- ACS, those undergoing PCI with stent placement, and pts with NSTEMI or STEMI.
- Continue for 6–12 mo after insertion of drug-eluting stent (DES), and 4–6 wk after insertion of bare metal stent (BMS).
- Peripheral arterial disease
- AF when warfarin/coumadin is contraindicated
- Ischemic cerebrovascular disease, carotid or vertebral artery dissection (3–6 mo), postcarotid endarterectomy (long term), and carotid artery stenting (DAPT for 30 d).

Perioperative Risks

- Plt dysfunction
- Bleeding if $P2Y_{12}$ RB not stopped 5 d before surgery; ASA to be continued if possible
- Coronary event due to stent thrombosis after DES implantation if $P2Y_{12}$ RB stoppedl risk of ST to be balanced against risk of delay to surgery

Worry About

- Increased bleeding intra- and postop
- Surgery undertaken <30 d after BMS insertion or <6 mo after DES insertion due to increased stent thrombosis risk

Overview/Pharmacology

- Inhibitor of plt aggregation through action at plt ADP receptor
- Two types:
  - Thienopyridine derivatives (clopidogrel, ticlopidine, prasugrel): Prodrugs—metabolized by the liver to active metabolites. Irreversibly bind to the receptor, thus inhibiting plt aggregation for the life span of the plt.
  - Direct acting $P2Y_{12}$ RBs (cangrelor, ticagrelor, elinogrel): Competitively bind to receptors causing conformational changes. Reversible concentration-dependent effect.

Drug Class/Mechanism of Action/Usual Dose

- Clopidogrel: 300-600 mg loading (PO), 75 mg daily for maintenance. Used pre-PCI, ischemic stroke/TIA (if pt is ASA-intolerant), NSTEMI (with ASA), AF if intolerant of warfarin (with ASA). Genetic polymorphisms—CYP2C19 poor metabolizers; need 150 mg maintenance. Half-life 7–9 h.
- Prasugrel: 60 mg loading (PO), 5-10 mg daily for maintenance. Used with ASA for ACS undergoing PCI (alternative to clopidogrel). Half-life 7 h, plt function recovers in 2–3 d. More effective and faster than clopidogrel, but higher risk of bleeding.
- Cangrelor: IV preparation. Used for ACS/PCI if pt has not yet received oral $P2Y_{12}$ RB. 30 mg/kg bolus then 4 mg/kg per min infusion for 2 h or duration of intervention. Half-life 3–6 min, rapid recovery of plt function (5 min).
- Ticagrelor: With ASA for pts with ACS. 180 mg (PO), then 90 mg twice daily. Alternative to clopidogrel for PCI. More rapid onset of action and more potent than clopidogrel/prasugrel.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV		ACS/MI, stroke, PVD	Pulse	ECG, BP
CNS	Dizziness, headache, vertigo, intracranial hemorrhage	Intracranial hemorrhage	Decreased LOC	CT (if required)
GI	Abdominal pain, diarrhea, constipation, nausea, GI bleeding	GI hemorrhage	Stool guaiac	
GU	Acute renal failure (uncommon with cangrelor)			Renal function
DERM	Pruritus, ecchymosis, rash	Rash, pruritus		
HEME	Anemia, purpura, epistaxis, bleeding, thrombocytopenia (rare)	TTP (rare)		FBC, coagulation screen

Key References: Oprea AD, Pepescu WM: Perioperative management of antiplatelet therapy, *Br J Anaesth* 111(Suppl 1):i3–i17, 2013; Levine GN, Bates ER, Bittl JA, et al.: 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery, *Circulation* 134(10):e123–e155, 2016.

Perioperative Implications

Preoperative Concerns

- Significantly increased risk of surgical bleeding if $P2Y_{12}$ RB is discontinued <7 d before surgery

Bleeding Risk

- If procedure involves a low bleeding risk (e.g., dental extraction, plastic surgery), continue DAPT.
- If intermediate bleeding risk, stop $P2Y_{12}$ RB, continue ASA.
- If high risk bleeding, postpone surgery if possible. If urgent, stop DAPT and consider bridging therapy.

Urgent Procedures

- Plt transfusion to counteract effects; however, be aware of the risk of ST.
- If plts given within half-life of $P2Y_{12}$ RB, new plts can also be affected by drug.

Anticipated Problems/Concerns

- If on $P2Y_{12}$ RB for AF or primary prevention of cardiac/CNS events, drug may be stopped preop without major consequences.
- If $P2Y_{12}$ RBs are part of DAPT for pre- or post-PCI stenting, need to consider (1) appropriate and safe time frame between stent placement and embarking on surgery, (2) potential consequences of stopping DAPT, (3) urgency of intervention, and (4) bleeding risk associated with the intervention. Need to make a thorough risk-benefit analysis of stopping or continuing.
- Bridging therapy: Poor evidence for best practice. Options include unfractionated heparin or LMWH, short-acting glycoprotein IIb/IIIa inhibitors (tirofiban/eptifibatide), or cangrelor as an IV preparation.
- RA: A vertebral canal hematoma is a rare but potentially catastrophic complication of neuroaxial blockade. Actual risk of vertebral canal hematoma with $P2Y_{12}$ RBs is unknown; however, published international guidelines, including those from the American Society of Regional Anesthesia and Pain Medicine, support the recommendation of discontinuing for at least 7 d and extending up to 10 d for prasugrel because of its higher incidence of bleeding when compared with clopidogrel.

Management of Intraoperative Bleeding on Dual Antiplatelet Therapy

- Surgical management of bleeding.
- Plt transfusion to reverse effects of $P2Y_{12}$ RBs.
- Make sure other causes of coagulopathy are identified and treated (point-of-care testing if available).
- Other blood products as clinically indicated.
- No specific reversal agents to $P2Y_{12}$ RBs.

Penicillins

Lucy Waskell

Uses

- Prescribed for pts with infections due to sensitive organisms, primarily *Pneumococcus* and those in genera *Streptococcus*, *Staphylococcus*, *Neisseria*, *Pseudomonas*, *Proteus*, *Haemophilus*, *Helicobacter*, *Moraxella*, and so on; used as prophylaxis for subacute bacterial endocarditis (penicillin G benzathine).
- Can be administered PO, IM as regular or slow-release repository form, or IV.

Worry About

- Hypersensitivity reactions (0.7–4%): rash, fever, bronchospasm, vasculitis, serum sickness, exfoliative dermatitis, Stevens-Johnson syndrome, angioedema, anaphylaxis
- Hyperkalemia when penicillin G potassium is administered IV (1.7 mEq K^+/1 × 10^6 units penicillin G), especially if administered rapidly
- Plt dysfunction, defective hemostasis after ticarcillin, and penicillin G
- Rare bone marrow depression, granulocytopenia, hepatitis
- Headaches, seizures after 1 dose of 5 MU of penicillin G procaine
- Clearance lower in neonates and infants
- After ingestion, nausea and diarrhea, rarely *Clostridium difficile* pseudomembranous colitis

Overview/Pharmacology

- Used to treat wide spectrum of infectious diseases.
- Many penicillins are acid-labile (pH 2 destroys antibiotic); often not administered orally.
- Actively and rapidly excreted by renal tubule.
- Half-life markedly increased in anuria.
- Dosage should be decreased in renal failure.
- Other organic acids (e.g., probenecid) can compete at the renal tubule for excretion, prolonging half-life of the antibiotic.
- High concentration in urine.
- Ampicillin and amoxicillin often administered with β-lactamase inhibitors such as clavulanate and sulbactam.
- Ticarcillin and piperacillin marketed in combination with β-lactamase inhibitors clavulanate, and tazobactam respectively.

Drug Class/Mechanism of Action/Usual Dose

- Organic acids consisting of a β-lactam ring to which is attached a side chain and a thiazolidine ring; they inhibit bacterial cell wall synthesis primarily by inhibiting the transpeptidase reaction, which is essential for bacterial cell-wall synthesis.
- Dose and route of administration depend on type of penicillin used and severity of disease treated.

Drug Effects

Drug	Absorption After Oral Dose	Resistance to Penicillinase	Dose IV	Antimicrobial Spectrum	Side Effects
Penicillin G	Poor; about one third of dose; taken on empty stomach	No	1–10 MU q4–6h	*Streptococcus, Neisseria*	Increased K^+ (1.7 mEq K^+/1 × 10^6 units penicillin G); greater than 20 1 × 10^6 U/d can cause seizures; inhibits platelet aggregation
Penicillin V	Moderate; 2–5 times greater than penicillin G	No	0.5 g q6h PO	Like penicillin G	K^+ salt
Dicloxacillin	Good (30–80% of dose taken on empty stomach)	Yes	0.5–1 g PO q6h	*Staphylococcus aureus*	90–95% bound to albumin; not removed by dialysis
Ampicillin	Good; taken on empty stomach	No	1–2 g q6h (250–500 mg q6h PO)	Gram + cocci, gram negative, *H. influenza, Escherichia coli, P. mirabilis*	
Amoxicillin	Good (better absorption than ampicillin)	No	0.75–1.5 g PO q8h	Like ampicillin	Colitis when taken with clavulanate
Ticarcillin	Poor	No	50–75 mg/kg q6h	*Pseudomonas, Enterobacter, Proteus* (indole +) + ampicillin spectrum	CHF secondary to Na^+ overload; 5 mEq Na^+/g; low K^+ secondary to obligatory cation excretion with anion; decline in platelet aggregation
Piperacillin	Poor	No	2–6 g q8h	*P. aeruginosa, Enterobacter, some Klebsiella,* other gram negatives, gram + *cocci, Listeria monocytogenes,* ampicillin spectrum	Same as ticarcillin: 2 mEq Na^+/g

Key Reference: Petri WA: Penicillins, cephalosporins, and other β-lactam antibiotics. In Brunton LL, Chabner B, Knollman B, editors: *Goodman & Gilman's the pharmacological basis of therapeutics,* ed 12, New York, 2011, McGraw-Hill, pp 1477–1504; Bhattacharyya RP, Grad YH, Hung DT: Genomics and infectious disease. In Kasper D, Fauci A, Hauser S, et al, editors: *Harrison's principles of internal medicine,* ed 19, New York, 2015, McGraw-Hill, Chapter 146.

Perioperative Implications

Preoperative Concerns

- Is pt allergic to any penicillins? What exactly happens when the drug is taken (rash vs. anaphylaxis)?
- If pt is on large doses of penicillin G, ticarcillin, or piperacillin, are serum electrolytes normal?
- Hemostasis, especially platelet aggregation, may be inhibited by the antibiotics.
- If pt has renal insufficiency or failure, dose of antibiotic should be q12h or less frequently.

Induction/Maintenance/Postoperative Period

- Penicillins should have no effect on induction or maintenance unless allergic reaction occurs; no known interactions with any anesthetic agents.

Anticipated Problems/Concerns

- Relate to administration of large amounts of Na^+, K^+, and organic anions (acids). Possible bleeding problems due to platelet dysfunction.

Phencyclidine

Davide Cattano

Uses

- DEA Schedule I drug of abuse with no present medical indications; street terms for PCP include angel dust, supergrass, killer weed, embalming fluid, rocket fuel, wack, and ozone.
- Common routes of administration: Smoking (often laced in marijuana cigarettes), oral ingestion; less common is IV injection.
- Experimentally used for animal models of schizophrenia, neurodegenerative diseases and seizure disorders, ischemic neuroprotection, and anesthesia-induced neurotoxicity.

Risk

- Psychosis, seizures, anticholinergic-type syndrome.
- Experimentally, PCP causes irreversible brain damage through excitotoxicity, with the typical bull's eye neuronal cell and vacuolization.

Perioperative Risks

- Aggressive and/or psychotic behavior, hypertension, stroke, hyperthermia, rhabdomyolysis, aspiration

Worry About

- Kidney failure, aspiration, malignant Htn, prolonged action

Overview/Pharmacology

- Effects due to parent compound, highly lipid-soluble, pK_a of 8.6, peak effects in 15 min when smoked and 2 h by ingestion, distribution in 4 h, elimination takes up to 48 h. Metabolites are active and present for weeks in chronic users.
- Metabolized in the liver; urinary excretion of metabolites at low doses, excretion of free drug at high doses, only a small fraction of the drug is excreted unchanged.
- Produces an acute state of intoxication lasting 4–6 h but may produce a chronic state of psychosis that can last up to several days. With low to moderate doses, acute intoxication includes staggering gait, slurred speech, nystagmus, numbness of extremities, sweating, catatonic muscular rigidity, blank stare, changes in body image, disorganized thought, drowsiness, apathy, anterograde amnesia, and possibly aggressive behavior.
- With moderate to high doses, intoxication includes elevated HR and BP, hypersalivation, sweating, fever, repetitive movements, and muscle rigidity on stimulation.
- With high doses, anesthesia, stupor, coma, and convulsions can occur.

Drug Class/Mechanism of Action/Usual Dose

- Arylcyclohexylamine
- Acts at the *N*-methyl-D-aspartate receptor as a noncompetitive antagonist but a weak dopamine, serotonin, and noradrenergic agonist; there is also PCP-induced dephosphorylation of ERK ½ and Akt and dephosphorylation of GSK3-beta (activation) that is prevented by lithium.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Tachycardia, Htn	Quantification, chronicity, acuity of drug exposure	Vital signs Diaphoresis	Blood, urine toxicology screens
RESP	Tachypnea vs. depression	Concurrent drug exposure (e.g., alcohol)	Respiratory rate Sat O_2%	
CNS	Psychosis, coma, convulsions, analgesia	Pupils, speech, reflexes		
ANS	Hypersalivation vs. dry mouth, hyperthermia		Observation, temp	

Key References: Lodge D, Mercier MS: Ketamine and phencyclidine: the good, the bad and the unexpected, *Br J Pharmacol* 172(17):4254–4276, 2015; Olney JW, Labruyere J, Price MT: Pathological changes induced in cerebrocortical neurons by phencyclidine and related drugs, *Science* 244(4910):1360–1362, 1989.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- No elective cases if pt has potentially taken PCP within 72 h.
- Steps to increase elimination of PCP from body; hydration and diuretics are supportive measures.
- Appropriate premedication (lorazepam, clonidine/dexmedetomidine).

Induction/Maintenance

- Ketamine is contraindicated (cross-tolerance) unless used cautiously to treat addiction and/or withdrawal symptoms (rare, deescalating doses); probably avoid nitrous oxide and isoflurane.
- Do not use selective beta-blockers with alpha effects (labetalol)
- Clonidine and dexmedetomidine

Postoperative Period

- Psychosis (acute vs. withdrawal), rhabdomyolysis, anticholinergic syndrome
- Precaution with muscle relaxant reversal

Anticipated Problems/Concerns

- Phenothiazines, anticholinergics, acidification of urine.
- There is no withdrawal, but addiction tolerance is common.

Phenothiazines

Eric Schnell

Uses

- Phenothiazine compounds are clinically useful antipsychotic and antiemetic medications.
- Phenothiazine antihistamines such as promethazine (phenergan) and prochlorperazine (compazine) are highly effective antiemetics.
- Phenothiazine neuroleptics such as chlorpromazine (thorazine) are used in the treatment of schizophrenia and psychosis.
- Chlorpromazine can also effectively treat uncontrollable hiccups and acute migraine headaches.

Perioperative Risks

- Common side effects of sedation and delirium may be particularly notable in the postop period and in susceptible pts.
- Severe extrapyramidal symptoms may arise from antidopaminergic activity.
- Tardive dyskinesia may result from long-term use and may be irreversible.
- Contraindicated in Parkinson disease; may worsen tremor and Parkinsonism.
- Autonomic dysfunction may result from sympatholytic and anticholinergic effects.
- Cardiac conduction defects and arrhythmias may occur with acute or chronic dosing, most commonly manifesting as a long QT interval.
- Accidental arterial injection or venous extravasation of promethazine can cause tissue necrosis.
- Neuroleptic malignant syndrome is a potentially fatal reaction to phenothiazines involving hyperthermia, rhabdomyolysis, tachycardia, and arrhythmias.

Pharmacokinetics/Pharmacodynamics

- Phenothiazines undergo hepatic metabolism; use caution in pts with hepatic dysfunction.
- Inactive metabolites excreted in bile/urine; pharmacokinetics rarely affected by renal failure.
- Phenothiazines are highly protein-bound (>90%).
- Prochlorperazine and promethazine have clinical half-lives of approximately 4–8 h after IV administration.

Drug Class/Mechanism of Action/Usual Dose

- Phenothiazines antagonize many receptors, primarily dopamine receptors (D_2-type) but also muscarinic receptors, serotonin receptors, alpha$_1$ adrenergic receptors and H_1 histamine receptors.
- Phenothiazine neuroleptics mediate their antipsychotic effects by blocking mesolimbic D_2 receptors, but D_2 blockade in striatum causes extrapyramidal side effects.
- Phenothiazine antiemetics are weak antipsychotics but potent H_1 histamine antagonists and antimuscarinic agents.
- Prochlorperazine is used at doses of 2.5–10 mg administered IV, IM, or PO q4–6h (max 40 mg/d) or 25 mg PR q12h.
- Promethazine is used at doses of 6.25–25 mg IV/IM q4–6h, IV doses given in diluted form slowly into a well-functioning large-vein IV line.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
ANS	Alpha$_1$ adrenoceptor blockade, antimuscarinic action		Orthostatic hypotension, tachycardia/bradycardia	Orthostatics
CNS	Extrapyramidal symptoms Neuroleptic malignant syndrome Sedation Decreased seizure threshold	Acute or chronic Muscle cramps, delirium	Akathisia, tardive dyskinesia Rigidity, tachycardia, hyperthermia, arrhythmias Lethargy, delirium	CK, K^+, uric acid EEG
CARDIO	Conduction defects: Long QT, ventricular and supraventricular arrhythmias	Can cause sudden death	Tachycardia, bradycardia, irregular rate	ECG
RESP	Respiratory depression	May potentiate opioids	Low respiratory rate	SpO_2, ABG, $ETCO_2$
VASC	Tissue necrosis (promethazine)	Arterial injection or tissue extravasation	Gangrene	
HEME	Leukopenia, agranulocytosis	Usually with chronic dosing only		CBC

Key References: Ohlow MJ, Moosman B: Phenothiazine: the seven lives of pharmacology's first lead structure, *Drug Discov Today* 16(3–4):119–131, 2011; Kwok J, Flood P: Drugs used for psychopharmacologic therapy. In Flood P, Rathmell JP, Shafer S, editors: *Stoelting's pharmacology & physiology in anesthetic practice*, ed 5, Philadelphia, 2015, Wolters Kluwer, pp 822–844.

Perioperative Implications

Preoperative Concerns

- Obtain baseline ECG for all pts taking chronic phenothiazines to assess cardiac conduction and QT interval.
- Neuroleptic malignant syndrome may present in pts undergoing chronic treatment but may be precipitated by other antidopaminergic agents such as metoclopramide.

Induction/Maintenance

- Autonomic insufficiency from long-term use may contribute to profound intraop hypotension.

Adjuvants/Regional Anesthesia/Reversal

- Treat extrapyramidal side effects with diphenhydramine, benztropine, or benzodiazepines.
- Neuroleptic malignant syndrome is treated with bromocriptine, dantrolene, and aggressive hydration/monitoring.

Postoperative Concerns

- Clinically significant respiratory depression if given to pts <2 y old or those with pulm disease, especially if combined with opioids.
- Arrhythmias and prolonged QT.
- Increased risk of sedation and delirium, particularly in elderly pts.

Drug Interactions

- Increased risk of extrapyramidal symptoms if given with other antidopaminergic medications (typically metoclopramide).
- May increase concentration of other hepatically metabolized (CYP2D6) drugs (some beta-blockers and tricyclic antidepressants).

Anticipated Problems/Concerns

- Assess mental status, respiratory status, and CV function after administration, particularly in the early postop period.

Phenoxybenzamine

Michael F. Roizen

Uses

- Incidence in USA: 3600 per y
- Rx for preop pheochromocytoma; occasionally for chronic Rx of pheochromocytoma and sympathetic hyperactivity states, carcinoid syndrome, BPH

Perioperative Risks

- Drug interactions: Sometimes requires very high doses of α-adrenergic agents to produce vasoconstriction.
- Vasodilation, orthostatic hypotension accentuated in hypovolemic pts.

Worry About

- Occasionally associated with confusional states.
- Associated with fatigue and prolonged sedation.
- Drop attacks on preop standing to urinate.
- Cost, which has increased since 1979 for this not-on-patent drug from $0.10 a tablet to $9.75 a tablet at the wholesale level (a 100-fold increase, as now there is apparently only one manufacturer).

Overview/Pharmacology

- α_1 blocker (relatively selective, α_1 being greater than α_2) by covalent (irreversible) binding to a receptor; compensatory response calls for production or availability of more (spare) receptors.
- Effect develops slowly; peak effect not attained for 2 h after IV or 4 h after oral administration.
- Absorption from GI tract incomplete.
- Renal excretion of 50% in 12 h, 80% in 24 h.
- Half-life of effect over 24 h; effects accumulate for at least 4–6 d.
- High lipid solubility at body pH.

Drug Class/Mechanism of Action

- α_1 blocker (a haloalkylamine).
- Chronically taken:
  - Decreases α_1 effects in pheochromocytoma.
  - High doses inhibit release of H_2 serotonin (occasionally used in carcinoid syndrome).
  - Ameliorates or prevents Raynaud phenomenon.
- Vasodilator for chronic treatment of CHF (occasionally), but worry about toxicity of promoting cancer when taken chronically.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Vasodilation of mucous membranes of nasopharynx; miosis	Nasal congestion	Mouth breathing	
CV	Antihypertensive agent Postural hypotension, reflex tachycardia, increased CO	Orthostatic dizziness	Orthostatic vital signs	Hct ECG
GI	Increased intestinal motility, causes diarrhea	Orthostatic hypotension		
ENDO	Stimulates insulin release Increased presynaptic norepinephrine release (blockade of presynaptic α_2 receptors inhibiting release of norepinephrine)			
GU	Increased blood volume, Na^+ retention inhibits contraction of vas deferens	Impairs ejaculation		BUN, Cr, lytes
CNS	Depression, sedation, fatigue, extrapyramidal symptoms rarely, N/V, motor excitability rare		CNS exam	

Key References: Kinney MA, Narr BJ, Warner MA: Perioperative management of pheochromocytoma, *J Cardiothorac Vasc Anesth* 16(3):359–369, 2002; Witteles RM, Kaplan EL, Roizen MF: Safe and cost-effective preoperative preparation of patients with pheochromocytoma, *Anesth Analg* 91(2):302–304, 2000.

Perioperative Implications/Possible Drug Interactions

Preoperative Period

- Make sure pt is not hypovolemic.
- Interaction with methyldopa (Aldomet): Urinary incontinence
- Preop treatment: Major goal is to avoid pheochromocytoma crisis; preop and intraop goals are management of extra-adrenal surgery, same as for adrenal surgery. If is not on α-blocker before surgery, try to delay until appropriate degree of α-blockade is achieved. Increase dose of phenoxybenzamine by 10 mg bid to qid every third day until appropriately blocked. Judge appropriate level of blockade by:
  - No BP readings higher than 165/90 mm Hg (even during psychological stress) for 48 h before surgery.
  - Orthostatic hypotension present, but BP on standing should not be lower than 80/45 mm Hg.
  - ECG free of ST-T changes due to cardiomyopathy.
  - Absence of other signs of catecholamine excess and presence of blockade effects such as nasal stuffiness.

Induction/Maintenance

- Can produce increased sedation; lower anesthetic requirements by one-third (not studied but anecdotally reported).

Muscle Relaxants

- No interactions known

Regional Anesthesia/Reversal

- No interactions known

Anticipated Problems/Concerns

- May need very high doses of vasopressors to increase vascular resistance, BP in pt taking large doses.
- CNS dysfunction by itself.

Phenylephrine (Neo-Synephrine)

Arvind Rajagopal | Kenneth J. Tuman

Uses

- Prescribed mainly as nasal decongestant or ophthalmically for treatment of mydriasis, capillary decongestion.
- Reliable vasopressor in treatment of hypotension.
- Used in obstetric anesthesia for hypotension after spinal. More effective as a prophylactic infusion than bolus doses.
- Prolongs local anesthetic duration in regional anesthesia.
- Available as parenteral IM/IV and various ophthalmic and/or nasal preparations.

Perioperative Risks

- Risk of Htn increases left heart work; may precipitate myocardial ischemia, MI.
- Infusions to augment systolic BP incidence of myocardial ischemia in pts undergoing carotid endarterectomy.
- Increased pulm vascular resistance, right heart work.
- Bradycardia may occur (usually not severe) related to baroreceptor reflex.
- Decreased renal, splanchnic blood flow.
- Systemic absorption of topical preparations may cause Htn, headache, tremulousness, myocardial ischemia.

Worry About

- Increase preload, afterload may worsen LV failure in pts with LV dysfunction.
- Raised PA pressures may worsen RV dysfunction.
- May decrease renal blood flow.

Overview/Pharmacology

- Direct α_1-agonist activity causes systemic and PA vasoconstriction, resulting in increased impedance to forward flow, reduced BP.
- Rapidly metabolized by MAO.
- IV duration less than 5 min.
- May terminate supraventricular tachycardia by vagal reflex from baroreceptor stimulation.
- Increased SVR during CPB.
- Increased perfusion pressure to vital organs in hypovolemic pts until volume is restored, CPR.
- May be used in conjunction with nitroglycerin to elevate coronary perfusion pressure in hypotensive pts with myocardial ischemia.
- Decreasing R-to-L shunts in pts with cyanotic spells (TOF)
- Vasopressor of choice in hypertrophic cardiomyopathy, systolic anterior motion of mitral valve and aortic stenosis, when increased inotropy or tachycardia undesirable.
- Advantageous in catecholamine-depleted pts (chronic cocaine or amphetamine abuse), or in those on tricyclic antidepressants or MAO inhibitors, when indirect vasopressors are unpredictable.

Drug Class/Mechanism of Action/Usual Dose

- Synthetic noncatecholamine activates predominantly α-adrenergic receptors (postsynaptic, heart, iris), triggers release of intracellular calcium, resulting in smooth muscle contraction.
- Differs structurally from epinephrine only in lacking 4-hydroxyl group on benzene ring.
- Usual adult dosage
  - IV bolus: 50–100 μg
  - IV infusion: 20–200 μg/min
  - Ophthalmic solutions: 2.5–10%
  - Supraventricular tachycardia dose: 150–800 μg titrated to raise BP

Assessment Points

System	Effect	PE	Test
HEENT	Mydriasis without cycloplegia Increased production of aqueous humor		
CV	Vasoconstriction of veins and arteries Increased systolic and diastolic BP Decreased HR	BP HR	PCWP ECG
RESP	Increased PVR		PCWP, PAP
RENAL	Increased renal blood flow	UO	BUN, Cr

Key References: Dellinger RP, Levy MM, Carlet JM, et al.: Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008, *Intensive Care Med* 34(1):17–60, 2008; Habib AS: A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. *Anesth Anal* 114(2):377-390, 2012.

Perioperative Implications

Preoperative Concerns

- Assess LV function and Hx of CAD.
- Consider arterial catheter if phenylephrine infusion anticipated (carotid endarterectomy, relative hypovolemia).
- Assess renal function (Cr).
- For nasal intubations, phenylephrine can be used as a nasal vasoconstrictor in a mixture with 3–4% lidocaine.

Induction/Maintenance

- Monitor ECG for signs of ischemia due to increased ventricular work or coronary artery spasm.
- May decrease hepatic blood flow due to α-adrenergic–mediated vasoconstriction of portal venous vasculature.

Adjuvants/Regional Anesthesia/Reversal

- Duration may be prolonged in pts on MAO inhibitors.
- Side effects with ophthalmic use occur within 20 min; usually self-limited.
- 2.5% nasal, ophthalmic solutions recommended in infant and elderly populations or in pts with CAD.

Anticipated Problems/Concerns

- Can be titrated slowly to avoid overshoot (with resultant Htn).
- Can be used when severe hypotension presents immediate danger to compromised myocardium or other end organ (e.g., brain).
- With a failing heart, increasing afterload and preload may increase left-sided filling pressures enough to precipitate pulm edema.

Phenytoin

Bozena R. Jachna | Lee A. Fleisher

Uses

- Management of generalized tonic-clonic (grand mal) and complex partial seizures
- Prophylaxis against seizures after trauma or surgical intervention
- Treatment of ventricular arrhythmias, especially those associated with digitalis or tricyclic antidepressant toxicity
- Treatment of prolonged QT interval
- Treatment of epidermolysis bullosa and chronic pain syndromes

Overview/Pharmacology

- Drug of choice for status epilepticus
- Treatment for acute and chronic seizures
- Onset of action: 30–60 min
- Protein binding >90% in adults
- Elimination half-life: 22 h
- 95% hydroxylated and conjugated in liver with glucuronic acid for renal excretion
- Therapeutic range: 10–20 μg/mL

Drug Class/Mechanism of Action/Usual Dose

- Hydantoin derivative
- In the CNS, helps to limit nerve impulse generation, thereby limiting spread of seizure focus by:
  - Decreasing influx of Na^+ ions across cell membranes in the motor cortex
  - Decreasing presynaptic Ca^{2+} release
  - Decreasing extracellular K^+ concentration
- In the heart, works to limit reentrant arrhythmias by:
  - Prolonging the effective refractory period and suppressing ventricular pacemaker automaticity
  - Shortening the action potential for status epilepticus (IV and PO dosages are the same)
- Pediatric: Loading dose, 15–20 mg/kg in single or divided doses, then 5 mg/kg per d in divided doses
- Adult: Loading dose, 10–15 mg/kg, then 5–6 mg/kg per d in 3 divided doses
- For treatment of cardiac arrhythmias: 1.5 mg/kg IV every 5 min for maximum dose of 15 mg/kg or 1.5 g

Perioperative Risks

- Hypotension, bradycardia, cardiac arrhythmias and/or collapse with rapid IV administration (likely due to propylene glycol vehicle)
- Venous irritation and/or pain
- Decreased efficacy of muscle relaxants

Concerns

- Pts with renal failure, jaundice, or other causes of hypoalbuminemia may exhibit phenytoin toxicity.
- Acute administration may lead to delayed emergence.
- Increased P450 clearance may cause decreased effectiveness of certain drugs: Antibiotics, oral contraceptives, procainamide, midazolam, and oral anticoagulants.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Nystagmus at toxic levels >20 mg/mL	Gingival hyperplasia with chronic use		
CV	Hypotension, bradycardia, cardiac arrhythmias with rapid administration		Vital signs, monitoring	
RESP	Respiratory depression		Saturation, respiratory rate monitoring	
DERM	Rash; Stevens-Johnson syndrome (rare)			
GI/HEPAT	Constipation, vomiting, nausea, hepatitis; increased hepatic drug metabolism; toxicity in low-albumin states; avoid or limit ethyl alcohol use	GI irritation if not taken with food		Albumin
HEME	Folic acid depletion, hyperglycemia, leukopenia, thrombocytopenia, agranulocytosis			CBC with differential
RENAL	Toxicity in uremic pts			BUN/Cr
CNS	Ataxia, diplopia, drowsiness, lethargy, coma, nystagmus, mood changes		CNS exam	

Key References: University of Maryland Medical Center: Dilantin overdose. <http://umm.edu/health/medical/ency/articles/dilantin-overdose>, 2016 (Accessed 11.07.16); Hayashi T, Higuchi H, Tomoyasu Y, et al.: Effect of carbamazepine or phenytoin therapy on blood level of intravenously administered midazolam: a prospective cohort study, *J Anesth* 30(1):166–169, 2016.

Perioperative Implications

Preoperative Concerns

- Pts with renal or liver disease or decreased nutritional states can have increased levels of free phenytoin.

Induction/Maintenance

- Rapid administration of phenytoin may cause hypotension, bradycardia, and arrhythmias. Administer at rate of less than 50 mg/kg per min.
- Larger doses of nondepolarizing muscle relaxants may be required.
- Shorter duration of nondepolarizing muscle relaxants.
- IV-administered midazolam may have a weaker effect in pts medicated with phenytoin.
- Concern with too rapid administration of vehicle (depending on vehicle).

Contraindications

- Hypersensitivity to phenytoin, other hydantoins.
- Pregnancy: Phenytoin crosses the placenta, resulting in congenital malformations (the "fetal hydantoin syndrome"), which results in wide-set eyes, broad mandible, and finger deformities.
- Lactating states, enters breast milk.
- Isolated cases of malignancies: Neuroblastomas have been reported.

Phenytoin Syndrome

- Fever
- Rash
- Psychiatric changes, slurred speech, dizziness, insomnia
- Tremor
- Constipation
- Hepatitis
- Rarely seen: SLE-like syndrome, lymphadenopathy, Stevens-Johnson syndrome, blood dyscrasias, lymphoma, coarsening of facial features, hypertrichosis.

Physostigmine, Eserine

Jeffrey S. Shiffrin

Uses

- Central anticholinergia; used for diagnosis and treatment in patients with a Hx of anticholinergic ingestion and/or exposure: Atropine, scopolamine, belladonna, jimson weed, toxic mushrooms, tricyclics, phenothiazines, antihistamines, benzodiazepines, opiates, inhalation anesthetics, propofol, GHB.
  - "Blind as a bat": Mydriasis and loss of accommodation
  - "Dry as a bone": Urinary retention and dry mucous membranes
  - "Hot as a hare": Hyperthermia from loss due to sweating
  - "Red as a beet": Cutaneous vasodilation; counteracts hyperthermia
  - "Mad as a hatter": Fluctuating consciousness, delirium, disorientation, decreased social restraint, slurred speech, incoordination, hallucinations, phantom behaviors, coma, paranoia during recovery
- Postop delirium from agitation to excessive somnolence. Best indication for treatment of combined central and peripheral anticholinergia.
- Glaucoma, ciliary muscle contraction = miosis = facilitates outflow of aqueous humor.
- Treatment for antimuscarinic xenobiotic toxicity (a chemical compound that is foreign to a living organism; e.g., benzodiazepines, tricyclics, antihistamines, jimson weed).
- Reversal of NMB (neostigmine a better choice as it avoids CNS effects).
- Hereditary ataxias.
- Alzheimer disease (may improve short-term memory but not used clinically).
- Analgesia (decreases morphine consumption postop).

Perioperative Risk

- Cholinesterase inhibition = excess acetylcholine. Can lead to three sets of problems: Analogous to organophosphorus compound poisoning, a cholinergic crisis (basically the opposite of anticholinergia syndrome above)
  - Muscarinic cholinergic (parasympathetic) over-stimulation (DUMBELS): D = Defecation, diarrhea, diaphoresis, GI distress; U = urination; M = miosis; B = bronchorrhea, bronchospasm, bradycardia; E = emesis (nausea); L = lacrimation; S = salivation
  - Nicotinic cholinergic excess (continuing depolarization of motor endplate, leading to fasciculations at low doses and progressive weakness at high doses)
  - CNS (anxiety, confusion, tremors, seizures, respiratory depression, coma)

Worry About

- Reactive airway disease
- Peripheral vascular disease
- Diabetes
- Bowel or bladder obstruction
- Preexisting intraventricular conduction delay, long-QT syndrome
- Preexisting AV block
- Pregnancy (class C)
- Sulfite allergy (contains sodium bisulfite preservative)

Overview/Pharmacology

- Physostigmine is a parasympathomimetic carbamate derived from the beans and/or seeds of an aquatic leguminous plant (calabar or ordeal bean). Used in the Old Calabar region of Nigeria as part of the Esere witchcraft ritual (believed to test the guilt or innocence of a person accused of a crime).

- Characterized and named *Physostigma venenosum balfour* in 1857 by John Balfour.
- Active alkaloid isolated and called physostigmine by Jobst and Hesse 1864 and independently by Vee and Leven who named it serine in 1865.
- Reversibly binds acetylcholinesterase (AchE), thus inhibiting acetylcholine degradation and increasing synaptic acetylcholine.
- Tertiary amine structure allows penetration of blood brain barrier.
- Prototypical carbamate insecticide.
- Early medical use by 1935 as miotic agent for glaucoma pts, myasthenia gravis treatment, atropine antidote, and reversal agent for curare-induced paralysis.

Drug Class/Mechanism of Action/ Usual Dose

- Physostigmine is a tertiary amine and a competing substrate for cholinesterase enzymes, thus decreasing the breakdown of acetylcholine.
- 1.5 mg given over 60 min = Vd 2.4 ± L/kg; half-life is 16.4 ± 3.2 min; peak plasma concentration 3 ± 0.5 ng/mL; clearance 0.1 L/min per kg.
- Inhibition of plasma cholinesterase within 2 min of infusion start. Half-life of plasma cholinesterase inhibition = 83.7 ± 5.2 min.
- For glaucoma: Not commonly used owing to systemic absorption and side effects. Replaced by other agents. Physostigmine ointment placed 1–3 times daily. Physostigmine solution 0.25%, 0.5% used 1–4 times daily while holding pressure over medial canthus/tear duct to minimize absorption.
- For reversal of central anticholinergia: Physostigmine salicylate (antilirium) 1 mg/mL; dose = 0.04 mg/kg or 1–2 mg IV/IM. IV given slowly, no more that 1 mg/min every 20–60 min as effective and necessary or until side effects develop.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
OPHTH	Constriction of pupils	Glaucoma topical application	Miosis, conjunctival hyperemia	Decreased IOP, red eye
CV	Bradycardia/tachycardia Vasoconstriction/vasodilation, decreased cardiac contractility	Variable depending on CNS vs. peripheral effects and use of other meds (ganglionic blockers, alpha- and beta-blockers)	Slow or irregular HR, asystole, or tachycardia, Htn, or hypotension	ECG, BP
RESP	Bronchoconstriction Bronchorrhea		Wheezing Secretions, "frothing at the mouth"	Auscultation
GI	Parasympathetic stimulation, abdominal cramps		Diarrhea, defecation	
GU	Bladder stimulation		Urination	
CNS	Excess acetylcholine	Somnolence, delirium, coma		

Key References: Taylor P: Anticholinesterase agents. In Brunton L, Chabner B, Knollman B, editors: *Goodman & Gilman's the pharmacological basis of therapeutics*, ed 12, New York, 2011, McGraw Hill, 2011, pp 239–254; Lepousé C, Lautner CA, Liu L, et al.: Emergence delirium in adults in the post-anaesthesia care unit, *Br J Anaesth* 96(6):747–753, 2006.

Perioperative Implications

Preoperative Concerns

- Scopolamine, antihistamines, benzodiazepines (especially in the elderly) can contribute to central anticholinergia.
- Use of jimson weed (belladonna) or hallucinogenic mushrooms.
- Interaction with vasopressors (possible Htn, tachycardia).
- Long-QT syndrome or AVB (increases chance for asystole).
- Tricyclic antidepressant use (asystole has occurred in the treatment of tricyclic overdose).

Induction/Maintenance

- Not used

Postoperative Period

- Many if not all anesthetics can cause anticholinergic signs and symptoms.
- Differential diagnosis: Metabolic (hyper/hypoglycemia, electrolyte imbalance, sepsis, MH, NMS; respiratory (hypoxia, hypercarbia); neurologic (CVA, seizures); psychiatric (narcolepsy, psychosis); iatrogenic (residual NMB, bladder distention, prolonged anesthetic effects/sensitivity).

Anticipated Problems/Concerns

- Physostigmine can be very effective in reversing excessive sedation or agitation associated with anticholinergia. However, anticholinergia is usually self-limited and is a diagnosis of exclusion (although it is confirmed by a positive response to physostigmine). Physostigmine is possibly a better treatment than benzodiazepine for combined central and peripheral anticholinergia. Also, physostigmine side effects are unpredictable and can be severe (asystole, seizures). In general, they are limited to exaggerated parasympathetic effects: N/V, stomach pain, salivation, urination, defecation, miosis, inability to focus, lacrimation, sweating, bronchospasm, bronchorrhea, dyspnea, bradycardia or tachycardia, hypotension or Htn, irregular pulse, and muscular twitching; but weakness, seizures, collapse, coma, pulm edema, and death (i.e., cholinergic crisis) can occur.
- Avoid in pts receiving other cholinergic agents (methacholine, bethanechol).
- Avoid in pts receiving depolarizing NMBs (succinylcholine).
- Atropine is the antidote for physostigmine overdose and central cholinergic symptoms.
- Avoid if long-QT syndrome on ECG.
- Glycopyrrolate is the antidote for peripheral cholinergic excess.

Procainamide (Procan, Procanbid, Pronestyl)

Henry Liu | Rayhan A. Tariq

Uses

- Treats recurrent or sustained hemodynamically stable monomorphic VT (IIa/C)/(IIa/C).* Not indicated for asymptomatic PVCs.
- Treats focal atrial tachycardia in hemodynamically stable pts (IIa/C).
- Treats recurrent atrial flutter (only in combination with AV-nodal-blocking agent) (IIb/A).
- Treats SVT during pregnancy.
- As a backup drug in hemodynamically stable pt with SVT (if adenosine is not successful).

*The first number and lowercase letter refer to the ACC/AHA system of classifying guidelines while the uppercase letter refers to the level of evidence.

Perioperative Risks

- Potential for hypotension secondary to ganglionic blockade more likely than myocardial depression.
- Nausea in pts on oral procainamide (related to levels of N-acetyl procainamide?).
- Chronic use can cause lupus-like syndrome; 25–50% of pts develop rash, small-joint arthralgias positive ANA. Resolves with cessation or administration of N-acetyl procainamide.

Worry About

- Ventricular dysrhythmias if plasma concentration of N-acetyl procainamide (NAPA) >30 μg/mL.
- QT_c prolongation.
- CNS toxicity.
- Hypotension.
- Procainamide-induced lupus syndrome.
- Bone marrow aplasia in 0.5% of pts; may be fatal, mechanism unknown.
- Hypokalemia may exacerbate toxicity.
- Avoid use in pts with myasthenia gravis; it can exacerbate symptoms.

Overview/Pharmacology

- Analog of procaine.
- Na^+ channel blocker (intermediate recovery).
- Decreases automaticity, slows phase 4 depolarization, prolongs refractory periods, thus reducing repolarization abnormalities.
- Highly lipophilic, but no relationship between drug properties and volume of distribution.

- Major metabolite NAPA does not block Na^+ channels but equipotent in prolonging action potentials.
- Rapid hepatic conjugation by N-acetyl transferase (half-life 3–4 h) to active metabolite NAPA.
- Renal excretion of unchanged drug as well as NAPA (half-life 6–8 h)
- Procainamide and NAPA have different pharmacologic effects, so sum of concentrations should not be used to guide therapy.
- Slow acetylators more likely to develop lupus-like symptoms; often resolve with administration of NAPA.
- Can cause serious drug interactions with drugs such as ondansetron (QT_c prolongation), flecainide, amiodarone, and others.

Drug Class/Mechanism of Action/Usual Dose

- Class IA antiarrhythmic; Na^+-channel blocker.
- Marked slowing of conduction by blocking sodium channels (SA node and intraventricular conduction).
- IV loading dose (adult): 15–18 mg/kg (if renal impairment, reduce to 12 mg/kg); infuse slowly over 25–30 min; may repeat q5min as needed, not to exceed 1 g.
- IV maintenance dose: 1–4 mg/min IV (reduce infusion by 1/3 in moderate renal and 2/3 in severe renal impairment).
  - Narrow therapeutic window: therapeutic plasma levels are procainamide 4–10 μg/mL, NAPA 15–25 μg/mL
  - Toxic level: Procainamide >10 μg/mL.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Slowing of conduction	Assess for clinically symptomatic bradycardia, heart block, CHF	Auscultation of heart sounds, ECG	Continuous ECG monitoring
RESP	Lupus-related pleuritis or pneumonia	Assess for dyspnea	Auscultation of lung fields	O_2 saturation monitoring
CNS	High plasma concentrations may cause confusion/disorientation and/or seizures; rarely muscle weakness	Evaluate regimen, pt compliance	Monitor blood levels of procainamide and NAPA	Neurologic assessment

Key References: deSouza IS, Martindale JL, Sinert R: Antidysrhythmic drug therapy for the termination of stable, monomorphic ventricular tachycardia: a systematic review, *Emerg Med J* 32(2):161–167, 2015; Pedersen CT, Kay GN, Kalman J, et al.: EHRA/HRS/APHRS expert consensus on ventricular arrhythmias, *Europace* 16(9):1257–1283, 2014.

Perioperative Implications

Preoperative Concerns
- Hx of arrhythmia, ischemic or structural heart disease.
- Ventricular dysfunction.
- Plasma concentration of procainamide.
- May be used to treat contractions in pts with myotonic dystrophies; should be continued periop.

Induction/Maintenance
- Caution with drugs that slow cardiac conduction (e.g., other Na^+ channel blockers, betablockers) and drugs that prolong QT interval
- Use of other Na^+ channel blockers
- Local anesthetic toxicity with major conduction blocks
- Arrhythmias with high plasma concentration of procainamide
- Myocardial depressive effect worsened by hyperkalemia
- Potentiates activity of neuromuscular blockade

Postoperative Period
- Toxicity
- Arrhythmias caused by slowed conduction

Anticipated Problems/Concerns

- Monitor for clinical signs of toxicity: Torsades, heart block, arrhythmias, confusion, lupus syndrome.
- Not well tolerated for long-term control of atrial tachycardias because of dosing regimen, complications.
- In renal pts: Concentrations of procainamide and NAPA may rise to toxic levels; therefore reduce dose, monitor levels of both.

Propylthiouracil—Antithyroid Drugs

Michael F. Roizen

Uses

- RX for hypothyroidism. In USA, 7.5% of pregnant women plus an additional 500,000 people per y develop hyperthyroidism.
- Rx for goiter associated with hyperthyroidism; second drug to methimazole due to greater side effects with PTU except in pregnancy (methimazole has greater side effects on fetus during pregnancy).
- Definitive Rx for control of hyperthyroidism in anticipation of spontaneous remission.
- Rx for hyperthyroidism in conjunction with ^{131}I or ^{125}I to hasten recovery while awaiting effects of radiation therapy.
- Secondary Rx for hyperthyroidism to control disorder in preparation for surgery.

Perioperative Risks

- Side effects of drug: Hypothyroidism; liver failure, especially in pts with liver transplants; be careful in pregnancy.

Worry About

- Agranulocytosis (less than 0.5% of treated pts develop this side effect) and liver problems

Overview/Pharmacology

- Antithyroid drug: Absorbed within 20–30 min; effect begins to decrease in 2–3 h (half-life of methimazole estimated to be 6–13 h).
- Drug and metabolites cleared by renal excretion.
- Antithyroid drugs cross placenta, can be found in breast milk.

Drug Class/Usual Dose

- Antithyroid drug (thioureylene): Interferes directly with synthesis of thyroid hormones by preventing incorporation of iodine into tyrosyl residual thyroglobulin; inhibits coupling of iodotyrosyl residues to form iodothyronines by inhibiting peroxidase enzyme.
- Depletes preformed hormone over time; only then do clinical effects become noticeable (half-life of thyroid hormones is >3 d in circulation).
- Other useful antithyroid drugs include those inhibiting conversion of less active T_4 into more active T_3, such as propranolol; methimazole and carbimazole do not appear to do so with anti–β-blocker effect (e.g., propranolol and others); those that inhibit release of preformed thyroid hormone (e.g., iodine). Also temporarily inhibits synthesis and decreases vascularity of thyroid glands.

Chronic Rx Uses

- Decreased hyperthyroidism and thyrotoxicosis
- Decreased goiter size in hyperthyroidism

Acute Rx Uses
- Relieves symptoms of hyperthyroidism while waiting for ^{131}I or ^{125}I to take effect.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Goiter shrinkage; occasionally goiter develops if hypothyroidism occurs	Snoring, hoarseness, neck pain	Ask pt to vocalize "e"; examine airway, neck	Check CXR (PA, lateral), lateral neck films; if needed, CT scan of neck
CV		Assess CV response to Rx		Rhythm strip or full ECG if CV system is involved by either Hx or PE
GI	Rare hepatotoxicity			SGPT, SGOT
HEME	Mild anemia, thrombocytopenia; agranulocytosis as toxic reaction to propylthiouracil or methimazole (0.05–0.12% of pts)	Hx of sore throat or fever often heralds agranulocytosis	Skin/mucous membranes for infection/petechiae; purpura if at risk	CBC with plt count; differential leukocyte count
DERM		Rare depigmentation of hair		
MS		Pain/stiffness in joints (rare side effect)		
GU	Placenta: Crosses placental barrier and is excreted in breast milk			
CNS		Headache, paresthesia are rare side effects. Shaking, anxiety, emotional instability are signs that hyperthyroidism not yet controlled.	Reflex speed, tremor, nervousness, mental status	
ENDO	Need to assess if euthyroid	Refer to all other systems, especially reflex speed, tremor, heat intolerance, weight loss, fatigue, weakness, anorexia, increased appetite	Reflex speed; HR	Free T_4 level if unable to assess if euthyroid by Hx, PE

Key References: Farling PA: Thyroid disease, *Br J Anaesth* 85(1):15–28, 2000; Nayak B, Burman K: Thyrotoxicosis and thyroid storm, *Endocrinol Metab Clin North Am* 35(4):663–686, 2006; Ross DS: Antithyroid drugs. In Cooper DS, Mulder JE, editors: Waltham, MA, 2015, UpToDate. www.uptodate.com/contents/antithyroid-drugs-beyond-the-basics (Accessed 07.07.2016).

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns
- Assess euthyroid state (see Assessment Points table).
- Fairly certain sign that remission may have occurred is decrease in size of goiter.

Induction/Maintenance
- No interactions known

Adjuvants/Regional Anesthesia/Reversal
- No interactions known

Postoperative Concerns
- Resumption not necessary if surgery to correct hyperthyroidism was successful.
- Be careful with pts who have Hx of liver disease and who are pregnant or breastfeeding.
- Short half-life makes resumption in nonthyroid surgery necessary ASAP, or give medication IV.

Anticipated Problems/Concerns
- Assess for hyperthyroidism, agranulocytosis, and liver dysfunction.

Proton Pump Inhibitors

Benjamin T. Cobb | Norman Randolph | Mark S. Weiss

Uses
- PPIs are used for the prevention and treatment of ulcers in the stomach, esophagus, or duodenum that are caused or exacerbated by stomach acids.
- People in USA receive approximately 21 million prescriptions annually.
- Worldwide, $13.6 billion worth of PPIs are consumed annually.
- PPIs are administered for the treatment of dysphagia, peptic and duodenal ulcer disease, gastroesophageal reflux, Barrett esophagus, Zollinger-Ellison syndrome, ulcers caused by NSAIDs, and eosinophilic esophagitis. PPIs are also used in the treatment of ulcers caused by *Helicobacter pylori*.

Perioperative Risks
- N/V, diarrhea, flatulence, abdominal pain.
- Interstitial nephritis and rhabdomyolysis.
- Possible mildly exaggerated effects of thiopental and/or other potent vasodilators.
- Inhibit CYP450 liver enzymes: (1) Drugs such as clopidogrel (Plavix) cannot be metabolized to active form and (2) PPIs increase free carvedilol levels.
- Displace protein-bound drugs (e.g., warfarin, sulfonylureas, thiopental, methotrexate).

Overview/Pharmacology
- Administered in an inactive (lipophilic) form in which they can enter the target cell. The acid environment in the cell protonates the drug and converts it into the activated form that binds to the proton pump.
- Metabolized by the liver, excreted by kidney and colon.
- Inhibit the cytochrome P450 system, causing variation in other medication effects.
- Displace protein-bound drugs, thus increasing their effects.

Drug Class/Mechanism of Action/Usual Dose
- PPIs suppress gastric acid production by binding to H+/K+ ATPase (i.e., the proton pump) in gastric parietal cells, causing long lasting suppression of acid secretion. The proton pump is at the terminal stage of acid production, and PPIs are up to 99% effective in decreasing gastric acid content as well as increasing the gastric pH.
- Omeprazole 20–40 mg PO for chronic GI symptoms
- Pantoprazole 40–80 mg IV q12–24h for acute GERD and GI bleeding
- Alternatives: antacids, sucralfate, tricyclic antidepressants, H_2-receptor antagonists, other PPIs (esomeprazole, lansoprazole), endoscopic interventions, and surgical interventions

Assessment Points

System	Effect	Assessment by Hx	PE	Test
RESP	URI, cough, asthma		Tachypnea, diminished breath sounds	ABG, CXR
GI	Abdominal pain, diarrhea	N/V, diarrhea	Compensatory tachypnea, abdominal tenderness	Endoscopy, upper GI series, KUB, ABG
ENDO	Hyperglycemia, hypercholesterolemia			Glucose, lipid panel
HEME	Anemia, thrombocytopenia	Dyspnea, bleeding, bruising	Hematomata, petechiae	CBC, bleeding time
HEPAT	Hepatocellular damage	Nausea, emesis, anorexia	Hepatomegaly, jaundice	AST, ALT, alk phos, PT/INR, PTT
Toxicity				
CV	Angina pectoris, arrhythmia, decreased magnesium levels	Chest pain	Hypotension, dyspnea	ECG/lyte panels
DERM	Rash	Pruritus, excoriations	Acneiform, erythematous, pruritic, or eczematoid lesions	
RENAL	Interstitial nephritis, pyelonephritis	Oliguria, anuria, hematuria	Edema, rales, pruritis	BUN/Cr, UA, CXR
CNS	Headache, tinnitus, drowsiness, dizziness		Sweating, confusion, convulsions	

Key References: Esomeprazole strontium (esomeprazole strontium)—drug summary. PDR.net. <http://www.pdr.net/drug-summary/Esomeprazole-Strontium-esomeprazole-strontium-3332.2474>, 2016 (Accessed 07.07.16); Gouda BB, Lydon AM, Badhe A, et al.: A comparison of the effects of ranitidine and omeprazole on volume and pH of gastric contents in elective surgical patients, *Eur J Anaesthesiol* 21(4):260–264, 2004.

Perioperative Implications

- Relatively few in the periop period.
- May cause acute renal injury.

Possible Drug Interactions

- May displace protein-bound drugs (e.g., warfarin [Coumadin], diazepam [Valium], sulfonylureas, thiopental [Pentothal], methotrexate, phenytoin [Dilantin]), increasing concentration in the blood and thus augmenting their effects.
- Inhibition of CYP450 liver enzymes. For example, the action of clopidogrel (Plavix) is inhibited by blocking conversion to its active form.
- May decrease the absorption of ketoconazole, decreasing its effectiveness.

Anticipated Problems/Concerns

- Increased risk of *Clostridium difficile* infection.
- May increase risk of myocardial infarction.
- Increased risk of osteoporosis with prolonged use, leading to hip, wrist, or spine fractures; use caution in performing RA.
- Hypomagnesemia may present as tetany, seizures, and cardiac arrhythmias.
- Decreased acid production with prolonged use may decrease the absorption of vitamin B_{12}.

Pseudoephedrine

Lori B. Heller | Lee A. Fleisher

Uses

- An OTC sympathomimetic commonly used as a nasal decongestant or for opening obstructed eustachian ostia.
- Used in the symptomatic treatment of reactive airway disease; however, appears to be ineffective as a bronchodilator.
- Also used for treatment of ejaculatory dysfunction and as a starting material for illicit drug manufacturing.
- Abuse and addiction to OTC stimulants does occur, particularly in those with eating disorders or erratic work hours, such as truck drivers. Associated with myocardial injury and withdrawal symptoms in this setting.

Perioperative Risks

- Concern about the coadministration of other sympathomimetic agents because of the possibility of additive effects and increased toxicity.
- Pressor effects of pseudoephedrine are more pronounced in:
  - Hypertensive pts
  - Pts taking β-adrenergic blocking drugs
  - Pts taking SNRIs
- May increase heart irritability
- MAO inhibitors, by increasing the quantity of NE, potentiate pseudoephedrine's indirect pressor effects; infrequently, a hypertensive crisis may result.
- May also reduce the antihypertensive effects of reserpine and methyldopa.

Overview/Pharmacology

- Acts directly on α- and, to a lesser degree, β-adrenergic receptors. Has an indirect effect by releasing NE from its storage sites.
- α-adrenergic effects result from inhibition of the production of cAMP by inhibiting the enzyme adenylyl cyclase, whereas β-adrenergic effects result from stimulation of adenylyl cyclase activity.
- Acts directly on α-receptors in the mucosa of the respiratory tract, producing vasoconstriction; this shrinks mucous membranes, thus reducing edema and congestion.
- May relax bronchial smooth muscle by stimulating β-adrenergic receptors, but this effect is not consistent.
- Readily and completely absorbed; elimination is predominantly renal and pH-dependent.

Drug Class/Dose

- Direct and indirect sympathomimetic
- Half-life is 6 h for standard preparation and 12 h for extended-release form.
- Adults and children ≥12 y of age: 60 mg q4–6h with a maximum dosage of 240 mg/d.
- Children 6–11 y of age: 30 mg q4–6h with a maximum dosage of 120 mg/d.
- Children 2–5 y of age: 15 mg q4–6h with maximum dosage of 60 mg/d.
- Children <2 of age: No USA FDA-approved dosing.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, dysrhythmias, cardiac irritability	Palpitations	BP/HR	ECG
HEENT	Mucosal vasoconstriction Reduction of volume of nasal mucosa Drainage of sinus secretions, opening of obstructed ostia	Nasal congestion Head stuffiness	Absence of hyperemia of nasal mucosa	
NEURO	Nervousness, excitability, restlessness, dizziness, weakness, insomnia, headaches, drowsiness		Tremors, anxiousness	
GU/RENAL	Urinary retention	Difficulty voiding, emptying bladder completely	Tachycardia, Htn	Bladder US, postvoid residuals
GI	N/V		Abdominal tenderness	

Key References: Kanfer I, Dowse R, Vuma V: Pharmacokinetics of oral decongestants, *Pharmacotherapy* 13(6 Pt 2):116S–128S, 1993; Werler MM: Teratogen update: pseudoephedrine, *Birth Defects Res A Clin Mol Teratol* 76(6):445–452, 2006.

Perioperative Implications

Preoperative Concerns
- Oral administration of usual doses to normotensive pts usually produces minimal effects.
- Possible Htn, tachycardia in sensitive pts.
- Those with concomitant hyperthyroidism, ischemic heart disease, or prostatic hypertrophy may be more at risk.
- May increase irritability of the heart muscle and result in multifocal PVCs.
- May be teratogenic; avoid use in pregnant pts if possible; avoid use in breastfeeding women.
- Geriatric pts may be especially sensitive.
- Overdose may cause hallucinations, CNS depression, seizures, and death.

Monitoring
- Routine

Induction
- Increased absorption of pseudoephedrine with antacid administration

Airway
- Improvement of airway edema and congestion related to mucosal hyperemia is often seen.

Maintenance
- Careful administration/titration of other sympathomimetic drugs

Regional Anesthesia
- Pts may be more prone to urinary retention with regional techniques that block sacral roots.

Postoperative Concerns
- Resumption of drug should not pose particular problems once vital signs are stable.

Anticipated Problems/Concerns
- Caution in administering other sympathomimetic agents.
- β-adrenergic blocking drugs may increase pressor effect.
- Antihypertensive effects of reserpine; methyldopa may be diminished.

Pyridostigmine Bromide

J. Lance LaFleur | Krishna Boddu | Lee A. Fleisher

Uses
- Therapy for MG, which is caused by decreased postsynaptic ACh receptors.
- Antagonism of nondepolarizing NMBDs.
- Therapy for glaucoma.
- Therapy for atony of GI and urinary tracts.

Perioperative Risks
- Muscarinic effects on GI, respiratory, and CV systems.
- Prolonged response to succinylcholine if administered shortly afterward by inhibition of pseudocholinesterase and increased postsynaptic depolarization.
- Paralysis may be prolonged by excessive doses, which can produce a depolarizing NMB

Pharmacology
- Oxydiaphoretic (acid-transferring) inhibitor of AChE.
- Transfers a carbamate group to AChE and forms a covalent bond at the esteratic site.
- Quaternary ammonium ion, which is poorly lipid soluble; does not effectively penetrate GI tract or blood-brain barrier (no CNS side effects).
- Onset is within 10–15 min (vs. 5–10 min for neostigmine); duration is 4 h (similar to neostigmine).
- 20% as potent as neostigmine.
- Renal excretion accounts for approximately 75% of elimination.
- Very large volume of distribution with extensive tissue storage.
- Oral bioavailability is 7.6 ± 2.4%.

Drug Class/Mechanism of Action/Usual Dose
- Reversibly inhibits AChE, which increases the concentration of ACh at the motor endplate.
- May be administered PO, IV, or IM
- Dose is 0.1–0.4 mg/kg IV.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Bradyarrhythmias, hypotension	Presyncope, angina, confusion	HR, BP, orthostasis	ECG
RESP	Increased secretions, bronchospasm	Dyspnea, wheezing	Auscultation	PFTs
GI	Increased secretions, increased motility, spasms	Diarrhea, abdominal pain	Palpation	Lytes

Key References: Barash PG, Cullen BF, Stoelting RK: *Clinical anesthesia*, ed 5, Philadelphia, 2006, Lippincott Williams and Wilkins, pp 297–300, 848; Blichfeldt-Lauridsen L, Hansen BD: Anesthesia and myasthenia gravis, *Acta Anaesthesiol Scand* 56(1):17–22, 2012.

Perioperative Implications

Preoperative Concerns
- In MG pts, skeletal muscle response to repetitive impulses is augmented by increased availability of Ach.
- Chronic administration in MG pts may alter effects of NMBDs, and some may consider omission or reduction of morning dose on the day of surgery.

Induction/Maintenance
- Although nicotinic effects are desirable, muscarinic effects should be attenuated by an anticholinergic (typically glycopyrrolate 0.05 mg per 1 mg of pyridostigmine).

Postoperative Period
- Incidence of recurarization in renal pts is not increased as clearance of both AChE inhibitors and NMBDs is similarly affected.
- MG pts taking >750 mg/d have greater potential for respiratory insufficiency.
- Myasthenic and cholinergic crises may occur after periop alterations in AChE inhibitor therapy.

Anticipated Problems/Concerns
- If maximal dose of pyridostigmine (0.4 mg/kg, or 20 mg in adults) fails to antagonize the residual blockade, it is not advisable to redose the AChE inhibitor, as this may lead to further motor weakness.
- Causes of inadequate antagonism include profound blockade, respiratory acidosis, hypokalemia, hypermagnesemia, hypothermia, verapamil, and antibiotics such as aminoglycosides and polypeptides.

Rifampin

Matthew B. Ellison | Matthew P. Jordan | Manuel C. Vallejo

Uses
- Antibiotic therapy for TB (yearly incidence 2.96:100,000 in USA) and *Neisseria meningitidis* infection (yearly incidence 0.3:100,000 in USA).
- Also used to treat Hansen disease (leprosy) and Legionnaires disease and as prophylaxis against *Haemophilus influenzae* type B.
- Treatment of opioid-induced pruritus associated with the cholestatic jaundice of malignancy
- Administered PO or IV
- 10% of pts receiving rifampin develop chemical hepatitis; 16 deaths per 500,000 receiving drug.

Perioperative Risks
- Hepatic dysfunction, most likely in presence of preexisting liver disease and when used in combination with other hepatotoxic agents like isoniazid.
- Decreased duration of action of narcotics and barbiturates due to P450 (CYP2D6) enzyme induction.
- Pts receiving antiarrhythmic therapy, digoxin, theophylline, phenytoin, or glucocorticoid therapy may need increased doses of these drugs due to enzyme induction.

Overview/Pharmacology
- Complex macrocytic antibiotic approved by FDA in 1971.
- Water-soluble at acidic pH; inhibits gram-positive and many gram-negative organisms, incl *Escherichia coli*, *Pseudomonas*, *Proteus*, *Klebsiella*, *Neisseria meningitidis*, *H. influenzae*, *Mycobacterium tuberculosis*.
- Increases in vitro activity of streptomycin and isoniazid.

- Primarily eliminated by biliary clearance (30–40%) with up to 30% of the dose excreted in urine.
- Half-life 3–5 h; increased with hepatic dysfunction.

Worry About

- Induces hepatic microsomal (P450, CYP2D6) activity and decreases half-life of hepatically metabolized drugs; this effect may last for several weeks after the drug is discontinued.
- Theoretically increases risk of halothane hepatitis.
- Hemolytic anemia, thrombocytopenia (rare).

Drug Class/Mechanism of Action/Dose

- Semisynthetic derivative of rifamycin B, produced by *Streptomyces mediterranei*.
- Inhibits DNA-dependent RNA polymerase in bacteria and mycobacteria; nuclear eukaryotic RNA polymerase not affected.
- Administered for chemoprophylaxis of meningococcal infections, with beta lactams for staphylococcal endocarditis, osteomyelitis, and methicillin-resistant *Staphylococcus aureus* infections; also used in conjunction with isoniazid and streptomycin for active TB.
- Typical adult and pediatric dose: Tuberculosis—10 mg/kg/d or 10 mg/kg PO twice weekly (max 600 mg); *Neisseria meningiditis*—600 mg q12h for 2 d; *Haemophilus influenzae* Type B prophylaxis—600 mg/d PO/IV for 4 d.
- Possible interaction of rifampin with 5HT3 and opioid system as well as mediators of itching proposed. Dose: 300 mg IV 3 times daily.
- Should be administered PO 1 h before or 2 h after meals.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL		Fatigue, drowsiness, dizziness, ataxia, confusion, weakness		
HEENT	Secreted in saliva, tears		Orange sputum, tears, conjunctiva, sweat	
GI	Hepatic dysfunction (rare with normal pre-Rx hepatic function)	N/V	Jaundice	Elevated transaminases
HEME	Thrombocytopenia, hemolytic anemia	Bruising/ bleeding		Plt count, Hgb/Hct, microscopic exam
RENAL	Interstitial nephritis, ATN, renal failure (with high doses)		Orange urine	Cr clearance, light-chain proteinuria

Key References: Wallace R, Philley J, Griffith D: Antimycobacterial agents. In Bennett J, Dolin R, Blaser M, editors: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 8, Philadelphia, PA, 2015, Elsevier, pp 463–478; Stoelting R, Hillier S: Antimicrobials. In Stoelting R, Hillier S, editors: *Pharmacology & physiology in anesthetic practice*, ed 4, Philadelphia, PA, 2006, Lippincott Williams & Wilkins, pp 542–543.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- Decreased duration of action of benzodiazepines, narcotics, barbiturates due to hepatic (P450, CYP2D6) enzyme induction.
- Adequacy of preexisting drug regimens should be verified (see Special Considerations).

Induction/Maintenance

- Decreased narcotic and analgesic efficacy: barbiturates, methadone, diazepam, midazolam; beta-blockers have increased clearance, decreased duration of action.
- Halothane metabolism increases, with increased risk of hepatotoxicity.

Adjuvants/Reversal

- Mycobacteria quickly develop resistance when rifampin is used alone (within 40 h); administer with isoniazid and/or streptomycin.

Special Considerations

- Risk of hepatic dysfunction increased periop due to preexisting hepatic disease and alcohol use.
- Delays oral absorption of ASA.
- Decreases in half-life requiring larger doses to maintain adequate therapeutic levels: Digoxin, digitoxin, quinidine, propranolol, metoprolol, verapamil, coumadin, theophylline, phenytoin, prednisone, cortisol, cyclosporine, oral hypoglycemic agents, ketoconazole, fluconazole
- Can precipitate opioid withdrawal symptoms in an opioid-dependent pt by enhancing the hepatic enzymatic metabolism of opioids.
- May increase metabolism of oral contraceptives and anticoagulants, thus decreasing the effectiveness of these medications.

Anticipated Problems/Concerns

- 10% of pts may develop hepatitis; pts with preexisting liver disease are at higher risk.
- Rifampin induces microsomal enzyme activity in the liver, resulting in decreased efficacy and duration of action of hepatically metabolized drugs; this may last for weeks after the drug is discontinued.

Selective Estrogen Receptor Modulators

Lyndsay M. Hoy | Lee A. Fleisher

Uses

- Critical components in treatment algorithm for invasive and/or in situ breast cancer, breast cancer chemoprevention in high-risk pts, and postmenopausal osteoporosis (raloxifene only)

Perioperative Risks

- VTE, particularly if the pt has a history of recent chemotherapy, prior irradiation, or long-term SERM use
- Microvascular complications following free-flap breast reconstruction surgery

Worry About

- Periop SERM management
- Endometrial cancer (tamoxifen only)
- Unpleasant side effect profile affecting pt quality of life and medication adherence

Overview/Pharmacology

- SERMs inhibit breast tumor growth via competitive antagonism of estrogen; also decrease bone demineralization and improve lipid profile via estrogen agonist properties.
- Shape of ligand binding to ERs is highly influential in determining spectrum of estrogen agonist/antagonist expression in target tissues.
  - SERMs competitively bind to shape-sensitive ligand binding domain on ERs, triggering a complex cascade of molecular networks.
  - SERM-ER complex undergoes conformational dynamic changes to become estrogenic or antiestrogenic, thereby recruiting subsequent cofactors and promoting or degrading specific gene transcription via posttranslational modification of multiple kinase pathways.
  - Differential expression of two ER isoforms (alpha, beta) at target sites with varying levels of ligand affinity, cofactor binding, and estrogen activity may contribute to intrinsic SERM success vs. resistance.

Mechanism of Action/Usual Dose

- Tamoxifen
  - Routinely used for prevention of breast cancer in women at high risk and also as adjuvant endocrine therapy in pts who are ER-positive.
  - Metabolically activated to hydroxylated metabolites with high ER affinity.
  - Long half-life (2 wk).
  - Blocks effects of endogenous estrogen in normal and neoplastic breast tissue; conversely produces estrogen-like effects in uterus, bone, liver, and coagulation system.
  - Adjuvant tamoxifen therapy for 5–10 y may reduce 15-y risk of mortality and local breast cancer recurrence.
  - Administered as a 20-mg pill taken daily.
- Raloxifene
  - Alternative to tamoxifen for women at increased risk of uterine cancer; unlike tamoxifen, lacks estrogen activity in uterus.
  - Estrogen effects on bone/lipids; estrogen antagonist effects on breast/uterus.
  - Only agent currently approved for prevention and treatment of postmenopausal osteoporosis.
  - Short-acting.
  - Administered as 60-mg pill taken daily.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Vasomotor symptoms (T, R) Stroke (T, R) Cataracts (T)	Hot flashes, night sweats		
CV	Possible cardioprotective effect (T)			
RESP	Pulm embolus (T, R)	Respiratory distress	Tachypnea	CXR, ABG, V/Q scan, spiral CT
ENDO	Decreased cholesterol (T, R)			Lipid panel
HEPAT	Fatty liver (T)			LFTs, hepatic US/CT
GYN	Endometrial hyperplasia (T) Menstrual irregularities (T) Sexual dysfunction (T)	Irregular menstrual cycle Reduced libido, dyspareunia		Uterine US
HEME	Thromboembolic event (T, R)			Coag
ONC	Reduced risk of breast cancer (T, R) Increased risk of endometrial cancer (T)			ER/PR status

R, Raloxifene; *T*, tamoxifen.

Key References: Maximov PY, Lee TM, Jordan VC: The discovery and development of selective estrogen receptor modulators (SERMs) for clinical practice, *Curr Clin Pharmacol* 8(2):135–155, 2013; Mirzabeigi MN, Nelson JA, Fischer JP, et al.: Tamoxifen (selective estrogen-receptor modulators) and aromatase inhibitors as potential perioperative thrombotic risk factors in free flap breast reconstruction, *Plast Reconstr Surg* 135(4):670–679, 2015.

Perioperative Implications

Preoperative Concerns

- Consider discontinuation of SERMs 2–4 wk preop, particularly if surgery is associated with moderate/high risk of VTE.

Adjuvants/Regional Anesthesia/Reversal

- No contraindications/known reactions

Postoperative Period

- Ideal time to restart SERM therapy postop should be considered on individual pt basis in conjunction with surgical and oncologic teams.

Anticipated Problems/Concerns

- SERMs may increase risk of VTE during periop period.
- Correlation between length of periop SERM cessation and oncologic outcome (i.e., altered progression of disease if SERM held for >1 mo) unknown. However, full compliance with SERM therapy clearly associated with reduction in long-term mortality.

Serotonin: Agonists, Antagonists, and Reuptake Inhibitors

David F. Stowe

Uses

- Serotonin (5-hydroxytryptophan [5-HT]) not given as a drug; is a neurotransmitter that plays many roles within the body; serotonin levels can be affected by drugs called serotonin agonists and antagonists
- Partially selective receptor *agonists* used mostly for Rx of acute migraine headaches; they include:
  - Sumatriptan (Imitrex) 5–20 mg IN, 25–100 mg/d PO
  - Naratriptan (Amerge) 2.5 mg/d PO
  - Rizatriptan (Maxalt) 5 mg/d PO
  - Zolmitriptan (Zomig) 5 mg IN, 2.5 mg/d PO
- Partially selective receptor 5-HT_3 *antagonists* used to treat N/V
  - Metoclopramide (Reglan) 5–15 mg qid PO, 2–10 mg IV, 10–20 mg IM (used to treat GERD, gastroparesis, N/V)
  - Dolasetron (Anzemet) 12.5 mg IV or 100 mg PO 30–60 min before emergence to prevent postop N/V or before chemotherapy
  - Ondansetron (Zofran) 4–8 mg tid PO to prevent N/V due to emergence or emetogenic chemotherapy treatment
  - Granisetron (Kytril) 10 µg/kg IV, 1 mg bid PO, TD patch (Sancuso) for prevention of N/V due to chemotherapy and for postop N/V
  - Palonosetron (Aloxi) 0.25 mg IV 30 min before and days after chemotherapy
- SSRIs (all used PO to treat major depression and personality disorders (e.g., OCD, PTSD)
  - Citalopram (Celexa) 20–40 mg/d PO (fewest side effects)
  - Escitalopram (Lexapro) 10 mg/d PO
  - Fluoxetine (Prozac, Sarafem) 20–80 mg/d PO
  - Paroxetine (Paxil, Pexeva) 20–50 mg/d PO
  - Sertraline (Zoloft) 50–200 mg/d PO (least tolerated)

Perioperative Risks

- Sumatriptan, etc: Not for pts with IHD, angina, Prinzmetal angina, severe Htn
- Metoclopramide, etc: Not for pts with pheochromocytoma, long-QT syndrome, or those taking MAOIs or TCA; may worsen mental depression/Parkinson disease; antagonized by narcotics; may cause tardive dyskinesis.
- SSRIs can cause serotonin syndrome (hyperthermia, muscle rigidity, myoclonus, rapid mental change) if given in the presence of MAOIs; may increase coumadin, digitalis effects by reducing plasma protein binding; increased suicide risk in pts <24 y of age.

Worry About

- Sumatriptan and other 5-HT agonists: Pts may have exacerbation of anginal symptoms, experience drowsiness, dizziness, flushing.
- Ondansetron, granisetron, etc: Chemotherapy pts may exhibit increased N/V during anesthesia.
- SSRIs: Serotonin syndrome: Increased threshold for N/V; concomitant use of MAOIs; displacement of other drugs highly bound to plasma protein (digoxin, antianginals, beta-blockers, tricyclic antidepressants); increased bleeding with coumadin, so monitor prothrombin time.

Overview/Pharmacology

- 90% of serotonin is secreted by enterochromaffin cells of GI tract; released into plasma by unclear mechanisms including neuronal stimuli; some taken up, much is stored in plts; 5-HT receptors on vascular endothelium stimulate release of NO to promote vasodilation, but receptors on vascular smooth muscle promote vasoconstriction. Excess release involved in carcinoid syndrome due to enterochromaffin cell neoplasm. As an amine neurotransmitter, serotonin is also secreted, stored, and released by raphe nuclei in brain stem (serotonergic neurons).
- Serotonergic neurons diffusely innervate most regions of CNS; with other neurotransmitters, is involved in modulating mood, depression, sexual function, anxiety, migraine headache, sleep, appetite, temp regulation, perception of pain and itch, regulation of BP.
- Abn in secretion or receptor activation likely underlies mental depression, migraine headache, sensitivity to pain, sleep pattern, and central BP control. In CNS, 5-HT receptor activation increases K^+ conductance to promote membrane hyperpolarization, leading to a mostly inhibitory action. As a CNS neurotransmitter, 5-HT modulates effects of other monoamine transmitters (e.g., norepinephrine, dopamine, other transmitters such as Ach, glycine, and GABA). Inhibition of 5-HT reuptake elevates mood and normalizes behavior.
- Side effects of SSRIs: Sexual dysfunction, weight gain, sleep dysfunction, withdrawal symptoms.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Htn, IHD (agonists)	MAO drug interaction	BP	Drug levels
	Longer P-R and QT_c intervals (antagonists)	Dysrhythmias, bleeding	ECG	INR
	Hypotension (SSRIs)		BP	
	Serotonin syndrome (SSRIs)		BP, CNS	
	Altered drug levels (SSRIs)		Bleeding	
ENDO	Carcinoid syndrome (increased 5-HT)	Diarrhea, abdominal pain, asthma, flushing, increased glucose, dizziness, drowsiness, PAT, SVT		5-HT, kallikreins
HEME	Leukopenia (antagonists)			CBC
CNS	Psychosis, depression, altered mood, seizure disorder	Mental disorder	CNS evaluation	Drug levels

Key References: Lacasse JR, Leo J: Serotonin and depression: a disconnect between the advertisements and the scientific literature, *PLoS Med* 2(12):e392, 2005; Meltzer HY, Massey BW, Horiguchi M: Serotonin receptors as targets for drugs useful to treat psychosis and cognitive impairment in schizophrenia, *Curr Pharm Biotechnol* 13(8):1572–1586, 2012.

Perioperative Implications

- Avoid narcotics in pts with carcinoid syndrome (surgery or 5-HT antagonists usually used to treat carcinoid tumor).
- Use caution in giving metoclopramide; pt must not be taking MAOIs—for example, isocarboxazid (Marplan), phenelzine (Nardil), or tranylcypromine (Parnate).
- Check pt's drug profile for Hx of migraine; increased risk of coronary vasoconstriction with sumatriptan.
- Check pt's drug profile for Hx of schizophrenia; may have low WBC count if taking clozapine.
- If pt is taking an SSRI, lowered threshold for N/V.
- Check pt's drug profile for Hx of major depression; if taking coumadin or digitalis, levels may be increased.

Sildenafil Citrate

John G. Augoustides | Lee A. Fleisher

Uses

- Treatment of erectile dysfunction (Viagra)
- Sildenafil (Revatio) is used to improve the ability to exercise in people with pulm arterial Htn
- Oral sildenafil is used as part of multimodal management of severe periop pulm Htn and right ventricular dysfunction in clinical settings such as:
  - Heart transplantation
  - Pulm Htn associated with CHD
  - Pulm Htn associated with mitral valve disease

Perioperative Risks

- None for elective surgery based on the half-life of sildenafil.
- Drug may still be present in emergent surgery.

Worry About

- Potentiation of vasodilating agents
- Hx of coronary ischemia or congestive heart failure
- Severe hepatic impairment

Overview/Pharmacology

- Sildenafil citrate was discovered by accident during testing as a treatment for heart disease.
- Terminal half-life 4–6 h.
- Total protein binding 96%, also distributed in tissues.
- Bioavailability 41%.
- Metabolized in liver via the cytochrome P450 isoenzymes, 3A4 (major route) and 2C9 (minor route).
- Active *N*-desmethyl metabolite.
- Peak plasma concentration reached in 60 min.
- Excreted via feces (80%), kidney (13%), and semen (<0.001% of a dose).
- Metabolism may be delayed after a high-fat meal and in pts with liver disease.
- Contraindicated in pts with hypersensitivity to sildenafil products and those taking nitroglycerin or other organic nitrates.
- Precautions: Anatomic deformities of the penis, conditions predisposing pts to priapism, bleeding disorders or active peptic ulceration, retinitis pigmentosa or other retinal abn, coronary ischemia or CHF, multidrug antihypertensive regimens.
- Excretion in breast milk is unknown.

Drug Class/Mechanism of Action

- Potent and selective inhibitor of PDE V.
- PDE V isoform is responsible for breaking down cGMP in the corpus cavernosum. cGMP relaxes smooth muscle to cause local vasodilatation and swelling of corpora as they fill with blood.
- With sexual arousal, NO is produced in cavernosal tissue to stimulate the secretion of cGMP.
- Sildenafil inhibits PDE V, causing a 35% increase in cGMP levels.
- Sildenafil inhibits PDE V in the lung, thus increasing cGMP levels in the lung to cause pulm vasodilatation and improvement in pulm Htn.

Usual Dose

- Supplied in 100-, 50-, and 25-mg tablets.
- May be taken 0.5–4 h prior to sexual activity.
- Dose ranges from 25–100 mg, with a maximum frequency of once a d orally.
- Dose adjustments required in pts with severe renal and hepatic impairment.
- For geriatric pts (above 65 y of age), starting dose should be 25 mg.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT	Activity on PDE VI (PDE VI is important for phototransduction in the retina)	Transient disturbance of blue-green color discrimination	
CV	Dilation of systemic blood vessels	Transient drop in BP, flushing, Hx of nitrate use	Low BP
GI	Relaxation of lower esophageal sphincter	Dyspepsia, diarrhea	
CNS		Headache, dizziness	
RESP	Mucosal vasodilation	Nasal congestion	

Key References: Schwartz BG, Kloner RA: Drug interactions with phosphodiesterase-5 inhibitors for the treatment of erectile dysfunction or pulmonary hypertension, *Circulation* 122(1):88–95, 2010; Vassalos A, Peng E, Young D, et al.: Pre-operative sildenafil and pulmonary endothelial-related complications following cardiopulmonary bypass: a randomised trial in children undergoing cardiac surgery, *Anaesthesia* 66(6):472–480, 2011.

Perioperative Implications

- Risk primarily related to emergent cases based on half-life.
- Caution with the concomitant use of hypotensive agents.
- Precautions to prevent reflux and regurgitation.
- Pts on regular sildenafil for pulm vasodilation will have significant pulm Htn that is often assoc with significant underlying lung disease and right ventricular dysfunction.
- Pts on regular sildenafil for pulm vasodilation may require aggressive periop management of severe pulm Htn to maintain adequate cardiac output. Adequate pulm vasodilation may require periop therapy with IV inodilators such as milrinone and/or inhaled selective pulm vasodilators such as NO or prostacyclin.
- A randomized trial of preop sildenafil did not show reduction in pulm vascular resistance.

Drug Interactions

- Concurrent use of nitrates may cause hypotension.
- Drug interactions with cytochrome P450 inhibitors (e.g., ketoconazole, erythromycin, cimetidine) can be expected; during concomitant therapy a lower dose is suggested.

Statins

Frederic T. Billings IV

Uses

- Incidence in USA: Estimated 20 million
- Primary indications include:
  - Hyperlipidemia: HMG-CoA reductase inhibitors (statins) are powerful drugs for lowering LDL cholesterol concentrations, and certain statins—atorvastatin in high doses and rosuvastatin—increase concentrations of healthy HDL cholesterol.
  - Primary and secondary prevention of CV disease: CV benefits (reduction in myocardial infarction and stroke) in pts with hypercholesterolemia. Benefits also in normocholesterolemic pts with elevated markers of inflammation (e.g., CRP, Jupiter trial).
  - Unproven benefits: Conflicting data on effect of statins to reduce risk of sepsis, thrombotic disease, acute kidney injury following surgery or radiocontrast administration, ARDS, or mortality in ICU patient populations. Recent (2010–2015) multicenter clinical trials testing the impact of statins on these acute illnesses have largely been negative despite prior promising data.

Perioperative Risks

- Myopathy: Incidence among nonoperative chronic statin users is 2–11% for myalgias, 0.5% for myositis, <0.1% for rhabdomyolysis. Incidence increased in severe renal insufficiency (CrCl <30 mL/min). Reversible following statin discontinuation.
- Hepatic dysfunction: Incidence of persistent elevations in aminotransferases is 0.5–3%; it is 0.1% for a 10-fold increase in alanine aminotrasferase. Effect is reversible following statin discontinuation.
- The incidence of myopathy and transaminitis increases when cytochrome P-450 3A4 inhibitors—including cyclosporine, tacrolimus, azole antifungals, fenofibrates, protease inhibitors, and macrolide antibiotics—are used together with statins that are extensively metabolized by cytochrome P-450 3A4 (lovastatin, simvastatin, and to a lesser extent atorvastatin).
- Lipophilic statins may be associated with more adverse events than hydrophilic statins.
- Data do not suggest, however, that periop statin use increases risk of periop myopathy or hepatic dysfunction.

Overview/Pharmacology

- Statins inhibit the reduction of HMG-CoA to mevalonate, the rate-limiting step in cholesterol biosynthesis. Statins primarily inhibit hepatocyte cholesterol synthesis and increase LDL receptor transcription and hepatic LDL cholesterol uptake. Consequently statins reduce systemic concentrations of LDL cholesterol by 25–55%. Plasma HDL cholesterol levels may rise by 8–10% with atorvastatin and rosuvastatin.
- The reduction in intracellular isoprenoid synthesis, which reduces prenylation of small GTPases (e.g., Rac, Rho), may mediate the beneficial pleiotropic (non-lipid-lowering) effects of statins observed in preclinical studies and small human studies. These effects include stabilization of atherosclerotic plaque, reduction of inflammation, reversal of endothelial dysfunction (through upregulation of eNOS), decreased thrombogenicity, and reduced generation of reactive oxygen species (through inhibition of NADPH-oxidase assembly). These effects are observed within 6–18 h in rodents and cells.
- Statins are orally administered once daily, and peak plasma concentrations are achieved in 1–3 h.
- The hepatic cytochrome P-450 system metabolizes most statins to active and inactive metabolites, and statins are primarily excreted in bile.

Pharmacokinetics

Statin	Dose (mg)	Elimination Half-Life, hr	Protein Binding	Solubility	Cytochrome P-450 Isozyme	Active Metabolites	Renal Excretion, %
Atorva-	10–80	15–30	80–90	Lipophilic	3A4	Yes	2
Fluva–	20–80	0.5–2.3	>99	Lipophilic	2C9	No	<6
Lova–	20–80	2.9	>95	Lipophilic	3A4	Yes	10
Prava–	10–40	1.3–2.8	43–55	Hydrophilic		No	20
Rosuva–	5–40	19	88	Hydrophilic	2C9	No	10
Simva–	10–80	2–3	94–98	Lipophilic	3A4, 3A5	Yes	13

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEPAT	Transaminitis	Asymptomatic	None	LFTs
MS	Myositis	Myalgia, cramps, aches	Muscle tenderness	Creatinine kinase

Key References: Chan WW, Wong GT, Irwin MG: Perioperative statin therapy, *Expert Opin Pharmocother* 14(7):831–842, 2013; Lewicki M, Ng I, Schneider AG: HMG CoA reductase inhibitors (statins) for preventing acute kidney injury after surgical procedures requiring cardiac bypass. *Cochrane Database Syst Rev* (3):CD010480, 2015.

Perioperative Implications

- Pts with coronary disease or a coronary disease risk equivalent (DM, symptomatic carotid artery disease, peripheral arterial disease, abd aortic aneurysm, chronic kidney disease, or multiple risk factors that confer a 10-y risk of CHD greater than 20%) should receive chronic statin therapy. Therefore pts on statin therapy should be examined preop for coronary and peripheral vascular disease.
- Concern for statin accumulation and muscular and hepatic side effects among pts receiving major surgery led the ACC/AHA/NHLBI to recommend short-term periop discontinuation of statin administration. Periop observational studies, however, have not assoc statin use with an increased risk of myopathy or rhabdomyolysis, and preoperative cessation of statin therapy (withdrawal) was associated with CV harm in some studies of pts undergoing cardiac and major vascular surgery.
- Some randomized trials and large observational studies suggest beneficial pleiotropic effects of statins administered in the periop period. Trials of statin use in critically ill pts have demonstrated no effect on ARDS, pneumonia, or sepsis.
- In the DECREASE III trial, 497 vascular surgery pts were randomly assigned to either 80 mg of extended-release fluvastatin daily or placebo at least 30 d before the procedure and continued for at least 30 d after surgery. The primary endpoint of myocardial ischemia within 30 d of surgery occurred significantly less often in the fluvastatin group (10.8% vs. 19.0%; hazard ratio 0.55, 95% CI 0.34–0.88). The secondary endpoint of the composite of death from CV

causes and myocardial infarction also occurred significantly less often in the fluvastatin group (4.8% vs. 10.1%; hazard ratio 0.47, 95% CI 0.24–0.94). There was no evidence of an increase in skeletal muscle or hepatic injury in the fluvastatin group. (Note: Recent concern regarding the quality of the DECREASE trials has questioned these results.)

- Among percutaneous coronary intervention pts, statin therapy administered 12 h before catheterization reduced composite of myocardial ischemic events and death in several placebo controlled RCTs.
- Statin therapy is recommended as early as possible before surgery for pts undergoing elective major vascular surgery who have not been receiving a statin.
- Statin therapy should not be discontinued for fear of side effects in the periop period in statin-usings.
- Physician-scientists hope that pleiotropic effects of statin therapy will provide periop protection for heart, brain, and kidney. As yet, there are no data to support this indication for statin use.

Tacrolimus (FK-506)

Aisling Conran | Lee A. Fleisher

Uses

- Rescue of primary immunosuppressant Rx following liver, lung, heart, pancreas, and limb transplant.
- Approximate number of candidates: 3000 awaiting liver transplant and 9000 awaiting kidney transplant in USA; 15,000 living liver transplant and 50,000 kidney transplant recipients are chronically receiving immunosuppressants.
- Has been used to suppress the inflammation associated with ulcerative colitis.

Perioperative Risks

- Htn: CCBs may be effective in treating tacrolimus-associated Htn, but care is required. Interference with tacrolimus metabolism may necessitate a reduction in dose.
- Nephrotoxicity: Do not administer concurrently with cyclosporine; administer cautiously with other potentially nephrotoxic drugs (e.g., aminoglycoside antibiotics).
- Hypersensitivity may occur with IV formulation; pts should be monitored for 30 min after injection.
- May result in opioid-induced hyperalgesia.

Worry About

- Drug is metabolized by cytochrome P450 (3A) enzyme system. Other medications that inhibit or induce this enzyme may affect tacrolimus drug levels.

Overview/Pharmacology

- General effect: Macrolide antibiotic with potent immunosuppressive properties, often used for rescue therapy in liver transplant pts with rejection refractory to other immunosuppressants.
- Tacrolimus is metabolized by the liver; metabolites are primarily excreted in bile; elimination half-life of 8.5 h is prolonged with hepatic dysfunction.
- CCBs, cyclosporine, erythromycin, antifungal agents, and metoclopramide may increase blood levels of tacrolimus as a function of P450 inhibition.
- Anticonvulsants (carbamazepine, phenobarbital, phenytoin) and rifampin may decrease blood levels of tacrolimus secondary to induction of the cytochrome P450 system.
- Adverse effects requiring dose adjustments include nephrotoxicity, neurotoxicity, alterations in glucose metabolism, infection, and susceptibility to malignancy.

Drug Class/Mechanism of Action/Usual Dose

- Macrolide antibiotic, highly protein-bound (>75%), binds primarily to albumin and/or α_1-glycoprotein.
- Tacrolimus binds to calcineurin, blocking production of interleukin-2 and thereby inhibiting further T-lymphocyte proliferation and immunosuppression.
- Dosing: IV 0.05–0.1 mg/kg per d; PO 0.15–0.3 mg/kg per d in 2 divided doses.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL	Hypersensitivity, rash	Observe 30 min; have epinephrine 1:1000 available		
CV	Htn		BP/HR	
RESP	Pleural effusion, dyspnea			
GI	Diarrhea, N/V, constipation, abnormal liver function, anorexia, abdominal pain			LFTs
RENAL	Abn kidney function, oliguria			BUN, Cr
ENDO	Hyperkalemia, hypokalemia, hyperglycemia			K^+, glucose
HEME	Anemia, leukocytosis, thrombocytopenia			CBC
CNS	Headache, tremor, insomnia, paresthesias, mental status changes, circumoral numbness		Preop neurologic exam	

Key Reference: Siniscalchi A, Piraccini E, Miklosova Z, et al.: Opioid-induced hyperalgesia and rapid opioid detoxification after tacrolimus administration, *Anesth Analg* 106(2):645–646, 2008.

Perioperative Implications

Preoperative Concerns

- Continue all immunosuppressants through the periop period.
- Monitor levels: Therapeutic range is 5–30 ng/mL; maintenance level is 5–10 ng/mL.

Monitoring

- Consider frequent NIBP or arterial cath.

Induction/Maintenance

- Inducers of P450 system include phenobarbital, phenytoin, isoniazid; some volatile anesthetics may result in increased metabolism of tacrolimus.

Possible Drug Interactions

- CCBs, cyclosporine, erythromycin, antifungal agents, and metoclopramide may increase blood levels of tacrolimus as a function of P450 inhibition.
- Anticonvulsants (carbamazepine, phenobarbital, phenytoin), rifampin may decrease blood levels of tacrolimus secondary to induction of the cytochrome P450 system.
- Adverse effects requiring dose adjustments include nephrotoxicity, neurotoxicity, alterations in glucose metabolism, infection, and susceptibility to malignancy.

Anticipated Problems/Concerns

- Hypersensitivity may occur with IV formulation.

Tetracyclines

Jonathan G. Ma | Amir Elhassan | Alan David Kaye | D'andra J. Davis

Uses

- Administered PO (most common), IV (fewer side effects), IM (rare, painful), topically (eyes only).
- Original broad-spectrum antibiotic with activity against gram-positive and gram-negative bacteria; species of *Chlamydia, Rickettsia, and Mycoplasma* (in adults); some protozoa. One of few agents active against organisms without cell walls. Resistance is increasing worldwide.
- Secondary uses: Alternative drugs in the treatment of syphilis, treatment of respiratory infections caused by susceptible organisms, prophylaxis against infection in chronic bronchitis, treatment of leptospirosis, and in the treatment of acne.
- Selective uses:
  - Tetracycline for treatment of GI ulcers caused by *Helicobacter pylori*
  - Doxycycline for Lyme disease, prevention of malaria, and treatment of amebiasis
  - Minocycline for meningococcal carriers
  - Demeclocycline for management of pts with ADH-secreting tumors
- Usage in USA is about 20 million doses per y.

Perioperative Risks

- IV tetracycline frequently leads to thrombophlebitis, lessens efficacy of oral contraceptives.
- Decrease dose with age.
- Decrease dose in those with poor renal/hepatic function, because tetracycline accumulates in such pts and can lead to hepatic toxicity (instead, in pts with renal dysfunction, use doxycycline, which has an unchanged elimination half-life in such pts).
- Barbiturates may lower the half-life β; tetracycline will increase cone of digoxin or warfarin. Pts may exhibit GI distress, even *Clostridium difficile* colitis.

Worry About

- Tetracycline (especially first-generation) is absorbed poorly if given within 3 h of divalent or trivalent cations (Ca^{2+}, Al^{3+}, Mg^{2+}, Fe^{2+}, Bi^{3+}).
- Possibility of tetracycline-resistant bacterial enteritis as well as GI distress limits the oral doses of these antibiotics.
- Doxycycline should be administered only PO or IV.

Overview/Pharmacology

- Two generations: First (e.g., tetracycline) and second (e.g., doxycycline, minocycline).
- Classified as bacteriostatic (newest ones are possibly bactericidal).
- First-generation half-life β is 6–12 h; excreted in urine and feces.
- Second-generation drugs are more lipophilic, greater V_d, recirculation, half-life β 16–18 h; >90% of doxycycline is excreted in feces; safe for anephric pts.
- Adjust dose with age and for pts with impaired renal/hepatic function.
- After PO administration, drugs taken up in duodenum (especially first-generation drugs); peak level 2 h; IV peak level 1 h.

Drug Class/Mechanism of Action/Usual Dose

- Original broad-spectrum antibiotic.
- Effective against *Rickettsia, Mycoplasma, Chlamydia, Borrelia*, spirochetes, some fungi
- Local irritant (in sclerotherapy).
- Normal dose impairs bacterial protein synthesis; binds via a Mg^{2+} bridge to single active site of 30 S subunit of bacterial ribosome; prevents binding of aminoacyl tRNA to the mRNA-ribosome complex. Without this codon-anticodon interaction, formation of peptide chains cannot proceed.
- Inhibit collagenase (osteoarthritis), tumor-induced angiogenesis (chemotherapy)
- Usual dose: Doxycycline 100 mg PO twice daily.

Assessment Points

System	Effect	Assessment by Hx	Test
HEENT	Children: Brown teeth; risk greatest from second trimester to age 8 y		
CV	Frequently causes thrombophlebitis decrease Tumor-mediated angiogenesis		
HEPAT	Rare toxicity, especially with higher doses, IV route, or in pregnancy; usually reversible with drug cessation	Hepatitis	LFTs
GI	Irritation, distress, especially when given PO, higher doses may lead to superinfection (with *S. aureus or C. difficile*) Disturbances in the normal flora may lead to candidiasis (oral and vaginal)	Mild N/V, severe colitis	
HEME	May inhibit/suppress antibody production, leukotaxis, complement system		
GU	May aggravate uremia in susceptible pts; crosses placenta, excreted in breast milk		BUN
CNS	Penetrates CNS; may increase ICP during therapy, especially in infants Doxycycline and minocycline: Vestibular problems (dizziness and vertigo), especially in women; reversible	Vision change, headache Dizziness, nausea	
DERM	Phototoxic skin reaction, especially with first-generation drugs		
MS	Retards bone growth in preemies, decreases collagenase in joints		

Key References: Chopra I, Hawkey PM, Hinton M: Tetracyclines, molecular and clinical aspects, *J Antimicrob Chemother* 29(3):245–277, 1992; Stoelting RK: *Pharmacology and physiology in anesthetic practice*, Philadelphia, 2006, Lippincott-Raven; Trevor AJ, Katzung BG, Masters SB: *Katzung & Trevor's review of pharmacology*, New York, 2007, McGraw-Hill Medical.

Perioperative Implications

Preoperative Concerns

- May increase digoxin levels, higher prothrombin time if pt is on warfarin

Possible Drug Interactions

- Methoxyflurane, tetracycline may lead to renal failure
- Barbiturates may lower half-life of β.

Reversal

- May augment nondepolarizing NM blocker.

Novel Therapies—Potential Nonantibiotic Indications

- Minocycline found to be cytoprotective; may have protective role in cardiovascular pathology and activity against myocardial ischemia-reperfusion injury.
- Reduces tolerance to morphine; can reduce symptoms of allodynia and hyperalgesia.
  - Neuroprotective properties in neurogenerative diseases associated with glial activation thought critical in neuropathic pain.
  - Neuroprotective in cerebral ischemia, spinal cord injury, Parkinson disease, Huntington disease, and Alzheimer disease.
  - Minocycline shown to inhibit sevoflurane-induced apoptosis, inflammation, amyloid accumulation.
  - Minocycline may alleviate postop cognitive impairment.
- Tetracyclines have been used successfully for pleurodesis.

Anticipated Problems/Concerns

- Although resistance is rising, tetracyclines remain useful antibiotics, with nonantibiotic indications increasing.
- Contraindicated in pregnancy and childhood.

Thiazolidinediones

Jeffrey R. Kirsch | Dallas D. Regan

Uses

- Oral insulin sensitizing agents for the treatment of type 2 DM. Their use in recent years has declined due to concern for increased risk of new or worsening heart failure. Furthermore, questions have been raised about a possible association between TZD use and decreased bone mineral density and bladder cancer.

Perioperative Risks

- Hypoglycemia: Although these agents act primarily to sensitize peripheral tissues to insulin, TZDs carry a mild to moderate risk of hypoglycemia when combined with sulfonylureas or insulin.
- Hepatotoxicity: The first marketed TZD, troglitazone, was removed from the market in USA and UK due to potentially severe liver dysfunction. Currently available TZDs have not shown this same effect on liver function, but liver function tests are still recommended before initiation and as clinically indicated.
- CV risk: Associated with fluid retention and an increased risk of CHF. TZD administration has not been found to be an independent risk factor for myocardial infarction.

Worry About

- Precipitation of heart failure due to volume expansion and sodium retention.
- Hypoglycemia when TZDs are used in conjunction with insulin and sulfonylureas.
- Hyperglycemia, especially when TZDs are stopped in severe insulin resistance.

Overview/Pharmacology

- Orally administered and well absorbed; pioglitazone peaks in 2 h and rosiglitazone peaks in 1 h.
- Distribution: Drug and metabolites are extensively protein bound.
- Excretion and clearance: The two available drugs, pioglitazone and rosiglitazone, are metabolized by different cytochrome P450 isoenzymes, which may make them associated with drug–drug interactions. Primarily excreted in bile and eliminated in feces.
  - Pioglitazone metabolized by hydroxylation and oxidation.
  - Rosiglitazone metabolized by hydroxylation and *N*-demethylation.

Drug Class/Mechanism of Action/Usual Dose

- Peroxisome proliferator activated receptor agonists.
- Sensitizes peripheral tissue to the action of insulin and also preserves pancreatic β cells.
- The mechanism for efficacy is not fully understood. TZDs bind and antagonize one or more peroxisome proliferator-activated receptors (PPAR) subunits, regulating gene expression.
- PPARs control the genetic regulation of complex processes involved in adipogenesis, lipid metabolism, inflammation, and maintenance of metabolic homeostasis.
- PPAR activation in adipose tissue (primary site of action) results in changes to insulin signaling pathways, ultimately resulting in increased insulin sensitivity.
- Animal models have demonstrated that PPAR agonists improved insulin release as a result of the preservation of pancreatic β-cell. They do not, however, directly stimulate insulin secretion.
- Dose of pioglitazone is 15–45 mg/d (as once-daily preparation).
- Dose of rosiglitazone is 2–8 mg/d (as once-daily preparation).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GENERAL	Increased body weight (average of 3–5 kg)	Pre-drug body weight	Increased SQ fat and decreased visceral fat	Improved waist-hip ratio
CV	Increased fluid retention Vasodilatation Worsening heart failure, esp. in NYHA III & IV	Increased ankle swelling	Edema	
HEME	Increased anemia (dilutional)	Easily fatigued	Pallor	Decreased Hgb by up to 4 g/dL
MS	Increased risk of fractures	Spontaneous fractures; low impact fractures		X-ray
HEENT	Sinusitis, pharyngitis, URI	Coryza, headache, rhinorrhea		
GI	Hepatotoxicity (1:100,000)	Loss of appetite, abdominal pain	Jaundice, dark urine	LFTs
ENDO	Hypoglycemia (in combination with insulin and sulfonylureas)	Sweating, tremors, blurring of vision, palpitation	Tachycardia, altered consciousness	Glucose
OPHTH	Increased macular edema (rare)	Blurring of vision	Decreased visual acuity	Fundus exam
OB	Increased ovulation (increased chances of pregnancy in PCOS women)			

Key References: Della-Morte D, Palmirotta R, Rehni AK, et al.: Pharmacogenomics and pharmacogenetics of thiazolidinediones: role in diabetes and cardiovascular risk factors, *Pharmacogenomics* 15(16):2063–2082, 2014; Vann MA: Management of diabetes medications for patients undergoing ambulatory surgery, *Anesthesiol Clin* 32(2):329–339, 2014.

Perioperative Implications

Preoperative Concerns

- Recommend holding morning dose on the day of surgery.
- Due to the dynamic nature of diabetes, carefully question the pt about their individual signs and symptoms of hypoglycemia.
- Close monitoring of glucose levels due to the risk of hypoglycemia or hyperglycemia.
- Measurement of liver function tests only if clinically indicated.
- Due to the increased risk of fluid retention and heart failure (and disputably MI) associated with TZDs, careful attention should be directed toward obtaining a thorough CV history, physical, and review of symptoms.

Induction/Maintenance

- Intraop administration of insulin may be necessary. Glucose may be necessary to treat hypoglycemia.
- Closely monitor glucose levels because of the risk of hypoglycemia and hyperglycemia.

Postoperative Period

- Closely monitor glucose levels because of the risk of hypoglycemia and hyperglycemia.
- Resume drug therapy if no problem with fluid retention or CV event once the pt is able to eat and drink normally.

Anticipated Problems/Concerns

- Drug-drug interactions have been reported with fluoroquinolones (variable effects on blood glucose), beta-blockers (mask symptoms of hypoglycemia), ACE inhibitors (increased risk of hypoglycemia), and insulin (increased risk of hypoglycemia, fluid retention, and heart failure).
- If in doubt, stop or delay the resumption of TZDs.

Latest Developments

- Rosiglitazone has been pulled from the market in Europe and New Zealand over CV and bone fracture concerns.
- Further investigation has revealed that rosiglitazone primarily affects PPAR-gamma receptors, while pioglitazone exerts effects on both the gamma and alpha receptors. Pharmacogenomic studies have revealed that human genetic variability influences the effectiveness of treatment and perhaps more importantly, the side effect profile of TZDs.

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Thyroid Supplements

John M. Murkin

Uses

- More than 3 million chronic users in USA.
- T_4 prescribed for pts with chronic hypothyroidism.
- T_3 used in myxedema coma.
- T_3 successfully used as rescue therapy for cardiogenic shock after CPB.
- T_3 favorably administered to brain-dead donors before organ harvesting for heart or heart-lung transplantation. (Prophylactic use of T_3 has shown no benefit in recent randomized trials.)
- T_4 is generally administered PO; T_4 and T_3 can be administered IV.

Perioperative Risks

- Drugs (amiodarone, lithium, herbal supplements, catecholamines, radiopaque contrast media) and also cirrhosis, renal failure, sepsis, and operation (CPB) can induce euthyroid sick syndrome (reduced peripheral conversion of T_4 to T_3); may also precipitate myxedema coma.
- Amiodarone, a potent class III antiarrhythmic drug, is an iodine-rich compound with a structural resemblance to T_3 and T_4 and causes substantial iodine overload; with continued administration, may produce either thyrotoxicosis or hypothyroidism.

Worry About

- T_4 or T_3 can aggravate symptoms of myocardial ischemia.

Overview/Pharmacology

- Hypothyroidism (overt) estimated to affect 0.5–3.8% of adults and increases with age (over 15% of women at ≥age 60).
- After thyroidectomy, <30% of pts euthyroid at 10 y due to inadequacy or discontinuation of Rx.
- Reversal of clinical Sx of chronic hypothyroidism, including myocardial effusions, requires 2–4 mo Rx.
- Half-life of T_4 is 7 d; T_3 is 1.5 d.
- T_4 is a relatively inactive prohormone that undergoes monodeiodination in liver and kidney to biologically active T_3.

Drug Class/Mechanism of Action/ Usual Dose

- Thyroid hormone replacement Rx.
- T_3 binding to specific membrane receptor proteins augments membrane transport activity, mitochondrial oxidative phosphorylation, and protein synthesis.
- Extranuclear effects of T_3 occur within min, increasing myocardial mitochondrial and transmembrane transport activity.
- Nuclear effects of T_3 occur within 0.5–1 h, involving transcription and translation of myocardial enzymes and contractile proteins.
- Direct effect of T_3 decreases arterial smooth muscle tone.
- Usual dosage of T_4 is 0.15 mg/d PO.
- Acute Rx: T_4, 0.3–0.5 mg by slow IV infusion followed by 0.1–0.15 mg/d, or T_3, 0.005–0.01 mg IV.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Chronotropy, inotropy, reduced SVR Arrhythmogenesis	Less fatigue Palpitations	HR, reflexes	FT_4E, TSH, ECG
RESP	Restoration of hypoxic, hypercapnic ventilatory drive			
GI	Increased protein synthesis; enhanced hepatic, renal clearance/excretion functions		Normal skin turgor	
ENDO	Thermogenesis	Reversal of cold intolerance	Skin warm to touch	

Key Reference: Kohl BA, Schwartz S: Surgery in the patient with endocrine dysfunction, *Anesthesiol Clin* 27(4):687–703, 2009.

Perioperative Implications/Possible Drug Interactions

Preoperative Concerns

- Thyroid hormones increase breakdown of vitamin K–dependent clotting factors, which can alter coagulation status.
- Chronic amiodarone therapy may produce hyper- or hypothyroidism and has been specifically associated with thyrotoxicosis.
- Preop low free T_3 syndrome (FT_3 <2.23 pmol/L) has been associated with an increased risk of low cardiac output and death in coronary revascularization pts.

Induction/Maintenance

- T_4 administration is advocated in the management of organ donors; oral T_4 achieves approximately 91–93% of the bioavailability of IV thyroxine and also facilitates hemodynamic stability comparable with IV administration.
- Exaggerated Htn and tachycardia can occur with agents such as ketamine and exogenous catecholamines including ephedrine and epinephrine in pts on both acute and chronic thyroid hormone replacement.

Adjuvants/Regional Anesthesia/Reversal

- Anticholinergics with minimal CV effects (e.g., glycopyrrolate) preferred over atropine.
- Caution in the presence of spinal anesthesia; T_3 administration may produce aggravated hypotension.

Postoperative Period

- Cirrhosis, sepsis, renal failure, surgery may all decrease peripheral conversion of T_4 to T_3 (euthyroid sick syndrome) and precipitate hypothyroidism.

Anticipated Problems/Concerns

- In critically ill pts, T_3 replacement can produce detrimental increases in oxygen requirements (especially myocardial) and protein catabolism without improving mortality rates.

Tissue Plasminogen Activator

Alan David Kaye | Burton D. Beakley | Ken F. Mancuso

Uses

- Clinical indications for thrombolysis in treatment of pulmonary embolism, acute ischemic stroke, acute MI, and occluded central venous access devices.
  - MI: Administration as soon as possible from symptom onset
  - Stroke: Administration within 3 h from onset of symptoms
- Rapid clot lysis by t-PA offers advantages in comparison with streptokinase.
- May be used in combination with other anticoagulants such as heparin and aspirin. Also may be combined with beta-blockers, morphine, nitroglycerin, and plt IIb/IIIa blockers.

Perioperative Risks

- Increased risk of bleeding during surgery; if severe, possible need for blood transfusion, fresh frozen plasma, cryoprecipitate, and plt infusion therapy.
- Strict blood pressure monitoring with intraop Htn posing increased risk of intracranial hemorrhage (0.8% with acute MI therapy and 6% with acute ischemic stroke therapy).
- Incomplete restoration of coronary blood flow and persisting thrombogenicity may lead to cardiac instability and risk for periop infarction.

Worry About

- Severe hemorrhagic complications and intracranial hemorrhage.
- Invasive procedures: Damage to blood vessels during vascular access procedures can cause severe bleeding, especially at noncompressible sites (e.g., subclavian vein).
- Risk for hematoma formation causing damage via mass effect to surrounding tissue/vessels (e.g., ulnar nerve during arterial cannulation).
- Contraindication for spinal/regional anesthesia.
- Bleeding at venipuncture sites.

Overview/Pharmacology

- Thrombolytic agent: Natural t-PA is produced by vascular endothelial cells and is naturally released from the endothelium in response to venous occlusion, physical activity, stress, or vasoactive medications. Responsible for most of the body's effort to prevent excessive thrombosis.
- Accelerates the conversion of plasminogen (bound to fibrin) to plasmin, resulting in fibrinolysis as site of clot.
- Time-dependent, because older thrombi develop extensive fibrin polymerization, making them more resistant to thrombolysis.
- t-PA (alteplase) is commercially produced using cDNA for natural t-PA, which is then is transfected into a mammalian cell line.
- Initial thrombolytic response is seen within 30 min when given IV. Half-life is about 5 min; elimination half-time is about 30–50 min. Some 80% is cleared from plasma within 10 min of stopping a standard infusion, and clearance is via the liver.

- Plasminogen activator inhibitors, also released by endothelial cells, oppose the action of t-PA and may be a factor in preventing uncontrolled fibrinolysis.

Drug Class/Mechanism of Action/ Usual Dose

- Thrombolytic agent. Binds to fibrin threads of thrombus and converts enmeshed plasminogen to plasmin, which initiates localized fibrinolysis. For this reason, unlike streptokinase, t-PA can be considered fibrin-specific; t-PA lacks effect on circulating plasminogen, thereby limiting systemic effects.
- For STEMI:
  - Accelerated infusion (<67kg) dose: 15mg IV once, then 0.75 mg/kg (max 50 mg) over 30 min, then 0.5 mg/kg (max 35 mg) over 60 min.
  - Accelerated infusion (>67 kg) dose: 15 mg IV once, then 50 mg over 30 min, then 35 mg over 60 min; max 100 mg total.
  - 3-h infusion (<65 kg) dose: 1.25 mg/kg IV over 3 h; 60% of dose over 1 h with 6-10% of dose as IV bolus, then 20% over second h, then 20% over third h.
  - 3-h infusion (>65 kg) dose: 100 mg IV over 3 h; 60 mg over 1 h with 6-10% of dose as IV bolus, then 20 mg over second h, then 20 mg over third h; max 100 mg total.
- Amount of salvaged myocardium is directly related to the time until the occluded artery is reopened. GUSTO I investigators showed 84% patency within 6 h of front-loaded t-PA.
- In acute ischemic stroke, 0.9 mg/kg IV with 10% given as loading bolus over 1 min and remainder infused over 60 min. Dose not to exceed 90 mg.
- In pulm embolism, 100 mg IV over 2 h. Start heparin at end of t-PA infusion.
- More rapid lysis, less systemic fibrinolysis, not antigenic and rarely associated with allergic reaction when compared with streptokinases, but t-PA is more expensive.

Assessment Points

System	Effect	Assessment by Hx	PE	Treatment
CV	Bleeding from vascular puncture sites	Hematoma Check for retroperitoneal bleed in presence of femoral puncture	Hgb	Manual compression Rarely is blood transfusion necessary
	Severe bleeding during surgery	Check if heparin or plt IIb/IIIa blockers are being given	Hgb Plts APTT	Transfusion of blood, FFP, cryoprecipitate Factor VIII and Plts may be needed; consider using TEG to guide therapy
	Effects of ancillary treatment	Check for ongoing beta-blocker, nitroglycerin, or morphine treatment		Discontinue if necessary; however, beta blockade has considerable benefit with little risk in most pts
	Reperfusion arrhythmias	Can occur on restoration of blood flow to ischemic myocardium	CV stability	Antiarrhythmics
CNS	Intracranial hemorrhage	Signs of stroke or raised ICP	Neurologic assessment Urgent CT, MRI	Supportive BP control (risk is increased in presence of heparin)

Key References: GUSTO Investigators: An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction, *N Engl J Med* 329(10):673–682, 1993; Schellinger PD, Fiebach JB, Mohr A, et al.: Thrombolytic therapy for ischemic stroke—a review. Part I—Intravenous thrombolysis, *Crit Care Med* 29(9):1812–1818, 2001.

Perioperative Implications

- High bleeding risk with invasive line placement
- Risk of hypotension on anesthetic induction with adjuvant nitroglycerin infusion
- Severe Htn may predispose to or exacerbate hemorrhagic stroke
- Residual thrombus is highly thrombogenic, posing risk of rethrombosis
- Contraindication to regional/spinal anesthesia
- Increased need for transfusions
- Close monitoring of neurologic function preop and postop

Tranexamic Acid

Alan David Kaye | Adam M. Kaye | Shilpadevi S. Patil | Debbie A. Chandler | Elyse M. Cornett

Uses

- To prevent bleeding due to fibrinolysis after surgery or trauma (cardiac surgery with and without cardiopulmonary bypass; liver transplantation; orthopedic surgery including spine; GU surgery; peripartum hemorrhage). Bleeding can be diagnosed clinically or via lab tests (prolonged thrombin time, reduced fibrinogen levels, increased D-dimer levels, classic teardrop shape on thromboelastography).
- Antifibrinolytic choice in cardiac surgery has shifted from aprotinin to TXA and epsilon-aminocaproic acid (ε-ACA) owing to the concern that aprotinin may be associated with an increased risk of cardiovascular or cerebrovascular events, renal dysfunction, or renal failure.
- TXA in 6% hydroxyethyl starch 130/0.4 prime solution decreases blood loss and chest tube drainage in CABG with no renal or postop complications.
- The reduction of blood loss in orthopedic surgery is of great importance, especially in hip or knee arthroplasty and spinal surgery. TXA administered at 10–15 mg/kg IV reduces blood loss, reduces relative risk of transfusion, and poses no increased risk of thromboembolism.
- Effective in reducing periop blood loss and transfusion requirements in neonates and children undergoing craniosynostosis reconstruction surgery and repair of congenital heart defects.
- TXA application in trauma is supported by firm clinical evidence. IV loading of 1 g TXA within 8 h of trauma then followed by IV infusion of 1 g TXA over 8 h significantly reduced all-cause mortality and death due to bleeding.
- PPH is a major cause of maternal mortality. TXA is used as a complement to uterotonics and appears to be a promising drug for the prevention and treatment of PPH after both vaginal and cesarean delivery.
- Used to reduce placental bleeding and conization of the cervix.
- For short-term use (2–8 d) in pts with hemophilia or von Willebrand disease to reduce or prevent hemorrhage and to reduce the need for replacement therapy during and following tooth extraction.
- To treat primary menorrhagia, gastric and intestinal hemorrhage, urinary tract bleeding, recurrent epistaxis, and hereditary angioneurotic edema. The drug also inhibits induced hyperfibrinolysis during thrombolytic treatment with plasminogen activators.
- Used in pts with hemophilia or those receiving anticoagulation who are about to undergo oral surgery.

Perioperative Risks

- Side effects: N/V, diarrhea, and abdominal pain are the most common adverse effects (in approximately 30% of pts with oral use).
- Giddiness has been reported.
- Hypotension (if the drug is injected too rapidly).

Worry About

- Potential for thrombotic complications secondary to the inhibition of fibrinolysis

Overview/Drug Class

- A synthetic lysine analogue. Prevents plasmin formation and therefore fibrinolysis by occupying plasminogen's lysine-binding site for fibrin.
- Has a structure similar to that of lysine and reversibly binds to lysine-binding sites for fibrin on plasminogen, thereby blocking the binding of plasminogen to fibrin. Plasminogen activators are located on the fibrin clot. Without localized binding of plasminogen to fibrin, it cannot be converted to plasmin.
- Because fibrinolysis requires plasminogen (and plasmin) binding to fibrin, fibrinolysis is inhibited.
- A competitive inhibitor of plasminogen activation and, at much higher concentrations, a noncompetitive inhibitor of plasmin. Suppresses fibrinolysis by inhibiting activation of plasminogen.
- Other antifibrinolytic medications incl ε-ACA (lysine analogue) and aprotinin (serine protease inhibitor).
- Reductions in mortality rates with TXA doses of 4.5–6 g daily for 5–7 d (in most studies) produced statistical significance between TXA and placebo.

- TXA was associated with reductions in mortality of 5–54% in pts with upper GI bleeding compared with placebo. Meta-analysis indicated a reduction of 40%.
- Administered either PO at 25 mg/kg every 6–8 h or IV at 10 mg/kg every 6–8 h beginning on the d prior to surgery.
- In adults, the minimum concentration of TXA necessary to completely prevent fibrinolysis is 17.5 ug/mL.
- In children aged 2 d-4 y, body weight is less accurate at predicting the distribution and elimination of TXA. Dosing is recommended by age rather than body weight. Other factors that do not affect the distribution and elimination of TXA in children are body surface area, pump prime volume, ultrafiltrate volume, and body temperature.
- Neonatal plasma requires a significantly lower concentration of TXA than adult plasma.
- In neonates the minimum concentration of TXA to completely prevent fibrinolysis is 6.54 µg/mL.
- Absorption after oral use is 30–50%; bioavailability is not affected by food.
- An antifibrinolytic concentration of drug remains in serum up to 7–8 h.
- The protein binding to plasminogen is approximately 3% at therapeutic plasma levels; it does not bind to serum albumin.
- The half-time of elimination when administered orally is 120 min.
- Urinary excretion is the main route of elimination via glomerular filtration.
- Overall renal clearance is equal to overall plasma clearance, and >90% of the dose is excreted unchanged in 24 h.
- Pts with renal insufficiency should have their doses reduced according to creatinine clearance. Only a small fraction of TXA is metabolized.
- TXA is 6–10 times more potent in terms of binding to plasminogen/plasmin than ε-ACA.
- Concurrent administration of heparin does not influence the activity of TXA.
- Pharmacokinetic properties: Maximum plasma concentrations of TXA can be attained within 3 h after an oral dose. Elimination after IV administration is triexponential, and over 95% of each dose is eliminated unchanged in the urine.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Retinal degeneration is associated with prolonged use; incidence 25–100% and dose-dependent (animal studies)	Visual changes	Ophthalmologic exam in pts receiving TXA every 4–5 d	Visual acuity Visual field Color vision Eyeground
CV	Hypotension (with rapid infusion)	Mental status changes, nausea	BP monitoring, HR, ECG	
RENAL	Reduce dose in pts with renal insufficiency			BUN/Cr, CrCl
GI	N/V, diarrhea, abdominal discomfort			
OB	Category B No well-controlled studies in pregnant females	Crosses placenta and appears in cord blood at concentration equal to that in maternal blood		
IMMUNE	Male mice receiving TXA up to 5 g/kg per d have been found to develop leukemia			

Key References: Fergusson DA, Hérbert PC, Mazer CD, et al.: A comparison of aprotinin and lysine analogues in high-risk cardiac surgery, *N Engl J Med* 358(22):2319–2331, 2015; Kagoma YK, Crowther MA, Douketis J, et al.: Use of antifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: a systematic review of randomized trials, *Thromb Res* 123(5):687–696, 2009.

Perioperative Implications

Airway
- No interactions known

Preinduction/Induction
- If given IV, inject slowly to avoid hypotension.

Maintenance
- No interactions known

Emergence
- No interactions known

Adjuvant/Regional Anesthesia/Reversal
- No interactions known

Contraindications
- Acquired defective color vision: Prohibits measuring one endpoint of toxicity.
- Subarachnoid hemorrhage: Cerebral edema and cerebral infarction may be caused by TXA in pts with subarachnoid hemorrhage.

Active Thromboembolic Disease
- Caution in the setting of DIC, in which inhibition of fibrinolysis may aggravate the hypercoagulable state.
- Reduced dose in renal insufficiency.

Anticipated Problems/Concerns

- Potential for increased thrombotic events.
- Timing of administration appears to be critical for optimal effect of hemostasis without increasing risk of thromboembolism.
- Single-dose administration of TXA is not effective in treating maximum reduction of blood loss.

Trimethaphan

Stephen T. Robinson

Uses

- Production of controlled hypotension during surgery to reduce bleeding into the surgical field
- Rapid reduction of BP in the treatment of hypertensive emergencies
  - Treatment of acute dissecting aortic aneurysm, particularly when preexisting conditions make the use of beta=blockers a relative contraindication
  - Emergency treatment of pulm edema in pts with pulm Htn associated with systemic Htn
- May serve as an alternative to sodium nitroprusside for pts who are resistant to this drug or can be mixed with nitroprusside to decrease risk of cyanide toxicity from nitroprusside

Perioperative Risks

- High doses may cause profound hypotension and, rarely, respiratory arrest.
- QRS prolongation has been seen during treatment.
- Tachycardia, angina, or syncope may occur without warning.
- Because of trimethaphan's ability to cross the placenta, its ganglionic blocking effects may decrease GI motility in the fetus, resulting in meconium ileus or neonatal paralytic ileus.
- CNS examination is limited by production of mydriasis.

Worry About

- Contraindicated in pts with shock, anemia, hypovolemia, uncorrected respiratory insufficiency, or neonates at risk for paralytic or meconium ileus.
- Orthostatic hypotension; may cause severe hypotension.
- Difficult to obtain since it is no longer manufactured in USA.

Overview/Pharmacology

- Rapid-acting ganglionic acetylcholine blocker, onset within 1–3 min.
- Peak response within 5–10 min.
- Duration of action: 10–15 min for single dose.
- Affects both parasympathetic and sympathetic pathways.
- Renally excreted, mostly unchanged.
- Most side effects are due to parasympathetic blockade and respond to dose reduction or discontinuation.
- Cardiac output may increase in pts with CHF or decrease in pts with normal heart function.
- Tachyphylaxis may occur during continuous IV infusion.

Drug Class/Mechanism of Action/ Usual Dose

- A short-acting ganglionic blocking agent.
- Prevents stimulation of postsynaptic receptors by competing with acetylcholine for these receptor sites.

- Hypotensive effect is primarily through sympathetic blockade by lowering SVR.
- Hypotensive effect is also mediated through direct vasodilation and histamine release (especially at higher rates of administration).
- Usual adult dosage:
  - For controlled hypotension during surgery: Initial: IV infusion, 3–4 mg/min, adjusted according to response; maintenance: IV infusion, 0.3–6 mg/min.
  - For hypertensive emergency: Initial: IV infusion, 0.5–1 mg per min, adjusted according to response; maintenance: IV infusion, 1–5 mg/min.
- Pts on concomitant antihypertensive medications require lower doses.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT	Mydriasis with cycloplegia	Visual changes	
CV	Vasodilation, tachycardia, hypotension, lowered SVR	Angina, syncope	Orthostatic hypotension
RESP	Rare respiratory arrest (uncertain etiology)		
GI	Decreased secretions, lower tone/motility	Dry mouth Paralytic ileus, constipation, N/V, diarrhea, reflux	
GU	Bladder atony Lower potency	Oliguria or anuria, incomplete emptying Erectile and ejaculation dysfunction	UO
CNS	Less increase in ICP compared with other vasodilators secondary to preserved cerebral autoregulation		
OB	Crosses placenta, may lower fetal GI motility, causing meconium or paralytic ileus		

Key References: Taylor P: Agents acting at the neuromuscular junction and autonomic ganglia. In Hardman JG, Limbird LE editors: *Goodman and Gillman's the pharmacological basis of therapeutics*, 10th ed. New York, 2001, McGraw-Hill, pp 210–211; Trivedi HK, Patel D, Weir MR: Hypertensive urgencies and emergencies. In Singh AK, Agarwal R, editors: *Core concepts in hypertension in kidney disease*. New York, 2016, Springer, pp 203-218.

Perioperative Implications

Preoperative Concerns

- Assess Hx of CAD; check baseline ECG.
- Assess volume status.
- Consider arterial line if trimethaphan infusion is anticipated.

Induction/Maintenance

- May prolong block from succinylcholine or nondepolarizing neuromuscular blockers.
- For controlled hypotension during surgery, it is recommended that infusion be stopped prior to wound closure.
- Monitor ECG for signs of ischemia due to decreased cardiac perfusion from hypotensive state.

Postoperative Period

- Mydriasis from drug may interfere with neurologic checks of postop neurosurgery pts.
- Risk for paralytic ileus is increased when drug infusion is continued for longer than 48 h.
- Pts continued on trimethaphan infusions postop should be monitored in the ICU
- Oral antihypertensive agents should be instituted and thimethaphan discontinued as soon as pt can take oral medication and BP has stabilized.

Anticipated Problems/Concerns

- Not ideal for prolonged infusions because tachyphylaxis can develop within first 48 h of therapy, although this may be attenuated by concomitant use of a diuretic.

Acknowledgment

The author would like to acknowledge Dr. Tor Sandven's contribution to this chapter in the previous edition.

Valproate

Diana Ayubcha | Taras Grosh

Uses

- Most widely prescribed antiepileptic drug worldwide.
- Used in treatment of epilepsy, acute mania, bipolar disease, impulse-control disorders, migraine headaches, and neuropathic pain.

Perioperative Risks

- Hemorrhage
- Platelet dysfunction
- Coagulopathy
- Hyperammonemic encephalopathy
- Seizures with subtherapeutic plasma concentration

Worry About

- Decreased factor VII levels, plt count and function, factor VIII, protein C, fibrinogen, factor XIII, increased lipoprotein (a) levels, acquired von Willenbrand disease.
- Serum valproate levels of >140 µg/mL may be related to low plt levels.
- Children with a trough level of >450 µmol/L or a daily dose of >40 mg/kg are more likely to develop thrombocytopenia.
- Nausea, gastric irritation, diarrhea, hyperammonemia, thrombocytopenia.
- Highly protein-bound (88–92%); may displace other protein-bound drugs and increase their plasma concentration (e.g., warfarin).

Overview/Pharmacology

- Inhibits CYP2C9, glucuronyl transferase, and epoxide hydrolase.
- Undergoes hepatic metabolism (glucuronide conjugation and oxidation) and renal excretion.
- 88–92% protein-bound and can be displaced by competing drugs, thereby increasing the plasma concentration of pharmacologically active drug.
- IV and PO doses are equivalent.
- Inhibits drug-metabolizing enzymes rather than inducing them, like other AEDs.
- Inhibits metabolism of lamotrigine and phenobarbital.
- Plasma concentration decreases with carbapenems.
- May increase the plasma concentrations of a variety of drugs, including zidovudine, lorazepam, nimodipine, paroxetine, amitriptyline, nortriptyline, nitrosoureas, and etoposide.

Drug Class/Mechanism of Action/ Usual Dose

- Antiepileptic
- Delays reactivation of Na+ channels during high-frequency neuronal firing, producing an inhibitory effect on creation of action potentials until neuronal discharge is blocked; works at both Na+ and Ca+ channels.
- Increases synthesis and release of GABA reduces GHB, and inhibits NMDA
- Usual dose: 500–3000 mg/d in 2–4 divided doses.
- Therapeutic trough 50–100 µg/mL.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mydriasis		Eye exam	
GI	Nausea Vomiting Dyspepsia			Endoscopy
ENDO	Pancreatitis	LUQ abdominal pain radiating to the back	Abdominal pain with palpation	Glucose, AST, ALT, CT, MRI, ERCP, endoscopic (US)
HEME	Agranulocytosis Thrombocytopenia Aplastic anemia	Epistaxis Easy bruising	Hematoma Petechiae	Coagulation factors, fibrinogen, plt count, bleeding time, PT, PTT, vWF level, TEG
HEPAT	Hepatocellular toxicity, Alpers-Huttenlocher syndrome (especially in pts <2 y of age)	Nausea Anorexia Bleeding	Hepatomegaly Biopsy exam for microvesicular steatosis, severe hepatocellular necrosis Fever, rash, lymphadenopathy, peripheral eosinophilia, coagulopathy	LFT, liver biopsy, PT/INR
DERM	Stevens-Johnson syndrome Alopecia Rash			
RENAL	Hyperammonemic encephalopathy	Acute onset of impaired consciousness, focal neurologic symptoms, increasing seizure frequency	Encephalopathy	Urea levels Ammonia levels
CNS	Tremor, somnolence, potentiates depressive effects of ETOH			Blood alcohol level
OTHER	Teratogenicity weight gain, growth plate ossification Peripheral edema			Albumin level

Key References: Abdallah C: Considerations in perioperative assessment of valproic acid coagulopathy, *J Anaesthesiol Clin Pharmacol* 30(1):7–9, 2014; Perks A, Cheema S, Mohanraj R: Anaesthesia and epilepsy, *Br J Anaesth* 108(4):562–571, 2012.

Perioperative Implications

Preoperative Concerns

- History of concomitant bleeding diathesis.
- Obtain laboratory coagulation tests (coagulation factors, fibrin formation, fibrinogen, platelet count, bleeding time, PT, PTT, vWF level, TEG, LFT) when considerable blood loss is anticipated.
- Bleeding risk reversed with dose reduction or cessation.
- If anticipating blood loss, prepare platelets, blood products, and DDAVP.
- Performance of neuraxial anesthesia must be made on an individual basis.
- Continue periop and resume immediately postop for risk of seizure.
- Assess neuropsychiatric status.
- Review for other AEDs or other drug interactions with valproate.
- Increased sedation in elderly and with EtOH and/or benzodiazepine use.

Induction/Maintenance

- Anticonvulsants may stimulate hepatic microsomal enzymes, thus increasing the rate of biotransformation of volatile halogenated agents and posing increased risk of organ toxicity.
- Consider EEG.
- Mildly exaggerated effects of thiopental, propofol, benzodiazepines.

Adjuvants/Regional Anesthesia/Reversal

- Risks of neuraxial anesthesia must be reviewed on an individual basis in terms of bleeding history.
- Possible delayed emergence with GA.

Anticipated Problems/Concerns

- Screen for coagulopathy in pts on long-term valproate or multiple AEDs.
- With neuraxial anesthesia, risk of bleeding may be increased.
- May displace protein-bound drugs (warfarin, methotrexate, sulfonylurea, thiopental), thus augmenting drug's effect.

Vitamin B_{12} (Cyanocobalamin)

John K. Stene

Indications

- Incidence of deficiency in USA varies with age: 5% of those <55 y, 10% of those 55–64 y, 10–15% of those 65–74 y, and 24% of those 74–80 y old. Some 75% of those >64 y with vitamin B_{12} deficiency do not have anemia or even RBC abnormality. CDC states that 1 in 31 individuals 51 y of age or older are deficient in B_{12}.
- Prescribed for pernicious anemia and demyelinating CNS disease.
- Lack of gastric secretion of intrinsic factor leads to malabsorption of vitamin B_{12}; therefore IM route preferred. Recent studies have documented that high-dose oral replacement is effective. Strict vegetarian diet–induced deficiency state responds to oral supplementation.
- Until a person reaches midlife, he or she probably gets all the B_{12} needed from food (unless vegetarian). Autoimmune achlorhydric gastritis (pernicious anemia) decreases absorption because of loss of intrinsic factor. Pts are also almost certainly low on B_{12} if they have been taking a proton pump inhibitor for a long time, which seriously diminishes B_{12} absorption. B_{12} absorption also generally decreases with older age.
- Also associated with *Helicobacter pylori* infection, chronic alcohol ingestion, long-term metformin administration, and pancreatic exocrine deficiency conditions.

Worry About

- Permanent neurologic injury, classic combined system disease with paresthesias, balance problems with loss of position and vibratory sense, and lack of myelination in long tracts; preventable with recognition and cobalamin replacement.
- Interactions and neurologic injury with folate, methionine synthetase inhibitors, and nitrous oxide, which can produce rapid neurologic deterioration.
- Hyperhomocysteinemia, which causes thrombophilia and vascular disease, associated with adequate folate and B_{12} deficiency.

Overview/Pharmacology

- Vitamin B_{12} released from dietary proteins by acid and peptic action binds to intrinsic factor (gastric glycoprotein from parietal cells) in the GI tract, is absorbed from the ileum, bound to transcobalamin II in plasma for transport to tissues. Approximately 3 μg of cobalamin secreted into bile daily.
- Excess vitamin B_{12} administration increases urinary excretion.
- Vitamin B_{12} is enzymatically converted to two active forms: deoxyadenosylcobalamin and methyl-cobalamin.

- Deoxyadenosylcobalamin is a cofactor for mitochondrial mutase enzyme, which catalyzes L-methylmalonyl CoA to succinyl CoA.
- Methylcobalamin is a cofactor in methionine synthetase reaction (a methyl group is transferred from 5-methyltetrahydrofolate to homocysteine to form methionine and tetrahydrofolate); pivotal in normal synthesis of purines, pyrimidines, and a number of methylation reactions through formation of *N*-adenosylmethionine.

Drug Class/Mechanism of Action/ Usual Dose

- Water-soluble B-vitamin complex.
- Administered via the IM or deep SQ route in doses of 1–1000 μg.
- Oral dose of 1000–2000 μg is as effective as IM dosing in pernicious anemia.
- Needs glycoprotein (intrinsic factor 60,000 MW) produced by gastric parietal cells for its absorption; 0.5–4% absorbed by passive diffusion without intrinsic factor.
- RDA: 2.4 μg/d for adults.
- Vitamin B_{12} is a quiet, conscientious type: doesn't get much hype, yet works overtime to keep your brain, immune system, and ticker in good shape; may protect against Alzheimer disease, depression, stroke, and vision loss.
- Therapeutic 1000 μg IM every mo or 1000 μg orally per d.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GI	Achlorhydric or gastrectomy pts at risk; associated with atrophic glossitis	Burning and tingling of mouth	Small, slick, glistening tongue	Serum B_{12} decreased, homocysteine and methylmalonic acid increased
HEME	Megaloblastic anemia	Apathy, lassitude, fatigue	Pale skin and mucous membranes, especially nailbeds, palmar surfaces	Peripheral blood smear: Macrocytic hyperchromic RBCs Bone marrow: Megaloblasts, megakaryocytes Plt count
CNS	Degeneration of dorsal, lateral columns of spinal cord	Numbness, tingling in extremities, difficulty walking	Loss of vibration, vibration, position sense; ataxia, Romberg sign, muscle flaccidity	Serum B_{12} <200 pg/mL, serum methylmalonic acid >400 nmol/L, and serum homocysteine >21 μmol/L suggests B_{12} deficiency
PNS	Neuropathy	Paresthesias, dysesthesias of lower extremities		

Key References: Hillman RS: Hematopoietic agents: growth factors, minerals, and vitamins. In Hardman JG, Limbird LE, editors: *Goodman & Gilman's the pharmacological basis of therapeutics*, ed 9, New York, 1996, McGraw-Hill, pp 1311–1340; Stabler SP: Vitamin B_{12} deficiency, *N Engl J Med* 368(2):149–160, 2013.

Perioperative Implications/Possible Drug Interactions

- Folate administration reverses megaloblastic anemia but does not prevent (may precipitate) spinal cord degeneration.
- N_2O oxidizes vitamin B_{12}, reduces the activity of methionine synthetase.
- Effect of N_2O can be reversed by large doses of folic acid.

Anticipated Problems/Concerns

- Scavenging of waste anesthetic gas prevents OR personnel from developing vitamin B_{12} deficiency states due to prolonged exposure to N_2O.
- Extensive interaction between folate and vitamin B_{12} makes it imperative that pernicious anemia be treated with B_{12} at same time as folate to prevent CNS degeneration.

Warfarin (Coumadin)

Charise T. Petrovitch | Lee A. Fleisher

Uses

- Management of thromboembolic disorders: For prophylaxis, Rx, and prevention of recurrence of thromboembolic events including DVT, pulm embolism, thrombosis of grafts. Prevention of arterial emboli associated with prosthetic heart valves, nonvalvular AFib, acute MI. Prevention of MI, stroke, and recurrent MI. Rx for deficiency of antithrombin III, protein C, protein S.
- Unknown number of individuals receiving the drug.

Perioperative Risks

- Hemorrhage (minor to major life risk)
- Purple-toe syndrome or warfarin necrosis
- Teratogenicity in pregnancy (decreases synthesis of vitamin K-dependent clotting factors by fetus)
- Risk of thrombosis/bleeding if discontinued periop

Worry About

- Major drug interactions
- Many drugs affect action of warfarin. List is extensive and continually expanding. Be concerned about other drugs that potentiate bleeding (e.g., antiplatelet agents, ASA, NSAIDs); and drugs that displace warfarin from protein-binding sites or that increase or decrease vitamin K levels.

Overview/Pharmacology

- General effect: Anticoagulant with dose-dependent effect on coagulation

Pharmacokinetics/Pharmacodynamics

- Warfarin is a racemic mixture of R and S isomers (R-warfarin and S-warfarin).
- Racemic warfarin is absorbed rapidly from GI tract; reaches maximal plasma concentration in 90 min; has a half-life of 36–42 h; time to peak effect is 36–72 h; duration after discontinuation is at least 2–5 d.
- In circulation, bound to plasma proteins and accumulates in liver. R-warfarins are excreted in urine; S-warfarins are eliminated in bile.
- Warfarin resistance or decreased warfarin effect. When warfarin absorption from GI tract is impaired due to malabsorption syndromes, concurrent use of liquid paraffin laxatives, cholestyramine resin, or excessive amounts of certain antacids (e.g., Mg trisilicate).
  - Vitamin K intake increased through diet or administration of vitamin K IM or IV.
  - With induction of hepatic enzymes, increasing metabolism of warfarin. Enzyme inducers including anticonvulsants, barbiturates, primidone, carbamazepine, antimicrobials (e.g., griseofulvin, rifampin, nafcillin, ethanol) and smoking.
- Increased warfarin effect or warfarin sensitivity
  - Drugs displacing warfarin from albumin increase its bioavailability (NSAIDs, ASA, phenytoin sodium, oral hypoglycemic agents, sulfa drugs, nalidixic acid, estrogen, miconazole)
  - Deficiency of vitamin K enhances; occurs with malabsorption syndromes and during administration of liquid paraffin laxatives and clofibrate; after long-term use of oral antimicrobials that deplete intestinal bacterial source of vitamin K. Large doses of vitamin E antagonize the action of vitamin K; anabolic steroids, danazol impair synthesis of vitamin K-dependent clotting factors; olestra removes vitamin K.
  - Metabolism blocked by phenytoin, chloramphenicol, erythromycin, clofibrate, TCAs, cimetidine, sulfinpyrazone, and trimethoprim-sulfamethoxazole, thus increasing warfarin's effect. Disulfiram (Antabuse) significantly slows metabolism.
  - Certain cephalosporins have a warfarin effect themselves—thus they are contraindicated.
  - Elderly, febrile, and debilitated pts and those with hepatic dysfunction, hyperthyroidism, or heart failure may have increased warfarin effect.

Drug Class/Mechanism of Action/ Usual Dose

- Interferes with synthesis of 6 vitamin K–dependent proteins involved in coagulation sequence: Factors II, VII, IX, and X; proteins C and S. Before these proteins are released into circulation, they undergo reactions that convert glutamic acid residues to carboxyglutamic acid residues and require presence of reduced form of vitamin K.
- Inhibits cyclic interconversion between reduced form of vitamin K and its 2,3-epoxide (vitamin K epoxide).

- Defective clotting factors lacking a "carboxyl tail" are produced, impairing coagulation.
- Factor II has a half-life of 48 h; requires 3–4 d to drop to a level when PT significantly prolonged.
- Nonurgent need for anticoagulation: Adult with average body mass, 5 mg/d PO prolongs PT to 1.5 × control value in 36–48 h; if not achieved by third day, daily dose may be adjusted by an increase or decrease of 2.5 mg; goal: PT = 1.5–2 × control. Increases bleeding complications when PT is 2.5 × control. Once anticoagulation stabilized, warfarin dose should be adjusted to maintain INR of 2–3 for all indications except in the case of mechanical prosthetic cardiac valves, which require higher levels of anticoagulation.
- More urgent need: Heparin anticoagulation first; start warfarin, 10 mg for 2 d.

Assessment Points

System	Effect	Assessment by History	Physical Examination	Test
GI	Vitamin K deficiency may result from a poor diet, extrahepatic biliary obstruction, malabsorption, sterile gut	GI bleeding Tarry stools Hematemesis	Weight/height ratio (BMI)	Hct Fecal occult blood
ENDO	Vitamin K deficiency Hyperthyroidism, hypermetabolism potentiate warfarin effect		Malnourishment	PT/PTT INR
GU	Diuresis, pregnancy decreases effect; warfarin is teratogenic			PT/PTT INR
MS	Arthritis pain medications that affect platelets (e.g., ASA, NSAIDs) potentiate bleeding			

Key References: Douketis JD, Spyropoulos AC, Kaatz S, et al.: BRIDGE investigators: perioperative bridging anticoagulation in patients with atrial fibrillation, *N Engl J Med* 373(9):823–833, 2015; van Veen JJ, Makris M: Management of peri-operative anti-thrombotic therapy, *Anaesthesia* 70(Suppl 1):58–67, 2015.

Perioperative Implications

Preoperative Concerns

- Anticoagulation: Consider therapy with vitamin K (PO, IM, IV, SQ: 2.5–5 mg/70 kg) or FFP (15–20 mL/kg).
- Monitor this drug: PT, INR.
- Decision to continue warfarin in pt undergoing surgery depends on risk of thrombosis vs risk of bleeding. In pts with atrial fibrillation in the BRIDGE trial, forgoing bridging anticoagulation was noninferior to periop bridging with low-molecular-weight heparin for the prevention of arterial thromboembolism and decreased the risk of major bleeding.

Possible Drug Interactions

- Regional: Risk of spinal or epidural hematoma when performing a regional when pt is anticoagulated. Risk is theoretically increased with anticoagulant. Epidural cath thought to be associated with greater risk of spinal or epidural hematoma if no measurable anticoagulant effect from warfarin (e.g., PT normal), but if receiving warfarin, not known if risks of spinal or epidural hematoma are significant.

Anticipated Problems/Concerns

- Bleeding the most likely complication due to further depletion of clotting factors during surgery; factor depletion may follow massive transfusions or with development of DIC.
- If anticoagulation is reversed preop with large doses of vitamin K, warfarin resistance is possible initially; thrombosis a risk in this setting.
- If anticoagulation reversed with administration of FFP, anticoagulation is more easily achieved postop, but infectious risks are a concern.
- Preop dose of warfarin can be restarted with oral fluids; when risk of thromboembolism is considered to be especially high (as in pts with recurrent pulm emboli undergoing pelvic surgery) or a delay of more than 48 h is anticipated before warfarin can be restarted, postop heparin infusion is appropriate.

Androstenedione

Alan David Kaye | Mark R. Jones | Jessica Kaye | Adam M. Kaye

Uses

- Testosterone replacement therapy
- Treatment of hypogonadal men
- Age-related sarcopenia
- HIV-related muscle wasting
- Increase in bone mineral density
- Prevention of age-related frailty and falls

Perioperative Risks

- Coagulopathy
- Polycythemia

Overview

- Growing sales trend of 20–30% in USA for both medical and nonmedical use of AAS.
- AAS have been available since 1996 as an OTC nutritional supplement and were banned for sale by the Anabolic Steroid Control Act in 2004.
- Estimated 10% of AAS users are teens.
- Estimated 4.9% of male and 2.4% of female adolescents in USA have used legal androgenic/anabolic steroids.
- Current estimates indicate that there are as many as 3 million AAS users in USA.
- Surveys among community weight trainers attending gyms and health clubs indicate that AAS use is between 15% and 30%.
- AAS use is positively associated with use of alcohol, illicit drugs, and legal performance enhancing substances.
- As a major precursor to testosterone that is available without a prescription, it is purported to increase strength and athletic performance. However, significant effects on muscle strength have not been found in men after androstenedione administration, except following a large dose (1500 mg/d for 12 wk) of androstenedione given to hypogonadal men.
- AAS used to increase endogenous testosterone production to enhance athletic performance and recovery from exercise, to keep RBCs healthy, and to heighten sexual arousal and function.
- Popularity related to society's preoccupation with sustaining the male libido.

Pharmacology/Mechanism of Action/Usual Dose

- As a member of a group of compounds known as AAS, these synthetic derivatives of testosterone are thought to possibly restore sex drive and boost muscle mass.
- Testosterone enters the cell by passive diffusion and is converted by 5α-reductase to 5α-dihydrotestosterone, which binds to intracellular androgen receptors.
- Increase protein anabolism and decrease protein catabolism. Nitrogen balance is improved only when there is sufficient intake of calories and protein.
- Stimulate the production of RBCs by enhancing the production of erythropoietic stimulating factor.
- Impair preadipocyte differentiation into adipocytes and reduce subcutaneous abdominal adipose tissue in nonobese women.
- Supplementation of androstenedione in the setting of a rigorous 12-wk resistance-training program resulted in a return of baseline levels of testosterone levels and significant increases in estrone and estradiol levels. No increase in measurable lean body mass or muscular strength when compared with placebo.
- Androstenedione is produced in the gonads and adrenal glands of both males and females.
- It is synthesized from dehydroepiandrosterone and then converted to testosterone by the enzyme 17 β-hydroxysteroid dehydrogenase or to estrone by the aromatase enzyme complex.
- Usual dose:
  - Androstenedione is a direct precursor of testosterone and estrone in both males and females; it may increase testosterone levels.
  - Marketing claims include increased strength, greater fat-free mass, and improved libido; recommended doses are 100–300 mg/d or 50–100 mg twice daily taken 1 h before exercise or upon awakening. Only high doses of 1500 mg/d for 12 wk confirmed to increase muscle strength.
- Contraindications:
  - Pts with steroid-dependent carcinoma of the breast, prostate gland, and endometrium.
  - Women who are or may become pregnant.
  - Pt with serious cardiac, hepatic, or renal disease.
- Adverse effects:
  - Several AAS-induced CV concerns reported include Htn, left ventricular hypertrophy, impaired diastolic filling, arrhythmias, erythrocytosis, altered lipoprotein profile, and thrombosis.
  - AAS-induced elevations in liver enzymes (alanine- and aspartate-aminotransferases).
  - Dermatologic chances such as acne, striae, alopecia, and hirsutism are possible results induced by the action of the AAS on the skin and sebaceous glands.
  - Endocrine and/or reproductive effects include a dose-dependent depression of levels of luteinizing hormone and follicle-stimulating hormone due to the negative feedback loop of the hypothalamic-pituitary-gonadal axis.
  - Feminization (gynecomastia) in males due to the aromatization of exogenous testosterone to estrogen metabolites.
  - Male users may have their endocrine suppression lead to hypogonadotrophic hypogonadism, testicular atrophy, sperm morphology, infertility, and changes in libido.
  - Female-specific side effects of AAS incl hirsutism, increased facial hair, voice deepening, clitorial hypertrophy, oligomenorrhea, reduced breast tissue, and male-pattern baldness.
  - Restoration of hypothalamic–pituitary homeostasis, endogenous testosterone, and spermatogenesis may take between 3-12 mo after using AAS.

Assessment Points

System	Effect	Assessment by Hx	Test
CV	Decreased HDL, atherosclerosis	Angina	ECG, cholesterol
GI	Cholestasis, hepatocellular tumors, hepatitis, nausea		Liver enzymes, bilirubin
HEME	Polycythemia, chronic usage, suppression of clotting factors, sodium and water retention	Easy bruising	PT, PTT Lytes
CNS	Depression, anxiety, behavioral changes, headache		

Key References: Broeder CE, Quindry J, Brittingham K, et al.: The Andro Project: physiological and hormonal influences of androstenedione supplementation in men 35 to 65 years old participating in a high-intensity resistance training program, *Arch Intern Med* 160(20):3093–3104, 2000; Dodge T, Hoagland MF: The use of anabolic androgenic steroids and polypharmacy: a review of the literature, *Drug Alcohol Depend* 114(2–3):100–109, 2011.

Perioperative Implications

- Retention of sodium, chloride, potassium, calcium, inorganic phosphate, and water.
- N/V, rarely hepatocellular neoplasms and hepatitis.
- Suppression of clotting factors II, V, VII and X; bleeding in pts on concomitant anticoagulant therapy.
- Polycythemia.
- Increased serum cholesterol, decreased HDL.
- Pts with osteolytic lesions or who are semi-ambulatory may develop nephrocalcinosis.
- In geriatric pts, high risk of prostate hypertrophy and prostate carcinoma.

Possible Drug Interactions

- Metabolic effects of androgens may decrease blood glucose level and insulin requirements.
- Androgens decreased levels of thyroxin-binding globulin, resulting in decreased total T_4 serum levels and decreased resin uptake of T_3 and T_4.
- May interfere with androgenic or estrogenic drug therapy.

β-Sitosterol

Alan David Kaye | Mark R. Jones | Adam M. Kaye

Uses

- CHD and hypercholesterolemia.
- BPH and prostatitis.
- Gallstones.
- Enhances sexual activity.
- Prevents colon cancer.
- Boosts immune system.
- Topically for treating wounds and burns.
- Migraine headache, chronic fatigue syndrome, and symptoms of menopause.
- Asthma, allergies, bronchitis, SLE, and alopecia.
- Areas of potential application currently under investigation include the prevention of breast, ovarian, and lung cancers.

Overview

- β-sitosterol is one of the major plant sterols found in humans. Its chemical structure is similar to that of cholesterol with an ethyl group added at position 24.
- β-sitosterol is available in many nonprescription supplements and with dietary plant consumption.
- With a low absorption rate, it inhibits intestinal absorption of cholesterol by competing for limited space with cholesterol in mixed micelles and also accelerates the esterification rate of the lecithin cholesterol acyltransferase enzyme.
- In benign prostatic hyperplasia, it binds to prostatic tissue, inhibits prostaglandin synthesis in the prostate, and has anti-inflammatory activity.
- Enhances proliferative responses of T cells in vitro.
- Inhibits colon cancer growth in vitro.
- Alternative for pts seeking modest reductions in LDL-C (<15%): Higher doses (4 g/d) can lead to reductions in LDL-C up to 19.8%, equivalent to doubling the dose of statin in dyslipidemic pts.
- Reductions in triglycerides (6–9%) seen as well with 2 g/d doses of sterol.
- May alter CNS disease progression, especially disorders that are correlated with an altered cholesterol metabolism, such as AD, MS, and ALS-PDC.
- Some studies have shown anti-diabetic properties of β-sitosterol.

Pharmacology/Usual Dose

- The reduction of dietary cholesterol available to the body may be due to inhibition of absorption in the intestine.
- Large amounts of dietary β-sitosterol may displace cholesterol during absorption and increase fecal excretion.
- Inhibition of 5-alpha reductase prevents the conversion of testosterone to dihydrotestosterone. This reduction of androgens may reduce prostatic hyperplasia in the same manner that finasteride (Proscar) does.
- For hypercholesterolemia, usual dosage is 800 mg–6 g before meals; for severe cases, can be up to 15 g.
- For benign prostatic hyperplasia and prostatitis, implement 60–130 mg tid.
- About 175–200 mg is consumed daily in typical diet.
- Contraindications include sitosterolemia, which is an inherited lipid storage disease with increased absorption of cholesterol and β-sitosterol from diet. Elevated liver β-sitosterol competitively inhibits cholesterol catabolism, which will lead to hypercholesterolemia.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	CAD	Angina MI		ECG
RESP	Asthma	Wheezing	Wheezing	

Key References: Wong NC: The beneficial effects of plant sterols on serum cholesterol, *Can J Cardiol* 17(6):715–721, 2001; Vanmierlo T, Bogie JF, Mailleux J, et al.: Plant sterols: friend or foe in CNS disorders? *Prog Lipid Res* 58:26–39, 2015.

Perioperative Implications

- Obtain adequate Hx to determine indication since there may be significant comorbidity.
- No known periop implications.

Anticipated Problems/Concerns

Side Effects

- May cause N/V, indigestion, gas, diarrhea, or constipation.
- Interactions: Ezetimibe (Zetia) may reduce absorption of β-sitosterol.
- Antihyperlipidemic drugs such as atorvastatin (Lipitor), cholestyramine, and gemfibrozil have additive effects in lowering cholesterol level.
- Pravastatin (Pravachol) can lower the blood level of β-sitosterol.
- Increased risk of deficiency of fat soluble vitamins. β-sitosterol may reduce absorption and blood level of α- and β-carotene and vitamin E.
- Erectile dysfunction and loss of libido have been reported in pts on β-sitosterol.

Blue Cohosh *(Caulophyllum thalictroides)*

Christopher J. Cullom | Alan David Kaye

Uses

- Commonly used by midwives as a uterine stimulant and for induction of labor. Major uses, therefore, include (1) inducing labor; (2) as an emmenagogue; (3) as an antispasmodic; and (4) as an abortifacient.
- Properties also include anti-inflammatory, antipyretic, diuretic, expectorant, vasoconstrictor, and smooth muscle relaxants.
- According to a national survey, 64% of midwives still use blue cohosh to induce labor and 7–45% of women use herbal medications during pregnancy.

Risk

- Ingestion of the leaf or seeds can lead to severe toxicity.
- Case reports document seizures, renal failure, and resp distress after use.
- Avoidance is advised in diabetic pts due to concern for hyperglycemia and potential inhibition of antiglycemic medications.
- Reports of perinatal stroke, aplastic anemia, chest pain (angina), hypertension, acute MI, CHF, shock, and multi-organ hypoxia in infants following maternal use from the first trimester to right before delivery.
- Should not be used by women with estrogen-sensitive conditions or cancers, and in pts with diarrhea.
- Also causes mucous membrane irritation, diarrhea, and cramping, and constricts coronary arteries.
- Possesses several components that can be teratogens, cytotoxic, or lethal to embryos and/or can cause birth defects and congenital malformations.

Perioperative Risks

- Coronary artery vasoconstriction that can lead to myocardial ischemia
- Alteration in antiglycemic and antihypertensive drug levels
- Interaction with medications dependent on cytochrome P-450 enzymes

Worry About

- Differentiate from black or white cohosh, which have other physiologic effects.
- Product safety and efficacy profiles differ among manufacturers.
- Usage in pregnancy due to concern of uterine stimulation, teratogenicity, and neonatal multisystemic complications.
- Usage in pts with diabetes, hypertension, or acute history of tobacco/nicotine use.

Overview/Pharmacology

- Several alkaloids and saponins are considered responsible for the pharmacologic effects.
- Anagyrine, *N*-methylcytosine, and taspine are constituents identified likely to be teratogenic.
- *N*-methylcytosine acts similarly to nicotine, which can cause elevated BP, tachycardia, diaphoresis, abdominal pain, vomiting, fasciculations, and produce hyperglycemia in the developing fetus.
- Alkaloid components found to be cytochrome P-450 inhibitor based on in vitro studies, and thus may pose a risk of drug-drug interactions when taken with other medications dependent on CYP450 enzymes.
- Blue cohosh preliminarily appears to have estrogenic effects with enhancement of estradiol binding to estrogen receptors.

Etiology

- Berberidaceae or Leonticaceae family.
- Listed in the US Pharmacopoeia 1882–1905 as a labor inducer.
- Typically the dried rhizome/root parts are used.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Mucous membrane irritation	Complaints of oral irritation	Oral mucosa exam	
CV	Ischemia, Htn, tachycardia	Complaints of angina, dyspnea, or palpitations	Cardiac exam	ECG ± ECHO
GI	Increased GI motility, diarrhea, abdominal cramping	Changes in bowel movements (i.e., frequency, consistency), abdominal discomfort	Abdominal exam	
ENDO	Hyperglycemia	Fatigue, polydipsia, polyuria, vision changes, weight loss	Visual acuity exam	Blood glucose
OB/GYN	Uterine stimulation, estrogenic effects	Changes in contractions or menstruation	OB exam	Biophysical profile US, LH levels

Key References: Finkel RS, Zarlengo KM: Blue cohosh and perinatal stroke, *N Engl J Med* 351(3):302–303, 2004; Rader JI, Pawar RS: Primary constituents of blue cohosh: quantification in dietary supplements and potential for toxicity, *Anal Bioanal Chem* 405(13):4409–4417, 2013.

Perioperative Implications

Preoperative Concerns
- Reliable self-reporting of use by pts.
- Enhanced hyperglycemia in diabetics.
- Can be associated with coronary vasoconstriction.
- The ASA recommends holding all herbal products 2–3 wk prior to surgery since the half-life of most of these preparations are unknown, allowing for elimination out of the body.

Monitoring
- Use standard ASA monitors.
- Intraop blood glucose levels.

Airway/Maintenance
- No known effects

Preinduction/Induction
- Coronary vasoconstriction

Adjuvant
- May accentuate the response to vasopressors
- May attenuate effectiveness of antihypertensive medications
- Possible drug-drug interactions due to inhibitory effects on hepatic enzymes

Postoperative Period
- Monitor CV status (i.e., BP, pulse) and blood glucose levels.

Carnitine

Renyu Liu | Dajin Sun

Uses
- Treatment of primary carnitine deficiency and deficiency secondary to complications of several inborn errors of metabolism, such as organic acidemia and fatty acid oxidation defects in children and adults, and acquired medical or iatrogenic conditions such as valproate and zidovudine treatment, cirrhosis, chronic renal failure on dialysis, etc.
- Treatment of valproic acid poisoning and/or overdosing and prevention of valproic acid–induced hepatotoxicity.
- Used for ADHD, erectile dysfunction and male infertility, cardiomyopathy, PVD, CHF, chronic cardiac dysrhythmias, senile dementia, metabolic nerve diseases, HIV infection, tuberculosis, myopathies, renal failure–induced anemia, neuropathy, and neuropathic pain, etc. However, additional studies are needed to confirm these potential benefits.
- Experimental data indicated that carnitine might have neuronal protective effects against hypoxia/ischemia and neuronal inflammation. Clinical applications of these finding are unknown.

Perioperative Risks
- Periop risks are related to carnitine deficiency rather than carnitine itself.
- Hypoglycemia, lactic acidosis, and muscle weakness related to carnitine deficiencies and discontinuation of carnitine supplement.
- Case report indicates that pts with carnitine deficiencies may develop symptoms similar to those assoc with propofol infusion syndrome. Periop usage of carnitine as a metabolic supplement might be related to periop outcome.

Worry About
- Individuals with L-carnitine deficiency should continue this medication as scheduled preop to avoid acute hypoglycemia, lactic acidosis, etc. IV carnitine or dextrose-containing solutions may be needed for fasting individuals with L-carnitine deficiencies.

Overview/Pharmacology
- Carnitine (3-hydroxy-4-trimethylamino-butyric acid or β-hydroxy-gamma-N-trimethylamino-butyrate) is a quaternary ammonium compound biosynthesized from the amino acids lysine and methionine.
- Carnitine exists in two stereoisomers: L-carnitine, the biologically active form, and D-carnitine, the biologically inactive form, which may be harmful.
- About 75% of L-carnitine comes from the diet, particularly from red meat and dairy products. Endogenous synthesis combined with high tubular reabsorption is enough to prevent deficiency in healthy people. Thus carnitine deficiency is uncommon in healthy, well-nourished adults.
- Most of the body's carnitine is stored in skeletal muscle, but it is also found in other high-energy-demanding tissues such as those in the myocardium, liver, and adrenal glands. Carnitine is excreted in urine. Thus carnitine and its metabolite may accumulate in pts with renal failure.

Pharmacokinetics
- Formula: $C_7H_{15}NO_3$
- Mol. mass: 161.199 g/mol
- Bioavailability: <10%
- Protein binding: None
- Metabolism: Slightly
- Half life: 15 h
- Excretion: Urine (>95%)

Drug Class/Usual Dose
- Carnitine is available both as a prescription drug and as a food supplement.
- Pregnancy: Category B. Studies in bacteria have found no evidence of mutagenicity. No human data are available. Carnitine occurs naturally in human breast milk.
- Dosing: The usual supplementation dose is 100–300 mg/kg/d. For infants and children, recommended dosage is between 50–100 mg/kg per d in divided doses with a maximum of 3 g/d. IV L-carnitine is used for treatment of lactic acidosis and cardiomyopathy secondary to L-carnitine deficiency. The recommended dosage is a 50 mg/kg bolus injection over 2–3 min followed by an equivalent dosage over the next 24 h (divided every 3-4 h). Subsequent dosages would be based on responses.
- Overdosage: There have been no reports of toxicity from L-carnitine overdosage. Oral doses of 15 g/d have been well tolerated.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Seizures (rare)	Oral or IV L-carnitine. Reliable description of a witnessed seizure	Seizure activity Postseizure state Signs of other injuries	Rule out other etiology
GI	N/V, diarrhea	Oral or IV L-carnitine; it is important to differentiate between overdose and deficiency		Blood carnitine level, serum glucose, lactic acid
DERM	Body odor	Oral or intravenous L-carnitine	Odor	

Key References: Odle J, Adams SH, Vockley J: Carnitine. *Adv Nutr* 5:289-290, 2014. Steiber A, Kerner J, Hoppel CL: Carnitine: a nutritional, biosynthetic, and functional perspective, *Mol Aspects Med* 25(5–6):455–473, 2004.

Possible Drug Interactions

- Carnitine has not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods.
- L-carnitine might decrease the need for certain drugs such as glycosides, digoxin, diuretics, beta blockers, calcium channel blockers, hypolipidemia (cholesterol-altering) drugs, and nitroglycerin derivatives.
- L-carnitine might increase the effects of warfarin (Coumadin) and heparin.

Anticipated Problems/Concerns

- None

Chitosan

Joan Spiegel

Uses

- Sustained-release drug carrier (chitosan glutamate)
- Transdermal drug delivery
- Weight-loss agent (poor)
- Decreases cholesterol and triglycerides and increases HDL total cholesterol ratio
- Cleaning petrochemical spills
- Water purification agent
- Hydrogel-based chitosan bandages for hemostasis and antibacterial properties

Risk

- None known

Perioperative Risks

- None known

Worry About

- Theoretical inhibition of absorption of fat-soluble vitamins A, D, E, and K

Overview

- Chitosan is a naturally occurring marine polysaccharide fiber derived from a common byproduct of shellfish processing. (Chitosan is the deacetylated form of chitin, a sugar from the shells of crustaceans.)
- Recently ingenious medical applications have been developed that use chitosan as a pharmaceutical drug carrier (thermogel) effectively encapsulating various anti-inflammatory and chemotherapeutic agents and allowing it to function as a moiety for safe sustained release.

Etiology

- Chitosan is a completely indigestible fiber source with the ability to electrostatically attract and bond with negatively charged dietary lipids, thus prohibiting their absorption.
- The hemostatic activity of chitosan is due to ionic interaction between the positively charged chitosan polymer and the negatively charged cell membrane of the red blood cell. It works irrespective of the presence of fibrin to form a biodegradable plug.

Assessment Points

System	Effect	Test
CV	Improved cholesterol	Lipid profile
HEME	Improved hemostasis	None
GI	Stomach upset, steatorrhea, loss of fat-soluble vitamins	None

Key References: Koide S: Chitin-chitosan properties, benefits and risks, *Nutrition Res* 18:1091–1101, 1998; Ogle OE, Swantek J, Kamoh A: Hemostatic agents, *Dent Clin North Am* 55(3):433–439, 2011.

Perioperative Implications

- None known or studied

Chondroitin Sulfate

Rosemary M.G. Hogg

Uses

- CS has been recommended for use as a nutritional supplement to reduce joint pain and inflammation associated with osteoarthritis.
- CS has been shown to have both anti-inflammatory and antioxidant effects on articular tissue; it modulates the anabolic/catabolic balance of the extracellular matrix.
- CS is commonly used in conjunction with glucosamine to provide an alternative therapeutic option with minimal side effects as compared with traditional treatments such as NSAIDs.
- Studies have demonstrated modest but significant reductions in pain, joint swelling, and effusion with an improvement in functional status after the use of CS, in particular when used in conjunction with glucosamine and with results comparable in efficacy to celecoxib.
- Many such studies, however, are small or of short duration and may be unable to fully assess the long-term effects of CS on joint remodeling.
- The use of exogenous glycosaminoglycans such as chondroitin in novel targeted chemotherapeutic interventions for the treatment of malignancy is in an early phase. Additionally, intravesical CS may be used to reduce bladder pain from interstitial cystitis.

Perioperative Risks

- No specific anesthetic interactions or complications have been identified from the use of CS.
- Use should be avoided in pts with shellfish allergy.
- Hepatotoxicity has been recognized in a number of case reports in pts taking combined G-CS supplements

Worry About

- Markedly similar in structure to heparin; should be avoided in pts at risk of heparin-induced thrombocytopenia and other heparin sensitivities. In addition may cause derangement in INR results in pts concomitantly taking warfarin (Coumadin).
- Worsening of previously well-controlled asthma has been demonstrated with the use of CS.

Overview/Pharmacology

- Chondroitin is a sulfated glycosaminoglycan found in the proteoglycans of the extracellular matrix of many connective tissues including intraarticular cartilage.
- In vitro studies have demonstrated an inhibition of interleukin-1 and metalloproteinases in synovial tissue while increasing type II collagen production in articular chondrocytes. The highly charged sulfate groups found in CS have been shown to generate electrostatic forces, which provide resistance to cartilaginous compression.
- Bioavailability varies from 10% to 20% after oral administration. CS exhibits first-order kinetics at single doses of up to 3000 mg and is not metabolized by cytochrome P450, thus minimizing interactions with other medications.
- Clinical effects are demonstrated within 4 wk in most pts and have been shown to persist for up to 3 mo after discontinuation of treatment.

Drug Class/Usual Dose

- Classified as a nutritional supplement.
- May be manufactured by the enzymatic hydrolysis of a variety of animal sources including shark fins, porcine muzzles, bovine trachea, and chicken bones. Nonanimal chondroitin had been developed from microbial fermentation but is not currently commercially available.

- Usual recommended dose is 200–400 mg 2–3 times daily or 1000–1200 mg as a single daily dose. Higher doses have been used in clinical trials with no evidence of increased efficacy.
- Glucosamine 1500 mg is commonly combined with chondroitin in commercial preparations taken either once daily or in three divided doses. The optimal dose of CS, alone or in conjunction with glucosamine, is unclear from current literature.

Assessment Points

System	Drug Effect	Assessment by Hx	PE	Test
MS	Anti-inflammatory, reduction in joint degeneration	Assessment of pain and functionality scores	Joint tenderness and mobility	Radiologic loss of joint space
GI	Nausea or diarrhea (low incidence)	Subjective reporting of GI upset	Abdominal bloating	
CV	Arrhythmia, peripheral edema	Description of arrhythmia	Irregular pulse	ECG
DERM	Hair loss, periorbital swelling			

Key References: Singh JA, Noorbaloochi S, MacDonald R, et al.: Chondroitin for osteoarthritis, *Cochrane Database Syst Rev* 1:CD005614, 2015; Abe A, Kaye AD, Gritsenko K, et al.: Perioperative analgesia and the effects of dietary supplements, *Best Pract Res Clin Anaesthesiol* 28(2):183–189, 2014.

Anticipated Problems/Concerns

- Caution with anticoagulant medications

Chromium

Lee A. Fleisher

Uses

- Body building (ineffective)
- May aid in glycemic control of type II DM and gestational DM
- Hyperlipidemia
- Hypoglycemia (reactive)
- Obesity

Perioperative Risks

- Risks minimal
- Chronic ingestion associated in one case with thrombocytopenia, hepatic dysfunction, renal dysfunction

Worry About

- Nephrotoxicity

Overview

- A trace mineral
- Improves glucose tolerance in type II DM and gestational DM (in some studies)
- Shown to increase insulin sensitivity and decrease serum triglycerides
- Shown to alleviate symptoms of reactive hypoglycemia
- Popular as weight-loss and body-building supplement, but effect not supported in clinical trials

Drug Class/Mechanism of Action/Usual Dose

- Hypothesis: In normal functioning, it increases circulating insulin, resulting in binding of chromium to peripheral insulin-sensitive tissue; increases insulin receptor number; and activates insulin receptor kinase.
- Usual dosage recommended: 50–200 μg/d.
- Available orally or IV
- Taken as supplement of 200–1000 μg/d
- Mixed results in randomized clinical tests

Assessment Points

System	Effect	Test
RENAL	Nephrotoxicity	Cr
ENDO	Insulin sensitivity	Glucose

Key References: Hummel M, Standl E, Schnell O: Chromium in metabolic and cardiovascular disease, *Horm Metab Res* 39(10):743–751, 2007; Suksomboon N, Poolsup N, Yuwanakorn A: Systematic review and meta-analysis of the efficacy and safety of chromium supplementation in diabetes, *J Clin Pharm Ther* 39(3):292–306, 2014.

Perioperative Implications

- No known interaction

Cranberry

Christopher J. Cullom | Alan David Kaye

Uses

- Many cranberry juice consumers are aware of a beneficial link between cranberry juice and the prevention of UTIs.
- High in polyphenol activity.
- Potentially beneficial for prevention of upper GI ulcers, reducing the risks of CV disease, and improving oral hygiene.
- Native Americans and early American sailors used cranberries for treating wounds and blood poisoning, urinary illnesses, diarrhea, DM, and as an antiscorbutic agent.

Perioperative Risks

- Cytochrome P-450 inhibitor based on in vitro evidence, specifically CYP3A4 and CYP2C9.
- Based on in vivo studies, interaction with warfarin, midazolam, fluconazole, or drugs dependent on CYP enzymes appear unlikely, unless cranberry is consumed at large quantities or long durations, yet not excluded completely.
- There is some evidence for alteration in INR with administration of cranberry that warrants consideration.

Worry About

- Theoretical risk of oxalate urinary stone formation (if large volumes consumed daily).
- Consider potential interaction with anticoagulation effects of warfarin or other drugs dependent on CYP enzymes.

Overview/Pharmacology

- Cranberries are a fruit native to New England and belong to *Vaccinium macrocarpon*.
- Most popular form for consumption is the cranberry-juice cocktail, containing about 27% cranberry juice, sweetener, water, and vitamin C.
- Also available as juice concentrate, tablets, or capsules.
- Consist of 90% water and various organic substances such as quinic acid, malic acid, and citric acid as well as glucose and fructose.

Drug Class/Mechanism of Action/Usual Dose

- Increases concentration of hippuric acid and increases acidification of urine.
- Inhibits bacterial adherence to mucosal surface by at least two kinds of inhibitors: fructose and proanthocyanidins.
- Fructose and proanthocyanidins in cranberries inhibit type I–fimbriated *Escherichia coli* adhesion.
- Cranberry products have been shown to reduce the incidence of UTIs in women at 12 mo.

Assessment Points

System	Drug Effect	Assessment by Hx	PE	Test
HEENT	Reduces dental plaque, periodontal and gum disease	Toothache	Dental exam	
CV	Improves ability of LDL to resist oxidative stress (antioxidation)			ECHO of arteries
GU	Prevents UTI, stone formation	Frequency and urgency and painful urination	Cloudy urine, low back pain	UA culture
HEME	Potential warfarin interaction	H/o anticoagulant use	Petechiae, bleeding	CBC, PT, PTT, INR

Key References: Guay DRP: Cranberry and urinary tract infections, *Drugs* 69(7):775–807, 2009; Lilja JJ, Backman JT, Neuvonen PJ: Effects of daily ingestion of cranberry juice on the pharmacokinetics of warfarin, tizanidine, and midazolam, *Clin Pharmacol Ther* 81(6):833–839, 2007.

Perioperative Implications

Preoperative Concerns

- Hx of recurrent UTI, possible urolithiasis, need for antibiotics.

Induction/Maintenance

- Routine monitoring.
- Consider antibiotic coverage if a UTI is present.
- Drugs administered depend on cytochrome P-450.

Postoperative Concerns

- Immediate resumption not necessary.

Anticipated Problems/Concerns

- Assess for UTI, antibiotic use, urolithiasis, anticoagulation status, or drug interactions for medications dependent on CYP enzymes.

Creatine

R. Blaine Easley | Lee A. Fleisher

Uses

- Medical: Historically used to lower cholesterol and treat rare conditions of heart failure due to creatine deficiencies; it has proposed benefits to decrease myalgias and myositis with statins.
- Fitness: Increased usage of creatine over past decade to increase muscle mass and enhance physical performance. Initially used by professional athletes, it is now used as a nutritional supplement in almost all areas of exercise fitness (in both casual and competitive athletes).
- Incidence: Unknown incidence in the population.

Perioperative Risks

- Unknown. Theoretical problems in pts with impaired renal function; potential for drug interactions, though no definitive studies

Worry About

- Hypovolemia and/or dehydration if nutrition inadequate.

Overview/Pharmacology

- Commercially available as creatine citrate, creatine monohydrate, and creatine phosphate.
- Creatine exists intracellularly in skeletal muscle, cardiac muscle, brain, and testes as creatine phosphate, otherwise called phosphocreatine. Phosphocreatine contains a high-energy phosphate bond, used for short, intense muscle activity via the phosphagen energy system.
- Studies in animal and human subjects have demonstrated increase of cellular phosphocreatine levels in skeletal muscle following creatine ingestion. Few studies demonstrate an increase in muscle strength or endurance.
- Recent randomized trials have shown neither increased strength nor increased stamina.
- Increase in muscle mass is thought to be related to increase in intracellular H_2O content brought about by influx of phosphocreatine into myocyte.
- Creatine is eliminated from the body by renal excretion as creatinine, the anhydrous form of creatine.
- Creatine is usually ingested after being dissolved in fluid.
- Use creatine to increase muscle mass and performance. Special concern should be paid to athletes desiring weight loss (i.e., wrestlers, gymnasts, body builders, football players) in examining renal function.

Drug Class/Usual Dose

- Creatine is classified as a nutritional or dietary supplement; therefore, it is unregulated by the FDA.
- Typical usage: Initially 20–25 g ingested daily for 5–7 d, followed by 5–10 g daily for 10–12 wk. However, some individuals take higher dosages continually.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia/hypotension	Exposure	BP, HR	Lytes

Key Reference: Shao A, Hathcock JN: Risk assessment for creatine monohydrate. *Regul Toxicol Pharmacol* 45(3):242–251, 2006.

Possible Drug Interactions

Preoperative Concerns

- Because of the associated risk of hypovolemia/dehydration in pts using creatine, there are theoretical problems when used with the following classes of medications: diuretics, H_2 antagonists (e.g., cimetidine), NSAIDs, probenecid, and trimethoprim, or when taken near the time of exercise.

Induction/Maintenance

- No known interactions. May need bolus of intravascular fluids and careful attention to BP at time of induction.

Adjuvants/Regional Anesthesia/Reversal

- No known interactions. Consider pro/cons of NSAID usage intraop, especially if no assessment of renal function.

Dandelion

Burton D. Beakley | Alan David Kaye

Uses

- Rx for liver disease (e.g., liver congestion, hepatitis, jaundice)
- Rx for gallbladder disease
- Rx for appendicitis
- Rx for fluid retention (diuretic)
- Rx for appetite stimulate
- Less commonly used for mastitis, heartburn, boils, fevers, heart failure, among other uses
- Dietary supplement as a source of vitamins and minerals, including vitamin A, B, C, and D as well as minerals iron, potassium, and zinc

Perioperative Risks

- No clinical trial to date on hemodynamic instability.
- There is no clinical trial to date, but dandelion use may include risk of bleeding secondary to decreased clotting, especially if pt already taking blood thinners.
- Potential for lyte imbalances due to diuretic effects.
- Potential increase in stomach acid.

Worry About

- If used in combination with prescription diuretic drugs, effects of either or both drugs may be enhanced, leading to a hypovolemic state.
- Multiple minerals in dandelion may ↓ systemic absorption of PO-administered drugs (e.g., ciprofloxacin, famotidine, and esomeprazole).
- Given dandelion's ability to lower blood glucose, if used in combination with diabetic medications, there is risk for hypoglycemia.
- May worsen side effects of lithium.
- Too much vitamin A.

Overview/Pharmacology

- Dandelion leaves and root contain quercetin, luteolin, p-hydroxyphenylacetic acid, germacranolide acids, chlorogenic acid, cichoric acid, and monocaffeyltartaric acid. The leaves contain scopoletin, aesculetin, aesculin, cichoriin, arnidiol, and faradiol. The roots contain caffeic acid, taraxacoside, taraxasterol, and the polysaccharide inulin.
- Primary effect in relieving dyspepsia disorder is caused by taraxerol.
- Stimulates bile release by the liver and gallbladder, hence improving both bile flow (choleretic effect) and release (cholagogue effect).
- Diuretic activity comparable to that of furosemide has been demonstrated in mice; however, because dandelion replaces potassium lost through diuresis, metabolic complications occur only rarely.
- Insulin, a polysaccharide fiber composed of long chains of fructose-containing molecules contained in the plant, may act to buffer fluctuations in blood sugar levels.

Usual Dose

- Dosing of dandelion depends on several factors; there is no scientific data to determine a exact dosing requirement.
- Root used for general tonic and mild liver remedy up to tid.
  - Dried root: 2–8 g by infusion, or decoction
  - Fluid extract: 4–8 mL
  - Tincture, alcohol based: Not recommended secondary to high dosage required
  - Juice of fresh root: 4–8 mL
  - Powdered solid extract: 250–500 mg
- Leaf preparations used for diuretic effects tid.
  - Dried leaf by infusion: 4–10 g
  - Fluid extract: 4–10 mL

Toxicity

- Generally considered one of the safest medicinal plants used.
- Potential for allergic reaction when taken by mouth or applied to skin of sensitive pts.
- May be potentially toxic because of the high content of K, Mg, and other minerals, and vitamin A.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia	Orthostasis, polyurea, polydipsia	Decreased skin turgor, hypotension, tachycardia, orthostasis	Orthostatic BP, HR
GI	Increased gastric secretion	Diarrhea		
RENAL	Prerenal failure	Polyurea, polydipsia	As for CV	BUN/Cr
METAB	Hypoglycemia	Lightheaded, clammy, shaky	Sweaty	Blood glucose

Key References: Murray MT, Pizzorno Jr JE: *Taraxacum officinale* (dandelion). In Pizzorno Jr JE, Murray MT, editors: *Textbook of natural medicine*, ed 2, London, 1999, Churchill Livingstone, pp 979–982; Jellin JM, Gregory PJ, Batz F, et al (eds): *Dandelion. Natural medicines: pharmacist's letter/prescriber's letter natural medicines comprehensive database*, ed 13, Stockton, CA, 2012, Therapeutic Research Faculty, pp 511–512.

Perioperative Implications

Preoperative Concerns

- Unknown effects in pediatric and pregnant pts.
- Rely on pt self-report. ASA guidelines hold all herbal products 2–3 d prior to surgery, as half-lives of these products are unknown.
- Due to increased stomach acid production, antacids may not work as well.

Monitoring

- Routine.
- May require fluid bolus if there is an indication of hypovolemia and UO.
- Consider intraoperative blood glucose monitoring as indicated.

Regional Anesthesia

- Not clear but can potentially affect platelet function and increased bleeding risk.

Emergence/Extubation

- No known complications to date.

Postoperative Period

- Continue to assess volume status and treat accordingly.
- Potentially increased bleeding.
- Continue to monitor blood glucose in pts on diabetic medications.

Dehydroepiandrosterone

Alan David Kaye | Burton D. Beakley | Ethan Phan | Rachel J. Kaye

Uses

- Proposed uses DHEA with insufficient evidence:
  - Vasodilation, anti-inflammatory, antiatherosclerotic, antiaging
  - Physical performance: Increase muscle mass, strength, and energy
  - SLE, multiple sclerosis, osteoporosis, adrenal insufficiency, Crohn disease, COPD
  - Alzheimer disease, Parkinson disease, fibromyalgia
  - Depression, schizophrenia, chronic fatigue, anorexia nervosa, sleep disorders
  - CV disease, diabetes, obesity, metabolic syndrome
  - Improve menopausal symptoms, bone mineral density, and vaginal atrophy
  - Improve erectile dysfunction in men; cervical dysplasia, atrichia pubis, sexual dysfunction, and well-being in healthy women

Risk

- May cause hirsutism, acne, headache, insomnia, wt gain, alopecia, deepening of voice, and abnormal menses in women, or gynecomastia in men.
- Cardiac arrhythmias occur rarely, even with large doses.
- May worsen liver diseases and polycystic ovary syndrome and lower HDL levels. (It also decreases total cholesterol, LDL, and triglycerides.)
- Associated with cases of mania and palpitations.
- Diabetics may be prone to hyperglycemia.
- Unknown coagulation and vasoconstriction/dilation effects.
- Use contraindicated in pregnancy, endometriosis, leiomyoma; breast, ovarian, uterine, and prostate cancers.
- Possibly unsafe with more side effects if used long term and in larger doses (higher than 50–100 mg/d).

Perioperative Risks

- Single case report associated DHEA with cardiac arrhythmias and immune suppression.
- High DHEA levels can be associated with insulin resistance.
- Unknown effects on periop stress response, adrenal, and cardiac function.

Overview/Pharmacology

- DHEA is naturally produced by the adrenal gland and converted to other forms of androgens and estrogens in the liver and peripheral tissues.
- FDA categorized DHEA as an unapproved drug in 1985; reclassified as a dietary supplement by 1994.
- Popularized after a *New England Journal of Medicine* report that high levels correlated with fewer cardiac

events (Rancho-Bernardo study); later found to be untrue in a larger Rancho-Bernardo study.
- Banned by athletic agencies such as the NCAA, the NFL, and the Olympics.
- Marketed as a dietary supplement because it can be manufactured from natural sources, such as soy and wild yam. However, many of these products, depending on source and metabolism, are not converted into DHEA in humans and are not recommended or preferable.
- No data indicate benefits greater than long-term risk.
- Endogenous production in liver, adrenal gland, testes, and brain in minute quantities.
- Hepatic metabolism, urinary excretion with a 12-h half-life.
- Steroid hormone produced by adrenals, interconverted to testosterone, estrone, estradiol, androsterone.
- Considered a prohormone, so effects similar to those of anabolic steroids.
- May increase protein synthesis in skeletal muscles. However, increase of serum testosterone or enhancement of strength during resistance training is controversial. A placebo-controlled, randomized clinical trial reported in the *New England Journal of Medicine* in 2006 found that supplementation in the elderly had no significant beneficial effects on body composition, physical performance, insulin sensitivity, or quality of life.
- Decreasing serum cortisol levels may cause early activation of the anterior cingulate cortex (ACC) secondary to neuronal recruitment of the steroid sensitive ACC that may be involved in pre-hippocampal memory processing, thereby improving memory.
- DHEA levels decrease with CHF, oxidative stress, aging, and cancer.
- May have apoptotic effects in some cancer lines but is also shown to stimulate hormone-producing tumors.

Usual Dose
- 30–90 mg/d for depression, memory improvement, or cognition (two studies)
- 50–100 mg daily for 3–24 mo for possible improvements in well-being, cognitive function, body compositions
- 20-50 mg PO daily for adrenal insufficiency
- Vaginal: 10% cream; apply topically daily

Assessment Points

System	Effect	Hx Assessment	PE	Test
HEENT	Hirsutism			
CV	Anabolic steroids associated with sudden cardiac arrest, Htn; DHEA rarely causes arrhythmias	Determine chronic and acute dose and duration of self-administration; palpitations	HR	Preop ECG for chronic or excessive use, may show ventricular hypertrophy
GI	Anabolic steroids assoc with hepatitis, cholestatic jaundice			
HEME	Inhibits plt aggregation in vivo Antiglucocorticoid actions		Ecchymoses	Bleeding time, preop glucose for diabetics
DERM	Increased acneiform dermatitis			
GU	Hypogonadism with anabolic steroids, prostate tumor growth	Prostate exam		PSA
CNS	Anabolic steroids may cause aggressiveness; DHEA binds to NMDA, sigma, GABA receptors	Increased pituitary tumor growth		ACTH

Key References: Nair KS, Rizza RA, O'Brien P, et al.: DHEA in elderly women and DHEA or testosterone in elderly men, *N Engl J Med* 355(16):1647–1659, 2006; Labrie F, Archer D, Bouchard C, et al.: Intravaginal dehydroepiandrosterone (Prasterone), a physiological and highly efficient treatment of vaginal atrophy, *Menopause* 16(5):907–922, 2009.

Perioperative Implications

Preoperative Concerns
- Insulin resistance; check preop glucose.
- Synergism with corticosteroids.

Induction/Maintenance
- Unknown effects of inhibition of steroid synthesis if combined with etomidate or immunosuppressives for transplantation.

Postoperative Concerns
- Unknown effects on stress response

Anticipated Problems/Concerns
- Unpredictable CV effects

Echinacea (American Coneflower, Purple Coneflower, *E. Angustifolia, E. Purpurea, E. Pallida*)

Kirk Lalwani

Uses
- Purported immunostimulation and prevention and treatment of respiratory tract infections.
- Adjuvant in the treatment of other bacterial, viral, or fungal infections of the urinary and respiratory tract.
- Anti-inflammatory when used topically for conditions such as eczema, psoriasis, and herpes simplex.
- Promotes wound healing when used topically (i.e., in leg ulcers and burns).
- Adjuvant for cancer therapy and in the treatment of chronic fatigue syndrome.

Perioperative Risks
- No known drug interactions or toxicities
- No known sedative, CV, or coagulation effects relevant to anesthesia

Worry About
- Immunostimulation may counteract the effect of steroids and immunosuppressant drugs in transplant recipients and pts with autoimmune disease.

Overview
- Most common side effects are GI symptoms, allergic reactions, and rashes.
- Allergic reactions are more common in atopic individuals and individuals with a Hx of sensitivity to the Asteraceae-Compositae family of plants (e.g., ragweed, chrysanthemums, marigolds, daisies) and can be serious.
- Echinacea may exacerbate autoimmune diseases such as MS, SLE, rheumatoid arthritis, AIDS, tuberculosis, and pemphigus vulgaris.
- Echinacea may inhibit cytochrome P450 (CYP 1A2, 3A4) enzymes, altering levels of drugs metabolized by these enzymes.
- Tachyphylaxis may occur with prolonged, uninterrupted use.

Drug Class/Mechanism of Action/Usual Dose
- Increases phagocytosis and lymphocyte activity, possibly by release of TNF, IL-1, and interferon.
- Anti-inflammatory activity by inhibition of cyclooxygenase and 5-lipogenase.
- Promotes wound healing by protecting type 3 collagen from free radical damage and inhibiting bacterial hyaluronidase.
- Concentration of active ingredients varies widely according to species and preparation used.
  - 1–3 mL of the fluid extract or cold-pressed juice of plant (or root) 3 times daily.
  - 1 g of powdered root 3 times daily (capsules, tablets)
- Echinacea appears to modestly inhibit cytochrome P450 1A2 (CYP1A2), and to induce hepatic cytochrome P450 3A4 (CYP3A4), but inhibit intestinal CYP3A4 (opposing effects).

Assessment Points

System	Effect	Test
IMMUNE	Immunostimulation, anti-inflammatory activity	Phagocytic activation, IL-1 and TNF activity
HEPAT	P450 CYP1A2 inhibition	Caffeine clearance test

Key References: Karsch-Völk M, Barrett B, Linde K: Echinacea for preventing and treating the common cold, *J Am Med Assoc* 313(6):618–619, 2015; Charrois TL, Hrudey J, Vohra S, et al.: Echinacea, *Pediatr Rev* 27(10):385–387, 2006.

Perioperative Implications

- Possible antagonism of antirejection drugs used following bone marrow or organ transplantation.
- Possibly related to two case reports of liver failure, one in a child and one in an adult.

Ephedra (Ma-Huang)

Bracken J. De Witt

Uses

- Ephedra is a plant that contains a variety of ephedrine alkaloids, including ephedrine and pseudoephedrine.
- Dietary supplements containing ephedra were marketed in USA as agents that may aid in wt reduction and energy enhancement. Ephedra may be used in the manufacture of methamphetamine.
- In 2004, USA banned the sale of ephedra-containing supplements with a subsequent marked decrease in reported poisonings.
- Although banned in USA, sale of ephedra-containing supplements continues via internet resources.
- Some supplements have been marketed as "ephedrine-free" or as legal ephedra products, in which ephedra is replaced with other herbal stimulants such as bitter orange.
- Ephedra-containing substances are also known as ma-huang, Mormon tea, squaw tea, and herbal ecstasy.

Perioperative Risks

- Risks associated with an increase in the sympathetic nervous system activity and dysrhythmias and Htn

Worry About

- Lethal cardiac arrhythmias, Htn, myocarditis, MI, angina, increased thermogenesis
- Hemorrhagic and/or ischemic stroke, subarachnoid hemorrhage, cerebral vasculitis, seizures
- Bronchial dilation, acute hepatitis
- Preterm labor

Overview/Pharmacology

- Mechanism of action is via increases in sympathetic stimulation.
- Ephedrine is an indirect-acting sympathomimetic that exerts its effects mainly by stimulating release of norepinephrine.
- Other ephedrine alkaloids in ephedra have direct-acting effects on both α- and β-adrenoceptors.
- Ephedra is often packaged with guarana-derived caffeine, which may synergistically augment adrenergic stimulation.

Drug Class/Mechanism of Action/Usual Dose

- Works via stimulation of the sympathetic nervous system.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmias, Htn, myocarditis, MI, angina thermogenesis	Chest pain	BP Increased temperature	BP/HR, ECG, cardiac enzymes Temperature probe
GU	Acute hepatitis			LFTs
CNS	Stroke, subarachnoid hemorrhage, vasculitis, seizure	Decreased mental status Headache	Neuro exam	CT, vascular biopsy, EEG
RESP	Bronchial dilation			PFTs

Key References: Ang-Lee MK, Moss J, Yuan CS: Herbal medicines and perioperative care, *J Am Med Assoc* 286(2):208–216, 2001; Wang CZ, Yuan CS, Moss J: Anesthetic implications of complementary and alternative medications. In Miller RD, editor: *Miller's anesthesia*, ed 8, Philadelphia, 2015, Elsevier, pp 1226–1239.

Perioperative Implications

Preoperative Period

- Ephedra may produce adverse pt reactions with medications such as MAO inhibitors, digoxin, cold medications containing ephedrine, diuretics, and antihypertensives.
- Assess preop BP, HR, and ECG.
- Consider as a potential cause of preterm labor.

Preinduction/Induction Period

- Control hemodynamics before induction.
- Observe ECG for arrhythmias.

Maintenance Period

- Response to ephedrine may be hampered secondary to tachyphylaxis; therefore, control hypotension with direct-acting adrenergic agonists, like phenylephrine.
- Ephedra may interact with volatile anesthetics (e.g., enflurane) to promote dysrhythmias.

Postoperative Period

- Assess postop BP, HR, and ECG for CV changes.

Evening Primrose

John A. Helmstetter | Alan David Kaye

Uses

- Evening primrose oil (EPO) is obtained from the seed of the plant species *Oenothera biennis*.
- EPO is also known as fever plant, huile d'onagre, king's cureall, night willow-herb, scabish, suncups, and sundrops.
- EPO may be used as a food supplement for the essential fatty acids, linoleic acid (LA), and γ-linolenic acid (GLA).
- Infusion of the whole plant has been used for asthma, GI disorders, whooping cough, and as a sedative pain killer.
- Other evidence indicates that orally administered primrose oil does not relieve symptoms of premenstrual syndrome and does not have any effect in shortening the length of pregnancy and labor.
- EPO had been licensed in Britain for treatment of atopic eczema and cyclic and noncyclic mastalgia. Cochrane meta-analysis found that evening primrose oil capsules were ineffective for eczema.
- Other potential uses for EPO include PMS, psoriasis, MS, hypercholesterolemia, rheumatoid arthritis, Raynaud phenomenon, Sjögren's syndrome, postviral fatigue syndrome, asthma, and diabetic neuropathy. Without solid evidence it is effective, but with recurrent anecdotal evidence of beneficial outcomes.

Perioperative Risks

- Speculation that EPO may increase risk of temporal lobe epilepsy or reduce the seizure threshold in schizophrenic pts taking epileptogenic drugs (e.g., phenothiazines).
- EPO may cause a decrease in blood clotting.

Worry About

- Obstetrics: Oral EPO administration during pregnancy may have an association with a protracted phase of labor, prolonged rupture of membranes, oxytocin augmentation, vacuum extraction, and arrest of descent. One case report exists of transient petechiae and ecchymosis in a newborn after 6.5 g of oral EPO intake by the mother the week before birth.

Overview/Pharmacology

- EPO is a rich source of the essential fatty acids LA and GLA. These essential fatty acids are involved in prostaglandin biosynthetic pathways.
- DGLA, a metabolite of GLA, is a precursor of both the inflammatory prostaglandin series via arachidonic acid (AA), and the less inflammatory series (PGE_1).
- Actions of PGE_1 include anti-inflammatory, immunoregulatory, and vasodilatory properties; inhibition of plt aggregation and cholesterol biosynthesis; hypotension, and elevation of cyclic AMP.
- GLA has been shown to have a favorable effect on the DGLA:AA ratio. The increase in AA is smaller and less consistent when compared with the increase in DGLA. This is beneficial because DGLA leads to the less inflammatory prostaglandin series PGE_1.
- GLA is not normally obtained from the diet. The body relies on the metabolic conversion of LA to GLA. This conversion is rate limiting in the production of GLA. It has been shown that there is a reduced rate of conversion of LA to GLA in several clinical situations, incl aging, diabetes, CV disorders and high LDL cholesterol concentrations, high alcohol intake, viral infections, cancer, nutritional deficits, atopic eczema, and premenstrual syndrome. Dietary supplementation of GLA, via EPO, bypasses the rate-limiting conversion step and has a beneficial effect on the ratio of inflammatory to less inflammatory prostaglandin synthesis.

Drug Class/Mechanism of Action/Usual Dose

- Dose of EPO is specific for each condition being treated; for example, the EPO dose for atopic eczema is 6–8 g for adults or 2–4 g for children. These doses of EPO are based on standardized products containing 8% GLA. EPO may be swallowed directly, mixed with milk or another liquid, or taken with food. The clinical response is usually seen after 3–4 mo of continuous use.

Drug Effects

System	Effect*
CV	Inhibits increase of serum total cholesterol + VLDL + IDL + LDL cholesterol concentrations in the presence of excess cholesterol in the diet. Serves as an antioxidant in hyperlipemic states. Reduces oxidative stress by inhibiting lipid peroxidation and reinforcing the glutathione-dependent antioxidant defense system.
GI	Has antiulcer and cytoprotective effects on experimentally induced gastric lesions.
HEME	Reduces plt aggregation when subject fed an atherogenic diet.
DERM	May be used for Rx of atopic eczema. Treatment of atopic eczema with EPO is controversial. Clinical studies have been equivocal on whether symptoms of atopic eczema benefit from EPO. May be used for the treatment of limited scleroderma, or CREST syndrome. Clinical studies have been equivocal in relation to fatty acid placebos but have shown qualitative improvement in symptoms of Raynaud phenomenon.
GU	Has been used for PMS and to help reduce frequency of nighttime hot flashes during menopause. Treatment is controversial because clinical studies have not shown a clear benefit of EPO for PMS and menopause. Has been shown to be no better than fatty acid placebo or topical NSAIDs for treatment of mastalgia. Has been used by many midwives to hasten cervical ripening in an effort to shorten labor and ↓ incidence of postdate pregnancies. One retrospective study showed that EPO does not shorten gestation or ↓ length of labor. Moreover, it was found that EPO may be associated with above-mentioned adverse effects on labor.
CNS	Significantly reduced headache in women with PMS. Pts given both EPO and fish oil had fewer symptoms associated with headache, such as depression and fatigue. Animal studies suggest EPO may be useful in the treatment of diabetic neuropathy, although the exact physiologic mechanism remains to be demonstrated.
IMMUNE	In pts with mild RA, EPO has been shown to improve morning stiffness, and there was also improvement in the Ritchie articular index for each pt. Pts with severe RA did not exhibit improvement. Although not scientifically proved, EPO has been taken by asthmatics to gain the anti-inflammatory effects of PGE_1.

*EPO studies are in a preliminary phase; its effects have been proved only in animal models. The effects mentioned here have yet to be proved in humans.

Key References: Stonemetz D: A review of the clinical efficacy of evening primrose, *Holist Nurs Pract* 22(3):171–174, 2008; Evening primrose. *Natural medicines: pharmacist's letter/prescriber's letter natural medicines comprehensive database,* ed 13, Stockton, CA, 2012, Therapeutic Research Faculty, pp 608–611.

Perioperative Implications

Preoperative Concerns

- EPO may cause increased risk of developing temporal lobe epilepsy, specifically in pts taking known epileptogenic drugs such as phenothiazines. Seizures have not been seen in pts not taking phenothiazines.
- Insufficient evidence regarding its use with other drugs, such as antihypertensive agents or pressors, anticoagulants or antiplatelet agents, nonsteroidal anti-inflammatory drugs, as well as herbs and supplements that might affect plt aggregation.

Preinduction/Induction

- No known interactions

Maintenance

- No known interactions

Postoperative Period

- No known interactions

Fish Oil

Alan David Kaye | Rachel J. Kaye | Orlando J. Salinas

Uses

- Active ingredient for brain and retinal health (more than 40% of brain and retina is structural fat and more than 50% of fat in brain and retina is DHA).
- Decreases arrhythmias and deaths related to coronary artery disease.
- Important component for cell signaling.
- Data from the MIDAS trial indicate that 900 mg of DHA (about 3 g of fish oil) per d in pts with minimal cognitive dysfunction restored memory to that of a person 3.5 y younger.
- Data from a trial in non-breastfed infants indicate better IQ by about 16 points in babies who were formula fed with 20 mg of DHA per d compared with those fed formula without DHA.
- While reducing plasma concentrations of triglycerides, also reduces elevated VLDL and chylomicrons and causes slight elevation in HDL; tends to reduce risk of death from CAD as well as the risk of stroke.
- Lowers BP (minimal effect).
- Decreases the risk of arrhythmias and MI.
- Beneficial antithrombogenic from EPA (DHA has no anticlotting effect) and anti-inflammatory effects from DHA or EPA

- Management of collagen vascular diseases (lupus, psoriasis, Raynaud phenomenon) and promotion of symptomatic improvement in rheumatic disease.
- May prevent immunologic injury in pts with IgA nephropathy by retarding loss of renal function. May benefit renal transplant recipients treated with cyclosporine. Significant beneficial effects on diabetic nephropathy and macroangiopathy.
- Beneficial in chronic and severe mental disorders (bipolar disorder, depression, ADHD, dementia).
- Reduces inflammatory symptoms associated with inflammatory bowel diseases.
- Other uses: Dysmenorrhea, kidney stones, diabetic neuropathy, gout, migraine headaches, male infertility, osteoporosis, multiple sclerosis, cancer-related cachexia, modest reduction in cataract risks, may improve risk of depression.

Perioperative Risks

- Risks of long-term use not known. Variable increase in bleeding time with EPA (but not with DHA).

Worry About

- Coagulation disorders; >3 g/d can inhibit blood coagulation and potentially reduce platelet aggregability, thus increasing risk of bleeding.
- Large doses of fish oil have been linked to a theoretical increased incidence of cancer via an increase in free radicals and elevated oxidate stress (e.g., prostate cancer). However, it should be noted that another study has demonstrated that omega-3 fatty acids protect against death from prostate cancer.

Overview/Pharmacology

- Omega-3 fatty acids: EPA and DHA.
- Also known as cod liver oil, marine oil, menhaden oil, N-3 fatty acids, N3-polyunsaturated fatty acids, omega 3, omega-3 fatty acids, polyunsaturated fatty acids, salmon oil, W-3 fatty acids, algal DHA.
- Dietary supplements available in capsules or oil by brand names: Coromega, Solgar Omega 3 700, Nature Made, Spring Valley, Bounty, Barleans, LifeFitness DHA, Nature Made DHA, and others.
- Recent research has focused on omega-3 fatty acids and omega-6 fatty acids and their respective ratios, with 1:1 and 4:1 ratios having more omega-6 fats that appear to be beneficial (greater omega-3 fatty acids levels are associated with inflammation-mediated chronic disease).
- Fish oils and DHA supplements are not regarded as drugs and, except for Lovaza, are not regulated by the FDA.
- Have biologic effects on prostaglandins, thromboxanes, and leukotrienes; they increase levels of TXA_3 and decrease levels of TXA_2, thus stimulating formation of prostaglandin I_3, moderately reducing the formation of TXB_2 in platelet, and inhibiting aggregation and adhesion.
- Use results in reduced platelet aggregation (EPA) and vasoconstriction (DHA).
- Recent studies show a small increase in levels of LDL with large doses.
- Improves large artery endothelium-dependent dilation of hypercholesterolemics (both EPA and DHA) without affecting endothelium-independent dilation.
- Reduces blood viscosity by increasing deformability of RBCs.
- Substantial reduction of triglyceride levels; variable effects on cholesterol levels.

Drug Class/Usual Dose

- Not clear: Usual dosage is 2–9 g/d of fish oil or 20 mg per year of life up to age 45 (900 mg), where dose stays constant (DHA).

Assessment Points

System	Effect	Assessment by Hx	PE	Test
GI	Abdominal distention, belching, halitosis, heartburn, flatulence, diarrhea			
HEME	Prolongs bleeding time, inhibits platelet aggregation (EPA only)	Anticoagulant Rx, fatigue, weakness, bleeding problems	Vital signs	Bleeding time, Hct
ENDO	Mild glucose intolerance in pts with NIDDM	FBS		

Key References: Kris-Etherton PM, Harris WS, Appel LJ; American Heart Association Nutrition Committee: Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease, *Circulation* 106(21):2747–2757, 2002; Yurko-Mauro K, McCarthy D, Rom D, et al.: Beneficial effects of docosahexaenoic acid on cognitive function in age-related cognitive decline, *Alzheimers Dement* 6(6):456–464, 2010.

Perioperative Implications

Preoperative Concerns

- May reduce blood clotting and increase risk of bleeding (not an effect of DHA alone); pts on 3 g of fish oil per d can be switched to 900 mg of DHA a d with perhaps same antiarrhythmic and brain-function-preserving effects; half-life is variable depending on preparation. Ideally a pt having surgery or a pain procedure should be off fish oil for 7 d, allowing enough time for fish oil–induced blood thinning effects to be gone, but patient should also be switched to DHA at same time.

Induction/Maintenance

- No interactions known.

Adjuvants/Possible Drug Interactions

- Caution if pt is receiving heparin, warfarin, dipyridamole, ticlopidine, sulfinpyrazone, or aspirin.
- Can reduce vitamin E levels. Caution with herbals that have antiplatelet and/or anticoagulant constituents (angelica, clove, danshen, garlic, ginger, ginkgo, *Panax* ginseng, red clover, turmeric, willow, and others) with EPA, not DHA.

Anticipated Problems/Concerns

- Assess for possible adverse effects on the coagulation system.
- Rare side effects include abdominal pain with cramps, blurred vision, diarrhea, dizziness, fatigue, headache disorder, nausea.
- Medical-grade fish oil is now available (Lovaza), which reduces indirect risk of mercury polychlorinated biphenyls, dioxin, and dioxin-related compounds, as does DHA from algae (algal DHA).

Garlic *(Allium sativum)*

Amit Prabhakar | Alan David Kaye

Uses

- Administered orally and topically as a powder, oil, tablet, and raw clove. Allicin is the pharmacologically active component.
- Potentially beneficial to the CV system as an antihyperlipidemic (conflicting results in recent clinical trials); also useful as an antimicrobial (*Microsporum canis*, sporotrichosis, tinea pedis), antiplatelet (via increased thromboxane levels), fibrinolytic, antioxidant (increased catalase and glutathione peroxidase), antidiabetic, and vasoprotective agent (i.e., antihypertensive and protective of elastic properties of the aorta).
- Note: These indications are not approved by FDA, but garlic is generally recognized as safe. Interpretation of data must take into account publication bias (preferential publication of positive findings).

Perioperative Risks

- Increased bleeding diathesis via inhibition of platelets mediated by COX inhibition.

Worry About

- Major drug interactions: Anticoagulants, antidiabetic agents, ASA, NSAIDs, plt inhibitors, herbs (danshen, dong quai, feverfew, ginger, ginkgo biloba, ginseng, horse chestnut), thrombolytic agents.
- Garlic has dose-dependent side effects, including breath and body odor, possible stimulation of the uterus, GI irritation and heartburn, nausea, vomiting, diarrhea, allergic reactions, dermatitis, and other skin-related pathogenesis.

Overview/Pharmacology

- Intact cells of garlic bulbs contain alliin, an odorless, sulfur-containing amino acid. Crushed garlic causes the enzyme allinase to convert alliin to allicin—a potent antibacterial agent that is odoriferous and unstable. Ajoene, a self-condensation product of allicin, has antithrombotic activity. Fresh garlic releases allicin in the mouth during the chewing process. Dried garlic preparations lack allicin but contain alliin and allinase; they should be enteric-coated so that they will pass through the stomach into the small intestine, where alliin can be enzymatically converted to allicin. Allicin is unstable in oil. Allinase is inactivated by heat (cooking) and acid.
- Potency can vary substantially among manufacturers.
- Dosage: No clear consensus, but dosage varies with reason for use. Hypercholesterolemia/arteriosclerosis: German Commission E recommends 4 g/d (1.5–2 average-sized garlic cloves) of fresh garlic, or at least 5000 μg of allicin, or chewing one garlic clove daily. Extract standardized to 1.3% allicin is

recommended. For Htn or antibacterial effect, 2.5 g/d or 1 clove or 300 mg of extract.
- Treatment should be evaluated over a 3- to 6-mo period to determine efficacy. To treat *M. canis*, sporotrichosis, and tinea pedis, recommended oral dosage is 2–5 mg of allicin extract; topical treatment calls for applying sliced cloves or garlic extract (ajoene) to lesion 2–3 times daily for 1–2 wk.
- Usual dosage is 300 mg of extract 2–3 times daily standardized to at least 1.3% allicin (equivalent to approx 3 g or 1 fresh clove daily).
- Moderate daily consumption has no effects on normal individuals. Effects are not seen with cooked garlic.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Reduced BP, reduced LDL cholesterol			BP, lipid profile
RESP		Halitosis, sulfuric odor		
ENDO	Hypoglycemia	Insulin, oral hypoglycemic use		Fasting blood glucose
HEME	Bleeding	Anticoagulant use, coagulopathy, dysfunctional platelets, bleeding disorders	Hematomas; poor surgical hemostasis	Prolonged PT, INR, plts, Hgb/Hct
GU		more than 5 cloves daily		
Low dose	Enhanced peristalsis	Dyspepsia, eructation, pyrosis (heartburn), flatulence		
Large doses	Inhibited peristalsis; possible reduction in stomach cancer	Constipation		
CNS	Spontaneous spinal epidural hematoma	Headache, paralysis	Neurologic examination	CT scan
ALLERGY/IMMUNE	Allergic reaction	Garlic oil contact dermatitis	Facial/tongue swelling	

Key References: Tsai CW, Chen HW, Sheen LY, et al.: Garlic: health benefits and actions, *BioMedicine* 2:17–29, 2012; Gardner CD, Lawson LD, Block E, et al: Effect of raw garlic vs. commercial garlic supplements on plasma lipid concentrations in adults with moderate hypercholesterolemia: a randomized clinical trial, *Arch Intern Med* 167(4):346–353, 2007.

Perioperative Implications

Perioperative Concerns/Possible Drug Interactions
- High consumption may cause significant antiplatelet activity; ASA, NSAIDs, other platelet inhibitors, thrombolytic agents, and certain herbs may cause risk of bleeding, but no clinical data are available.
- Hypoglycemia may be increased in individuals receiving antidiabetic agents.
- Garlic can interfere with oral contraceptives.
- Garlic is not recommended for individuals with thyroid disease.

Monitoring
- Preop PT (INR), blood glucose levels

Airway
- Malodorous breath and skin

Preinduction/Induction
- No special concerns

Maintenance
- Monitor blood glucose levels.

Extubation
- No special risks

Adjuvants
- No special risks

Postoperative Period
- Theoretically increased risk of bleeding and hypoglycemia

Anticipated Problems/Concerns
- Possible increased risk of bleeding and hypoglycemia
- Pts who are avid garlic consumers should not double up doses to make up for missed doses while undergoing surgery.
- If on warfarin postop, pts should be warned against heavy consumption.

Ginger *(Zingiber officinale)*

Mark R. Jones | Alan David Kaye

Uses
- Ginger ranks 18th in recent herbal supplement sales.
- Has long been used in Ayurvedic and Chinese medicine for a wide variety of conditions including arthritis, rheumatism, constipation, indigestion, nausea, vomiting, motion sickness, and diabetes mellitus.
- In vivo human studies show ginger to be effective in management of N/V postop and in association with pregnancy. Clinical research demonstrates potential effectiveness of ginger for dysmenorrhea, vertigo, morning sickness, and osteoarthritis.
- In vivo animal studies show ginger has significant anti-inflammatory, antithrombotic, hypotensive, glucose-lowering, and lipid-lowering effects.
- In vitro studies show ginger has significant antioxidant, antitumorigenic, anti-inflammatory, antiviral, and antimicrobial effects.
- Anecdotal or inconsistent evidence for ginger treatment in chemotherapy-induced nausea and vomiting, migraine headache, myalgia, and rheumatoid arthritis.

Perioperative Risks
- No toxic or unpleasant side effects reported in human studies with therapeutic doses.
- High doses may prolong bleeding time due to inhibition of thromboxane synthetase and stimulation of prostacyclin.
- High doses may lower BP.

Worry About
- Potential additive or synergistic effects with antiplatelet agents, heparin, or warfarin, which may increase bleeding risks.
- Potential hypotensive effect and additive effect with calcium channel blockers.
- Preliminary research demonstrates that ginger increases insulin levels. Therefore it could have an additive effect with any antidiabetes drugs and result in hypoglycemia (particularly important with NPO instructions).

Overview/Pharmacology
- Pungent constituents: Gingerol, shogaol, gingerdiols, vanilloids, sesquiterpene, monoterpene volatile oils, and diarylheptanoids. These constituents have a variety of pharmacologic properties, including antipyretic, antitussive, anti-inflammatory, sedative, antibiotic, and weak antifungal effects.
- Plasma concentration curve is defined by a two-compartment model with a terminal half-life of 7.2 min and total body clearance of 16.8 mL/min per kg.
- 92.4% of ginger is serum-protein–bound with elimination by the liver and gut flora.

Mechanism of Action
- Anti-5-HT_3 mediates antiemetic effects.
- Direct cholinergic agonist of postsynaptic M_3 receptors and an inhibitor of presynaptic muscarinic autoreceptors. May mediate GI prokinetic effects.
- The aqueous extract of red and white ginger rhizomes displays anticholinesterase inhibitory action, thereby increasing levels of Ach in the synaptic junction, which may improve cholinergic neurotransmission.
- Cyclo-oxygenase and lipo-oxygenase inhibition: Mediates anti-inflammatory and antithrombotic effects by decreasing levels of thromboxane B_2, prostaglandin E_2, and leukotrienes.
- Inhibition of cytokine and chemokine induction in vitro: Mediates anti-inflammatory effects.
- Insulin sensitization mediates hypoglycemic and lipid-lowing effects.
- Calcium channel inhibition mediates decrease in BP and negative inotropic and chronotropic effects.
- Vanilloid mediates induction of apoptosis: antitumorigenic effects.
- Antioxidant effects may be hepatoprotective and nephroprotective.

Usual Dosage/Indications
- Dosage: The total daily dose is typically 1–4 g with an onset of antiemetic effect within 25 min and duration up to 4 h.
- Doses as high as 15 g/d well tolerated in human trials.

- Indications:
  - May be used to prevent pregnancy-associated and postop N/V.
  - Shows promise as therapy for postchemotherapy N/V.
  - May be used to alleviate dyspepsia and loss of appetite.
  - May have anti-inflammatory and antithrombotic effects.
  - Taken before exercise, 4 g of ginger significantly decreases muscle soreness.
  - May be useful as an insulin sensitizer.
  - May be useful in decreasing serum lipid and cholesterol levels.
  - Recent in vivo animal studies of ginger have shown cognition-enhancing effects and a possible role in treatment of dementia.
- Contraindications: Must be used carefully in combination with antiplatelet drugs, warfarin, or heparin owing to potential for increased bleeding risks.

Assessment Points

System	Effects (Based on Animal/Human Studies)	Assessment by Hx	PE
CV	Hypotensive Augments inotropic effect by increase in Ca efflux across sarcoplasmic reticulum Large doses may lead to cardiac arrhythmias		BP/HR
GI	Increases gastric and intestinal motility as well as gastric, bile, and salivary secretions Antiemetic May be hepatoprotective		
RESP	Antitussive		
HEME	Inhibits thromboxane synthetase Acts as a prostacyclin agonist	Herb use Symptoms of bleeding Antiplatelet agents, heparin, or warfarin	
CNS	Prolongs duration of anesthesia induced by barbiturates Antipyretic through prostaglandin inhibition Large quantities may cause central nervous system depression		

Key References: Ali BH, Blunden G, Tanira MO, et al.: Some phytochemical, pharmacological and toxicological properties of ginger: a review of recent research, *Food Chem Toxicol* 46(2):409–420, 2008; Grzanna R, Lindmark L, Frondoza CG: Ginger—a herbal medicinal product with broad anti-inflammatory actions, *J Med Food* 8(2):125–132, 2005.

Perioperative Implications

Preoperative Period
- Possible interaction with antiplatelet agents or warfarin

Induction
- May potentiate barbiturates.
- May potentiate hypotension.

Postoperative Concerns
- May increase bleeding complications.

Anticipated Problems/Concerns
- May increase bleeding complications when used with antiplatelet drugs, warfarin, or heparin.
- Consider avoiding use in the presence of gallstone conditions.
- May potentiate periop hypotension.
- May cause hypoglycemia, requiring adjustment of DM medication regime.

Ginkgo biloba

Jonathan G. Ma | Jonathan P. Eskander | Alan David Kaye

Uses
- Antioxidant and polyphenol properties.
- Improved cognitive performance in pts with Alzheimer disease, particularly short-term visual memory and speed of cognitive processing, for 6 mo to 1 y.
- Improved cognitive performance in vascular dementia and may be neuroprotective in pts with preexisting cerebral ischemia.
- Used to improve symptoms of intermittent claudication, Raynaud phenomenon, and acrocyanosis. Evidence for effectiveness is debated.
- *Ginkgo biloba* extract (GBE) used in pts with normal-tension glaucoma and those with early diabetic retinopathy, improving measures of colored vision; also possibly effective in treating age-related macular degeneration, symptoms of vertigo and other equilibrium disorders, depression, anxiety, and vitiligo.
- GBE is believed to work via the dopaminergic system, which modulates prolactin secretion. One study has shown that it enhances the copulatory behavior of male rats.

Perioperative Risks
- Increased risk of bleeding and drug interactions; therefore the ASA recommends stopping 2–3 wk prior to surgery since the half-life of a given ginkgo preparation is unknown.
- Lack of safety data in certain populations; therefore not recommended for use in pregnancy, breastfeeding, and in children <12 y of age.
- Commonly reported side effects include N/V and diarrhea, headache, and bleeding.

Worry About
- Spontaneous bleeding can occur related to the inhibition of platelet aggregation.
- Risk of bleeding is further increased if combined with antithrombotic drugs (aspirin, NSAIDs, clopidogrel, dipyridamole), anticoagulant drugs (heparin, enoxaparin), and other herbal medicines known to increase bleeding (ginger, garlic, ginseng). Recent studies show that coagulation parameters were unchanged when GBE was coadministered with warfarin.
- Can decrease the effectiveness of numerous anticonvulsants (valproate, carbamazepine, phenobarbital, primidone, gabapentin, phenytoin); also ginkgotoxin, which is contained in a far greater concentration in the seeds, can cause seizures; anecdotal reports of seizure occurring after pts with and without epilepsy Hx took ginkgo leaf; finally, ginkgo has been shown to decrease alprazolam levels by 17% when GBE 120 mg taken 2 times daily.
- May enhance the effects of MAO inhibitors (phenelzine, selegiline, tranylcypromine) and increase the risk of serotonin syndrome when taken with SSRIs.
- Interactions have also been reported with CCBs, trazodone, acetylcholinesterase inhibitors, blood glucose–lowering medications, insulin, drugs for erectile dysfunction, and thiazide diuretics.
- Animal studies have shown that GBE induces pathologic changes in liver, thyroid gland, and nose, most notably an increase in liver tumors and thyroid gland follicle cell tumors. No human studies to verify these findings.

Overview
- Ginkgo (*Ginkgo biloba*) is one of the oldest tree species and GBE is one of the most common supplements used worldwide. Several extracts have been isolated.

Drug Class/Mechanism of Action/Usual Dose
- Active elements responsible for ginkgo's medicinal effects incl ginkgo flavone glycosides and terpene lactones, both obtained from the dry leaves.
- Extracts standardized to contain 24–27% of ginkgo flavone glycosides and 6% terpenes are commonly found in 40- to 80-mg oral capsules and recommended 3 times daily.
- Ginkgo has a wide range of properties: Antagonism of platelet activating factor, lowering of serum fibrinogen levels, stimulation of endothelium-derived relaxing factor, facilitation of prostacyclin release, and inhibition of nitric oxide.
- CNS effects are mainly attributed to ginkgo's antioxidant characteristics. By causing a decrease in superoxide release and acting as a scavenger of free radicals, ginkgo helps to prevent hypoxic damage to

brain tissue and improves cerebral metabolism. O_2 utilization in the brain may be improved and age-related changes in the animal hippocampus may be prevented.
- Additional studies indicate that ginkgo reversibly inhibits MAO-A and MAO-B, inhibits acetylcholinesterase, and decreases adrenal benzodiazepine receptors.
- Studies have shown that coadministration of warfarin with GBE or ginkoglide B (a platelet activating factor antagonist) influenced blood coagulation parameters. Ginkgo and its extracts were shown not to affect the clearance of warfarin enantiomers, suggesting that the herb does not significantly influence CYP1A2, CYP3A4, or CYP2C9 activity.

Assessment Points

System	Effect	Assessment by Hx	PE
HEENT	Increased ocular blood flow	Bleeding	Mucosal bleeding
CV	Vasodilation		BP/HR
HEME	Inhibition of platelet aggregation	Bleeding, bruising	Mucosal bleeding Petechiae
GI	N/V, diarrhea		
CNS	Increased cerebral blood flow Headache	Headache	
DERM	Contact dermatitis	Exposure	Rash

Key References: Jiang X, Williams KM, Liauw WS, et al.: Effect of ginkgo and ginger on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects, *Br J Clin Pharmacol* 59(4):425–432, 2005 ; Yeh KY, Pu HF, Kaphle K, et al.: *Ginkgo biloba* extract enhances male copulatory behavior and reduces serum prolactin levels in rats, Horm Behav 53(1):225-231, 2008 (epub 2007); Marcilhac A, Dakine N, Bourhim N, et al.: Effect of chronic administration of *Ginkgo biloba* extract or Ginkgolide on the hypothalamic-pituitary-adrenal axis in the rat, *Life Sci* 62(25):2329-2340, 1998.

Perioperative Implications

Preoperative Concerns
- Outside of potentially increased risk of bleeding, periop concern with ginkgo intake revolves around drug interactions.
- Minimal data on effects in pregnancy, breastfeeding, and pediatrics.
- Many pts do not account for alternative medicines when asked for medication lists by their physician.
- Inhibition of platelet aggregation can result in significant intraop bleeding; thus ginkgo should be D/C at least 36 h before elective surgery.

Monitoring
- Routine

Airway
- Avoid nasal intubation to minimize intranasal bleed.

Preinduction/Induction
- Avoid excessive hypotension with induction agents because ginkgo's subtle vasodilatory effects can further decrease BP; effects on the adrenal receptors minimize a normal stress response. Hence prolonged and excessive hypotension can jeopardize perfusion of vital organs.

Maintenance
- Side effects can be amplified with concomitant use of interacting drugs. Such concerns include bleeding, hypotension, seizures, sedation, serotonin syndrome, and cholinergic crisis.

Extubation
- No known concerns

Postoperative Period
- Avoid administering classes of drugs that may interact with ginkgo and potentiate its effects, as previously mentioned.

Novel Therapies
- Can improve cerebral oxygen supply, decrease cerebral oxygen extraction rate and consumption, reduce cerebral oxygen metabolic rate, and maintain balance of cerebral oxygen supply and demand in elderly pt with preexisting cerebral ischemia.
- May ameliorate neuropathic pain by scavenging reactive oxygen species, contribute to hypersensitivity neuropathic pain.

Ginseng

James G. Hilliard | Jeffery R. Kirsch

Uses
- Ginseng has been used for more than 2000 y in Chinese herbal medicine for a variety of proposed health benefits.
- Used as an adaptogen, it is believed to increase the body's resistance to stress and fatigue.
- Known to have antistress, antifatigue, antiviral, antifungal, antineoplastic, neuroprotective, and antihyperglycemic effects

Perioperative Risks
- Ginseng blocks morphine in a non–opioid-dependent manner.
- Ginseng has the ability to lower postprandial blood glucose in both pts with diabetes type 2 and nondiabetic pts.
- Ginseng may promote bleeding in surgical pts. Ginsenosides (the active ingredients) in American ginseng have been shown to inhibit platelet aggregation. Studies in lab rats show prolongation of the coagulation time of thrombin and activated partial thromboplastin. One study suggests that the antiplatelet activity of panaxynol, a constituent of ginseng, may be irreversible in humans. Given these findings, it may be prudent to recommend that pts discontinue ginseng use at least 7 d prior to surgery.

Worry About
- Reduced efficacy of opioids and unpredictable dosing requirements of analgesics.
- The development of hypoglycemia, especially in diabetic pts taking insulin or oral antihyperglycemic agents.
- May have additive effects when used with corticosteroids and may intensify the side effects of corticosteroids.
- May lead to development of headache, tremors, and manic episodes when used in pts receiving MAO inhibitors such as phenelzine.
- Interferes with the pharmacodynamics and drug-level monitoring of pts taking digoxin and may increase digoxin levels.
- May increase the risk of surgical bleeding owing to its antiplatelet effects and inhibition of the coagulation cascade.
- May have estrogen-like effects and should be avoided in pregnant or breastfeeding women and in children. Avoid the use of ginseng in pts with hormone-sensitive conditions, such as breast cancer, uterine cancer, or endometriosis.
- Consumption can increase and/or decrease BP. Caution should be used in those with hypertension or hypotension.

Overview
- *Ginseng* refers to several species of the genus *Panax* and comprises a family of plants (American ginseng, Asian ginseng, Chinese ginseng, Korean red ginseng, *Panax ginseng*: *Panax* spp., including *P. ginseng* C.C. *Meyer*, and *P. quinquefolius L.*, excluding *Eleutherococcus senticosus*).
- Dietary supplements are typically derived from American ginseng (*Panax quinquefolius*) or Asian ginseng.
- Siberian ginseng (*Eleutherococcus senticosus*) is a different genus and does not contain the ingredients believed to be active in the two forms used in supplements.
- Ginseng can be taken as fresh or dried roots, extracts, solutions, capsules, tablets, sodas, and teas; also used as a cosmetic agent.

Drug Class/Mechanism of Action/Usual Dose
- The active ingredients in American ginseng are panaxosides (saponin glycosides). The active ingredients in Asian ginseng are ginsenosides (triterpenoid glycosides).
- Most of the pharmacologic actions of ginseng are attributed to the ginsenosides belonging to a group of compounds known as *steroidal saponins*.

Drug Effects		
System	**Effect**	**Test**
CV	Tachycardia, palpitations, Htn with other cardiac stimulants, edema	HR, BP
HEME	Decreases effectiveness of warfarin, inhibits coagulation cascade	INR, PT, PTT
NEURO	Excessive use: Somnolence, hypertonia, nervousness, and excitability mania in pts on phenelzine Reduces analgesic effect of morphine	
ENDO	Hypoglycemia	Blood glucose
GYN	Mastalgia, postmenopausal bleeding	Hct

Key References: Volger BK, Pittler MH, Ernst E: The efficacy of ginseng. a systematic review of randomized clinical trials, *Eur J Clin Pharmacol* 55(8):567–575, 1999; Tokuyama S, Takahashi M: Pharmacological and physiological effects of ginseng on actions induced by opioids and psychostimulants, *Japan J Pharm* 117(3):195–201, 2001.

Perioperative Implications

Preoperative Concerns
- Check coagulation studies; monitor blood glucose.

Monitoring
- Standard

Induction
- Increased amounts of opioids may be required to blunt adrenergic response to intubation.

Airway
- No specific concerns

Postoperative Concerns
- Monitor blood glucose level, monitor for signs of excessive postop bleeding.
- Increased amounts of opioids may be required to manage postop pain.

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Glucosamine Sulfate

Bridget Perrin Pulos

Uses
- For pain associated with OA, particularly of the knee
- IBD
- Other inflammatory disorders, such as rheumatoid arthritis, psoriasis
- Possible benefits for wound healing and prevention of migraines

Perioperative Risks
- No convincing evidence of increased periop risk owing to glucosamine therapy
- No known significant interactions with commonly administered anesthetic drugs

Worry About
- Potential increase in INR in pts on warfarin who initiate glucosamine therapy, or increase glucosamine dose

Overview
- Available without a prescription in North America.
- Classified as a food additive, not regulated by the USA FDA, made from crustacean skeletons.
- As monotherapy, little consistent evidence of therapeutic effect.
- Often used in combination with other drug supplements, such as chondroitin.
- In combination with chondroitin, may prolong the time to total knee replacement in those with severe OA.
- Side-effect profile is indistinguishable from placebo and better than that of NSAIDs.
- High oral bioavailability with substantial first-pass metabolism, freely diffusable with a 28- to 58-h half-life.

Drug Class/Mechanism of Action/Usual Dose
- Glucosamine is a component of the extracellular matrix of articular cartilage, found naturally in the body.
- Recommended oral dose is 1500 mg/d or 500 mg 3 times per d.
- Precise mechanism of action of glucosamine is unknown; thought to aid in cartilage repair, normalize cartilage metab, and have mild anti-inflammatory properties.

Assessment Points		
System	**Effect**	**Test**
HEME	May potentiate warfarin or increase risk of bleeding when taken with other drugs that increase risk of bleeding	PT/INR if pt is on warfarin
ENDO	No consistent effect	Glucose if otherwise indicated

Key References: Fransen M, Agaliotis M, Nairn L, et al.: Glucosamine and chondroitin for knee osteoarthritis: a double blind randomized placebo-controlled clinical trial evaluating single and combination regimens, *Ann Rheum Dis* 74(5):851–858, 2015; Altman RD: Glucosamine therapy for knee osteoarthritis: pharmacokinetic considerations, *Expert Rev Clin Pharmacol* 2(4):359–371, 2009.

Perioperative Implications
- Glucosamine therapy has no significant periop or anesthetic implications. No need to interrupt therapy for a surgical procedure, no reason to modify an anesthetic plan due to glucosamine, and there is no urgency with regard to restarting therapy postop.

Glycine

Alan David Kaye | Rachel J. Kaye | Mark R. Jones

Uses
- Inhibitory neurotransmitter in the brain stem and spinal cord.
- Glycine and GABA receptors may mediate the effects of inhaled anesthetics.
- A nonessential amino acid sold as a natural sugar substitute, a sedative, and an antacid; used to promote muscle growth and decrease Sx of BPH; also as a polyphenol and an antipsychotic.
- Glycine 1.5% used as a nonhemolytic irrigation solution during TURP.
- Antagonists of glycine binding to NMDA receptor complex are used as anticonvulsants.
- Attempts to use glycine and other NMDA agonists in schizophrenia have had little success.
- Intrathecal glycine is not different from placebo in the treatment of complex regional pain syndrome.

Perioperative Risks

- Incidence of TURP syndrome, a complication of TURP surgery, is 0.5–8%; mortality rate is 0.2–0.8%, even up to 25% in severe cases.
- Operative hysteroscopy intravascular absorption syndrome (OHIAS) can rarely result during hysteroscopy for endometrial ablation, septum resection, myomectomy, or polypectomy. The thick uterine wall necessitates distention pressures higher than those required for irrigation during TURP.
- Clinical presentation of glycine toxicity and hyponatremia may be difficult to distinguish from sepsis or DIC; most commonly presents 30–45 min after the completion of surgery, although can occur from 15 min after starting irrigation up to 24 h postop.
- Glycine metabolized to ammonia can lead to hyperammonemic encephalopathy.

Worry About

- Glycine irrigation is contraindicated in pts with anuria.
- TURP syndrome is thought to be due to hyponatremia, hypoosmolality, and elevated glycine levels due to absorption of irrigation fluid. Manifestations probably related to the glycine load include myocardial depression, hemodynamic changes, and visual disturbances. Other symptoms include burning sensations in the face, N/V, weakness, confusion, seizure, and coma.
- Glycine irrigation should be used with caution in pts with CHF.
- Recent case reports have demonstrated transient postop blindness following use of large quantities of glycine delivered through a rotatory pump set at an inappropriately high pressure and OHIAS, similar to TURP syndrome with hyponatremia, hypoosmolality, hyperglycinemia, and volume overload, including pulm edema.

Overview/Pharmacology

- Smallest amino acid; glycogenic; major inhibitory neurotransmitter.
- Glycine is inhibitory on ligand-gated, strychnine-sensitive Cl^- channel receptors but excitatory on strychnine-insensitive NMDA receptors, where it is a cofactor for activation of the NMDA receptor by L-glutamate.
- Glycine metabolism: Primarily transamination to serine and deamination to ammonia, which is converted to urea and excreted by the kidneys. A portion of absorbed glycine is excreted unchanged by the kidneys.
- Studies indicate that there are better irrigating fluids than glycine solution during monopolar TURP. In some studies, glycine has been at best equal but never superior to alternative fluids. Unlike alternate solutions, glycine has toxic properties that add to patient safety concerns associated with massive fluid absorption.

Drug Class/Usual Dose

- Glycine 1.5% solution is used as an irrigation solution during endoscopic procedures, especially TURP. It is nontoxic, has a refractive index close to that of water, and is nonhemolytic despite a hypotonic osmolality of 200–220 mOsm/L.
- Homeopathic use for BPH at 780 mg/d for 2 wk and then 390 mg for the next 3 mo.
- Glycine 30–60 g/d improves negative symptoms of schizophrenia.
- NMDA receptor allows influx of Na^+ and Ca^{2+}. Overstimulation of this channel leads to Ca^{2+} overload in neurons, which has been shown to be neurotoxic. Glycine antagonists at the NMDA receptor potentiate GABA receptor-mediated events, leading to increased Cl^- conductance, membrane hyperpolarization, and neuroprotection. Glycine site antagonists decrease the release of excitatory amino acids, such as glutamate, which are known to potentiate cerebral ischemic injury.
- Possible drug interactions: Clozapine, haloperidol, olanzapine, risperidone.

Hyperekplexia

- Hereditary disorder characterized by exaggerated startle reflex in response to unexpected acoustic, tactile, and other stimuli.
- Neonates with hyperekplexia may present with hypertonia, developmental delays, apnea, and sudden death.
- In some cases, a mutation encoding the postsynaptic inhibitory glycine receptors (GLRA1, GLRB) or presynaptic glycine transporter (SLC6A5), resulting in abnormal glycinergic neurotransmission, is present.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	T-wave depression or inversion, increased long-term risk of MI Htn or hypotension may occur in TURP syndrome	Homeopathic use or glycine 1.5% irrigation		BP, HR, ECG
HEME	Antagonists associated with aplastic anemia	Homeopathic glycine use	Skin/mucous membranes for infection/petechiae	CBC, peripheral smear, bone marrow biopsy
GU	Metabolites oxalate and glycolate may produce renal failure	TURP with glycine irrigation or homeopathic use		Chem 7
GI	Gastric antacid			
CNS	Glycine accumulates in cells, which increases cerebral edema, hyponatremia, hypotonicity. Direct toxicity account for neurologic symptoms in TURP syndrome Encephalopathy through ammonia metabolite; mitigates negative Sx of schizophrenia	Headache, N/V, visual changes, seizure, weakness, encephalopathy, lethargy	Mental status, visual acuity, strength	Serum, Na serum osmolality
RESP	Pulm edema (decreased with spinal anesthesia)	TURP	SOB, wheeze, frothy sputum	CXR, SpO_2

Key References: Hawary A, Mukhtar K, Sinclair A, et al.: Transurethral resection of the prostate syndrome: almost gone but not forgotten, *J Endourol* 23(12):2013–2020, 2009; Chau A, Roitfarb M, Carabuena JM, et al.: Anesthetic management of a parturient with hyperekplexia, *A A Case Rep* 4(8):103–106, 2015.

Perioperative Implications

Preoperative Period

- Elicit recent Hx of glycine use as homeopathic treatment.
- Anuria is a contraindication to use of glycine irrigation; caution with oliguric pts.

Induction/Maintenance

- No known interactions with homeopathic doses of glycine
- If pt is using glycine as a homeopathic antipsychotic, affect/mental status may be problematic given underlying disease and side-effect profile of this drug.
- Risk of TURP syndrome/OHIAS. Be aware of the degree of blood loss and amount of irrigation used. If RA used, monitor for symptoms of glycine toxicity: N/V, visual changes, weakness. Also monitor for hemodynamic instability; ECG changes, hypotension or Htn.
- With intraop onset of TURP syndrome/OHIAS, surgery should be terminated as soon as possible.

Postoperative Concerns

- TURP syndrome can occur within 15 min of beginning irrigation or as late as 24 h postop. Monitor for signs of changing mental status, hemodynamic instability, and seizures.
- Seizures, if caused by glycine activity on NMDA receptors, can be treated with NMDA receptor antagonists or glycine antagonists. Mg^{2+}, which may be low after TURP, exerts a negative effect on NMDA receptors, so a trial of Mg^{2+} therapy may be warranted.

Kava

Amy O. Soleta

Uses

- Treatment of anxiety, stress, nervousness
- Treatment of insomnia
- Treatment of muscular aches and pains
- Traditionally used in the South Pacific during religious and cultural ceremonies to achieve relaxation and for medicinal purposes

Perioperative Risks

- No data exist to quantify risk of adverse effects
- ASA recommends stopping herbal supplements as long as 2 wk prior to elective procedures.

Worry About

- Risk of hepatotoxicity, especially when combined with other hepatotoxic drugs
- Oversedation when combined with ethanol or other sedative drugs
- Potential to affect hemodynamic stability and coagulation

Overview/Pharmacology

- Oral administration: Peak effect 1.8 h, elimination half-life 9 h, metabolized in liver by cytochrome P450.
- Effects on various ion channels leading to decreased excitability of CNS.
- Enhanced binding and regulation of GABA receptors, leading to anxiolysis, sedation, muscle relaxation, and anticonvulsive effects
- Inhibition of limbic system, leading to decreased emotional excitability and mood enhancement
- Weak Na channel antagonism, leading to potential anticonvulsant effects
- Inhibition of calcium channels, leading to inhibition of vascular smooth muscle
- Reduced reuptake of dopamine and norepinephrine
- Inhibition of COX, leading to antithrombotic, analgesic, and anti-inflammatory effects

Usual Dose

- Highly variable dosing based on growing and harvesting conditions, plant parts and extraction techniques used, and dosage form chosen by manufacturer
- Active compounds are kavapyrones
- Anxiolysis: 105–210 mg kavapyrones daily for 3-4 wk

Toxicity

- Risk of hepatotoxicity; caution with concomitant use of other hepatotoxic herbs
- Potentiation of sedation with ethanol, barbiturates, benzodiazepines, opioids
- Risk of MAOI toxicity if taken with MAOIs

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Sedation	Headache, dizziness, dyskinesia	Mental status	Vital signs
CV	Hypotension	Lightheadedness, orthostasis	Decreased BP and HR	Vital signs
GI	Hepatotoxicity	Nausea, vomiting, abdominal pain, fatigue	Jaundice, ascites, edema	LFTs
RENAL	Decreased RBF	Oliguria, nausea	Peripheral edema, hypotension, tachycardia	Fluid challenge, BUN/Cr, lytes, urinalysis
HEME	Abnormal platelet aggregation	Use of other anticoagulants or antiplatelets, easy bruising, prolonged bleeding	Petechiae, hypovolemia	Elevated PT/INR, PTT, abnormal platelet function

Key References: Raduege KM, Kleshinski JF, Ryckman JV, et al.: Anesthetic considerations of the herbal, kava, *J Clin Anesth* 16(4):305–311, 2004; Horlocker TT, Wedel DJ, Rowlingson JC, et al.: Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition), *Reg Anesth Pain Med* 35(1):64–101, 2010.

Perioperative Implications

Preoperative Concerns

- Rely on pt self-report.
- Sedation.
- Consider preop LFTs, BUN/Cr, and coagulation studies if concern for concomitant disease.

Monitoring

- Standard

Regional Anesthesia

- No significant added risk, but use caution if combined with other anticoagulant/antiplatelet agents.

Emergence/Extubation

- Prolonged due to excess sedation

Postoperative Period

- Continue to monitor for increased sedation.
- Potential for prolonged bleeding.

Licorice *(Glycyrrhiza glabra)*

R. Blaine Easley

Uses

- One of the top 10 herbal medications utilized in USA.
- Historically used to improve immune function and treat a variety of conditions including PUD, duodenal ulcers, cough and/or bronchitis, atherosclerosis, chronic fatigue syndrome, various cancers, AIDS, and Addison disease. Most recently a study has demonstrated its effectiveness in relieving postop sore throat.

Perioperative Risks

- Unknown. Theoretical problems in pts with impaired renal function, Htn, chronic liver disease, cardiac arrhythmias, and hypertonia.
- Potential for drug interactions. Pseudohyperaldosteronism has been produced experimentally in healthy subjects taking >100 g/wk.

Worry About

- Pseudohyperaldosteronism: Documented mineralocorticoid effects that result in fluid retention, hypernatremia, hypokalemia, and edema.
- Hypertension: Direct effects on vascular smooth muscle tone independent of mineralocorticoid properties.
- Vasospasm and/or headache: Recent case reports of cerebral artery spasm causing severe headache, visual disturbances, and potential ischemia.
- Hypokalemia and/or muscle weakness: Chronic usage related to hypokalemic myopathies, muscle cramps, and skeletal muscle spasms.
- Arrhythmias: Rare side effect but more worrisome in pts with Hx of arrhythmias requiring medication (e.g., digoxin).
- Paresthesias: Numbness in extremities may be a sign of licorice toxicity.

Overview/Pharmacology

- Licorice is the common name given to various substances derived from the plant root *Glycyrrhiza glabra*, also known as Spanish licorice. This plant is a perennial that grows 3–7 feet high and originated in Europe and Asia. Also called sweet root and licorice root.
- Glycyrrhizin and/or glycyrrhizic acid (the glucoside form) and glycyrrhetinic acid (the glycoside form) are the most important substances or metabolites found in licorice. The roots also contain coumarins, flavonoids, volatile oils, and plant sterols.
- Licorice and its components are metabolized and excreted by the liver and kidneys.
- Mineralocorticoid effects of licorice, via glycyrrhetinic acid, result from the inhibition of 11-β-hydroxysteroid dehydrogenase (an enzyme that normally inactivates cortisol by converting its C11 alcohol to a ketone). Excess glucocorticoids then bind to mineralocorticoid receptors and produce a mineralocorticoid response, as evidenced by increased sodium retention and Htn. Thus licorice ingestion creates a syndrome of hyperaldosteronism characterized by hypernatremia, Htn, hypokalemia, and suppression of the renin-angiotensin system.
- Glycyrrhetinic acid also inhibits 15-hydroxy-prostaglandin dehydrogenase and prostaglandin reductase. These two enzymes are important in the metabolism of prostaglandin E and F_2, perhaps explaining licorice's immunologic benefits, effects on reducing cough and/or bronchospasm, protection of gastric mucosa, and benefit by decreased platelet aggregation.
- Glabridin has antioxidant and potential wound/ulcer healing properties.

Drug Class/Usual Dose

- Made from peeled and unpeeled dried root compounded and sold as a powder, dry extract, and liquid extract. In some preparations, such as DGL, harmful

components have been removed. Unfortunately preparation and advertising of these compounds is unregulated by the FDA.
- Licorice is taken in the following manner
  - Dried root: 1–5 g PO 3 times daily up to 6 wk (indication: general use).
  - Extract: (1:1 preparation) 2–5 mL PO 3 times daily up to 6 wk (indication: general use)
  - DGL extract: 1.5–3 g/d for peptic ulcer
  - DGL extract: 380–760 mg PO 20 min before meals for peptic ulcer

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CNS	Headache Visual changes Paresthesias	Exposure/use of licorice	Visual acuity Sensory exam	Neurologic consult, possible MRI
CV	Hypovolemia Hypervolemia Htn Arrhythmia	Exposure/use of licorice	BP/HR, consider orthostatics	ECG rhythm strip
GI	Black stools (rare) Laxative effect	Report of loose dark stool	Abdominal exam	Stool guaiac
HEME	Decreased clotting (rare)	Bleeding problems	Plts, PT/PTT	
ENDO	Hyperglycemia Hypernatremia Hypokalemia	Exposure/use of licorice Weight gain, increased urination		Serum chemistries

Key References: Kaye AD, Clarke RC, Sabar R, et al.: Herbal medicines: current trends in anesthesiology practice—a hospital survey, *J Clin Anesth* 12(6):468–471, 2000; Ruetzler K, Fleck M, Nabecker S, et al.: A randomized, double-blind comparison of licorice versus sugar-water gargle for prevention of postoperative sore throat and postextubation coughing, *Anesth Analg* 117(3):614–621, 2013.

Possible Drug Interactions

Preoperative Period

- Multiple adverse drug interactions reported in pts using licorice preparations and prescription medications. Licorice can interfere with the function of hormone supplements (e.g., birth control pills), oral hypoglycemic agents, and corticosteroids. Lyte imbalances and GI symptoms can be worsened by usage of licorice with diuretics and laxatives. Digoxin usage and licorice-induced hypokalemia can be potentially arrhythmogenic.
- Lyte abnormalities of hypokalemia, hypernatremia, and metabolic alkalosis should be sought and corrected before surgery in high-dose frequent users.
- Pt should be instructed to discontinue use of the herbal medicine approx 2 wk before elective surgery.

Induction/Maintenance

- No known interactions with licorice metabolites. However, pseudohyperaldosteronism should be considered and anesthetic management directed at the problems of hypokalemia, Htn, and fluid status. Placement of an arterial line and/or central venous line should be considered in symptomatic pts. (See Hyperaldosteronism, Secondary.)

Adjuvants/Regional Anesthesia/Reversal

- No known interactions. Consider pros and cons of NSAID use intraop, especially if no assessment of renal function. Careful attention to neurologic exam and/or paresthesias before initiation of regional technique.

Emergence/Extubation

- No known interactions. Acute topical preop and postop administration (by gargle) has been used without adverse effect to prevent postop sore throat. However, hypokalemia with or without a Hx of muscle weakness could potentially modify response to nondepolarizing muscle relaxants.

Postoperative Concerns

- Failure of resolution of preop symptoms attributed to licorice use with D/C of licorice-containing compound should prompt investigation of other causes.
- Continued monitoring of fluid and lyte status. If problems with hypokalemia continue despite potassium supplementation, consider potassium-sparing diuretics (e.g., triamterene) or a competitive aldosterone antagonist (e.g., spironolactone); investigate other possible causes.

Melatonin (*N*-Acetyl-5-Methoxytryptamine, Bevitamel, Vitamist, Melatonex)

Ori Gottlieb

Uses

- Regulates sleep-wake cycles.
- Prescribed for jet lag, shift work, depression.
- Use as antineoplastic, antidelirium, and anticonvulsant is under investigation.
- Questionable benefit in treating breast cancer and migraines.
- Categorized as a nutraceutical (unregulated).

Risks

- Not controlled by FDA; therefore quality and potency may vary.
- May interact with other CNS-acting medications such as hypnotics, sedatives, or psychotropics.
- Not recommended in children or pregnant/breast-feeding women owing to insufficient data
- May cause excessive somnolence.
- Use of animal-source melatonin products is not recommended because of risk of viral contamination or infection.

Overview/Pharmacology

- Secretion modulated by hypothalamic enzymes in response to a dark environment.
- Exogenous routes of administration: Oral tablets, capsules, lozenges, teas, sprays.
- Unlike endogenous melatonin, oral doses undergo first-pass hepatic metabolism with a bioavailability of 30–50%.
- Crosses the blood-brain barrier.
- Mean elimination half-life is 45 min. Only 0.01% of melatonin is excreted unchanged in urine.
- Pharmacologic tolerance to melatonin has not been described.
- Alcohol may potentiate side effects.

Usual Dose

- Taken 1–2 h before usual sleep time.
- Significant individual dose variation.
  - Insomnia: 1–4 mg PO in evening.
  - Insomnia with depression: 5–10 mg PO in evening.
  - Jet lag: 3–6 mg PO in evening on the destination's sleep schedule; may require up to 5 nights to become effective.
  - Tinnitus: 3 mg PO in evening.
  - Circadian disruption/blindness
  - Adults: 5–7 mg PO in evening.
  - Children: 2.5–7.5 mg PO in evening.

Endogenous Actions

- Secreted by the pineal gland in response to the absence of photic stimuli (known as the "darkness hormone").
- Reduces the body's core temperature in preparation for sleep.
- Secretion peaks during the pediatric years and decreases with age.
- Is involved in some way with reproductive function. Receptors have been found in reproductive tissues.
- Endogenously produced melatonin may have a significant role in deferring a number of free radical–related diseases and some pathophysiologic changes associated with aging.

Exogenous Actions

- Resets the body to the environmental clock and allows pts to normalize physiologic and behavioral sleep patterns.
- Used commonly as a preventive and therapeutic agent against jet lag.
- Useful in individuals with poor circadian synchrony, such as the visually impaired.

Perioperative Implications

- The ASA recommends that all herbal medications be D/C 2–3 wk prior to elective surgery because it takes 5–6 half-lives for an agent to leave the body; moreover, these substances lack uniform data regarding uptake, distribution, and elimination as they are not considered drugs by the USA FDA. Over 90 herbal products are associated with bleeding; this can be a specific problem intraop or when placement of a regional anesthetic is being considered for postop pain management.

Phytosterols

Lee A. Fleisher

Uses

- Naturally occurring in human diet.
- Used as supplements, especially in margarines, to reduce cholesterol levels.
- May also possess anti-inflammatory, antipyretic, antineoplastic, and immune-modulating properties.
- Some recent evidence questions the beneficial effect of phytosterols and the potential for increased CV risk.

Perioperative Risks

- None known

Worry About

- Pts may be taking phytosterols because of hypercholesterolemia and occult CAD.

Overview/Pharmacology

- Phytosterols (including plant sterols and stanols) are natural components of edible vegetable oils such as sunflower seed oil; as such, they are natural constituents of the human diet.
- It is difficult to incorporate free sterols into edible fats and/or oils because of their insolubility, whereas sterols esterified to fatty acids are more fat soluble.
- In the intestine, most sterol esters are hydrolyzed to free sterols as part of the normal digestive process.
- Plant stanols are hydrogenation products of the respective plant sterols (e.g., campestanol and/or campesterol, sitostanol and/or sitosterol) and are found in nature at very low levels.
- Enrichment of foods such as margarines with plant sterols and stanols is one of the recent developments in functional foods to enhance the cholesterol-lowering ability of traditional food products.
- May reduce the absorption of some fat-soluble vitamins. Randomized trials have shown that plant sterols and stanols lower blood concentrations of β-carotene by about 25%, concentrations of α-carotene by 10%, and concentrations of vitamin E by 8%.

Drug Class/Usual Dose

- Consumption of plant sterols and stanols lowers blood cholesterol levels by inhibiting the absorption of dietary and endogenously produced cholesterol from the small intestine. Plant sterols and/or stanols are only very poorly absorbed themselves.
- This inhibition is related to the similarity in physicochemical properties of plant sterols and stanols and cholesterol and may be related to two mechanisms:
  - The greater the amount of plant sterols and/or stanols, the lower the solubility and perhaps the greater the amount of cholesterol precipitated. Cholesterol in the crystalline form cannot be absorbed.
  - Competition for space in mixed micelles.
- Being marketed in new margarine formulations.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypercholesterolemia	CAD, angina	Chest pain	ECG
GI	Malabsorption of some vitamins			

Key References: Weingärtner O, Böhm M, Laufs U: Controversial role of plant sterol esters in the management of hypercholesterolaemia, *Eur Heart J* 30(4):404–409, 2009: Rocha VZ, Ras RT, Gagliardi AC, et al.: Effects of phytosterols on markers of inflammation: a systematic review and meta-analysis, *Atherosclerosis* 248:76–83, 2016.

Possible Drug Interactions

- No known drug interactions

Anticipated Problems/Concerns

- None known

Red Yeast Rice (Cholestin)

Alan David Kaye | John N. Cefalu | Amit Prabhakar

Uses

- Chinese traditional medicine for therapy of pts with cardiovascular diseases
- Hypercholesterolemia
- Prevention of coronary events, stroke, and TIA
- Treatment of dyslipidemia in statin-intolerant pts
- Prostate and colon cancer
- Possible diabetes treatment

Perioperative Risks

- Obtain adequate Hx to determine indication for taking red yeast rice.

Worry About

- Chemical composition of red yeast rice is not controlled by the FDA and may vary by manufacturer.
- Relatively contraindicated in liver disease. Hepatotoxicity is worsened in combination with other hepatotoxic drugs.

Overview

- Prepared by growing red yeast (*Monascus purpureus*) on rice to produce a red product.
- Contains 10 mevinic acids include monacolin K, also known as lovastatin.
- Popular in Asian countries.
- Available in several preparations in USA.

Drug Class/Mechanism of Action/Usual Dose

- HMG-CoA reductase inhibitor, essentially a natural statin and its homologues, additionally contains unsaturated fatty acids, flavonoids, plant sterols, and other biologically active substances.
- Inhibits conversion of HMG-CoA to mevalonic acid, an early precursor of cholesterol.
- Usual dose is 600–2400 mg daily.
- Xuezhikang (from red yeast rice) reduces expression of mediators of oxidative stress induced in diabetes mellitus and protects pancreatic islet cells from hyperglycemic injury. Xuezhikang, which is purified from cholestin, has been shown to decrease blood glucose levels by improving glucose tolerance and insulin secretion in db/db mice. Xuezhikang has also been shown to protect islets from hyperglycemic injury with conserved β-cell content and microenvironment. Xuezhikang potently inhibits the expression of key factors in oxidative stress and causes an upregulated expression of glucose-sensing tissue.
- Reduces matrix metalloproteinases 2 and 9 and CRP levels involved in vascular remodeling.
- Red yeast rice can significantly increase adiponectin and can significantly lower LDL-C and total cholesterol levels. Adiponectin correlates positively with HDL-C while serum leptin correlates negatively with triglycerides. Therefore red yeast rice has a potentially protective effect in obesity-related and cardiovascular diseases.
- Xuezhikang from red yeast rice has been shown to upregulate eNOS expression in vascular endothelia and RBCs, increasing plasma nitric oxide and improving abnormal hemorheology in high cholesterol diet–induced atherosclerotic rats. Therefore the elevated eNOS/NO and improved hemorheology may be beneficial in atherosclerosis.

Assessment Points

System	Effect	Test
CV	Reduces VLDL, LDL, and triglyceride levels Reduces matrix metalloproteinases and CRP involved in vascular remodeling Increases adiponectin levels Reduces eNOS regulatory factor Increases expression of eNOS.	VLDL, LDL, HDL, triglycerides Matrix metalloproteinases 2 and 9 and CRP Adiponectin, LDL-C, HDL, triglycerides, leptin
HEPAT	Rare hepatocellular damage and cholestasis	AST, ALT
MS	Rare myopathy, myalgia, and rhabdomyolysis	CPK
ENDO	Reduces pancreatic B-cell destruction and oxidative stress	Pancreatic B-cell numbers

Key References: Becker DJ, Gordon RY, Halbert SC, et al.: Red yeast rice for dyslipidemia in statin-intolerant patients. A randomized trial, *Ann Intern Med* 150(12):830–839, 2009; Cicero AF, Derosa G, Parini A, et al.: Red yeast rice improves lipid pattern, high-sensitivity C-reactive protein, and vascular remodeling parameters in moderately hypercholesterolemic Italian subjects, *Nutr Res* 33(8):622–628, 2013.

Perioperative Implications

Preoperative Concerns

- Lovastatin has been designated as pregnancy category X by the FDA. Thus red yeast rice should be avoided in pregnancy and lactation.

Preinduction/Induction

- Succinylcholine is contraindicated in myopathies associated with elevated serum CPK values.

S-Adenosyl-L-Methionine

Alan David Kaye | Katherine Stammen | Sudipta Sen | Elyse M. Cornett

Uses

- As an antiaging, antidisease therapeutic agent.
- May protect against the hepatotoxic effect of certain drugs (e.g., alcohol, acetaminophen, phenobarbital, and steroids).
- Depression, mild to moderate and adolescent.
- Anxiety, PMS.
- Heart disease.
- Liver disease, cirrhosis, intrahepatic cholestasis, disorders of porphyrin, and bilirubin metabolism.
- Osteoarthritis, tendinitis, bursitis, chronic low back pain.
- Dementia, Alzheimer disease, Parkinson disease.
- MS, migraine, seizure, spinal cord injury.
- Chronic lead poisoning.
- Disorder of porphyrin and bilirubin metabolism.
- Chronic fatigue syndrome.
- Intellectual enhancement, ADHD.
- Postop SAMe therapy can benefit residual liver function of pts with cirrhosis, especially pts suffering marked ischemia reperfusion injury.
- SAMe supplementation restores hepatic antioxidant glutathione (GSH) deposits. Depleted glutathione is associated with alcoholism, acetaminophen toxicity, Alzheimer disease, Crohn disease, diabetes, heart disease, and stroke.

Perioperative Risks

- N/V, flatulence, diarrhea, irregular or accelerated HR
- Anxiety

Overview/Pharmacology

- SAMe is produced endogenously by ATP activation of methionine, which is produced by the body from dietary protein.
- SAMe is required in numerous transmethylation reactions involving nucleic acids, proteins, phospholipids, amines, and other neurotransmitters. The synthesis of SAMe is linked with folate and cyanocobalamin metabolism; deficiencies of both these vitamins have been found to reduce SAMe concentrations in the CNS.
- May improve methylation by different mechanisms in several neurologic and psychiatric disorders.
- Is well tolerated with oral use and free of serious side effects. The oral supplement was developed in the 1970s and has been touted as a multipurpose treatment ever since.
- Exogenously administered SAMe has a low bioavailability due to rapid first-pass metabolism by the liver.
- Peak plasma concentration reached in 3–5 h.
- Half-life of 100 min.
- Excreted in urine and feces.
- Crosses the blood-brain barrier.
- Metabolized to homocysteine; remethylated to form methionine, which can form more SAMe.
- Tosylate salt has 1% oral bioavailability.
- Butane disulfonate salt has 5% oral bioavailability.

Mechanism of Action

- Contributes to the synthesis, activation, and metabolism of hormones, neurotransmitters, nucleic acid, proteins, phospholipids, and some drugs.
- SAMe crosses the blood-brain barrier and is involved in transmethylation and folate and monoamine metabolism as well as in membrane function and neurotransmission.
- SAMe plays a role in more than 100 biochemical reactions: increases levels of serotonin, dopamine, norepinephrine, phosphatides, and proteoglycans.
- Improves intrahepatic cholestasis. SAMe supplementation seems to improve hepatic function and reverse imbalances of various enzymes. In liver disease, deficiencies of MAP often lead to reductions in cysteine and choline, which can lead to depletion of glutathione. SAMe restores levels of glutathione, decreases inflammation, and increases methylation of DNA.
- Stimulates growth of articular cartilage.
- Relieves joint pain, possibly owing to analgesic or anti-inflammatory effects. May stimulate articular cartilage growth and repair as a result of chondrocyte proteoglycan synthesis. May antagonize TNF-alpha, which may be beneficial in arthritic pts.
- Antidepressant effect is probably due to increased serotonin turnover and elevated dopamine and norepinephrine levels or alterations in cellular membrane fluidity, which would facilitate signal transduction across membranes and increase the efficiency of receptor-effector coupling.
- In liver disease, restores depleted biochemical factors.
- In myelopathy of AIDS, replenishes depleted endogenous SAMe.

Usual Dose

- For depression, 400–1600 mg daily PO or 200–400 mg daily IV to speed onset of action of tricyclic antidepressants.
- Addition of betaine to SAMe counteracts high levels of homocysteine; combination more effective than SAMe alone for treatment of depression.
- For osteoarthritis, 200 mg 3 times PO or 400 mg IV.
- For alcoholic liver disease, cirrhosis, or intrahepatic cholestasis, 1200–1600 mg/d PO or 800 mg/d IV.
- For AIDS myelopathy, 800 mg/d IV for 14 d.
- For fibromyalgia, 800 mg/d PO.

Assessment Points

System	Effect	Assessment by Hx	PE
GI	N/V, diarrhea	GI complaints	KUB
MS	Osteoarthritis	Stiff joints	ROM

Key References: Guo T, Chang L, Xiao Y, et al.: S-adenosyl-L-methionine for the treatment of chronic liver disease: a systematic review and meta-analysis, *PLoS ONE* 10(3):e0122124, 2015; Su ZR, Cui ZL, Ma JL, et al.: Beneficial effects of S-adenosyl-L-methionine on post-hepatectomy residual liver function: a prospective, randomized, controlled clinical trial, *Hepatogastroenterology* 60(125):1136–1141, 2015.

Perioperative Implications

Drug Interactions

- Additive serotonergic effects and serotonin syndrome–like effects with antidepressants include SSRIs
- Due to serotonergic properties, the following should be avoided with SAMe (in view of the risks of serotonin syndrome–like effects): dextromethorphan (Robitussin DM, other cough syrups), meperidine (Demerol), pentazocine (Talwin), tramadol (Ultram), sumatriptan (Imitrex), and other 5-$HT_{1B/1/D}$ receptor agonists.
- Additive side effects like hyperthermia, agitation, confusion, and coma when used with MAOIs.
- Other side effects may include dry mouth, nausea, gas, diarrhea, headache, anxiety, nervousness, restlessness, and insomnia.
- Large doses of SAMe may cause mania (abn elevated mood). People with bipolar disorder (manic depression) should not take SAMe because it may worsen manic episodes.
- Taking levodopa (L-DOPA) for Parkinson disease may lower the levels of SAMe in the body. This contributes to depression and increases the side effects of levodopa.
- SAMe decreases effectiveness of levodopa.
- SAMe concentrations can be lowered in the presence of guanidinoacetate (also known as glycocyamine) supplementation. Glycocyamine is a direct precursor of creatine, which is a popular nutritional supplement.
- SAMe does not improve outcome or reduce the occurrence of adverse events for chronic liver diseases such as cholestasis and viral hepatitis.

Contraindications

- Pts taking MAO inhibitors or within 2 wk of their discontinuation
- Concurrent use with antidepressant drugs, including MAOIs, can lead to additive stimulatory effects. Agitation, tremor, insomnia, nervousness, irregular or accelerated heart rate are theoretical concerns.
- Parkinson disease with levodopa treatment.

Saw Palmetto

Joan Spiegel

Uses

- BPH
- Urinary tract inflammation (prostatitis)
- Underactive bladder
- Male- and female-pattern baldness
- Aphrodisiac
- Breast augmentation

Perioperative Risks

- No established interactions with anesthetic agents

Worry About

- Saw palmetto has been implicated in hepatitis, cholecystitis, bleeding diatheses, conduction defects, and erectile dysfunction. No studies confirm these effects.
- Unsubstantiated pharmacologic effects such as increasing the action of benzodiazepines

Overview

- Saw palmetto extract is an extract of the fruit of *Serenoa repens* from the American dwarf palm tree. Saw palmetto's active ingredients include fatty acids, plant sterols, and flavonoids.
- Saw palmetto has hormonal (estrogenic) effects as well as direct inhibitory effects on androgen receptors. There are also possible anti-inflammatory effects (from the berries of the plant).
- Saw palmetto has not been evaluated by the FDA.
- Saw palmetto is possibly ineffective for its intended use, the treatment of BPH.

Etiology

- Mechanism of action: Saw palmetto exhibits antiestrogenic and antiandrogenic effects by inhibiting the actions of 5-alpha reductase enzyme (thereby preventing the conversion of testosterone to dihydrotestosterone, a cause of BPH and baldness).

Possible Drug Interactions

- Any medication that alters male sex hormones should not be taken with saw palmetto. Examples include finasteride and flutamide.
- Drugs that affect coagulation should also not be consumed with saw palmetto; these include Coumadin and anti-inflammatory agents (clopidogrel, ibuprofen, aspirin)
- Because saw palmetto may have hormone-like effects, it may make oral contraceptives less effective, thus raising the risk of unplanned pregnancy.
- Tannins in saw palmetto may interfere with iron absorption.
- Tinctures may contain large amounts of alcohol and thus cause N/V when taken with metronidazole or disulfiram.

Assessment Points

System	Effect	Test
GI	Occasional upset, hepatitis, and cholecystitis (very rare)	LFTs
HEME	Bleeding, iron deficiency	None, iron studies, Hgb
GU	Improved urinary symptoms (conflicting data)	None
ENDO	Breast enlargement (unproved) Prevent hair involution due to dihydrotestosterone (unproved)	None

Key References: *Serenoa repens*, *Altern Med Rev* 3(3):227–229, 1998; Bent S, Kane C, Shinohara K, et al.: Saw palmetto for benign prostatic hyperplasia, *N Engl J Med* 354(6):557–566, 2006; Tacklind J, Macdonald R, Rutks I, et al.: *Serenoa repens* for benign prostatic hyperplasia, *Cochrane Database Syst Rev* 12:CD001423, 2012.

Perioperative Implications

Preoperative Concerns

- Self-reporting of other herbal supplements
- Unknown effects in children; interference with birth control and in lactating mothers

Intraoperative Concerns

- None known

Postoperative Period

- Routine

St. John's Wort *(Hypericum perforatum)*

Theodore G. Cheek | Lee A. Fleisher

Uses

- More than 3% of presurgical pts report using St. John's wort.
- Taken mainly for depression, although pts may take it for a variety of reasons including anxiety, viral and bacterial infections, menstrual cramps, HIV, cancer, chest congestion, hemorrhoids, skin wounds, and burns.
- Efficacy in treating depression is controversial.
- Most integrative medical specialists will use every other alternative first because of drug interactions; this is at best a third-line medication. Others such as S-adenosyl-L-methionine are equally or more effective and without undesirable drug interactions or other side effects.

Worry About

- Drug interactions: May prolong sedative effects of other drugs including anesthetics and sedatives. There are case reports of a severe hypertensive response to vasopressors such as ephedrine or phenylephrine in pts taking St. John's wort.
- Induces cytochrome P450 enzymes; promotes metabolism and decreased blood levels of warfarin, cyclosporine, digoxin, CCBs, and steroids; even renders birth control pills and menopausal drug therapies ineffective. Watch for unplanned and sometimes unwanted pregnancies due to this effect.)
- Serotonin-like syndrome (Htn, tachycardia, agitation, restlessness).
- Unpredictable effects due to lack of strict regulation.

Overview/Pharmacology

- Classified as a dietary supplement and not subject to FDA; pharmacologic activity can be unpredictable and highly variable in different preparations. Hypericum extract (0.3% hypericin) is marketed to be taken PO at 300 mg 3 times daily.
- Contains many complex chemicals, but hypericin and hyperforin are responsible for the antidepressant effects.
- Absorbed within 40 min of oral administration.
- Mainly metabolized by the liver and cleared by renal excretion; elimination half-time 43 h.

Mechanism of Action/Usual Dose

- May act as a nonspecific reuptake inhibitor of serotonin, norepinephrine, and dopamine.
- Appears to work differently from conventional antidepressants.
- MAO inhibition reported in early studies but not confirmed in follow-up studies.
- Usually taken as a capsule consisting of the plant extract; typical dosage is 300–500 mg of hypericum extract 3 times daily.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Photosensitivity			
CV	Rarely, Htn, tachycardia, and serotonin-like syndrome	Dosage taken; determine whether patient is also taking an SSRI	BP/HR	ECG
GI	Nausea			
DERM	Rarely, rash			
CNS	Restlessness, fatigue, antidepression			

Key References: Skidmore-Roth L editor: *Mosby's handbook of herbs and natural supplements*, ed 3, St Louis, 2006, Mosby, pp 957–963; Abe A, Kaye AD, Gritsenko K, Urman RD, Kaye AM: Perioperative analgesia and the effects of dietary supplements, *Best Pract Res Clin Anaesthesiol* 28(2):183–189, 2014.

Perioperative Implications

Preoperative Concerns

- Hx can include dose, duration, preparation taken, and reason for use.
- Best to discontinue at least 1 wk preop so as to clear the drug from the body.
- May see as much as a 50% decrease in effect of warfarin. Consider alternatives to warfarin.
- Can decrease digoxin levels, possibly by induction of a P-glycoprotein transporter.
- Serotonin-like syndrome, especially when combined with an SSRI, tricyclics, or MAO inhibitor.

Induction/Maintenance/Emergence

- May prolong anesthesia via potentiation of central effects of inhaled agents, sedatives, and opioids.

Anticipated Problems/Concerns

- Effects may be variable among different preparations owing to lack of standardization.
- Anticipate decreased effects of certain drugs such as warfarin, cyclosporine, beta-blockers, CCBs, steroids, and digoxin.
- May prolong the sedative effects of anesthetics.
- Watch for serotonin-like syndrome (Htn, tachycardia, agitation, restlessness).

Valerian *(Valeriana officinalis)*

Lee A. Fleisher

Uses

- Treatment of:
  - Insomnia (valerian is present in virtually all herbal sleep aids)
  - Anxiety
  - Depression
  - Htn
  - GI hyperactivity
  - Headaches
  - Muscle spasms
  - Benzodiazepine withdrawal

Perioperative Risks

- Potential for valerian withdrawal exists if usage is stopped suddenly after chronic high-dose administration. This withdrawal can present as delirium, tachycardia, and diaphoresis.
- Chronic dosing with high-dose valerian has been linked with cardiac failure and emergence delirium.

Worry About

- No direct drug interactions are reported.
- Valerian may act synergistically with sedative anesthetics, leading to prolonged emergence.
- Valerian can potentiate medications such as barbiturates, benzodiazepines, opioids, antidepressants, and alcohol.

Overview

- Valerian is a native herb of temperate regions; its name is believed to be derived from the Latin word *valere*, meaning to be healthy or strong. It has been used for centuries as a sleep aid by Greeks, Romans, Chinese, American Indians, and Europeans.
- Prior to the introduction of barbiturates to the US National Formulary, valerian was indicated for treatment of unrest and nervous sleep disturbance. It has since been dropped from the US National Formulary.
- Valerian contains many constituents that work synergistically, including volatile oils, valepotriates, monoterpene alkaloids, and furanofuran lignans.
- Volatile oils: These oils give valerian a pungent odor due to the release of isovaleric acid. The sesquiterpene skeleton present on volatile oils such as valerenic acid, valeranone, and kessyl glycol is a proposed primary source of pharmacologic effects. These components have been shown to act on the amygdaloid body in the brain and to inhibit breakdown of GABA, thus leading to sedation.
- Valepotriates: Have a furanopyranoid monoterpene skeleton, which can be found in glycosylated forms known as iridoids. The compounds have been shown in animal experiments to decrease spontaneous motility after oral administration.

Mechanism of Action/Usual Dose

- Produces dose-dependent sedation and hypnosis mediated mainly through the $GABA_A$ receptor, the adenosine A_1 receptor, and, as recently noted, the $5\text{-}HT_{5a}$ receptor.
- Tablets: 300-400 mg PO 30 min-1 h prior to sleep.
- Tea: 1 cup of boiling water over 1–2 teaspoons (2–3 g) of the root and infused for 10–15 min. One may drink up to 2 cups daily.
- Tincture: 2–6 mL (½-1 teaspoon) up to 3 times daily.

Assessment Points

System	Effect	Test
CV	High-output cardiac failure Hypotension Arrhythmias Dilates coronary arteries	Rule out other causes of high-output cardiac failure: Sepsis, beriberi, cardiac shunt, or Paget disease ECG, ECHO
HEPAT	CYPA 4 inhibitor Hepatotoxicity	Baseline LFTs
CNS	Sedation Hypnosis Anticonvulsive effect Headache Restlessness Hallucinations Ataxia	Sleep studies: May improve sleep latency and slow-wave sleep EEG
GI	Nausea Intestinal irritability	Decrease dose or stop ingestion
MS	Muscle relaxation	

Key References: Ang-Lee MK, Moss J, Yuan CS: Herbal medicines and perioperative care, *J Am Med Assoc* 286(2):208–216, 2001; Abe A, Kaye AD, Gritsenko K, Urman RD, Kaye AM: Perioperative analgesia and the effects of dietary supplements, *Best Pract Res Clin Anaesthesiol* 28(2):183–189, 2014.

Perioperative Implications

- The valepotriate component of valerian may alkylate DNA, which could be potentially cytotoxic or carcinogenic. It has been recommended that valerian not be used in pregnancy or while breast feeding.
- Cessation of valerian consumption prior to surgical intervention should be decided on an individualized basis. If a 2- to 3-wk taper is not feasible, then pts should continue taking valerian. Benzodiazepines can be used to treat withdrawal symptoms should they develop.