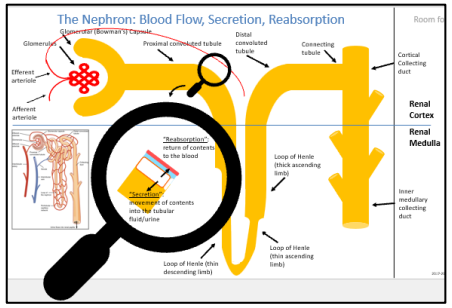
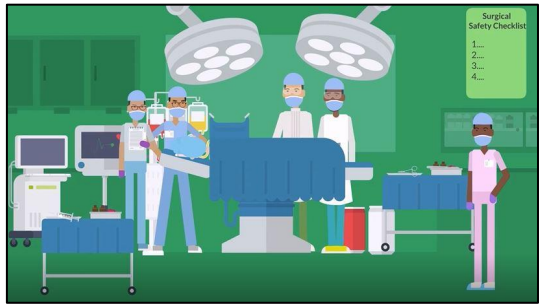
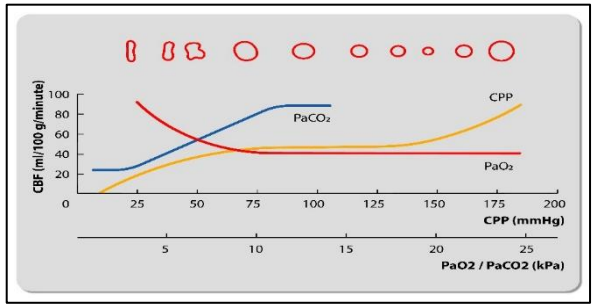
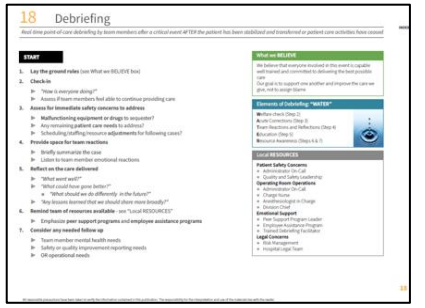
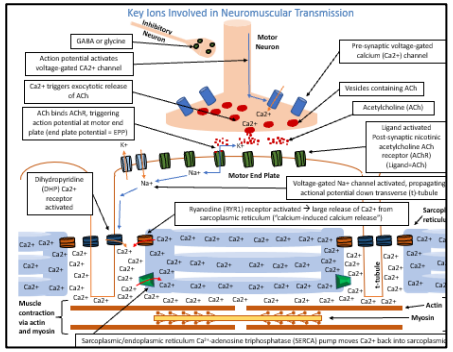








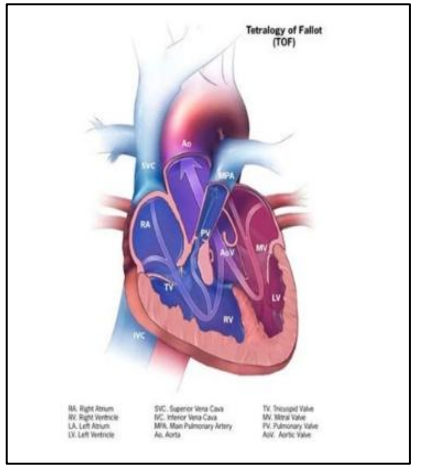


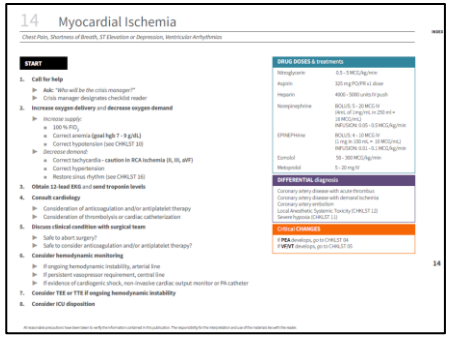
Data-Driven Didactics Review Session 2024:

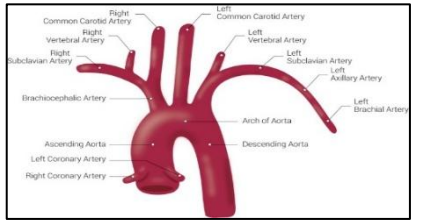
Lifelong Learning in Anesthesia

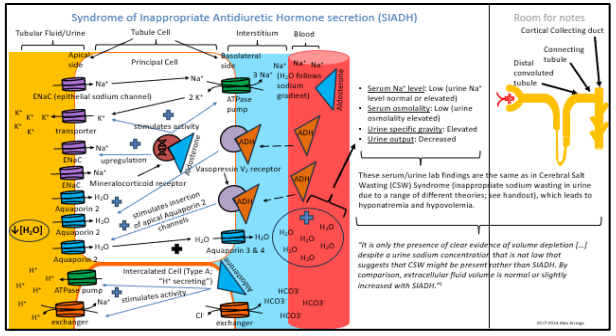
Alexander Arriaga, MD, MPH, ScD
@AlexArriagaMD

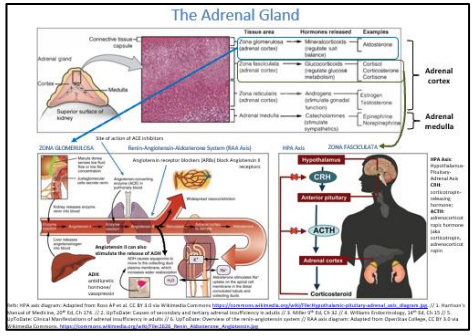
datadrivendidactics.org

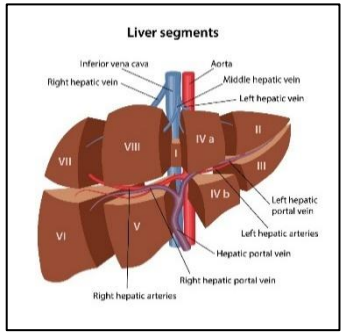












Room for notes

Goal and Objectives

Overall Goal:

- To provide, at a key moment, a data-driven and lifelong-learning style anesthesia review.

Objectives:

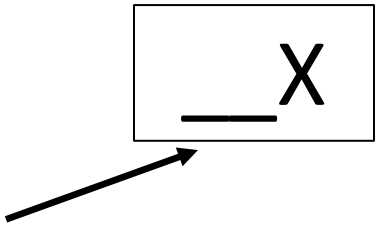
By the end of this session, participants should be able to:

- State anesthesia implications regarding selected high-yield anesthesia topics to guide further learning.
- Apply high-yield, evidence-based anesthesia knowledge towards lifelong learning in anesthesia.

This talk represents of the presenter and not necessarily the supporting agencies (views=mine). Dr. Arriaga is an Editor on the Patient Safety Editorial Board for the American Society of Anesthesiologists, and a Question Editor/Board Examiner for the American Board of Anesthesiology, both of which provide a stipend for work that is otherwise done in a volunteer capacity. The presenter does not believe that any of these represent a conflict of interest. A fee is not charged for this session. All reasonable precautions have been taken to verify the information contained in this lecture. The responsibility for the interpretation and use of the information lies with the reader. Attempts have been made to cite and squeeze references into individual slides, understanding that this makes slides crowded. Expanded citations/references for a given slide can be provided on request.

Room for notes

Format for this session and slides



- Will review topics, by category. Weighted priority given to key topics.
  - *Numbers on upper right-hand corner signify that the slide addresses topics asked "X" number of times on in-training exams, based on publicly available data, "intended to help plan continuing medical education," "help…identify specific strengths and weaknesses," and/or "assist and support you in the design of your educational program."*[1]
- ***After years of experience reviewing (1) how to create a PowerPoint slide & (2) literature on methods of learning (including active learning): these slides are methodically created to prioritize the stated objective: a data-driven and lifelong-learning style anesthesia review.***
- This review attempts to help learners that range from those who struggle with lifelong learning, to those who are already experts.
- Residents who have not done certain specialty rotations have generally enjoyed the "review" of something new.
- Feel free to ask questions.

1. American Board of Anesthesiology In-training reports, program summary keywords, and Gaps in Knowledge reports. The keywords are provided to programs nationwide, and over the years, they are/were publicly available at www.openanesthesia.org. Gaps in Knowledge reports are also provided to programs nationwide and/or publicly available at www.theaba.org. The design of this educational program was informed by these keywords, development of original didactic content, an overall review of the literature, and implementation of medical education methods previously published (PMID's 34923227, 34872825).

Room for notes

Renal

"The kidney is one of the most highly differentiated organs in the body."

~ Harrison's Principles of Internal Medicine, 21st Ed.

Room for notes

The Nephron

44X*

Room for notes

Glomerular (Bowman's) Capsule

Glomerulus

Proximal convoluted tubule

Distal convoluted tubule

Connecting tubule

Cortical Collecting duct

Efferent arteriole

Afferent arteriole

Renal Cortex

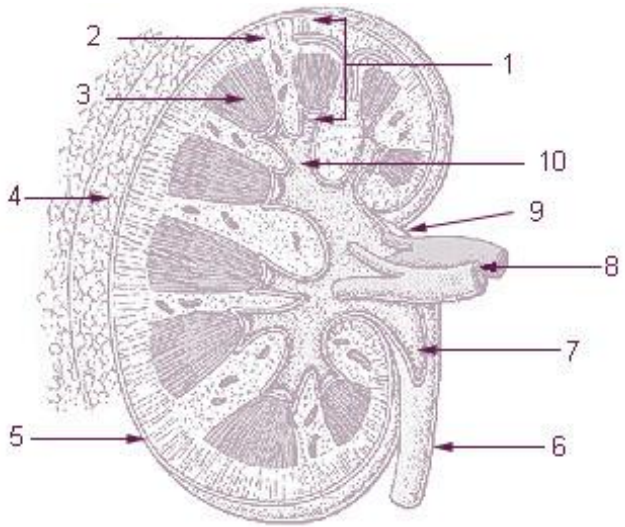
Renal Medulla

Loop of Henle (thick ascending limb)

Loop of Henle (thin descending limb)

Inner medullary collecting duct

Loop of Henle (thin ascending limb)



1. Renal parenchyma; 2. **Renal Cortex**; 3. **Renal Medulla**; 4. Perineural fat; 5. Renal Capsule; 6. Ureter; 7. Renal pelvis; 8. Renal artery and vein; 9. Renal hilus; 10. Renal calyx

* This count is the sum for the nephron/animation slides in this section that do not already have X counts at the top of the slide. This count is an underestimate, as some topics covered in this section are X-counted instead in the endocrine section to avoid double-counting

The Nephron: Blood Flow, Secretion, Reabsorption

Room for notes

Glomerular (Bowman's) Capsule

Glomerulus

Proximal convoluted tubule

Distal convoluted tubule

Connecting tubule

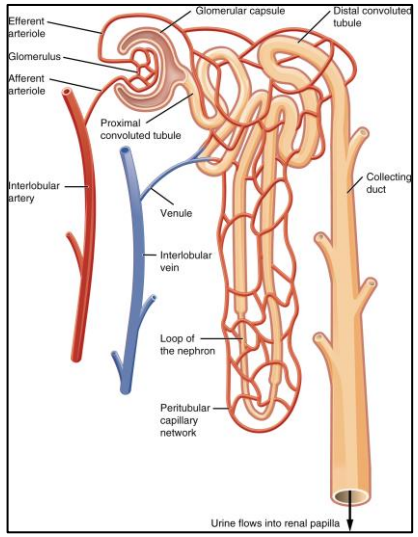
Cortical Collecting duct

Efferent arteriole

Afferent arteriole

Renal Cortex

Renal Medulla



"Reabsorption": return of contents to the blood

"Secretion": movement of contents into the tubular fluid/urine

Loop of Henle (thick ascending limb)

Inner medullary collecting duct

Loop of Henle (thin descending limb)

Loop of Henle (thin ascending limb)

Countercurrent Multiplication: key process for water reabsorption and excretion of concentrated urine

Room for notes

Glomerulus

Efferent arteriole

Afferent arteriole

Proximal convoluted tubule

Distal convoluted tubule

Connecting tubule

Cortical Collecting duct

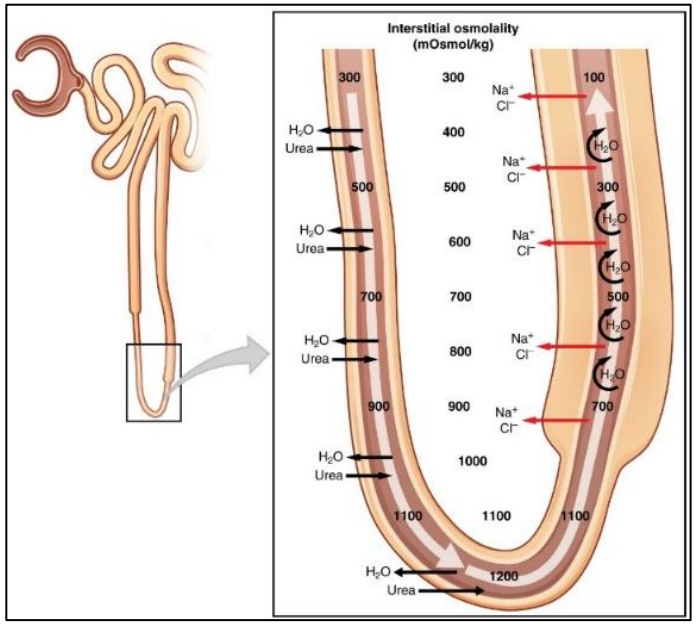
Loop of Henle (thin descending limb): highly permeable to water.[1]

Loop of Henle (thick ascending limb): relatively impermeable to water and actively reabsorbs NaCl, creating a concentrating gradient in the renal medulla. [1,3,4]

Renal Cortex

Renal Medulla

"NaCl absorption by the thick ascending limb is the primary initiating event."[1]



H_2O
H_2O
H_2O

NaCl
NaCl
NaCl

300
700
1000
1200

100
500
800

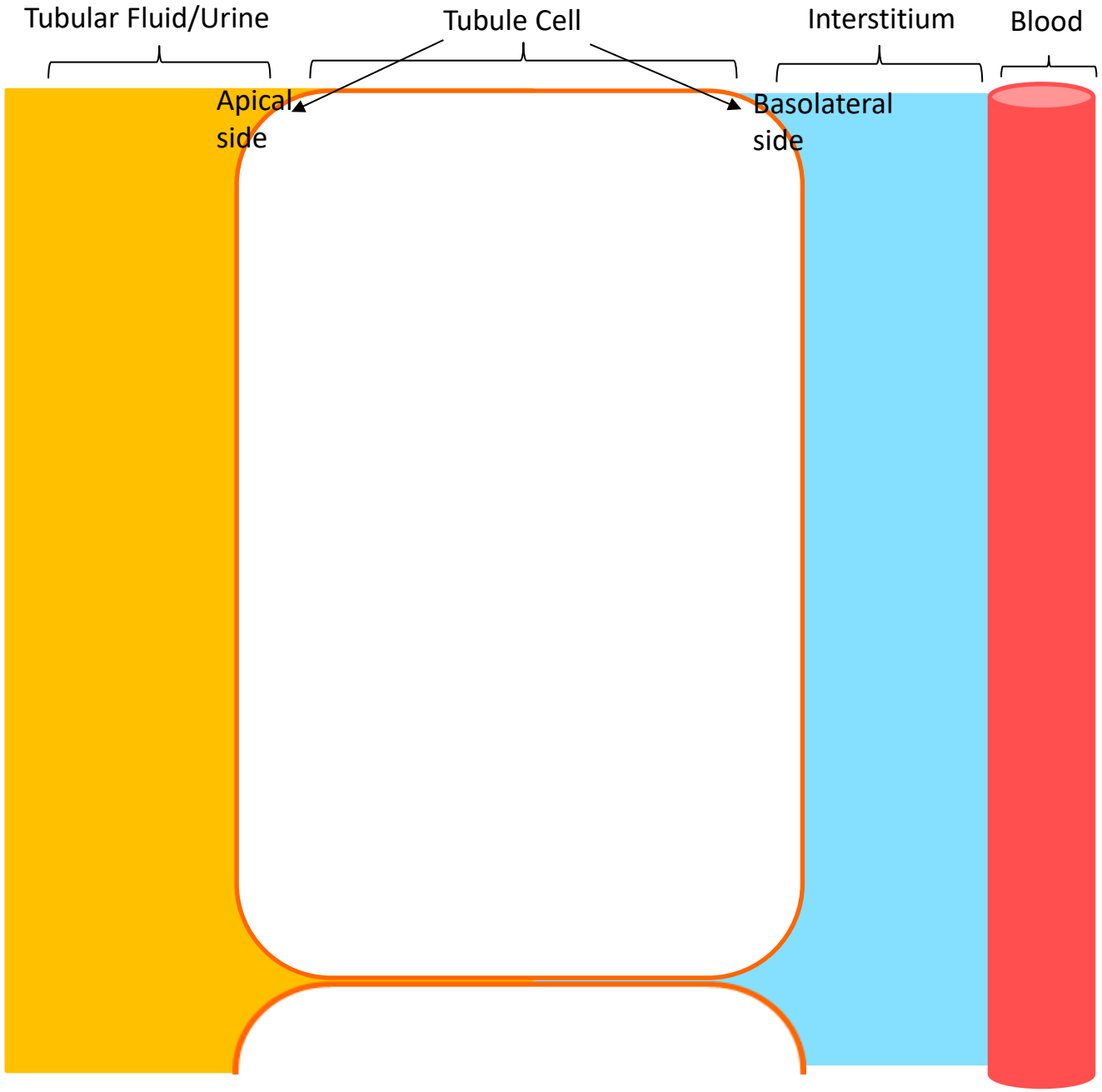
"Because of the **countercurrent** flow of tubular fluid in the descending limb (fluid flowing into the medulla) and ascending limb (fluid flow out of the medulla), this **single effect** could be **multiplied**, resulting in an osmotic gradient within the medullary interstitium, where the tip of the papilla has an osmolality of 1200 mOsm/kg H_2O compared to 300 mOsm/kg H_2O at the corticomedullary junction."[2]

"[A]t any point along the loop of Henle the fluid in the ascending limb has an osmolality less than fluid in the adjacent descending limb. This osmotic difference is termed the **single effect**."[2]

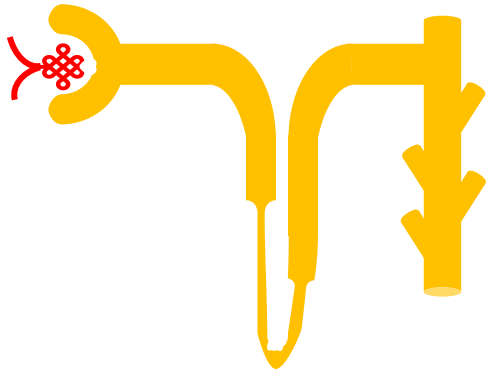
Loop of Henle (thin ascending limb): relatively impermeable to water.[1,3,4]

% Na^+ reabsorbed, by nephron site[5]	%
Proximal convoluted tubule	67%
Loop of Henle (thick ascending limb)	25%
Distal tubule	5%
Collecting Duct	~~3~~%

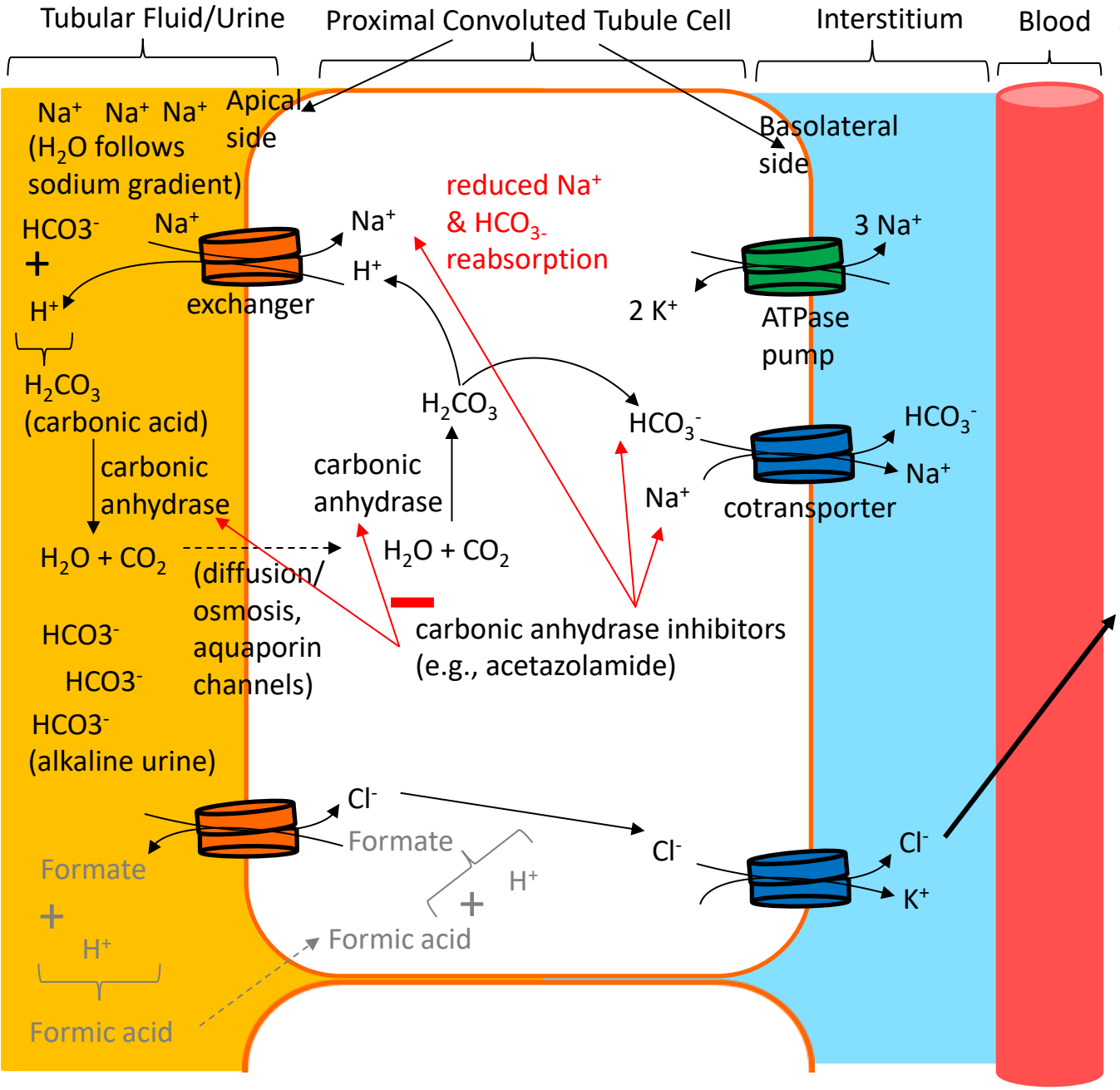
Template for nephron cell (to follow along and actively retain information)



Room for notes



Carbonic Anhydrase Inhibitors

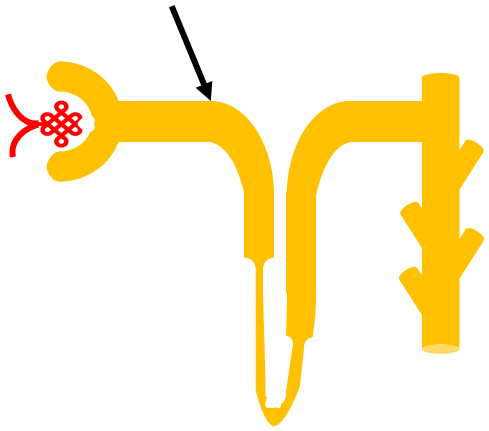


Acetazolamide: carbonic anhydrase inhibitor; diuretic largely via action at the proximal convoluted tubule. Other possible uses include (1) altitude sickness/high-altitude cerebral edema (facilitates renal acid/base compensation for respiratory alkalosis caused by high altitude); (2) seizure disorder (CNS carbonic anhydrase inhibition can slow down abnormal/ excessive discharge from CNS neurons); (3) idiopathic intracranial hypertension (reduces the rate of CSF production); (4) glaucoma (carbonic anhydrase inhibition leads to decreased aqueous humor formation → reduced intraocular pressure); (5) metabolic alkalosis.

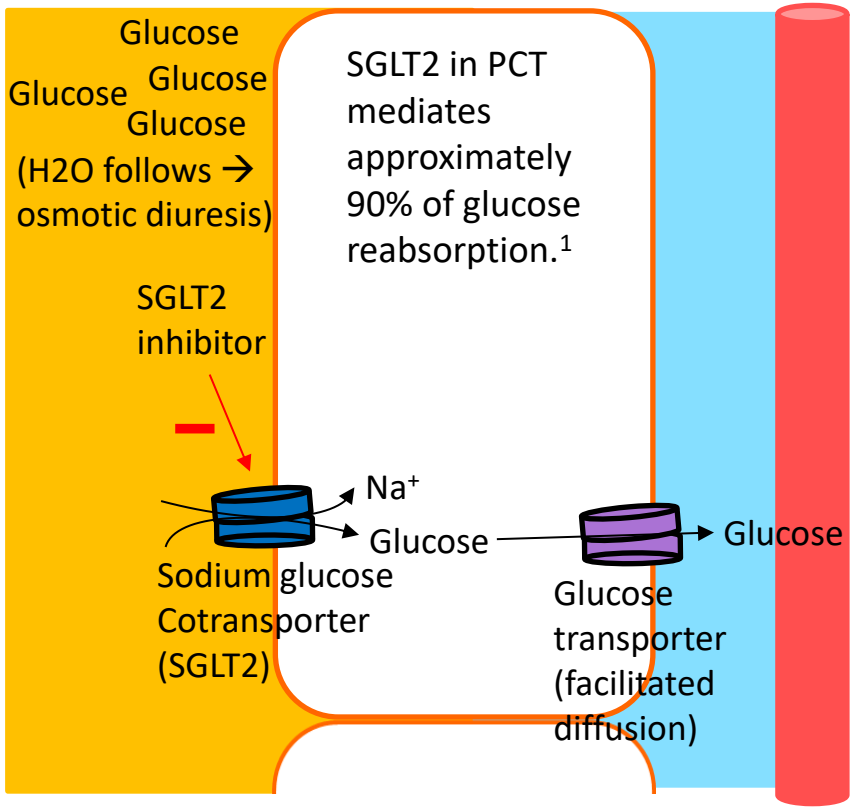
- Hyperchloremic metabolic acidosis due to increased Cl^- absorption and decreased HCO_{3-} reabsorption.
- Hypokalemia can occur from increased potassium secreted in distal nephron (in exchange for sodium reabsorption) to compensate for the increased sodium in tubular fluid/urine.
- Weak diuretic because (1) remainder of nephron works to compensate for the increase volume of tubular fluid; (2) eventual compensation for metabolic acidosis attenuates the diuretic effect.

Room for notes

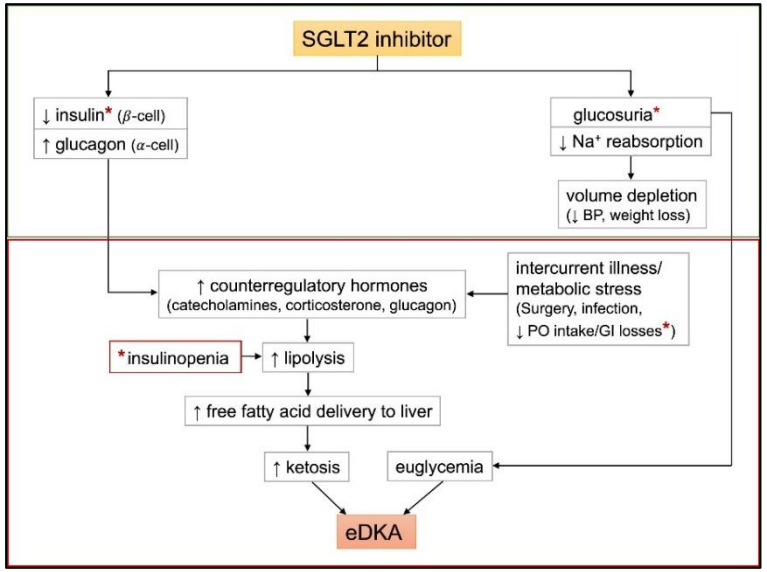
Proximal convoluted tubule



SGLT2 inhibitors and Euglycemic Diabetic Ketoacidosis



SGLT2 inhibitors can increase risk of "euglycemic" (serum glucose <250 mg/dL) diabetic ketoacidosis (eDKA) in pts w/diabetes mellitus, particularly when DKA risk is increased (e.g., infection, illness, surgery).[1]



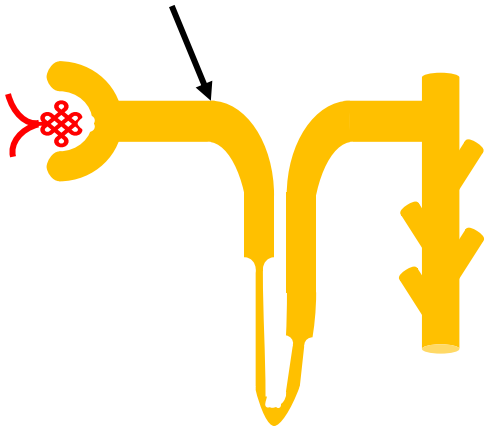
FDA communication 2020 (revised 2022): "To lessen the risk of developing ketoacidosis after surgery, FDA has approved changes to the prescribing information for SGLT2 inhibitor medicines. Health care professionals should consider stopping canagliflozin, dapagliflozin, and empagliflozin at least three days before, and ertugliflozin at least four days before scheduled surgery."

- Signs/Symptoms of ketoacidosis include: abdominal pain, nausea/emesis, myalgias, fatigue, leukocytosis, mild elevation in amylase levels, elevated urine ketones.[1,2]
- "Serum ketones [e.g., serum beta-hydroxybutyrate level] should be obtained in any patient with nausea, vomiting, or malaise while taking SGLT2 inhibitors, and patients should be counseled to withhold SGLT2 inhibitor therapy until these symptoms resolve."[1,3]

FDA communication on SGLT2 inhibitors: https://www.fda.gov/drugs/drug-safety-and-availability/fda-revises-labels-sglt2-inhibitors-diabetes-include-warnings-about-too-much-acid-blood-and-serious // Wang et al. PMID 32734242. Red asterisks depict theorized mechanisms for combined carbohydrate deficiency and insulinopenia. Creative Commons License CC BY-NC-ND 4.0 // 1. UpToDate: Sodium-glucose cotransporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus. // 2. Barash 9th Ed, Ch 47 // 3. UpToDate: Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis// 4. Thompson A et al 2024 PMID 39316661

Room for notes

Proximal convoluted tubule



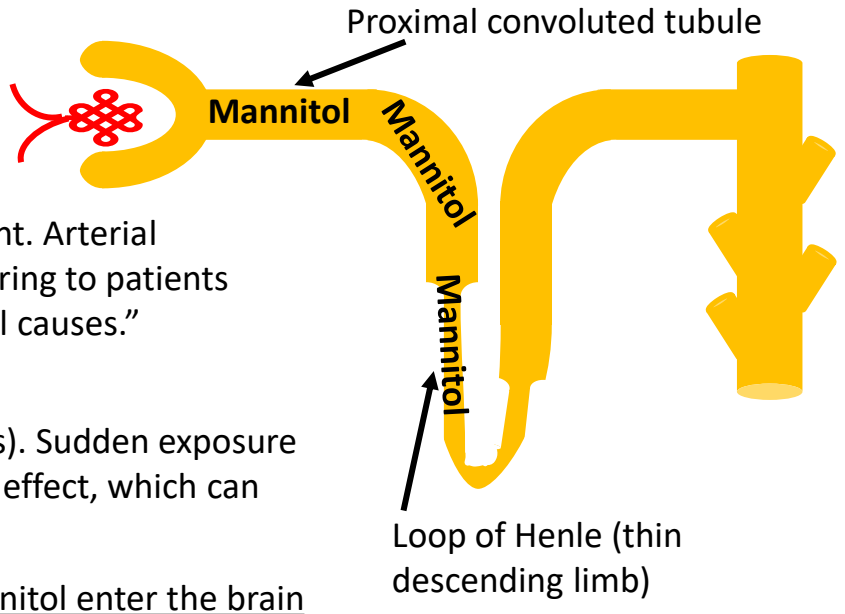
2024 ACC/AHA Periop CV Guidelines for Noncardiac Surgery: recommend holding SGLT2 inhibitors for 3-4 days preop (same timeline as FDA communication) "to reduce the risk of perioperative metabolic acidosis."[4]

Mannitol

Room for notes

Mannitol: osmotic diuretic; causes urinary excretion of water and sodium; preferentially causes more water diuresis than sodium loss → may cause **hypernatremia**.* Diuresis may cause **hypovolemia** and hypotension.[1-3]

Use of mannitol to reduce intracranial pressure (ICP) and/or brain volume: mannitol can withdraw water from brain tissue → water is then excreted in the urine with the mannitol.[3,4] Other theory: "While mannitol was previously thought to reduce intracranial pressure through simple brain dehydration, [mannitol reduces intracranial pressure] at least in part, through reducing blood viscosity, leading to improved microcirculatory flow of blood constituents and consequent constriction of the pial arterioles, resulting in decreased cerebral blood volume and intracranial pressure."[3]



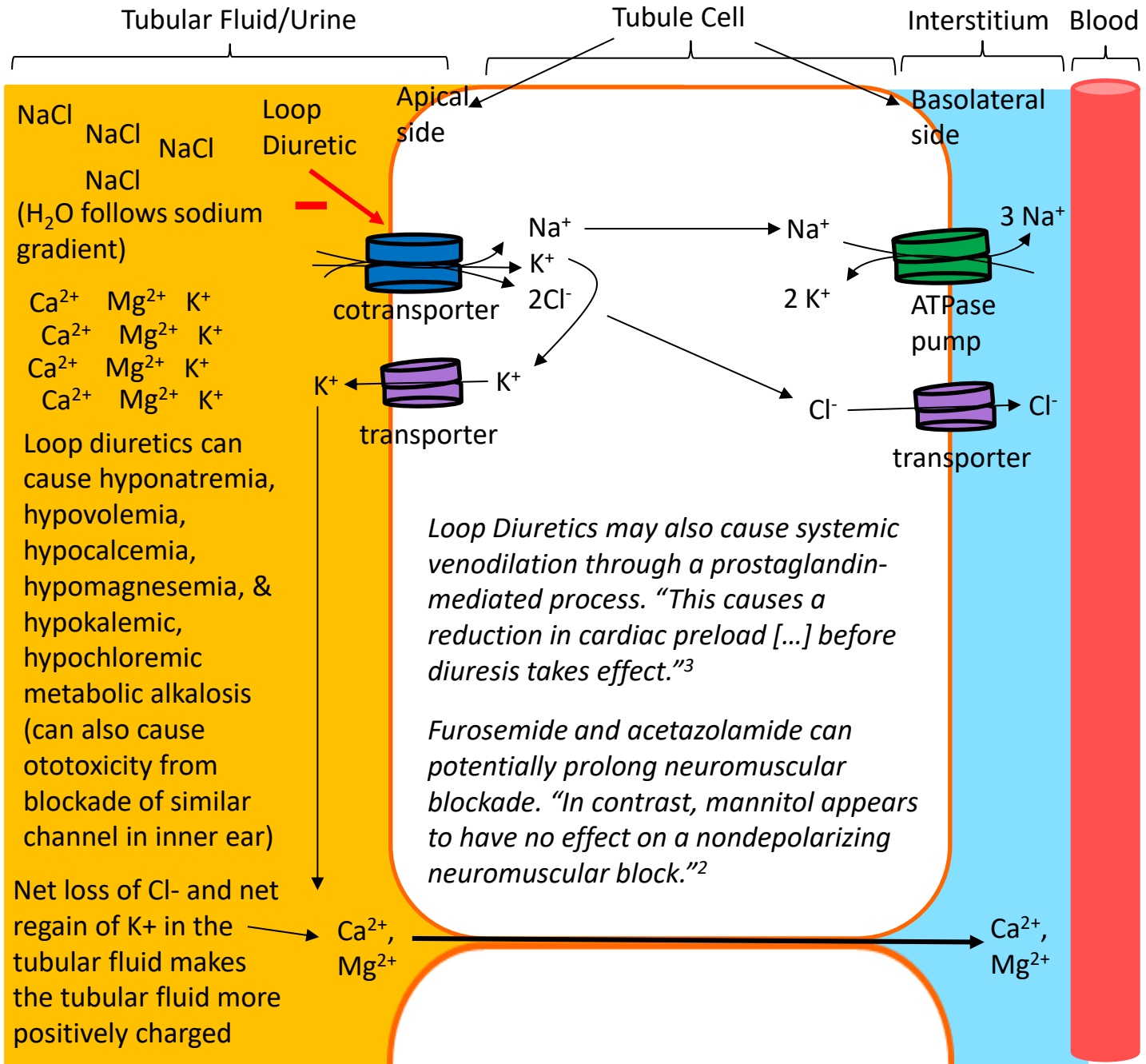
Brain Trauma Foundation (BTF) Guidelines for the Management of Severe Traumatic Brain Injury, 4th Ed**
"Mannitol is effective for control of raised intracranial pressure (ICP) at doses of 0.25 g/kg to 1 g/kg body weight. Arterial hypotension (systolic blood pressure <90 mm Hg) should be avoided. Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes."

FAQ's, other theories, and clinical practice
Does mannitol initially increase ICP? "Mannitol should be administered by infusion (e.g., over 10 to 15 minutes). Sudden exposure of the cerebral circulation to extreme hyperosmolarity [from too rapid administration] can have a vasodilatory effect, which can produce brain engorgement and increased ICP, both of which do not occur with slower administration."[5]

Does mannitol require the blood-brain barrier to be intact? If it is not intact (e.g., tumor, trauma), will the mannitol enter the brain parenchyma and cause cerebral edema? "The possibility that the mannitol that gains access to the parenchyma aggravates swelling had resulted in varying degrees of reluctance among clinicians to administer mannitol. Most clinicians nonetheless find it to be a mainstay of ICP management. There is the concern that it will only be effective when some degree of blood–brain barrier (BBB) integrity is preserved in a significant portion of the brain. Clinicians respond to this concern by making empiric use of this agent; that is, if it is effective in reducing ICP or improving conditions in the surgical field, repeated doses are administered."[5]

1. Bell R. BJA Education; PMID: 35614905. // 2. UpToDate Mechanism of action of diuretics. // 3. Brain Trauma Foundation. Guidelines for the management of severe TBI, 4th Ed (Executive Summary & Complete Guidelines). Available at: https://braintrauma.org/coma/guidelines-current // 4. UpToDate: Mannitol (systemic): Drug information // 5. Miller 10th Ed, Ch 53 // * If mannitol is given to patients with severe renal insufficiency, the mannitol may be retained in the bloodstream, and the osmotic pull of water into the bloodstream can cause a dilutional hyponatremia. ** While the current BTF recommendations for mannitol are listed as "not supported by evidence meeting current standards," the authors state it was retained in the 4th Ed guidelines[11] to maintain sufficient recognition of the potential need for hyperosmolar therapy to reduce intracranial pressure."

Loop Diuretics

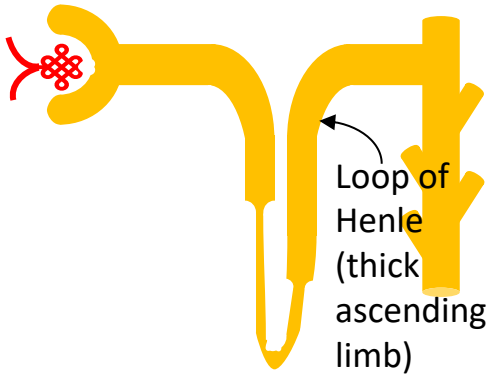


"Loop diuretics are the most potent diuretics available, increasing the excretion of Na + to as much as 25% of the amount filtered."[1]

Inhibition of NaCl transport at the thick ascending limb of the Loop of Henle → impaired concentrating ability of the kidney → decreased water reabsorption both upstream (e.g., descending limb of Loop of Henle) and downstream (e.g., collecting ducts)

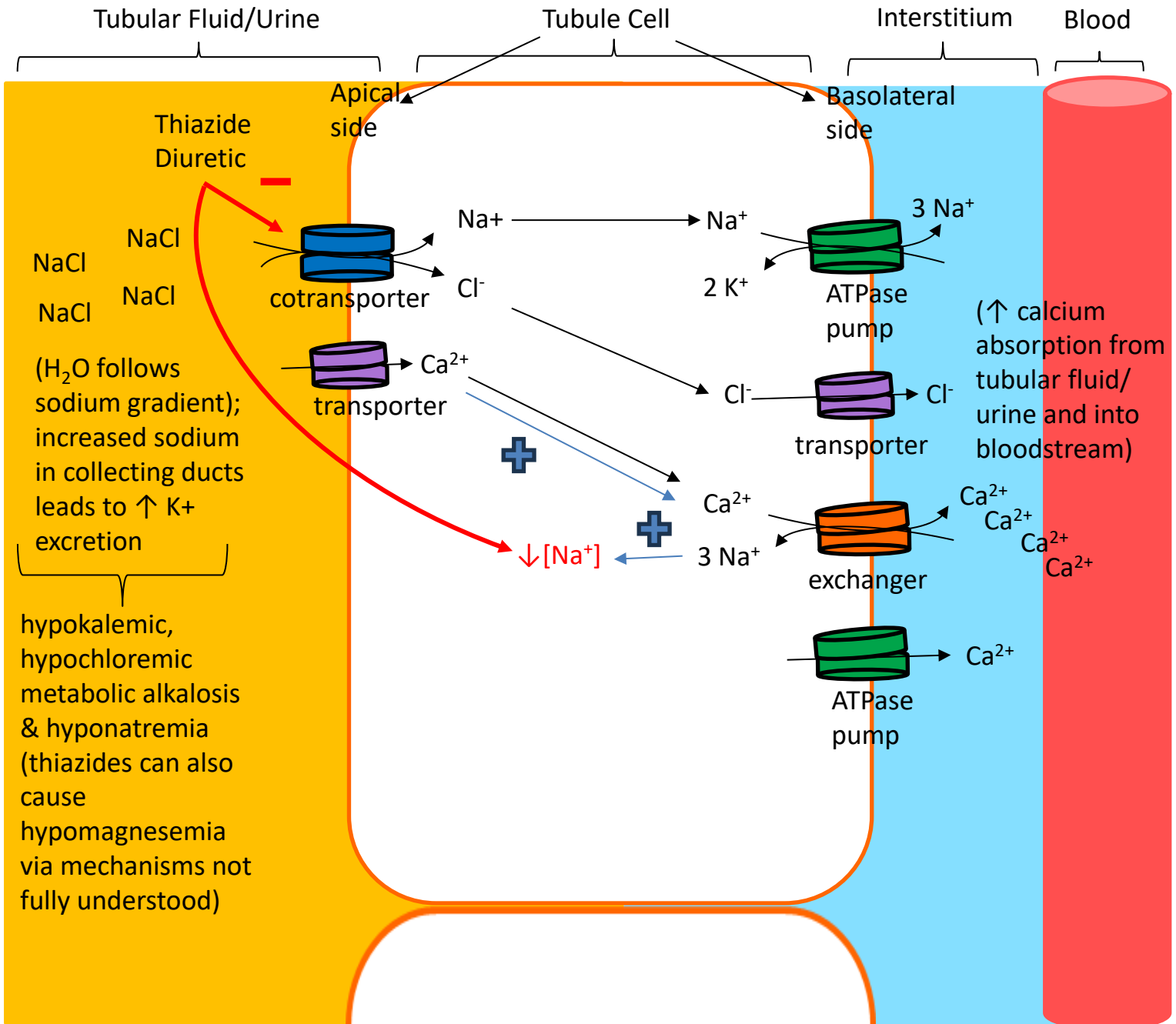
Use of furosemide in combination with mannitol to reduce brain volume: <u>theorized mechanisms include</u>: In addition to furosemide causing diuresis of fluid brought into the vascular space by mannitol, other theories exist (such as disruption of the ability of central neurons and glia to restore their volume in response to fluid lost from mannitol)."[4]

Room for notes



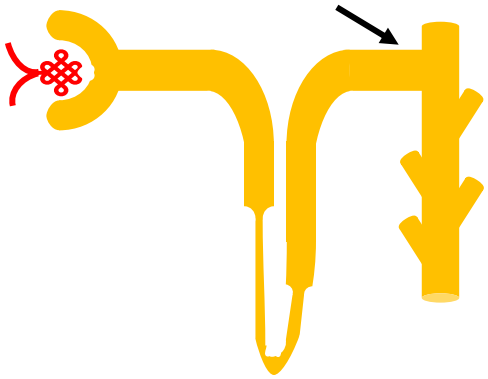
Refs: 1. Koeppen's Renal Physiology, 6th Ed, Ch 10 // 2. Miller 10th Ed Ch 24 // 3. Bell R. BJA Education; PMID: 35614905 // 4. Miller's Anesthesia 10th Ed Ch 53 // A. Harrison's 21st Ed, Ch 309 // B. Berne & Levy's Physiology 8th Ed, Ch 35 // Other Refs: Miller 10th Ed Ch 15

Thiazide Diuretics

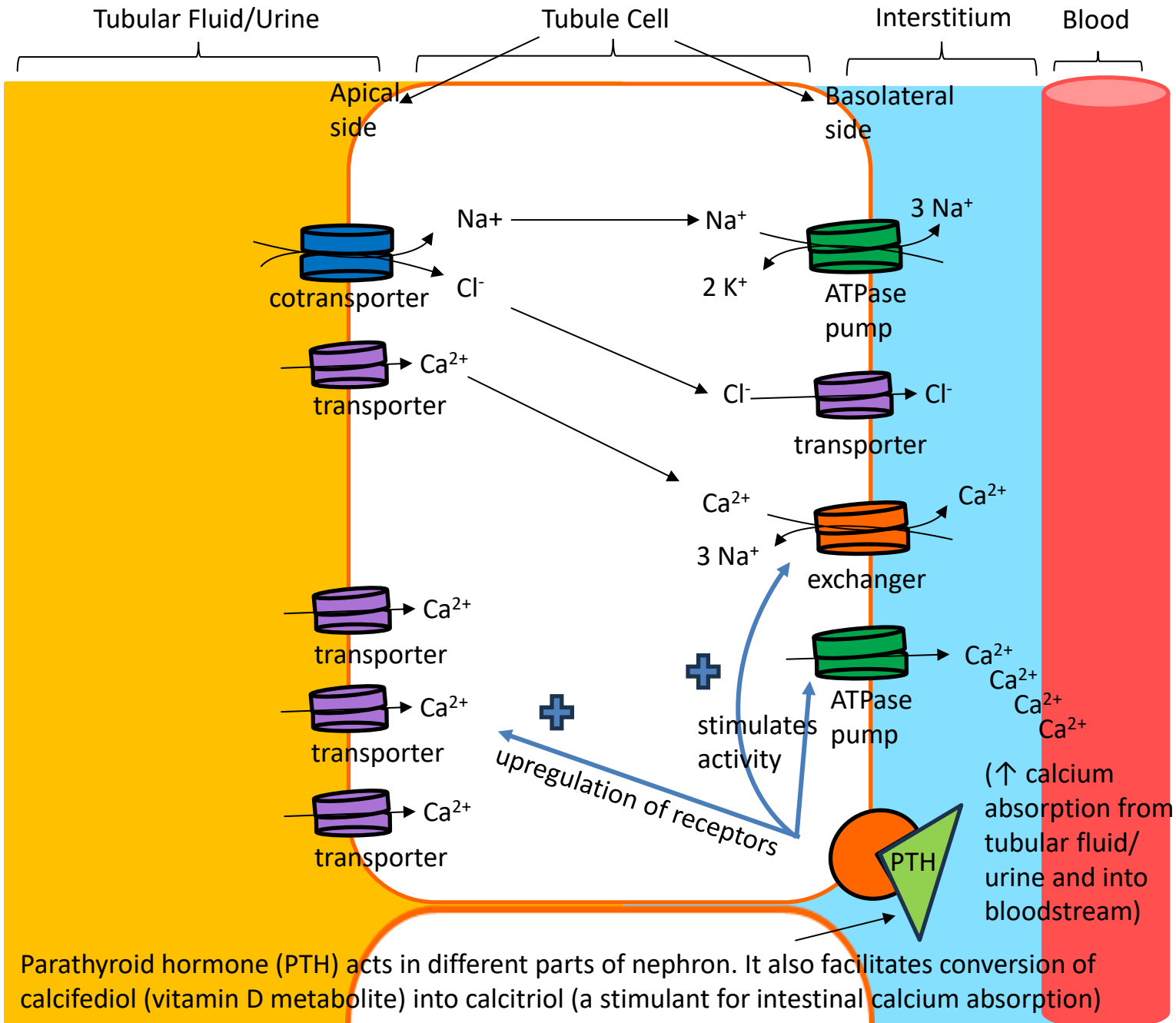


Room for notes

Distal convoluted tubule



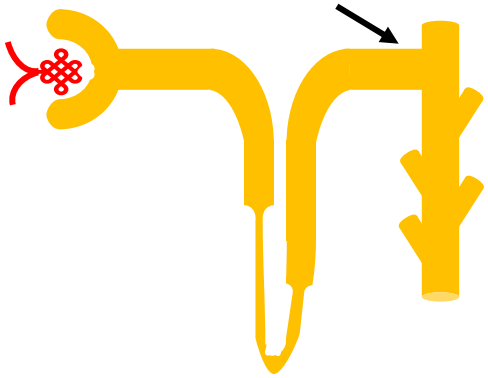
Parathyroid Hormone



Parathyroid hormone (PTH) acts in different parts of nephron. It also facilitates conversion of calcifediol (vitamin D metabolite) into calcitriol (a stimulant for intestinal calcium absorption)

Room for notes

Distal convoluted tubule



Renin-Angiotensin-Aldosterone System

Room for notes

Glomerular (Bowman's) Capsule

Glomerulus

Proximal convoluted tubule

Distal convoluted tubule

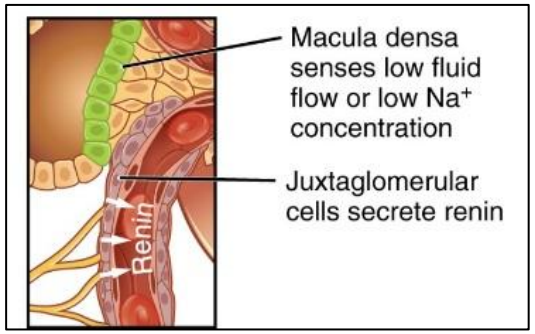
Connecting tubule

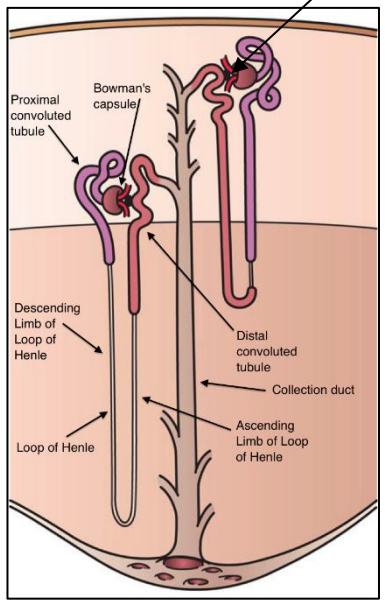
Cortical Collecting duct

Macula densa

Efferent arteriole

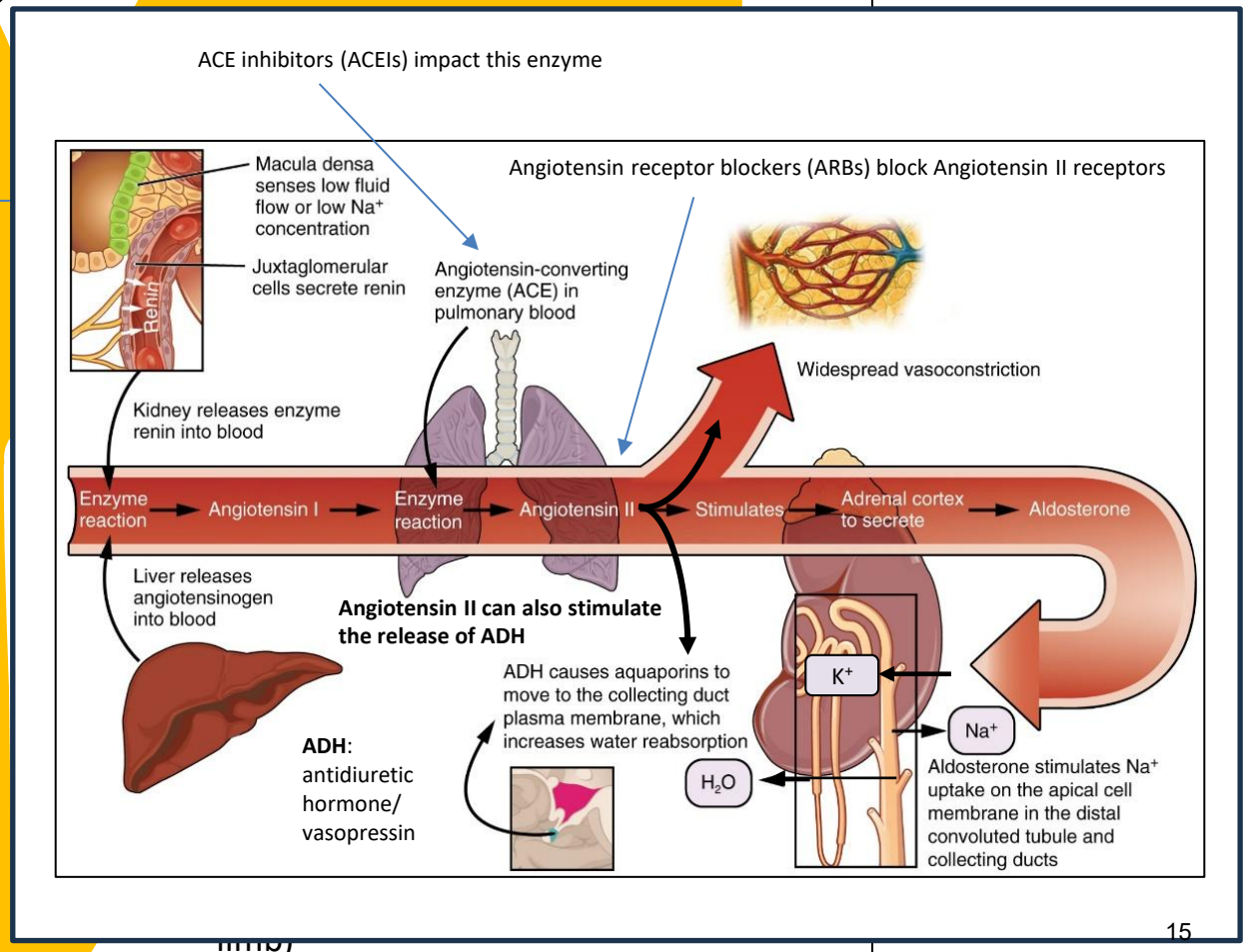
Afferent arteriole





"Near the end of the thick ascending limb, the nephron passes between the afferent and efferent arterioles of the same nephron. This short segment of the thick ascending limb abutting the glomerulus is called the macula densa."[1]

Loop of Henle (thin descending limb)



Angiotensin II, NSAIDS, ACEIs, and ARBs

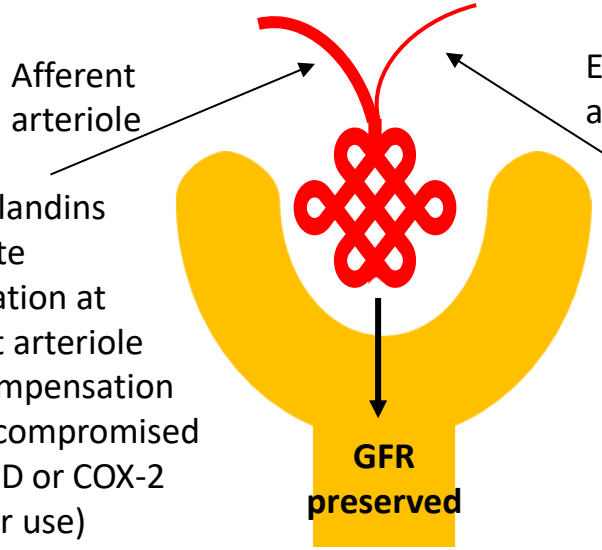
11X
Including next slide

Room for notes

Prostaglandins work together with angiotensin II to preserve GFR in settings of low renal perfusion:

- Prostaglandins stimulate vasodilation of afferent glomerular arterioles and Angiotensin II causes constriction of the efferent glomerular arterioles → increased glomerular capillary pressure → increased GFR (or preserved GFR in setting of low renal perfusion).[1-4]

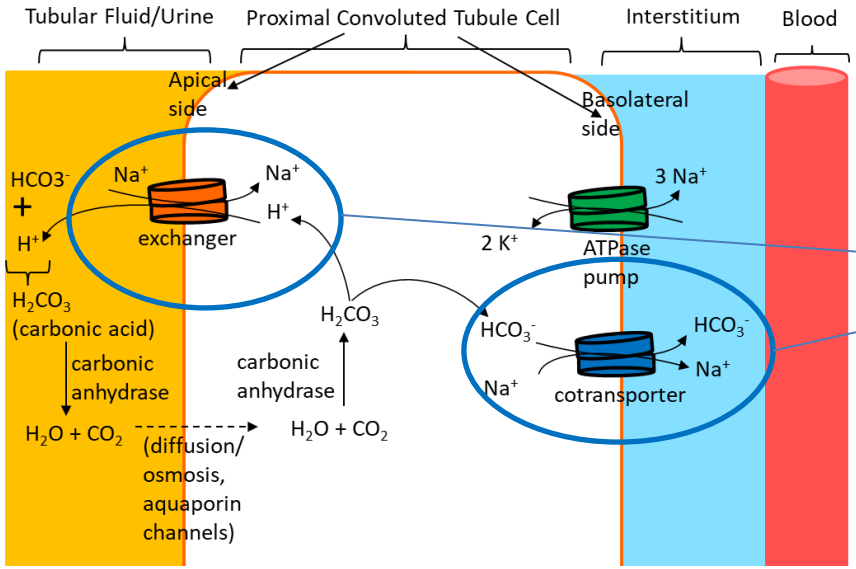
Compensation for Low Renal Perfusion[1-4]



Prostaglandins stimulate vasodilation at afferent arteriole (this compensation can be compromised by NSAID or COX-2 inhibitor use)

Angiotensin II stimulates vasoconstriction at efferent arteriole (this compensation can be compromised by ACE-I or ARB use)

Angiotensin II also works at Proximal Tubule



Stimulated by Angiotensin II, which leads to increased Na^+ reabsorption.[6]

- Side effects of ACE-I's and ARB's can include reduction in GFR, hyperkalemia (via decreased aldosterone secretion), and cough & angioedema (more common with ACE-I's). ACE-I's and ARB's are contraindicated in pregnancy.[5]
- ACE-I and/or ARB therapy may improve survival in patients with acute myocardial infarction who are not hypotensive or have other contraindications.[7]

"[S]epsis, hypercalcemia, severe liver failure, calcineurin inhibitors [e.g., tacrolimus, cyclosporine], and radiocontrast agents can act through various vasoconstrictor mediators to increase afferent arteriolar resistance. In addition, sepsis and contrast agents may have direct toxic effects on the tubules."[4]

Angiotensin-converting enzyme inhibitors (ACEIs) and Angiotensin receptor blockers (ARBs): To hold or not to hold preop?

Controversy and Recent Evidence:

Miller 10th Ed, Ch 38: "The impact of continuation or discontinuation of [ACEIs/ARBs] in the perioperative setting is controversial" **Barash 9th Ed, Ch 23:** "The perioperative management of [ACEIs] and [ARBs] is controversial."

UpToDate (Perioperative Medication Management): "In general, patients who continue [ACEIs] and ARBs appear to have higher rates of [periop] hypotension, but lower rates of postoperative hypertension. No association between cardiovascular outcomes or mortality has been demonstrated with perioperative continuation of [ACEIs] or ARBs."

JAMA 2024 RCT "Stop-or-Not Trial" (PMID 39212270): "Among patients who underwent major noncardiac surgery, a strategy of [continuing ACEIs or ARBs] before surgery was not associated with a higher rate of postoperative complications than a discontinuation strategy." (Intraop hypotension more frequent when ACEIs/ARBs were continued, but did not lead to complications "likely [due to] rapid [intraoperative] correction […] and the overall short duration of low blood pressure."

Selected Recommendations:

Miller 10th Ed, Ch 28 (Preoperative Evaluation): "In general, long-term antihypertensive treatment should be continued up to the day of surgery, except possibly for [ACEIs] or [ARBs]. Administration of these medications within 24 hours [preop] is associated with increased risks of [intraop] hypotension. Thus, it is reasonable to withhold these medications for 24 hours before surgery" "Importantly, failure to resume ACEI and ARB therapy [postop] is itself associated with adverse outcomes."

UpToDate (Perioperative medication management): "We individualize the decision to continue or discontinue [ACEIs] based on the indications […], the patient's blood pressure, and the type of surgery and anesthesia planned. When there is a high concern for perioperative hypotension, we withhold [ACEIs] and ARBs on the morning of surgery. […] [W]hen the indication is for heart failure or poorly controlled hypertension, we continue them to avoid further exacerbation of these conditions."

2024 ACC/AHA et al Guidelines/Noncardiac Surgery (mentions Stop-or-Not Trial as still pending): "an individualized approach to perioperative management of ACEi or ARBs is warranted."

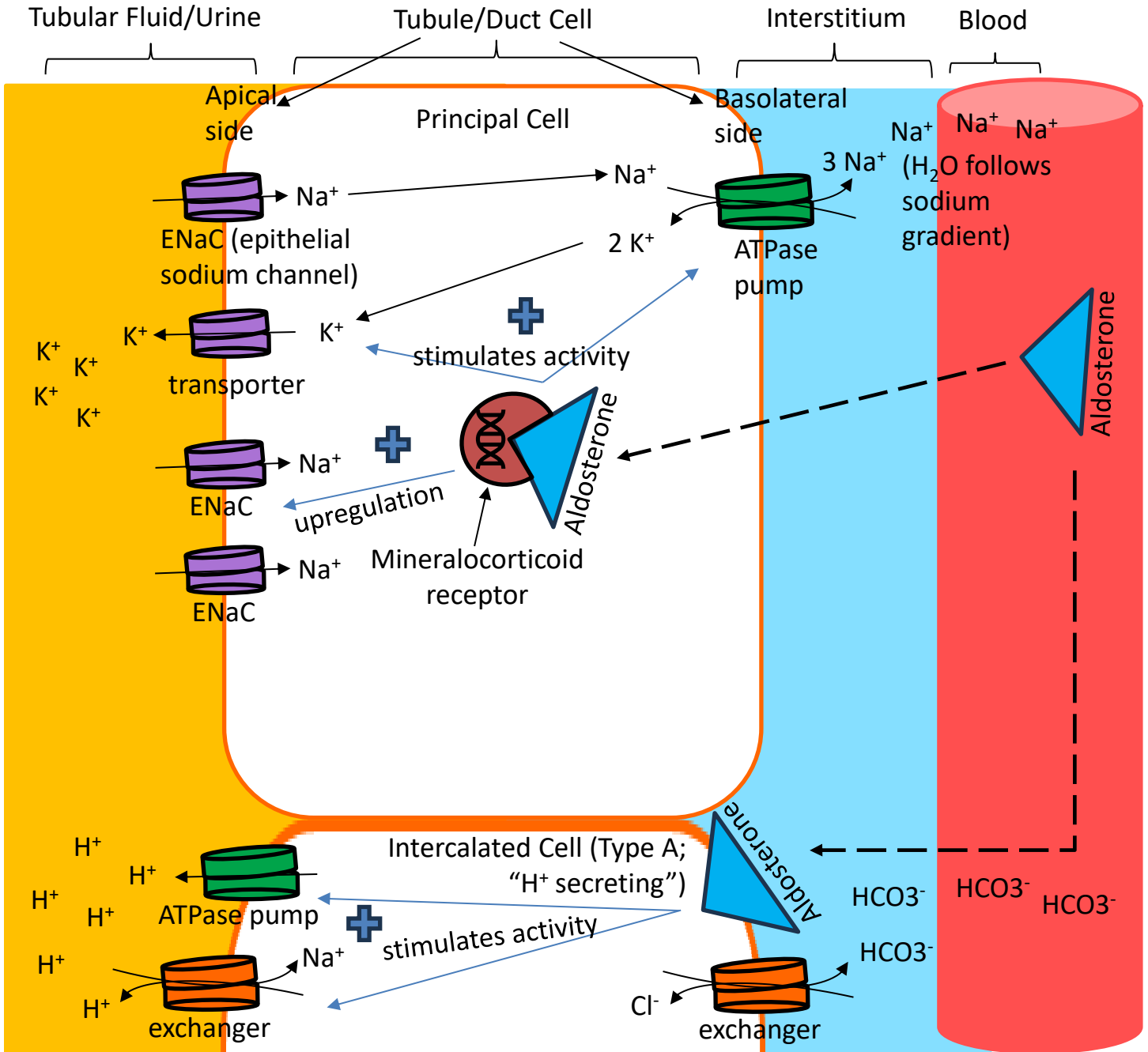
- "In [patients with controlled BP] on chronic renin-angiotensin-aldosterone system inhibitors (RAASi) for hypertension undergoing elevated-risk [noncardiac surgery], omission 24 hours [preop] may be beneficial to limit [intraop] hypotension."
- "In patients on chronic RAASi for HFrEF, perioperative continuation is reasonable."

Room for notes

What about diuretics?
Miller 10th Ed, Ch 28: Discontinue on the day of surgery, except for thiazide diuretics taken for hypertension.

UpToDate (Perioperative Medication Management): Continue if taking for heart failure with fluid balance that is hard to control. Discontinue if taking for hypertension or well-controlled heart failure.

Normal Aldosterone Effects as part of Renin-Angiotensin-Aldosterone System



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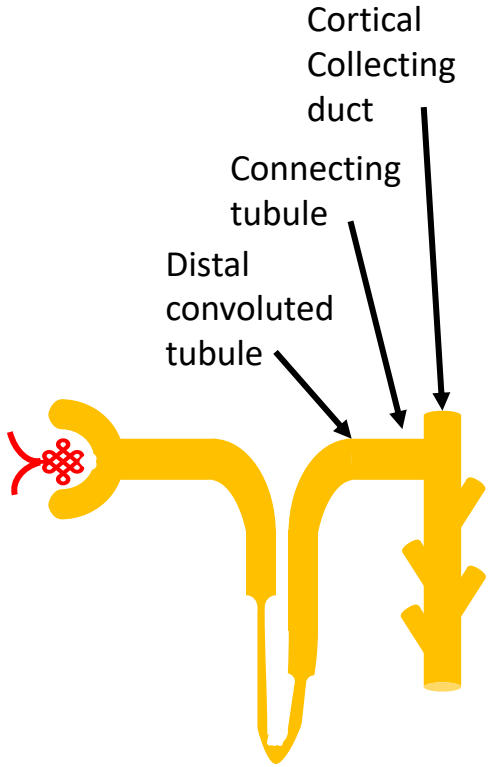
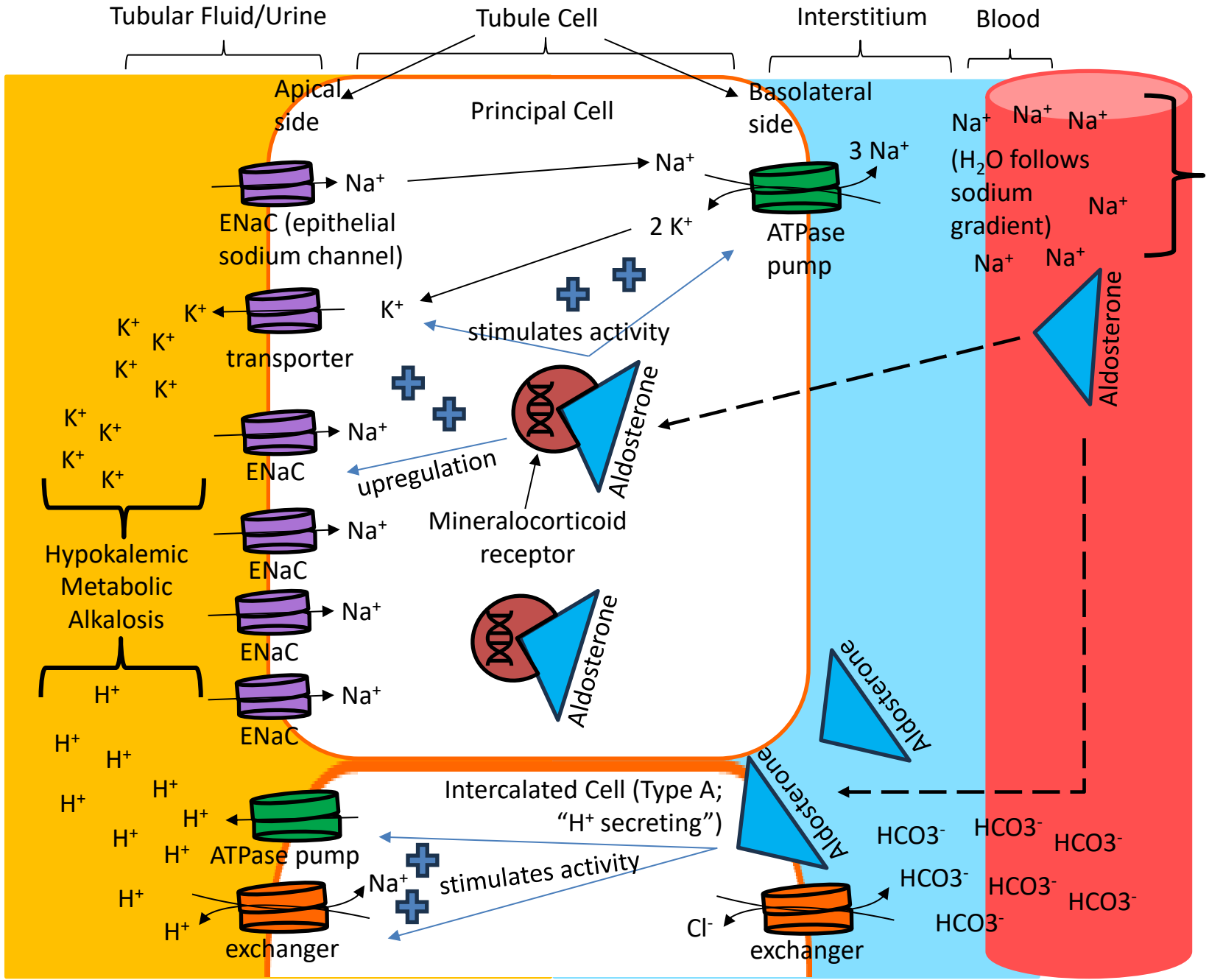


Primary Hyperaldosteronism



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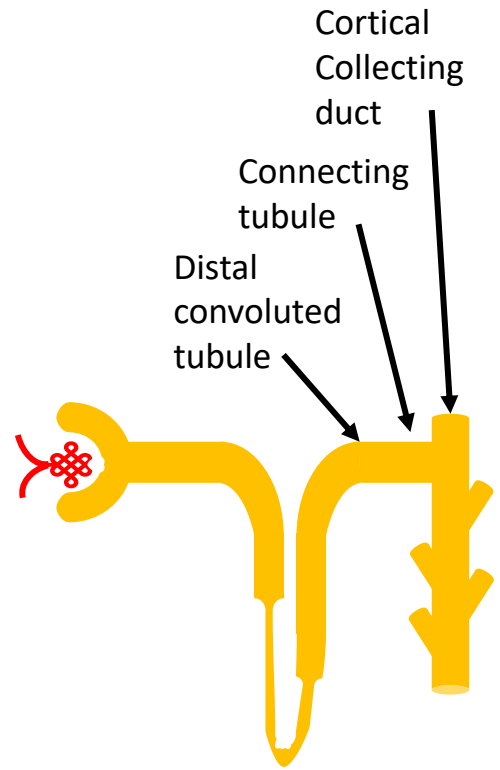
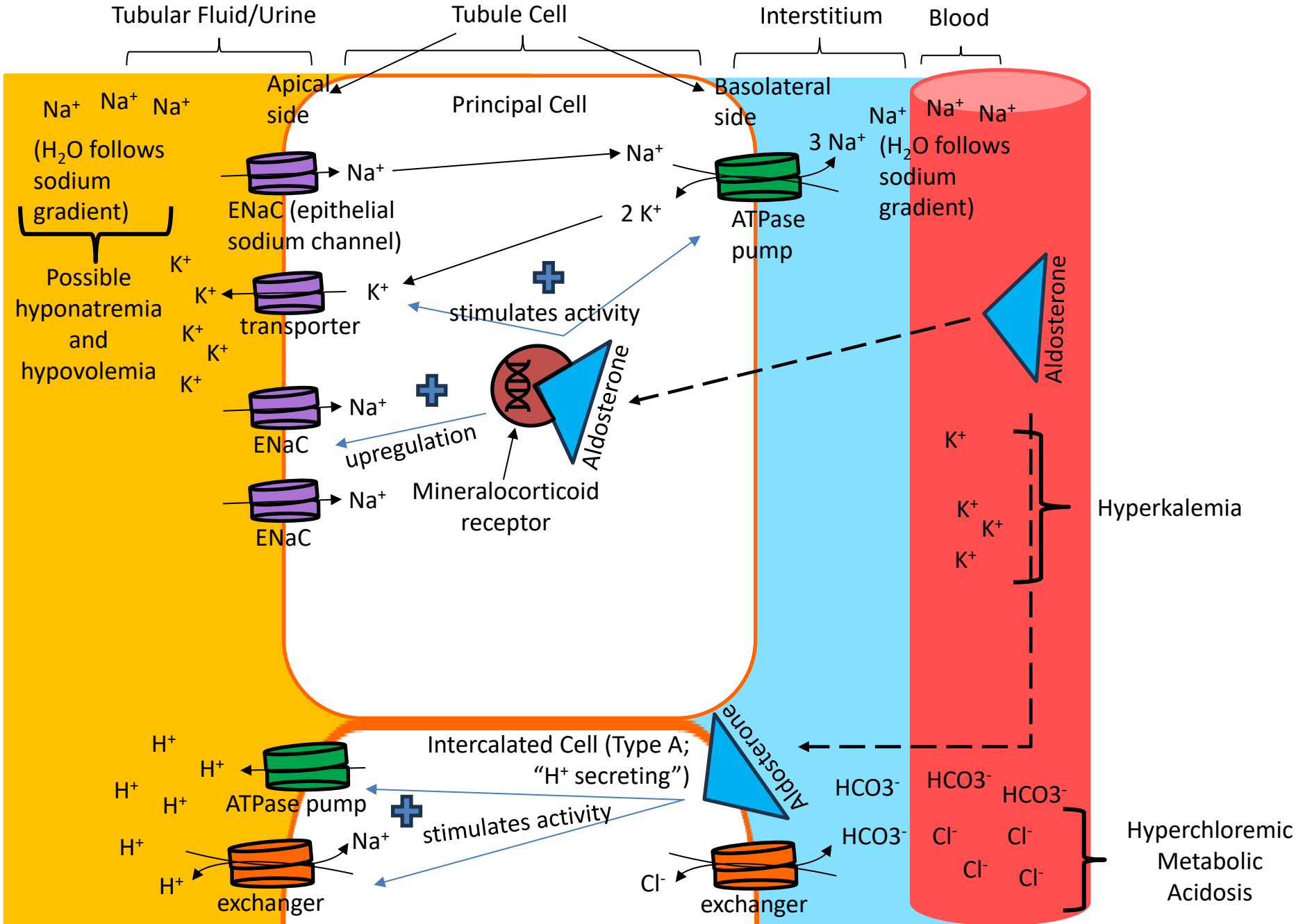


Primary Adrenal Insufficiency (Mineralocorticoid Component)



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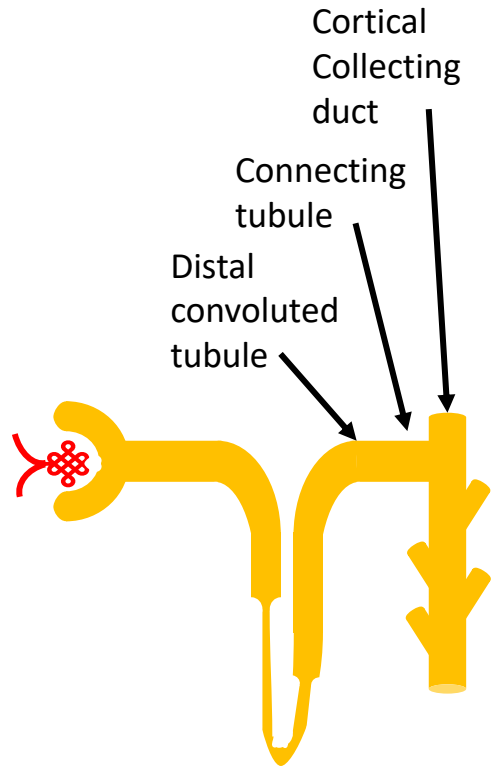
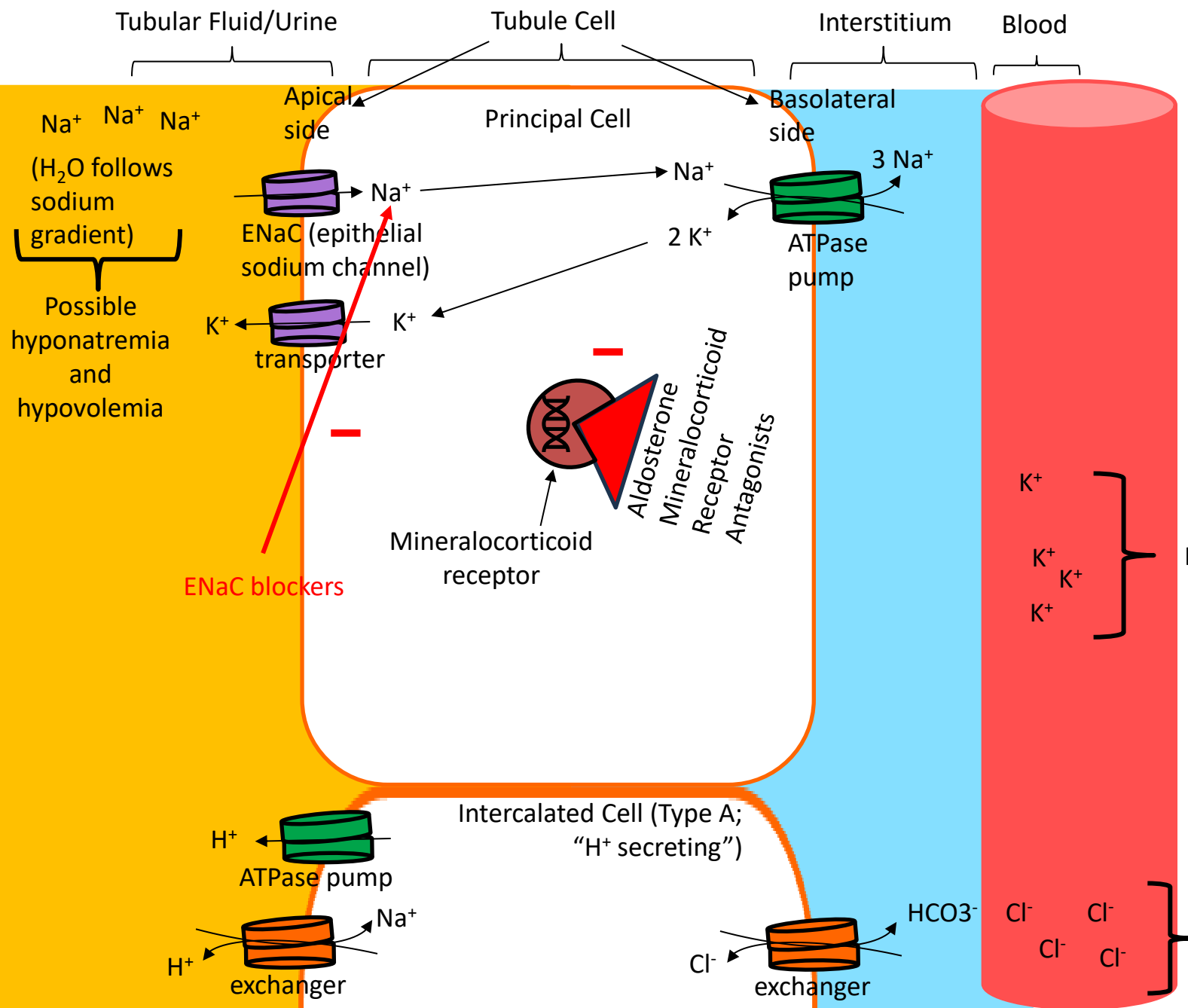


Potassium-Sparing Diuretics



Primary Adrenal Insufficiency (Mineralocorticoid Component)

Aldosterone Mineralocorticoid Receptor Antagonists (Spironolactone, Eplerenone, Finerenone)

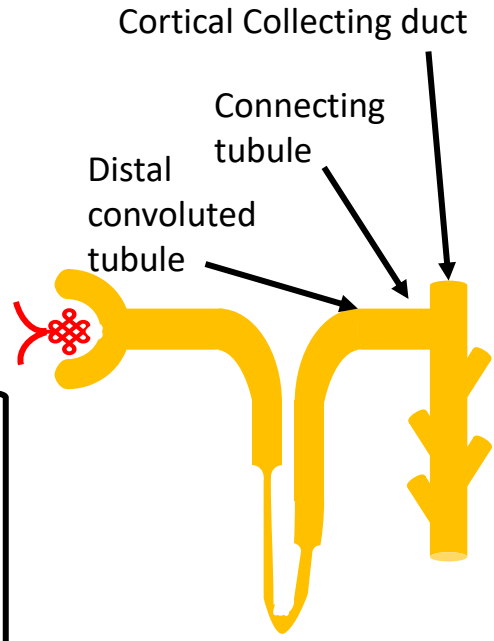
Hyperkalemia

ENaC (epithelium sodium channel) blockers (Amiloride, Triamterene)

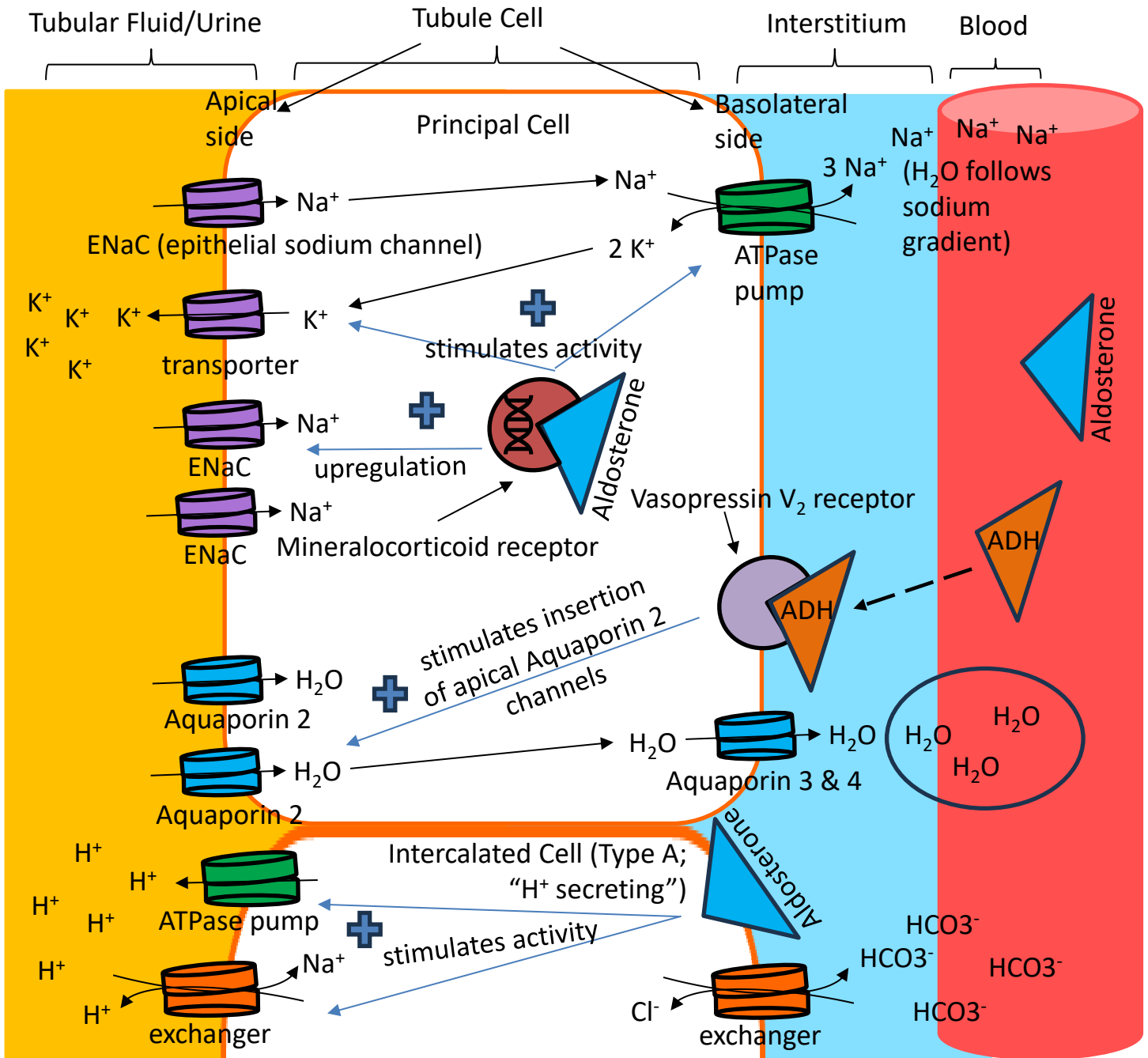
Hyperchloremic Metabolic Acidosis

Potassium-sparing diuretics

Room for notes

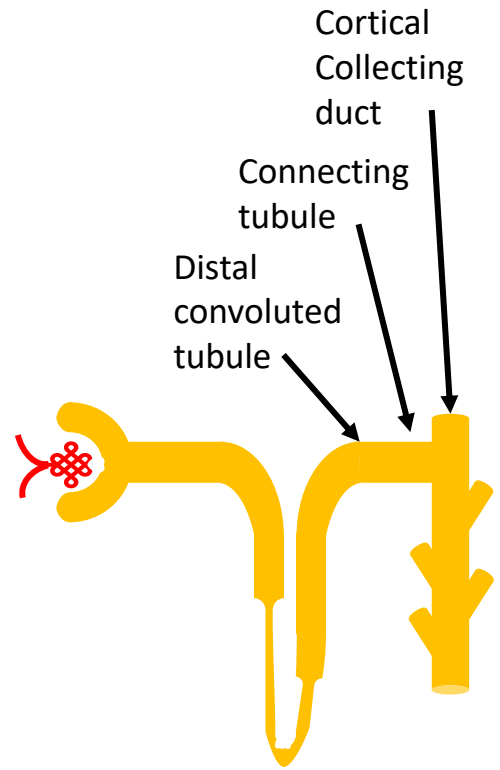


Antidiuretic Hormone (ADH)

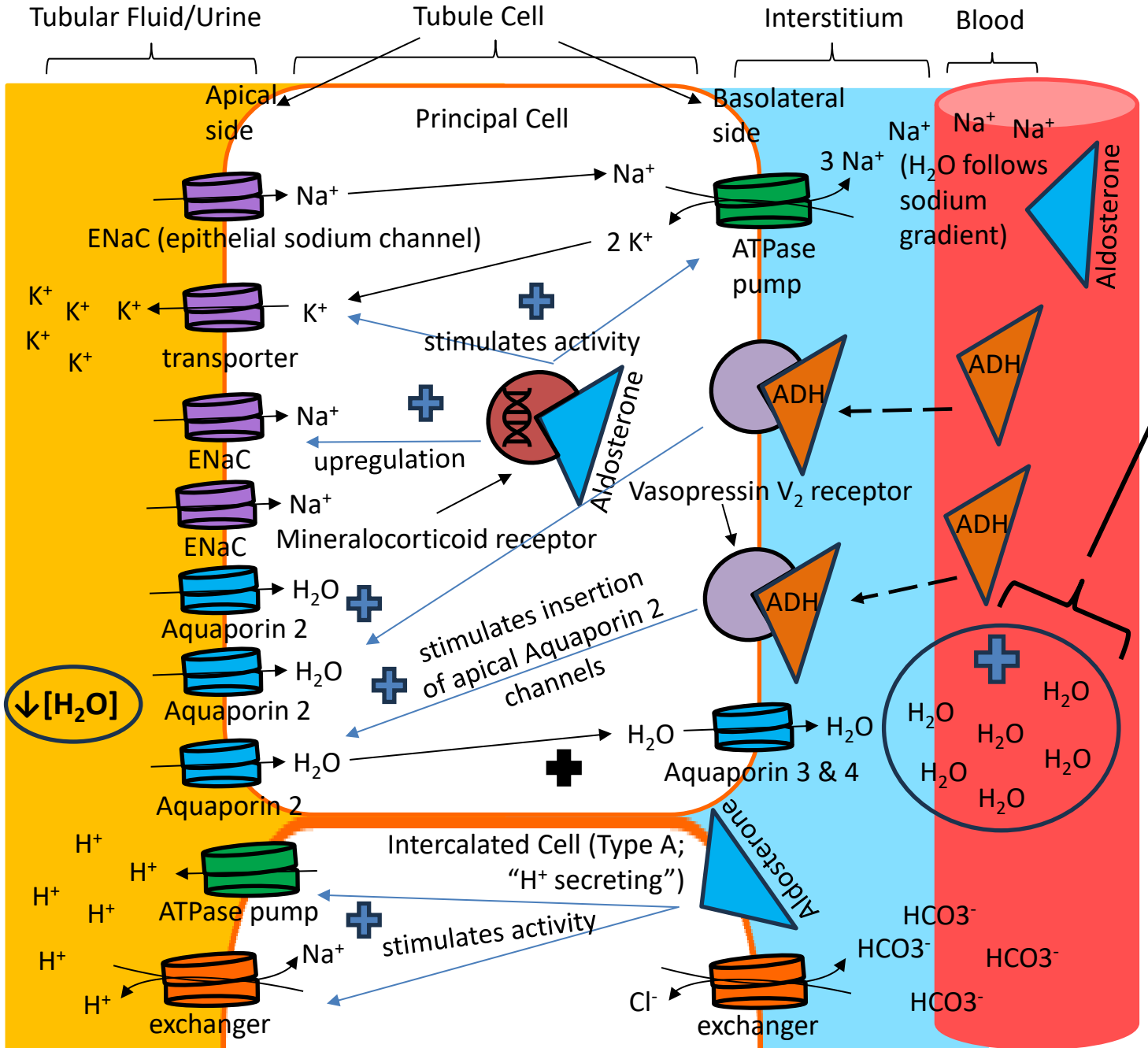


Normal Effects of ADH in response to small increases in plasma osmolality (≥ 1-2% increase) or notable hypovolemia (≥ 10-15% reduction in blood volume)

Room for notes



Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH)

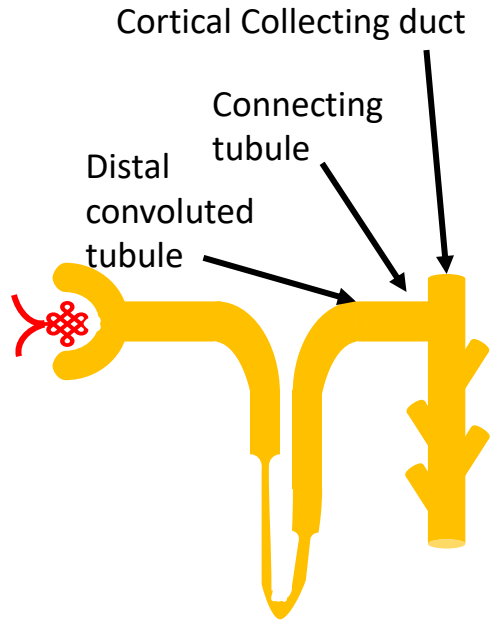


- Serum Na^+ level: Low (urine Na^+ level normal or elevated)
- Serum osmolality: Low (urine osmolality elevated)
- Urine specific gravity: Elevated
- Urine output: Decreased

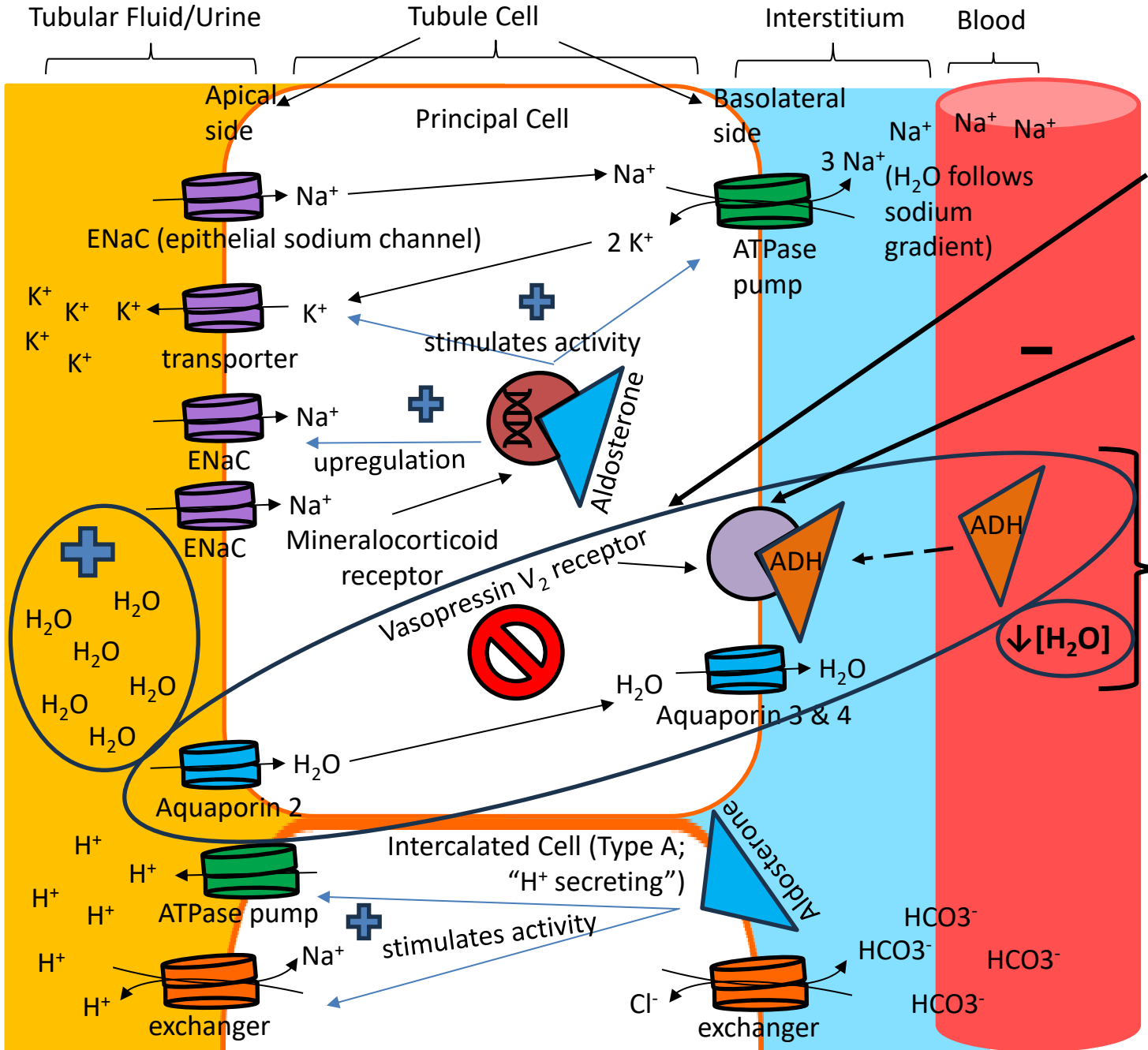
These serum/urine lab findings are the same as in Cerebral Salt Wasting (CSW) Syndrome (inappropriate sodium wasting in urine due to a range of different theories; see handout), which, in the case of CSW, leads to hyponatremia and hypovolemia.

"It is only the presence of clear evidence of volume depletion […] despite a urine sodium concentration that is not low that suggests that CSW might be present rather than SIADH. By comparison, extracellular fluid volume is normal or slightly increased with SIADH."[1]

Room for notes



Arginine Vasopressin Resistance (Peripheral Nephrogenic Diabetes Insipidus [DI])



"[Arginine vasopressin resistance (nephrogenic DI)] may result from defects in the V2 receptor, Aquaporin-2, or any of the regulatory proteins that govern cellular responses to ADH."[1]

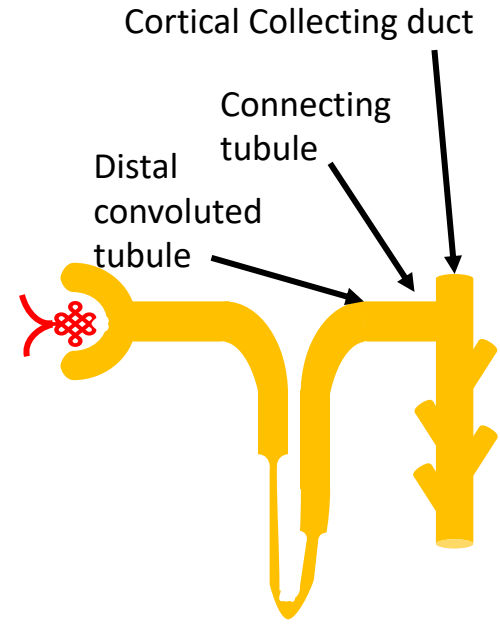
Vasopressin receptor antagonists (aka, vaptans) can cause selective water diuresis; sometimes used to treat SIADH or other forms of hyponatremia.[2,3]

- Serum Na^+ level: High (urine Na^+ level normal or decreased)
- Serum osmolality: High (urine osmolality decreased)
- Urine specific gravity: Low
- Urine output: Elevated

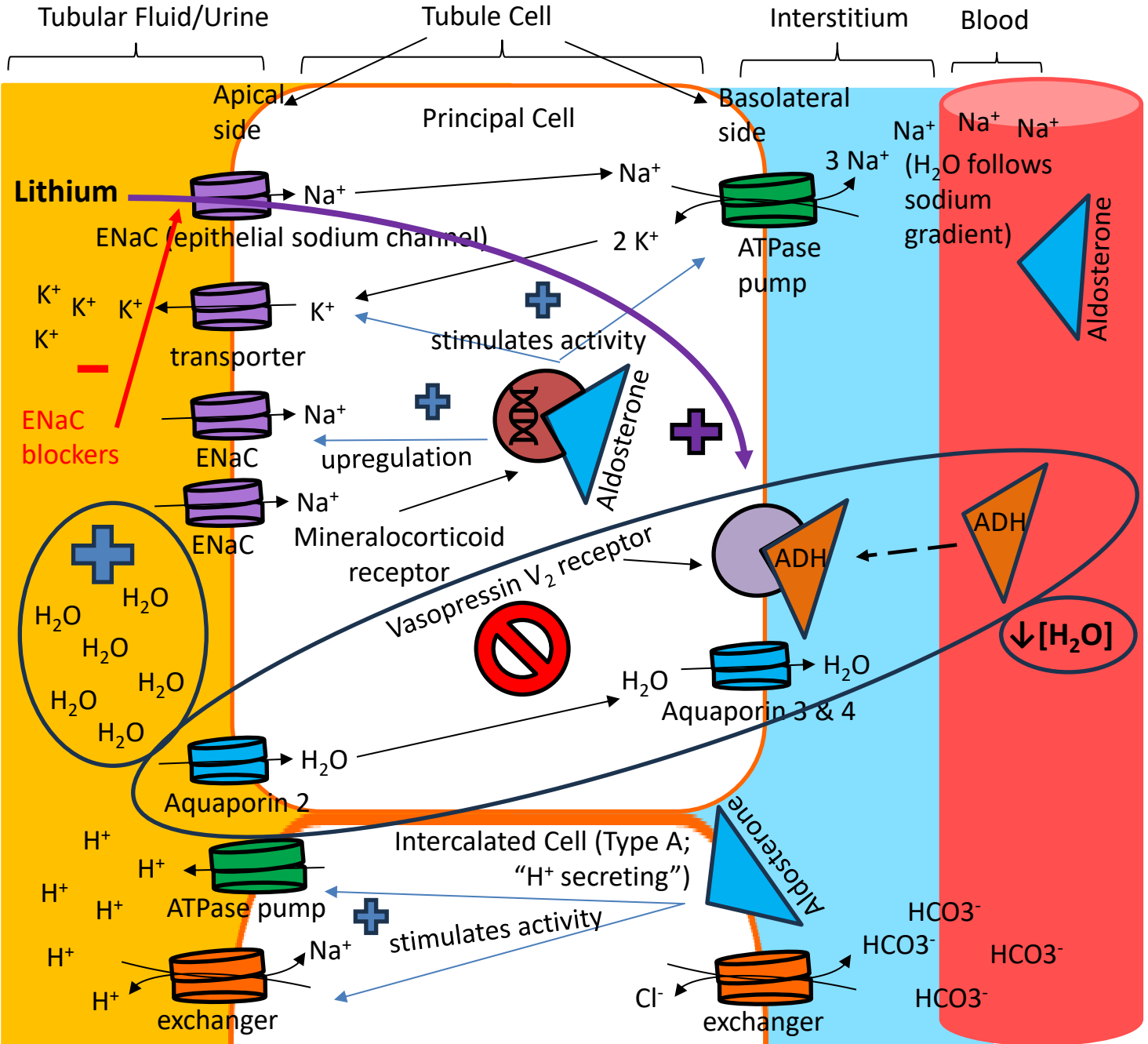
These serum/urine lab findings are same as in Arginine Vasopressin Deficiency (Central Neurogenic DI)

*"Neurogenic and nephrogenic DI are differentiated based on the **response to desmopressin (DDAVP),** [a synthetic analog of ADH which] leads to concentration of the urine in the presence of neurogenic, but not nephrogenic, DI."*[4] *"If DI is confirmed, basal plasma arginine vasopressin (AVP) should be measured on unrestricted fluid intake. If AVP is normal or elevated […], the patient probably has nephrogenic DI. [I]f plasma AVP is low or undetectable, the patient has either pituitary DI or primary polydipsia."*[5]

Room for notes



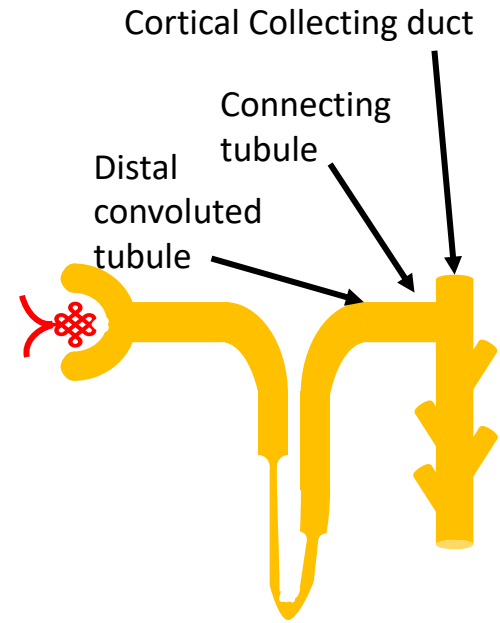
Lithium, Arginine Vasopressin Resistance (Nephrogenic DI), and ENaC blockers



"The lithium ion resembles Na^+, K^+, magnesium, and Ca^{2+} ions, and therefore may affect the distribution and kinetics of all these electrolytes. Lithium enters cells via Na^+ channels and tends to accumulate within the cells."[1]

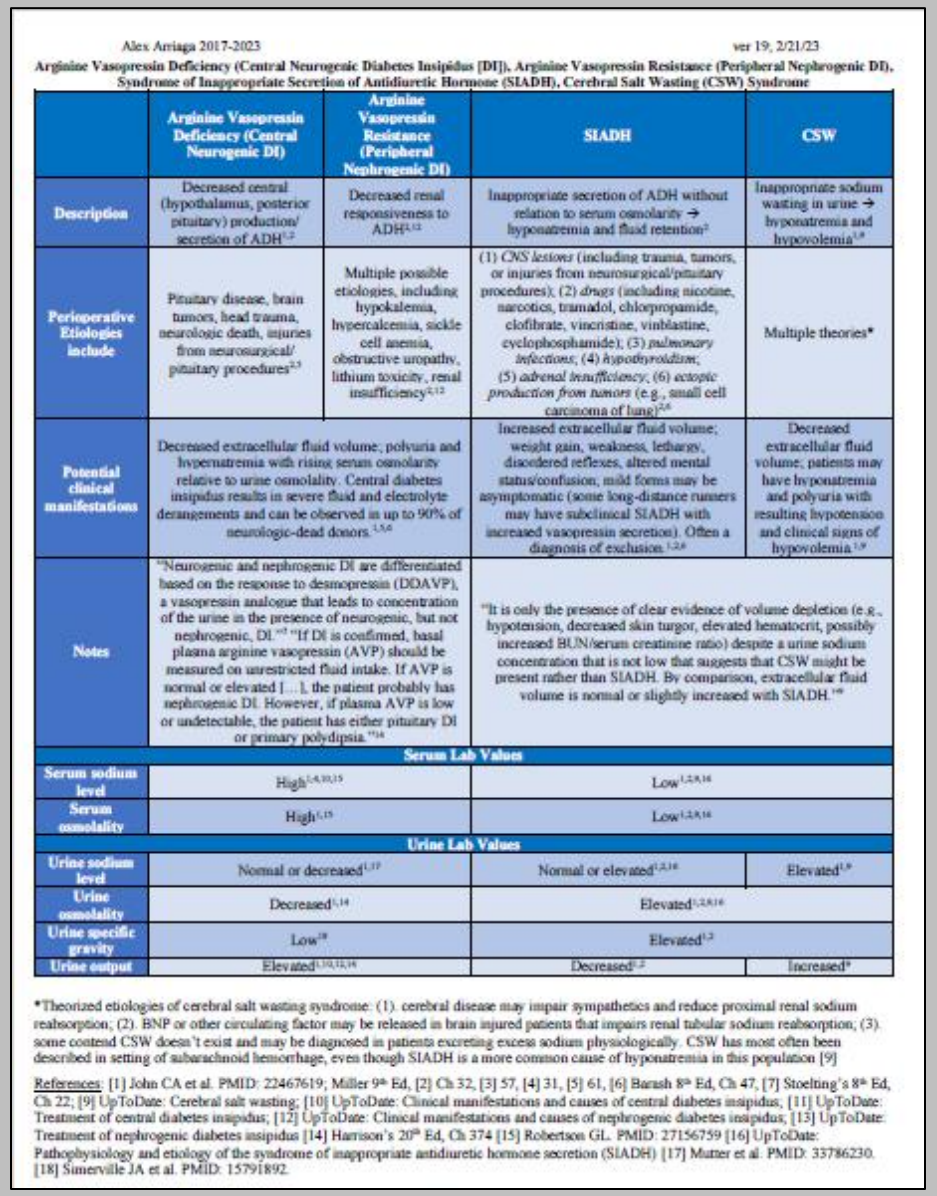
- Lithium use can lead to arginine vasopressin resistance (nephrogenic DI). Theorized mechanism: lithium enters collecting ducts via ENaC channels and accumulates.[2,3]
- Amiloride (ENaC blocker) is sometimes used for the treatment of lithium-induced arginine vasopressin resistance (nephrogenic DI).[2,3]
- Lithium can prolong duration of both depolarizing and nondepolarizing paralytics, via both presynaptic (inhibition of neuromuscular transmission) and postsynaptic (inhibition of muscular contraction) theorized mechanisms.[1]

Room for notes



Syndrome of Inappropriate antidiuretic hormone (SIADH) vs Arginine Vasopressin Deficiency/Resistance (Diabetes Insipidus [DI]) vs Cerebral Salt Wasting Syndrome (CSW)

Room for notes



Alex Arriaga 2017-2023 ver 19, 2/21/23

Arginine Vasopressin Deficiency (Central Neurogenic Diabetes Insipidus [DI]), Arginine Vasopressin Resistance (Peripheral Nephrogenic DI), Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH), Cerebral Salt Wasting (CSW) Syndrome

	Arginine Vasopressin Deficiency (Central Neurogenic DI)	Arginine Vasopressin Resistance (Peripheral Nephrogenic DI)	SIADH	CSW
Description	Decreased central (hypothalamus, posterior pituitary) production/ secretion of ADH[1,2]	Decreased renal responsiveness to ADH[1,12]	Inappropriate secretion of ADH without relation to serum osmolarity → hyponatremia and fluid retention[2]	Inappropriate sodium wasting in urine → hyponatremia and hypovolemia[1,9]
Perioperative Etiologies include	Pituitary disease, brain tumors, head trauma, neurologic death, injuries from neurosurgical/ pituitary procedures[2,3]	Multiple possible etiologies, including hypokalemia, hypercalcemia, sickle cell anemia, obstructive uropathy, lithium toxicity, renal insufficiency[2,12]	(1) *CNS lesions* (including trauma, tumors, or injuries from neurosurgical/pituitary procedures); (2) *drugs* (including nicotine, narcotics, tramadol, chlorpropamide, clofibrate, vincristine, vinblastine, cyclophosphamide); (3) *pulmonary infections*; (4) *hypothyroidism*; (5) *adrenal insufficiency*; (6) *ectopic production from tumors* (e.g., small cell carcinoma of lung)[2,6]	Multiple theories*
Potential clinical manifestations	Decreased extracellular fluid volume; polyuria and hypernatremia with rising serum osmolarity relative to urine osmolality. Central diabetes insipidus results in severe fluid and electrolyte derangements and can be observed in up to 90% of neurologic-dead donors.[3,5,6]		Increased extracellular fluid volume; weight gain, weakness, lethargy, disordered reflexes, altered mental status/confusion; mild forms may be asymptomatic (some long-distance runners may have subclinical SIADH with increased vasopressin secretion). Often a diagnosis of exclusion.[1,2,6]	Decreased extracellular fluid volume; patients may have hyponatremia and polyuria with resulting hypotension and clinical signs of hypovolemia.[1,9]
Notes	"Neurogenic and nephrogenic DI are differentiated based on the response to desmopressin (DDAVP), a vasopressin analogue that leads to concentration of the urine in the presence of neurogenic, but not nephrogenic, DI."[2] "If DI is confirmed, basal plasma arginine vasopressin (AVP) should be measured on unrestricted fluid intake. If AVP is normal or elevated [...], the patient probably has nephrogenic DI. However, if plasma AVP is low or undetectable, the patient has either pituitary DI or primary polydipsia."[16]		"It is only the presence of clear evidence of volume depletion (e.g., hypotension, decreased skin turgor, elevated hematocrit, possibly increased BUN/serum creatinine ratio) despite a urine sodium concentration that is not low that suggests that CSW might be present rather than SIADH. By comparison, extracellular fluid volume is normal or slightly increased with SIADH."[9]	
Serum Lab Values				
Serum sodium level	High[1,9,10,15]		Low[1,2,9,16]	
Serum osmolality	High[1,15]		Low[1,2,9,16]	
Urine Lab Values				
Urine sodium level	Normal or decreased[1,15]		Normal or elevated[1,2,16]	Elevated[1,9]
Urine osmolality	Decreased[1,14]		Elevated[1,2,9,16]	
Urine specific gravity	Low[14]		Elevated[1,2]	
Urine output	Elevated[1,10,12,14]		Decreased[1,2]	Increased*

*Theorized etiologies of cerebral salt wasting syndrome: (1). cerebral disease may impair sympathetics and reduce proximal renal sodium reabsorption; (2). BNP or other circulating factor may be released in brain injured patients that impairs renal tubular sodium reabsorption; (3). some contend CSW doesn't exist and may be diagnosed in patients excreting excess sodium physiologically. CSW has most often been described in setting of subarachnoid hemorrhage, even though SIADH is a more common cause of hyponatremia in this population [9]

References: [1] John CA et al. PMID: 22467619; Miller 9th Ed, [2] Ch 32, [3] 57, [4] 31, [5] 61, [6] Barash 8th Ed, Ch 47, [7] Stoelting's 8th Ed, Ch 22; [9] UpToDate: Cerebral salt wasting; [10] UpToDate: Clinical manifestations and causes of central diabetes insipidus; [11] UpToDate: Treatment of central diabetes insipidus; [12] UpToDate: Clinical manifestations and causes of nephrogenic diabetes insipidus; [13] UpToDate: Treatment of nephrogenic diabetes insipidus [14] Harrison's 20th Ed, Ch 374 [15] Robertson GL. PMID: 27156759 [16] UpToDate: Pathophysiology and etiology of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) [17] Mutter et al. PMID: 33786230. [18] Simerville JA et al. PMID: 15791892.

Terminology Update:

"Confusion between diabetes insipidus and diabetes mellitus has led to occasional medication errors resulting in patient-safety concerns; in addition, the name 'diabetes insipidus' does not reflect the underlying pathophysiology of disease. As a result, the Endocrine Society, European Society of Endocrinology, Pituitary Society, Society for Endocrinology, European Society for Paediatric Endocrinology, Endocrine Society of Australia, Brazilian Endocrine Society, and Japanese Endocrine Society all proposed to change the names of these disorders. Arginine vasopressin deficiency (AVP-D) is the new name for central diabetes insipidus, and arginine vasopressin resistance (AVP-R) is the new name for nephrogenic diabetes insipidus."[1]

1. UpToDate: Arginine vasopressin deficiency (central diabetes insipidus): Treatment

Arginine Vasopressin Deficiency (Central Neurogenic Diabetes Insipidus [DI]), Arginine Vasopressin Resistance (Peripheral Nephrogenic DI), Syndrome of Inappropriate Secretion of Antidiuretic Hormone (SIADH), Cerebral Salt Wasting (CSW) Syndrome

	Arginine Vasopressin Deficiency (Central Neurogenic DI)	Arginine Vasopressin Resistance (Peripheral Nephrogenic DI)	SIADH	CSW
Description	Decreased central (hypothalamus, posterior pituitary) production/ secretion of ADH[1,2]	Decreased renal responsiveness to ADH[2,12]	Inappropriate ADH secretion independent of serum osmolarity → hyponatremia and fluid retention[2]	Inappropriate sodium wasting in urine → hyponatremia and hypovolemia[1,9]
Perioperative Etiologies include	Pituitary disease, brain tumors, head trauma, neurologic death, injuries from neurosurgical/ pituitary procedures[2,5]	Multiple possible etiologies, including hypokalemia, hypercalcemia, sickle cell anemia, obstructive uropathy, lithium toxicity, renal insufficiency[2,12]	(1) *CNS lesions* (including trauma, tumors, injuries from neurosurgical/pituitary procedures); (2) *drugs* (including nicotine, narcotics, tramadol, chlorpropamide, clofibrate, vincristine, vinblastine, cyclophosphamide); (3) *pulmonary infections*; (4) *hypothyroidism*; (5) *adrenal insufficiency*; (6) *ectopic tumor production* (e.g., small cell lung cancer)[2,6]	Multiple theories*
Potential clinical manifestations	Decreased extracellular fluid volume; polyuria and hypernatremia with rising serum osmolarity relative to urine osmolality. Central diabetes insipidus results in severe fluid and electrolyte derangements and can be observed in up to 90% of neurologic-dead donors.[1,5,6]		Increased extracellular fluid volume; weight gain, weakness, lethargy, disordered reflexes, altered mental status/confusion; may be asymptomatic if mild (some long-distance runners may get subclinical SIADH with increased vasopressin secretion). Often diagnosis of exclusion.[1,2,6]	Decreased extracellular fluid volume; patients may have hyponatremia & polyuria → hypotension & hypovolemia.[1,9]
Notes	"Neurogenic and nephrogenic DI are differentiated based on the response to desmopressin (DDAVP), [which] leads to concentration of the urine in the presence of neurogenic, but not nephrogenic, DI."[7] "If DI is confirmed, basal plasma arginine vasopressin (AVP) should be measured on unrestricted fluid intake. If AVP is normal or elevated […], the patient probably has nephrogenic DI. [I]f plasma AVP is low or undetectable, the patient has either pituitary DI or primary polydipsia."[14] Desmopressin is sometimes used in management of arginine vasopressin deficiency (central DI), including in the context of deceased organ donor management.		"It is only the presence of clear evidence of volume depletion (e.g., hypotension, decreased skin turgor, elevated hematocrit, possibly increased BUN/serum creatinine ratio) despite a urine sodium concentration that is not low that suggests that CSW might be present rather than SIADH. By comparison, extracellular fluid volume is normal or slightly increased with SIADH."[9]	
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Serum osmolality	High[1,15]		Low[1,2,9,16]	
Urine Lab Values				
Urine sodium level	Normal or decreased[1,17]		Normal or elevated[1,2,16]	Elevated[1,9]
Urine osmolality	Decreased[1,14]		Elevated[1,2,9,16]	
Urine specific gravity	Low[18]		Elevated[1,2]	
Urine output	Elevated[1,10,12,14]		Decreased[1,2]	Increased[9]

*Theorized etiologies of cerebral salt wasting syndrome: (1). cerebral disease may impair sympathetics and reduce proximal renal sodium reabsorption; (2). BNP or other circulating factor may be released in brain injured patients that impairs renal tubular sodium reabsorption; (3). some contend CSW doesn't exist and may be diagnosed in patients excreting excess sodium physiologically. CSW has most often been described in setting of subarachnoid hemorrhage, even though SIADH is a more common cause of hyponatremia in this population [9]

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Perioperative Oliguria: Prerenal vs. Intrarenal vs Postrenal

15X

Room for notes

Fractional Excretion of Sodium (FENa; %) = $[(Urine_{Na} \times Serum_{Cr})/(Serum_{Na} \times Urine_{Cr})] \times 100$

FENa greatest clinical value when patient has[1]
Oliguric AKI
No preexisting CKD
No diuretics in system

"A variety of studies have confirmed that the FENa [better] differentiates prerenal disease from ATN than other laboratory tests. The urine sodium concentration, the urine-to-serum creatinine ratio, and the urine osmolality all have a much lower predictive value."[1]

FENa	FEUrea	Interpretation[1]	Note
< 1%	<35%	Prerenal	Interpretation of both FENa and FEUrea unclear if pt on SGLT2 inhibitor
1-2%	--	Pre or intrarenal	
> 2%	50-65%	Intrarenal ATN	
FEUrea helpful for patients on diuretics (FENa can be >2% in hypovolemic patients with CKD or on diuretics)			

Other lab tests[2-4,8]

Test	Value/Notes	More Novel Serum Biomarkers[5,9-11]
Urine specific gravity	> 1.015 for prerenal hypovolemia	*(Both are active areas of study)* Cystatin C: accumulates in setting of renal insufficiency; less affected by muscle mass /diet than creatinine. Proenkephalin A 119-159 (penKid): correlates to GFR; may be associated with subclinical AKI in critical illness. *2024 ITE Knowledge Gaps*: "Cystatin C is an accurate biomarker of renal function"
Urine osmolality	> 500 mosmol/kg for prerenal; < 450 mosmol/kg (often < 350 mosmol/kg) in ATN	
Urine microscopy	Muddy brown granular casts for ATN	
Urine sodium	< 20 mEq/L for prerenal (assuming no Na^+ wasting disease); higher in ATN (> 40 mEq/L)	
BUN/$Serum_{Cr}$ ratio	Greater than 20:1 mg/dL for prerenal; 10:1 to 15:1 (normal) for ATN	
Rate of $Serum_{Cr}$ rise over time	Faster rise (greater than 0.3 to 0.5 mg/dL) in ATN	
Other tests: (1) Fluid/diuretic challenge, if indicated; (2) POCUS (e.g., cardiac ultrasound [U/S]; venous excess U/S score); (3) CVP; (4) variation in stroke volume, pulse pressure, IVC diameter or SVC diameter; (5) Passive leg raise test		

Postrenal Oliguria (ureter, bladder, and/or urethra obstruction) workup may include: Confirm foley not kinked (if applicable); H&P-guided GU-tract imaging (e.g., renal and/or bladder ultrasound).[4]

Broader Differential for what may have caused Oliguria or ATN: **H**ard **C**ase **T**o **SOLVE**: **H**ypotension (intraop ↓BP), **C**ardiac (CHF, venous congestion), **T**oxins, **S**epsis, **O**ther (renal syndromes, surgical-induced trauma or emboli), **L**iver (splanchnic sequestration & systemic vasodilation), **V**entilation (positive pressure ventilation & PEEP can affect venous return, cardiac output, & renal perfusion [laparoscopy & other surgical pressure may ↓ renal perfusion via direct compression]; permissive hypercapnia can promote renal vasoconstriction), **E**ndocrine (pain/stress/hypotension can trigger renin-angiotensin-aldosterone system, ADH, & cortisol release, as well as suppression of atrial natriuretic peptide → Na^+ & H_2O retention [volatiles may also induce Na^+ & H_2O retention via mechanisms not fully understood]).[3-7]

Renal Protection for Procedures with High Contrast Load or Aortic Cross-Clamping

14X

Contrast-induced nephropathy (CIN): "serum creatinine increase of 0.5 mg/dL or a 25% increase from the baseline within 48 to 72 hours after iodinated contrast medium administration." Risk factors: CRI (increases risk 20X), hx renal dz, prior renal surgery, proteinuria, DM, HTN, gout, nephrotoxic drugs (NSAIDS, aminoglycosides, diuretics).[1] Metformin and Contrast Dye: CIN can lead to metformin retention & lactic acidosis. Evidence mixed; may be more relevant in patients with pre-existing abnormal renal function.[2]

Medications to protect kidneys from contrast induced nephropathy (in addition to hydration and maintaining urine output)

Medication	Comments
Sodium bicarbonate (IV intraop), acetylcysteine (PO pre-op)	Hypothetical benefit: "urinary alkalinization and scavenging of reactive oxygen species mitigate renal tubular epithelial-cell injury from the use of iodinated contrast material."[4] PRESERVE trial (NEJM 2018; randomized trial; 5,177 pts at high risk for renal complications undergoing angiography): no benefit to IV sodium bicarb over saline or for oral acetylcysteine over placebo for several outcomes (death, need for dialysis, persistent decline in kidney function at 90 days, or prevention of contrast-induced acute kidney injury).[4] "The two most important factors that contribute to CIN are…contrast load and…preexisting kidney disease."[3]

Aortic Cross-Clamp: Risk of AKI during elective infrarenal aortic reconstruction (most often from ATN) is ~3%. Suprarenal clamping decreases renal blood flow more substantially. Renal sympathetic blockade from epidural does not necessarily reduce this risk.[3]

Medications to possibly preserve renal function before/during aortic cross-clamp *("Significant controversy exists regarding the use of these drugs, as well as the mechanisms by which they may offer a protective effect."[3])*

Medication	Possible positive effects[3]	Notes
Mannitol (possible dose: 12.5g to 25g per 70kg as osmotic diuretic before aortic cross-clamp)	(1) Improved renal cortical blood flow during infrarenal cross-clamp; (2) reduced renal ischemia-induced changes (e.g., vascular endothelial cell edema, vascular congestion); (3) free-radical scavenging; (4) decreased renin production;(5) increased renal prostaglandin synthesis	May cause: electrolyte changes; hypovolemia → decreased renal perfusion.
Loop diuretics, low-dose dopamine (possible dose: 1-3 mcg/kg/min)	Increase in intraoperative renal blood flow and urine output	
Fenoldopam (selective dopamine type 1 agonist)	Preferential dilation of renal and splanchnic vascular beds	

Room for notes

2024 ACC/AHA Periop CV Guidelines for Noncardiac Surgery: "in patients with diabetes or impaired glucose tolerance, continuation of metformin during the perioperative period is reasonable to maintain glycemic control."[5]

1. Barash 9th Ed Ch 33. // 2. Iodinated contrast media chapter in Meyler's Side Effects of Drugs, 16th Ed // 3. Miller 9th Ed, Ch 56 // 4. Weisbord et al. NEJM 2018; 378:603-14 // 5. . Thompson A et al 2024 PMID 39316661

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References for Slides "The Nephron" & "The Nephron: Blood Flow, Secretion, Reabsorption": 1. 10-part labeled image of kidney: https://commons.wikimedia.org/wiki/File:Illu_kidney.jpg. Public Domain. // 2. Harrison's 21st Ed, Ch 309 // 3. Bua S et al. Ch 14. Carbonic anhydrase inhibitors as diuretics. In Carbonic Anhydrases 2019; https://doi.org/10.1016/B978-0-12-816476-1.00014-9 // 4. Miller's Anesthesia, 10th Ed, Ch 15 // 5. Image of blood flow in nephron: OpenStax College, CC BY 3.0 via Wikimedia Commons. https://commons.wikimedia.org/wiki/File:2626_Renin_Aldosterone_Angiotensin.jpg // 6. Bell R. BJA Education; PMID: 35614905

References for Slide "Countercurrent Multiplication: key process for water reabsorption and excretion of concentrated urine": 1. Harrison's 21st Ed, Ch 309 // 2. Berne & Levy's Physiology 8th Ed, Ch 35 // 3. Bell R. BJA Education; PMID: 35614905 // 4. Miller 10th Ed Ch 15 // 5. Koeppen's Renal Physiology, 6th Ed, Appendix // Countercurrent Multiplication Image: OpenStax College, CC BY 3.0, via Wikimedia commons https://commons.wikimedia.org/wiki/File:2621_Loop_of_Henle_Countercurrent_Multiplier_System.jpg

References for Slide "Carbonic Anhydrase Inhibitors": 1. Harrison's 21st Ed, Ch 309 // 2. Koeppen's Renal Physiology, 6th Ed, Ch 8 // 3. Bell R. BJA Education; PMID: 35614905 // 4. UpToDate: Mechanism of action of diuretics // 5. UpToDate: Acetazolamide: Drug Information // 6. Sarafidis et al. Diuretics in clinical practice. Part II. Expert Opin Drug Saf; PMID: 20095916 // 7. UpToDate: Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment // 8. UpToDate: High-altitude illness: Physiology, risk factors, and general prevention.

References for slide "Thiazide Diuretics and Parathyroid Hormone": 1. Harrison's 21st Ed, Ch 309 // 2. Bell R. BJA Education; PMID: 35614905 // 3. Goodman's Basic Medical Endocrinology, 5th Ed, Ch 10 // 4. UpToDate: Mechanism of Action of Diuretics // 5. UpToDate: Hydrochlorothiazide: Drug Information // 6. Sarafidis et al. Diuretics in clinical practice. Part II. Expert Opin Drug Saf; PMID: 20095916.

References for slide "Renin-Angiotensin-Aldosterone System": 1. Koeppen's Renal Physiology, 6th Ed, Ch 2 // Image depicting renin-angiotensin-aldosterone system: Adapted from OpenStax College, CC BY 3.0 via Wikimedia Commons. https://commons.wikimedia.org/wiki/File:2626_Renin_Aldosterone_Angiotensin.jpg // Image depicting location of macula densa in relation to glomerulus: Holly Fischer, CC BY 3.0 via Wikimedia commons. https://commons.wikimedia.org/wiki/File:Kidney_Nephron.png. // Harrison's 21st Ed Ch 309.

References for slide "Angiotensin II, NSAIDS, ACE-I's, and ARB's": 1. Harrison's 21st Ed, Ch 309 // 2. Harrison's 21st Ed, Ch 310 // 3. Koeppen's Renal Physiology, 6th Ed, Ch 3 // 4. Abuelo JG. NEJM 2007; PMID: 17715412 // 5. UpToDate: Major side effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers // 6. Goodman's Basic Medical Endocrinology, 5th Ed, Ch 9 (including Fig 9.21) // 7. UpToDate: Angiotensin converting enzyme inhibitors and receptor blockers in acute myocardial infarction: Recommendations for use.

References for slides "Normal Aldosterone Effects as part of Renin-Angiotensin-Aldosterone System," "Primary Hyperaldosteronism," "Primary Adrenal Insufficiency (Mineralocorticoid Component)," and "Potassium-Sparing Diuretics": 1. Harrison's 21st Ed, Ch 309 // 2. Goodman's Basic Medical Endocrinology, 5th Ed, Ch 4 (including Fig 4.26 & 4.30) // 3. Goodman's Basic Medical Endocrinology, 5th Ed, Ch 9 // 4. William's Endocrinology, 15th Ed, Ch 13 // 5. William's Endocrinology, 15th Ed, Ch 14 // 6. Koeppen's Renal Physiology, 6th Ed, Ch 10 // 7. Koeppen's Renal Physiology, 6th Ed, Ch 8 (including figure 8.4) // 8. UpToDate: Mechanism of Action of Diuretics (including figure 4) // 9. Miller's Anesthesia, 10th Ed, Ch 15 (including fig 15.14) // 10. Bell R. BJA Education; PMID: 35614905 // 11. Sarafidis et al. Diuretics in clinical practice. Part II. Expert Opin Drug Saf; PMID: 20095916.

References for slide "Antidiuretic Hormone (ADH)" and "Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH)": 1. UpToDate: Cerebral Salt Wasting // 2. Harrison's 21st Ed, Ch 309 // 3. Goodman's Basic Medical Endocrinology, 5th Ed, Ch 9 // 4. Koeppen's Renal Physiology, 6th Ed, Ch 5 (including Fig 5.6) // 5. UpToDate: Mechanism of Action of Diuretics (including figure 4) // 6. UpToDate: Vasopressin, Desmopressin: Drug Information // 7. Miller's Anesthesia 10th Ed, Ch 15 (including fig 15.13) // 8. Barash's Anesthesia 9th Ed, Ch 50.

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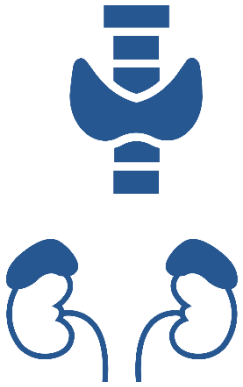
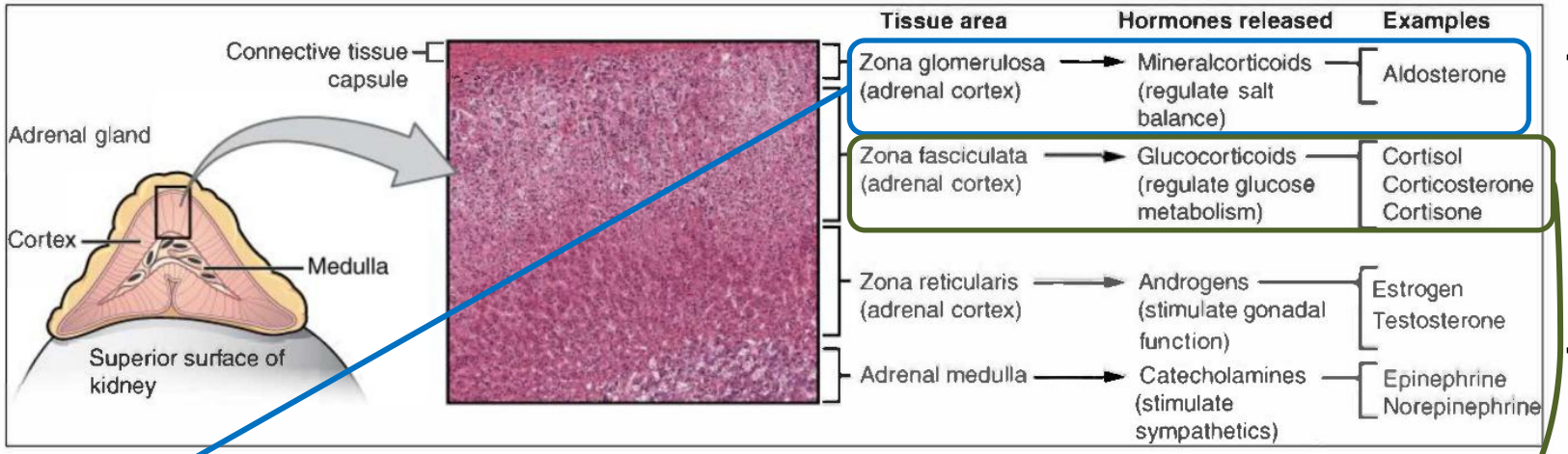


Endocrine

References for slide “Pheochromocytoma”: 1. Miller’s Anesthesia, 10th Ed, Ch 28 // 2. Miller 10th Ed Ch 29 // 3. Stoelting’s Anesthesia and Coexisting Disease 8th Ed, Ch 22// 4. Anesthesia and Uncommon Diseases 6th Ed, Ch 13 // 5. Endocrine Society Clinical Practice Guideline on Pheochromocytoma and Paraganglioma (PMID: 24893135) // 6. Treatment of pheochromocytoma in adults (UpToDate) // 7. Clinical presentation and diagnosis of pheochromocytoma (UpToDate) // Additional references for table “Serum Thyroid Function Tests in Clinical Conditions”: 1. UpToDate: “Laboratory assessment of thyroid function” // 2. Stoelting 8th Ed Ch 22 // 3. Harrison Principles of Internal Medicine 21st Ed Ch 383 & 384 // 4. UpToDate “Pathogenesis of Graves’ Disease” // 5. UpToDate “Pathogenesis of Hashimoto’s thyroiditis (chronic autoimmune thyroiditis)” // 6. UpToDate “Disorders that cause hypothyroidism” // 7. UpToDate “Central hypothyroidism” // 8. UpToDate “Drug interactions with thyroid hormones” // 9. UpToDate “Disorders that cause hypothyroidism” //10. Miller 10th Ed Ch 29 // Hypothalamus/pituitary image 1147605182 via Shutterstock license. Thyroid icon 4832971 via Noun Project License. Adrenal icon 716572 Public Domain via Noun Project

Room for notes

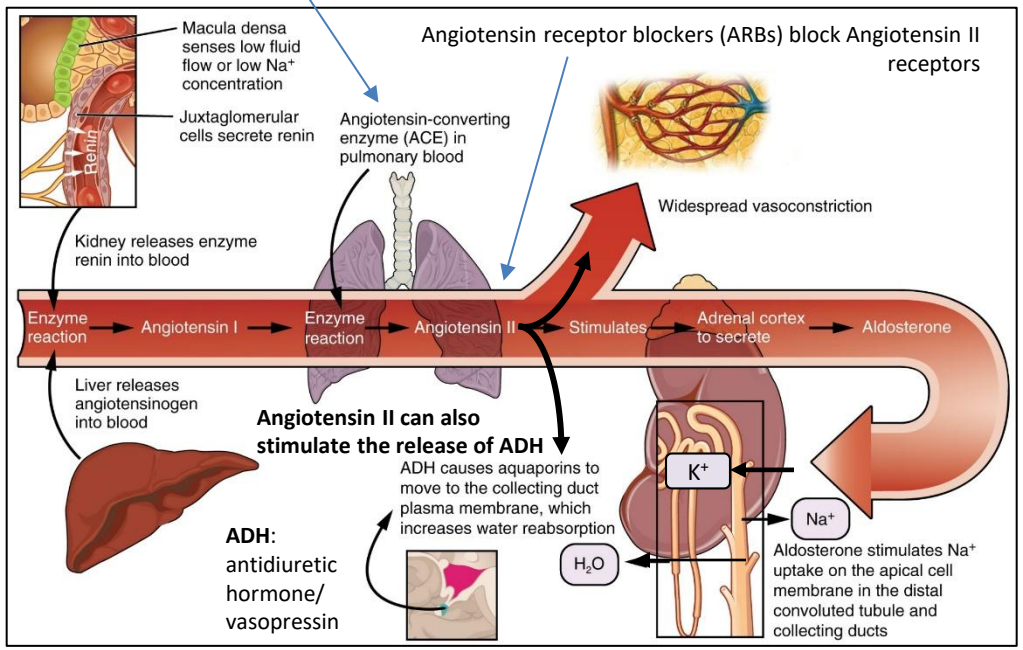
The Adrenal Gland



Site of action of ACE inhibitors

ZONA GLOMERULOSA

Renin-Angiotensin-Aldosterone System (RAA Axis)



ADH: antidiuretic hormone/ vasopressin

HPA Axis

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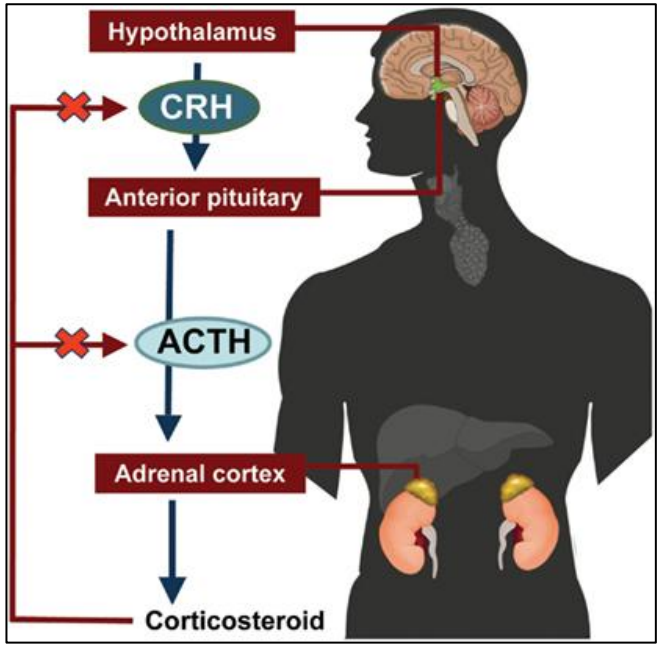

HPA Axis: Hypothalamus-Pituitary-Adrenal Axis
CRH: corticotropin-releasing hormone;
ACTH: adrenocorticotropic hormone (aka corticotropin, adrenocorticotropin

Refs: HPA axis diagram: Adapted from Ross AP et al. CC BY 3.0 via Wikimedia Commons https://commons.wikimedia.org/wiki/File:Hypothalamic-pituitary-adrenal_axis_diagram.jpg. // 1. Harrison's Manual of Medicine, 20th Ed, Ch 174. // 2. UpToDate: Causes of secondary and tertiary adrenal insufficiency in adults // 3. Miller 10th Ed, Ch 29 // 4. Williams Endocrinology, 14th Ed, Ch 15 // 5. UpToDate: Clinical Manifestations of adrenal insufficiency in adults // 6. UpToDate: Overview of the renin-angiotensin system // RAA axis diagram: Adapted from OpenStax College, CC BY 3.0 via Wikimedia Commons. https://commons.wikimedia.org/wiki/File:2626_Renin_Aldosterone_Angiotensin.jpg

Room for notes

Adrenal Insufficiency

14X

Room for notes

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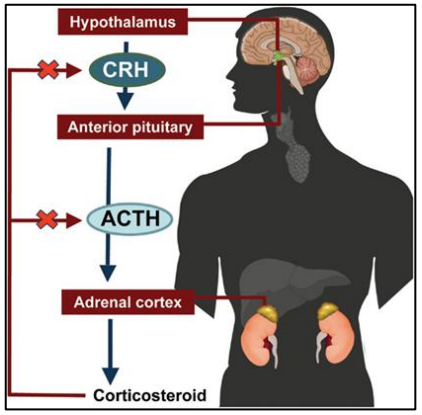
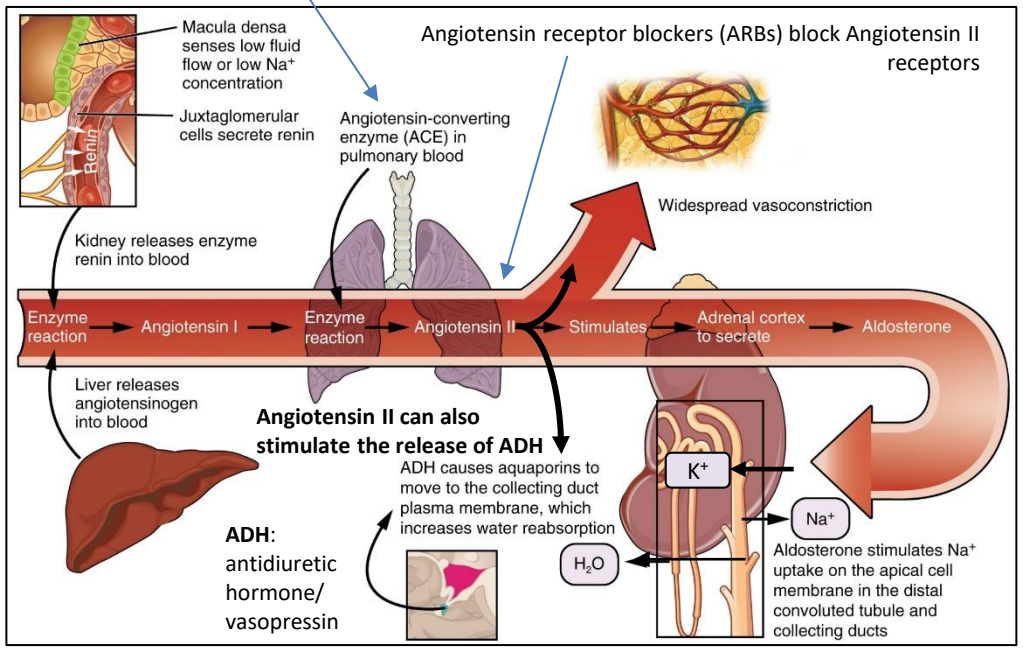


- Primary adrenal insufficiency (aka, Addison disease): associated with local destruction of adrenal tissue. Causes include autoimmune or congenital disease, infection, malignancy, intra-adrenal hemorrhage, congenital disease, or bilateral adrenalectomy.[1,3] *May cause both mineralocorticoid (zona glomerulosa; aldosterone) and glucocorticoid (zona fasciculata; corticosteroid) deficiency. Patients might also be on androgen supplementation*.
- Central adrenal insufficiency: Pathology involving: (1) pituitary gland interfering with adrenocorticotropic hormone (ACTH; aka, corticotropin) secretion (secondary adrenal insufficiency) OR (2)hypothalamus interfering w/corticotropin releasing hormone (CRH) secretion (tertiary adrenal insufficiency).[2,3] *Adrenal effect often limited to glucocorticoid deficiency (i.e., RAA axis intact).*
- Etomidate can case transient adrenal suppression of cortisol synthesis & release.[6]

Site of action of ACE inhibitors

ZONA GLOMERULOSA

Renin-Angiotensin-Aldosterone System (RAA Axis)



Lab findings in selected Adrenal Pathologic States[3-7]

Lab	Adrenal Insufficiency
Na+	**Decreased** • *Mineralocorticoid component* → aldosterone deficiency leads to sodium loss & possible hypovolemia • *Glucocorticoid component* → cortisol deficiency stimulates increased vasopressin (ADH) secretion.
K+	• **Increased** in *Primary* adrenal insufficiency (from mineralocorticoid/aldosterone deficiency). Patients may have hyperkalemic acidosis & subsequent arrythmia/myocardial conduction defects). • *Note: K+ may be unchanged in secondary (pituitary)/tertiary (hypothalamus)* adrenal insufficiency if renin-angiotensin-aldosterone system (& mineralocorticoid function) intact.
Glucose	Hypoglycemia in some cases (from glucocorticoid deficiency).

Refs: HPA axis diagram: Adapted from Ross AP et al. CC BY 3.0 via Wikimedia Commons https://commons.wikimedia.org/wiki/File:Hypothalamic-pituitary-adrenal_axis_diagram.jpg. // 1. Harrison's Manual of Medicine, 20th Ed, Ch 174 // 2. UpToDate: Causes of secondary & tertiary adrenal insufficiency in adults // 3. Miller 10th Ed, Ch 29 // 4. Williams Endocrinology, 14th Ed, Ch 15 // 5. UpToDate: Clinical Manifestations of adrenal insufficiency in adults // 6. Stoelting 8th Ed Ch 22 // 7. Miller 10th Ed Ch 28

Adrenal Cortex Pathologic States: Periop Considerations

9X

Room for notes

Lab findings in selected Adrenal Pathologic States (cont'd)		
Lab (serum)	**Glucocorticoid Excess – exogenous or endogenous (Cushing Syndrome)***	**Primary hyperaldosteronism & Secondary hyperaldosteronism**
Na+	**Increased** (may have hypertension and hypervolemia)**	
	** Most glucocorticoids have some mineralocorticoid properties. High cortisol doses (greater than 30mg/day), including from excess ACTH production, can bind to mineralocorticoid receptors & cause Na^+/water retention & depletion of potassium & hydrogen ions.[1-2]	Aldosterone stimulates Na+ and fluid retention, as well as potassium excretion.
K+	**Decreased** (may have hypokalemic alkalosis)**	
Glucose	Hyperglycemia & sometimes diabetes mellitus (glucocorticoids inhibit peripheral glucose use by cells, stimulate gluconeogenesis, & have anti-insulin action)	--

* *Cushing Disease:* excess glucocorticoids from an ACTH-producing pituitary tumor. Acute ectopic ACTH is most commonly from a paraneoplastic syndrome from small cell lung cancer.[2-3]

- Full Handout: Lab findings in selected Adrenal Pathologic States.

Condition	Perioperative Considerations Include
Adrenal Insufficiency or Adrenal Crisis	Treatment of hypovolemia, hyperkalemia, and hyponatremia; assess for stress-dose glucocorticoid supplementation. Patients may already be on fludrocortisone for mineralocorticoid supplementation.[1]
Cushing Syndrome	Control of glucose, volume, and electrolyte status; HTN management.[1]
Hyperaldosteronism	Correction of electrolyte status; HTN management. If patient still hypokalemic, be cautious of hyperventilation, which can further decrease serum K+ concentration. Patients may be on potassium-sparing diuretics (see handout).[2]

Refs: 1. Miller 10th Ed, Ch 29 // 2. Stoelting 8th Ed, Ch 22 // 3. Miller 10th Ed, Ch 28

Lab Findings in Selected Adrenal Pathologic States

Alex Arriaga 2017-2023 ver 7; 11/19/23

Lab findings in selected Adrenal Pathologic States[3-7]

Lab (serum)	Adrenal Insufficiency	Glucocorticoid Excess - exogenous or endogenous (Cushing Syndrome)	Primary hyperaldosteronism*** and Secondary hyperaldosteronism
Na+	**Decreased** • *Mineralocorticoid component* → aldosterone deficiency leads to sodium loss & possible hypovolemia • *Glucocorticoid component* → cortisol deficiency stimulates increased vasopressin (ADH) secretion.	**Increased** (from mineralocorticoid activation; patients may have associated hypertension and hypervolemia) ➔ High doses of cortisol (greater than 30mg/day), including from excess ACTH production, can bind to mineralocorticoid receptors and cause sodium/water retention and depletion of potassium & hydrogen ions. Most glucocorticoids have some mineralocorticoid properties.[3,7] ➔ Aldosterone stimulates Na+ and fluid retention, as well as potassium excretion.	
K+	• **Increased** in *Primary* adrenal insufficiency (from mineralocorticoid/aldosterone deficiency). Patients may have hyperkalemic acidosis & subsequent arrythmia/myocardial conduction defects). *Note: K+ may be unchanged in secondary (pituitary)/tertiary (hypothalamus) adrenal insufficiency* if renin-angiotensin-aldosterone system (& mineralocorticoid function) intact.	**Decreased** (from mineralocorticoid activation; patients may have hypokalemic alkalosis)	
Ca++	Increased in some cases, often if coexisting thyrotoxicosis or acute renal insufficiency; elevated BUN may be seen in some cases.	--	
Glucose	Hypoglycemia in some cases (from glucocorticoid deficiency).	Hyperglycemia & sometimes diabetes mellitus (glucocorticoids inhibit peripheral glucose use by cells, stimulate gluconeogenesis, & have anti-insulin action)	--
Notes	• Primary Adrenal Insufficiency: serum cortisol concentration inappropriately low and baseline plasma ACTH inappropriately high. Stimulation with cosyntropin (ACTH analog) leads to subnormal change in cortisol level.[9] • Secondary Adrenal Insufficiency: serum cortisol and baseline plasma ACTH concentrations inappropriately low.	• The term *"Cushing Disease"* is sometimes used to refer to excess glucocorticoids from an ACTH-producing pituitary tumor. Acute ectopic ACTH syndrome is most commonly a paraneoplastic syndrome from small cell lung cancer.[6,7] • Cushing syndrome patients may have easy bruising despite normal coagulation profiles.	***JW Conn originally reported on the aldosterone-producing adenoma. Many subtypes of primary aldosteronism have since been described.[1] • Primary aldosteronism patients may also have hypomagnesemia and abnormal glucose tolerance.[7] Serum renin levels may be low in primary hyperaldosteronism and high in secondary hyperaldosteronism.[7] • Chronic licorice ingestion (contains glycyrrhizic acid → pathway mimicking mineralocorticoid excess) can cause findings similar to primary hyperaldosteronism despite low plasma aldosterone.[7,8]

Potassium-sparing diuretics commonly used in the treatment of hyperaldosteronism[****-1-3,7]

1. Spironolactone or Eplerenone: aldosterone mineralocorticoid-receptor antagonists that can stop potassium loss and fluid retention from mineralocorticoid excess (works primarily at the distal convoluted tubule to decrease Na+ reabsorption, which increases water reabsorption and increases K+ retention).
   - Side effects of spironolactone include gynecomastia, irregular menses, and mastodynia.
2. Triamterene: inhibits Na+ reabsorption at distal convoluted tubule, which decreases water reabsorption and increases K+ retention.
3. Amiloride: inhibits Na+ reabsorption at distal convoluted tubule, the cortical collecting tubule, and collecting duct, which decreases water reabsorption and increases K+ retention.

**** Chronic potassium supplementation is also sometimes used as part of treatment of hyperaldosteronism.

Refs: 1. UpToDate: Treatment of primary aldosteronism // 2. Epocrates: Spironolactone, eplerenone, triamterene, amiloride // 3. Miller 9th Ed, Ch 32 // 4. Williams Endocrinology, 14th Ed, Ch 15 // 5. UpToDate: Clinical Manifestations of adrenal insufficiency in adults // 6. Miller 9th Ed, Ch 31 // 7. Stoelting's Anesthesia & Coexisting Disease 8th Ed Ch 22 // 8. Apparent mineralocorticoid excess syndromes (including chronic licorice ingestion) // 9. UpToDate: Initial testing for adrenal insufficiency: Basal cortisol and the ACTH stimulation test.

Room for notes

Lab findings in selected Adrenal Pathologic States[3-7]

Lab (serum)	Adrenal Insufficiency	Glucocorticoid Excess - exogenous or endogenous (Cushing Syndrome)	Primary hyperaldosteronism*** and Secondary hyperaldosteronism
Na^+	**Decreased** • *Mineralocorticoid component* → aldosterone deficiency leads to Na^+ loss & possible hypovolemia • *Glucocorticoid component* → cortisol deficiency stimulates increased antidiuretic hormone (ADH) secretion.	**Increased** (from mineralocorticoid activation; patients may have associated hypertension and hypervolemia) → High doses of cortisol (greater than 30mg/day), including from excess ACTH production, can bind to mineralocorticoid receptors and cause sodium/water retention and depletion of potassium & hydrogen ions. Most glucocorticoids have some mineralocorticoid properties.[3,7] → Aldosterone stimulates Na^+ and fluid retention, as well as potassium excretion.	
K^+	• **Increased** in *Primary* adrenal insufficiency (from mineralocorticoid/aldosterone deficiency). Patients may have hyperkalemic acidosis & subsequent arrythmia/myocardial conduction defects). *Note: K^+ may be unchanged in secondary (pituitary)/tertiary (hypothalamus) adrenal insufficiency if renin-angiotensin-aldosterone system (& mineralocorticoid function) intact.*	**Decreased** (from mineralocorticoid activation; patients may have hypokalemic alkalosis)	
Ca^{2+}	Increased in some cases, often if coexisting thyrotoxicosis or acute renal insufficiency; elevated BUN may be seen in some cases.	--	
Glucose	Hypoglycemia in some cases (from glucocorticoid deficiency).	Hyperglycemia & sometimes diabetes mellitus (glucocorticoids inhibit peripheral glucose use by cells, stimulate gluconeogenesis, & have anti-insulin action)	--
Notes	• Primary Adrenal Insufficiency: serum cortisol concentration inappropriately low and baseline plasma ACTH inappropriately high. Stimulation with cosyntropin (ACTH analog) leads to subnormal change in cortisol level.[9] • Secondary Adrenal Insufficiency: serum cortisol and baseline plasma ACTH concentrations inappropriately low.	• The term "*Cushing Disease"* is sometimes used to refer to excess glucocorticoids from an ACTH-producing pituitary tumor. Acute ectopic ACTH syndrome is most commonly a paraneoplastic syndrome from small cell lung cancer.[6,7] • Cushing syndrome patients may have easy bruising despite normal coagulation profiles.	***JW Conn originally reported on the aldosterone-producing adenoma. Many subtypes of primary aldosteronism have since been described.[1] • Primary aldosteronism patients may also have hypomagnesemia and abnormal glucose tolerance.[7] Serum renin levels may be low in primary hyperaldosteronism and high in secondary hyperaldosteronism.[7] • Chronic licorice ingestion (contains glycyrrhizic acid → pathway mimicking mineralocorticoid excess) can cause findings similar to primary hyperaldosteronism despite low plasma aldosterone.[7,8]

Potassium-sparing diuretics that may be used in the treatment of hyperaldosteronism**:**[1-3,7]

1. Spironolactone or Eplerenone: aldosterone mineralocorticoid-receptor antagonists that can stop potassium loss and fluid retention from mineralocorticoid excess. They work primarily at the distal convoluted tubule to decrease Na^+ and water reabsorption, which increases K^+ retention and can lead to hyperkalemia. Other side effects of spironolactone include gynecomastia, irregular menses, and mastodynia.
2. Amiloride or Triamterene: inhibits Na^+ reabsorption at distal convoluted tubule, cortical collecting tubule, and collecting duct, which decreases water reabsorption and increases K^+ retention (can lead to hyperkalemia).

**** Chronic potassium supplementation is also sometimes used as part of treatment of hyperaldosteronism.

Refs: 1. UpToDate: Treatment of primary aldosteronism // 2. Epocrates & UpToDate Drug Info: Spironolactone, eplerenone, triamterene, amiloride // 3. Miller 9th Ed, Ch 29 // 4. Williams Endocrinology, 15th Ed, Ch 13// 5. UpToDate: Clinical Manifestations of adrenal insufficiency in adults// 6. Miller 9th Ed, Ch 28// 7. Stoelting Anesthesia & Coexisting Dz 8th Ed Ch 22// 8. Apparent mineralocorticoid excess syndromes (including chronic licorice ingestion)// 9. UpToDate: Initial testing for adrenal insufficiency: Basal cortisol & the ACTH stimulation test.

Perioperative ("stress dose") Steroid Supplementation

4X

Room for notes

- "Cortisol is one of the few hormones essential for life."[4]
- "It is clear that inadequate corticosteroid coverage can cause death, but what is not so clear is what dose of steroid should be recommended for replacement therapy."[1]
- Prednisone 5mg/day or less than 3 weeks of corticosteroids (regardless of dose): continue usual long-term corticosteroid regimen.[7]
- Prednisone greater than 20mg/day for over 3 weeks, or patient with Cushing syndrome: see table.
- "The need for supplementation is unclear for patients who have taken prednisone (or its equivalent) at a daily dose of 5 to 20 mg for more than 3 weeks."[7]
- Recommended reading: Liu et al. Perioperative Steroid Management. Anesthesiology 2017. PMID: 28452806

Perioperative ("stress-dose") Steroid Supplementation Considerations (pts taking prednisone 20mg/daily [or equivalent] for over 3 weeks)[4-7]

Procedure type	Corticosteroid Supplementation
Superficial	Usual dose
Minor	Usual dose + hydrocortisone (50mg IV pre-incision + periop 24 hr taper, such as 25mg IV q8hr x 3, then usual dose)
Moderate	
Major	Usual dose + hydrocortisone (100mg IV pre-incision + periop taper, such as 50mg IV q8hr, tapered by half until at usual dose)

Steroid Conversion table[1-6]

Steroid	Relative Glucocorticoid Activity	Relative Mineralocorticoid Activity	Equivalent Glucocorticoid Dose in mg (IV/PO)*
Hydrocortisone	1	1	20
Dexamethasone	30	0	0.5
Prednisone	4	0.8	5
Methylprednisolone	5	0.5	4
Fludrocortisone	5	200	**

* For example: glucocorticoid equivalents for 20mg prednisone: 80mg hydrocortisone, 16mg methylprednisolone, or 2mg dexamethasone. **Fludrocortisone (aka 9-alpha-fluorocortisol) often given in doses lower than that which stimulate major glucocorticoid activity, given potent mineralocorticoid effect.

Refs: 1. Miller 10th Ed, Ch 29 // 2. Williams Endocrinology Ch 15 // 3. Anes & Uncommon Dis 6th Ed Ch 13 // 4. Stoelting 8th Ed Ch 22 // 5. PMID 28452806 // 6. UpToDate: The management of the surgical patient taking glucocorticoids // 7. Miller 10th Ed Ch 28

ICU Corticosteroid Treatment Considerations

3X

Room for notes

Society of Critical Care Medicine (SCCM) Guidelines:[1-3,6]

Diagnosis of Critical Illness-Related Corticosteroid Insufficiency (CIRCI; one approach): Random plasma cortisol less than 10 micrograms/dL AND change in baseline cortisol of less than 9 micrograms/dL 60 min after giving cosyntropin (an ACTH/corticotropin analog).

Conditions where corticosteroids recommended or suggested:

- Adults with septic shock
- Adults hospitalized with ARDS
- Severe bacterial community-acquired pneumonia
- Bacterial Meningitis
- Cardiac arrest (ICU admission after cardiac arrest)
- Cardiopulmonary bypass surgery (perioperative corticosteroid use)
- Severe or critical COVID-19 (consider dexamethasone over other corticosteroids)

Conditions where no corticosteroid treatment recommended:

- Influenza
- Major trauma

Conditions where high-dose/short duration corticosteroids (>400mg/day hydrocortisone equivalent for < 3 days) is not recommended:

- Adults with septic shock.

Cosyntropin (ACTH) Stimulation Test in the diagnosis of primary adrenal insufficiency:[4]

- In primary adrenal insufficiency: endogenous ACTH is already elevated → giving cosyntropin should lead to little to cortisol response.
- In secondary adrenal insufficiency from hypopituitarism: hypopituitarism causes adrenal atrophy → giving cosyntropin may lead to a subnormal cortisol response.

"An inadequate serum cortisol response to ACTH stimulation establishes the diagnosis of adrenal insufficiency but does not distinguish between the primary and secondary forms."[4] (Baseline ACTH levels, CRH testing, and/or other testing may be needed for this).

What causes CIRCI?

- Possibly due to suboptimal cortisol production relative to body demands in critical illness.
- Diagnostic criteria and clear definition of CIRCI are a subject of debate.[5]

SCCM infographic: 2024 Guidelines for corticosteroid use in sepsis, ARDS, & community-acquired pneumonia

SCCM infographic: Surviving Sepsis Campaign 2021: Guidelines for vasoactive management

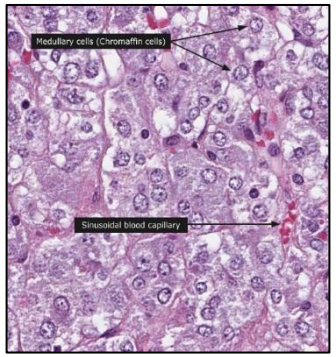
Refs: 1. Diagnosis and Management of Critical Illness-Related Corticosteroid Insufficiency in Critically Ill Patients (Parts 1 and 2) 2017; PMIDs 28938253, 29095205 // 2. Surviving Sepsis Management of Sepsis and Septic Shock 2021; PMID: 34605781 // 3. Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU First Update 2021 // 4. UpToDate: Initial testing for adrenal insufficiency: Basal cortisol and the ACTH stimulation test. // 5. UpToDate "Glucocorticoid therapy in septic shock for adults" // 6. Guidelines on use of corticosteroids in sepsis, acute respiratory distress syndrome, and community-acquired pneumonia (2024 focused update); PMID 38240492. The latest guidelines for the Society of Critical Care Medicine (SCCM) can be found at www.sccm.org.

Pheochromocytoma

11X

Room for notes

- Pheochromocytoma: catecholamine-secreting tumor from chromaffin cells of adrenal medulla. *Tumors can also arise from sympathetic ganglia (catecholamine-secreting paragangliomas) or other non-adrenal sites (extra-adrenal pheochromocytoma)*. Associated familial disorders (e.g., MEN type II, neurofibromatosis type I).
- Common symptoms: episodic headaches, sweating, tachycardia, HTN, palpitations, orthostatic hypotension.
- Diagnostic testing includes (institutional variation): urinary and/or plasma metanephrines and/or catecholamines (would expect increased levels); imaging (MRI/CT; sometimes nuclear studies).
- Preop preparation: alpha-blockade (usually at least 7-14 days preop) **before** beta-blockade (unopposed alpha-stimulation can worsen HTN, lead to catecholamine-induced cardiomyopathy & subsequent pulmonary edema; alpha-stimulated HTN w/beta-blocked depressed cardiac function can lead to heart failure). Correct hypovolemia if indicated.



Perioperative alpha blockers and adjuncts	
Phenoxybenzamine	irreversible nonspecific alpha-blocker (side effects: orthostatic hypotension/dizziness, fatigue, nasal congestion)
Prazosin, Terazosin, Doxazosin	selective alpha-1 blockers (less side effects, but incomplete alpha-blockade could lead to more intraoperative hypertension).
Adjuncts	calcium channel blockers, clonidine, labetalol, magnesium, metyrosine (inhibits catecholamine synthesis)

Intraoperative considerations for pheochromocytoma
Arterial line and adequate vascular access
Hypertension treatment*: sodium nitroprusside; nicardipine; phentolamine
Hypotension treatment*: Phenylephrine, Vasopressin
Caution/avoid: sympathomimetics (e.g., ketamine, ephedrine), histamine releasing agents (e.g., morphine), succinylcholine, glucagon, metoclopramide, high-dose corticosteroids.[5,6]

Multiple Endocrine Neoplasia (MEN) syndromes	
I	primary hyper**P**arathyroidism, **P**ituitary and entero-**P**ancreatic tumors, other tumors
IIa	Pheochromocytoma, medullary thyroid cancer, parathyroid hyperplasia; other types
IIb	Pheochromocytoma, medullary thyroid cancer, others (neuromas, ganglioneuromas)

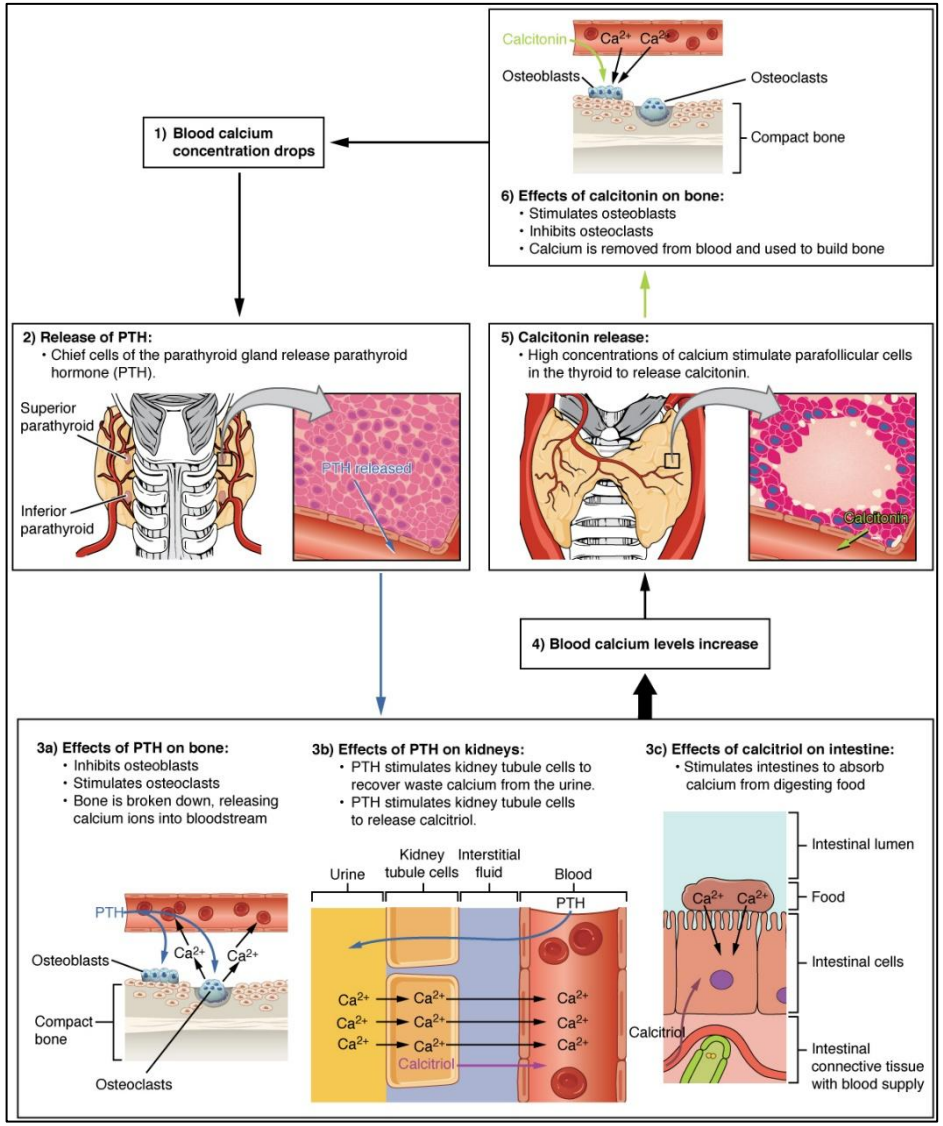
*Miller 9th Ed, Ch 32: "Virtually all anesthetic drugs and techniques…have been used with success…because of ease of use, the preference is to give phenylephrine for hypotension and nitroprusside or nicardipine for hypertension." Miller 10th Ed Ch 29: "All anesthetic techniques are acceptable as long as hemodynamic control is achieved." Stoelting 8th Ed, Ch 22: "Mixtures of antihypertensive drugs such as nitroprusside, esmolol, diltiazem, and phentolamine have been recommended to control refractory hypertension." Phentolamine is cited in some sources, and other sources state its onset/duration is too long compared to other agents. // Histology chromaffin cells: Adrenal gland, detail2, magnification 1, CC-BY-NC 4.0 via Human Protein Atlas, available at www.proteinatlas.org. See Endocrine title slide for references.

Parathyroid & Calcium

15X
Including next slide

Room for notes

Parathyroid-Calcium Physiology



Hyperparathyroidism:[1-3]

- Primary hyperparathyroidism: parathyroid hormone (PTH) excess from primary parathyroid gland disorder (often single gland adenoma or hyperplasia, but other causes include carcinoma). Almost always leads to hypercalcemia.
- Secondary hyperparathyroidism: chronic hypocalcemia (e.g., from renal failure, malabsorption) → parathyroid hyperplasia → PTH excess.
- Tertiary hyperparathyroidism: chronic secondary hyperparathyroidism → hyperplastic parathyroid glands that secrete excess PTH independent of physiologic feedback.

Hyperparathyroidism & neuromuscular blockade:[2]

- "Coexisting skeletal muscle weakness [from hyperparathyroidism] suggests the possibility of decreased requirements for muscle relaxants, whereas hypercalcemia might be expected to antagonize the effects of nondepolarizing muscle relaxants. In view of the unpredictable response to muscle relaxants, careful titration is recommended."

Refs: 1. Miller 10th Ed, Ch 28 // 2. Stoelting 8th Ed Ch 22 // 3. Miller 10th Ed Ch 29 // 4. UpToDate "Clinical Manifestations of hypercalcemia" // 5. UpToDate "Clinical manifestations of hypocalcemia" // 6. UpToDate "Treatment of hypercalcemia" // 7. Epocrates for medications named // 8. UpToDate: "Treatment of hypocalcemia" // Image: OpenStax College, CC BY 3.0 via Wikimedia Commons https://commons.wikimedia.org/wiki/File:1817_The_Role_of_Parathyroid_Hormone_in_Maintaining_Blood_Calcium_Homeostasis.jpg

Parathyroid & Calcium (cont'd)

Signs/Symptoms of Hypercalcemia[2-4]	
Renal	Kidney stones, polyuria/polydipsia, hypovolemia
Musculoskeletal	Bone pain, skeletal demineralization, fractures
GI	Anorexia, constipation, emesis, pancreatitis, peptic ulcer disease
Neuro/Psych	Mood disturbances, lethargy, confusion, memory impairment
ECG	Shortened QT interval

Acute Hypocalcemia Basics[2,3,5,8]

Clinical manifestations include:

- *Neuromuscular/Psych/Respiratory*: tetany, paresthesias, laryngeal stridor, laryngospasm, bronchospasm, seizures, mood disturbances, Chvostek and Trousseau's signs
- *Cardiac*: prolonged QT interval, arrhythmia, hypotension, heart failure,

Treatment considerations include:
Calcium gluconate & calcium chloride; magnesium repletion; vitamin D supplementation

Treatment considerations for acute hypercalcemia[3,6,7]	
Normal saline hydration	Hypercalcemic pts can be hypovolemic; saline hydration may promote calcium excretion
Bisphosphonates	Inhibits osteoclast recruitment/function
Calcitonin	Inhibits bone resorption of calcium into bloodstream via osteoclast inhibition
Phosphate repletion	Increasing serum phosphate facilitates calcium excretion
Dialysis	Can remove calcium from body

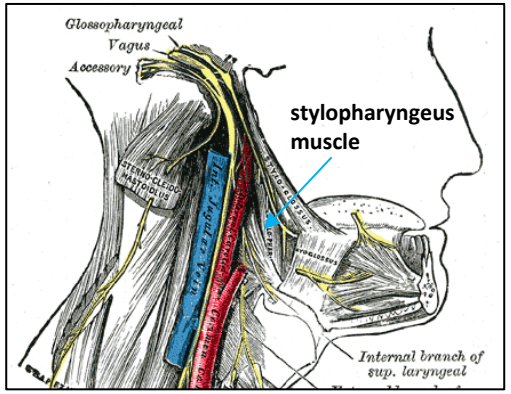
Other treatment: *Glucocorticoids* (decreases intestinal calcium absorption over days); *Calcimimetics* (reduce PTH by serving as calcium-sensing receptor antagonists); *denosumab* (inhibits osteoclasts by binding to receptor activator of nuclear factor kappa-B ligand [RANKL]); +/- *furosemide* (can inhibit calcium reabsorption in loop of Henle, but may exacerbate hypovolemia – may have more application in patients with CHF getting saline hydration)

Refs: 1. Miller 10th Ed, Ch 28 // 2. Stoelting 8th Ed Ch 22 // 3. Miller 10th Ed Ch 29 // 4. UpToDate "Clinical Manifestations of hypercalcemia" // 5. UpToDate "Clinical manifestations of hypocalcemia" // 6. UpToDate "Treatment of hypercalcemia" // 7. Epocrates for medications named // 8. UpToDate: "Treatment of hypocalcemia" // Image: OpenStax College, CC BY 3.0 via Wikimedia Commons https://commons.wikimedia.org/wiki/File:1817_The_Role_of_Parathyroid_Hormone_in_Maintaining_Blood_Calcium_Homeostasis.jpg

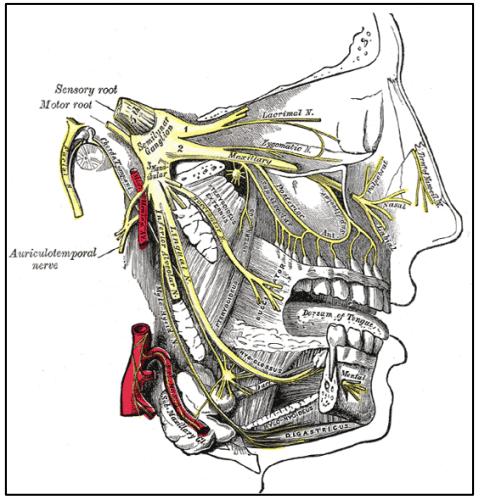
Room for notes

“Image/Buzzwords Co-slides”: Airway Anatomy & Innervation

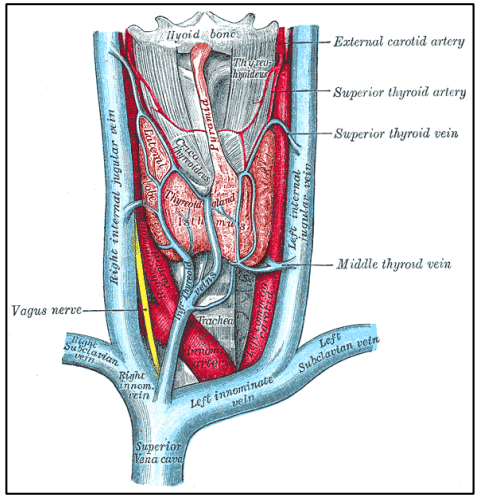
Glossopharyngeal Nerve (CN IX)



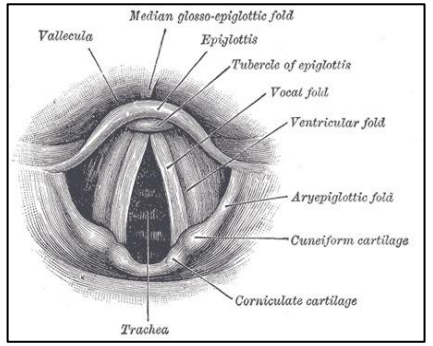
Trigeminal Nerve (CN V)



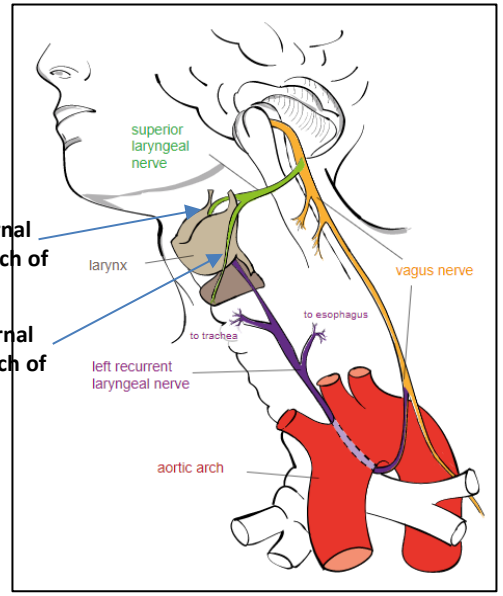
Thyroid Anatomy



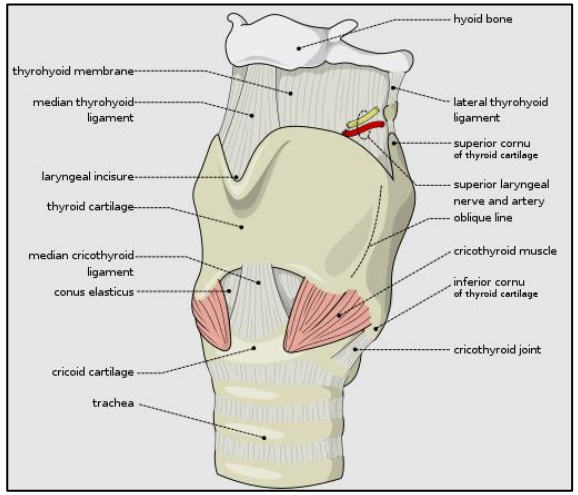
Laryngoscopic view of larynx



(Left) Vagus Nerve (CN X)

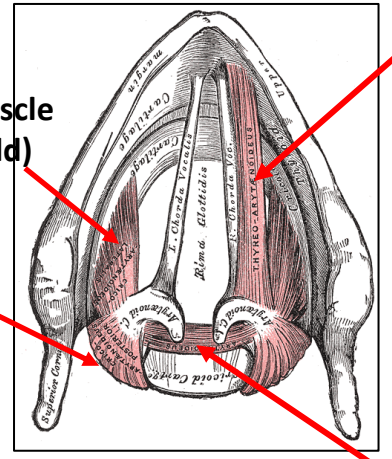


Cricothyroid muscle



Lateral cricoarytenoid muscle (an adductor of vocal fold)

Posterior cricoarytenoid muscle (only abductor of vocal fold)



2022 ITE Gaps in Knowledge: Laryngeal injury is a strong contraindication to transtracheal jet ventilation.

Thyroarytenoid muscle (plays role in adduction and voice pitch [shortens/relaxes vocal ligaments and rotate arytenoids in opposition of posterior cricoarytenoids] [Note: pitch is largely mediated by cricothyroid muscle])

Transverse interarytenoid muscle (pulls arytenoid cartilages towards each other [plays role in closure of opening between vocal folds])

Room for notes

"Image/Buzzwords Co-slides": Airway Anatomy and Innervation

34X

Room for notes

Trigeminal Nerve (CN V): sensory to nasal mucosa and nasal cavity (V2: maxillary branch).

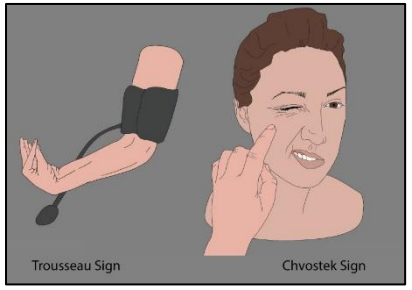
Glossopharyngeal nerve (CN IX): sensory to posterior third of tongue, walls of pharynx, & anterior surface of epiglottis.

- Gag/Pharyngeal Reflex: most sensory from CNIX (some sensory from CNV2 [nasopharynx] and CN X).
  - Motor innervation: Stylopharyngeus muscle innervated by CNIX (elevates larynx and elevates/dilates pharynx to facilitate swallowing food). All *other pharyngeal muscles are innervated by the pharyngeal branch of CN X.*

Vagus Nerve (CN X):

- Superior Laryngeal Nerve (SLN):
  - Internal Branch: sensory to posterior surface of epiglottis, aryepiglottic folds & arytenoids (also: base of tongue).
  - External Branch: motor innervation to cricothyroid muscle (voice pitch).
- Recurrent Laryngeal Nerve (RLN): (1) sensory innervation to vocal folds & trachea. (2) motor innervation to all muscles of larynx except cricothyroid muscle.
  - *Unilateral injury*: hoarseness (injured cord: paramedian position); *Bilateral injury*: dyspnea, stridor, partial/complete airway obstruction (bilateral cords: paramedian position).
  - **Laryngospasm Reflex**: most sensory via internal branch of SLN; motor primarily via RLN (several laryngeal muscles).[1] Periop, usually occurs from irritation of airway, vocal cords, or other noxious stimuli during light plane of anesthesia. Tx: See handout.
  - Airway obstruction after thyroid/parathyroid surgery: history/physical to differentiate RLN injury vs hematoma; hypocalcemia (from severe hypoparathyroidism due to inadvertent removal of all four parathyroid glands) not usually a cause until 24-96 hours postop (see table "Acute Hypocalcemia Basics").
  - The RLN can be injured during head/neck surgery (e.g., thyroid, parathyroid, cervical spine, carotid endarterectomy), cardiothoracic surgery (e.g., patent ductus arteriosus (PDA) repair [left RLN]), interscalene block, & other procedures.
  - Posterior cricoarytenoid muscle: the only abductor of the larynx (i.e., only muscle to open the true vocal folds). It opposes the action of the lateral cricoarytenoid muscles.

Chvostek & Trousseau signs of hypocalcemia
Chvostek sign: tapping facial nerve at angle of jaw produces contracture of ipsilateral facial muscles.
Trousseau sign: upper arm BP cuff inflated above systolic BP for few minutes → carpopedal spasm (finger contraction; inability to open hand).



Barash 9th Ed, Ch28 & 47 // Miller 10th Ed Chs 29, 40, & 66 // Cumming's Otolaryngology 7th Ed Ch 53 // KJ Lee's Essential Otolaryngology: Head and Neck Surgery, 12th Ed. Chs 36 & 50 // Jain et al. PMID 31613499 // Image: Omerovic et al. CC-BY-4.0, PMID: 31194466 // 1. Laryngospasm in anaesthesia https://doi.org/10.1093/bjaceaccp/mkt031

Laryngospasm

Loss of EtCO2 due to vocal cord closure, often during stage 2 anesthesia

16

Signs and Symptoms

- Inspiratory stridor, accessory muscle use, sternal retractions, paradoxical chest movement, airway obstruction, ↓SpO_2, ↓HR, loss of $EtCO_2$

Treatment

- Notify team to cease stimulation/surgery
- Give 100% O_2, evaluate ventilation
- Apply CPAP and jaw thrust
- Confirm or establish adequate IV access
- Deepen anesthesia with IV and/or inhaled agents. Consider propofol 1-3 mg/kg
- Give succinylcholine 0.1-2 mg/kg (if no IV: 2-4 mg/kg IM)
- If bradycardia, give atropine 0.02 mg/kg IV (if no IV: 0.04 mg/kg IM)
- Consider direct laryngoscopy to secure the airway and/or suction
- Avoid further patient stimulation during stage 2 anesthesia
- If further airway instrumentation needed, consider airway topicalization with lidocaine
- Monitor for negative pressure pulmonary edema (pink frothy secretions). If present, consider ETT, PPV, PEEP, ICU

Differential Diagnosis

- Circuit disconnect or obstruction
- Upper airway obstruction
- Lower airway obstruction/bronchospasm

Laryngospasm

Revision June 2018

"Bilateral pressure at the *laryngospasm notch* between the condyle of the mandible and the mastoid process can be effective at treating laryngospasm." This may work via autonomic pathways causing vocal cord relaxation, or simply arousing a semi-conscious patient out of light anesthesia.[1,2]

- Video of this technique (NEJM Letter to Editor):[3] https://youtu.be/eIdWRYOQenQ?feature=shared

Room for notes

Society for Pediatric Anesthesia Critical Event Checklists. Revision Packet March 2023. Latest update available at http://www.pedsanesthesia.org // OpenAnesthesia: Laryngospasm https://www.openanesthesia.org/keywords/laryngospasm/ // 1. Miller 10th Ed, Ch 40 // 2. Smith's Anesthesia for Infants and Children 10th Ed, Ch 19 // 3. PMID: 24670183

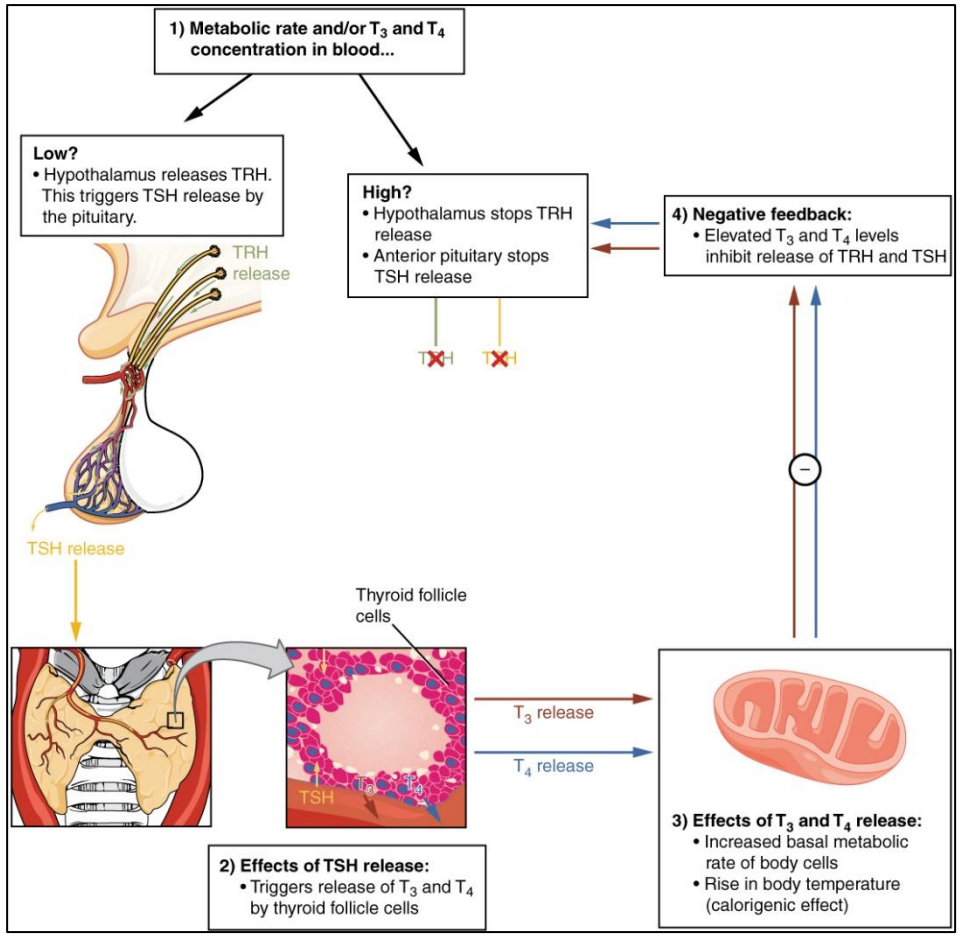
Thyroid

4X

Including next two slides

Room for notes

Thyroid Hormone Homeostasis



Serum Thyroid Function Tests in Clinical Conditions*[1-9]			
TSH	**Free T4**	**T3**	**Interpretation**
Low	High/ Normal	High	Hyperthyroidism (Ddx includes Graves' disease, iodine or thyroid hormone excess, toxic nodular hyperthyroidism, destructive thyroiditis w/thyroid hormone release)
Normal/ High	High	High	TSH-mediated hyperthyroidism (such as TSH-secreting pituitary adenoma), thyroid hormone resistance
High	Low	Low/ Normal	Primary Hypothyroidism (e.g., Hashimoto's thyroiditis)
Low/ Normal **	Low	Low/ Normal	DDx includes Central/Secondary hypothyroidism (e.g., anterior pituitary dysfunction, hypothalamic disease)

TRH: thyrotropin-releasing hormone; TSH: thyroid-stimulating hormone

Terminology:[10]

- T_4 (aka thyroxine): prohormone made by thyroid gland.
- T_3: hormone produced both directly by thyroid gland and indirectly via enzymatic deiodination of T_4.
- "Many investigators believe that all effects of thyroid hormones are mediated by T3[, while] T4 functions only as a prohormone."

Refs at section title slide. * Complex algorithms exist for thyroid dysfunction workup. This table is intended as a referenced synopsis and not a comprehensive guide. **TSH level could be slightly high in some instances of central hypothyroidism (e.g., biologically inactive TSH). Graves' Disease: autoimmune disease due to thyroid-stimulating antibodies that bind to TSH receptors expressed primarily on the thyroid gland. Hashimoto's thyroiditis: chronic autoimmune thyroiditis; thyroid gland may have goitrous enlargement. Image: OpenStax College, CC BY 3.0 via Wikimedia Commons https://commons.wikimedia.org/wiki/File:1813_A_Classic_Negative_Feedback_Loop.jpg

Hyperthyroidism

Room for notes

- Thyrotoxicosis: A condition characterized by clinical manifestations of thyroid hormone excess.[5,7]
- Thyroid Storm: Rare condition characterized by severe clinical manifestations of thyrotoxicosis.[5]

Hyperthyroidism[1-6]	
Clinical manifestations can include:	• Tachycardia, arrhythmias, palpitations, tremors, weight loss, diarrhea; proptosis (in Graves' Disease). • *Thyroid Storm*: progressively severe symptoms, may also include hyperthermia, severe arrythmia, hypotension, CHF, mood disorders, altered mental status, coma.
Perioperative Treatment considerations (goal euthyroid before elective procedures):	
(1) Thionamides (e.g., propylthiouracil [PTU], methimazole)	PTU inhibits conversion of T4 to T3. Given ideally for at least several weeks preop (they decrease de novo thyroid hormone synthesis within hours, but do not impact release of preformed thyroid hormone). Note: agranulocytosis is rare but feared side effect.
(2) Beta-blockers	Propranolol inhibits conversion of T4 to T3. Can treat tachydysrhythmias and rate control.
(3) Iodine	Wolff-Chaikoff effect: Large doses of iodine can transiently inhibit organification of iodine in the thyroid gland. *Used cautiously* or after thionamides to prevent iodine from being used as substrate, particularly in patients with toxic adenoma or toxic multinodular goiter.
(4) Glucocorticoids	Reduces T4 to T3 conversion; may also treat underlying autoimmune process if present.
(5) Other medications	*Cholestyramine* (bile acid sequestrant; interferes w/enterohepatic circulation & recycling of thyroid hormone); *Plasmapheresis* (can remove cytokines, antibodies, & thyroid hormones); *Lithium* (blocks thyroid hormone release, but carries renal, neurologic, & other side effects).
(5) Other intraoperative	Treatment of hyperthermia if thyroid storm (e.g., cooling blankets, acetaminophen); fluid resuscitation & electrolyte repletion as needed.

Refs: 1. Miller 10th Ed Ch 28 // 2. Miller 10th Ed Ch 29 // 3. Steolting 8th Ed Ch 22 // 4. Anesthesia and Uncommon Disease 6th Ed Ch 13 // 5. UpToDate "Thyroid Storm" // 6. UpToDate "Anesthesia for patients with thyroid disease and for patients who undergo thyroid or parathyroid surgery" // 7. Health Harvard Dictionary (https://www.health.harvard.edu/q-through-z#T-terms)

Hypothyroidism

Room for notes

- Often detected subclinically, with elevated TSH and normal thyroid hormone levels.
- Myxedema Coma: Rare condition characterized by severe clinical manifestations of hypothyroidism.
- Hypothyroidism & airway exam: "Hypothyroidism is often associated with amyloidosis, which may produce an enlarged tongue, cardiac conduction abnormalities, and renal disease….The tongue may be enlarged in a hypothyroid patient even in the absence of amyloidosis…"[2]
- Hypothyroidism & MAC requirements: Possible increased sensitivity to anesthetics[2-4] → some advocate for careful dosing, but also note "the effect of thyroid activity on [MAC] of volatile anesthetics is negligible"[3] & "There is no evidence that these patients have a reduced MAC for contemporary inhaled anesthetics."[5]

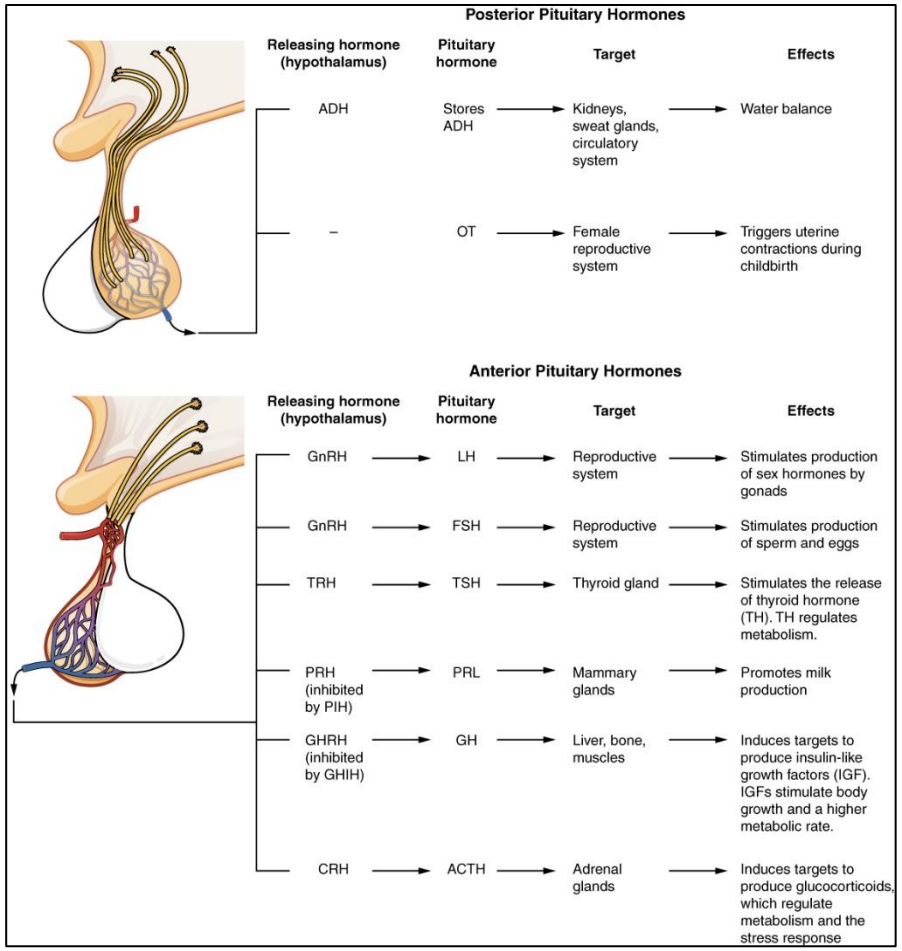
Hypothyroidism[1-6]	
Clinical manifestations can include:	• Slowness in mentation, reflexes, & movement; cold intolerance; respiratory depression, OSA; bradycardia; weight gain; nonpitting edema; impaired free water clearance, possibly w/hyponatremia. • *Myxedema coma*: progressively severe symptoms, which may also include delirium/unconsciousness; hypothermia; hypoventilation; bradycardia, hypotension, CHF, pericardial/pleural effusions; hypoglycemia; dilutional hyponatremia.
Perioperative Treatment considerations include (goal euthyroid before elective procedures):	
(1) Stress-dose steroids (?)	"Addison disease (with…relative steroid deficiency) is more common in hypothyroidism,…some endocrinologists routinely treat patients…with stress dose steroids perioperatively…the possibility that this steroid deficiency exists should be considered if the patient becomes hypotensive perioperatively."[2]
(2) IV thyroid hormone replacement (?)	"For patients in myxedema coma who require emergency surgery, liothyronine (T3 hormone) can be given intravenously (with fear of precipitating myocardial ischemia, however) while supportive therapy is undertaken"[2]
(3). Other	Fluid resuscitation, electrolyte repletion, glucose management, warming as needed.

Refs: 1. Miller 10th Ed Ch 28 // 2. Miller 10th Ed Ch 29 // 3. Stoelting 8th Ed Ch 22 // 4. Anesthesia & Uncommon Diseases 6th Ed Ch 13 // 5. UpToDate "Anesthesia for patients with thyroid disease and for patients who undergo thyroid or parathyroid surgery" // 6. UpToDate "Myxedema Coma"

Pituitary - Misc

12X

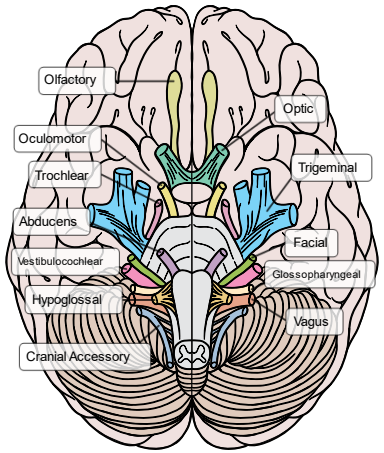
Room for notes

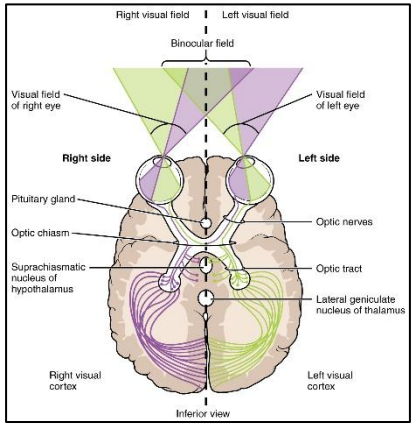


Pituitary hypersecretion from functioning microadenoma – most common hormones: Prolactin (galactorrhea, amenorrhea, infertility), growth hormone (acromegaly), and ACTH (Cushing syndrome).[2,6,7]

Nonfunctioning pituitary macroadenoma: impaired vision is most common presenting symptom, usually bitemporal hemianopsia from optic chiasmal compression.[7] If growth causes healthy pituitary destruction (may eventually lead to panhypopituitarism): gonadotropin deficiency (amenorrhea, impotence) is most common initial hormone deficiency (nonfunctioning adenomas are usually gonadotroph cells).[3,7]

Sheehan syndrome (pituitary infarction → pituitary apoplexy after obstetric hemorrhage/hypotension): may present with postpartum lactation difficulty, cold intolerance, fatigue, refractory hypotension. Treatment includes prompt hormonal therapy (such as corticosteroids, thyroid replacement, and desmopressin [DDAVP]). Other acute causes of pituitary apoplexy: severe hypertension, trauma.[1,2]





ADH: antidiuretic hormone/vasopressin; OT: oxytocin; GnRH: gonadotropin-releasing hormone; LH: luteinizing hormone; FSH: follicle-stimulating hormone; TRH: thyrotropin-releasing hormone; TSH: thyroid-stimulating hormone; PRH: prolactin-releasing hormone; PIH: prolactin-inhibiting hormone; PRL: prolactin; GHRH: growth hormone-releasing hormone; GHIH: growth hormone-inhibiting hormone; GH: growth hormone; CRH: corticotropin-releasing hormone; ACTH: adrenocorticotropic hormone (aka corticotropin, adrenocorticotropin). Refs: Acromegaly image 2216232369 via Shutterstock license // 1. Miller 10th Ed Ch 28 // 2. Miller 10th Ed Ch 29 // 3. Stoelting 8th Ed Ch 22 // 4. AACE Acromegaly guidelines PMID 21846616 // 5. UpToDate: Anesthesia for transphenoidal pituitary surgery // 6. Miller 10th Ed Ch 53 // 7. UpToDate: Causes, presentation, and evaluation of sellar masses // Pituitary hormones & Optical fields: OpenStax College, CC BY 3.0 via Wikimedia Commons; https://commons.wikimedia.org/wiki/File:1420_Optical_Fields.jpg https://commons.wikimedia.org/wiki/File:1810_Major_Pituitary_Hormones.jpg

Acromegaly: Anesthetic Considerations

4X

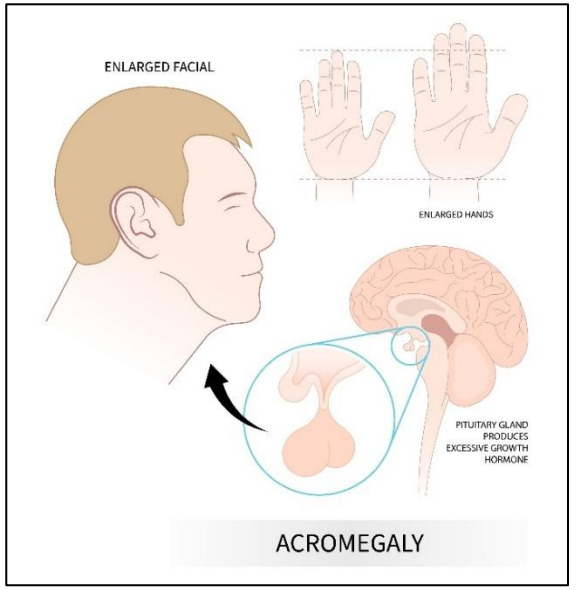
Room for notes

Patients with acromegaly may have:[1-7]

- Difficult airway (enlarged jaw, tongue, epiglottis, & other laryngeal/pharyngeal tissue, possibly narrowing glottic opening). These patients may also have hoarseness (recurrent laryngeal nerve may be stretched by growth of surrounding structures) or voice changes (from changes to laryngeal tissue).
- Carpal tunnel syndrome (enlarged bone and connective tissue may compromise ulnar and other collateral flow to radial artery – may be relevant to arterial line placement).
- Other multisystem comorbidities, including OSA, cardiomyopathy, diabetes mellitus (growth hormone can antagonize insulin action, leading to glucose intolerance), headaches, visual deficits, excessive sweating, joint pains, menstrual irregularities, gonadal dysfunction, other hormonal tumors (e.g., MEN type-I).

If patient presenting for transsphenoidal tumor excision:

- *2022 ITE Gaps in Knowledge*: "During transsphenoidal resection of a pituitary tumor, allowing hypercapnia can improve conditions for tumor visualization."
- If patient on CPAP/BiPAP for OSA: Consider discussion w/surgeon regarding postop options after transsphenoidal tumor excision.
- Value of smooth emergence: coughing, straining, hypertension can increase risk of epistaxis or CSF leak. Laryngospasm requiring extended positive pressure ventilation is even less ideal than in other scenarios.



Adjunct treatments for growth hormone secreting nonoperative pituitary adenomas may include:[2-4]

- Radiation therapy
- Dopamine agonists (e.g., bromocriptine, cabergoline): inhibit anterior pituitary secretion via dopamine receptor stimulation.
- Somatostatin analogs (e.g., octreotide, lanreotide): inhibits multiple hormones, including growth hormone.
- Growth hormone receptor antagonists (e.g., pegvisomat).

Refs: Acromegaly image 2216232369 via Shutterstock license // 1. Miller 10th Ed Ch 28 // 2. Miller 10th Ed Ch 29 // 3. Stoelting 8th Ed Ch 22 // 4. AACE Acromegaly guidelines PMID 21846616 // 5. UpToDate: Anesthesia for transsphenoidal pituitary surgery // 6. Miller 10th Ed Ch 53 // 7. UpToDate: Causes, presentation, and evaluation of sellar masses // 8. UpToDate: Physiology of growth hormone.

Neuro & Neuromuscular

Room for notes

References for image “Key Ions Involved in Neuromuscular Transmission”: Miller’s Anesthesia, 10th Ed, Ch 31 // Pollard’s Cell Biology, 3rd Ed, Ch 17 // JIvory96, CC BY-SA 4.0, via Wikimedia Commons (https://commons.wikimedia.org/wiki/File:Ca2%2B_sparks.jpg) // https://en.wikipedia.org/wiki/File:NMJ_Signalling_1.jpg CC BY-SA 3.0 // https://open.oregonstate.education/aandp/chapter/10-3-muscle-fiber-excitation-contraction-and-relaxation/ CC BY-SA 4.0 // Litman RS et al. Anesthesiology 2018; PMID 28902673 // Roderick et al. PMID: 12781146.

Neuro: Electroconvulsive Therapy (ECT)

20X

- Sympathetic swings: initial parasympathetic response and bradycardia (followed by a sympathetic surge). Some pre-treat with glycopyrrolate/atropine (also reduces secretions).
- Caution in patients with risks from hemodynamic swings: e.g., pheochromocytoma, severe coronary disease, sensitivity to increased ICP (ECT briefly increases cerebral blood flow).
- Common agents use to decrease ECT hemodynamic response: labetalol, esmolol, calcium channel blockers (Barash 9th Ed, Ch 33). Diltiazem may reduce seizure duration. Dexmedetomidine and remifentanil also studied as adjuncts.
- Paralysis: succinylcholine popular. Rocuronium/sugammadex being explored but dosing not well established (Miller 9th Ed, Ch 28).

Induction Agent	Effect on Seizure Duration
Methohexital	No change
Etomidate	Increases
Ketamine	Increases
Propofol	Decreases

Adjunct	Effect on Seizure Duration
Midazolam	Decreases
Lidocaine	Decreases
Dexmedetomidine	No change
Remifentanil	No change vs increased

* **Methohexital** (1 to 1.5 mg/kg) has less effect on seizures than other induction agents and has been a traditional "gold standard."

Refs: Barash 9th Ed Ch 33 // Miller 10th Ed, Ch 24// Kadiyala et al 2018; PMID: 29870425 // Deiner et al 2009; PMID: 19359878 // Stripp et al 2018; PMID: 28462732 // Soehle et al 2018; PMID: 29994943 // Tess A et al. Medical consultation for electroconvulsive therapy. UpToDate (June11'19) // Wajima et al 2001; PMID: 11323371 // Wajima et al 2002; PMID: 12500511.

Room for notes

Air/Fat/Amniotic Fluid Embolism

14X

- Most sensitive test to detect venous air embolism: TEE (0.02mL/kg air)
  - Most sensitive noninvasive test: precordial Doppler (0.05 mL/kg air)
- High risk for venous air embolism: posterior fossa procedure; sitting position craniotomy.
- Fat embolism buzzwords: orthopedic trauma patient (such as long bone/pelvic fracture); hypoxemia, hypotension, tachycardia, tachypnea/respiratory alkalosis, thrombocytopenia; petechial rash.
- Amniotic fluid embolism buzzwords: labor & delivery patient; hypotension, hypoxemia, tachycardia, dyspnea, loss of consciousness, generalized bleeding/coagulopathy/ disseminated intravascular coagulation (DIC).

Handouts: Crisis Checklists for Air Embolism (Venous), Hypotension, and Hypoxia; Society for Pediatric Anesthesia Pedi Crisis Checklist for Hypotension


1 Air Embolism – Venous

Decreased end-tidal CO_2, decreased oxygen saturation, hypotension

START

Critical CHANGES

1 Call for help and a code cart
- Ask: *"Who will be the crisis manager?"*

2 Turn FIO_2 to 100%

3 Turn off nitrous oxide

4 Stop source of air entry
- Fill wound with irrigation
- Lower surgical site below level of heart, if possible
- Search for entry point (including open venous lines)

5 Consider...
- Positioning patient with left side down
  - Continue appropriate monitoring while repositioning
- Placing bone wax or cement on bone edges
- Transesophageal echocardiography (TEE) if diagnosis unclear
- Using ETCO$_2$ to monitor progression and resolution of embolus or for assessment of adequate cardiac output

Miller 10th Ed, Ch 53 and 60. // Mirski et al 2007; PMID: 17197859 // Chestnut's Obstetric Anesthesia 6th Ed, Ch 38. //Ariadne Labs Operating Room Crisis Checklists. See https://www.ariadnelabs.org/ for latest version. With permission via Creative Commons BY-NC-SA (https://creativecommons.org/licenses/by-nc-sa/4.0/).

Room for notes

01 Air Embolism - Venous

Decreased end-tidal CO_2, decreased oxygen saturation, hypotension

INDEX

01

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Turn FiO_2 to 100%**
   - Turn off nitrous oxide
3. **Stop source of gas entry**
   - Fill wound with irrigation and/or apply bone wax to bone edges
   - Lower surgical site below level of heart if possible
   - Search for entry point (including open venous lines)
   - Desufflate if concern for CO_2 embolism
4. **Support hemodynamics**
   - Escalate vasopressor support as needed
   - Turn down anesthetic agents
5. **Consider...**
   - Positioning patient with left side down, if feasible
     - Continue monitoring during positioning
   - Removing PEEP in patients with PFO at risk for paradoxical embolism
   - Avoid spontaneous ventilation; paralyze as needed
   - Use $ETCO_2$ to monitor progression and resolution of embolism or for assessment of cardiac output
   - If diagnosis is unclear, call for TEE
   - If ongoing hemodynamic instability, call for ECMO or cardiopulmonary bypass
6. **Continuing care**
   - Consider hyperbaric oxygen treatment within 6 hours for evidence of paradoxical embolism

DIFFERENTIAL diagnosis

Amniotic Fluid Embolism
Cement Embolism
Venous Thromboembolism / Pulmonary Embolism
Non-embolic causes of hypotension (CHKLST 10)
Non-embolic causes of hypoxia (CHKLST 11)

Critical CHANGES

If **PEA** develops, *go to* CHKLST 04

Excerpt Vasopressor Support (from Hypotension Crisis Checklist):

DRUG DOSES & treatments

ePHEDrine	5 - 25 mg IV — *or* — 50 mg IM x 1
Phenylephrine	BOLUS: 50 - 200 MCG IV (1mL of 10 mg/mL in 100 mL = 100 MCG/mL) INFUSION: 0.5 - 1 MCG/kg/min
Norepinephrine	BOLUS: 5 - 20 MCG IV (4mL of 1mg/mL in 250 ml = 16 MCG/mL) INFUSION: 0.05 - 0.5 MCG/kg/min
Vasopressin	BOLUS: 1 - 2 units IV (1 mL of 20 units/mL in 19 mL = 1 unit/mL) INFUSION: 0.01 - 0.04 units/min
EPINEPHrine	BOLUS: 4 - 10 MCG IV (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01 - 0.1 MCG/kg/min

Room for notes

10 Hypotension

Unexplained drop in blood pressure refractory to initial treatment

INDEX

START

1. **Call for help**
   - Ask: *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Check...**
   - Measurement artifact
   - $ETCO_2$ - adequacy of perfusion
   - Heart rate
     - If BRADYCARDIA, *go to* CHKLST 03
     - If TACHYCARDIA, *go to* CHKLST 16
   - Rhythm
     - If PEA, *go to* CHKLST 04
     - If VF / VT, *go to* CHKLST 05
3. **Inspect surgical field for bleeding**
   - If BLEEDING, *go to* CHKLST 09
4. **Run IV fluids wide open**
5. **Give vasopressors** and titrate to response
   - MILD hypotension:
     - Give ePHEDrine or phenylephrine
   - SIGNIFICANT / REFRACTORY hypotension:
     - Administer norepinephrine; consider escalating to add vasopressin or EPINEPHrine
6. **Turn FiO_2 to 100%** and **minimize volatile anesthetics**
7. **Consider...**
   - Trendelenburg position
   - Additional IV access
   - Arterial line
   - Point of care ultrasound or echocardiography for diagnosis
   - Mechanical circulatory support

DIFFERENTIAL diagnosis

Volume / Vasoplegia (Vasodilation)
- Occult bleeding
- Anaphylaxis, *go to* CHKLST 02
- Drug overdose or error
- Sepsis
- Hypoxia, *go to* CHKLST 11
- Hypocalcemia
- Adrenal insufficiency
- Reperfusion

Obstructed Blood Flow
- Mechanical or surgical manipulation
- Insufflation during laparoscopy
- Vascular compression
- Tamponade
- Increased PEEP
- Pneumothorax

Cardiac Function
- Myocardial ischemia, *go to* CHKLST 14
- Heart failure
- Emboli (pulmonary, fat, amniotic, CO_2, air), *go to* CHKLST 01
- Bone cementing
- Malignant hyperthermia, *go to* CHKLST 13

DRUG DOSES & treatments

ePHEDrine	5 - 25 mg IV *— or —* 50 mg IM x 1
Phenylephrine	BOLUS: 50 - 200 MCG IV (1mL of 10 mg/mL in 100 mL = 100 MCG/mL) INFUSION: 0.5 - 1 MCG/kg/min
Norepinephrine	BOLUS: 5 - 20 MCG IV (4mL of 1mg/mL in 250 ml = 16 MCG/mL) INFUSION: 0.05 - 0.5 MCG/kg/min
Vasopressin	BOLUS: 1 - 2 units IV (1 mL of 20 units/mL in 19 mL = 1 unit/mL) INFUSION: 0.01 - 0.04 units/min
EPINEPHrine	BOLUS: 4 - 10 MCG IV (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01 - 0.1 MCG/kg/min

REFRACTORY VASOPLEGIA treatment

Methylene Blue	1 - 2 mg/kg in 100mL NS over 20 - 60 minutes
	Consider pharmacy consultation
Hydrocortisone	100 mg IV

HYPOCALCEMIA treatment

Calcium Gluconate	1 - 3 g IV
— or —	
Calcium Chloride	0.5 - 1 g IV

10

Room for notes

Methylene blue: thought to treat low blood pressure/ vasoplegia via interference with the nitric oxide-cyclic guanylate monophosphate (CGMP) pathway, thus inhibiting its vasorelaxant effect on smooth muscle.[1,2]

Hypotension

Sustained low blood pressure with patient at risk for end-organ hypoperfusion, typically > 20% below baseline

- Ensure oxygenation/ventilation
- Turn anesthetic agents down or off
- Check cuff size and transducer position
- Consider placing arterial line
- Give appropriate treatment (see table below)

Age	BP (mmHg)*	
infant	MAP 30 or post-conceptual age in weeks	
3 mo – 1 yr	65 – 68	< 5th% Systolic BP
1 – 3 yr	68 – 74	
4 – 12 yr	70 – 85	
> 12 yr	85 – 92	

* Numbers are only a guide and vary by patient and situation

Mean Arterial Pressure (MAP) values

	↓ Preload	↓ Contractility	↓ Afterload
Causes	▪ Hypovolemia/hemorrhage ▪ Vasodilation ▪ Impaired venous return ▪ Tamponade ▪ IVC compression (prone, obese, surgical) ▪ Pneumothorax/ pneumoperitoneum/PE ▪ Increased PIP or PEEP	▪ Negative inotropic drugs (anesthetic agents) ▪ Arrhythmias ▪ Hypoxemia ▪ Heart failure (ischemia) ▪ Hypocalcemia/blood product administration	▪ Drug-induced vasodilation ▪ Sepsis ▪ Anaphylaxis ▪ Adrenal crisis ▪ Hypocalcemia ▪ Thyroid crisis
Treatment	▪ Expand circulating blood volume (administer fluids rapidly, consider PRBCs and albumin) ▪ Trendelenberg position ▪ Place or replace IV; consider intraosseous line	▪ Start inotrope if needed: DOPamine 2-20 MICROgrams/kg/min IV infusion, or EPINEPHrine 1-10 MICROgrams/kg IV bolus then EPINEPHrine 0.02-1 MICROgrams/kg/min IV infusion ▪ Calcium chloride 10-30 mg/kg IV or Calcium gluconate 50 mg/kg IV ▪ Review ECG (rhythm, ischemia), send ABG, Hgb, electrolytes	▪ Start vasopressor if needed: phenylephrine 1-20 MICROgrams/kg IV bolus, then phenylephrine 0.1-2 MICROgrams/kg/min IV infusion, or norepinephrine 0.05-2 MICROgrams/kg/min IV infusion ▪ Go to 'Anaphylaxis' card, if appropriate. ▪ Administer steroids for adrenal crisis

13 Hypotension Revision Jan 2023

Society for Pediatric Anesthesia Critical Event Checklists. Revision Packet March 2023. Latest update available at http://www.pedsanesthesia.org

Room for notes

11 Hypoxia

Unexplained oxygen desaturation

INDEX

START

1. **Call for help**
   - **Ask:** "*Who will be the crisis manager?*"
   - Crisis manager designates checklist reader
2. **Turn FiO_2 to 100%** at high gas flows
   - Confirm inspired FiO_2 = 100% on gas analyzer
   - Confirm presence of end-tidal CO_2
3. **Hand-ventilate** to assess compliance
4. **Listen** to breath sounds
5. **Check…**
   - Blood pressure, pulse, airway pressures
   - Capnogram waveform
   - Endotracheal tube/supraglottic device position
   - Pulse oximeter placement and limb perfusion
   - Circuit integrity: disconnection, kinks, holes
6. **Consider initial stabilization actions**
   - Suction secretions
   - Remove circuit and use self-inflating bag
   - Alveolar recruitment maneuver and PEEP titration
   - Bronchodilator therapy
   - Deepen anesthetic and paralysis
   - Optimize positioning and insufflation pressure
7. **Consider causes - see DIFFERENTIAL Diagnosis**
8. **If hypoxia persists, consider ECMO**

DRUG DOSES & treatments

Albuterol	3 MDI puffs per ETT 2.5 mg via nebulizer
EPINEPHrine	10 - 20 MCG IV, repeat PRN (1 mg in 100 mL = 10 MCG/mL)

Additional DIAGNOSTIC TESTS

Fiberoptic bronchoscopy
Chest x-ray
Electrocardiogram
Transesophageal Echocardiogram
Arterial or venous blood gas
Lung ultrasound

DIFFERENTIAL diagnosis

Airway / Breathing
- Right mainstem intubation
- Aspiration
- Atelectasis
- Bronchospasm
- Anaphylaxis (CHKLST 02)
- Hypoventilation
- Laryngospasm
- Obesity / positioning
- Pneumothorax
- Pulmonary edema
- Auto-PEEP

Circulation
- Embolism (CHKLST 01)
- Heart disease
- Tamponade
- Septic shock
- Severe hypotension (CHKLST 10)

Artifacts
- Dyes (e.g. methylene blue)
- Hemoglobinopathies (e.g. methemoglobinemia)

11

Room for notes

Complications of Subarachnoid Hemorrhage (SAH)

8X

Room for notes

- ECG changes that can occur after SAH: profound "canyon" T wave inversions, nonspecific T-wave abnormalities, QT prolongation, ST-segment depression, and U-waves. "There is typically no relationship between the ECG changes and echocardiographic myocardial dysfunction. ECG abnormalities [alone] do not herald evolving or impending cardiac disease." [Miller 10th Ed, Ch 53]
  - Echocardiography sometimes independently done (SAH can cause a catecholamine mediated myocardial "stunning" injury).
- Neurogenic Pulmonary edema: increased ICP can activate sympathetics → catecholamine surge → increased pulmonary capillary pressure → destruction of capillary/alveolar walls → leakage of fluid.
- Peak occurrence of cerebral vasospasm: 3 days – 2 weeks after SAH; peak at 7 days → some consider SAH surgery early (0-3 days) or late (>10 days).
  - Triple H therapy: hypervolemia, hypertension, hemodilution (controversial).
  - Calcium channel blockers: may mitigate vasospasm (nicardipine) or complications from vasospasm (nimodipine).
- Syndrome of inappropriate secretion of antidiuretic hormone (SIADH), Arginine Vasopressin Deficiency/Resistance (Diabetes Insipidus [DI]) and Cerebral Salt Wasting Syndrome (CSW): see handout in renal section.

Hunt-Hess Classification for Intracranial Aneurysm/SAH Severity by Clinical Symptoms

Grade	Clinical Symptoms
1	Asymptomatic (or minimal headache/nuchal rigidity)
2	Moderate/severe headache, nuchal rigidity; no neuro deficit except cranial nerve palsy
3	Confusion, drowsiness, mild focal neuro deficit
4	Stupor, hemiparesis (moderate/severe), early decerebrate rigidity
5	Deep coma, decerebrate rigidity, moribund
If severe comorbidities and severe vasospasm on imaging, use next highest grade.	

Miller 10th Ed., Ch 53. // Cottrell/Patel 6th Ed, Ch 23 // Hunt WE, Hess RM. J Neurosurg 1968. PMID: 5635959.

Glasgow Coma Scale

6X

Eye-Opening Response	Verbal Response	Motor Response
4= Spontaneous	5= Oriented (name, place, date)	6= Follows commands
3= To sound	4= Confused	5= Localizes pain
2= To pressure	3= Words (inappropriate speech)	4= Normal flexion
1= None	2= Sounds (incomprehensible moans/groans)	3= Abnormal Flexion to pain (decorticate posturing – slow movements, arms across chest, rotation of forearms, clenching of thumbs, extension of legs)
	1=None	2= Extension to pain (decerebrate posturing)
		1= None
"NT" is used for a given category if it is non-testable (for example: E4, VNT, M5)		

- Less than 8, intubate: "Advanced Trauma Life Support Guidelines suggest that head injured patients should be intubated if their Glasgow coma scale is less than 8."
- Video demonstration available at: www.glasgowcomascale.org (https://youtu.be/v6qpEQxJQO4)

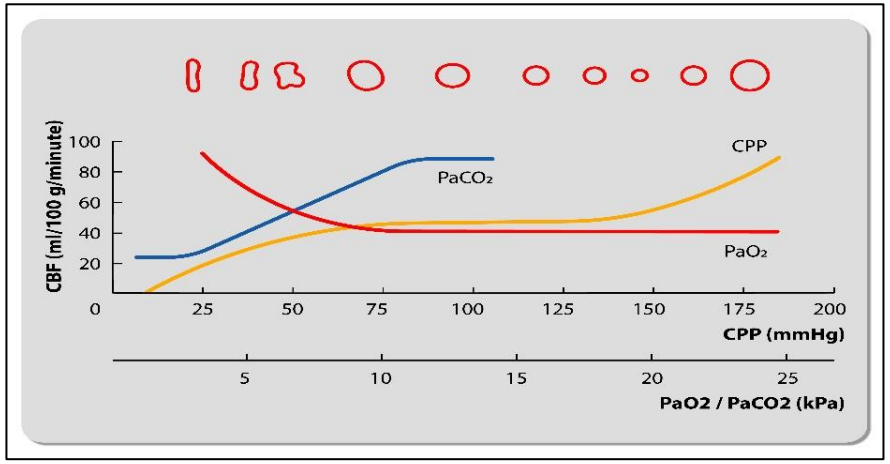
Wilson MH, Habig K, Wright C, et al. Pre-hospital emergency medicine. The Lancet 2015, 386: 2526-34. // https://www.glasgowcomascale.org/downloads/GCS-Assessment-Aid-English.pdf?v=3 Accessed Jan 2, 2021. // Galvagno et al. Advanced Trauma Life Support ® Update 2019: Management and applications for adults and special populations. Anesthsiol Clin 2019; 37: 13-32.

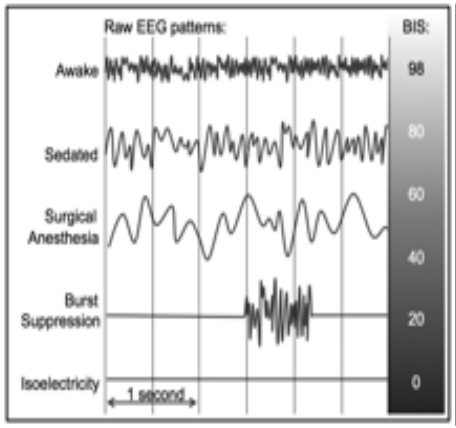
Room for notes

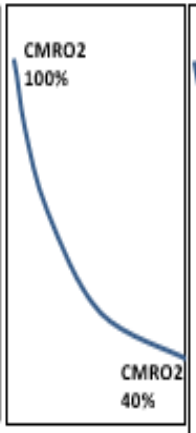
Factors affecting Cerebral Blood Flow (CBF)

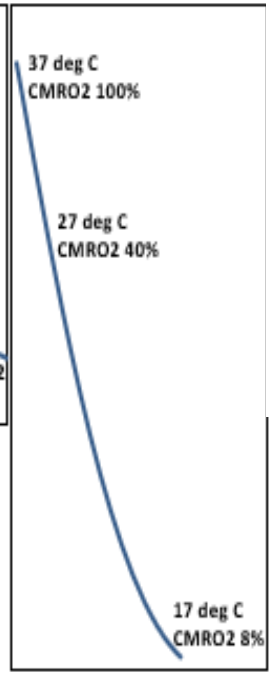
20X

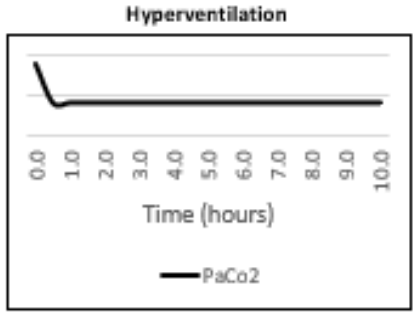
Room for notes

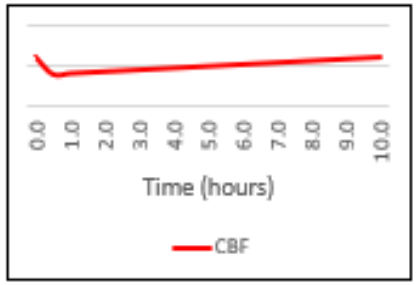


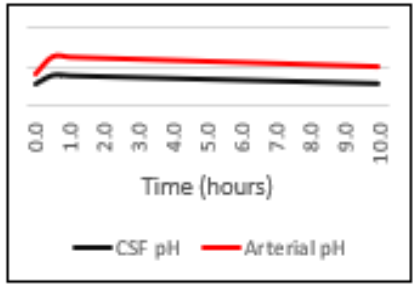












Anesthetics, CBF, and CMR			
	Agent	CBF	CMR
Intravenous	Midazolam	↓	↔
	Fentanyl	↓	↓
	Propofol	↓	↓
	Etomidate	↓	↓
	Dexmedetomidine	↓	↓
	Remifentanil	*	↔
	Sufentanil	↓	↓
	Morphine	↓	↓
	Ketamine	↑	↑
Inhalational	Sevoflurane	↑	↓
	Isoflurane	↑	↓
	Desflurane	↑	↓
	Halothane	↑	↓
	N2O**	↑	↑

Cerebral Perfusion Pressure (CPP):
CPP = MAP – ICP (or MAP – CVP , if CVP > ICP)

Cerebral Blood Flow (CBF):
CBF = CPP/CVR

Factors influencing cerebral blood flow include: PaO2, PaCO2, cerebral metabolic rate, mean arterial pressure (cerebral perfusion pressure), vasopressors, blood viscosity, and neurogenic pathways.

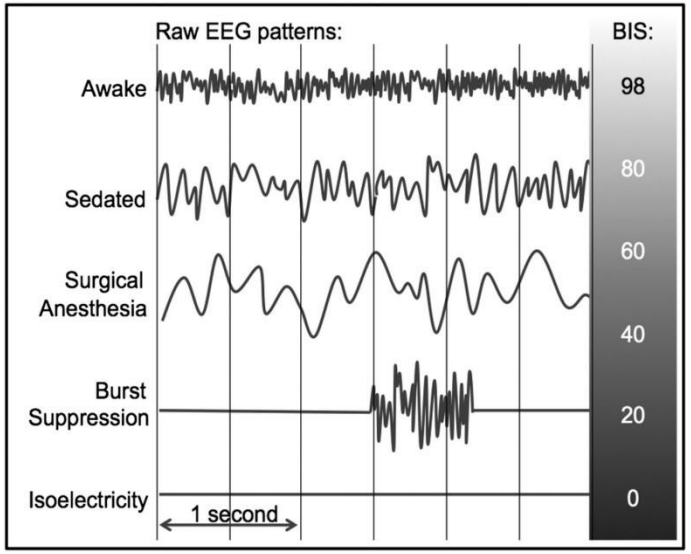
Miller 10th Ed: Ch 10, 53 // Barash 9th Ed, Ch 37 // Cole et al. PMID: 18091252 // Albrecht et al. PMID: 3109079 // EEG image: Wildes et al. PMID: 27311914 Creative Commons CC-BY-NC 4.0. // Autoregulation image: 2044990829, used via license from Shutterstock// Meng et al. PMID 25401418 // Gelb et al. PMID 18227320 // *, **: see subsequent slide w/table

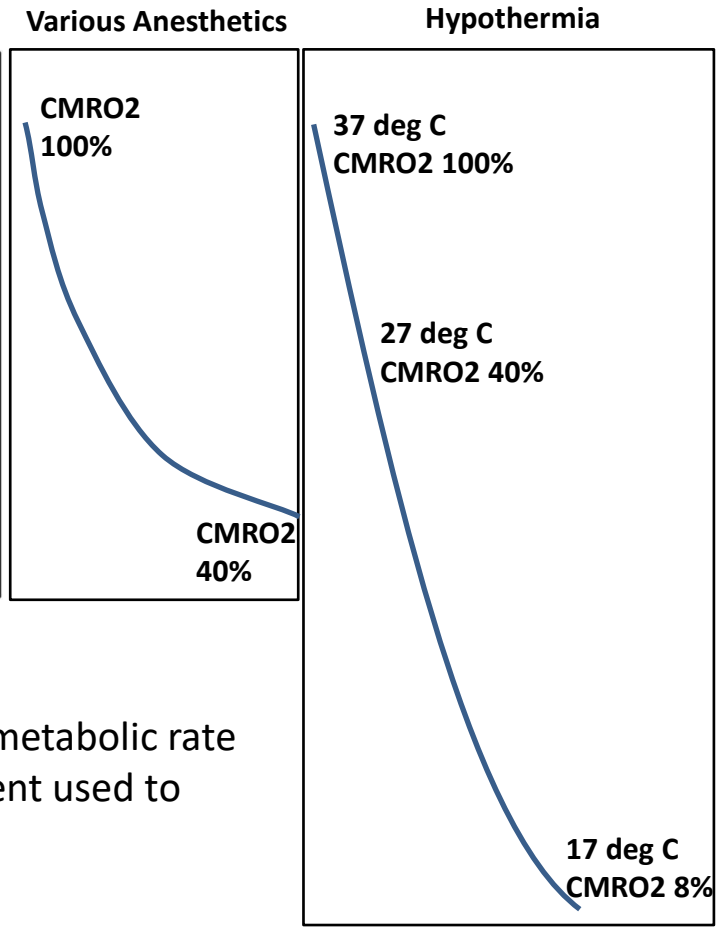
Factors affecting Cerebral Blood Flow (CBF)

Room for notes

Miller, 10th Ed, Ch 10:

Neurovascular (flow-metabolism) coupling: Increased neuronal activity → increased local brain metabolism → "this increase in [cerebral metabolic rate (CMR)] is associated with a proportional change in CBF."





Anesthetics:

- "When complete [EEG] suppression is achieved, the cerebral metabolic rate of oxygen ($CMRO_2$) is similar irrespective of the anesthetic agent used to achieve EEG suppression."

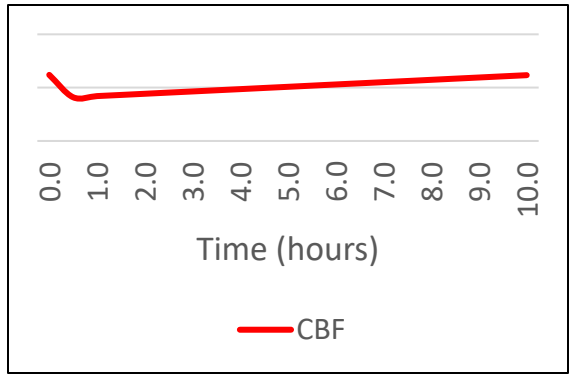
Temperature:

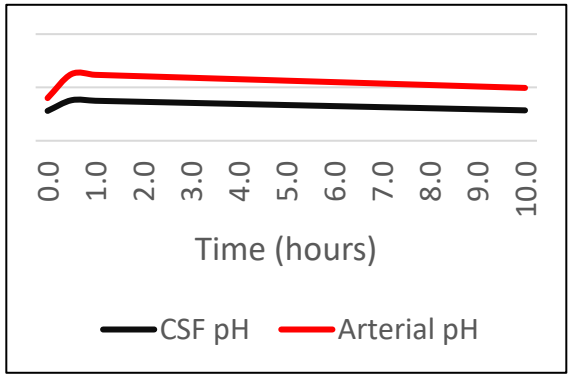
- "The CMR decreases by 6-7% per degree Celsius of temperature reduction….In contrast to anesthetic drugs, temperature reduction beyond that at which EEG suppression first occurs *does* produce a further decrease in the CMR."

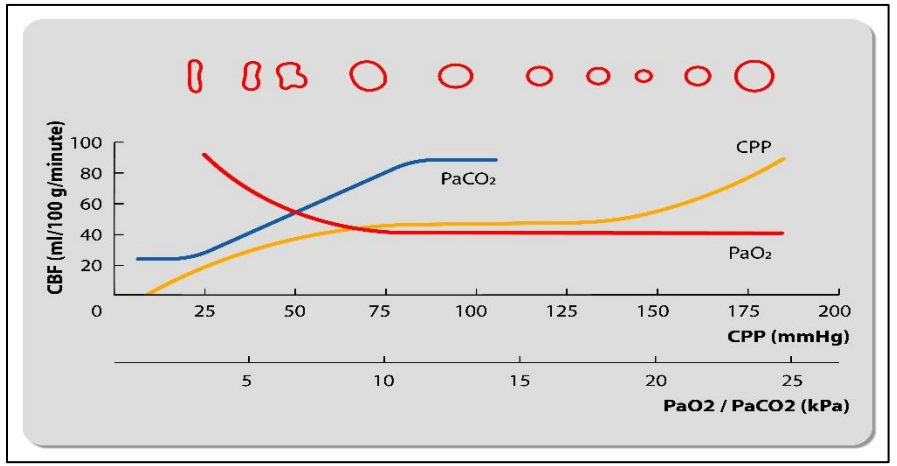
Miller 10th Ed: Ch 10 // EEG image: Wildes et al. PMID: 27311914 Creative Commons CC-BY-NC 4.0.

Factors affecting Cerebral Blood Flow (CBF)

Hyperventilation







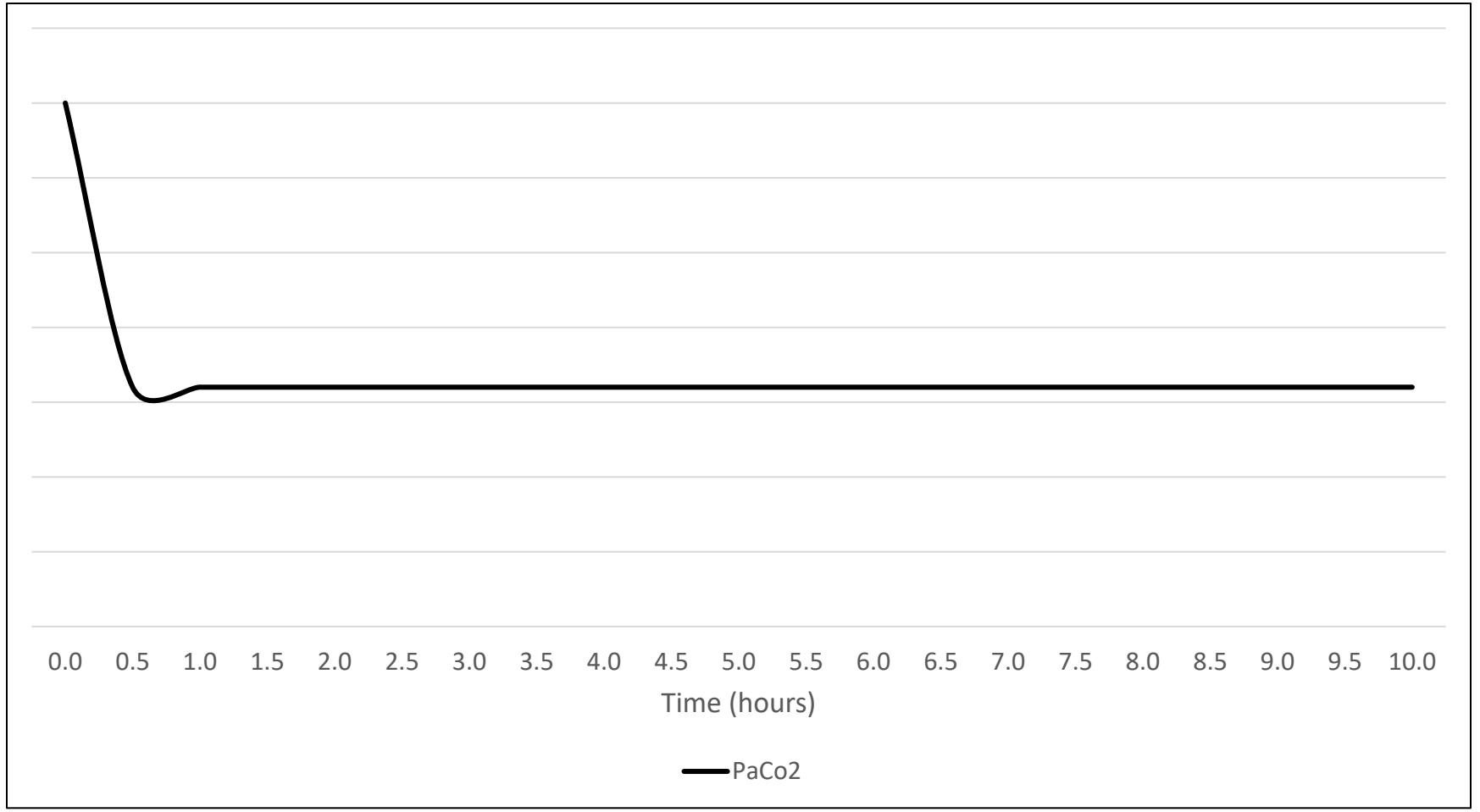
Miller, 10th Ed, Ch 10:

- "CBF varies directly with PaCO2 […] within the [physiologic] range [~25-75mm Hg]." The CBF responsiveness to PaCo2 is attenuated if there is moderate/severe hypotension.
- "Changes in PaO2 from 60 to more than 300 mm Hg have little influence on CBF. [A PaO2 reduction] below 60 mm Hg rapidly increases CBF." [Below 60mmHg], the relationship between [pulse oximetry measured hemoglobin saturation] and CBF is inversely linear."
- "The CBF changes in response to alterations in PaCO2 rapidly occur, but they are not sustained. Despite the maintenance of an increased arterial pH [from hyperventilation], CBF returns toward normal over [6-8 hours] because the pH of cerebrospinal fluid (CSF) gradually returns to normal levels as a result of extrusion of bicarbonate."
- "In contrast with *respiratory* acidosis, acute systemic *metabolic* acidosis has little immediate effect on CBF because the [blood brain barrier] excludes H+ from the perivascular space."

Room for notes

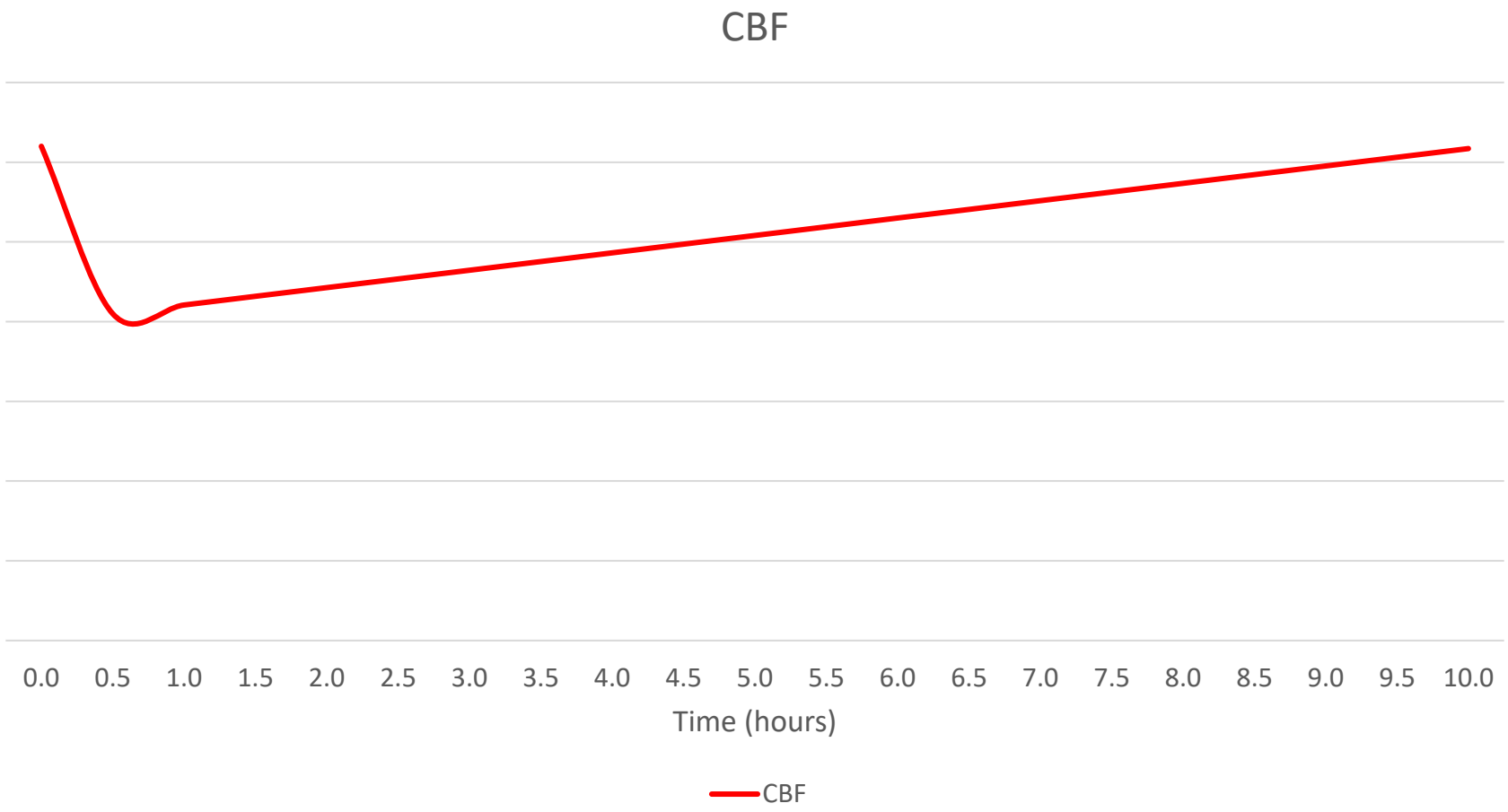
Miller 10th Ed: Ch 10, 53 // Albrecht et al. PMID: 3109079. // Autoregulation image: 2044990829, used via license from Shutterstock. // Meng et al. PMID 25401418 // Gelb et al. PMID 18227320

PaCO2 during substantial/sustained hyperventilation



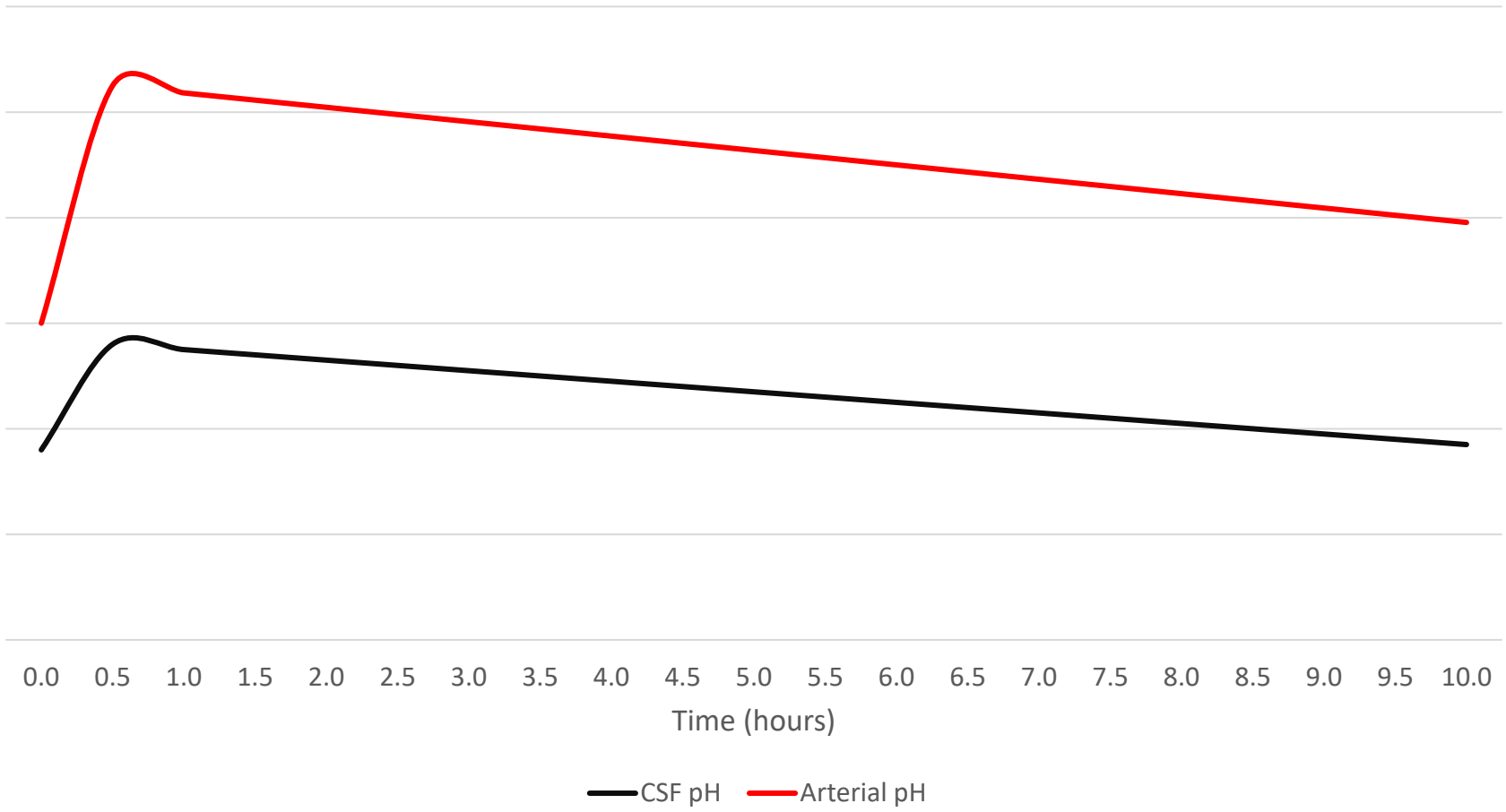
Room for notes

CBF during substantial/sustained hyperventilation



Room for notes

pH (CSF and arterial) during substantial/sustained hyperventilation



Room for notes

Factors affecting Cerebral Blood Flow (CBF)

Miller, 10thEd, Ch 10:

- "The net effect of volatile anesthetics on CBF is […] a balance between a reduction in CBF caused by CMR suppression and an augmentation of CBF caused by the direct cerebral vasodilation."

- ***Remifentanil**: "[S]edative doses of remifentanil alone can cause minor increases in CBF. With larger doses of with the concomitant administration of anesthetic adjuvants, CBF is either unaltered or modestly reduced."

- ****Nitrous Oxide**: "When N2O is administered alone, very substantial increases in CBF and ICP can occur.
  - These substantial increases are somewhat attenuated when nitrous oxide is given with a volatile anesthetic.
  - "[W]hen N2O is administered in combination with intravenous drugs, including barbiturates, benzodiazepines, narcotics, and propofol, [the] cerebral-vasodilating effect [from nitrous oxide] is [more] attenuated or even completely inhibited."

Anesthetics, CBF, and CMR			
	Agent	CBF	CMR
Intravenous	Midazolam	↓	↔
	Fentanyl	↓	↓
	Propofol	↓	↓
	Etomidate	↓	↓
	Dexmedetomidine	↓	↓
	Remifentanil	*	↔
	Sufentanil	↓	↓
	Morphine	↓	↓
	Ketamine	↑	↑
Inhalational	Sevoflurane	↑	↓
	Isoflurane	↑	↓
	Desflurane	↑	↓
	Halothane	↑	↓
	N2O**	↑	↑

Room for notes

Miller 10th Ed: Ch 10, 53 // Barash 9th Ed, Ch 37 // Cole et al. PMID: 18091252

Factors affecting Cerebral Blood Flow (CBF) - Misc

Room for notes

Miller, 10th Ed, Ch 10:

- **Viscosity**: "…viscosity is not a target of manipulation [for CBF] in patients at risk as a result of cerebral ischemia, with the possible exception of those with hematocrit values higher than 55%.."
- **Neurogenic regulation of cerebral blood flow (i.e. innervation from sympathetics)**: "The nature and influence of such pathways in humans are not known, and their manipulation for the purposes of clinical management remains to be systematically investigated."
- **Vasodilators**: "Most drugs used to induce hypotension, [including] sodium nitroprusside, nitroglycerin, […] hydralazine, and calcium channel blockers, reduce cerebral tone and cause cerebral vasodilation. As a result, CBF either increases or is maintained at pretreatment levels…"
- **Pressors**: "When basal pressure is within the normal autoregulation range, an increase in systemic pressure either does not affect CBF or increases CBF only modestly."
- **Age**: "…both CBF and CMRO2 decrease by 15-20% at the age of 80 years."
- **Succinylcholine:** "Although succinylcholine *can* produce increases in ICP [~5mmHg in the lightly anesthetized…], it can still be used for a rapid-sequence induction…[there should be] proper attention to…CO2 tension, arterial blood pressure,…and depth of anesthesia and after defasciculation…."

Cerebral Perfusion Pressure (CPP):
CPP = MAP – ICP (or MAP – CVP , if CVP > ICP)

Mean Arterial Pressure (MAP):
MAP = DP + (1/3)(SP-DP) or DP + (1/3)(PP)

Cerebral Blood Flow (CBF):
CBF = CPP/CVR

ICP: Intracranial Pressure; CVP: central venous pressure ; CVR: cerebrovascular resistance; DP: diastolic pressure; SP: systolic pressure; PP: pulse pressure

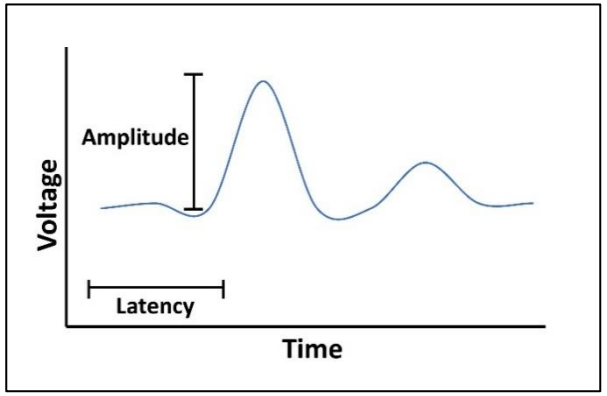
Ref: Barash 9th Ed, Ch 37 // https://www.ncbi.nlm.nih.gov/books/NBK538226/

Factors affecting SSEP's

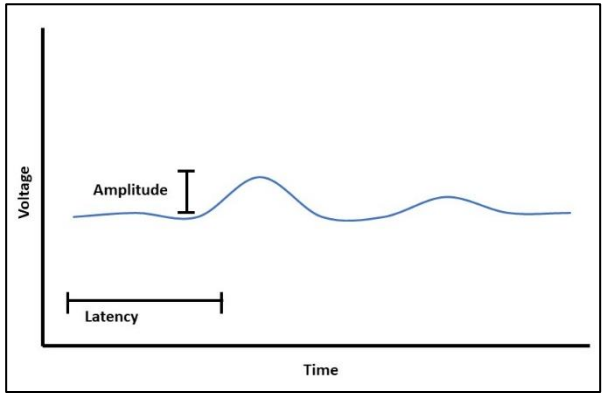
15X

- Latency: time from application of stimulus to onset or peak of the response. (Miller 10th Ed, Ch 35)
- Amplitude: voltage of the recorded response. (Miller 10th Ed, Ch 35)
- Concerning signal change: "The commonly used definitions…include a decrease in the amplitude by 50% or an increase in the latency by 10%." (Barash 9th Ed, Ch 37)
- General factors affecting SSEP's (such as decreased amplitude or increased latency) include: surgical trespass or distraction (for example, retractor causing ischemia), some anesthetic drugs/concentrations (see below), hypothermia, hypoperfusion/hypotension. (Miller 10th Ed, Ch 35 & Barash 9th Ed, Ch 37)
- Anesthetic techniques affecting SSEP's: Volatile anesthetics cause decrease in amplitude and increase in latency in nearly linear/dose-dependent fashion. Robust signals have been obtained up to 0.5 MAC. N2O has more depressant effect on signal amplitude than latency. (Barash 9th Ed, Ch37)
- High-Yield Recommended Reading: Barash, 9th Ed, Ch 37, p. 986-987 (Neuromonitoring).
- Handout: PediCrisis Checklist for Loss of Evoked Potentials

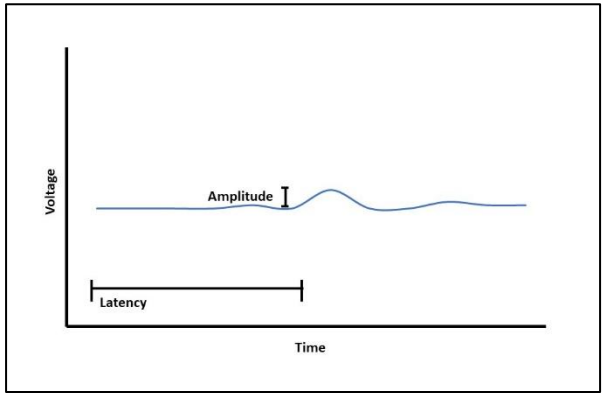
SSEP Basic Waveform



N2O depresses amplitude more than increased latency

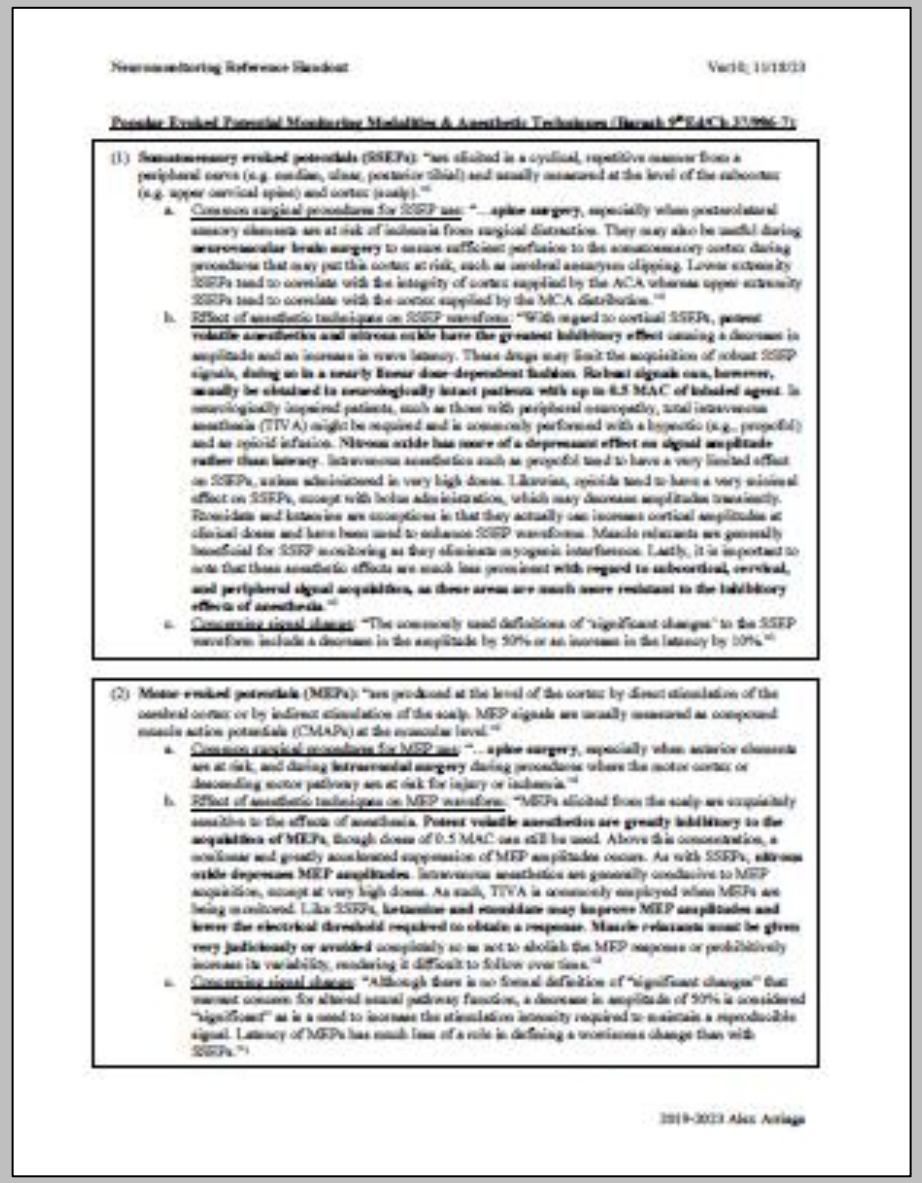


Volatiles decrease amplitude and increase latency



Room for notes

Neuromonitoring Reference Handout



Neuromonitoring Reference Handout Ver10; 11/18/23

Popular Evoked Potential Monitoring Modalities & Anesthetic Techniques (Barash 9th Ed/Ch 37/996-7):

(1) **Somatosensory evoked potentials (SSEPs):** "are elicited in a cyclical, repetitive manner from a peripheral nerve (e.g. median, ulnar, posterior tibial) and usually measured at the level of the subcortex (e.g. upper cervical spine) and cortex (scalp)."[1]

a. Common surgical procedures for SSEP use: "…**spine surgery**, especially when posterolateral sensory elements are at risk of ischemia from surgical distraction. They may also be useful during **neurovascular brain surgery** to ensure sufficient perfusion to the somatosensory cortex during procedures that may put this cortex at risk, such as cerebral aneurysm clipping. Lower extremity SSEPs tend to correlate with the integrity of cortex supplied by the ACA whereas upper extremity SSEPs tend to correlate with the cortex supplied by the MCA distribution."[1]

b. Effect of anesthetic techniques on SSEP waveform: "With regard to cortical SSEPs, **potent volatile anesthetics and nitrous oxide have the greatest inhibitory effect** causing a decrease in amplitude and an increase in wave latency. These drugs may limit the acquisition of robust SSEP signals, **doing so in a nearly linear dose-dependent fashion. Robust signals can, however, usually be obtained in neurologically intact patients with up to 0.5 MAC of inhaled agent**. In neurologically impaired patients, such as those with peripheral neuropathy, total intravenous anesthesia (TIVA) might be required and is commonly performed with a hypnotic (e.g., propofol) and an opioid infusion. **Nitrous oxide has more of a depressant effect on signal amplitude rather than latency**. Intravenous anesthetics such as propofol tend to have a very limited effect on SSEPs, unless administered in very high doses. Likewise, opioids tend to have a very minimal effect on SSEPs, except with bolus administration, which may decrease amplitudes transiently. Ketamine and ketamine are exceptions in that they actually can increase cortical amplitudes at clinical doses and have been used to enhance SSEP waveforms. Muscle relaxants are generally beneficial for SSEP monitoring as they eliminate myogenic interference. Lastly, it is important to note that these anesthetic effects are much less prominent **with regard to subcortical, cervical, and peripheral signal acquisition, as these areas are much more resistant to the inhibitory effects of anesthesia.**"[1]

c. Concerning signal change: "The commonly used definitions of 'significant changes' to the SSEP waveform include a decrease in the amplitude by 50% or an increase in the latency by 10%."[1]

(2) **Motor evoked potentials (MEPs):** "are produced at the level of the cortex by direct stimulation of the cerebral cortex or by indirect stimulation of the scalp. MEP signals are usually measured as compound muscle action potentials (CMAPs) at the muscular level."[1]

a. Common surgical procedures for MEP use: "…**spine surgery**, especially when anterior elements are at risk, and during **intracranial surgery** during procedures where the motor cortex or descending motor pathways are at risk for injury or ischemia."[1]

b. Effect of anesthetic techniques on MEP waveform: "MEPs elicited from the scalp are exquisitely sensitive to the effects of anesthesia. **Potent volatile anesthetics are greatly inhibitory to the acquisition of MEPs**, though doses of 0.5 MAC can still be used. Above this concentration, a nonlinear and greatly accelerated suppression of MEP amplitudes occurs. As with SSEPs, **nitrous oxide depresses MEP amplitudes**. Intravenous anesthetics are generally conducive to MEP acquisition, except at very high doses. As such, TIVA is commonly employed when MEPs are being monitored. Like SSEPs, **ketamine and etomidate may improve MEP amplitudes and lower the electrical threshold required to obtain a response. Muscle relaxants must be given very judiciously or avoided** completely so as not to abolish the MEP response or prohibitively increase its variability, rendering it difficult to follow over time."[1]

c. Concerning signal change: "Although there is no formal definition of "significant changes" that warrant concern for altered neural pathway function, a decrease in amplitude of 50% is considered "significant" as it is used to increase the stimulation intensity required to maintain a reproducible signal. Latency of MEPs has much less of a role in defining a worrisome change than with SSEPs."[1]

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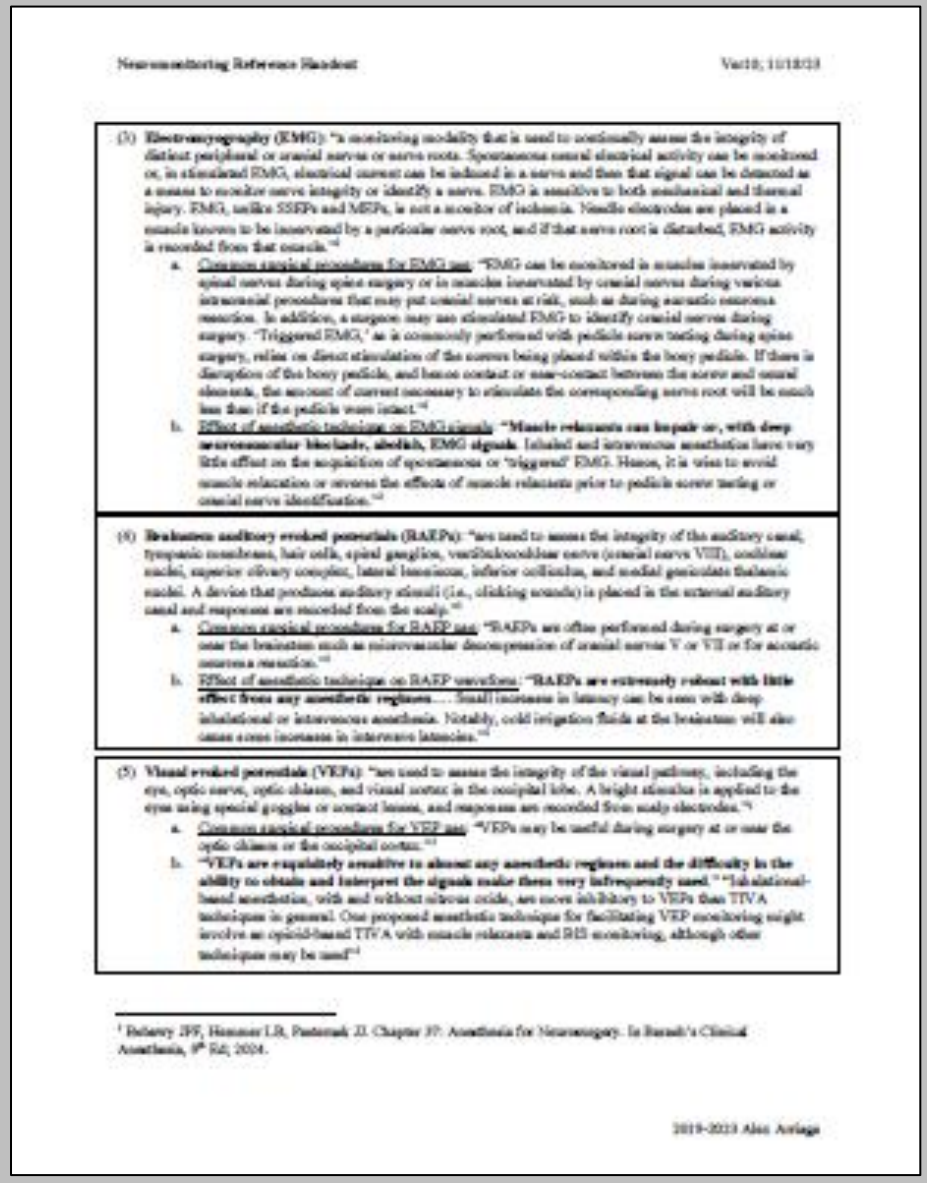

Neuromonitoring Reference Handout Ver10; 11/18/23

(3) **Electromyography (EMG):** "a monitoring modality that is used to continually assess the integrity of distinct peripheral or cranial nerves or nerve roots. Spontaneous neural electrical activity can be monitored or, in stimulated EMG, electrical current can be induced in a nerve and then that signal can be detected as a means to monitor nerve integrity or identify a nerve. EMG is sensitive to both mechanical and thermal injury. EMG, unlike SSEPs and MEPs, is not a monitor of ischemia. Needle electrodes are placed in a muscle known to be innervated by a particular nerve root, and if that nerve root is disturbed, EMG activity is recorded from that muscle."[1]

a. Common surgical procedures for EMG use: "EMG can be monitored in muscles innervated by spinal nerves during spine surgery or in muscles innervated by cranial nerves during various intracranial procedures that may put cranial nerves at risk, such as during acoustic neuroma resection. In addition, a surgeon may use stimulated EMG to identify cranial nerves during surgery. 'Triggered EMG,' as is commonly performed with pedicle screw testing during spine surgery, relies on direct stimulation of the screws being placed within the bony pedicle. If there is disruption of the bony pedicle, and hence contact or near-contact between the screw and neural elements, the amount of current necessary to stimulate the corresponding nerve root will be much less than if the pedicle were intact."[1]

b. Effect of anesthetic technique on EMG signals: **"Muscle relaxants can impair or, with deep neuromuscular blockade, abolish, EMG signals**. Inhaled and intravenous anesthetics have very little effect on the acquisition of spontaneous or 'triggered' EMG. Hence, it is wise to avoid muscle relaxation or reverse the effects of muscle relaxants prior to pedicle screw testing or cranial nerve identification."[1]

(4) **Brainstem auditory evoked potentials (BAEPs):** "are used to assess the integrity of the auditory canal, tympanic membrane, hair cells, spiral ganglion, vestibulocochlear nerve (cranial nerve VIII), cochlear nuclei, superior olivary complex, lateral lemniscus, inferior colliculus, and medial geniculate thalamic nuclei. A device that produces auditory stimuli (i.e., clicking sounds) is placed in the external auditory canal and responses are recorded from the scalp."[1]

a. Common surgical procedures for BAEP use: "BAEPs are often performed during surgery at or near the brainstem such as microvascular decompression of cranial nerves V or VII or for acoustic neuroma resection."[1]

b. Effect of anesthetic technique on BAEP waveform: **"BAEPs are extremely robust with little effect from any anesthetic regimen**…. Small increases in latency can be seen with deep inhalational or intravenous anesthesia. Notably, cold irrigation fluids at the brainstem will also cause some increases in intravenous latencies."[1]

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a. Common surgical procedures for VEP use: "VEPs may be useful during surgery at or near the optic chiasm or the occipital cortex."[1]

b. **"VEPs are exquisitely sensitive to almost any anesthetic regimen and the difficulty in the ability to obtain and interpret the signals make them very infrequently used."** "Inhalational-based anesthetics, with and without nitrous oxide, are more inhibitory to VEPs than TIVA techniques in general. One proposed anesthetic technique for facilitating VEP monitoring might involve an opioid-based TIVA with muscle relaxants and BIS monitoring, although other techniques may be used"[1]

[1] Doherty JW, Hemmer LB, Pasternak JJ. Chapter 37: Anesthesia for Neurosurgery. In Barash's Clinical Anesthesia, 9th Ed; 2024.

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Room for notes

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[1] Bebawy JPF, Hemmer LB, Pasternak JJ. Chapter 37: Anesthesia for Neurosurgery. In Barash's Clinical Anesthesia, 9th Ed; 2024.

Loss of Evoked Potentials

Management of signal changes during spine surgery

- Notify all members of health care team. Call a "time out"
- Loss of evoked potentials (EP) requires definitive steps to re-establish perfusion/remove mechanical cause; MEP loss for > 40 min may increase possibility of long term injury
  - Assure the presence of attending surgeon, attending anesthesiologist, senior neurologist or neurophysiologist, and experienced nurse
  - Each service: review situation, report on management and corrective actions taken
    - Surgeon: rule out mechanical causes for loss/change including traction weights
    - EP technologist: rule out technical causes for loss/change
    - Anesthesiologist: assure no neuromuscular blockade is present; reverse NMB if necessary
- Check patient positioning (neck, upper and lower extremities)
- Review the anesthetic and consider improving spinal cord perfusion by modifying:
  - Mean arterial pressure: MAP > 65 mmHg using ePHEDrine 0.1 mg/kg IV (MAX 10 mg/dose) and/or phenylephrine 0.3-1 MICROgrams/kg IV (MAX 100 MICROgrams/dose), with repeated doses as needed
  - Hemoglobin: if anemic, transfuse RBC to improve oxygen delivery
  - pH and $PaCO_2$: ensure normocarbia or slight hypercarbia (↑ I/E ratio, ↓ PEEP)
  - Temperature: ensure normothermia
  - Check for "unintended" drugs given (e.g. neuromuscular blocker)
  - Decrease depth of anesthetic and ensure N_2O is under 50%
- Discuss feasibility of a useful wake-up test:
  - Patient is appropriate candidate if capable of following verbal commands
- Consider high-dose steroid if no improvement:
  - MethylPREDNISolone 30 mg/kg IV over one hour, then 5.4 mg/kg/hour IV for 23 hours

Room for notes

Autonomic Hyperreflexia; Postoperative Vision Loss

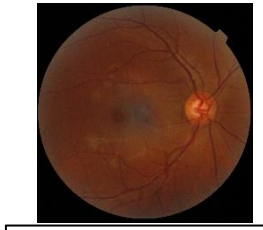
19X

Autonomic dysreflexia/hyperreflexia:

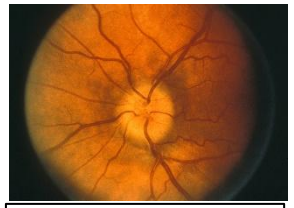
- Patient population: Weeks/months after spinal cord injury at T7 or above.
- Abnormal response: profound hypertension (with headache, sweating, flushing, bradycardia, arrythmias) after stimulus (e.g., surgical; distended bladder) below level of injury.
- Pathophysiology: disruption of descending inhibitory tracts (w/intact sympathetic reflex arcs).
- Treatment: Ideally prevention (consider regional/general anesthesia even if procedure to insensate location). Spinal may be preferred over epidural for denser block and avoidance of sacral sparing. Consider risk/benefit of mild/moderate sedation for minor procedures. Succinylcholine may cause hyperkalemia.

Perioperative Visual Loss (POVL): Anterior vs. Posterior ischemic optic neuropathy (ION) vs. Central Retinal Artery Occlusion (AION vs. PION vs. CRAO) vs. Acute Angle Glaucoma :

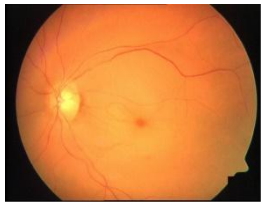
- Ophthalmic artery is a branch of the internal carotid artery. ION & CRAO cause painless vision loss.
- Buzzwords: *AION*: cardiac surgery, optic disc edema. *PION*: prone spine surgery, high blood loss, normal funduscopic exam. *CRAO*: external eye compression, retrobulbar hemorrhage from nerve block or head/neck surgery, decreased arterial flow (hypotension; thromboembolic event); impaired venous drainage; "cherry red macula."
- Acute angle glaucoma: PAINFUL and red globe, blurry vision, headache, nausea.
- Risk Factors for ION after prone spine surgery: (1) obesity; (2) anesthesia duration; (3) estimated blood loss; (4) lower % colloid for nonblood replacement; (5) male sex; (6) Wilson frame use. (PMID: 22185873)
- Risk Factors for ION after cardiac surgery: (1) carotid artery stenosis; (2) stroke; (3) diabetic retinopathy (decreased risk in uncomplicated DM2); (4) macular degeneration; (5) glaucoma; (6) cataract. Female sex associated w/decreased risk. (PMID: 28244936).
  - High-Yield NEJM video on ION and POVL: https://youtu.be/zxPKDyFBNUE
  - QR Code: Appdx#1 of Practice Advisory Periop Visual Loss/Spine Surgery



Normal Exam



Optic Disc Edema

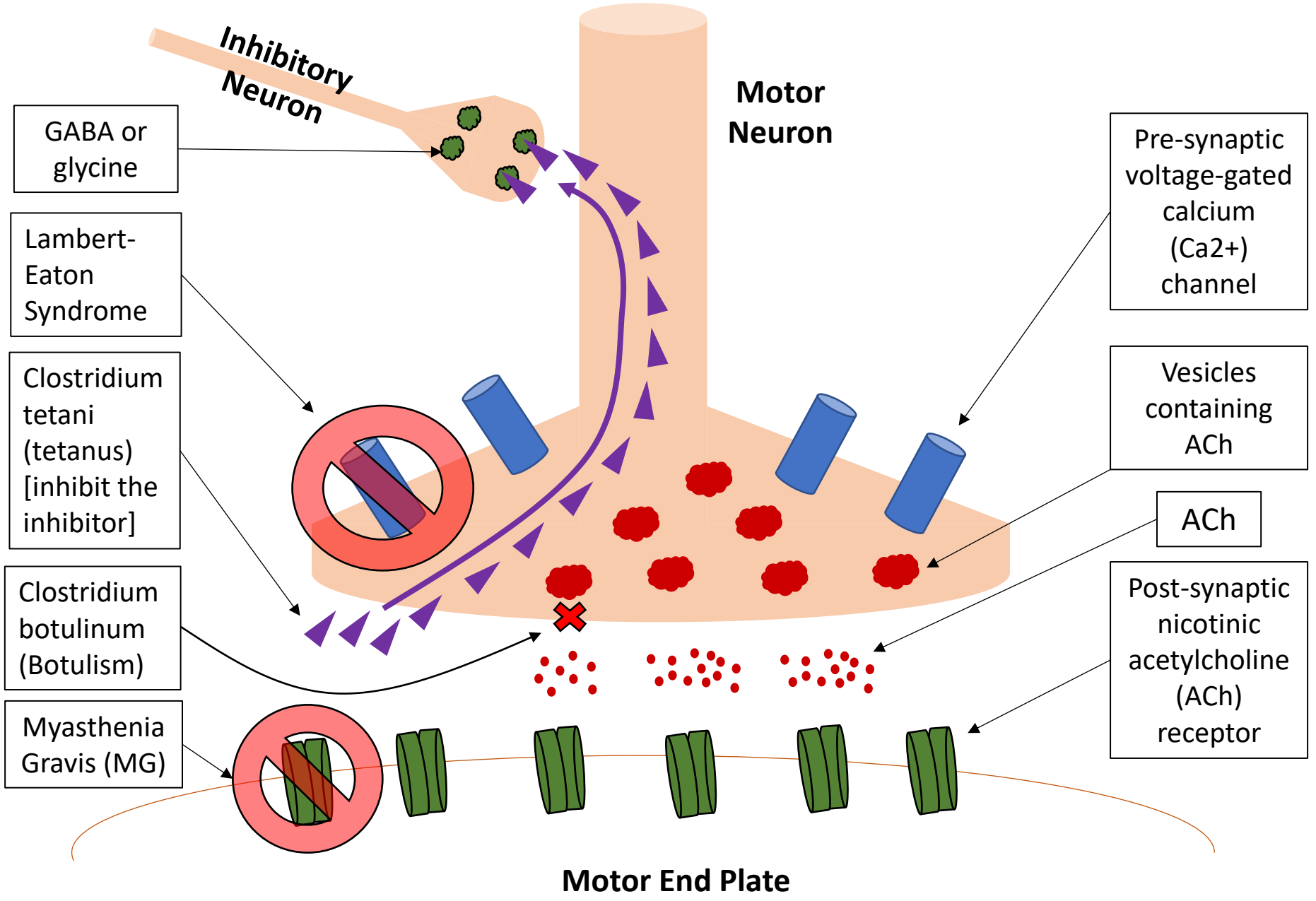


CRAO

Barash 9th Ed, Ch 37 // CRAO Image: Achim Fieß, et al, CC BY 2.0 via Wikimedia Commons https://upload.wikimedia.org/wikipedia/commons/f/f6/Cherry_Red_Spot_Fiess.jpg // Miller 10th Ed Ch 30 // Optic disc edema: ICEH, via Creative Commons license CC BY-NC 2.0 https://www.flickr.com/photos/communityeyehealth/7603596592 // Normal eye exam: Ske., CC BY-SA 3.0 via Wikimedia Commons (https://upload.wikimedia.org/wikipedia/commons/7/7f/Retinography.jpg) // PMID: 26083207; 22185873; 28244936.

Room for notes

"Image/Buzzwords Co-slides": Myasthenia Gravis, Lambert-Eaton, Botulism, Tetanus



Room for notes

"Image/Buzzwords Co-slides": Myasthenia Gravis, Lambert-Eaton, Botulism, Tetanus

30X

Room for notes

- Myasthenia Gravis (MG): autoantibodies against post-synaptic nicotinic acetylcholine receptors. **Resistant to succinylcholine** (decreased functional receptors)**; sensitive to nondepolarizers** (or unpredictable effect; sugammadex increasingly considered for reversal). Predictors for post-operative ventilation include:

Myasthenic History	Pulmonary History
Disease duration > 6 years	Other significant pulmonary disease
Bulbar (speech/swallow) symptoms preop	Vital capacity less than 2.9L
History of myasthenic crisis	
Pyridostigmine dose > 750mg/day	

- Lambert-Eaton Myasthenic Syndrome: autoantibodies against presynaptic voltage-gated calcium channels. **Sensitive to succinylcholine AND sensitive to nondepolarizers**.
  - Often a paraneoplastic syndrome: small cell lung cancer is a common underlying malignancy.
  - Unlike MG: (1) more likely to have proximal limb weakness than respiratory, ocular, or bulbar; (2) strength increased with repeated effort; (3) autonomic dysfunction more likely.
- Clostridium botulinum (botulism) and Clostridium tetani (tetanus)
  - Botulinum toxin: neurotoxin prevents acetylcholine vesicle release from presynaptic membrane
    - Pain management: via muscle relaxation and reduction in spasticity
  - Tetanus: retrograde transport of toxin → preferentially affects inhibitory neurons → rigidity/spasms

Miller 10th Ed, Ch 31 // UptoDate: Anesthesia for the patient with myasthenia gravis. // Barash, 9th Ed, Ch 59 // Berkowitz 2018; PMID: 30273248. // Patil et al 2016; PMID: 26879873.

Anticholinesterase/Organophosphate (OP) poisoning (for example: certain insecticides, nerve agents)

25X

Room for notes

Cholinergic Crisis:

- Muscarinic Signs: DUMBBELS (Diarrhea, Urination, Miosis [pupil constriction], Bronchorrhea/Bronchospasm, Bradycardia, Emesis, Lacrimation, Salivation/Sweating). If crosses blood/brain barrier: seizures, confusion.
- Nicotinic Signs (mostly skeletal/somatic): fasciculations followed by weakness/paralysis.
  - Overdose of a nicotinic anticholinesterase (such as neostigmine) can cause a "cholinergic crisis" (Neostigmine dose for minimal blockade: 30 micrograms/kg.[2] Dose for moderate to shallow neuromuscular blockade (sugammadex now preferred when not contraindicated for rocuronium/vecuronium): 30-70 micrograms/kg).
- *Myasthenic crisis (i.e., autoimmune destruction of post-synaptic acetylcholine receptors) vs. Cholinergic crisis (e.g., too much pyridostigmine): pure myasthenic crisis lacks muscarinic signs.*

- Emergency Pharmacological treatment:
  - Atropine: anticholinergic; titrate to dried secretions/pupillary dilatation/HR>80bpm.
  - Benzodiazepines: OP's can cause seizures.
  - Pralidoxime: reactivates cholinesterase by binding to OP; atropine must also be administered (pralidoxime does not significantly relieve respiratory depression or muscarinic anticholinesterase effects).[1]

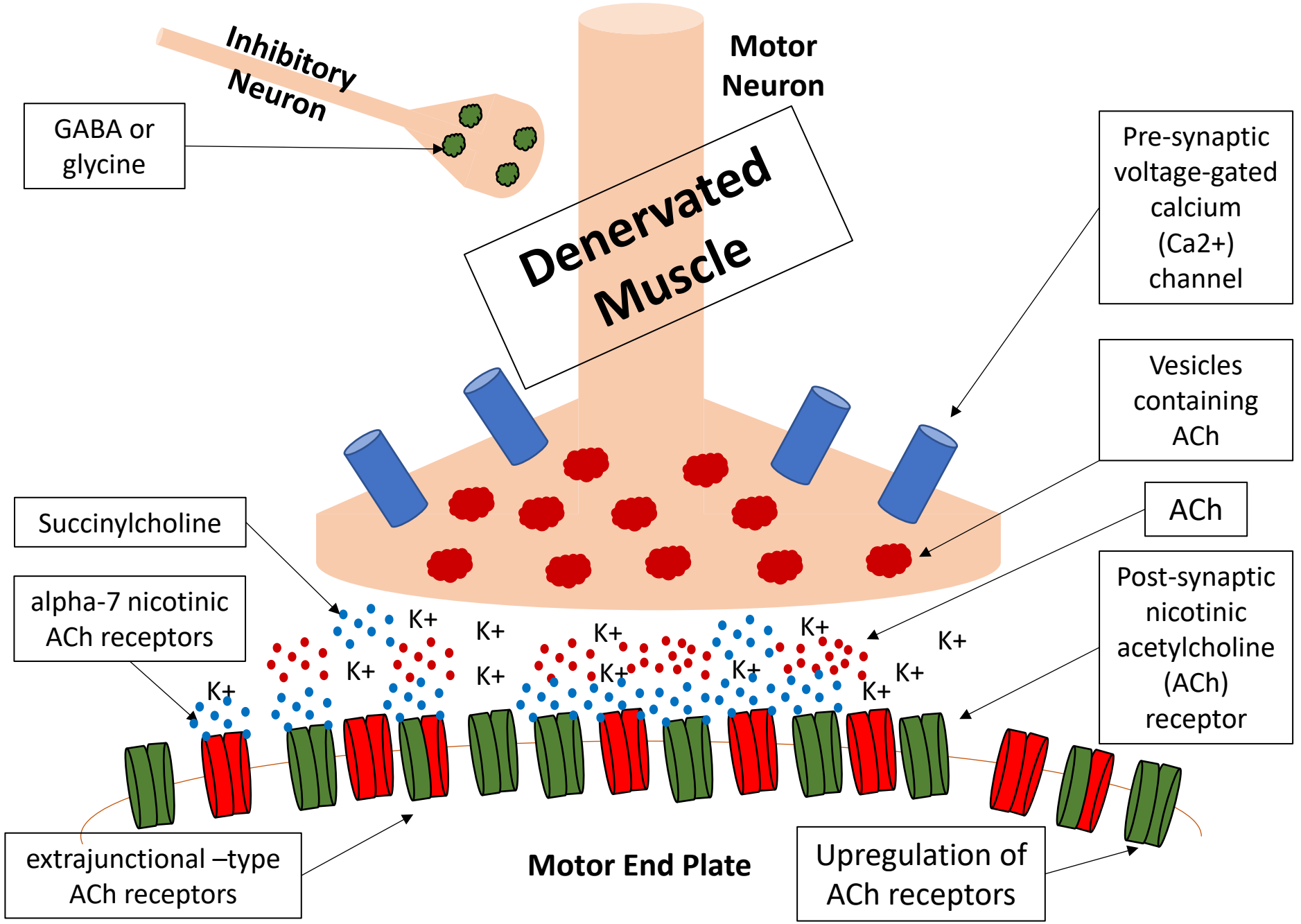
Combo autoinjectors are sometimes used

Prevention/prophylaxis of OP poisoning: "Pyridostigmine is an appropriate medication for *prophylaxis* against possible nerve agent exposure, whereas atropine and pralidoxime chloride would be appropriate for treatment after exposure" (2019 ITE Gaps in Knowledge Report).

- Pyridostigmine does not cross blood-brain barrier; it forms a reversible complex with cholinesterase that protects from irreversible inhibition by OP's.[1]

UpToDate: Myasthenic crisis (5/15/20). // 1. Pralidoxime & Pyridostigmine – Epocrates & ClinicalKey Drug Monograph // 2. PMID: 36520073 // Miller 10th Ed Ch 64. // Barash 9th Ed Ch 59. // ITE Gaps in Knowledge Report. Available at www.theaba.org.

Upregulation in denervated muscle



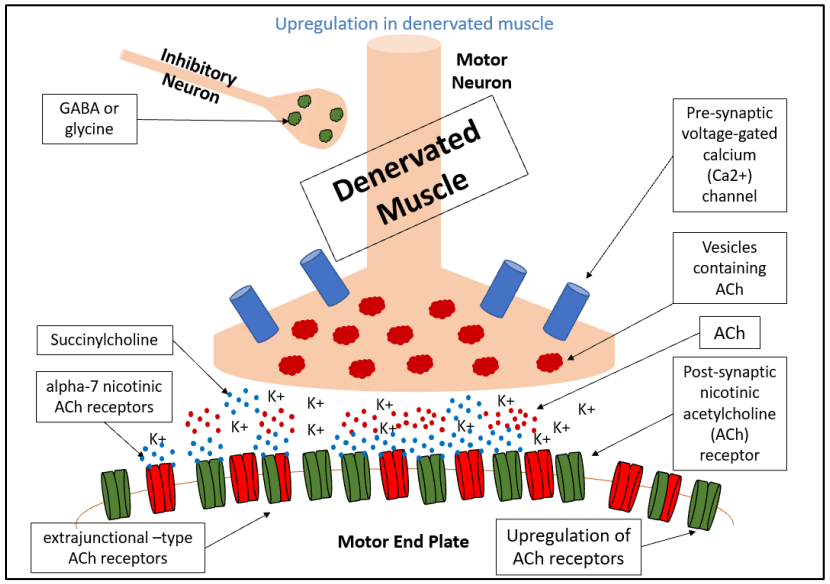
Room for notes

Succinylcholine & Related Topics

38X

Room for notes

Succinylcholine and Denervated Muscle



Recommended high-yield reading:

1. Martyn JAJ. Succinylcholine-induced hyperthermia in acquired pathologic states: etiologic factors and molecular mechanisms. Anesthesiology 2006; 104: 158-69.
2. Miller 10th Ed, Ch 24, pages 676-681 (Pharmacology of Succinylcholine)

Patients particularly susceptible to hyperkalemia from succinylcholine (normal rise in serum K^+ from Sux: 0.5mEq/dL):

1. CNS & upper motor neuron lesions (e.g., stroke, tumors/masses), especially if weakness.
2. Demyelinating diseases (MS, Guillain-Barre Syndrome).
3. Many muscular disorders (e.g., muscular dystrophy, myotonic dystrophy).
4. Severe burns or crush injuries (starting 24 hours after the injury and PEAKS 7-10 days after the injury).
5. Prolonged immobility or neuromuscular blockade.
6. Severe metabolic acidosis and hypovolemia.

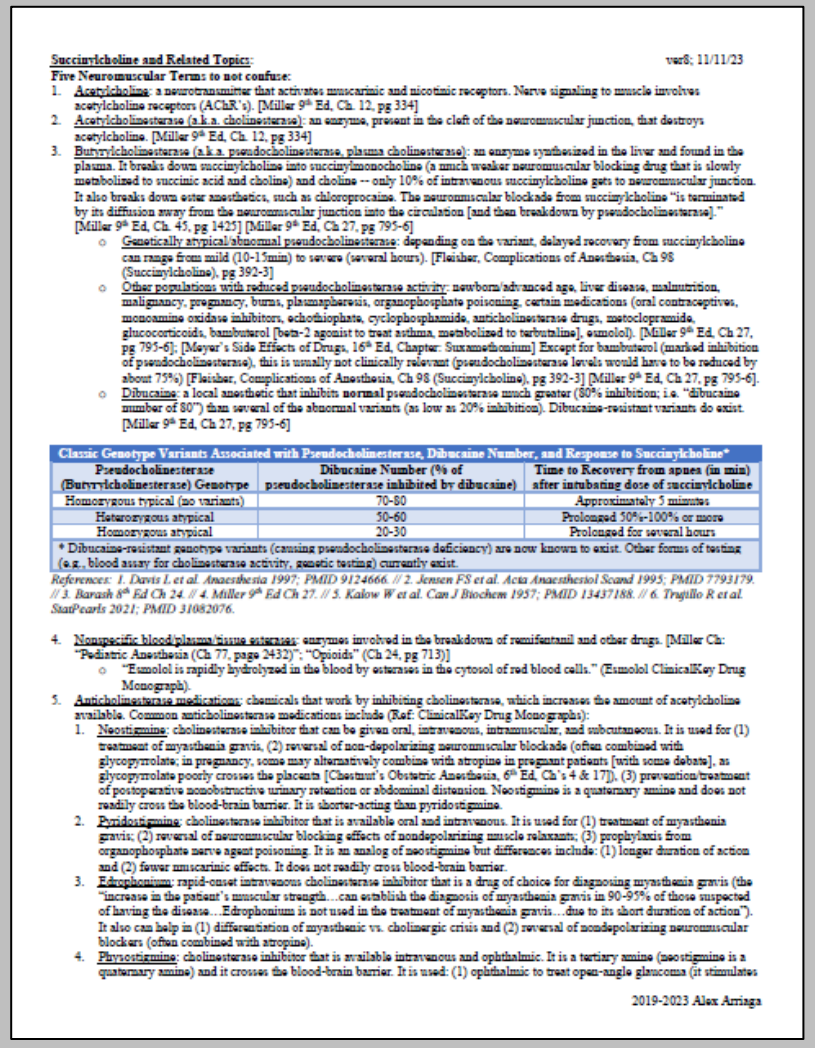
Upregulation of neuromuscular junction (NMJ) and extrajunctional cholinergic receptors is thought to be the etiology (muscular dystrophy etiology may be rhabdomyolysis).

2023 Gaps in Knowledge: "Minor surgery is associated with succinylcholine-associated myalgias." [also noted in Miller 10th Ed, Ch 24, pg. 680]

Handout: Succinylcholine & Related Topics

Martyn JAJ et al. Neuromuscular physiology and pharmacology. In Miller's Anesthesia, 10th Ed, Ch 11 // Miller 10th Ed, Ch 24 // ITE Gaps in Knowledge Report. Latest update available at www.theaba.org.

Handout: Succinylcholine & Related Topics



Succinylcholine and Related Topics: ver8; 11/11/23

Five Neuromuscular Terms to not confuse:

1. Acetylcholine: a neurotransmitter that activates muscarinic and nicotinic receptors. Nerve signaling to muscle involves acetylcholine receptors (AChR's). [Miller 9th Ed, Ch. 12, pg 334]
2. Acetylcholinesterase (a.k.a. cholinesterase): an enzyme, present in the cleft of the neuromuscular junction, that destroys acetylcholine. [Miller 9th Ed, Ch. 12, pg 334]
3. Butyrylcholinesterase (a.k.a. pseudocholinesterase, plasma cholinesterase): an enzyme synthesized in the liver and found in the plasma. It breaks down succinylcholine into succinylmonocholine (a much weaker neuromuscular blocking drug that is slowly metabolized to succinic acid and choline) and choline -- only 10% of intravenous succinylcholine gets to neuromuscular junction. It also breaks down ester anesthetics, such as chloroprocaine. The neuromuscular blockade from succinylcholine "is terminated by its diffusion away from the neuromuscular junction into the circulation [and then breakdown by pseudocholinesterase]." [Miller 9th Ed, Ch. 45, pg 1425] [Miller 9th Ed, Ch 27, pg 795-6]
   - Genetically atypical/abnormal pseudocholinesterase: depending on the variant, delayed recovery from succinylcholine can range from mild (10-15min) to severe (several hours). [Fleisher, Complications of Anesthesia, Ch 98 (Succinylcholine), pg 392-3]
   - Other populations with reduced pseudocholinesterase activity: newborn/advanced age, liver disease, malnutrition, malignancy, pregnancy, burns, plasmapheresis, organophosphate poisoning, certain medications (oral contraceptives, monoamine oxidase inhibitors, echothiophate, cyclophosphamide, anticholinesterase drugs, metoclopramide, glucocorticoids, bambuterol [beta-2 agonist to treat asthma, metabolized to terbutaline], esmolol). [Miller 9th Ed, Ch 27, pg 795-6]; [Meyer's Side Effects of Drugs, 16th Ed, Chapter: Suxamethonium] Except for bambuterol (marked inhibition of pseudocholinesterase), this is usually not clinically relevant (pseudocholinesterase levels would have to be reduced by about 75%) [Fleisher, Complications of Anesthesia, Ch 98 (Succinylcholine), pg 392-3] [Miller 9th Ed, Ch 27, pg 795-6].
   - Dibucaine: a local anesthetic that inhibits **normal** pseudocholinesterase much greater (80% inhibition; i.e. "dibucaine number of 80") than several of the abnormal variants (as low as 20% inhibition). Dibucaine-resistant variants do exist. [Miller 9th Ed, Ch 27, pg 795-6]

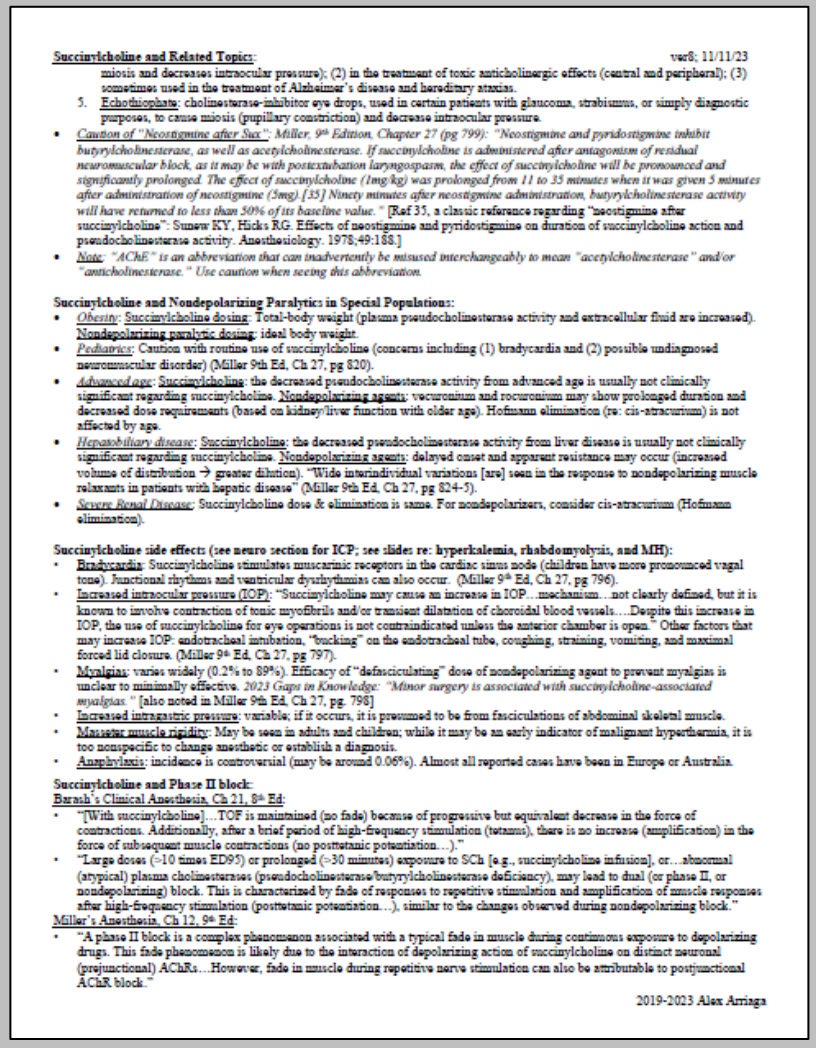
Classic Genotype Variants Associated with Pseudocholinesterase, Dibucaine Number, and Response to Succinylcholine*

Pseudocholinesterase (Butyrylcholinesterase) Genotype	Dibucaine Number (% of pseudocholinesterase inhibited by dibucaine)	Time to Recovery from apnea (in min) after intubating dose of succinylcholine
Homozygous typical (no variants)	70-80	Approximately 5 minutes
Heterozygous atypical	50-60	Prolonged 50%-100% or more
Homozygous atypical	20-30	Prolonged for several hours

* Dibucaine-resistant genotype variants (causing pseudocholinesterase deficiency) are now known to exist. Other forms of testing (e.g., blood assay for cholinesterase activity, genetic testing) currently exist.

References: 1. Davis L et al. Anaesthesia 1997; PMID 9124666. // 2. Jensen FS et al. Acta Anaesthesiol Scand 1995; PMID 7793179. // 3. Barash 8th Ed Ch 24. // 4. Miller 9th Ed Ch 27. // 5. Kalow W et al. Can J Biochem 1957; PMID 13437188. // 6. Trujillo R et al. StatPearls 2021; PMID 31082076.

4. Nonspecific blood/plasma/tissue esterases: enzymes involved in the breakdown of remifentanil and other drugs. [Miller Ch: "Pediatric Anesthesia (Ch 77, page 2432)"; "Opioids" (Ch 24, pg 713)]
   - "Esmolol is rapidly hydrolyzed in the blood by esterases in the cytosol of red blood cells." (Esmolol ClinicalKey Drug Monograph).
5. Anticholinesterase medications: chemicals that work by inhibiting cholinesterase, which increases the amount of acetylcholine available. Common anticholinesterase medications include (Ref: ClinicalKey Drug Monographs):
   1. Neostigmine: cholinesterase inhibitor that can be given oral, intravenous, intramuscular, and subcutaneous. It is used for (1) treatment of myasthenia gravis, (2) reversal of non-depolarizing neuromuscular blockade (often combined with glycopyrrolate; in pregnancy, some may alternatively combine with atropine in pregnant patients [with some debate], as glycopyrrolate poorly crosses the placenta [Chestnut's Obstetric Anesthesia, 6th Ed, Ch's 4 & 17]), (3) prevention/treatment of postoperative nonobstructive urinary retention or abdominal distension. Neostigmine is a quaternary amine and does not readily cross the blood-brain barrier. It is shorter-acting than pyridostigmine.
   2. Pyridostigmine: cholinesterase inhibitor that is available oral and intravenous. It is used for (1) treatment of myasthenia gravis; (2) reversal of neuromuscular blocking effects of nondepolarizing muscle relaxants; (3) prophylaxis from organophosphate nerve agent poisoning. It is an analog of neostigmine but differences include: (1) longer duration of action and (2) fewer muscarinic effects. It does not readily cross blood-brain barrier.
   3. Edrophonium: rapid-onset intravenous cholinesterase inhibitor that is a drug of choice for diagnosing myasthenia gravis (the "increase in the patient's muscular strength…can establish the diagnosis of myasthenia gravis in 90-95% of those suspected of having the disease…Edrophonium is not used in the treatment of myasthenia gravis…due to its short duration of action"). It also can help in (1) differentiation of myasthenic vs. cholinergic crisis and (2) reversal of nondepolarizing neuromuscular blockers (often combined with atropine).
   4. Physostigmine: cholinesterase inhibitor that is available intravenous and ophthalmic. It is a tertiary amine (neostigmine is a quaternary amine) and it crosses the blood-brain barrier. It is used: (1) ophthalmic to treat open-angle glaucoma (it stimulates



Succinylcholine and Related Topics: ver8; 11/11/23

miosis and decreases intraocular pressure); (2) in the treatment of toxic anticholinergic effects (central and peripheral); (3) sometimes used in the treatment of Alzheimer's disease and hereditary ataxias.

5. Echothiophate: cholinesterase-inhibitor eye drops, used in certain patients with glaucoma, strabismus, or simply diagnostic purposes, to cause miosis (pupillary constriction) and decrease intraocular pressure.

- *Caution of "Neostigmine after Sux": Miller, 9th Edition, Chapter 27 (pg 799): "Neostigmine and pyridostigmine inhibit butyrylcholinesterase, as well as acetylcholinesterase. If succinylcholine is administered after antagonism of residual neuromuscular block, as it may be with postextubation laryngospasm, the effect of succinylcholine will be pronounced and significantly prolonged. The effect of succinylcholine (1mg/kg) was prolonged from 11 to 35 minutes when it was given 5 minutes after administration of neostigmine (5mg) [35] Ninety minutes after neostigmine administration, butyrylcholinesterase activity will have returned to less than 50% of its baseline value."* [Ref 35, a classic reference regarding "neostigmine after succinylcholine": Sunwe KY, Hicks RG. Effects of neostigmine and pyridostigmine on duration of succinylcholine action and pseudocholinesterase activity. Anesthesiology. 1978;49:188.]
- *Note: "AChE" is an abbreviation that can inadvertently be misused interchangeably to mean "acetylcholinesterase" and/or "anticholinesterase." Use caution when seeing this abbreviation.*

Succinylcholine and Nondepolarizing Paralytics in Special Populations:

- *Obesity*: Succinylcholine dosing: Total-body weight (plasma pseudocholinesterase activity and extracellular fluid are increased). Nondepolarizing paralytic dosing: ideal body weight.
- *Pediatrics*: Caution with routine use of succinylcholine (concerns including (1) bradycardia and (2) possible undiagnosed neuromuscular disorder) (Miller 9th Ed, Ch 27, pg 820).
- *Advanced age*: Succinylcholine: the decreased pseudocholinesterase activity from advanced age is usually not clinically significant regarding succinylcholine. Nondepolarizing agents: vecuronium and rocuronium may show prolonged duration and decreased dose requirements (based on kidney/liver function with older age). Hofmann elimination (re: cis-atracurium) is not affected by age.
- *Hepatobiliary disease*: Succinylcholine: the decreased pseudocholinesterase activity from liver disease is usually not clinically significant regarding succinylcholine. Nondepolarizing agents: delayed onset and apparent resistance may occur (increased volume of distribution → greater dilution). "Wide interindividual variations [are] seen in the response to nondepolarizing muscle relaxants in patients with hepatic disease" (Miller 9th Ed, Ch 27, pg 824-5).
- *Severe Renal Disease*: Succinylcholine dose & elimination is same. For nondepolarizers, consider cis-atracurium (Hofmann elimination).

Succinylcholine side effects (see neuro section for ICP; see slides re: hyperkalemia, rhabdomyolysis, and MH):

- Bradycardia: Succinylcholine stimulates muscarinic receptors in the cardiac sinus node (children have more pronounced vagal tone). Junctional rhythms and ventricular dysrhythmias can also occur. (Miller 9th Ed, Ch 27, pg 796).
- Increased intraocular pressure (IOP): "Succinylcholine may cause an increase in IOP…mechanism…not clearly defined, but it is known to involve contraction of tonic myofibrils and/or transient dilatation of choroidal blood vessels…Despite this increase in IOP, the use of succinylcholine for eye operations is not contraindicated unless the anterior chamber is open." Other factors that may increase IOP: endotracheal intubation, "bucking" on the endotracheal tube, coughing, straining, vomiting, and maximal forced lid closure. (Miller 9th Ed, Ch 27, pg 797).
- Myalgias: varies widely (0.2% to 89%). Efficacy of "defasciculating" dose of nondepolarizing agent to prevent myalgias is unclear to minimally effective. *2023 Gaps in Knowledge: "Minor surgery is associated with succinylcholine-associated myalgias."* [also noted in Miller 9th Ed, Ch 27, pg. 798]
- Increased intragastric pressure: variable; if it occurs, it is presumed to be from fasciculations of abdominal skeletal muscle.
- Masseter muscle rigidity: May be seen in adults and children; while it may be an early indicator of malignant hyperthermia, it is too nonspecific to change anesthetic or establish a diagnosis.
- Anaphylaxis: incidence is controversial (may be around 0.06%). Almost all reported cases have been in Europe or Australia.

Succinylcholine and Phase II block:

Barash's Clinical Anesthesia, Ch 21, 8th Ed:

- "[With succinylcholine]…TOF is maintained (no fade) because of progressive but equivalent decrease in the force of contractions. Additionally, after a brief period of high-frequency stimulation (tetanus), there is no increase (amplification) in the force of subsequent muscle contractions (no posttetanic potentiation…)."
- "Large doses (>10 times ED95) or prolonged (>30 minutes) exposure to SCh [e.g., succinylcholine infusion], or…abnormal (atypical) plasma cholinesterases (pseudocholinesterase/butyrylcholinesterase deficiency), may lead to dual (or phase II, or nondepolarizing) block. This is characterized by fade of responses to repetitive stimulation and amplification of muscle responses after high-frequency stimulation (posttetanic potentiation…), similar to the changes observed during nondepolarizing block."

Miller's Anesthesia, Ch 12, 9th Ed:

- "A phase II block is a complex phenomenon associated with a typical fade in muscle during continuous exposure to depolarizing drugs. This fade phenomenon is likely due to the interaction of depolarizing action of succinylcholine on distinct neuronal (prejunctional) AChRs…However, fade in muscle during repetitive nerve stimulation can also be attributable to postjunctional AChR block."

2019-2023 Alex Arriaga

Rapidly differentiating the terms acetylcholine, acetylcholinesterase, pseudocholinesterase, nonspecific blood/plasma/tissue esterases, and anticholinesterases should be fluent anesthesiology vocabulary.

Room for notes

Succinylcholine and Related Topics: ver9; 12/4/24

Five Neuromuscular Terms to not confuse:

1. Acetylcholine: a neurotransmitter that is involved in muscle contraction via activation of nicotinic receptors at the neuromuscular junction (acetylcholine receptors [AChR's]). [Miller 10th Ed, Ch. 11, pg 226]
2. Acetylcholinesterase (a.k.a. cholinesterase): an enzyme, present in the cleft of the neuromuscular junction, that destroys acetylcholine. [Miller 10th Ed, Ch. 11, pg 226]
3. Butyrylcholinesterase (a.k.a. pseudocholinesterase, plasma cholinesterase): an enzyme synthesized in the liver and found in the plasma. It breaks down succinylcholine into succinylmonocholine (a much weaker neuromuscular blocking drug that is slowly metabolized to succinic acid and choline) and choline -- only 10% of intravenous succinylcholine gets to neuromuscular junction. It also breaks down ester anesthetics, such as chloroprocaine. The neuromuscular blockade from succinylcholine "is terminated by its diffusion away from the neuromuscular junction into the circulation [and then breakdown by pseudocholinesterase]." [Miller 10th Ed, Ch. 41, pg 1279] [Miller 10th Ed, Ch 24, pg 677]
    - Genetically atypical/abnormal pseudocholinesterase: depending on the variant, delayed recovery from succinylcholine can range from mild (10-15min) to severe (several hours). [Fleisher, Complications of Anesthesia, Ch 98 (Succinylcholine), pg 392-3]
    - Other populations with reduced pseudocholinesterase activity: newborn/advanced age, liver disease, malnutrition, malignancy, pregnancy, burns, plasmapheresis, organophosphate poisoning, certain medications (oral contraceptives, monoamine oxidase inhibitors, echothiophate, cyclophosphamide, anticholinesterase drugs, metoclopramide, glucocorticoids, bambuterol [beta-2 agonist to treat asthma, metabolized to terbutaline], esmolol). [Miller 10th Ed, Ch 24, pg 677]; [Meyer's Side Effects of Drugs, 16th Ed, Chapter: Suxamethonium] Except for bambuterol (marked inhibition of pseudocholinesterase), this is usually not clinically relevant (pseudocholinesterase levels would have to be reduced by about 75%) [Fleisher, Complications of Anesthesia, Ch 98 (Succinylcholine), pg 392-3] [Miller 10th Ed, Ch 24, pg 677].
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4. Nonspecific blood/plasma/tissue esterases: enzymes involved in the breakdown of remifentanil and other drugs. [Miller 10th Ed, Ch 72, pg 2275; Miller 10th Ed, Ch 22, pg 590)]
    - "Esmolol is rapidly hydrolyzed in the blood by esterases in the cytosol of red blood cells." (Esmolol ClinicalKey Drug Monograph).
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- *Pediatrics*: Caution with routine use of succinylcholine (concerns including [1] bradycardia; [2] hyperkalemia/cardiac arrest/rhabdomyolysis, particularly if undiagnosed neuromuscular disorder) (Miller 10th Ed, Ch 24, pg 678, 700).
- *Advanced age*: Succinylcholine: the decreased pseudocholinesterase activity from advanced age is usually not clinically significant regarding succinylcholine. Nondepolarizing agents: vecuronium and rocuronium may show prolonged duration and decreased dose requirements (based on kidney/liver function with older age). Hofmann elimination (re: cis-atracurium) is not affected by age.
- *Hepatobiliary disease*: Succinylcholine: the decreased pseudocholinesterase activity from liver disease is usually not clinically significant regarding succinylcholine. Nondepolarizing agents: delayed onset and apparent resistance may occur (increased volume of distribution → greater dilution). "Wide interindividual variations [are] seen in the response to nondepolarizing muscle relaxants in patients with hepatic disease" (Miller 10th Ed, Ch 24, pg 703-705).
- *Severe Renal Disease*: Succinylcholine dose & elimination is same. For nondepolarizers, consider cis-atracurium (Hofmann elimination).

Succinylcholine side effects (see neuro section for ICP; see slides re: hyperkalemia, rhabdomyolysis, and MH):

- Bradycardia: Succinylcholine stimulates muscarinic receptors in the cardiac sinus node (children have more pronounced vagal tone). Junctional rhythms and ventricular dysrhythmias can also occur. (Miller 10th Ed, Ch 24, pg 678).
- Increased intraocular pressure (IOP): "Succinylcholine may cause an increase in IOP…mechanism…not clearly defined, but it is known to involve contraction of tonic myofibrils and/or transient dilatation of choroidal blood vessels….Despite this increase in IOP, the use of succinylcholine for eye operations is not contraindicated unless the anterior chamber is open." Other factors that may increase IOP: endotracheal intubation, "bucking" on the endotracheal tube, coughing, straining, vomiting, and maximal forced lid closure. (Miller 10th Ed, Ch 24, pg 679).
- Myalgias: varies widely (0.2% to 89%). Efficacy of "defasciculating" dose of nondepolarizing agent to prevent myalgias is unclear to minimally effective. *2023 Gaps in Knowledge: "Minor surgery is associated with succinylcholine-associated myalgias."* [expanded explanation available in Miller 10th Ed, Ch 24, pg. 680]
- Increased intragastric pressure: variable; if it occurs, it is presumed to be from fasciculations of abdominal skeletal muscle.
- Masseter muscle rigidity: May be seen in adults and children; while it may be an early indicator of malignant hyperthermia, it is too nonspecific to change anesthetic or establish a diagnosis.
- Anaphylaxis: incidence is controversial (may be around 0.06%). Almost all reported cases have been in Europe or Australia.

Succinylcholine and Phase II block:

Barash's Clinical Anesthesia, 9th Ed, Ch 21:

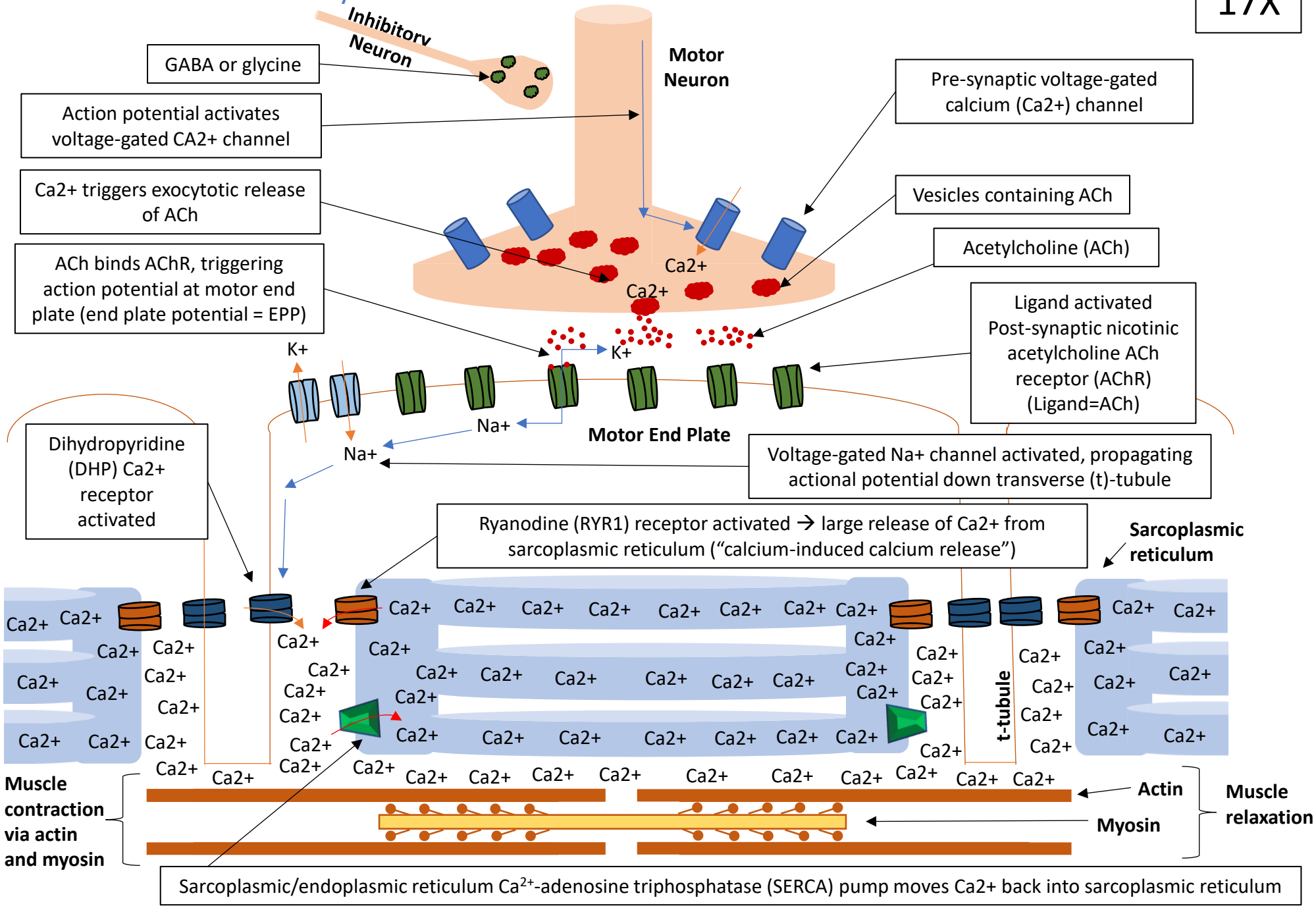
- "[With succinylcholine]…There is a lack of fade, both to train-of-four stimulation and tetanic stimulation, and absence of posttetanic potentiation [i.e., no amplification in contractions after delivery of tetanic stimulation].
- "Under certain conditions, succinylcholine can induce a different type of blockade that is termed *phase II block.* In the past, it has also been referred to as 'dual block' or 'nondepolarization block.' It has some features in common with the classic blockade induced by nondepolarizing neuromuscular blocking drugs, including fade to train-of-four and tetanic stimulation. A phase II block occurs after administration of a single large dose of succinylcholine ($\geq$ 10 x ED_{95}), repeated doses, or a prolonged continuous infusion."

Miller's Anesthesia, 10th Ed, Ch 11**:**

- "A phase II block is a complex phenomenon associated with a typical fade in muscle during continuous exposure to depolarizing drugs. This fade phenomenon is likely due to the interaction of depolarizing action of succinylcholine on distinct neuronal (prejunctional) AChRs…However, the mechanism of fade in muscle during repetitive nerve stimulation after [nondepolarizing muscle relaxants] is due to simultaneous […] pre-and postjunctional AChR [block]"

Key Ions Involved in Neuromuscular Transmission

17X



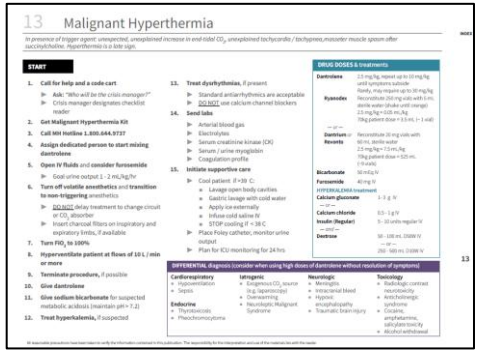
Room for notes

Malignant Hyperthermia

17X

Room for notes

- Mechanism: abnormal RYR1 gene (most common) →abnormal ryanodine receptor → significant release of calcium from sarcoplasmic reticulum after triggering agent → uncontrolled muscle contractions → lactic acidosis → muscle breakdown causes hyperkalemia.
- Triggering agents: Volatile anesthetics (e.g., sevoflurane, desflurane, isoflurane), succinylcholine.
- ABG: mixed metabolic and respiratory acidosis (increased lactic acid; inability to hyperventilate enough to release CO2).
- MH vs thyroid storm: Thyroid storm patient may have hyperthyroidism history. Thyroid storm is usually not associated with rigidity, elevated CK, or lactic acidosis. Hypokalemia (not hyperkalemia) is common in thyroid storm. ABG can be helpful.
- Known associated conditions include: Central/Multimini Core disease (Core Myopathies), King-Denborough syndrome (see Litman article for more).
- Testing options: (1) Muscle biopsy contracture studies (halothane, caffeine); (2) genetic testing.
- Dantrolene mechanism: complex; reduces pathologic concentrations of calcium. Can cause muscle weakness. "…whether dantrolene directly inhibits RyR1 or requires additional intermediates…remains to be clarified."[1] *Avoid calcium channel blockers in treatment of MH*.
- Handout: MH Crisis Checklist.
- QR Code: Litman RS et al. Anesthesiology 2018. PMID 28902673.



References: 1. Miller 10th Ed, Ch 31 // Barash 9th Ed, Ch 24 // Cote et al. A Practice of Anesthesia for Infants and Children. 6th Ed, Ch 41. // Openanesthesia: MH vs thyroid storm (available at https://www.openanesthesia.org/mh_vs-_thyroid_storm/) // Litman RS et al. Anesthesiology 2018; PMID 28902673 // Figure: Ariadne Labs Operating Room Crisis Checklists. See www.ariadnelabs.org for latest version. With permission via Creative Commons BY-NC-SA (https://creativecommons.org/licenses/by-nc-sa/4.0/).

13 Malignant Hyperthermia

In presence of trigger agent: unexpected, unexplained increase in end-tidal CO_2, unexplained tachycardia / tachypnea, masseter muscle spasm after succinylcholine. Hyperthermia is a late sign.

START

1. **Call for help and a code cart**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Get Malignant Hyperthermia Kit**
3. **Call MH Hotline 1.800.644.9737**
4. **Assign dedicated person to start mixing dantrolene**
5. **Open IV fluids** and **consider furosemide**
   - Goal urine output 1 - 2 mL/kg/hr
6. **Turn off volatile anesthetics** and **transition to non-triggering** anesthetics
   - DO NOT delay treatment to change circuit or CO_2 absorber
   - Insert charcoal filters on inspiratory and expiratory limbs, if available
7. **Turn FiO_2 to 100%**
8. **Hyperventilate patient at flows of 10 L / min or more**
9. **Terminate procedure,** if possible
10. **Give dantrolene**
11. **Give sodium bicarbonate** for suspected metabolic acidosis (maintain pH > 7.2)
12. **Treat hyperkalemia,** if suspected
13. **Treat dysrhythmias**, if present
    - Standard antiarrhythmics are acceptable
    - DO NOT use calcium channel blockers
14. **Send labs**
    - Arterial blood gas
    - Electrolytes
    - Serum creatinine kinase (CK)
    - Serum / urine myoglobin
    - Coagulation profile
15. **Initiate supportive care**
    - Cool patient if >39 C:
      - Lavage open body cavities
      - Gastric lavage with cold water
      - Apply ice externally
      - Infuse cold saline IV
      - STOP cooling if < 38 C
    - Place Foley catheter, monitor urine output
    - Plan for ICU monitoring for 24 hrs

DRUG DOSES & treatments

Dantrolene	2.5 mg/kg, repeat up to 10 mg/kg until symptoms subside
Ryanodex	Rarely, may require up to 30 mg/kg Reconstitute 250 mg vials with 5 mL sterile water (shake until orange) 2.5 mg/kg = 0.05 mL/kg 70kg patient dose = 3.5 mL (~ 1 vial)
— *or* —	
Dantrium *or* **Revonto**	Reconstitute 20 mg vials with 60 mL sterile water 2.5 mg/kg = 7.5 mL/kg 70kg patient dose = 525 mL (~9 vials)
Bicarbonate	50 mEq IV
Furosemide	40 mg IV
HYPERKALEMIA treatment	
Calcium gluconate	1- 3 g IV
— *or* —	
Calcium chloride	0.5 - 1 g IV
Insulin (Regular)	5 - 10 units regular IV
— *and* —	
Dextrose	50 - 100 mL D50W IV — or — 250 - 500 mL D10W IV

DIFFERENTIAL diagnosis (consider when using high doses of dantrolene without resolution of symptoms)

Cardiorespiratory
- Hypoventilation
- Sepsis

Endocrine
- Thyrotoxicosis
- Pheochromocytoma

Iatrogenic
- Exogenous CO_2 source (e.g. laparoscopy)
- Overwarming
- Neuroleptic Malignant Syndrome

Neurologic
- Meningitis
- Intracranial bleed
- Hypoxic encephalopathy
- Traumatic brain injury

Toxicology
- Radiologic contrast neurotoxicity
- Anticholinergic syndrome
- Cocaine, amphetamine, salicylate toxicity
- Alcohol withdrawal

Room for notes

Multiple Sclerosis; Muscular/Myotonic Dystrophy

12X

Room for notes

Multiple Sclerosis (MS): autoantibodies against myelin in the Central Nervous System (CNS).

- Some avoid spinal anesthesia if MS exacerbation: demyelination may render the spinal cord more susceptible to local anesthetics. Epidurals have been used successfully.
- Avoid hyperthermia: as little as 1 deg Celsius can affect demyelinated nerve conduction → exacerbation.
- Consider avoiding succinylcholine, particularly if exacerbation: risk of hyperkalemia.

Muscular Dystrophy: X-lined recessive mutations of the gene for dystrophin.

- Duchenne (more severe) and Becker (milder) are the most common.
- Increased risk of cardiomyopathy, conduction, and/or other cardiac disease: consider preop EKG/Echo.
- Avoid succinylcholine: risk of rhabdomyolysis, hyperkalemia, MH-like syndrome.
  - Increased sensitivity to nondepolarizing muscle relaxants (consider sugammadex).
- Some avoid volatile anesthetics: rare risk of MH-like event [Miller 10th Ed Ch 31].

Myotonic dystrophy:

- Prolonged muscle contraction (myotonia) & progressive muscle weakness/wasting.
- Factors increasing periop pulmonary risk: weakness, chronic aspiration, impaired cough reflex.
- Increased risk of cardiac disease (similar considerations as muscular dystrophy)
- Avoid Succinylcholine, Neostigmine, hypothermia/shivering: may cause exaggerated contracture (also, see muscular dystrophy succinylcholine considerations). Consider rocuronium/sugammadex.
- "There is no case report in the literature linking DM [myotonic dystrophy, aka *dystrophia myotonica, DM]* to MH." [Miller 10th Ed, Ch 31]

Miller 10th Ed, Ch 31. // Stoelting's Anesthesia and Co-existing Disease, 7th Ed, Ch 13. // Litman RS et al. Anesthesiology 2018; PMID 28902673.

Periodic Paralyses; Mitochondrial Myopathies

11X

Room for notes

Periodic Paralyses: weakness, often with changes in serum K+

- Hyperkalemic variant: can be precipitated after potassium-rich meal, fasting, strenuous exercise followed by rest, stress, cold, glucocorticoids, pregnancy.
  - Often admitted preop for dextrose-containing IV solutions while NPO
  - Avoid succinylcholine, neostigmine, potassium, sudden temperature changes, hypoglycemia: can increase serum K+.
  - Be prepared to treat hyperkalemia (insulin, glucose, calcium, etc).
- Hypokalemic variant: can be precipitated by carbohydrate or salt-rich meal (or solutions with high glucose or sodium content), exercise, stress, pregnancy, menstruation, hypothermia, and medications causing a shift of potassium (such as insulin). (Miller 10th Ed, Ch 31)

Mitochondrial Myopathies:

- Wide variety of molecular defects from mutations in mitochondrial or nuclear DNA.
- May involve brain, nerves, and muscle, or be subclinical.
- "All inhalational anesthetics and propofol depress mitochondrial function at several levels…ventricular dysrhythmias have been reported after a small dose of bupivacaine"
- "…[while] any anesthesia technique might be used in children with mitochondrial myopathies…*all* children with mitochondrial myopathies must be monitored closely when administering any type of anesthetic." (Cote, 6th Ed, Ch 24)

Miller 10th Ed, Ch 31. // Cote, 6th Ed, Ch 24.

Delayed Emergence

22X

Room for notes

- **<u>Drugs that may prolong neuromuscular blockade include</u>**: Volatile anesthetics (desflurane > sevoflurane > isoflurane), local anesthetics, procainamide, calcium-channel-blockers, furosemide, acetazolamide, magnesium, lithium, dantrolene, tamoxifen, and some antibiotics (metronidazole, aminoglycosides, lincosamides [clindamycin], polymyxins, tetracyclines). Also: more than one nondepolarizing neuromuscular blocker at the same time (e.g., rocuronium [rapid-sequence induction] → cis-atracurium [maintenance]).
  - *Long-term anticonvulsants can cause accelerated recovery from neuromuscular blockade.*
  - "The cephalosporins and penicillins have not been reported to potentiate neuromuscular block. […] mannitol appears to have no effect on a nondepolarizing neuromuscular block." [Miller 10th Ed, Ch 24]
  - <u>High-Yield Reading</u>: Miller 10th Ed, Ch 24, pgs 697-700.

<table>
<tr><th colspan="5">Causes of Delayed Emergence: "Don't Miss The Criteria for Extubation"</th></tr>
<tr><th>Drugs (& possible reversal agent[s])</th><th>Metabolic</th><th>Temperature</th><th>CVA</th><th>Extra</th></tr>
<tr><td>- Residual anesthetic agents
- Opioids (naloxone)
- Benzodiazepines (flumazenil)
- Nondepolarizing paralytics (sugammadex for rocuronium or vecuronium; neostigmine/glycopyrrolate)</td><td>Hypoglycemia</td><td rowspan="4">Hypothermia</td><td rowspan="4">Cerebrovascular accident (CVA)/transient ischemic attack (TIA)</td><td>Pseudocholinesterase deficiency</td></tr>
<tr><td rowspan="3">Drugs that prolong neuromuscular blockade (see above)</td><td>Hypercarbia/ acidosis</td><td>Myasthenia Syndromes</td></tr>
<tr><td>Hypocalcemia</td><td rowspan="2">Other disease processes, including neuromuscular disease</td></tr>
<tr><td>Hypermagnesemia</td></tr>
</table>

Handout: Crisis Checklist for Delayed Emergence

Miller 10th Ed, Ch 24 and 76. // Naguib et al. PMID: 7669466

06 Delayed Emergence

Prolonged unresponsiveness following general anesthesia or abnormal neurologic exam following general anesthesia

INDEX

06

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Ensure all anesthetic medications have been stopped**
3. **Check for and correct hypoxemia, hypercarbia, hypothermia, or hypotension**
   - Consider signs of increased intracranial pressure (widened pulse pressure, bradycardia, irregular respirations)
4. **Check for and treat residual drug effects**
   - Neuromuscular blockade (check TOF)
   - Opiates and hypnotics
5. **Send labs**
   - Arterial blood gas, electrolytes, glucose
6. **Correct electrolyte abnormalities**
7. **Perform neurologic examination**
   - If unresponsive: pupil changes, gag reflex, level of arousal
   - If responsive: stroke assessment
     - Facial droop - show teeth in smile
     - Pronator drift - eyes closed, extend arms with palms up for 10 seconds
     - Speech assessment - say "you can't teach old dogs new tricks"
     - Assess for severe sudden headache
   - Consider **STAT head CT** and **neurology consult** for abnormal exam

DRUG DOSES & treatments

Naloxone	40 MCG IV (0.4 mg to total 10 mL = 40 MCG/mL) Repeat q 2 minutes *If no response to 400 MCG, consider non-opiate causes*
Flumazenil	0.2 mg IV Repeat dose q 1 minute Max dose 1 mg *AVOID in chronic benzodiazepine use or seizure history*
Sugammadex	2 - 4 mg/kg IV

DIFFERENTIAL diagnosis

High spinal
Serotonin syndrome
Myxedema coma or thyroid storm
Concomitant head injury
Hepatic or uremic encephalopathy
Neurosurgical complications
- Hemorrhage
- Vascular occlusion
- Elevated ICP

Postictal state following intraoperative seizure
Medication error
Local Anesthetic Systemic Toxicity (CHKLST 12)
Central anticholinergic syndrome

Room for notes

Monitoring & Antagonism of Neuromuscular Blockade

11X

Room for notes

Synopsis: ASA 2023 Practice Guidelines on Monitoring and Antagonism of Neuromuscular Blockade (NMB; all doses intravenous):[1]

NMB Monitoring	Antagonism of NMB
Use quantitative monitoring (TOF ratio ≥ 0.9 before extubation via adductor policis; recommend against using eye muscles) over qualitative assessment (e.g., peripheral nerve stimulator without TOF monitoring)	Recommend sugammadex over neostigmine for deep (TOF=0; posttetanic count ≥ 1; 4mg/kg), moderate (TOF 1 to 3; 2mg/kg if at least 2 twitches), and shallow (TOF=4; TOF ratio ≤ 0.4; 2mg/kg) blockade from rocuronium or vecuronium (16mg/kg if immediately after 1.2 mg/kg rocuronium)
Avoid clinical assessment alone (sustained head lift, grip strength, tidal volumes) to assess NMB recovery	Neostigmine reasonable alternative to sugammadex if minimal (TOF ratio 0.4 to ≤ 0.9) blockade (minimal blockade dose not to exceed 40 mcg/kg)
If only single dose of succinylcholine given, use NMB monitoring to guide extubation when there are clinical signs of delayed succinylcholine recovery	Patients with TOF ratio ≥ 0.9 do not require pharmacological antagonism. *For cis-atracuricum*, use neostigmine when at minimal blockade (confirm TOF ratio ≥ 0.9 before extubation or wait 10 min after neostigmine)

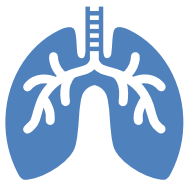
Other FDA sugammadex considerations (sugammadex "dosing is based on actual body weight"):[2]

Specific Populations	If need reintubation after sugammadex (up to 4mg/kg) given
Sugammadex "[may reduce efficacy of hormonal contraceptives] for up to 7 days. Advise female patients of reproductive potential using hormonal contraceptives to use an additional, non-hormonal contraceptive for the next 7 days following [sugammadex] administration."	Can use 1.2 mg/kg rocuronium if at least 5 minutes since sugammadex (NMB onset may be delayed). Can use 0.6 mg/kg rocuronium or 0.1 mg/kg vecuronium if at least 4 hours since sugammadex. If 16mg/kg sugammadex given, wait at least 24 hours before rocuronium/vecuronium.
Sugammadex "not recommended for use in patients with severe renal impairment, including those requiring dialysis." Sugammadex "is known to be substantially excreted by the kidney."	*Caution with succinylcholine if before above waiting times* "because a substantial fraction of postjunctional nicotinic receptors can still be occupied by the neuromuscular blocking agent" (consider cis-atracurium* as alternative).

*Typical intubation doses:[3] *cisatracuricum*: 0.15-0.2mg/kg; vecuronium: 0.08-0.1 mg/kg; rocuronium: 0.6 mg/kg (non-RSI) or 1-1.2mg/kg (RSI)

1. 2023 ASA Practice Guidelines on Monitoring & Antagonism of Neuromuscular Blockade. Anesthesiology 2023 // 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022225lbl.pdf (sugammadex highlights prescribing info) // 3. Epocrates & UpToDate/Lexicomp for: cisatracurium, vecuronium, rocuronium // Miller 10th Ed Ch 24 // TOF: Tain-of-four count // RSI: rapid sequence intubation

Room for notes

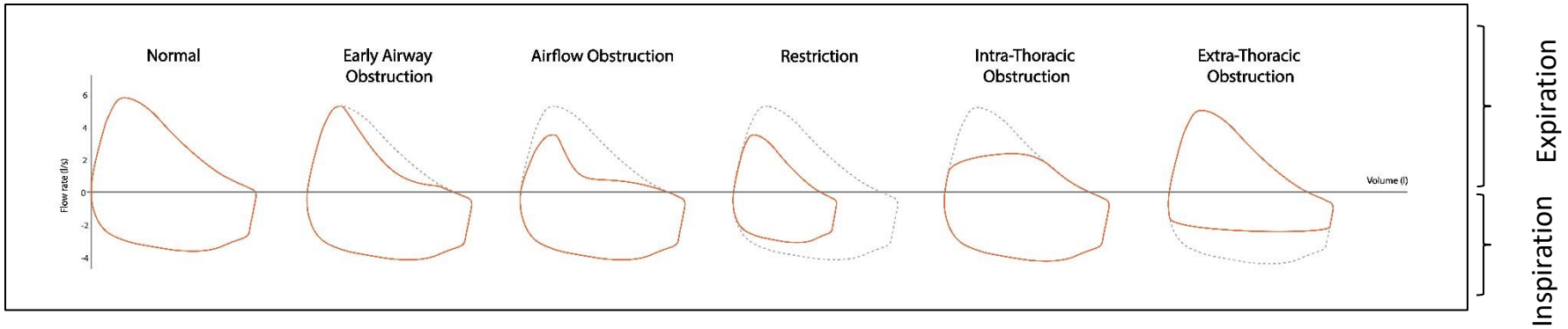


Thoracic & Pulmonary

4X

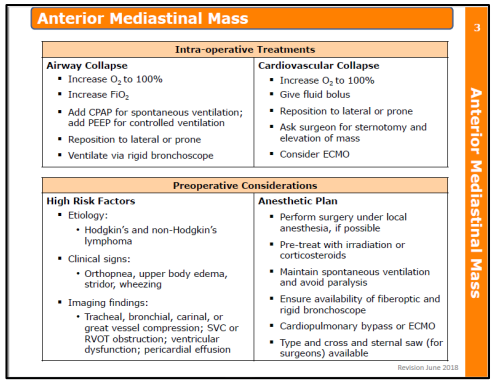
Thoracic/Pulmonary

Flow-Volume Loops:



What is the flow-volume loop for an anterior mediastinal mass?

- There are several different causes of tumors involving the mediastinum (e.g., thymoma, teratoma, thyroid tumor, lymphoma)
- While Flow-Volume loops may be used in work-up assessing location and dynamic extent of airway obstruction: "Flow-volume loops, specifically the exacerbation of a variable intrathoracic obstructive pattern (expiratory plateau) when supine, are unreliable for predicting which patients will have intraoperative airway collapse." (Miller 10th Ed, Ch 49)
- **History/physical and imaging are essential** (see preoperative considerations of Handout: PediCrisis Checklist for Anterior Mediastinal Mass).



Flow-Volume image: Fontan J; used under license from Shutterstock.com

Room for notes

Anterior Mediastinal Mass

Intra-operative Treatments	
Airway Collapse	**Cardiovascular Collapse**
▪ Increase O_2 to 100% ▪ Increase FiO_2 ▪ Add CPAP for spontaneous ventilation; add PEEP for controlled ventilation ▪ Reposition to lateral or prone ▪ Ventilate via rigid bronchoscope	▪ Increase O_2 to 100% ▪ Give fluid bolus ▪ Reposition to lateral or prone ▪ Ask surgeon for sternotomy and elevation of mass ▪ Consider ECMO

Preoperative Considerations	
High Risk Factors	**Anesthetic Plan**
▪ Etiology: • Hodgkin's and non-Hodgkin's lymphoma ▪ Clinical signs: • Orthopnea, upper body edema, stridor, wheezing ▪ Imaging findings: • Tracheal, bronchial, carinal, or great vessel compression; SVC or RVOT obstruction; ventricular dysfunction; pericardial effusion	▪ Perform surgery under local anesthesia, if possible ▪ Pre-treat with irradiation or corticosteroids ▪ Maintain spontaneous ventilation and avoid paralysis ▪ Ensure availability of fiberoptic and rigid bronchoscope ▪ Cardiopulmonary bypass or ECMO ▪ Type and cross and sternal saw (for surgeons) available

Revision June 2018

Society for Pediatric Anesthesia Critical Event Checklists. Revision Packet March 2023. Latest update available at http://www.pedsanesthesia.org

Room for notes

Thoracic/Pulmonary

12X

Room for notes

ARDS vs. TRALI vs. TACO

	ARDS[1]	TRALI[2]	TACO[2]
Timing	Acute onset or worsening respiratory symptoms (within one week of insult)	Acute onset (within 6 hrs of stopping transfusion) and no evidence of acute lung injury before transfusion	Acute onset (within 12 hrs of stopping transfusion – must have cardiac and ≥ 1 radiographic/clinical/oxygenation criteria)
Imaging	Bilat CXR/CT opacities not explained by pleural effusions, lobar collapse, lung collapse, pulmonary nodules	Radiographic evidence of bilateral infiltrates	Radiographic and/or clinical evidence of acute or worsening pulmonary edema***
Cardiac	Not fully explained by cardiac failure or fluid overload*	No evidence of left atrial hypertension (i.e., circulatory overload)	• Elevated BNP or NT-pro BNP • CV changes**** not explained by other medical condition • Evidence of fluid overload
Oxygenation	Moderate to severe impaired oxygenation, even with PEEP ≥ 5cmH2O**	Hypoxemia defined by ≥ 1 of the following: (1) P/F ≤ 300mmHg; (2) SpO2 < 90% (room air); (3) other clinical evidence	Evidence of acute or worsening respiratory distress*****

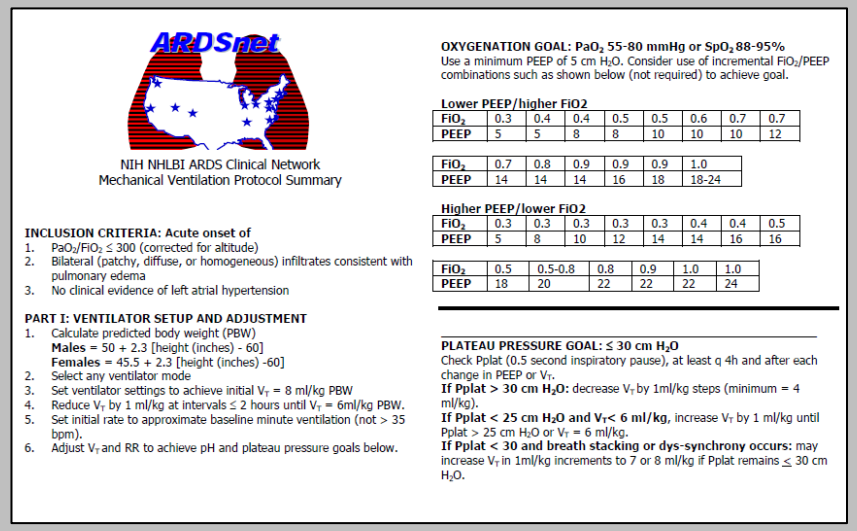
- ARDS Handout: ARDS Clinical Network (ARDSnet) Mechanical Ventilation Protocol Summary[3]
  - 2021 Lancet Review Article: Fundamental initial ICU care elements for ARDS pts include "lung protective ventilation strategy: goal tidal volume ≤ 6 mL/kg, plateau pressure ≤ 30 cm H2O, PEEP relative to FiO2 set according to ARDS Network grids or local practice, generally PEEP ≥ 5 cm H2O."[4]
  - Prone ventilation: Proposed advantages include (1) improved oxygenation; (2) improved ventilation/perfusion matching; (3) less overdistension (non-dependent lung regions); (4) less cyclical opening and closing (dependent lung regions). Sometimes used for severe or moderate-to-severe ARDS.[5] During COVID-19 pandemic, there was use "in awake non-intubated patients with acute hypoxaemic respiratory failure."[4] As with any prone positioning, ETT migration into mainstem bronchus or ETT kinking are possibilities (consider in differential if hypoxemia after prone positoning).[6]
- TRALI/TACO Treatment Considerations: Stop transfusion, alert blood bank, supportive care, consider ARDS treatment principles (TRALI), consider fluid mobilization/diuresis or treatment similar to cardiogenic pulmonary edema from other causes (TACO).

ATS/ESICM/SCCM Guidelines for ARDS Mechanical Ventilation:

*if no ARDS risk factors present, echo or other assessment should be done to exclude hydrostatic pulmonary edema. **(Mild: PaO2/FiO2 [P/F] 201-300mmHg; Moderate: P/F 101-200mmHg; Severe: P/F <100mmHg). *** crackles on lung auscultation, orthopnea, cough, a third heart sound and pinkish frothy sputum in severe cases. **** Elevated central venous pressure, evidence of left heart failure including tachycardia, hypertension, widened pulse pressure, jugular venous distension, enlarged cardiac silhouette and/or peripheral edema. ***** dyspnea, tachypnea, cyanosis and decreased oxygen saturation values in the absence of other specific causes.

References on next slide

Handout: ARDSnet Mechanical Ventilation Protocol Summary



NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of
1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT
1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%
Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FiO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.
If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H_2O.

pH GOAL: 7.30-7.45
Acidosis Management: (pH < 7.30)
If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCO_2$ < 25 (Maximum set RR = 35).

If pH < 7.15: Increase RR to 35.
If pH remains < 7.15, V_T may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).
May give $NaHCO_3$
Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I: E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING
A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:
1. $FiO_2 \leq 0.40$ and PEEP ≤ 8 OR $FiO_2 \leq 0.50$ and PEEP ≤ 5.
2. PEEP and FiO_2 ≤ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

B. SPONTANEOUS BREATHING TRIAL (SBT):
If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with FiO2 ≤ 0.5 and PEEP ≤ 5:
1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H_2O with PS ≤ 5
2. Assess for tolerance as below for up to two hours.
   a. $SpO_2 \geq 90$: and/or $PaO_2 \geq 60$ mmHg
   b. Spontaneous $V_T \geq 4$ ml/kg PBW
   c. RR ≤ 35/min
   d. pH ≥ 7.3
   e. No respiratory distress (distress= 2 or more)
      - HR > 120% of baseline
      - Marked accessory muscle use
      - Abdominal paradox
      - Diaphoresis
      - Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING
(Different from the spontaneous breathing criteria as PS is not allowed)

1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H_20 **without pressure support or IMV assistance.**

References from previous slide:

1. ARDS Definition Task Force. ARDS: The Berlin Definition. JAMA 2012. PMID: 22797452
2. CDC National Health Safety Network Biovigilance Protocol. Available at http://www.cdc.gov/nhsn.
3. NIH NHLBI ARDS Clinical Network. Mechanical Ventilation Protocol Summary. Available at http://www.ardsnet.org/tools.shtml.
4. **Meyer et al. Acute respiratory distress syndrome. Lancet 2021; 398: 622-37. PMID: 33894835**
5. **Guérin et al. Prone position in ARDS patients: why, when, how and for whom. Intensive Care Med 2020; 46: 2385-96. PMID: 33169218.**
6. Guérin et al. Prone positioning in severe acute respiratory distress syndrome (PROSEVA study). NEJM 2013. PMID 23688302
7. Miller 10th Ed, Ch 45
8. Goldberg et al. State of the art management of transfusion-related acute lung injury (TRALI). Curr Pharm Des 2012; PMID 22621274.
9. UpToDate articles:
   1. ARDS: Clinical features, diagnosis, and complications in adults.
   2. Prone ventilation for adult patients with ARDS.
   3. Transfusion-related acute lung injury (TRALI).
   4. Transfusion associated circulatory overload (TACO).

Room for notes

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals $\leq$ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%

Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FiO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: $\leq$ 30 cm H_2O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.

If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains $\leq$ 30 cm H_2O.

pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)

If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCO_2$ < 25 (Maximum set RR = 35).

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Thoracic/Pulmonary

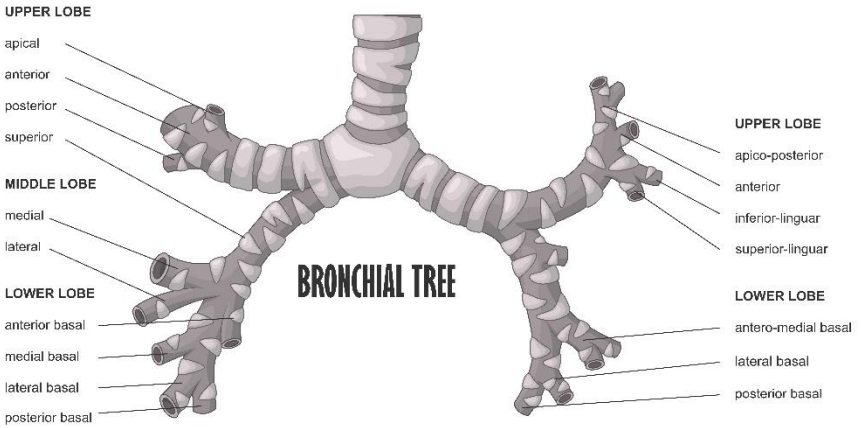
23X

Room for notes

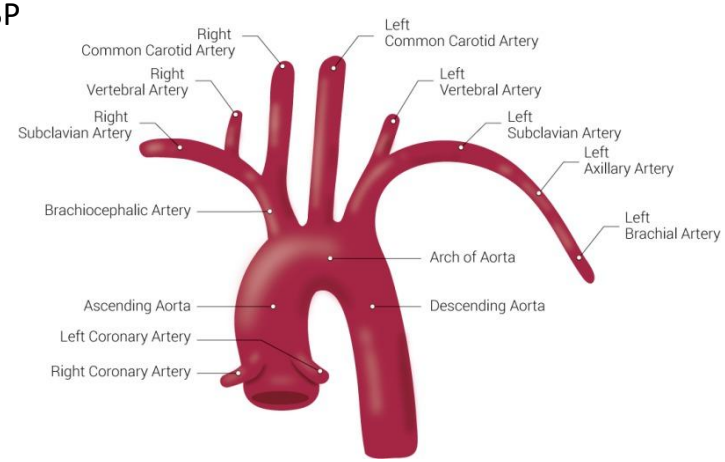
One Lung Ventilation topics:

- Key Bronchoscopy landmarks for Left Double Lumen Tube (DLT) placement: *Bronchoscope passed via tracheal lumen*: (1) edge of endobronchial cuff around entrance of left mainstem bronchus; (2) view of right upper lobe bronchus and three orifices (apical, anterior, posterior). *Bronchoscope passed via endobronchial lumen*: (3) visualization of bronchial bifurcation at end of left mainstem bronchus (left upper and left lower bronchi).
- Bronchial blockers: **Pros**: can be used with single-lumen ETT if challenging airway; can placed to achieve selective lobar collapse; **Cons**: failure to achieve desired lung separation from abnormal anatomy, lack of seal, or other malposition (most dangerous: balloon lodged above carina & total airway obstruction); could get caught in staple line if miscommunication.
- Hypoxemia during one-lung ventilation:

Less Disruptive	More Involved
FiO2 100%	Return to two-lung ventilation
Recheck positioning via bronchoscopy	CPAP to nondependent (operative) lung
Suction for mucus plugs	Ligate/Clamp ipsilateral pulmonary artery (i.e., during pneumonectomy)
PEEP to dependent (ventilated) lung	Urgent cardiopulmonary bypass

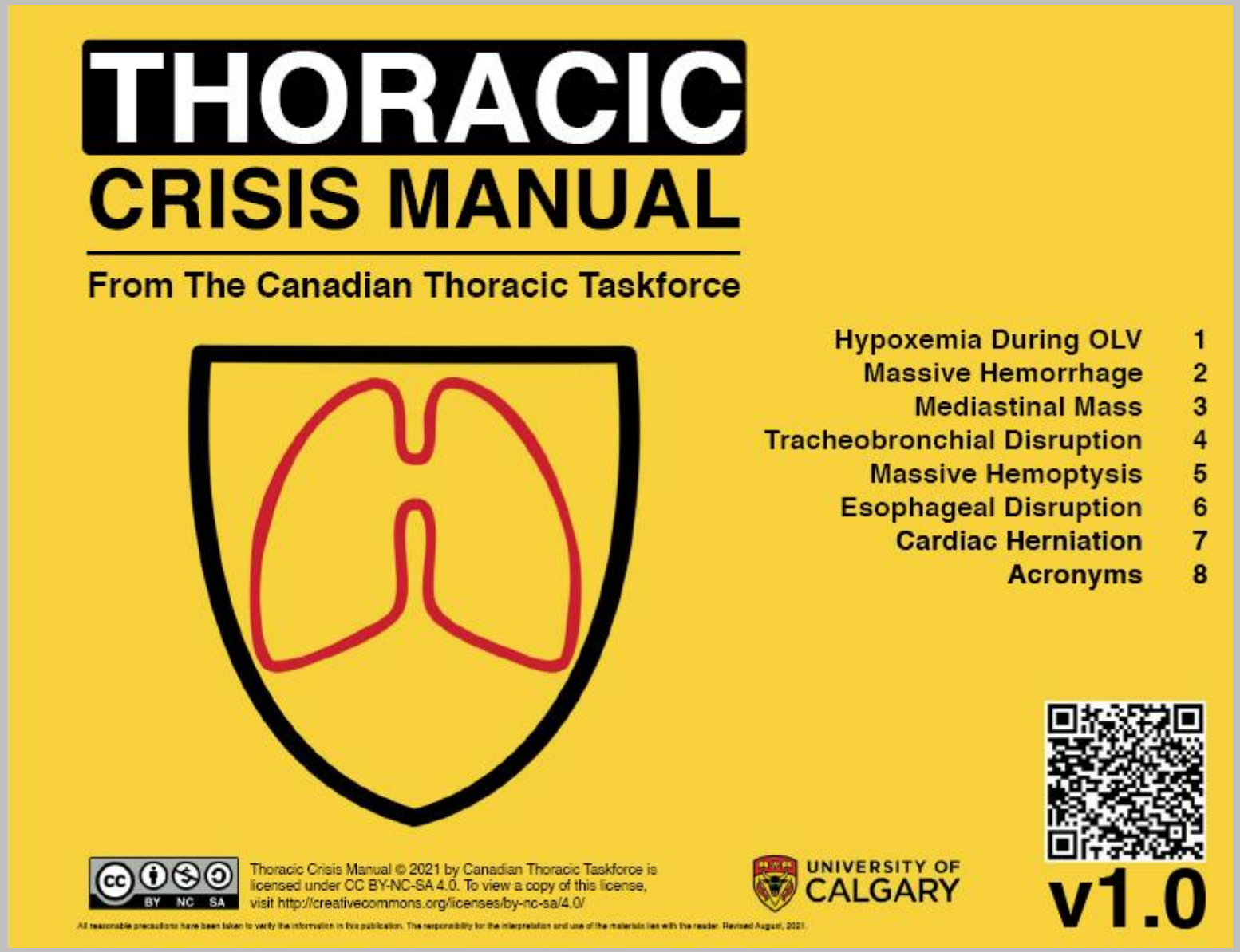


Mediastinoscopy & vascular compression: place pulseOx on Right finger to look for innominate artery (aka brachiocephalic artery) compression; Left BP cuff for systemic BP



Miller 10th Ed, Ch 49 // Bronchial tree image: 407075512, used via license from Shutterstock
Mediastinoscopy Image: Palmer B. StatPearls Creative Commons CC-BY-4.0 https://www.ncbi.nlm.nih.gov/books/NBK499911/figure/article-17736.image.f1/

Room for notes



Canadian Thoracic Taskforce. Thoracic Crisis Manual. See tinyurl.com/2hvu54xu for latest version. With permission via Creative Commons BY-NC-SA (https://creativecommons.org/licenses/by-nc-sa/4.0/).

1 Hypoxemia During One-Lung Ventilation

SpO_2 < 90% or PaO_2 < 60 mmHg despite 100% FiO_2

START

1. Increase to 100% FiO_2
2. Confirm position of lung isolation device
3. Recruit the ventilated lung
4. Optimize PEEP to the ventilated lung
5. Suction secretions from ventilated lung
6. Consider bronchodilator therapy to ventilated lung
7. Decrease volatile anesthetic or consider TIVA
8. Ensure normal cardiac output
9. Ensure adequate hemoglobin level
10. Notify surgeon of severe or refractory hypoxemia:
    - Call for help
    - O_2 insufflation/CPAP/HFJV to nonventilated lung
    - Resume two-lung ventilation
    - Consider pulmonary artery clamp to nonventilated lung
    - Consider inhaled nitric oxide (10-40 ppm)
    - Consider ECMO/CPB

RISK FACTORS

Right-sided surgery
Prior contralateral lung resection
Supine position
Normal FEV_1
Low PaO_2 on two-lung ventilation
High A-a gradient for CO_2

OXYGENATION TECHNIQUES

V_T 4-6 ml/kg IBW
I:E ratio 1:2 (routine)
- 1:1-1:2 (restrictive deficit)
- 1:4-1:6 (obstructive deficit)

Ventilated Lung:
- Recruitment maneuver
- PEEP 3-10 cm H_2O

Nonventilated Lung:
- CPAP 5-10 cm H_2O
- O_2 insufflation 2-3 L/min

HFJV: 100-200 RR, DP 15-30 psi, I:E 1:1-1:2

HYPOXEMIA & RIGID BRONCHOSCOPY

- Manual ventilation via bronchoscope
- Reposition bronchoscope above carina
- Suction secretions
- Retrieve tumor fragments
- Achieve pulmonary hemostasis
- Consider and manage pneumothorax

Thoracic/Pulmonary

25X

Carbon monoxide (CO) poisoning/carboxyhemoglobinemia: SpO2 falsely elevated relative to SaO2. Methemoglobinemia: SpO2 falsely approaches 85%. → Use Multiwavelength pulse oximeter ("Pulse CO-Oximeter" is Masimo trademark).

- Both increase oxyhemoglobin affinity for O2 → both cause left shift of oxyhemoglobin dissociation curve.
- p50: The PO2 at which hemoglobin is 50% saturated with oxygen.

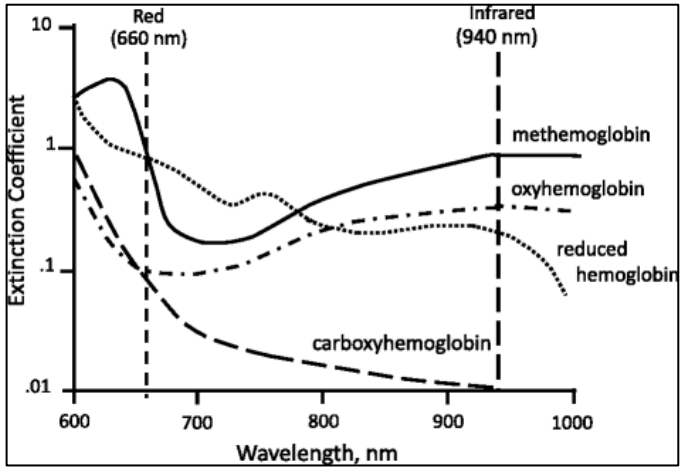
COHb level	Comments/Symptoms (COHb = Carboxyhemoglobin)
≤10%	Smokers
15-20%	Headaches, dizziness, confusion
>20%	Progression of symptoms: Nausea/vomiting, seizures, myocardial ischemia, organ dysfunction, coma, imminent death (>60-80%)
>25%	Hyperbaric oxygen therapy discussed/considered

Smoking cessation: Optimal time: 8 weeks preop. Some say "increased sputum/reactive airways" in short term after cessation. Many recommend immediate cessation preop regardless. Cessation drops carboxyhemoglobin → oxyhemoglobin dissociation curve shifts back to the right.

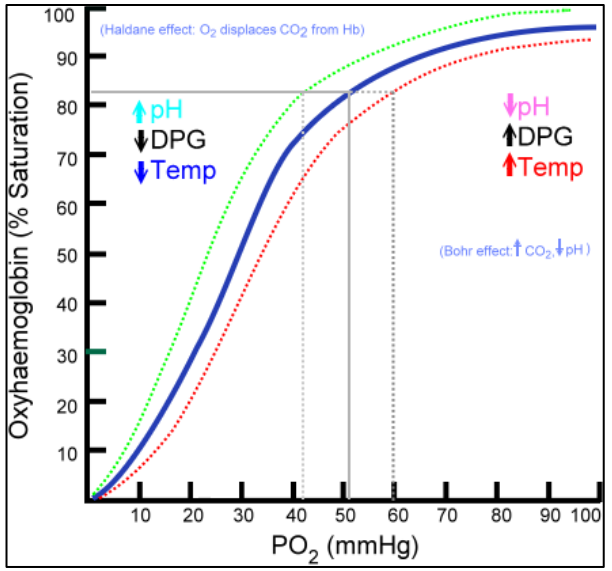
- ASA Statement on Smoking Cessation: "surgery may represent a teachable moment for…smoking cessation…patients should abstain from smoking…both **before** and after surgery."

Kahn Academy video on Haldane and Bohr effect (Dr. Rishi Desai): https://youtu.be/dHi9ctwDUnc

Pulse oximeter typically uses 660 & 940nm



Oxyhemoglobin Dissociation Curve



UptoDate. Strategies to reduce pulmonary complications in adults. // OpenAnesthesia CO Poisoning. // Extinction coefficients image: Jubran A. PMID 26179876. Creative Commons CC-BY-4.0 // Miller Basics 8th Ed, Ch 5. // Miller 10th Ed, Ch 12, 37, 71 // Dissociation Curve: Ratznium/Aaronsharpe. Wikimedia Commons public domain. https://commons.wikimedia.org/wiki/File:Oxyhaemoglobin_dissociation_curve.png // https://www.masimo.com/company/news/news-media/2005/ Accessed 12/18/19 // Barash 9th Ed, Ch 26 // Ferri's Clinical Advisor 2022: Carbon Monoxide Poisoning // ASA Statement on Smoking Cessation.

Room for notes

Hyperbaric Oxygen Therapy (HBOT)

12X

Common criteria for HBOT **in acute carbon monoxide (CO) poisoning:**[1]

- Neurologic impairment (including loss of consciousness, altered mental status, dizziness).
- Myocardial ischemia, arrhythmias, heart failure.
- HbCO higher than 25%
- Pregnant patient with signs of fetal distress.

HBOT Seizure: Can occur from oxygen toxicity to CNS. Tx: Decrease FiO2 to room air (21%). Benzodiazepine +/- anticonvulsants. Supportive care. Don't decompress chamber while pt convulsing (airway closure from seizure & failure to exhale could lead to pulmonary barotrauma & arterial gas embolism). Seizure hx doesn't increase risk (risk increases w/increasing pO2 and exposure time). Seizures rarely recur with further HBOT Tx.

HBOT, MAC, and N2O: "Because of its high MAC value (1.04), general anesthesia with N2O can usually only be obtained in a hyperbaric environment….The anesthetic state was associated with tachypnea, tachycardia, increases in systemic blood pressure, mydriasis, diaphoresis,…clonus,…A stable level of physiologic activity was difficult to maintain."[3]

Undersea & Hyperbaric Medical Society Hyperbaric Oxygen Therapy Indications[2]
Air or Gas Embolism
Arterial Insufficiencies (e.g., central retinal artery occlusion, selected problem wounds)
Carbon Monoxide Poisoning
Clostridial Myonecrosis (Gas Gangrene)
Compromised Grafts and Flaps
Acute Traumatic Ischemia (e.g., crush injury)
Decompression Sickness
Delayed Radiation Injuries
Sudden Sensorineural Hearing Loss
Intracranial Abscess
Necrotizing Soft Tissue Infection
Refractory Osteomyelitis
Severe Anemia
Thermal Burns

1. Miller 10th Ed Ch 71 // 2. https://www.uhms.org/resources/hbo-indications.html (14th Ed) // 3. Russel GB. Hyperbaric nitrous oxide as a sole anesthetic agent in humans. Anesth Analg 1990; 70:289-95 // UpToDate: Hyperbaric Oxygen Therapy.

Room for notes

Cardiac & Hematology

Room for notes

Cardiac & Hematology

45X+
(incl protamine reaction table and TEE resources)

- Bradycardia in patient with Heart Transplant: Transplanted heart may have total autonomic denervation of the heart. "Vagal maneuver" (stimulation of carotid sinus) may not work. Use **"ENIGmatic" drugs**: **E**pinephrine, **N**orepinephrine, **I**soproterenol, **G**lucagon.
- Heparin resistance attempting to go on bypass:
  - Most common cause: antithrombin III (AT3) deficiency → Tx: recombinant AT3 or FFP.
  - If patient has significant heparin induced thrombocytopenia/thrombosis (HITT) and needs cardiopulmonary bypass: consider direct thrombin inhibitor (e.g., bivalrudin).
- Contraindications to Intra-aortic balloon pump (IABP): severe aortic insufficiency; severe peripheral vascular disease.
- Handouts: [1] Cognitive Aid for Heparin Resistance, [2] Protamine Reaction (Zenati et al), and [3] Cardiac Tamponade (Society for Pediatric Anesthesia); [4] Left-sided Valvular lesions & HCM; [5] Selected online free TEE education video lectures.

American Society of Echocardiography (ASE) 2013 Guidelines for comprehensive TEE (includes 28 suggested views):	ASE and Society for Cardiovascular Anesthesiologists (SCA) 2013 Consensus Statement for Basic TEE (includes 11 views of basic TEE and typical distribution of RCA, LAD and LCx):	Classic 1999 ASE/SCA TEE article:	STS/SCA/AmSECT Guidelines for Anticoagulation during Cardiopulm Bypass:

STS: Society of Thoracic Surgeons. AmSECT: American Society of extracorporeal technology.

Room for notes

+ denotes that there are additional entries on these topics that pertain to echo imaging available via QR codes and video links provided

5. Heparin Resistance

Initiate for High (>400 u/kg) Heparin Management System (HMS) Recommended Dose

ACTIONS

1. PERFUSIONIST report suspicion of Heparin Resistance
   - Based upon HMS recommended dose – Threshold 400 u/kg
2. Administer HMS recommended bolus of heparin, check ACT
3. If **LOW**, administer additional **5 000 – 10 000 u** of heparin, check ACT
4. *Was patient on IV/SQ heparin preoperatively?* If **YES** proceed to **STEP 7**
5. IF **NO**, administer bolus of heparin to cumulative maximum 50 000 units, repeat ACT
6. If ACT remains unsatisfactory, proceed to **STEP 8**
7. **Assume** Antithrombin (AT) III Deficiency
   1. Administer 500 u **Antithrombin III (AT III)**
      - Ensure an additional dose is available after administration
      - Alternatively, administer 2 u Fresh Frozen Plasma or Cryo
   2. Repeat ACT
   3. If ACT low, administer additional 500 u **AT III**, repeat ACT
8. Consider
   1. Lower ACT target and perform OPCAB and administer a fixed heparin dose regimen
9. Start CPB when target ACT achieved or option from **Step 7** selected

DRUG DOSES

Heparin:	300 u/kg
Antithrombin III:	500-1000 IU IV
Bivalirudin:	0.75 mg/kg IV *bolus*
	1.75 mg/kg/hr IV *infusion*
	Target: ACT > 300

PHARMACY

(XXX) XXX-XXXX

OR **xXXXXX**

Heparin Allergy

Utilize Bivalirudin

From VA Boston Cardiac Surgery Crisis Checklists. With permission from Dr. M. Zenati and thanks to Yule S, Dias R, et al.

Room for notes

Protamine Reactions

	Type I	Type II	Type III
Clinical Presentation	• Mild hypotension • Normal airway pressures	• Moderate/severe hypotension • Anaphylactoid symptoms (e.g., bronchospasm, increased airway pressures)	• Severe hypotension • Pulmonary hypertension/elevated pulmonary artery pressures • Right heart failure
Pathophysiology (hypotheses)	• May be allergic (IgE) or nonallergic (IgG/complement)		• Heparin/protamine complex that lodge into pulmonary vasculature and release mediators.
Risk factors	• Previous protamine exposure (including protamine Hagedorn insulin), fish allergy, vasectomy, pre-existing hemodynamic instability/decreased LV function		

Treatment	• Volume resuscitation
	• Vasopressor support
	• Lower protamine infusion rate
		• Escalate vasopressor support (e.g., epinephrine, norepinephrine, calcium chloride)
		• Optimize intravenous/arterial access
		• Consider:
		  • Albuterol
		  • Milrinone
		  • Reheparinization/cardiopulomary bypass	

Miller's Anesthesia, 10th Ed, Ch 50 // Barash 9th Ed, Ch 39

Room for notes

3. Protamine Reaction

ACTIONS

1. First witness alerts READER of **"Protamine Reaction Emergency"**
   A. *Reader press&hold Vocera button and announce:*
   " Protamine Reaction Emergency"
   A. *Start crisis timer*
2. DISCONTINUE Protamine and Propofol
3. Volume Resuscitation: 1L Crystalloid
4. Open cardiac massage **by expert (avoid graft damage)**
5. Vasopressor or Inotropic Therapy (see drug doses at right)
6. If hypotension *refractory* to treatment modalities:
   A. Consider administration of **methylene blue**
   B. Repeat heparin (300 u/kg) and cannulation
   C. **Re-start pump if severe refractory hypotension lasting >5 min**

Signs and Symptoms of Protamine Reaction

Severe hypotension refractory to high-dose vasopressors

(MAP <50 mmHg)

Low systemic vascular resistance (<800 dyne/s/cm^{-5})

Central venous pressure < 5 mmHg

Capillary Wedge Pressure < 10 mmHg

Normal to Elevated Cardiac Index (> 2.5L/min/m^2)

Drug Doses

Ephedrine:	5-25 mg bolus IV q5min
Epinephrine:	1-10 mcg/min *IV infusion*
	10-100 mcg IV *bolus* prn
Methylene Blue:	1-2 mg/kg IV
Norepinephrine:	2-10 mcg/min *IV infusion*
Phenylephrine:	100-500 mcg bolus IV q5min
Methylprednisolone:	30 mg/kg IV over 30 min
Nebulized Albuterol:	1.25-5mg q4h

Guidelines for Protamine Administration

Dose: 1-1.3 mg/100 IU heparin

Prior to infusion, ready vasoactive therapy

Give slowly over 5-10 minutes

Pause infusion if hypotension develops

From VA Boston Cardiac Surgery Crisis Checklists. With permission from Dr. M. Zenati and thanks to Yule S, Dias R, et al.

Room for notes

Tamponade, Cardiac

Tamponade physiology occurs when increased pericardial pressure impairs diastolic filling

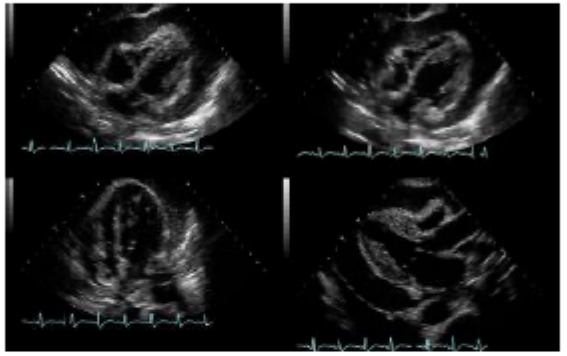
25

Signs & Symptoms

- Beck's Triad: muffled heart tones, distended neck veins, decreased systolic blood pressure
- Pulsus Paradoxus: cyclic inspiratory decrease in systolic BP of more than 10mmHg
- Electrical Alternans: cyclic alteration in magnitude of p waves, QRS complex & t-waves
- Typical presentation of acute tamponade = sudden hypotension, tachycardia & tachypnea; patient may be unable to lie flat

Diagnosis

- Echocardiography/ultrasound: diastolic compression or collapse of RA/RV, leftward displacement of ventricular septum, exaggerated increase in RV size with reciprocal decrease in LV size during inspiration



Treatment - imaging is key in deciding treatment

- Pericardiocentesis awake/local for large effusions prior to GA
- Surgical for postoperative tamponade (cause is often local collections of clotted blood)

Anesthetic Considerations

- Progressive decrease in SV with an increased CVP → systemic hypotension → cardiogenic shock
- Goals: maintain sympathetic tone and CO via ↑ HR and contractility/fluid bolus prn
  - Induction: Ketamine (1-2 mg/kg IV), muscle relaxant
  - If CV collapse: EPINEPHrine 0.05-0.1 MICROgrams/kg IV bolus or infusion (0.01-0.1 MICROgrams/kg/min)
  - Access: Large bore PIV; arterial line ideal but should not delay treatment in hemodynamically unstable patient
  - Avoid: cardiac depression, vasodilation, ↓ HR; ↑ airway pressure (will ↓ venous return) so may need small tidal volumes or hand ventilation

Differential Diagnosis

- CHF, PE
- If pulsus paradoxus: respiratory distress, airway obstruction, COPD, PE, RV infarction

First Published Nov 2018

Tamponade, Cardiac

Room for notes

Handout: Left-sided Valvular lesions & HCM

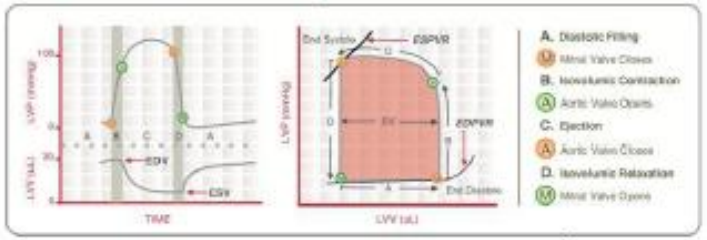
Anesthetic/Hemodynamic Goals for Left-sided Valvular lesions and Hypertrophic Cardiomyopathy:

Hemodynamic Goals

Lesion	Preload	Systemic Vascular Resistance	Heart Rate	Contractility
Aortic Stenosis (AS)	↑	↑	↓	→
Mitral Stenosis (MS)	↑	→ or ↑	↓	→
Mitral Regurgitation (MR)	↑	↓	↑	→
Aortic Insufficiency (AI)	↓	↓	↑	→
Hypertrophic Cardiomyopathy (HCM)	↑	↑	↓	↓

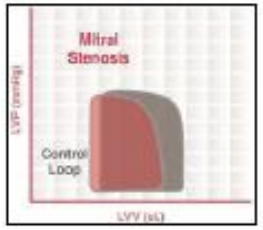
- Pts with AS and HCM are particularly dependent on "atrial kick" (sinus rhythm) → i.e. Afib is particularly detrimental. Systolic Anterior Motion: If HCM is severe, the anterior mitral valve leaflet or chordal structures can be pulled into the left ventricular outflow tract (LVOT) → LVOT obstruction and possible MR.

Standard Left Ventricular Pressure-Volume Loop:

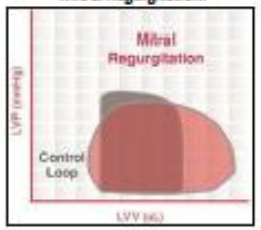


Pressure-Volume Loops for Left Ventricular Valvular Lesions:

Mitral Stenosis:



Mitral Regurgitation:



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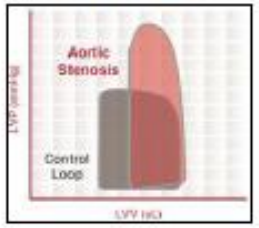

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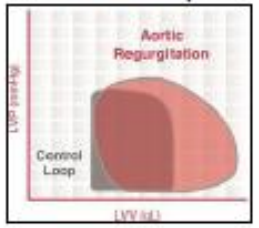


References: 1. Essential Clinical Anesthesia. Cambridge University Press, 2011. 2. Pressure-Volume Loops. https://commons.wikimedia.org/wiki/File:Cardiac_Pressure_Volume_Loops.jpg With permission via Creative Commons CC BY-SA 3.0, Andykenyon, via Wikimedia Commons. 3. Aortic Regurgitation, Mitral Regurgitation, Mitral Stenosis, Aortic Stenosis. https://commons.wikimedia.org/wiki/File:Aortic_regurgitation.jpg https://commons.wikimedia.org/wiki/File:Mitral_regurgitation.jpg https://commons.wikimedia.org/wiki/File:Mitral_stenosis.jpg https://commons.wikimedia.org/wiki/File:Aortic_stenosis.jpg With permission via Creative Commons CC BY 3.0, Bruce Blaus, via Wikimedia Commons. 4. Miller 9th Ed, Ch 54 (Anesthesia for Cardiac Surgical Procedures).

Room for notes

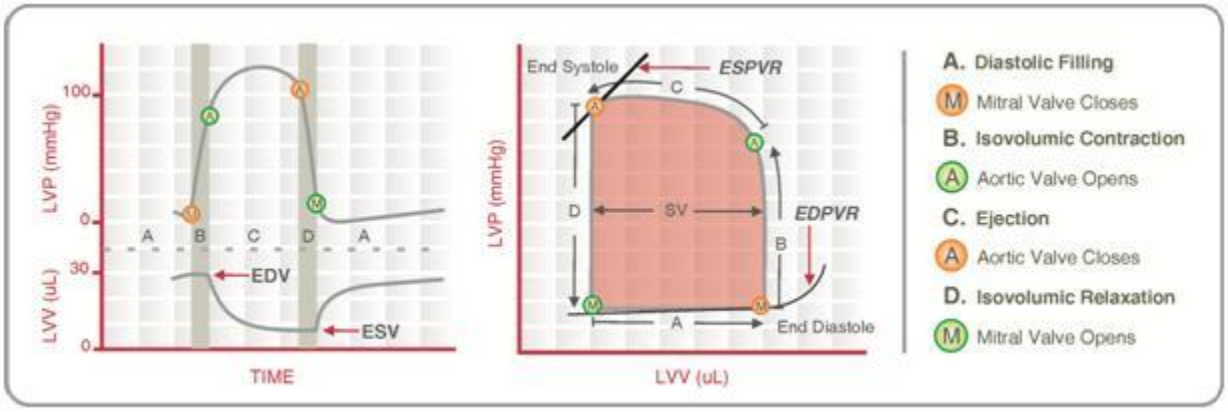
Anesthetic/Hemodynamic Goals for Left-sided Valvular Lesions and Hypertrophic Cardiomyopathy:

Hemodynamic Goals

Lesion	Preload	Systemic Vascular Resistance	Heart Rate	Contractility
Aortic Stenosis (AS)	↑	↑	↓	→
Mitral Stenosis (MS)	↑	→ or ↑	↓	→
Mitral Regurgitation (MR)	↑	↓	↑	→
Aortic Insufficiency (AI)	↓	↓	↑	→
Hypertrophic Cardiomyopathy (HCM)	↑	↑	↓	↓

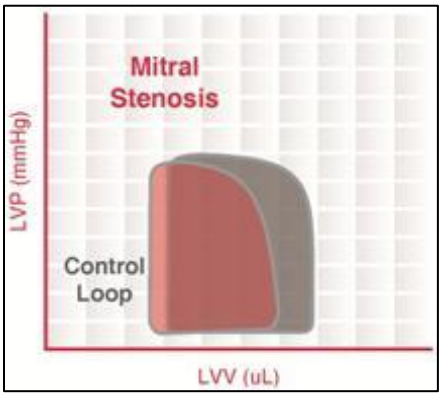
- Pts with AS and HCM are particularly dependent on "atrial kick" (sinus rhythm) → i.e. Afib is particularly detrimental. Systolic Anterior Motion: if HCM is severe, the anterior mitral valve leaflet or chordal structures can be pulled into the left ventricular outflow tract (LVOT) → LVOT obstruction and possible MR.

Standard Left Ventricular Pressure-Volume Loop:



Pressure-Volume Loops for Left Ventricular Valvular Lesions:

Mitral Stenosis:



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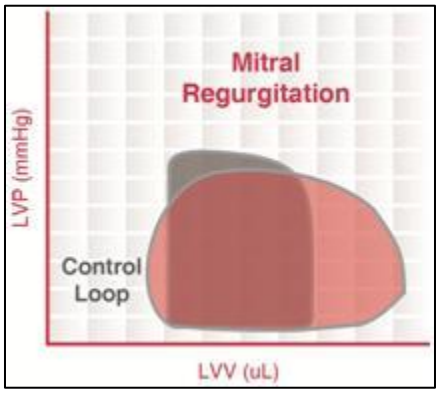

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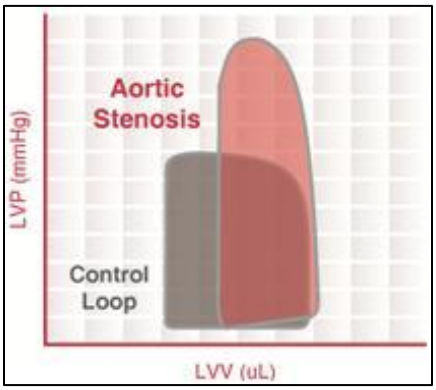
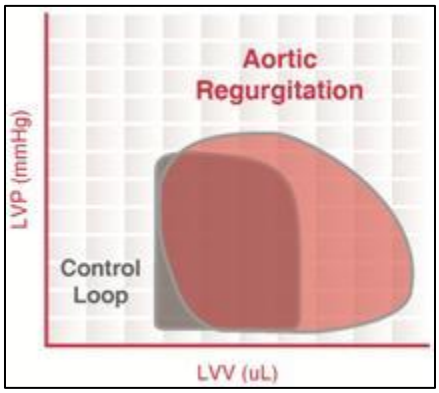


Aortic Insufficiency:



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2. Pressure-Volume Loop. https://commons.wikimedia.org/wiki/File:Cardiac_Pressure_Volume_Loop.jpg. With permission via Creative Commons CC BY-SA 3.0, Andyhenton, via Wikimedia Commons.
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Selected Free Online Anesthesia Education Videos Containing TEE Content

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3. Schell R. 20160121 High Yield Cardiac Keywords Parts 1 to 3, 2016. Part 1: https://youtu.be/ZtZfUshQtIc. Part 2: https://youtu.be/cwBi0nsoXRg. Part 3: https://youtu.be/ckRWFkoY-XIo.

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- TEE Rounds (https://www.openanesthesia.org/tee-rounds/)
    1. Many case-based TEE videos of varying lengths (the series was retired in 2020, with archive still available as of last search).
        - **November 2013: Cardiac Tamponade (11min-51sec):** https://vimeo.com/77304150.

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    1. This is a multi-part lecture series on the Basics: (1) Introduction to the Basic TEE Exam (10min); (2) TEE Imaging Planes and Orientation (35min); (3) TEE Probe Position and Orientation (9min); (4) Comprehensive Assessment of LV Function (19min); (5) Hemodynamics (12min); (6) Basics of the Aortic Valve (25min); (7) Basics of the Mitral Valve (15min); (8) Wall Motion Assessment (17min); (9) Assessment of the RV (19min).
- TEE Rounds (https://www.openanesthesia.org/tee-rounds/)
    1. Many case-based TEE videos of varying lengths (the TEE rounds series was retired in 2020 and is now available as a set of resources including more recent podcasts).
        - **November 2013: Cardiac Tamponade (11min-51sec): https://vimeo.com/77304150.**

Cardiac: Adult Advanced Life Support ("ACLS")

35X

Room for notes

2020 AHA ACLS Algorithms largely unchanged for cardiac arrest, tachycardia, and bradycardia

- 2018 American Heart Association (AHA) ACLS Updated statement: "**Amiodarone or lidocaine** may be considered for VF/pVT that is unresponsive to defibrillation."[1]
- *Of note: avoid lidocaine if cardiac arrest may be from Local Anesthetic Systemic Toxicity (LAST)![2]*

Epinephrine 1mg IV in adults for cardiac arrest: The alpha-adrenergic effects (vasoconstriction, increased aortic diastolic pressure) can increase coronary and cerebral perfusion pressure (Miller 9thEd/Ch86). Epinephrine also **decreases the cellular refractory period and stabilizes VF**.[3] Epinephrine also bronchodilates and **inhibits release of histamine from mast cells** (helpful in anaphylaxis). *Ongoing controversy surrounding increased myocardial work from 1mg epinephrine.*

- Update to "Anesthesia ACLS" (Anes Analg):[4] recommends titrating Epi 100-1,000 mcg IV.
- ASRA: Cardiac Arrest & Local Anes Syst Toxicity:[2] advise smaller Epi doses:"start with ≤ 1 mcg/kg."
- ACLS Cardiac Arrest preference (obtaining vascular access): IV → IO → CVC → ETT
- Handouts: (1) Crisis Checklists: Unstable Bradycardia, Cardiac Arrest (Asystole/PEA & VF/VT), Unstable Tachycardia, Myocardial Ischemia, and Anaphylaxis (special circumstances of ACLS); (2) Stanford Emergency Manual entry: SVT – Stable and Unstable
  - Most common cause of periop anaphylaxis (Barash 9th Ed/Ch 9 & refs[5,7-9] below):
    - Globally: neuromuscular blockers > antibiotics, chlorhexidine, dyes, ?sugammadex, latex
    - U.S. (limited data): antibiotics are perhaps > neuromuscular blockers
- Neonatal Resuscitation: see QR code. "Babies who are breathing well and/or crying […] should not need […] suctioning, even if the amniotic fluid is meconium stained. Avoiding unnecessary suctioning helps prevent the risk of induced bradycardia as a result of suctioning the airway."[6]

2020 AHA Neonatal Resuscitation Algorithm:[6]

Anesthesiology 2023 Review Article on Periop Anaphylaxis:[7]
"[T]he rank order may differ, potentially due to differences in clinical practice, differences in the environment or in reporting. From limited U.S. reporting, antibiotics are the most commonly reported causes of perioperative anaphylaxis. The situation is similar in the United Kingdom but is in distinct contrast to neuromuscular blocking agents most often implicated in European reports."

1. Panchal AR et al. Circulation 2018; PMID 30571262 // 2. Neal et al. Reg Anes Pain Med 2020; PMID: 33148630. // 3. Tovar OH et al. J Mol Cell Cardiol 1997; PMID 9201629 //4. Moitra et al. Anes Analg 2018; PMID: 30044297. // 5. Dewatcher et al. Curr Allergy Asthma Rep 2015; PMID 26139330 // Barash 9th Ed, Ch9. // 6. Aziz et al. Circulation 2020; PMID 33081528 // 7. Tacquard et al. Anesthesiology 2023; PMID 36413685 // 8. Tsur et al. Anaesthesia 2014; PMID 24848211 // 9. Hristovska et al. Anaesthesia 2018; PMID 29280475

03 Bradycardia - Unstable

HR < 50 bpm with hypotension, acutely altered mental status, shock, ischemic chest discomfort, or acute heart failure

INDEX

03

START

1. **Call for help and a code cart**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Turn FiO_2 to 100%**
   - Verify oxygenation/ventilation adequate
   - Consider securing airway
3. **Administer atropine**
4. **Stop surgical stimulation** (if laparoscopy, desufflate)
5. **If atropine ineffective:**
   - Consider EPINEPHrine or DOPamine

   — or —
   - Start transcutaneous pacing (see box)
6. **Consider...**
   - Assessing and treating underlying etiology (see differential diagnosis box)
   - If hemodynamically unstable, minimizing volatile anesthetics
   - Calling cardiology consult
7. **If bradycardia progresses to asystole or PEA arrest**
   - *go to* CHKLST 04

DRUG DOSES & treatments

Atropine	0.5-1 mg IV, may repeat up to 3 mg total
EPINEPHrine	BOLUS: 10 - 100 MCG IV, repeat as needed (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01 - 0.1 MCG/kg/min
— or —	
DOPamine	2 -20 MCG/kg/min IV infusion

OVERDOSE treatment

Beta-blocker	**Glucagon**	5 - 10 mg IV push
Calcium channel blocker	**Calcium chloride**	1g IV
	— or —	
	Calcium gluconate	3g IV
Digoxin	**Digoxin FAB**; consult pharmacy for patient-specific dosing	

DIFFERENTIAL diagnosis

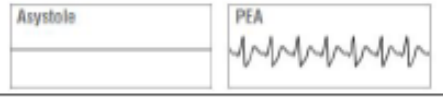
Drug effect or overdose	Hyperkalemia
Tension pneumothorax	Hypothermia
Auto-PEEP	Hypovolemia
Surgical stimulation	Local anesthesia systemic toxicity (CHKLST 12)
High spinal	Malignant Hyperthermia (CHKLST 13)
Acidosis	Myocardial ischemia (CHKLST 14)

TRANSCUTANEOUS PACING instructions

1. Place pacing electrodes front and back
2. Connect 3-lead ECG from pacing defibrillator
3. Turn monitor/defibrillator to PACER mode
4. Set PACER RATE (bpm) to 80/minute (adjust based on clinical response once pacing is established)
5. Start at 60 mA of PACER OUTPUT and increase until electrical capture (pacer spikes aligned with QRS complex)
6. Set final milliamperes 10 mA above initial capture level
7. Confirm effective capture
   - Electrically: assess ECG tracing
   - Mechanically: palpate femoral pulse

Room for notes

04 Cardiac Arrest - Asystole/PEA



Non-shockable pulseless cardiac arrest

INDEX

04

START

1. **Call for help and a code cart**
   - ▶ **Ask:** *"Who will be the crisis manager?"*
   - ▶ **Say:** *"The top priority is high-quality CPR"*
   - ▶ Crisis manager assigns roles - see ROLE assignments box
2. **Put backboard under patient**
   - ▶ Turn supine as soon as possible, but do not delay the start of compressions
3. **Turn FiO_2 to 100%, turn off volatile anesthetic**
4. **Start CPR and assessment cycle**
   - ▶ **Perform CPR**
     - ■ "Hard and fast" about 100-120 compressions/min to depth ≥ 2 inches
     - ■ Ensure full chest recoil with minimal interruptions
     - ■ 10 breaths/minute, do not over-ventilate
       - ● Bag-mask ventilation until able to place endotracheal tube
   - ▶ **Give EPINEPHrine 1mg IV**
     - ■ Repeat EPINEPHrine every 3-5 minutes
   - ▶ **Assess every 2 minutes (limit assessment to < 10 seconds)**
     - ■ Change CPR compression provider
     - ■ Check $ETCO_2$
       - If: No waveform, check for esophageal intubation
       - If: < 10 mmHg, evaluate CPR technique
       - If: Sudden increase to > 40 mmHg, may indicate return of spontaneous circulation
         - ○ Treat reversible causes, consider reading aloud differential diagnoses
     - ■ Check rhythm
       - If: Asystole/PEA continues:
         - ○ Resume CPR and assessment cycle (restart Step 4)
         - ○ Read aloud differential diagnosis (see list in right column)
       - If: VT/VF
         - ○ Resume CPR
         - ○ *go to* CHKLST 05
5. **Consider ECMO if refractory cardiac arrest**

DRUG DOSES & treatments

EPINEPHrine	1 mg IV, repeat every 3-5 minutes
TOXIN treatment	
Local anesthetic	*go to* CHKLST 12
Beta-blocker	**Glucagon** 5 - 10 mg IV push
Calcium Channel Blocker	**Calcium chloride** 1g IV
	— *or* —
	Calcium gluconate 3g IV
HYPERKALEMIA treatment	
Calcium chloride	0.5 - 1 g IV
— *or* —	
Calcium gluconate	1 - 3 g IV
Sodium bicarbonate (if pH < 7.2)	50 mEq IV
Insulin (Regular)	5 - 10 units IV
– *and* –	
Dextrose	50 - 100 mL D50W IV
	— *or* —
	250 - 500 mL D10W IV

ROLE assignments

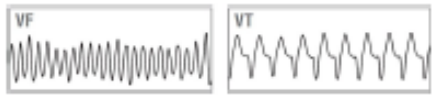
Chest compressions	Code cart
Airway	Time keeping
Vascular access	Checklist reader
Documentation	

DIFFERENTIAL diagnosis

Hypovolemia	Myocardial ischemia (CHKLST 14)
Hyper- or hypokalemia	Acidosis
Tamponade	Hypoxia (CHKLST 11)
Tension pneumothorax	Hypoglycemia
Auto-PEEP	LAST (CHKLST 12)
Embolism	Surgical stimulation
High neuraxial	
Intra-abdominal hypertension	

Room for notes

05 Cardiac Arrest - VF/VT



Shockable pulseless cardiac arrest

INDEX

START

1. **Call for help and a code cart**
   - **Ask:** *"Who will be the crisis manager?"*
   - **Say:** *"Shock patient as soon as the defibrillator arrives"*
   - **Crisis manager assigns roles** (see ROLE assignments box)
2. **Put backboard under patient**
   - Turn supine as soon as possible, but do not delay the start of compressions
3. **Turn FiO_2 to 100%; turn off volatile anesthetics**
4. **Start CPR - defibrillation - assessment cycle**
   - **Perform high-quality CPR**
     - "Hard and fast" about 100 - 120 compressions/min to depth ≥ 2 inches
     - Ensure full chest recoil with minimal interruptions
     - 10 breaths/minute; do not over-ventilate
       - Bag-mask ventilation until able to place endotracheal tube
   - **Defibrillate**
     - Shock at highest setting
     - Resume CPR immediately after shock
   - **Give EPINEPHrine**
     - Repeat EPINEPHrine every 3-5 minutes
   - **Give antiarrhythmics for refractory VF/VT after 2 shocks**
   - **Assess every 2 minutes**
     - Change CPR compression provider
     - Check $ETCO_2$
       If: No waveform, check for esophageal intubation
       If: < 10 mm Hg, evaluate CPR technique
       If: Sudden increase to > 40 mm Hg, may indicate return of spontaneous circulation
     - Treat reversible causes, consider reading aloud differential diagnoses
     - Check rhythm; if rhythm organized, check pulse
       If: VF/VT continues: Resume CPR cycles (restart Step 4)
       If: Asystole/PEA: *go to* CHKLST 04
5. **Consider ECMO**

DRUG DOSES & treatments

EPINEPHrine	1 mg IV, repeat every 3 - 5 minutes
ANTIARRHYTHMICS	
Amiodarone	1st dose: 300 mg IV 2nd dose: 150 mg IV
Lidocaine	1st dose: 1 - 1.5 mg/kg 2nd dose: 0.5 - 0.75 mg/kg
Magnesium	2 - 4 g IV for *Torsades de Pointes*

DEFIBRILLATOR instructions

1. Place electrodes on chest
2. Turn defibrillator ON, set to DEFIB mode, and increase ENERGY LEVEL. Biphasic: Follow manufacturer recommendation. (If unknown, use highest setting.)
   Monophasic: 360J
3. Deliver shock: press CHARGE, then press SHOCK

ROLE assignments

Chest compressions
Airway
Vascular access
Documentation
Code cart
Time keeping
Checklist reader

DIFFERENTIAL diagnosis

Hypovolemia
Hyper- or hypokalemia
Tamponade
Tension pneumothorax
Auto-PEEP
Embolism
High neuraxial
Intra-abdominal hypertension
Myocardial ischemia (CHKLST 14)
Acidosis
Hypoxia (CHKLST 11)
Hypoglycemia
LAST (CHKLST 12)

Room for notes

14 Myocardial Ischemia

Chest Pain, Shortness of Breath, ST Elevation or Depression, Ventricular Arrhythmias

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Increase oxygen delivery** and **decrease oxygen demand**
   - *Increase supply:*
     - 100 % FiO_2
     - Correct anemia **(goal hgb 7 - 9 g/dL)**
     - Correct hypotension (see CHKLST 10)
   - *Decrease demand:*
     - Correct tachycardia **- caution in RCA ischemia (II, III, aVF)**
     - Correct hypertension
     - Restore sinus rhythm (see CHKLST 16)
3. **Obtain 12-lead EKG** and **send troponin levels**
4. **Consult cardiology**
   - Consideration of anticoagulation and/or antiplatelet therapy
   - Consideration of thrombolysis or cardiac catheterization
5. **Discuss clinical condition with surgical team**
   - Safe to abort surgery?
   - Safe to consider anticoagulation and/or antiplatelet therapy?
6. **Consider hemodynamic monitoring**
   - If ongoing hemodynamic instability, arterial line
   - If persistent vasopressor requirement, central line
   - If evidence of cardiogenic shock, non-invasive cardiac output monitor or PA catheter
7. **Consider TEE or TTE if ongoing hemodynamic instability**
8. **Consider ICU disposition**

DRUG DOSES & treatments

Nitroglycerin	0.5 - 5 MCG/kg/min
Aspirin	325 mg PO/PR x1 dose
Heparin	4000 - 5000 units IV push
Norepinephrine	BOLUS: 5 - 20 MCG IV (4mL of 1mg/mL in 250 ml = 16 MCG/mL) INFUSION: 0.05 - 0.5 MCG/kg/min
EPINEPHrine	BOLUS: 4 - 10 MCG IV (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01 - 0.1 MCG/kg/min
Esmolol	50 - 300 MCG/kg/min
Metoprolol	5 - 20 mg IV

DIFFERENTIAL diagnosis

Coronary artery disease with acute thrombus
Coronary artery disease with demand ischemia
Coronary artery embolism
Local Anesthetic Systemic Toxicity (CHKLST 12)
Severe hypoxia (CHKLST 11)

Critical CHANGES

If **PEA** develops, *go to* CHKLST 04
If **VF/VT** develops, *go to* CHKLST 05

Room for notes

16 Tachycardia - Unstable

INDEX

Persistent tachycardia with hypotension, ischemic chest pain, altered mental status, or shock

START

1. **Call for help and a code cart**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Turn FiO2 to 100%** and **turn down volatile anesthetic**
3. **Analyze rhythm**
   - If **wide complex, irregular**: treat as VF, *go to* CHKLST 05
   - If **narrow complex, regular**: consider adenosine while awaiting cardioversion
4. **Prepare for immediate synchronized cardioversion**
   - Sedate conscious patients unless deteriorating rapidly
5. **Cardiovert per instructions in gray box**
   - If **cardioversion needed and unable to synchronize**, use high-energy unsynchronized shocks (biphasic - select highest setting, monophasic - 360 J)
6. **If resistant to electrical conversion, consider amiodarone**
7. **Consider cardiology consultation**

DRUG DOSES & treatments

Adenosine	6 mg rapid IV push If persistent, 12 mg rapid IV push *Caution in severe asthma*
Amiodarone	150 mg IV over 10 minutes May repeat x1

SYNCHRONIZED CARDIOVERSION instructions

1. Turn monitor/defibrillator ON, set to defibrillator mode
2. Place electrodes on chest
3. Engage synchronization mode
4. Adjust EKG if necessary until SYNC markers seen with each R-wave
5. Select energy level
6. Press charge button
7. Press and hold shock button
8. Check monitor, if tachycardia persists, increase energy level
9. Engage synchronization mode after delivery of each shock

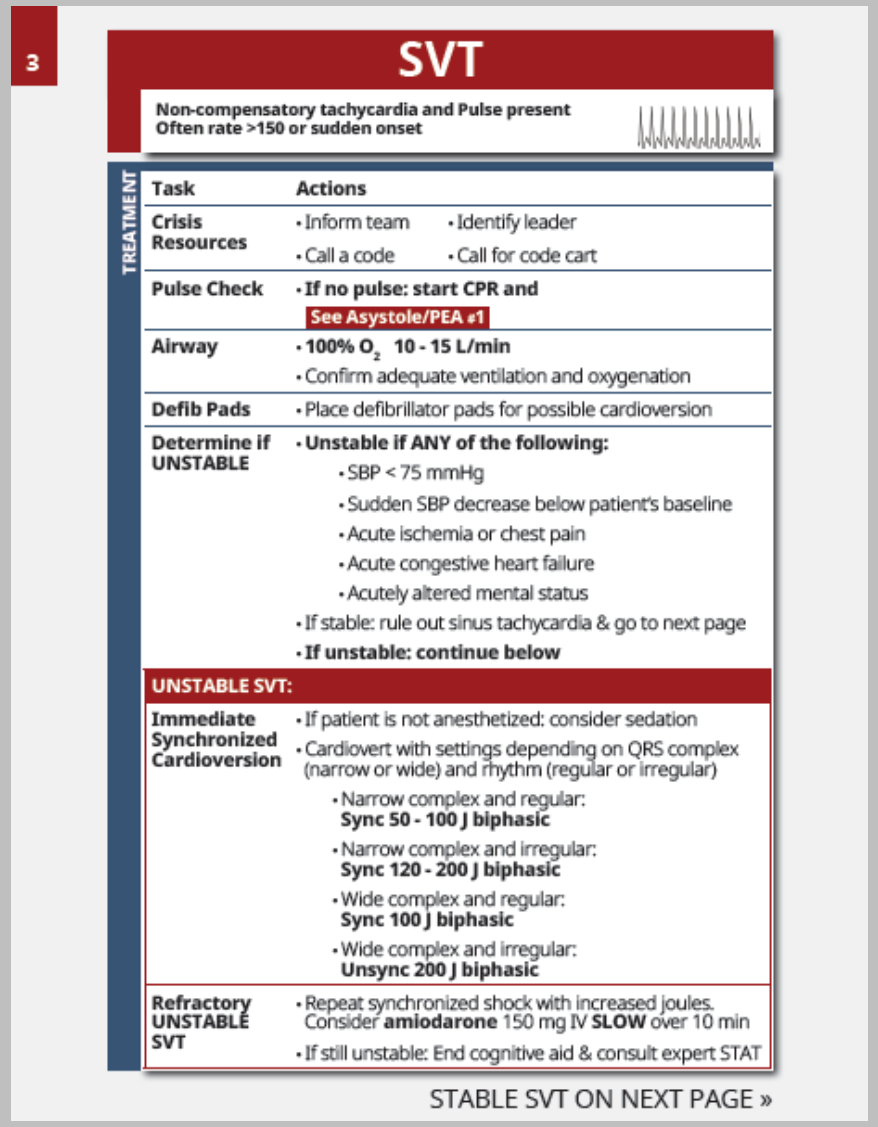
ENERGY Level

CONDITION	ENERGY LEVEL
Narrow complex, regular	50 J - 100 J
Narrow complex, irregular	120 J - 200 J biphasic; 200 J monophasic
Wide complex, regular	100 J
Wide complex, irregular	Treat as VF, *go to* CHKLST 05

Critical CHANGES

If **cardiac arrest** develops:
- Asystole/PEA, *go to* CHKLST 04
- VF/VT, *go to* CHKLST 05

Room for notes



3

SVT

Non-compensatory tachycardia and Pulse present
Often rate >150 or sudden onset

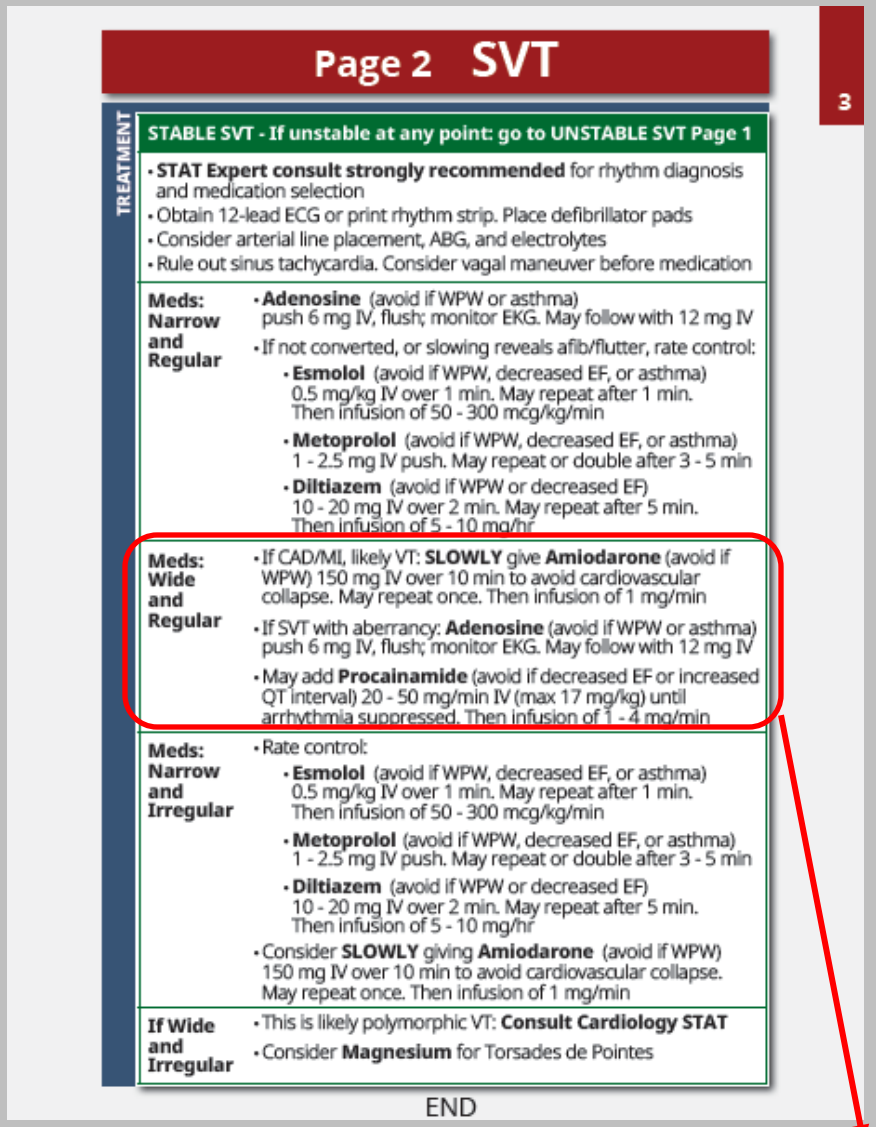
TREATMENT

Task	Actions
Crisis Resources	• Inform team • Identify leader • Call a code • Call for code cart
Pulse Check	• **If no pulse: start CPR and** See Asystole/PEA #1
Airway	• **100% O_2 10 - 15 L/min** • Confirm adequate ventilation and oxygenation
Defib Pads	• Place defibrillator pads for possible cardioversion
Determine if UNSTABLE	• **Unstable if ANY of the following:** • SBP < 75 mmHg • Sudden SBP decrease below patient's baseline • Acute ischemia or chest pain • Acute congestive heart failure • Acutely altered mental status • If stable: rule out sinus tachycardia & go to next page • **If unstable: continue below**

UNSTABLE SVT:

Immediate Synchronized Cardioversion	• If patient is not anesthetized: consider sedation • Cardiovert with settings depending on QRS complex (narrow or wide) and rhythm (regular or irregular) • Narrow complex and regular: **Sync 50 - 100 J biphasic** • Narrow complex and irregular: **Sync 120 - 200 J biphasic** • Wide complex and regular: **Sync 100 J biphasic** • Wide complex and irregular: **Unsync 200 J biphasic**
Refractory UNSTABLE SVT	• Repeat synchronized shock with increased joules. Consider **amiodarone** 150 mg IV **SLOW** over 10 min • If still unstable: End cognitive aid & consult expert STAT

STABLE SVT ON NEXT PAGE »



Page 2 SVT

3

TREATMENT

STABLE SVT - If unstable at any point: go to UNSTABLE SVT Page 1

- **STAT Expert consult strongly recommended** for rhythm diagnosis and medication selection
- Obtain 12-lead ECG or print rhythm strip. Place defibrillator pads
- Consider arterial line placement, ABG, and electrolytes
- Rule out sinus tachycardia. Consider vagal maneuver before medication

Meds: Narrow and Regular	• **Adenosine** (avoid if WPW or asthma) push 6 mg IV, flush; monitor EKG. May follow with 12 mg IV • If not converted, or slowing reveals afib/flutter, rate control: • **Esmolol** (avoid if WPW, decreased EF, or asthma) 0.5 mg/kg IV over 1 min. May repeat after 1 min. Then infusion of 50 - 300 mcg/kg/min • **Metoprolol** (avoid if WPW, decreased EF, or asthma) 1 - 2.5 mg IV push. May repeat or double after 3 - 5 min • **Diltiazem** (avoid if WPW or decreased EF) 10 - 20 mg IV over 2 min. May repeat after 5 min. Then infusion of 5 - 10 mg/hr
Meds: Wide and Regular	• If CAD/MI, likely VT: **SLOWLY** give **Amiodarone** (avoid if WPW) 150 mg IV over 10 min to avoid cardiovascular collapse. May repeat once. Then infusion of 1 mg/min • If SVT with aberrancy: **Adenosine** (avoid if WPW or asthma) push 6 mg IV, flush; monitor EKG. May follow with 12 mg IV • May add **Procainamide** (avoid if decreased EF or increased QT interval) 20 - 50 mg/min IV (max 17 mg/kg) until arrhythmia suppressed. Then infusion of 1 - 4 mg/min
Meds: Narrow and Irregular	• Rate control: • **Esmolol** (avoid if WPW, decreased EF, or asthma) 0.5 mg/kg IV over 1 min. May repeat after 1 min. Then infusion of 50 - 300 mcg/kg/min • **Metoprolol** (avoid if WPW, decreased EF, or asthma) 1 - 2.5 mg IV push. May repeat or double after 3 - 5 min • **Diltiazem** (avoid if WPW or decreased EF) 10 - 20 mg IV over 2 min. May repeat after 5 min. Then infusion of 5 - 10 mg/hr • Consider **SLOWLY** giving **Amiodarone** (avoid if WPW) 150 mg IV over 10 min to avoid cardiovascular collapse. May repeat once. Then infusion of 1 mg/min
If Wide and Irregular	• This is likely polymorphic VT: **Consult Cardiology STAT** • Consider **Magnesium** for Torsades de Pointes

END

- *2022 ITE Gaps in Knowledge*: "According to ACLS guidelines, procainamide is an appropriate therapeutic choice during the treatment of stable wide-complex tachycardia."

Room for notes

02 Anaphylaxis

Hypotension, bronchospasm, high peak-airway pressures, decreased breath sounds, tachycardia, urticaria

INDEX

02

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Give EPINEPHrine bolus**
   - Repeat bolus with increasing dose as needed
   - Consider EPINEPHrine infusion
3. **Establish/secure airway**
   - Turn FiO_2 to 100% or start supplemental oxygen
4. **Remove potential causative agents**
5. **Give fluid bolus**
6. **Consider...**
   - Minimize volatile anesthetics if patient remains unstable
   - Consider albuterol as adjunctive therapy for bronchospasm unresponsive to EPINEPHrine
   - Vasopressin bolus and/or infusion for patients with hypotension unresponsive to EPINEPHrine
   - Terminate procedure
   - Once hemodynamically stable:
     - Supplemental treatment with diphenhydrAMINE and corticosteroids
     - Tryptase level: Check within first hour, repeat at 4 and 18-24 hours

DRUG DOSES & treatments

EPINEPHrine	BOLUS: 10 - 50 MCG IV (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01- 0.1 MCG/kg/min If no IV access, 0.3 mg IM
Vasopressin	BOLUS: 1 -2 units IV (1 mL of 20 units/mL in 19 mL = 1 unit/mL) INFUSION: 0.03 units/min
Albuterol	2-3 puffs MDI 2.5 mg via nebulizer
Supplemental treatment	
diphenhydrAMINE	25 - 50 mg IV
Corticosteroids	Hydrocortisone 100 mg IV Methylprednisolone 1 mg/kg IV

Common CAUSATIVE AGENTS

Neuromuscular blocking agents
Antibiotics
Latex products
IV contrast and dyes
Sugammadex
Allogenic blood components, *go to* CHKLST 17
Chlorhexidine

Critical CHANGES

If **cardiac arrest** develops:
- Asystole/PEA, *go to* CHKLST 04
- VF/VT, *go to* CHKLST 05

If **airway obstruction** develops, *go to* CHKLST 07

Room for notes

18 Debriefing

INDEX

Real-time point-of-care debriefing by team members after a critical event AFTER the patient has been stabilized and transferred or patient care activities have ceased

START

1. **Lay the ground rules** (see What we BELIEVE box)
2. **Check-in**
   - *"How is everyone doing?"*
   - Assess if team members feel able to continue providing care
3. **Assess for immediate safety concerns to address**
   - **Malfunctioning equipment or drugs** to sequester?
   - Any remaining **patient care needs** to address?
   - Scheduling/staffing/resource **adjustments** for following cases?
4. **Provide space for team reactions**
   - Briefly summarize the case
   - Listen to team member emotional reactions
5. **Reflect on the care delivered**
   - *"What went well?"*
   - *"What could have gone better?"*
     - *"What should we do differently in the future?"*
   - *"Any lessons learned that we should share more broadly?"*
6. **Remind team of resources available** - see "Local RESOURCES"
   - Emphasize **peer support programs** and **employee assistance programs**
7. **Consider any needed follow up**
   - Team member mental health needs
   - Safety or quality improvement reporting needs
   - OR operational needs

What we BELIEVE

We believe that everyone involved in this event is capable well trained and committed to delivering the best possible care
Our goal is to support one another and improve the care we give, not to assign blame

Elements of Debriefing: "WATER"

Welfare check (Step 2)
Acute Corrections (Step 3)
Team Reactions and Reflections (Step 4)
Education (Step 5)
Resource Awareness (Steps 6 & 7)

Local RESOURCES

Patient Safety Concerns
- Administrator On-Call
- Quality and Safety Leadership

Operating Room Operations
- Administrator On-Call
- Charge Nurse
- Anesthesiologist in Charge
- Division Chief

Emotional Support
- Peer Support Program Leader
- Employee Assistance Program
- Trained Debriefing Facilitator

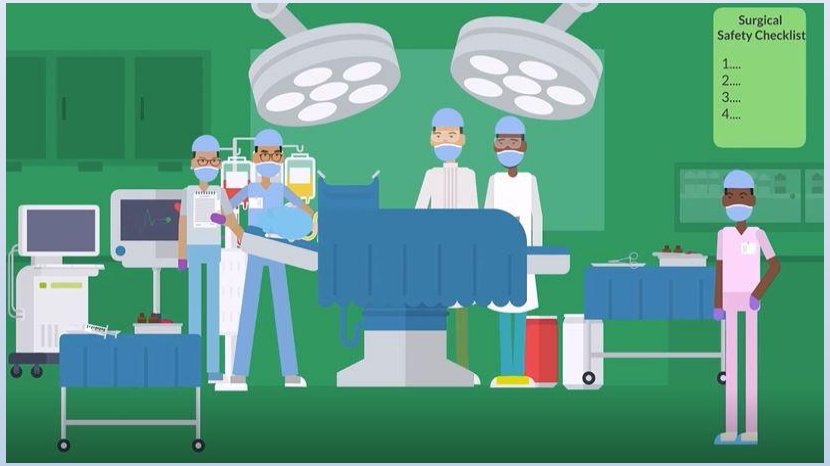
Legal Concerns
- Risk Management
- Hospital Legal Team

Room for notes

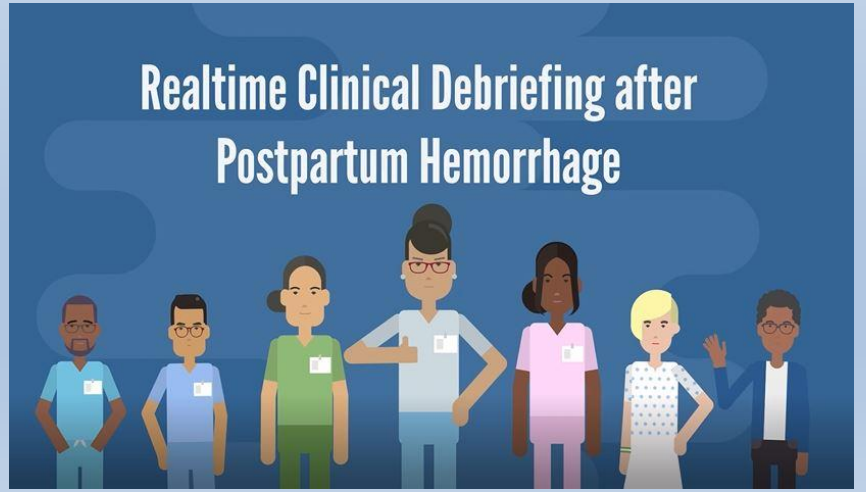
Additional Online Education Material on Realtime Perioperative Critical Event Debriefing

Online-module-style webpage on datadrivendidactics.org dedicated to literature, cognitive aids, and educational videos on realtime perioperative critical event debriefing

Postpartum Hemorrhage

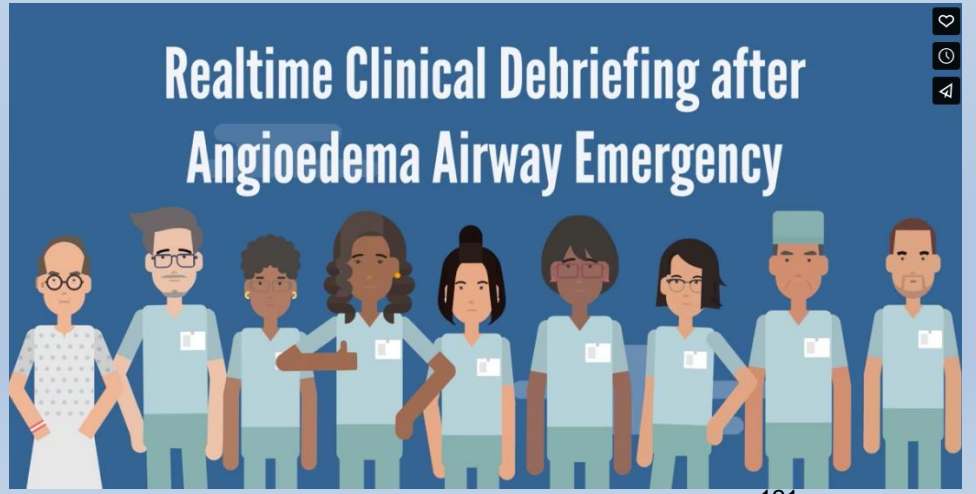


Postpartum hemorrhage simulation; includes topics from Obstetrics Section (OB Hemorrhage Crisis Checklist, uterotonics, antifibrinolytics, and other areas); second video gives practical example of debriefing checklist in use.



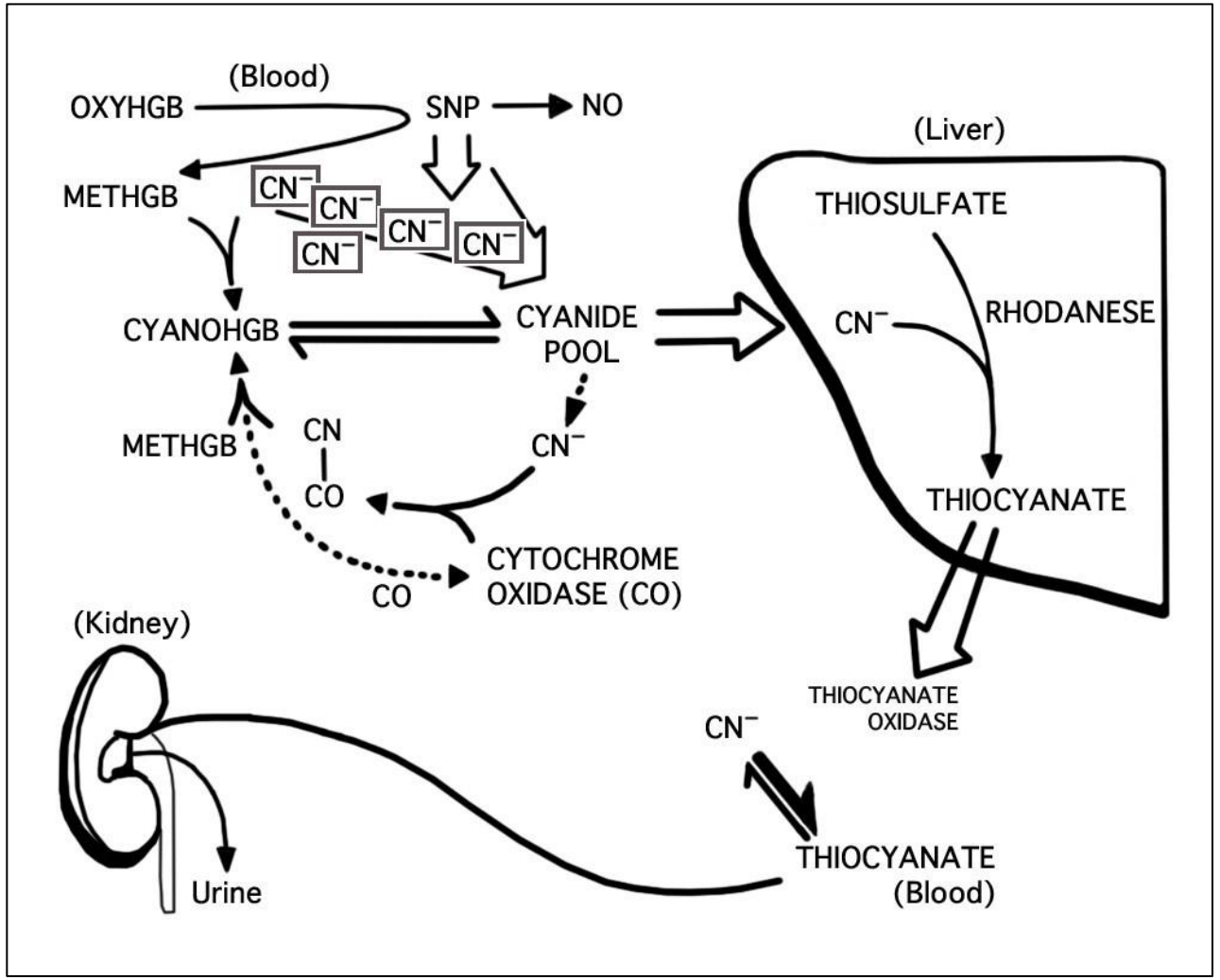
Angioedema Airway Emergency

Angioedema with airway compromise in the emergency department simulation; involves topics from Anatomy & Airway section (difficult airway management, beginning with awake fiberoptic intubation); second video gives practical example of debriefing checklist in use.



www.datadrivendidactics.org/debriefing-resources

“Image/Buzzwords Co-slides”: Sodium Nitroprusside, Cyanide, Methemoglobinemia



CN-: cyanide ions; CO: cytochrome oxidase; CYANOHGB: cyanomethemoglobin; METHGB: methemoglobin; NO: nitric oxide; OXYHGB: oxyhemoglobin; SNP: sodium nitroprusside

Image: Hammer et al. PMID 23631460, via Creative Commons CC BY 2.0 https://bmcanesthesiol.biomedcentral.com/articles/10.1186/1471-2253-13-9

Room for notes

"Image/Buzzwords Co-slides": Sodium Nitroprusside, Cyanide, Methemoglobinemia

15X

Room for notes

- Sodium Nitroprusside and Pathogenesis of Cyanide Toxicity (see figure):

1. OXYHGB donates electron to SNP to generate NO and 5 CN- . OXYHGB becomes METHGB, which can bind one cyanide ion to become CYANOHGB (a nontoxic compound).
2. If other CN- cannot be cleared, they bind to the ferric ion of mitochondrial cytochrome oxidase & block oxygen utilization in oxidative phosphorylation → anaerobic metabolism.
    - Diagnosis of cyanide toxicity: relevant history, **profound metabolic acidosis, elevated serum lactate,** bright red venous blood (as opposed to methemoglobinemia, which is chocolate brown), **mixed venous blood with INCREASED oxygen levels** (less oxygen taken up by cells). Initial nonspecific symptoms that can progress to cardiopulmonary collapse, seizures, and multisystem organ failure.
    - Treatment of cyanide toxicity: (1) Sodium thiosulfate: increases metabolism of CN- to thiocyanate (cleared by kidneys). Pts w/impaired renal function are at risk for thiocyanate toxicity (tinnitus, visual disturbances, delirium, seizures); (2) Nitrates (e.g., amyl nitrate, sodium nitrite) via their ability to produce METHGB; (3) Hydroxocobalamin(parenteral preparation of Vitamin B12): chelates CN- and inactivates it.

- Methemoglobinemia:
    - Notable causative drugs include: nitroprusside, nitrates, nitroglycerin, metoclopramide, cocaine and several local anesthetics – particularly benzocaine (in theory, also lidocaine & prilocaine, which are the components of EMLA cream).
    - METHGB prevents O2 binding to HGB & OXYHGB develops increased affinity for O2 → **left-shift of oxygen-hemoglobin dissociation curve, cyanosis, SpO2 inaccurately 85%** (need multiwavelength pulse oximeter ("Pulse CO-Oximeter" is Masimo trademark).
    - Treatment: Methylene blue (**UNLESS** patient has glucose-6-phosphate dehydrogenase [G6PD] deficiency – these patients can get hemolysis and worsened condition from methylene blue) +/- ascorbic acid (aka Vitamin C, which is ok to use in pts with G6PD deficiency).

Smith's Anesthesia for Infants and Children, 10th Ed, Ch 22. // Saeui et al. PMID 21075587. // Friederich JA et al. PMID: 7598246. // Hammer et al. PMID 23631460 // Henretig et al PMID 31018070 // Parker-Cote et al PMID 29417853 // UpToDate "Cyanide Poisoning" // UpToDate "Methemoglobinemia"

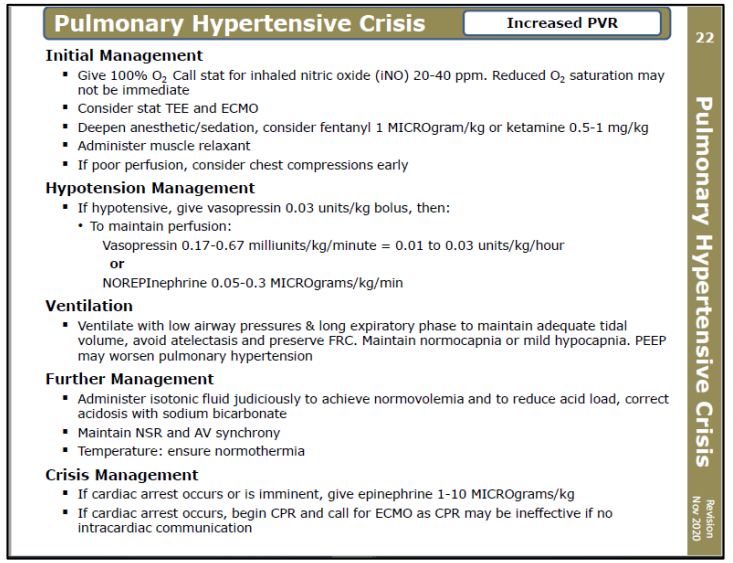
Nitric Oxide

5X

- Formed by endothelial cells or given via inhalation. **Inhaled** nitric oxide produces **selective pulmonary vasodilation** (smooth muscle relaxation from cGMP pathways).

- Indications:
  - Pulmonary hypertension
  - Persistent pulmonary hypertension of newborn
  - ARDS
  - Neonatal respiratory distress syndrome,
  - Altitude sickness
  - Chronic lung disease
  - Sickle cell disease (mechanism unclear, may cause peripheral vasodilation in these patients).

Handout: Pulmonary Hypertensive Crisis Checklist (Soc Ped Anes)



Pulmonary Hypertensive Crisis — Increased PVR

22

Initial Management
- Give 100% O_2. Call stat for inhaled nitric oxide (iNO) 20-40 ppm. Reduced O_2 saturation may not be immediate
- Consider stat TEE and ECMO
- Deepen anesthetic/sedation, consider fentanyl 1 MICROgram/kg or ketamine 0.5-1 mg/kg
- Administer muscle relaxant
- If poor perfusion, consider chest compressions early

Hypotension Management
- If hypotensive, give vasopressin 0.03 units/kg bolus, then:
  - To maintain perfusion:
    Vasopressin 0.17-0.67 milliunits/kg/minute = 0.01 to 0.03 units/kg/hour
    or
    NOREPInephrine 0.05-0.3 MICROgrams/kg/min

Ventilation
- Ventilate with low airway pressures & long expiratory phase to maintain adequate tidal volume, avoid atelectasis and preserve FRC. Maintain normocapnia or mild hypocapnia. PEEP may worsen pulmonary hypertension

Further Management
- Administer isotonic fluid judiciously to achieve normovolemia and to reduce acid load, correct acidosis with sodium bicarbonate
- Maintain NSR and AV synchrony
- Temperature: ensure normothermia

Crisis Management
- If cardiac arrest occurs or is imminent, give epinephrine 1-10 MICROgrams/kg
- If cardiac arrest occurs, begin CPR and call for ECMO as CPR may be ineffective if no intracardiac communication

Pulmonary Hypertensive Crisis

Revision Nov 2020

- Half-life: a few seconds. It should be slowly weaned and not abruptly discontinued.

- End products of metabolism: methemoglobin and nitrate.

Room for notes

Pulmonary Hypertensive Crisis Checklist. Society for Pediatric Anesthesia. // Nitric Oxide ClinicalKey Drug Monograph. Accessed 12/18/19.

Pulmonary Hypertensive Crisis

Increased PVR

22

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Pulmonary Hypertensive Crisis

Revision Nov 2020

Room for notes

Pulmonary Hypertensive Crisis

Mean PAP > Mean SAP

Recognition: Acute ↓ O2 sat, ↓ SBP, ↓EtCO2, ↑ CVP, ↑Airway pressures

Mechanism: Abrupt pulmonary vasoconstriction with resultant RV failure, ↓CO, and ↓ BP

Management

- Administer 100% oxygen
- Call for nitric oxide (iNO) ASAP
- Hyperventilation and alkalinization
- Support cardiac output
  - ✓ Adequate preload
  - ✓ Inotropes: dopamine, dobutamine, epinephrine
- Utilize pulmonary vasodilators
- Attenuate noxious stimuli: deepen anesthetic/sedation, administer narcotic
- Maintain NSR and AV synchrony
- Consider ECMO activation

Diagnostic studies

- ECG: New ST segment changes
- Echo: RVSP > ½ systemic, worsening TR, ↑ RV dilatation or dysfunction, systolic septal flattening

Pulm Vasodilator Class & Mechanism	Drug and Dosing
Nitric Oxide pathway:	
▪INHALED NO (iNO) Activates cGMP dependent signaling pathways. ↑ intracellular Ca uptake and smooth muscle relaxation	• iNO 10-40ppm
▪Phosphodiesterase Inhibitors ↓ PDE 3,5 effect thereby ↑ing intracellular cGMP levels	• Milrinone IV 0.25-0.75mcg/kg/min
Prostacyclin analogs ↑prostacyclin effect mediating pulmonary vasodilation, smooth muscle relaxation and inhibiting platelet aggregation.	• Epoprostenol IV 1-2ng/kg/min (maintenance) or 40ng/kg/min INHALED • Iloprost 2.5-5mcg INHALED

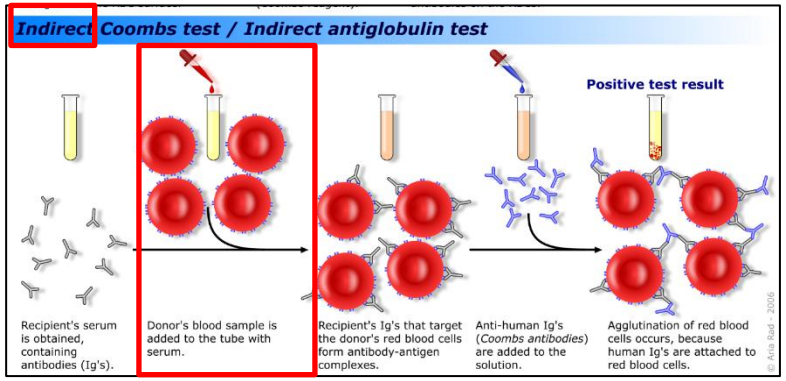
Society for Pediatric Anesthesia Critical Event Checklists. Prior version. Latest update available at http://www.pedsanesthesia.org/

Room for notes

Transfusions

21X

Room for notes

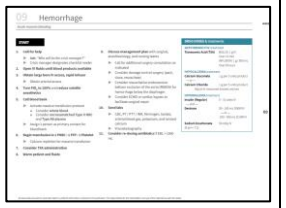


Antibody Screen vs. Crossmatch (both can be done via indirect Coombs test): **Antibody screen:** Recipient's serum mixed with commercially supplied RBCs [known to contain common antigens]. **Crossmatch**: Recipient's serum mixed with Donor RBCs.

Washed, Leukoreduced, Irradiated Blood Products:

- IgA deficiency and transfusion: Pt with anti-IgA antibodies and donor has IgA antigen → severe, often rapid, allergic reaction can occur.
  - Alternative option: **Washed** RBCs "so that all traces of donor IgA have been removed or with blood that lacks the IgA protein."[1]
- **Leukoreduced** blood products lower risk of: febrile reaction; HLA alloimmunization, CMV, transmission of variant Creutzfeld-Jakob disease, and leukocyte-induced immunomodulation. Many institutions implement "universal leukoreduction."[1]
- **Irradiated** cellular products (RBC, platelets, granulocytes – FFP and cryoprecipitate are noncellular and no not need irradiation): Prevents proliferation of donor T-lymphocytes (can cause graft-versus-host disease). Indications include critically ill children, marrow cell transplant recipients, immunodeficient patients and other select indications.[1]
  - *2021 ITE Gaps in Knowledge*: "Gamma radiation of blood is appropriate for immunodeficient patients."

Handout:
Hemorrhage Crisis Checklist



Citrate Intoxication & Transfusion: Citrate binds (chelates) calcium and can cause **hypocalcemia** (hypotension, narrow pulse pressure, arrhythmias, confusion, tetany) and coagulopathy (calcium is co-factor in coagulation cascade). **Patients at increased risk**: liver disease/liver transplant status, as well as pediatric patients (reduced citrate metabolism).[1-4]

Upper Figure: Coombs test schematic. Available at https://en.wikipedia.org/wiki/Coombs_test. Available by GNU Free Documentation License & Creative Commons Attribution-Share Alike 3.0 Unported license. // 1. Miller 10th Ed Ch 45 // 2. Miller 10th Ed. Ch 43 // 3. Miller 10th Ed Ch 56 // 4. Barash 9th Ed Ch 53

09 Hemorrhage

Acute massive bleeding

INDEX

START

1. **Call for help**
   - ▶ **Ask:** *"Who will be the crisis manager?"*
   - ▶ Crisis manager designates checklist reader
2. **Open IV fluids until blood products available**
3. **Obtain large bore IV access, rapid infuser**
   - ▶ Obtain arterial access
4. **Turn FiO_2 to 100%** and **reduce volatile anesthetics**
5. **Call blood bank**
   - ▶ Activate massive transfusion protocol
     - Consider **whole blood**
     - Consider **uncrossmatched Type O RBC** and **Type AB plasma**
   - ▶ Assign 1 person as primary contact for blood bank
6. **Begin transfusion in 1 PRBC : 1 FFP : 1 Platelet**
   - ▶ Calcium repletion for massive transfusion
7. **Consider TXA administration**
8. **Warm patient and fluids**
9. **Discuss management plan** with surgical, anesthesiology, and nursing teams
   - ▶ Call for additional surgery consultation as indicated
   - ▶ Consider damage control surgery (pack, close, resuscitate)
   - ▶ Consider resuscitative endovascular balloon occlusion of the aorta (REBOA) for hemorrhage below the diaphragm
   - ▶ Consider ECMO or cardiac bypass to facilitate surgical repair
10. **Send labs**
    - ▶ CBC, PT / PTT / INR, fibrinogen, lactate, arterial blood gas, potassium, and ionized calcium
    - ▶ Viscoelastography
11. **Consider re-dosing antibiotics** if EBL > 1500 mL

DRUG DOSES & treatments

ANTIFIBRINOLYTIC treatment

Tranexamic Acid (TXA)	BOLUS: 1 g IV Over 10 min INFUSION: 1 g/ 500 mL Over 8 hours

HYPOCALCEMIA treatment

Calcium Gluconate	1 g per 3 units product
— or —	
Calcium Chloride	1 g per 5 units product
Adjust to measured ionized calcium	

HYPERKALEMIA treatment

Insulin (Regular)	5 - 10 units IV
— and —	
Dextrose	50 - 100 mL D50W IV — or — 250 - 500 mL D10W IV
Sodium bicarbonate (if pH < 7.2)	50 mEq IV

09

Room for notes

Transfusions (cont'd)

12X

Room for notes

#1 cause of Transfusion-Associated Fatality (2017-2021/FDA): **Transfusion Associated Circulatory Overload (TACO) (32%);** #2: Transfusion related acute lung injury (TRALI) and possible TRALI (21%); #3: hemolytic transfusion reaction (HTR) due to non-ABO incompatibilities (14%); #4: Microbial contamination (13%); #5: Anaphylaxis (9%); #6: HTR due to ABO incompatibilities (7%); #7: transfusion reaction type not determined (3%); #8: Other (1%) (https://www.fda.gov/media/172382/download).[1]

Contents of cryoprecipitate: Fibrinogen, fibronectin, vWF, FVIII, and FXIII. [Barash 9th Ed/Ch 17]

Indications for FFP (Miller 10th Ed, Ch 45; based on ASA Practice Guidelines for Blood Management;):

1. "…correction of coagulopathy when [INR > 2], in the absence of heparin.
2. …correction of coagulopathy due to coagulation deficiencies in patients transfused with more than one blood volume (approximately 70 mL/kg) when coagulation studies cannot be easily or quickly obtained.
3. Replacement of known coagulation factor deficiencies with associated bleeding, disseminated intravascular coagulation (DIC), or both, when specific components are not available.
4. Reversal of warfarin anticoagulation when severe bleeding is present and prothrombin complex concentrations are not available."

❖ Barash 9th Ed/Ch 17 also adds: "Heparin resistance secondary to antithrombin deficiency when antithrombin concentrate is not available" and "treatment of hereditary angioedema when C1-esterase inhibitor is not available."

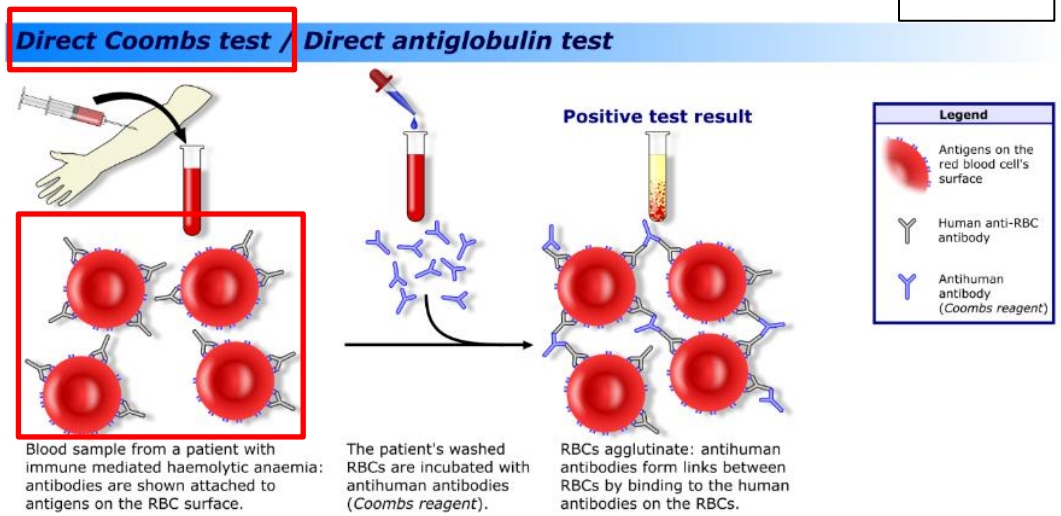
Suggested Criteria for Preop Transfusion of Non-RBC Blood Products (ASA 2015 Practice Guidelines for Blood Management):

1. FDA. Fatalities reported to FDA following blood collection and transfusion annual summary for fiscal year xxxx. https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/transfusiondonation-fatalities

Transfusion Reactions

15X

- Mild febrile vs hemolytic reaction: "A **direct antiglobulin test** readily differentiates a hemolytic reaction from a febrile reaction because this test rules out the attachment of antibodies to transfused donor RBCs…No consensus exists on whether the transfusion should be terminated when a febrile reaction occurs." [Miller 10th Ed, Ch45]
- Hemolytic transfusion reaction lab findings: low serum haptoglobin (hemolysis → hemoglobinemia → hemoglobin binds to haptoglobin), elevated indirect bilirubin and lactate dehydrogenase, hemoglobinuria, positive direct Coombs test, possible DIC.
- Delayed hemolytic transfusion reaction: May present 2-21 days after the transfusion (decreased hematocrit, jaundice, hemoglobinuria, and/or impaired renal function).
- Handout: Crisis Checklist for Transfusion Reaction.



Transfusion Reactions — Reactions may occur with any type of blood product

26

For All Reactions:

- Stop transfusion
- Disconnect donor product and IV tubing
- Infuse normal saline through clean tubing
- Examine blood product ID; determine correct pt
- Send product to Blood Bank
- Determine the type of reaction:

	Hemolytic	Non-Hemolytic	Anaphylactic
Signs	Hemoglobinemia, hemoglobinuria, DIC, ↓ BP, ↑ HR, bronchospasm	↓ BP, bronchospasm, pulmonary edema, fever, rash	Erythema, urticaria, angioedema, bronchospasm, tachycardia, shock
Treatment	▪ Furosemide 1-2 mg/kg IV (MAX 40 mg) ▪ Mannitol 0.25-1 g/kg ▪ Support BP to maintain renal perfusion ▪ Maintain urine output at least 1-2 mL/kg/hour ▪ Prepare for cardiovascular instability ▪ Send blood and urine sample to laboratory	▪ Treat fever ▪ Treat pulmonary edema ▪ Observe for signs of hemolysis	▪ Support airway and circulation as necessary ▪ EPINEPHrine 1-10 MICROgrams/kg IV ▪ DiphenhydrAMINE 1 mg/kg IV (MAX 50 mg) ▪ MethylPREDNISolone 2 mg/kg IV (MAX 60 mg) ▪ Maintain intravascular volume

Revision June 2020

Transfusion Reactions

Room for notes

Society for Pediatric Anesthesia Critical Event Checklists. Revision Packet March 2023. Latest update available at http://www.pedsanesthesia.org // Miller 10th Ed, Ch 45 // Hematology: Basic Principles and Practice 7th Ed, Ch 110. // Rad A. Coombs test schematic. https://en.wikipedia.org/wiki/Coombs_test. Available by GNU Free Documentation License & Creative Commons Attribution-Share Alike 3.0 Unported license. // https://www.ncbi.nlm.nih.gov/books/NBK448158/

17 Transfusion Reaction

INDEX

Hemolytic Reaction: *Cardiac instability, bronchospasm, bleeding, dark urine;* ***Non-hemolytic Reaction:*** *fever, rash, pulmonary edema;*
Anaphylactic Reaction: *hypotension, urticaria, bronchospasm*

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Disconnect any blood products infusing**
   - Check blood product labels for correct patient name and ABO compatibility
   - Send the blood product(s) back to the blood bank for evaluation
3. **Support hemodynamics with EPINEPHrine**
   - Repeat bolus with increasing dose as needed
   - Consider EPINEPHrine infusion
4. **Manage bronchospasm**
   - FiO_2 100%
   - Albuterol or EPINEPHrine
5. **Maintain urine output if hemolysis noted**
   - Volume load 20 mL / kg crystalloid. *Caution if signs of volume overload.*
   - Consider furosemide or mannitol to goal UOP 1-2 mL / kg / hr
6. **Monitor labs**
   - Arterial or venous blood gas, electrolytes
   - PT, aPTT, fibrinogen, viscoelastography
   - Direct antiglobulin (Coomb's) test, haptoglobin, LDH, free hemoglobin, tryptase
7. **Consider invasive lines**
   - Arterial line for ongoing hemodynamic instability
   - Central venous catheter for vasopressors
8. **Further treatment**
   - Consider hematology consult and ICU disposition

DRUG DOSES & treatments

EPINEPHrine	BOLUS: 10 -20 MCG IV (1 mg in 100 mL = 10 MCG/mL) INFUSION: 0.01 - 0.1 MCG/kg/min
Furosemide	40 mg IV
Albuterol	2-3 puffs MDI via ETT 2.5 mg via nebulizer

DIFFERENTIAL diagnosis

Anaphylaxis from other causes (CHKLST 02)
Hypotension (CHKLST 10)
Transfusion Related Acute Lung Injury (TRALI)
Transfusion-Associated Circulatory Overload (TACO)
Septic Shock
Other hemolytic anemias (idiopathic, HUS, HELLP)

17

Room for notes

von Willebrand disease (vWD)

2X

Von Willebrand factor (vWF): **synthesized in the endothelium and platelet**; vWF circulates as a complex with Factor VIII and acts as a ligand for platelet adhesion via the GPIb receptor. Disease can be quantitative or qualitative.

Desmopressin (DDAVP): analog of antidiuretic hormone/ vasopressin; stimulates release of vWF, factor 8, and plasminogen activator (no clinically significant tPA-like fibrinolysis). Typical IV dose: 0.3 mcg/kg over 30-60min. Intranasal spray also exists.

**** Avoid DDAVP in type 2B**: DDAVP in pts with type 2B → increased abnormal vWF → thrombocytopenia.

Type	Quantitative/Qualitative	Description	Notes on Treatment
1	Quantitative vVF defect	Most common (80% of cases)	Periop DDAVP often used
2A	Qualitative defect; patient may also have a quantitative component	Defect in platelet adhesion (2A also has deficiency of vWF multimers)	Factor 8 and/or vWF preparation may be needed
2M			
2N		Decreased vWF affinity for Factor 8	Factor 8 often needed (vWF may not suffice)
2B		**Increased** platelet binding affinity**	Often treated with (1) Factor 8 plus vWF or (2) cryoprecipitate
3	Quantitative (almost complete absence of vWF)	vWF levels may be undectectable	

Anes Uncomm Dz 6th Ed Ch 11 // Miller 9th Ed Ch 31 // Barash 9th Ed Ch 17// Stoelting 8th Ed Ch 23 // Hematology: Basic Principles and Practice 7th Ed, Ch 138

Room for notes

Hemophilia; Factor V Leiden; Porphyria

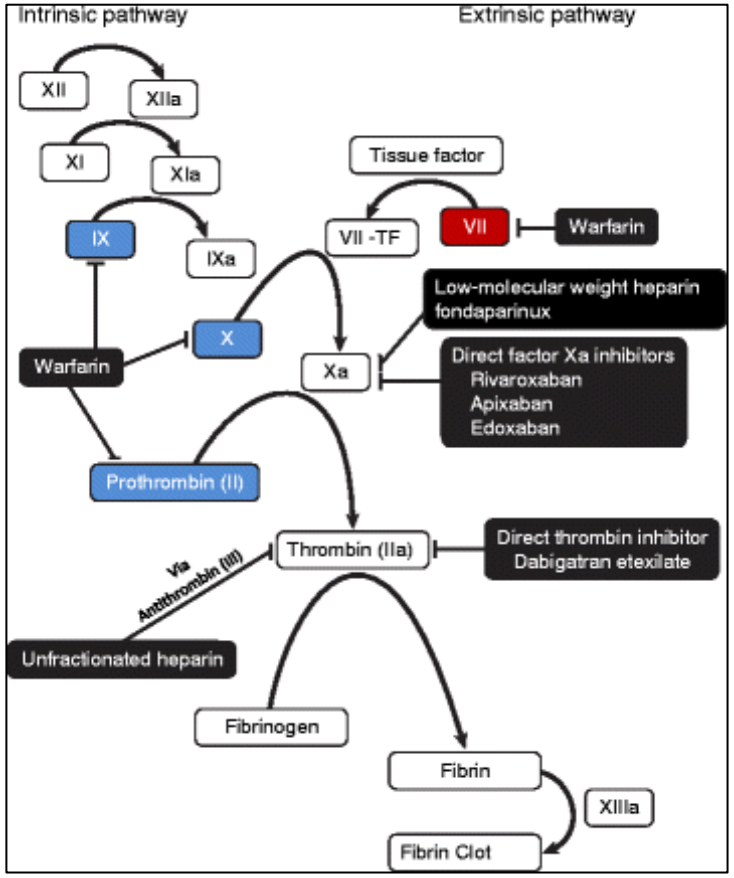
11X
Incl next slide

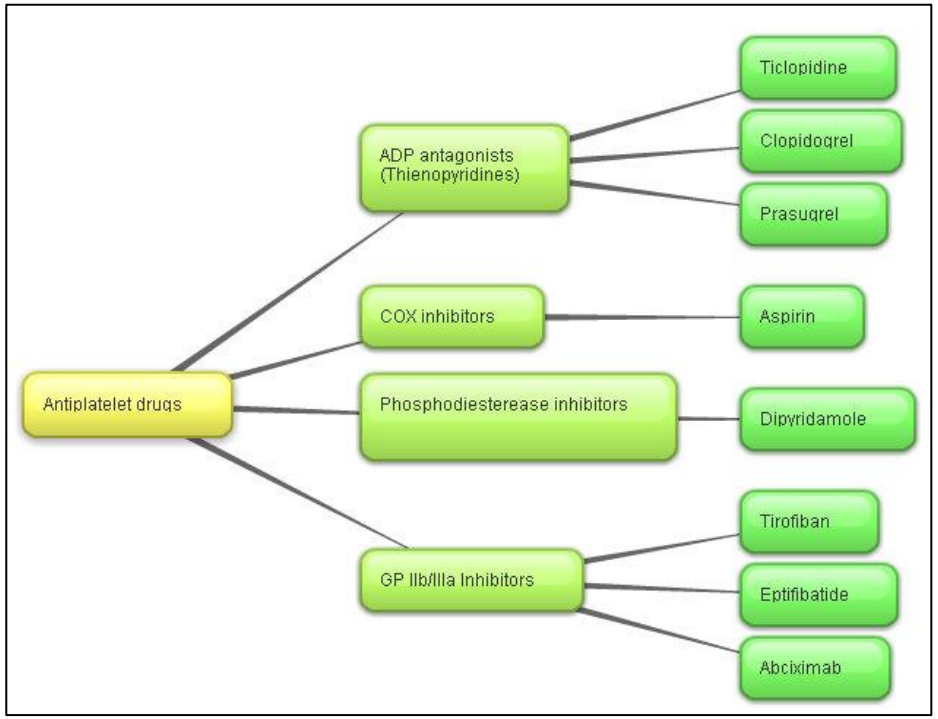
Room for notes

- Hemophilia A: defect in Factor VIII activity; Hemophilia B: deficiency of Factor IX activity.
  - Both X-linked; often present in childhood (spontaneous joint/deep muscle bleeding).
- Hemophilia A & elective procedures (assuming no Factor VIII antibodies): **Involve hematologist. Possible considerations**:
  - Minor procedure/mild hemophilia A: desmopressin (DDAVP) 30 min preop.
  - Major procedures: consider Factor VIII concentrate (or FFP, cryoprecipitate), as well as adjunct antifibrinolytics. [Miller 10th Ed, Ch 29]
- Hemophilia B & elective procedures (assuming no Factor IX antibodies): **Involve hematologist. Possible considerations**:
  - Minor procedure or mild bleeding episode: recombinant or purified Factor IX (or Factor IX-PCC).
  - Major procedures: recombinant or purified Factor IX (Factor IX-PCC has active clotting factors and can lead to thromboses if given for major procedure). [Miller 10th Ed, Ch 29]
- Patients with Hemophilia from Factor VIII or IX antibodies: Patients with "inhibitors to FVIII or FIX often respond to bypass agents such as rFVIIa or PCCs [prothrombin complex concentrates." [Barash 9th Ed/Ch 17] FEIBA (factor VIII inhibitor bypassing agent) can be considered for patient with Factor VIII antibodies [Miller 10th Ed Ch 29].
- Factor V Leiden: Mutation to Factor V that makes it insensitive to activated protein C (a natural anticoagulant) → hypercoagulable state. **Treatment:** "Only patients who present with a thrombotic event require anticoagulation." [Anes Uncomm Dx 6th ed]
- Acute Intermittent Porphyria: an inducible porphyria that results from defect in heme synthesis. **Agents that can trigger an attack include** (acute neurological/GI symptoms, hypertension/tachycardia): ketorolac, sulfonamides, barbituates, diazepam, phenytoin, and birth control pills. Ketamine and etomidate have been porphyrogenic in rats.

OpenAnesthesia: Hemophilia: Factor deficiencies. Srivastava A, et al. Guidelines for the management of hemophilia. *Haemophilia*. 2013;19(1):e1– e47.

Popular Antithrombotic (Anticoagulant/Antiplatelet) Agents





- Unfractionated heparin:[1] "acts at multiple sites in coagulation process; binds to antithrombin III, catalyzing inactivation of thrombin and other clotting factors."
- Enoxaparin, Dalteparin:[1] "binds to antithrombin III and accelerates activity, inhibiting thrombin and factor Xa (low-molecular weight heparin)."
- Fondaparinux: "selectively binds to antithrombin III, potentiating factor Xa neutralization and inhibiting thrombin formation (synthetic selective factor Xa inhibitor)."[1] Sometimes used as alternative to unfractionated heparin in patients with heparin-induced thrombocytopenia.[3]
- "Heparins act indirectly by binding to antithrombin (AT, formerly called AT III…)…which converts AT from a slow to a rapid inactivator of coagulation factors (e.g. thrombin [factor IIa], factor Xa)….Both unfractionated and low-molecular weight heparins inactivate factor Xa via AT. However, unfractionated heparin is a much more efficient inactivator of thrombin"[2]

1. Epocrates // 2. UpToDate "Heparin and LMW heparin: Dosing and adverse effects" // 3. UpToDate "Fondaparinux: Drug information" // Anticoagulants image: Brown KS et al. PMID 27659071. via Creative Commons CC-BY-4.0 // Antiplatelets image: Vtvu, CC BY-SA 3.0 via Wikimedia Commons (https://commons.wikimedia.org/wiki/File:Antiplatelet_agents_classification.jpg)

Room for notes

Self-Directed Deep Dive: Antithrombotics and Antihemorrhagics
WHO Anatomical Therapeutic Chemical (ATC) Classification System

V·T·E	Antithrombotics (thrombolytics, anticoagulants and antiplatelet drugs) (B01)		[hide]
Antiplatelet drugs	Glycoprotein IIb/IIIa inhibitors		Abciximab · Eptifibatide · Orbofiban · Roxifiban · Sibrafiban[§] · Tirofiban
	ADP receptor/$P2Y_{12}$ inhibitors		Thienopyridines (Clopidogrel · Prasugrel · Ticlopidine) · Nucleotide/nucleoside analogs (Cangrelor · Elinogrel · Ticagrelor)
	Prostaglandin analogue (PGI2)		Beraprost · Iloprost · Prostacyclin · Treprostinil
	COX inhibitors		Acetylsalicylic acid/Aspirin[#] · Aloxiprin · Carbasalate calcium · Indobufen · Triflusal
	Thromboxane inhibitors		Thromboxane synthase inhibitors (Dipyridamole (+ aspirin) · Picotamide · Terbogrel) · Receptor antagonists (Terbogrel · Terutroban[§])
	Phosphodiesterase inhibitors		Cilostazol · Dipyridamole · Triflusal
	Other		Cloricromen · Ditazole · Vorapaxar
Anticoagulants	Vitamin K antagonists (inhibit II, VII, IX, X)		Coumarins: Acenocoumarol · Coumatetralyl · Dicoumarol · Ethyl biscoumacetate · Phenprocoumon · Warfarin[#] · 1,3-Indandiones: Clorindione · Diphenadione · Phenindione · Other: Tioclomarol
	Factor Xa inhibitors (with some II inhibition)	Heparin group/ glycosaminoglycans/ (bind antithrombin)	**Low-molecular-weight heparin** (Bemiparin · Certoparin · Dalteparin · Enoxaparin · Nadroparin · Parnaparin · Reviparin · Tinzaparin) · Oligosaccharides (Fondaparinux · Idraparinux[§]) · Heparinoids (Danaparoid · Dermatan sulfate · Sulodexide)
		Direct Xa inhibitors ("xabans")	Apixaban · Betrixaban · Darexaban[§] · Edoxaban · Otamixaban[§] · Rivaroxaban
	Direct thrombin (IIa) inhibitors		Bivalent: Hirudin (Bivalirudin · Desirudin · Lepirudin[‡]) · Univalent: Argatroban · Dabigatran · Efegatran · Inogatran[§] · Melagatran[‡] · Ximelagatran[‡]
	Other		Antithrombin III · Defibrotide · Nafamostat · Protein C (Drotrecogin alfa[‡]) · Ramatroban · REG1
Thrombolytic drugs/ fibrinolytics	Plasminogen activators: r-tPA (Alteplase[#] · Reteplase · Tenecteplase · Desmoteplase[†]) · UPA (Saruplase · Urokinase) · Anistreplase · Monteplase · Streptokinase[#] · Other serine endopeptidases: Ancrod[‡] · Brinase · Fibrinolysin		
Non-medicinal	Citrate · EDTA · Oxalate		

[#]WHO-EM · [‡]Withdrawn from market · Clinical trials: ([†]Phase III · [§]Never to phase III)

V·T·E	Antihemorrhagics (B02)		[hide]
Antihemorrhagics (coagulation)	Systemic	Vitamin K	Phytomenadione (K_1) · Menadione (K_3)
		Coagulation factors	*intrinsic:* IX/Nonacog alfa · VIII/Damoctocog alfa pegol/Efmoroctocog alfa/Moroctocog alfa/Susoctocog alfa/Turoctocog alfa *extrinsic:* VII/Eptacog alfa *common:* X · II/Thrombin · I/Fibrinogen · XIII/Catridecacog *combinations:* Prothrombin complex concentrate (II, VII, IX, X, protein C and S)
		Other systemic	Batroxobin · Carbazochrome · Etamsylate · Fostamatinib · *thrombopoietin receptor agonist* (Romiplostim · Avatrombopag · Eltrombopag · Lusutrombopag)
	Local		Absorbable gelatin sponge · Calcium alginate · Collagen · Epinephrine/adrenalone · Fibrin glue · Oxidized cellulose · Tetragalacturonic acid hydroxymethylester · Thrombin · Hemostatic Powder Spray TC-325
Antifibrinolytics	*amino acids* (Aminocaproic acid · Tranexamic acid · Aminomethylbenzoic acid) · *serpins* (Aprotinin · Alfa1 antitrypsin · C1-inhibitor · Camostat) · unsorted (Ulinastatin)		

ASRA Guidelines for Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic therapy

Wikipedia: ATC code B01 (https://en.wikipedia.org/wiki/ATC_code_B01) and B02 (https://en.wikipedia.org/wiki/ATC_code_B02) // WHO Collaborating Centre for Drug Statistics Methodology (https://www.whocc.no/) //

Room for notes

Liver

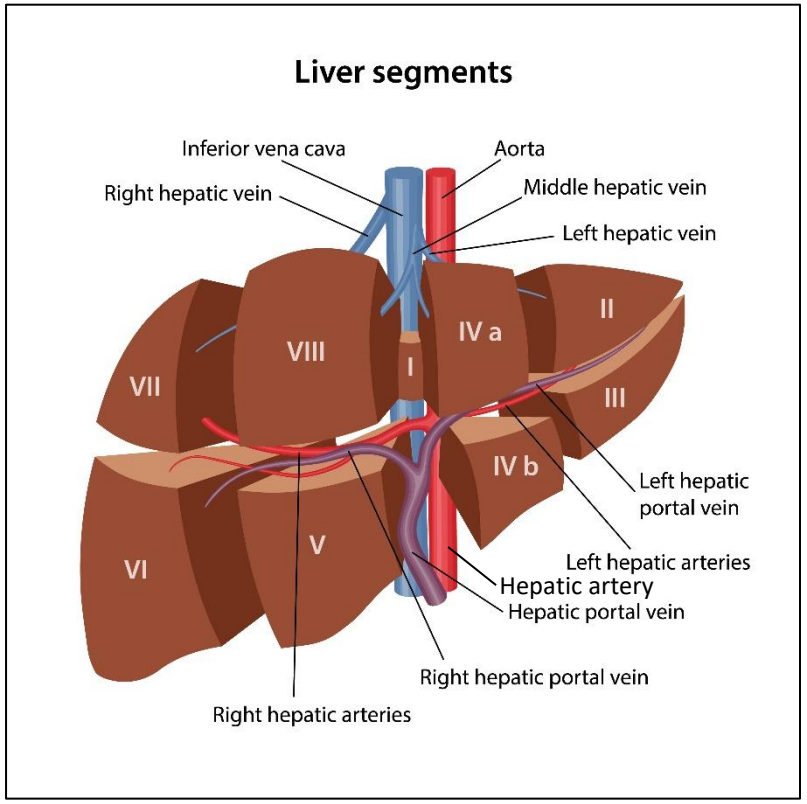
Room for notes

Liver: Anatomy, Physiology, and Hepatic Blood Flow

9X

Room for notes

- Blood Supply: 25% from hepatic artery; 75% from the portal vein. Each provides 50% of oxygen to liver.[1]
  - Hepatic veins drain to inferior vena cava (IVC). Increased central venous pressure (CVP; from positive pressure ventilation, congestive heart failure, excessive intravascular fluids) → increased pressure on hepatic veins → decreased hepatic flow and liver venous congestion.
    - Lower CVP's or higher stroke volume variations (SVV) are sometimes used to limit vascular congestion during hepatic resection.[1]
  - Portal blood flow (PBF) comes from splanchnic circulation and is dependent on cardiac output and mean arterial pressure (MAP).
- Volatile Anesthetics: isoflurane, sevoflurane, and desflurane decrease PBF in a dose-dependent manner via reduction in MAP and cardiac output.
  - *Hepatic Arterial Buffer Response (HABR)*: reduced PBF is matched with increase in hepatic arterial blood flow to maintain total hepatic blood flow (HABR is not preserved with halothane).
- Other Extrinsic factors that can decrease hepatic flow:[2]
  - Pain, hypoxemia, and surgical stress (especially if close to liver) → increased splanchnic vascular resistance → decreased hepatic flow.
  - Nonselective beta-blockers (e.g., propranolol) via decreased cardiac output (beta-1) and splanchnic vasoconstriction (beta-2).

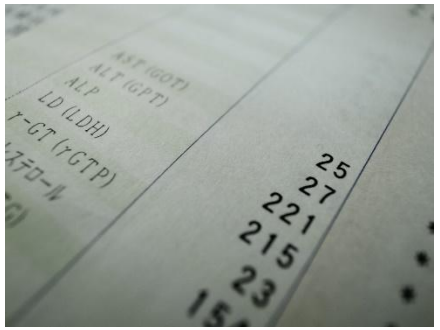


Refs: 1. Miller 10th Ed, Ch 14. // 2. Miller Basics of Anesthesia 8th Ed, Ch 28 // Image: Bolbot O; used under license from Shutterstock.com

Liver: Physiology, Protein Synthesis, and Labs

14X

- 80-90% of circulating proteins are synthesized in the liver.[1]
  - "The liver is the site of synthesis for all procoagulant and anticoagulant factors, with the exception of tissue thromboplastin (III), calcium (IV), and von Willebrand factor (VIII)."[2]
    - Vitamin-K-dependent coagulation factors/proteins: Factors II, VII, IX, X, and proteins C and S.
- Ratio of AST to ALT: ALT often higher than AST in hepatic injury; AST often higher than ALT in alcoholic liver disease and Wilson disease (genetic disorder causing excess copper accumulation).[1]
- Enterohepatic circulation: 95% of bile acids secreted into the duodenum are reabsorbed via the terminal ileum and returned to the liver.
- Bilirubin excretion: Bilirubin is product of heme catabolism. Hepatocytes convert unconjugated bilirubin into conjugated bilirubin (via bilirubin *glucuronyl transferase enzyme*) and excreted in bile.
  - *Gilbert's syndrome*: mild decreased activity of enzyme → unconjugated hyperbilirubinemia.
  - *Crigler-Najjar syndrome*: severe deficiency of enzyme (neonatal jaundice, brain damage).
  - Conjugated bilirubin is converted to urobilinogen in colon, which is excreted in urine/stool (pale stool and dark urine may be a sign of cholestasis). Some of the urobilinogen is reabsorbed to the liver via the enterohepatic circulation.
- Hemolysis vs. Hepatocellular Injury vs. Cholestasis:
  - Hemolysis associated with unconjugated hyperbilirubinemia;
  - Hepatocellular injury associated with increased AST & ALT (decreased in very advanced disease) and decreased albumin;
  - Cholestasis associated with increased alkaline phosphatase and gamma glutamyl transpeptidase (GGT).



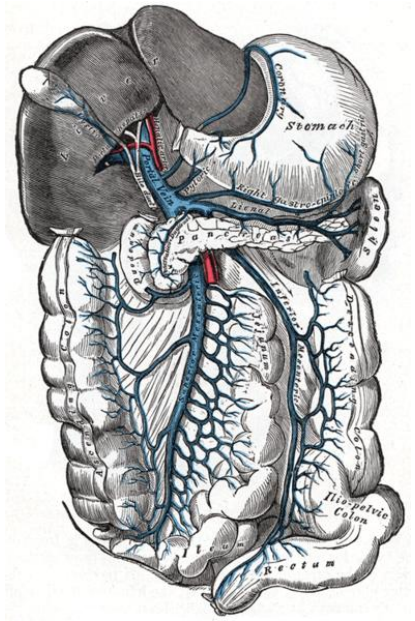
Refs: 1. Miller 10th Ed, Ch 14. // 2. Miller 10th Ed, Ch 56 // Image: "Result of liver function test" by matsuyuki is licensed with CC BY-SA 2.0. To view a copy of this license, visit https://creativecommons.org/licenses/by-sa/2.0/

Room for notes

Pathophysiology of End-Stage Liver Disease

3X

- Cirrhosis → fibrosis and destruction of hepatic vasculature → portal hypertension and release of vascular mediators (including nitric oxide) → splanchnic vasodilation, gastroesophageal varices, and portosystemic shunts. Portosystemic shunts can cause hepatic encephalopathy.[1]
  - Cardiovascular complications: Hyperdynamic circulation -- high cardiac output, low arterial blood pressure, low systemic vascular resistance, decreased effective circulating volume (more intravascular volume is sequestered in the splanchnic vascular bed).[1]
- Hepatorenal syndrome (HRS): advanced liver disease and acute kidney injury (AKI) in the absence of any apparent cause and refractory to volume expansion or stopping diuretics (diagnosis of exclusion).
  - *Pathophysiology*: Splanchnic vasodilation from cirrhosis → decrease in effective circulating volume → decrease in arterial blood pressure → activation of sympathetic, renin-angiotensin-aldosterone, and vasopressin systems → reduction in renal perfusion and glomerular filtration.[1]
- Hepatopulmonary syndrome (HPS)[1,2]: portal hypertension → intrapulmonary vascular dilations (IPVD; possibly due to release or failure-to-clear vasoactive mediators, such as nitric oxide) → PaO2 less than 70mmHg or alveolar-arterial oxygen gradient greater than 15mmHg on room air; ventilation-perfusion mismatch. Since IPVD's predominate in the bases of the lungs, some patients get:
  - Platypnea: dyspnea when going from supine to standing.
  - Orthodeoxia: decrease in PaO2 (more than 5% or 4mmHg) when going from supine to standing.
- Portopulmonary hypertension: pulmonary arterial hypertension that is otherwise unexplained in patient with portal hypertension. mPAP greater than 45 is contraindication to liver transplant.[1]



Refs: 1. Miller 10th Ed, Ch 14 & 56. //2. UpToDate: Hepatopulmonary syndrome in adults// Image: Gray H. Anatomy of the Human Body. Portal Vein. Public Domain, via Wikimedia Commons. Available at: https://commons.wikimedia.org/wiki/File:Gray591.png

Room for notes

Misc End-Stage Liver Disease

6X

- Kinetics of Neuromuscular blocking agents in end-stage liver disease:[1]
  - Vecuronium and Rocuronium (i.e., aminosteroid neuromuscular blocking agents) have a larger volume of distribution in cirrhotic patients → slower rate of onset and longer duration of action.
  - Some use rocuronium instead of cis-atracurium for liver transplant "because the duration of the neuromuscular block appears to be a useful predictor of primary allograft function."

Child-Turcotte Pugh (CTP) and Model for End-Stage Liver Disease (MELD) scores:

- Original MELD: included INR, bilirubin, creatinine. Newer ones add serum sodium (Na-MELD) and age (i-MELD).
- MELD calculators are available online: https://optn.transplant.hrsa.gov/resources/allocation-calculators/meld-calculator/
- Downsides of CTP include the subjectivity of ascites and encephalopathy scoring (and responsiveness to diuretics, lactulose, rifaximin) and ceiling/floor effects due to a min score of 5 and max of 15.
- "Studies comparing…CTP to MELD have yielded conflicting results likely due to small sample sizes and differences in primary outcome measures and surgical procedures…both scores should be used in conjunction with other available patient data when attempting to risk-stratify cirrhotic patients for nonhepatic surgery."

Child-Turcotte-Pugh Score (Class A: 5-6 points; B: 7-9; C: 10-15)		Points		
		1	2	3
Some Subjectivity	Encephalopathy grade	None	1-2	3-4
	Ascites	Absent	Slight	Moderate
	Bilirubin (mg/dL)	<2	2-3	>3
	Albumin (g/dL)	>3.5	2.8-3.5	<2.8
	International normalized ratio (INR)	<4	4-6	>6

Encephalopathy Grades (West Haven Criteria):[1] (1): Trivial lack of awareness; shortened attention span; disordered sleep; (2): Lethargy, behavioral change; asterixis; (3): Somnolence, confusion; gross disorientation; bizarre behavior; (4) Coma

Refs: 1. Miller 10th Ed, Ch 14 & 56. //2. UpToDate: Model for End-Stage Liver Disease (MELD) // Wiesner et al PMID: 11460223 // Pugh et al PMID: 4541913

Room for notes

Liver Transplantation

7X

Room for notes

Preanhepatic Phase: starts with surgical incision & ends with vascular exclusion and hepatectomy of liver.

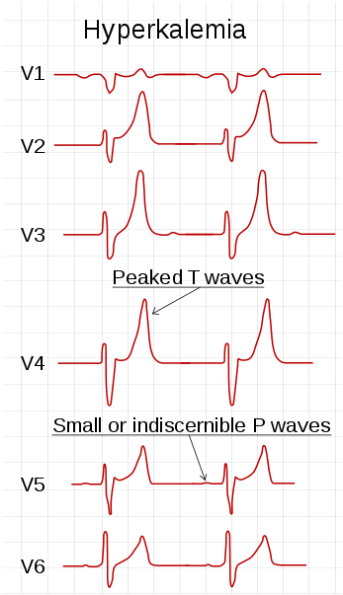
- Hypovolemia can occur from drainage of ascites. Preexisting coagulopathy & portal hypertension can increase bleeding risk. Hyperkalemia may occur from transfusions. Hypokalemia treated cautiously (neohepatic phase associated with hyperkalemia). Patient may have pre-existing hyponatremia.
- *Citrate intoxication* (the liver metabolizes citrate; citrate is present in blood products and can bind calcium → ionized hypocalcemia). Hypomagnesemia can also occur from citrate infusion. *ECG signs of hypocalcemia*: prolonged QT, heart block.[2,3]

Anhepatic Phase: starts with vascular exclusion of flow to liver and ends with graft reperfusion.

- In absence of venovenous bypass (which carries risk of embolic event), clamping IVC (suprahepatic and infrahepatic) can decrease venous return up to 50%. Venovenous bypass (VVB) or a "piggyback" technique (partial IVC clamping and IVC preservation) can decrease this issue. VVB risks include embolic events.

Neohepatic Phase: begins with reperfusion of the graft liver via portal vein.

- Risk of abrupt hyperkalemia and acidosis (donor liver often preserved in potassium-rich solution; ischemic time can cause acidosis). Calcium chloride and sodium bicarbonate may be initial drugs of choice.
- Associated with increase in preload and decrease in systemic vascular resistance and blood pressure.
- Postreperfusion syndrome (PRS): systemic hypotension and pulmonary hypertension within first 5 minutes of reperfusion.



Refs: 1. Miller 10th Ed, Ch 56. // 2. Miller 10th ed, Ch 43 // 3. Miller 10th Ed, Ch 29 // Image: hyperkalemia (Mikael Häggström, Public domain, via Wikimedia Commons; available at https://commons.wikimedia.org/wiki/File:ECG_in_hyperkalemia.svg. Accessed May 5, 2021)

Pediatrics

Room for notes

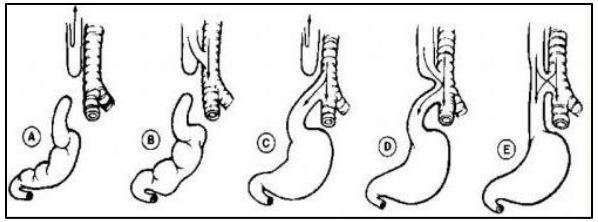
Pediatrics

15X

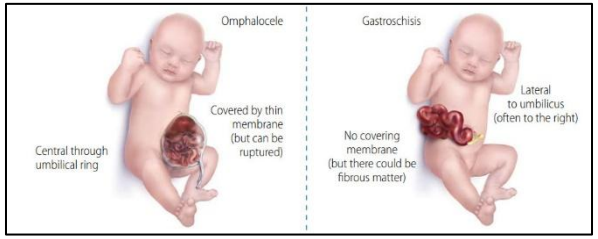
Tracheo-esophageal fistula (TEF):[1,2]

- Type C is most common; during repair: ideally, the ETT balloon should be distal to fistula but above carina (sometimes fistula is close to the carina).
- VACTERL (Vertebral, Anal, Cardiac, TE fistula, Renal, Limb) – consider Echo and other preop testing.

TE Fistula

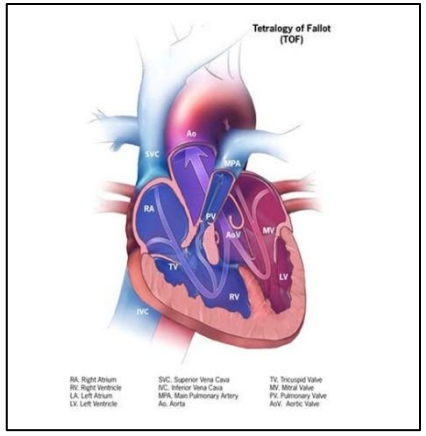


Omphalocele and Gastroschisis:[1,2]



- Omphalocele: herniated viscera/intestines emerge from umbilicus (covered by membranous sac) due to failure of gut migration from yolk sac into abdomen. Association w/several abnormalities (e.g., congenital heart disease, exstrophy of bladder, Beckwith-Wiedemann syndrome [macroglossia that can be associated w/airway difficulty, hypoglycemia, visceromegaly, polycythemia]).
- Gastroschisis: herniated viscera/intestines emerge in periumbilical area (exposed to air) from gestational occlusion of omphalomesenteric artery. Gut may be foreshortened & inflamed. Less often associated w/other abnormalities.
- Management: initial: protect viscera, avoid hypothermia. Abdominal closure may increase intraabdominal pressure, increase PEEP, impair venous return, & impair perfusion of liver/kidneys →altered drug metabolism (closure often staged; intrabdominal pressure sometimes monitored).

Tetralogy of Fallot:



- Anatomy: Right ventricular outflow tract obstruction (RVOT), ventricular septal defect, overriding aorta, right ventricular hypertrophy.
- **Tet-Spells:** Pathophysiology: transient near occlusion of RVOT, sometimes when infant agitated/upset (possibly from right ventricle/infundibular contractility, peripheral vasodilation, hyperventilation). Tx: reduce the right-to-left shunt: 100% FiO2, phenylephrine, knee-to-chest position (increases SVR), IV fluids. Also: beta-blockers (reduces contractility) & opioids (facilitates sedation & decreased minute ventilation).

1. Coté 6th Ed, Ch 37. // 2. Miller's 10th Ed, Ch 72 // TE Fistula figure: Salik et al. PMID 30570997 Creative Commons CC-BY-4.0. Omphalocele, Gastroschisis and Tetralogy Fallot images: CDC NCBDDD https://www.cdc.gov/ncbddd/birthdefects/omphalocele.html https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/quick-reference-handbook/gastroschisis.html#fig51 https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/quick-reference-handbook/tetralogy-of-fallot.html ; public domain; does not constitute endorsement or recommendation by U.S. Government, DHHS, or CDC; available free of charge at CDC website // OpenAnesthesia: Tetralogy of Fallot RX //

Room for notes

Pediatrics

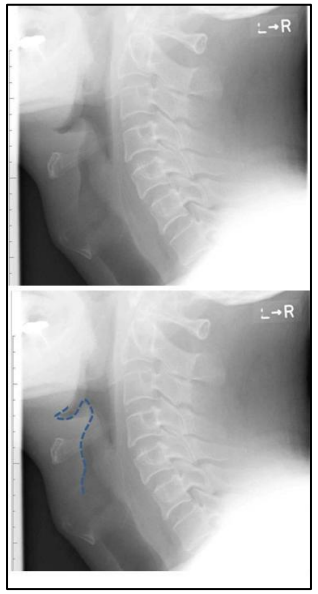
12X

Room for notes

Epiglottitis:

- Potentially life-threatening infection of supraglottic structures. Often caused by Haemophilus influenza B or Group A strep. Severe sore throat, stridor, drooling, patient sitting in tripod position. Induction: airway manipulation in O.R. with monitors on and surgeon present; maintain spontaneous ventilation (inhalational induction), avoid paralytics.
- Croup (laryngotracheo-bronchitis) is often less urgent, associated with barking cough, often caused by parainfluenzae virus.

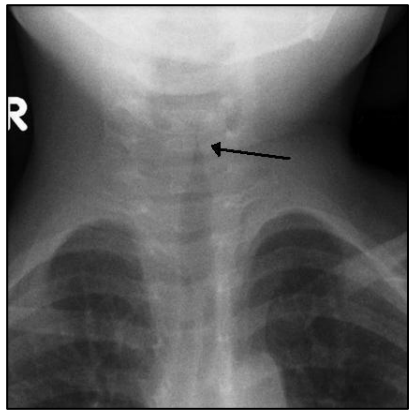
Epiglottitis: "Thumbprint sign"



Adult vs. Pediatric Normal Airway Anatomy:

- Pediatric airway: larynx/glottis higher in neck (closer to C3 than C5 [adults]). Some (controversial) say narrowest point of airway is cricoid cartilage (until age 5), as opposed to glottic opening (adults). Large tongue/occiput and omega-shaped epiglottis.

Croup: "Steeple sign"



Neonatal postoperative apnea:

- Most conservative approach: If under 60-weeks post-conceptual age (PCA): 24-hour observation (at least 12-hours if under 50 wks PCA). Some use caffeine and theophylline as stimulants. Some use pure regional/local anesthesia (i.e., no sedation). Other risk factors: anemia, apnea at home; small-for-gestational-age may be protective.

Grover C. NEJM 2011 PMID 21812674 // Epiglottitis image: https://commons.wikimedia.org/wiki/File:Compare_epiglottis.jpg; CC BY-SA 3.0, via Wikimedia Commons // Lee FE-H. Murray and Nadel's textbook of Emergency Medicine. 2016 // Croup image: https://commons.wikimedia.org/wiki/File:Croup_steeple_sign.jpg, CC BY-SA 3.0, via Wikimedia Commons // OpenAnesthesia: Postoperative apnea: post conceptual age // Miller 10th Ed Ch 72 // Barash 9th Ed Ch 43

Pediatric ETT Size; Peds Syndromes/Airway

10X

Peds ETT Size[1,2]	Peds ETT Insertion Distance[1,2]
Uncuffed ETT for children above age 2 yrs (mm Inner Diameter [ID]): **(Age [in years]/4) + 4** (or 4.5) • Equivalent formula: (Age in yrs + 16)/4 • 1-2yrs: 4.0-5.0 ID ETT; 6mo-1yr: 3.5-4.0 ID ETT; Neonate-6mo: 3.0-3.5 ID ETT; 1000-2500g: 3.0 ID ETT; (2.5 if 1000g)	Oral ETT from lips to mid-trachea: • Less than 1,000 g in weight: 6 cm; 1,000 to 3,000 g: 7 to 9 cm; term neonate: 10 cm; infants and children: **10 + age (years) mm**. • Alternatives: [Age (years)/2] + 12 ; [Weight (kg)/5 + 12]; **ID of ETT x 3**.
Cuffed ETT (mmID): **(Age [in years]/4) + 3** (for children <2 years) or + 3.5 (for those >2 years).	

Syndromes Associated with Airway Difficulties Include:[1,2]	
Pierre Robin sequence	hypoplastic mandible, pseudomacroglossia, high-arched cleft palate"
Treacher Collins syndrome	malar, mandibular hypoplasia and +/- cleft lip, choanal atresia, cervical spine deformity, congenital heart disease, macrostomia or mircostomia
Crouzon syndrome	maxillary hypoplasia, inverted V-shaped palate, ocular proptosis, criosynostosis, +/- large tongue
Apert syndrome	maxillary hypoplasia, narrow palate, craniosynostosis, flat facies, hypertelorism, +/- cleft palate, congenital heart disease, hydronephrosis, polycystic kidneys, esophageal atresia, syndactyly
Trisomy 21	small mouth, hypoplastic mandible, protruding tongue, cervical spine subluxation, associated with cardiac disease (ASD, VSD, AV canal defects), hypotonia, duodenal atresia, mental handicap

High-Yield Recommended Read: Cote 6th Ed Ch14, Table e14.1: Syndromes/Disease Processes Associated with Airway Difficulties. *Deep dive*: Smith's Anesthesia for Infants and Children, 10th Ed, Appendix D (Index of syndromes and their pediatric anesthetic implications).

1. Cote's A Practice of Anesthesia for Infants and Children, 6th Ed, Ch 14. // 2. Barash 9th Ed Ch 43

Room for notes

Pediatrics

41X

Including PONV guidelines

Room for notes

- Pyloric Stenosis:[1-5] "this procedure is never a surgical emergency"[3]
  - Early metabolic abnormality: hypokalemic, hypochloremic metabolic alkalosis (from vomiting). Reason for paradoxical aciduria: kidneys prioritize addressing the hypovolemia over the alkalosis. Aldosterone secretion increases, which leads to reabsorption of sodium (and H_20) and excretion of K^+ & H^+ (which only exacerbates the alkalosis). IV Fluid: Consider Normal Saline or D5 ½ NS with K^+.
- 4-2-1 Rule (hourly IV fluid requirement): [1,3,6]
  - 4ml/kg/hr for first 10kg; 2ml/kg/hr for next 10kg; 1mL/kg/hr for every kg after 20kg.
    - 4-2-1 may be overestimate for acutely ill children (who may have increased ADH secretion).
    - "The amount of fluid needed for ongoing losses during the perioperative period largely depends on the type of procedure as well as on the pathological state of the child."[3]
  - Hypotension is late sign of hypovolemia. Other signs to look for: tachycardia, decreased skin turgor/cap refill, decreased urine output.
- Spinal block in infant vs. adults:[7,8]
    - Infants have less hemodynamic changes from spinal. Dural sac (closer to S3 than S1 [adults]) and end of spinal cord extend lower (i.e., conus medullaris closer to L3 than L1 [adults]).
- Fetal Hemoglobin:[9] Has more affinity for oxygen than adult hemoglobin (left shift of oxyhemoglobin dissociation curve; i.e., P50 lower than adult).
- Risk Factors for PONV in children (& adults) and management algorithms:

  See 2020 SAMBA/ASER Guidelines (see QR code):

Pediatric Reference Vital Signs[10-15]**

Age	HR (bpm)	BP (mmHg)	RR (breaths /min)
Pre-mature	110-170	55-75/35-45	40-70
0-3 mo	100-160	65-85/45-55	65-55
3-6 mo	90-120 (160)*	70-90/50-65	30-45 (55)*
6-12 mo	80-120 (160)*	80-100/55-65	22-40 (50)*
1-3 yr	70-110 (150)*	90-105/55-70	20-30
3-6 yr	65-110 (120)*	95-110/60-75	20-25
6-12 yr	60-95 (110)*	100-120/60-75	14-22
12+ yr	55-85 (110)*	110-135/65-85	12-20

1. Cote's A Practice of Anesthesia for Infants and Children, 6th Ed, Ch 9 // 2. Cote 6th Ed Ch 37 // 3. Miller 10th Ed Ch 72 // 4. UpToDate: Infantile hypertrophic pyloric stenosis // 5. Zaghal et al PMID 34038653 // 6. UpToDate: Assessment of systemic perfusion in children // 7. Miller 10th Ed Ch 74 // 8. Cote 6th Ed Ch 42 // 9. Cote 6th Ed Ch 38 // 10. Cote 6th Ed Ch 2 // 11. Smith's Anesthesia for Infants and Children 10th Ed Ch 5 // 12. Barash 9th Ed Ch 43 // 13. Nelson Textbook of Pediatrics 21st Ed Ch 81 // 14. Nelson 21st Ed Ch 449 // 15. UpToDate: The pediatric physical examination: General principles and standard measurements. // * Upper limit seen in some literature, at times representing an upper percentile. ** Literature and institutional variation exists, as well as variation by height, weight and sex. This table is intended as a referenced synopsis and not a comprehensive guide.

Geriatrics

Room for notes

Geriatrics: Physiologic Changes of Aging

41X

Room for notes

CNS: Increased: (1) sensitivity to anesthesia; (2) risk of postop delirium/cognitive dysfunction.[1]

Cardiac: arterial stiffening/increased afterload; diastolic dysfunction more common; decreased ability of sympathetic and autonomic system to respond to physiologic derangement.[1]

Pulmonary: **increased closing capacity (point at which small airways close)**, increased work of breathing, decreased respiratory response to hypoxia and hypercarbia, increased risk for aspiration/pneumonia, diaphragm weakens and chest wall thickens.[1]

Parameter	Geriatric
Functional Residual Capacity	↑
Minute Ventilation	↔
Tidal Volume	↓
Respiratory Rate	↑
Closing Capacity	↑
Tracheal Compliance	↔
Airway Resistance	↑

Renal: *"In healthy patients, serum creatinine is unlikely to change significantly between the ages of 40 and 70."* [2019 ITE Gaps in Knowledge] – Older patients may have "normal" serum creatinine levels as well as decreased lean muscle mass.

- **Meperidine**: renal excretion of normeperidine (toxic metabolite) decreases w/age.[2]
- **Morphine**: Renal insufficiency can lead to morphine-6-glucuronide accumulation (has activity at the mu-opioid receptor).[3]
- **Paralytics**: *Succinylcholine*: no change (decreased in pseudocholinesterase usually not clinically significant). *Cis-atracurium*: Organ-independent Hofmann elimination (cis-atracurium helpful for patients with ESRD) is usually not affected by age. *Rocuronium/Vecuronium*: depends on kidney/liver function (caution in patients with ESRD).[4]

MAC decreases by about 6% for every decade after 20-30 years. *Infants/children*: (1) For isoflurane, desflurane (and halothane): MAC increases about 30% from full-term birth to age 6 months, then goes back down and progressively decreases into adulthood; (2) For sevoflurane: MAC highest at full-term birth (3.3%), slight decrease at 1-6 months (3.2%), with drop to about 2.5% from age 6 months to 10 years and progressive decreases into adulthood.[1-2,5-6]

- **Fentanyl, remifentanil, and sufentanil** are approximately twice as potent in older patients. *2021 ITE Gaps in Knowledge*: "The onset of action of remifentanil is altered in a geriatric patient compared to a 40-year-old patient." (possible slower onset and offset; potentially from lower cardiac output, slower blood-brain equilibration).[2]

1. Miller 10th Ed Ch 61 // 2. Barash 9th Ed Ch 34 // 3. Miller 10th Ed Ch 55 // 4. Miller 10th Ed Ch 24 // 5. PMID 35483048 // 6. Coté 6th Ed Ch 7

Emergence Excitement/Delirium (Postoperative)

5X

Room for notes

Emergence Excitement: "…a transient confusional state that is associated with emergence from general anesthesia. […] Unlike delirium, emergence excitement typically resolves quickly and is followed by an uneventful recovery." More common in children, particularly if volatile anesthetics used.[1]

- **Pediatric Anesthesia Emergence Delirium scale**: scoring system for emergence delirium based on the following criteria: (1) eye contact w/caregiver; (2) purposeful actions; (3) awareness of surroundings; (4) restlessness; (5) inconsolability.[2,3]

Hypoactive vs Hyperactive Delirium Infographic (BMJ)[5]

Delirium (postoperative):

- "acute cognitive disruption characterized by inattention, a fluctuating course, and cognitive disturbance."[4]

Treatment of Postoperative Delirium:

- Nonpharmacologic: Supportive care; limit benzodiazepines, meperidine, and drugs with atropinic properties (except glycopyrrolate); frequent reorientation; ensure any assistive devices and glasses/hearing aids present; facilitate patient's circadian rhythm; provide any familiar objects or individuals; search for underlying cause (e.g., infection, pain, hypoxemia, electrolyte disturbances, hypoglycemia, urinary retention, constipation, inadequate nutrition, neurologic insult).
- Pharmacologic: If refractory agitation/if needed, can consider typical (e.g., haloperidol) and atypical antipsychotics (e.g., risperidone, olanzapine, quetiapine, ziprosidone).[1,6]

Popular perioperative medications with anticholinergic properties that are on the 2019 Beers Criteria® for Potentially Inappropriate Medication (PIM) use in Older Adults (American Geriatrics Society)
Diphenhydramine
Scopolamine
Promethazine
Hydroxyzine

2023 Gaps In Knowledge: "Hypoactive delirium is treated with intravenous haloperidol."[7]

1. Miller 10th Ed Ch 76 // 2. Barash 9th Ed Ch 43 // 3. PMID 15114210 // 4. Miller 10th Ed Ch 78 // 5. PMID 28546253 // 6. Barash 9th Ed Ch 34 // 7. ABA Gaps in Knowledge Report. Latest edition available at www.theaba.org // Miller 10th Ed, Ch 61. // AGS 2019 Updated Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. PMID: 30693946.

Geriatrics: Perioperative Neurocognitive Disorders (PND)

5X

Perioperative Neurocognitive Disorders (PND): "overarching term for [periop] cognitive impairment or change, including delirium"[1]

Old Nomenclature	New Nomenclature[1-3]
Preexisting cognitive impairment	Mild or Major Neurocognitive Disorder (preoperative diagnosis)
Postoperative Delirium	Delirium (postoperative)
Postoperative Cognitive Dysfunction	1-30 days postop: Delayed neurocognitive recovery
	30 days-12 months postop: Mild or Major Neurocognitive Disorder Postoperative
	Beyond 12 months postop: Mild or Major Neurocognitive Disorder

Risk factors for Postoperative Neurocognitive Disorders:[1,4,5]

Most Mentioned		Other Potential Factors	
Age	Debated: surgical procedure type	History of delirium	Frailty
Preexisting cognitive impairment (new term: "Mild/Major Neurocognitive Disorder")	Widely debated: Anesthesia type (e.g., regional vs. general; volatile vs. total intravenous anesthesia).	ASA physical status	Smoking
		Activities of Daily Living (ADL) Impaired	Polypharmacy, including psychotropic meds

Regional Anesthesia (RA) vs General Anesthesia (GA) & PND: widely debated. Historically, some RA vs GA studies had patients getting RA w/deep sedation. PND may result of preexisting vulnerabilities & the surgery itself.[1]

Hip Fracture Surgery in Older Adults: -- Recent Studies Include:
NEJM 2021 Randomized Trial (REGAIN):[6] "Spinal anesthesia for hip-fracture surgery in older adults was not superior to general anesthesia with respect to survival and recovery of ambulation at 60 days." Postop delirium incidence similar w/two types of anesthesia.
JAMA 2022 Randomized Trial (RAGA):[7] "In patients aged 65 years and older undergoing hip fracture surgery, regional anesthesia without sedation did not significantly reduce the incidence of postoperative delirium compared with general anesthesia."
Ann Intern Med 2022 (REGAIN follow-up):[8] "Severe pain is common after hip fracture. Spinal anesthesia was associated with more pain in the first 24 hours after surgery and more prescription analgesic use at 60 days compared with general anesthesia."
Anesthesiology 2023 (REGAIN follow-up):[9] "Long-term outcomes [365 days] were similar with spinal versus general anesthesia."

Room for notes

ASA 2025 Practice Advisory: Periop Care of Older Adults Scheduled for Inpatient Surg:[10]

- Neuraxial or general anesthesia (TIVA or inhaled) can be chosen. Regarding postop delirium, (1) no superiority for neuraxial vs general & (2) inconclusive evidence for TIVA vs inhaled.

- Dexmedetomidine "is reasonable to consider" to lower postop delirium risk (but also consider bradycardia & hypotension risk).

- If patient has cognitive impairment or frailty, consider changes such as multidisciplinary care team (including geriatric expert) involvement, as well as patient/family education on delirium risk.

1. Miller 10th Ed Ch 78 //2. PMID 30325806 //3. PMID 37944401 //4. PMID 27127918 //5. PMID 31834869 //6. PMID 34623788 //7. PMID 34928310 //8. PMID 35696684 //9. PMID 37831596 //10. PMID 39655991

Pain

Room for notes

Pain

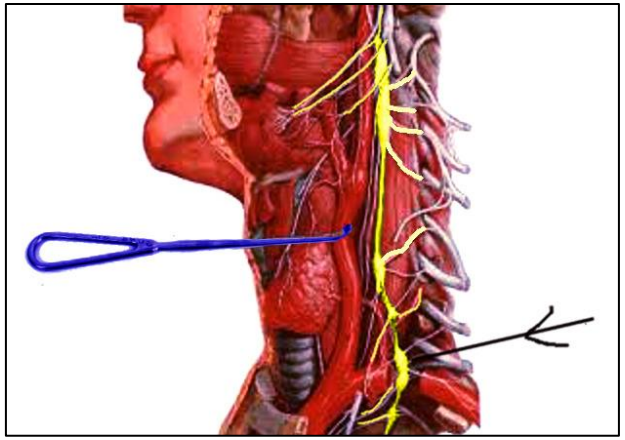
15X

Room for notes

Complex Regional Pain Syndrome (CRPS):

- **"SAT Exam Injury"**: **S**udomotor symptoms/sympathetic dysfunction, **A**llodynia/hyperalgesia, **T**rauma, **E**xclude other causes, **I**njury (CRPS type II: known nerve injury; if only the other criteria present: CRPS type I). Pain should not just be limited to a single nerve distribution.
- Treatment (adapted from Rho et al*): (1) Physical therapy (& biopsychosocial approach); (2) non-opioid, tricyclic antidepressant, gabapentin, +/- mild opioid analgesics; (3) diagnostic sympathetic block; (4) somatic block (if sympathetic block fails); (5) spinal cord stimulator/ intrathecal medications.

Stellate Ganglion



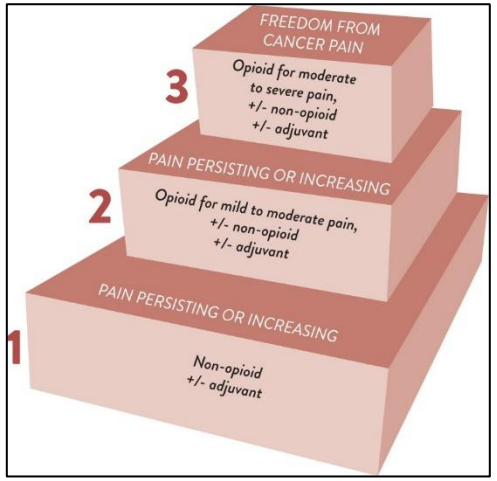
Stellate Ganglion Block	
Indications/Uses	Sympathetically-mediated pain at head/neck/upper extremity (such as CRPS), vascular insufficiency, intractable angina, hyperhidrosis, phantom limb pain, neuropathic pain (such as post-herpetic neuralgia)
Stellate ganglion location	Over head of 1st rib at junction of T1 transverse/uncinate process. It is the fusion of the superior thoracic ganglion & inferior cervical ganglion. Block is typically at C6 or C7 level (volume spread).
Signs of successful block	Horner's syndrome (miosis [constricted pupil]), ptosis, anhidrosis), nasal congestion, venodilation hand/forearm, increase in temperature of blocked limb ≥ 1 deg Celsuis
Complications/ other side effects	hoarseness (RLN), dyspnea (phrenic nerve), neuraxial/spinal block, seizures, hematoma, nerve injury, pneumothorax, esophageal perforation

Image: https://www.ncbi.nlm.nih.gov/books/NBK539807/ via Creative Commons CC-BY-4.0. // OpenAnesthesia: Stellate Ganglion Block: effects // * Noted to be adapted from Rho et al, Mayo Clin Proc 2002 // Miller's Basics of Anesthesia, 8th Ed, Ch 44

Pain

17X

Room for notes



WHO Cancer Pain Ladder:

- WHO 1986 examples: *Non-opioids*: aspirin, acetaminophen; *weak opioid*: codeine; *strong opioids*: morphine, hydromorphone, methadone, buprenorphine; *adjuvant drug classes:* anticonvulsants, neuroleptics, anxiolytics, antidepressants, corticosteroids.
- WHO 2018 update: "a cancer pain management ladder is useful as a teaching tool and as a general guide to pain management based on pain severity…it cannot replace individualized therapeutic planning…"
- "Step 4": interventional therapy (nerve block, epidural, spinal cord stimulator, etc).

Celiac Plexus Block:

- Celiac plexus is at T12-L1 level. Provides sensory innervation and sympathetic outflow to pancreas, liver, gallbladder, spleen, kidneys, and GI tract from distal stomach to splenic flexure. Commonly considered in management of pancreatic cancer pain.
- Agent: alcohol can be given with small amount of local anesthesia to reduce pain on injection; phenol painless on injection.
- Most common complications: diarrhea, orthostatic hypotension. Rare complications: paraplegia (artery of Adamkiewicz injury), aorta/vena cava puncture, retroperitoneal hemorrhage, visceral organ injury, pneumothorax, local anesthetic systemic toxicity.
- Other blocks: Hypogastric block (many pelvic cancers); Ganglion impar block (perineal/rectal cancers)
  - *2021 ITE Gaps in Knowledge*: "Ganglion impar block would be appropriate for the treatment of pain resulting from radiation-induced proctitis."

1. Cancer pain relief. Geneva: World Health Organization; 1986 http://apps.who.int/iris/bitstream/handle/10665/43944/9241561009_eng.pdf // 2. (including image: WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. Geneva: World Health Organization; 2018. Creative Commons License: CC BY-NC-SA 3.0 IGO https://www.ncbi.nlm.nih.gov/books/NBK537489/ // Miller 10th Ed Ch 47 // Miller Basics 8th Ed Ch 44 //OpenAnesthesia: celiac plexus block: complications // Practical Management of Pain, 5th Ed, Ch 59

Pain

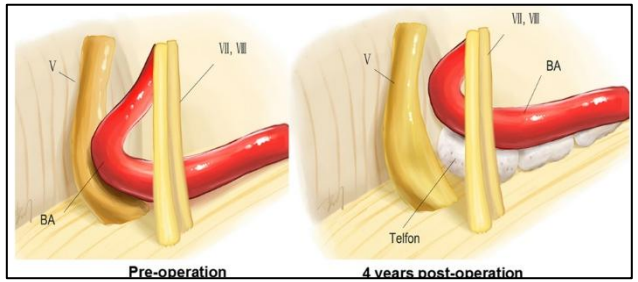
20X

Room for notes

Trigeminal neuralgia:

- Most common cause: vascular compression of trigeminal nerve root by blood vessel(s) (often the superior cerebellar artery)
- Most effective/first-line agent: carbamazepine or oxcarbazepine (feared side effect: aplastic anemia).
- Alternative treatment options include: Surgical referral (surgical microvascular decompression a popular consideration), gabapentin, pregabalin, lamotrigine, baclofen.[1,2]

Microvascular Decompression for Trigeminal Neuralgia



Post-herpetic neuralgia:

•Can last 7 days pre and 6 months post shingles vesicles.

•Most common dermatomes: thoracic and trigeminal.

•Risk Factors: Severe pain and/or sensory abnormalities during acute herpes zoster; older age.

•Prevention/Treatment: antivirals, tricyclics, serotonin-norepinephrine reuptake inhibitors, gabapentin, lidocaine, sympathetic blockade (e.g., stellate ganglion block). Zoster vaccine (live-attenuated): FDA licensed for pts > 50yrs, recommended for pts > 60 yrs, including those w/previous zoster.

Rib Fracture Pain Management:

- Therapy is focused on minimizing pulmonary complications from the fracture.
- Regional options include epidural, paravertebral block, intercostal block(s)
- Regarding systemic absorption: (Intercostal > Caudal > Lumbar/Thoracic > Peripheral nerve block): intercostal has the highest amount of local anesthesia systemic absorption.

1. Trigeminal Neuralgia (UpToDate) // 2. Cruccu et al NEJM 2020, PMID: 32813951 // Kroger AT. Immunization. In Principles of Infectious Disease, 8th Ed // OpenAnesthesia: Trigeminal Neuraglia, Anesthetic Absorption: regional anesthesia techniques, rib fractures // Image: Wang et al. BMC Neurology; Creative Commons CC-BY-4.0 PMID 31481028. // Miller 10th Ed Ch 62

Obstetrics

Room for notes

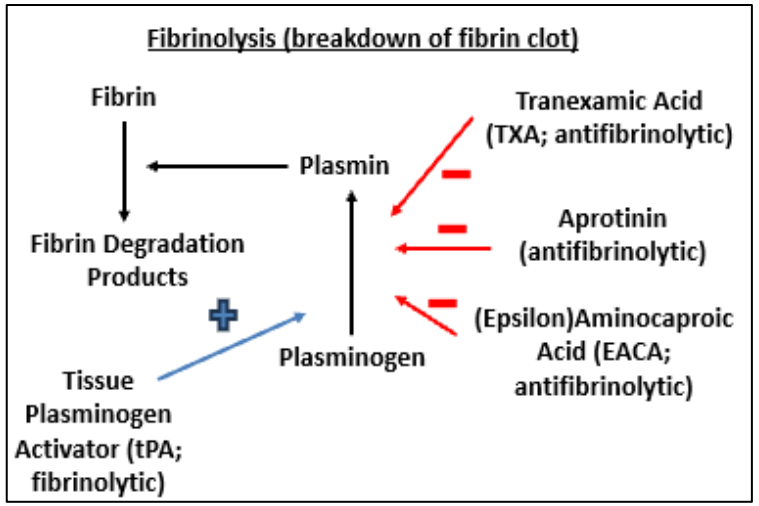
Obstetrics: Hemostasis, Uterotonics, Uterine Relaxants

30X

Room for notes

Uterotonics:

- Oxytocin (aka Pitocin; relaxes vascular smooth muscle; lowers SVR → can cause hypotension & tachycardia)
- Methylergonovine (aka Methergine; increases uterine contraction force/frequency; can cause increase in BP; caution in patients with hypertension [pre-eclampsia]).
- Carboprost (aka 15-methyl prostaglandin F-2-alpha; aka Hemabate; synthetic prostaglandin; can cause bronchospasm; caution in patients with asthma).
- Misoprostol (aka Cytotec; prostaglandin; produces uterine contractions).



Tranexamic Acid (TXA; antifibrinolytic; inhibits plasminogen's affinity to bind multiple proteins)

- *World Maternal Antifibrinolytic (WOMAN) Trial (Lancet 2017)*: Randomized controlled trial; TXA, especially given within 3 hours of giving birth, was associated with decreased death due to bleeding from postpartum hemorrhage.[1]

Other TXA within-3-hours Lancet Studies include:

- *Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 2 (CRASH-2) Trial (Lancet 2010 & 2011)*:[2-3] TXA given within 3 hours after injury in bleeding trauma patients reduced risk of death due to bleeding (possibly harmful if given after 3 hours).

- *CRASH-3 Trial (Lancet 2019):*[4] TXA, given within 3 hours of injury, reduced head injury-related death in patients with traumatic brain injury (TBI).

Uterine Relaxants:

- Nitroglycerin and volatile anesthetics most popular.
- Beta-agonists (terbutaline) and magnesium sometimes used.

Handout: OB Hemorrhage Crisis Checklist

Chestnut OB Anesthesia, 6th Ed, Ch 37 // Epocrates drug reference for selected agents. // 1. PMID: 28456509 // 2. PMID: 20554319 // 3. PMID: 21439633 // 4. PMID: 31623894 // UpToDate: Alteplase: Drug information; Perioperative blood management: Strategies to minimize transfusions; Intraoperative use of antifibrinolytic agents; Initial management of moderate to severe hemorrhage in the adult trauma patient // Note: Aprotinin discontinued in United States (safety concerns); was reintroduced in Europe. // PMID 29200009.

15 OB Hemorrhage

INDEX

Cumulative Blood Loss (intrapartum and postpartum) > 1000mL in vaginal or cesarean delivery or blood loss associated with signs or symptoms of hypovolemia within 24 hours after delivery

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
   - Crisis manager designates a person to monitor estimated blood loss
2. **Announce vital signs and cumulative blood loss every 10 minutes**
3. **Open IV fluids** and **establish adequate IV access**
   - Warm patient and fluids
   - Insert bladder catheter
   - Consider arterial access
4. **Turn FiO_2 to 100%** or **start supplemental oxygen**
   - Minimize volatile anesthetics
5. **Prepare for transfusion**
   - Assign 1 person as primary contact with Blood Bank
   - Activate massive transfusion protocol
   - Request rapid transfuser device
6. **Send STAT labs**
   - CBC, BMP, Type and Screen, fibrinogen, PT, aPTT, lactate
   - Viscoelastography
7. **Give uterotonic agents and tranexamic acid**
8. **Begin transfusion**
   - Transfuse with products in ratio of 4 PRBCS : 4 FFP : 1 Platelet
   - Target fibrinogen > 200 mg/dL
     - 10 units cryoprecipitate, expected rise 100 mg/dL
     - Fibrinogen concentrate 4g, expected rise 100 mg/dL
9. **Surgical team: perform exam and uterine massage**
   - Consider the differential diagnosis (see box)
   - Consider D+C, laceration repair, uterine tamponade
   - If bleeding unresponsive, consider uterine artery ligation or hysterectomy, or Interventional Radiology for embolization

DRUG DOSES & treatments

Oxytocin (Pitocin)
3 units IV BOLUS or 5-10 units IM BOLUS
— followed by —
10 - 40 units in 500 - 1000 mL IV INFUSION
Caution in hypotension

Methylergonovine maleate (Methergine)
0.2 mg IM q 2 - 4 hours
DO NOT administer IV
Caution in hypertension, cardiac disease

Carboprost tromethamine (Hemabate)
250 MCG q 15 - 90 min IM x8 max
DO NOT administer IV
Caution in asthma, HTN

miSOPROStol (Cytotec)
800 - 1000 MCG PR/buccal/SL x1 dose

Tranexamic Acid (TXA)
1000mg IV over 10 min, repeat x1 after 30 min

Calcium Chloride
1 g per 5 units product
— or —
Calcium Gluconate
1 g per 3 units product

DIFFERENTIAL diagnosis

- **Tone** (uterine atony)
- **Trauma** (lacerations or uterine rupture)
- **Tissue** (retained placenta)
- **Thrombin** (clotting factor deficiency)

15

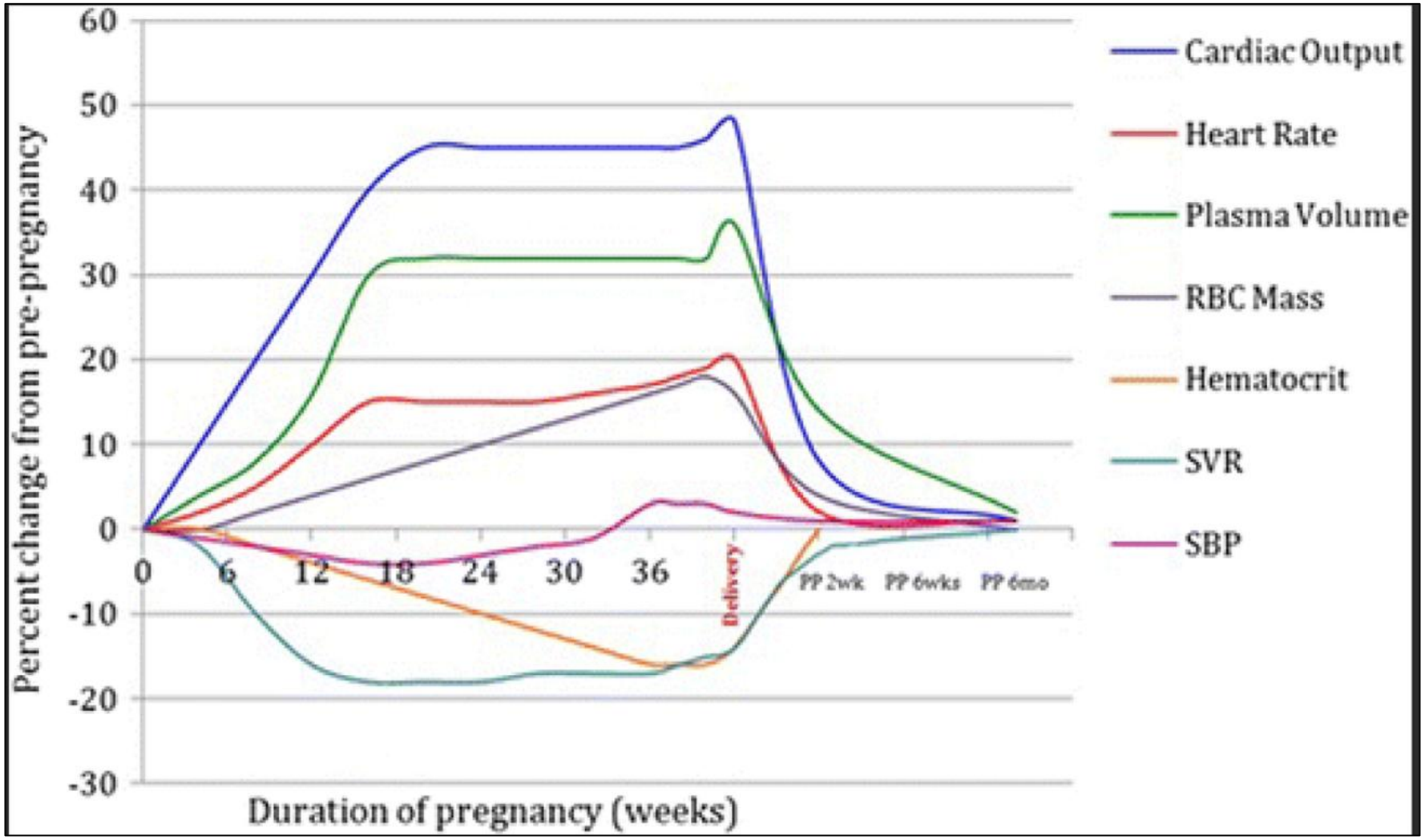
Room for notes

Physiologic Changes of Pregnancy

Hemodynamic Changes and Time Course

47X

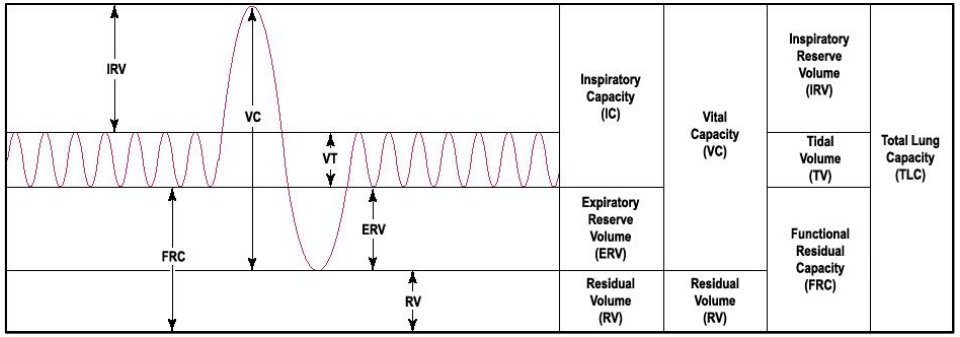
(incl next slides on physiologic changes of pregnancy)



Ordoñez et al. https://doi.org/10.1186/s40949-021-00058-y Creative Commons CC-BY-4.0 //

Room for notes

Physiologic Respiratory Changes Throughout Life



Parameter	Term Neonate	Term Gestation	Obesity	Geriatric
Functional Residual Capacity	↓/↔[1,2,4]	↓ (-20%)**[5]	↓**[3]	↑[11]
Minute Ventilation	↑[1]	↑ (+45%)*****[5]	↓/↔[7,9]	↔[12]
Tidal Volume	↔ [1,4]	↑ (+45%)*****[5]	↓[7]	↓[12]
Respiratory Rate	↑[1]	↑[7]	↑/↔[7]	↑[12]
Closing Capacity	↑[1,2]	↔***[5]	↔***[9]	↑******[10,13]
Tracheal Compliance	↑****[4]	↔	↔	↔
Airway Resistance	↑[4]	*[5,7]	↑[8,9]	↑[12]
Common causes of decreased FRC: PANGOS (Pregnancy, Ascites, Neonate, General Anesthesia, Obesity, Supine Position) **Common causes of increased closing capacity**: ACLS (Advanced age, Chronic bronchitis, LV failure, Smoking/Surgery)				

- *2022 ITE Gaps in Knowledge*: "Normal $PaCO_2$-$ETCO_2$ gradient is close to zero in healthy, full term parturients." (Increased cardiac output and basilar atelectasis from pregnancy → reduction in alveolar dead space [which is what causes $PaCo_2$ to be slightly higher than $ETCO_2$ in nonpregnant patients])[5]

* Pulmonary resistance decreases; upper airway changes can lead to increased airflow resistance/snoring; if pregnancy and obesity, airway resistance may increase from reduction of lung volumes. ** Decrease in FRC is accompanied by a decrease in expiratory reserve volume. In both pregnancy and obesity, this is related to mass effect (i.e., compression of lung parenchyma). *** Closing capacity may not change, but reduced FRC relative to normal closing capacity may cause increased airway closure. **** May be due to cartilaginous immaturity; dynamic collapse with inspiration/expiration may be more likely. ***** Results from hormonal changes (progesterone is respiratory stimulant) and increase in CO2 production at rest. $PaCO_2$ declines to 30mmHg by week 12 of gestation. ****** Increased chest wall rigidity and decreased respiratory muscle strength can lead to increased closing capacity (the point at which small airway collapse).

1. Miller Basics 8th Ed Ch 34 // 2. Cote 6th Ed Ch 13 // 3. Miller 10th Ed Ch 12 // 4. Cote 6th Ed Ch 2 // 5. Chestnut 6th Ed Ch 2 // 6. Anesth Uncomm Dz 6th Ed Ch 6 // 7. Chestnut 6th Ed Ch 49 // 8. Stoelting 7th Ed Ch 19 // 9. Nunn & Lamb's Applied Respiratory Physiology, 9th Ed Ch 15 // 10. Miller 10th Ed Ch 61 // 11. Barash 9th Ed Ch 34 // 12. Brocklehurst's Textbook of Geriatric Medicine and Gerontology //13. PMID 14557122 // with acknowledgement to Joseph Mintz, MD

Room for notes

Other Physiologic Changes of Pregnancy

Renal Changes and Time Course		
Parameter	**Change**	**Notes**
GFR	Increase	Increased 50% by 3rd month of pregnancy; remains elevated until 3 months postpartum.[1]
Renal Blood Flow	Increase	Rises 60%-80% by mid-pregnancy; it is 50% greater than nonpregnant values in 3rd trimester.[1]
Creatinine Clearance	Increase	Increases early in pregnancy; reaches max by end of 1st trimester; slight decrease near-term.[2] 2020 ITE Gaps in Knowledge: *"The increase in creatinine clearance that occurs with pregnancy returns to prepregnant levels 8 to 12 weeks postpartum."*
BUN	Decrease	Decreases to 8-9 mg/dL by end of 1st trimester; stays there until term.[2]
Serum Cr concentration	Decrease	Decreases progressively to 0.5-0.6mg/dL by end of pregnancy.[2]

Coagulation System Changes at Term Gestation	
Pro-coagulants that increase	Factors I, VII, VIII, IX, X, XII, and von Willebrand factor
Anti-coagulants that decrease	Antithrombin III, Protein S
Unchanged factors include	Protein C (anti-coagulant); Factor II and Factor V (pro-coagulants)

Potential EKG/Echocardiographic Changes	
Echocardiography changes	LV hypertrophy; tricuspid, pulmonic, and mitral regurgitation
EKG Changes	Increased heart rate; shortened PR and uncorrected QT interval; depressed ST segments and isoelectric low-voltage T waves in left-sided precordial and limb leads

1. Miller 10th Ed, Ch 58. // 2. Chestnut 6th Ed, Ch 2. // GFR: Glomerular filtration rate; BUN: Blood Urea Nitrogen; Cr: creatinine

Room for notes

Obstetrics: Misc

16X

Room for notes

- Primary determinant of local anesthetic:
  - Potency: Lipid Solubility (aka "Meyer Overton correlation").
  - Onset: pKa (example: lidocaine has low pKa). *Exception*: 2-Chloroprocaine (pKa is high, but low systemic toxicity, so high concentration used).
  - Duration: Protein binding. *2020 ITE Gaps in Knowledge: "The duration of action of epidural bupivacaine is not greatly affected by the addition of epinephrine."*

- Placental transfer of medications:
  - Drugs that poorly cross the placenta to the Fetus: Heparin, Insulin, Glycopyrrolate, Paralytics (nondepolarizing and succinylcholine).
  - Fetal trapping of lidocaine (concept would also apply to mepivacaine): Fetal pH more acidic than maternal pH, lidocaine is a weak base → lidocaine gets "trapped" on fetal side. Bupivicaine diffuses poorly to placenta because of protein binding. Chloroprocaine poorly transfers to placenta because it is rapidly eliminated on maternal side by plasma cholinesterase.

- Transient Neurologic Symptoms:
  - Buttock/thigh/leg pain w/in 24 hrs, usually after spinal anesthesia, lasting up to 10 days. No bladder/bowel symptoms (as opposed to cauda equina syndrome).
  - "The likelihood of TNS is highest after intrathecal **lidocaine** and **mepivacaine,** and are far less frequent with bupivacaine and other local anesthetics….TNS occur more commonly in patients who are placed in the **lithotomy** position for surgery." [Miller's 9th Ed, Ch 45]

1. Miller 10th Ed, Ch 41 // 2. Chestnut 6th Ed, Ch 13, 33. // Brown et al. PMID: 934571

Obstetrics: Misc

13X
Incl next slide

Room for notes

- Fetal Heart Rate Decelerations
  - Early: Compression of fetal head, possible reflex vagal response to mild hypoxia (not ominous).
  - Variable: Umbilical cord compression against fetus → decreased umbilical blood flow.
  - Late: Uteroplacental insufficiency
- Maternal hypotension can cause fetal bradycardia: consider treating borderline hypotension in mom if the fetal tracing is nonreassuring.
- Antiphospholipid syndrome: hypercoagulable state that can cause recurrent pregnancy loss.
- Pain dermatomes of labor: First stage: T10-L1; Second stage: S2-S4. Sensory block for a c-section: T4-S4 (afferent nerves innervating abdominal/pelvic organs accompany sympathetic fibers – sympathetic trunk is T5 to L1).
- Non-obstetric surgery during pregnancy (ASA/ACOG joint opinion)[1]:
  - Medically necessary surgery should not be delayed regardless of trimester; elective surgery should be postponed until after delivery.
  - Consider corticosteroids if viable premature gestational age.
  - Perioperative DVT risk screening/prophylaxis should be provided.
  - "[F]etal monitoring should be individualized and, if used, based on gestational age, type of surgery, and facilities available."
  - Fetal monitoring may apply if: (1) fetus is viable; (2) monitoring physically possible; (3) OB surgery provider available; (4) parturient gives informed consent; (5) surgery can be safely altered/interrupted for emergency delivery.
  - If fetal monitoring: (1) institution should have neonatal/pediatric services; (2) OB provider with c-section privileges, as well as an individual qualified to interpret fetal heart rhythms, should be readily available.
  - "No currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard concentrations at any gestational age. There is no evidence that in utero human exposure to anesthetic or sedative drugs has any effect on the developing fetal brain; and there are no animal data to support an effect with limited exposures less than 3 hours in duration."

1. American Society of Anesthesiologists (ASA)/American College of Obstetricians and Gynecologists (ACOG) Joint Document on Nonobstetric Surgery During Pregnancy. Committee Opinion # 775 // Chestnut 6th Ed, Ch 8, 23, 26, 40 //

Preeclampsia & Imitators

Diagnostic Criteria for Preeclampsia

Blood Pressure:

- Systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure

or

- *Severe feature*: Systolic blood pressure of 160 mm Hg or more, or diastolic blood pressure of 110 mm Hg or more, in patient not already on antihypertensive therapy. (Severe hypertension can be confirmed within a short interval [minutes] to facilitate timely antihypertensive therapy).

"Intravenous hydralazine or labetalol and oral nifedipine are the three agents most commonly used for [acute onset severe hypertension in pregnancy]"[1]

and

Proteinuria:

- 300 mg or more per 24-hour urine collection (or this amount extrapolated from a timed collection)

or

- Protein/creatinine ratio of 0.3 or more

or

- Dipstick reading of 2+ (used only if other quantitative methods not available)

or

Severe features:

- Thrombocytopenia (platelet count less than 100 x 10^9/L
- Impaired liver function not accounted for by alternative diagnoses and as indicated by abnormally elevated blood concentrations of liver enzymes (to more than twice the upper limit normal concentrations), or by severe persistent right upper quadrant or epigastric pain unresponsive to medications
- Renal insufficiency (serum creatinine concentration more than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses
- Visual disturbances

Gestational HTN: BP elevation criteria without proteinuria or above findings; Chronic HTN in Pregnancy: HTN predates pregnancy or 20wks gestation; Chronic HTN w/Superimposed Preeclampsia: Chronic HTN plus preeclampsia; Imitators of preeclampsia: Handout

1. ACOG Practice Bulletin 203 and 222 (and 2024 practice update to 222); PMIDs: 32443079, 30575676, and 38569186. The latest ACOG Clinical Guidance documents can be accessed at www.acog.org/clinical .

Room for notes

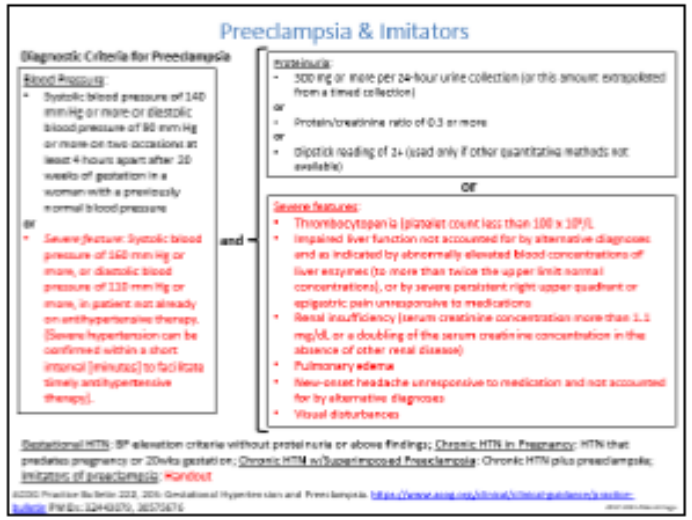
2024 ACOG Update (to ACOG Practice Bulletin 222): "There are insufficient data to recommend management strategies after a positive or negative test result [of the biomarker study sFlt-1:PIGF ratio (serum soluble fms-like tyrosine kinase-1:placental growth factor ratio)] […] the test is a complementary risk-stratification screen to add to the diagnostic work-up of preeclampsia with severe features. […] Avoid in patients who did not meet inclusion criteria [for its primary study]: e.g., avoid testing in asymptomatic, nonhospitalized individuals less than 23 weeks or more than 35 weeks of gestation and in postpartum individuals."

Preeclampsia and Imitators

Room for notes

Preeclampsia and Imitators:

Diagnostic Criteria for Preeclampsia:

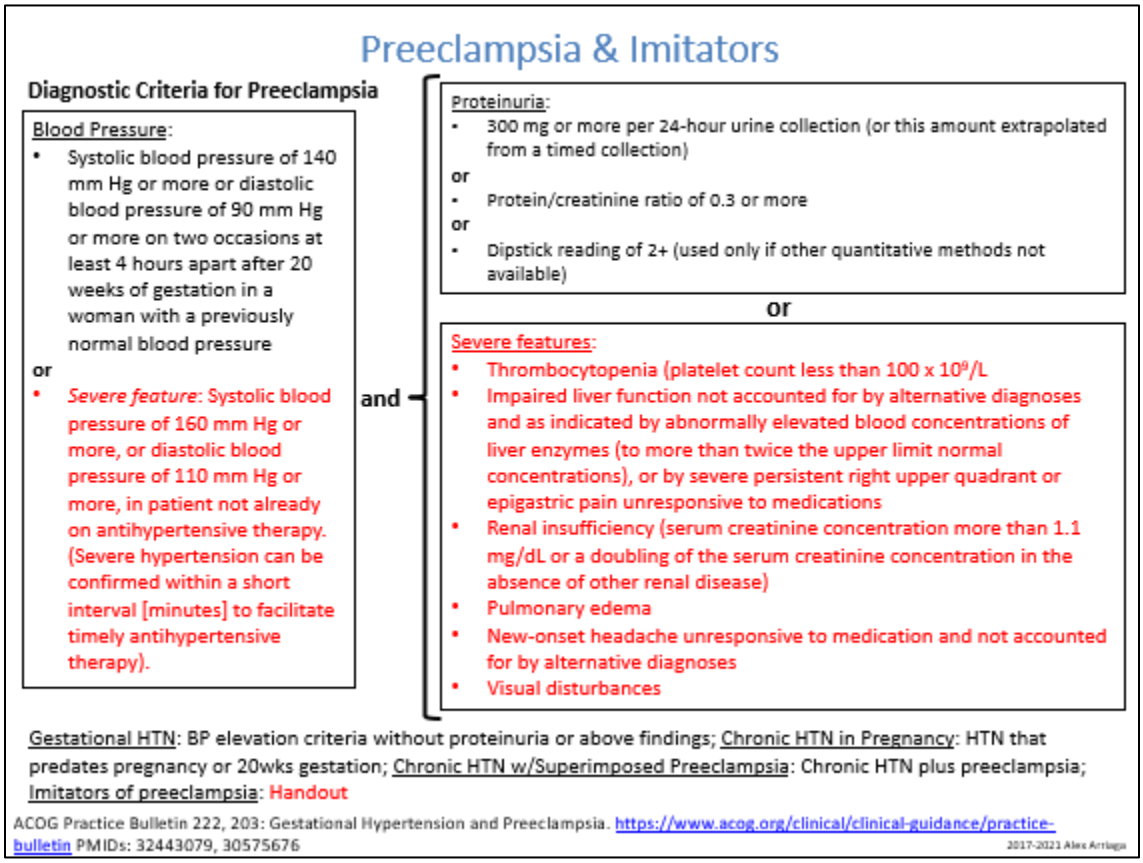


Excerpts on Imitators of Preeclampsia (from UptoDate article on *Preeclampsia: Clinical features and Diagnosis*):

- Antiphospholipid syndrome: "hypertension, proteinuria, thrombocytopenia and other signs of end-organ dysfunction can be seen in antiphospholipid syndrome. The absence of laboratory evidence of antiphospholipid antibodies excludes this diagnosis."
- Acute Fatty Liver of Pregnancy (AFLP): "Anorexia, nausea and vomiting are common clinical features of AFLP. Low-grade fever can be present in AFLP, but does **not** occur in preeclampsia/HELLP. AFLP is associated with more serious liver dysfunction. Hypoglycemia and DIC are common features, while unusual in preeclampsia/HELLP. AFLP is also usually associated with more significant renal dysfunction compared to preeclampsia/HELLP."
- TTP or HUS: "Although neurologic abnormalities and acute renal failure are often seen in TTP & HUS, respectively they are not always seen, and these disorders may be indistinguishable from severe preeclampsia/HELLP syndrome. Preeclampsia/HELLP begins to resolve within 48 hours after delivery, while TTP & HUS does not resolve with delivery. Distinguishing among TTP, HUS and related thrombotic microangiopathy syndromes may be challenging."
- Exacerbation of systemic lupus erythematosus (SLE): "Flares of SLE are likely to be associated with hypocomplementemia and increased titers from anti-DNA antibodies, by comparison, complement levels are usually, but not always, normal or increased in preeclampsia. Acute onset, accelerated HTN is more likely to be due to preeclampsia than a lupus flare."

SOAP Consensus Statement on Neuraxial Procedures in Obstetric Patients with Thrombocytopenia: "Through a systematic review and modified Delphi process, the taskforce concluded that the best available evidence indicates the risk of spinal epidural hematoma associated with a platelet count ≥70,000 × 10^6/L is likely to be very low in obstetric patients with thrombocytopenia secondary to gestational thrombocytopenia, immune thrombocytopenia (ITP), and hypertensive disorders of pregnancy in the absence of other risk factors. Ultimately, the decision of whether to proceed with a neuraxial procedure in an obstetric patient with thrombocytopenia occurs within a clinical context. Potentially relevant factors include, but are not limited to, patient comorbidities, obstetric risk factors, airway examination, available airway equipment, risk of general anesthesia, and patient preference." (Anesth Analg 2021; PMID: 33861047)

Diagnostic Criteria for Preeclampsia:



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Obstetrics: Misc

20X

- Risk factors for Post-Dural Puncture Headache (PDPH): Female sex, younger age, prior PDPH history, pregnancy, vaginal delivery (vs c-section), large bore needle, multiple dural punctures, cutting needle (if using cutting needle, insert needle with bevel parallel to long axis of spine), dural puncture with patient in sitting position (weigh benefit of lateral decubitus against operator experience). *May/might be associated w/PDPH*: history of headaches, smoking, operator inexperience.[1,2]
- Pneumocephalus buzzwords: often abrupt onset frontal headache immediately after dural puncture
- Magnesium toxicity: (Tx: calcium, loop diuretics, supportive care)

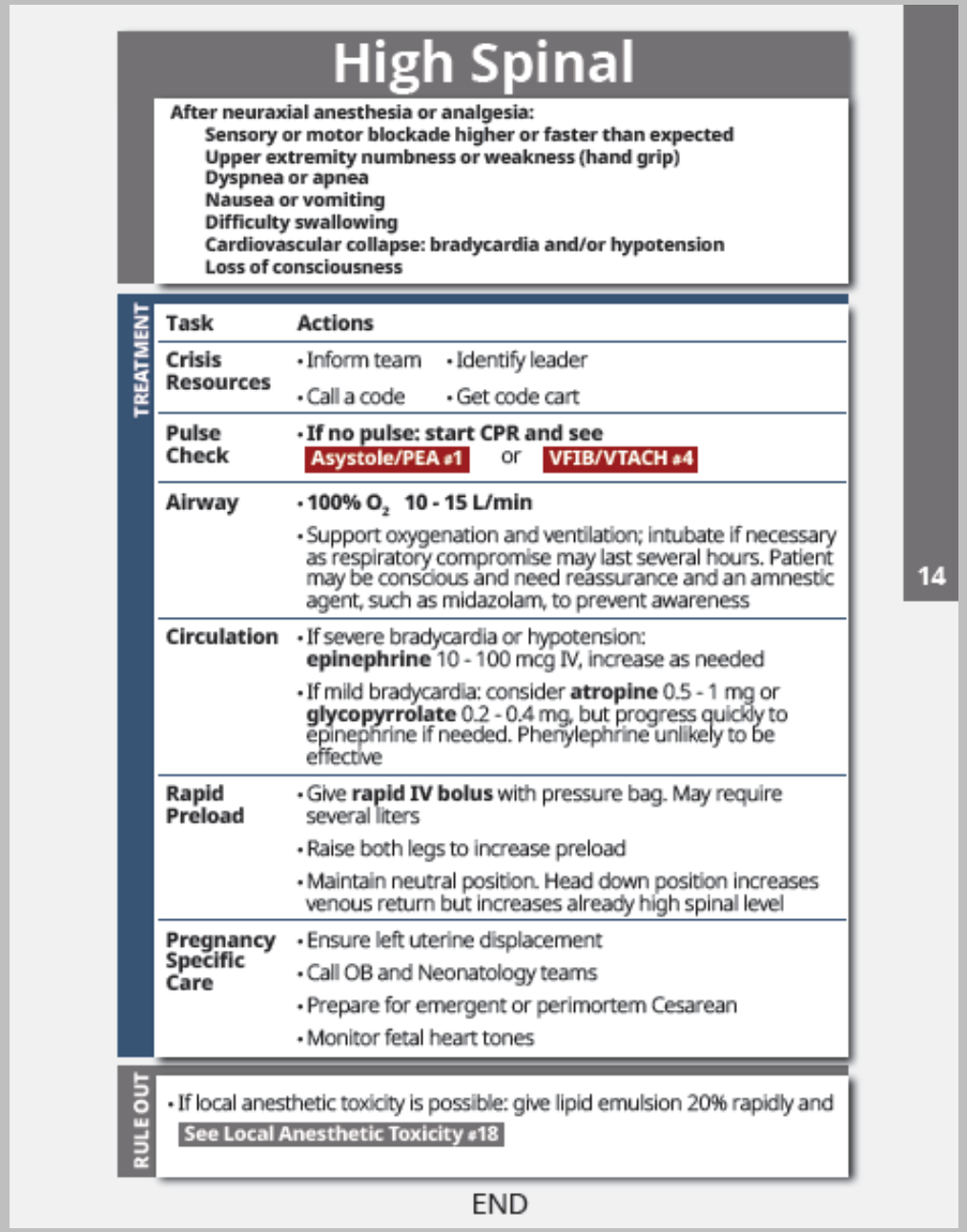
Infographic of PDPH multidisciplinary guidelines (ASRA, SOAP, & others)[2]

Serum Mg level (mg/dL)	Comments/Signs/Symptoms
1.7-2.4	Normal range
5-9	Therapeutic range for seizure prophylaxis in preeclampsia w/severe features (side effects may include sedation, weakness, and EKG changes: widened QRS, long PR)
~12	Loss of deep tendon/patellar reflexes
15-20	Respiratory arrest
25	Asystole

- APGAR: **A**ppearance: acrocyanotic (trunk pink, extremities blue)=1; **P**ulse: <100bpm=1; **G**rimace (instead of active cough and sneezing)=1; **A**ctivity: some extremity flexion instead of active movement=1; **R**espiratory effort: irregular, slow, shallow, or gasping=1
- Handout: High Spinal (Stanford Emergency Manual Entry)

Chestnut OB Anesthesia, 6th Ed, Ch 30 // 2. PMID 37582578 // Chestnut 6th Ed Ch's 9 and 35.

Room for notes



Room for notes

Regional

Room for notes

Peripheral Nerve Blocks

84X
incl images & L.A.S.T.

Side Effects/Complications of Interscalene Block:

- **Ipsilateral phrenic nerve block and diaphragmatic paralysis** "are inevitable […] may cause subjective […] dyspnea […] respiratory compromise can occur [if] severe preexisting respiratory disease or contralateral phrenic nerve dysfunction." (Miller 10th Ed, Ch 42)
- **Pneumothorax:** "should be considered if cough or chest pain is produced while exploring for the nerve." (Barash 9th Ed, Ch 36)
- **Severe hypotension, bradycardia, and syncope (sometimes referred to as Bezold-Jarisch reflex)**: "[C]an occur in awake, sitting patients undergoing shoulder surgery [under an interscalene block]. The cause is presumed to be stimulation of intracardiac mechanoreceptors by decreased venous return, producing an abrupt withdrawal of sympathetic tone and enhanced parasympathetic output." (Miller 10th Ed Ch 42)
- "**Epidural and intrathecal injections** have occurred with this block, primarily when done under general anesthesia." (Miller Ch 10th Ed, Ch 42)
- Other complications: intravascular injection with CNS toxicity/seizures, Horner syndrome [miosis/constricted pupil, ptosis, anhidrosis], partial blockade of vagus/recurrent laryngeal nerve (hoarseness, and dysphagia). (Barash 9th Ed Ch 36 and Miller 10th Ed, Ch 42)

Complications of Axillary nerve Block: Systemic toxicity (especially if transarterial approach and large volume of local anesthetic), nerve injury, hematoma, infection.

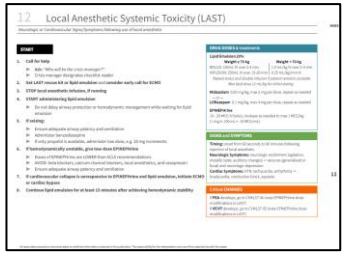
Local Anesthetic Systemic Toxicity (L.A.S.T):

- Key medication in treatment: Lipid Emulsion 20%
- Epinephrine smaller doses preferred (≤ 1 mcg/kg)
- Key medications to avoid: beta-blockers, calcium channel blockers, vasopressin, local anesthetics.

"ASRA Best" Video Gallery (includes peripheral nerve block videos)

ASRA 2020 Checklist for Local Anesthetic Systemic Toxicity

Handout: Crisis Checklist for Local Anesthetic Systemic Toxicity


12 Local Anesthetic Systemic Toxicity (LAST)

Room for notes

12 Local Anesthetic Systemic Toxicity (LAST)

Neurologic or Cardiovascular Signs/Symptoms following use of local anesthetic

INDEX

START

1. **Call for help**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Get LAST rescue kit or lipid emulsion** and **consider early call for ECMO**
3. **STOP local anesthetic infusion, if running**
4. **START administering lipid emulsion**
   - Do not delay airway protection or hemodynamic management while waiting for lipid emulsion
5. **If seizing:**
   - Ensure adequate airway patency and ventilation
   - Administer benzodiazepine
   - If only propofol is available, administer low dose, e.g. 20 mg increments
6. **If hemodynamically unstable, give low-dose EPINEPHrine**
   - Doses of EPINEPHrine are LOWER than ACLS recommendations
   - AVOID: beta blockers, calcium channel blockers, local anesthetics, and vasopressin
   - Ensure adequate airway patency and ventilation
7. **If cardiovascular collapse is unresponsive to EPINEPHrine and lipid emulsion, initiate ECMO or cardiac bypass**
8. **Continue lipid emulsion for at least 15 minutes after achieving hemodynamic stability**

DRUG DOSES & treatments

Lipid Emulsion 20%

Weight ≥ 70 kg	Weight < 70 kg
BOLUS: 100mL IV over 2-3 min	1.5 mL/kg IV over 2-3 min
INFUSION: 250mL IV over 15-20 min	0.25 mL/kg/min IV

Repeat bolus and double infusion if patient remains unstable
Max lipid dose 12 mL/kg for initial dosing

Midazolam 0.05 mg/kg, max 2 mg per dose, repeat as needed
— *or* —
LORazepam 0.1 mg/kg, max 4 mg per dose, repeat as needed

EPINEPHrine
10 - 20 MCG IV bolus, increase as needed to max 1 MCG/kg
(1 mg in 100 mL = 10 MCG/mL)

SIGNS and SYMPTOMS

Timing: onset from 60 seconds to 60 minutes following injection of local anesthetic
Neurologic Symptoms: neurologic excitement (agitation, metallic taste, auditory changes) -> seizures (generalized or focal) and neurologic depression
Cardiac Symptoms: HTN, tachycardia, arrhythmia -> bradycardia, conduction block, asystole

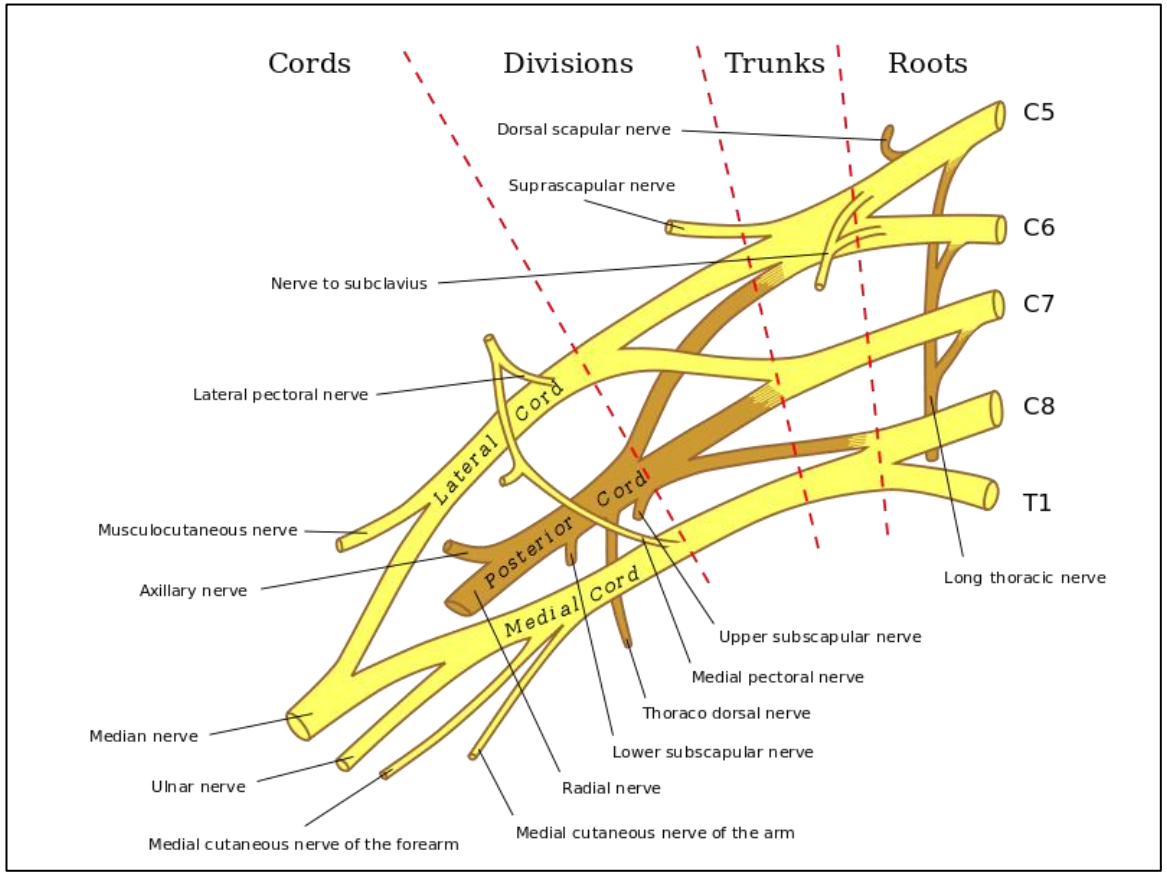
Critical CHANGES

If **PEA** develops, *go to* CHKLST 04 (note EPINEPHrine dose modifications in LAST)
If **VF/VT** develops, *go to* CHKLST 05 (note EPINEPHrine dose modifications in LAST)

12

Room for notes

Brachial Plexus Anatomy



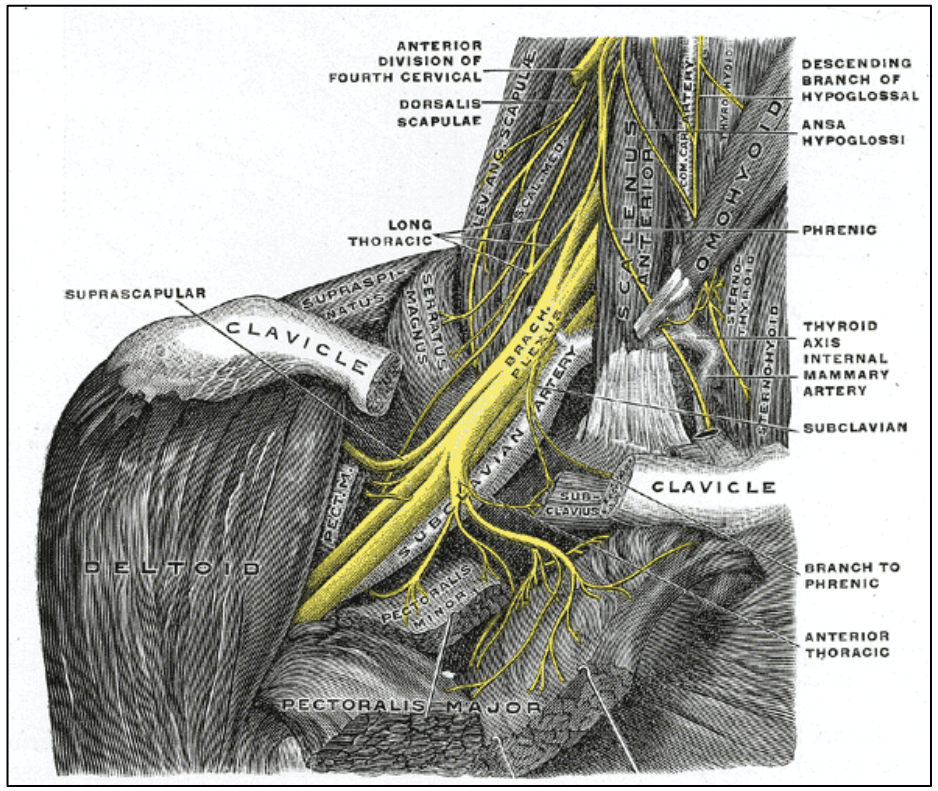
- Interscalene Block: Used for shoulder surgery. "Blockade occurs at the level of the **superior and middle trunks**….blockade of the inferior trunk (C8 through T1) is often incomplete"
- Supraclavicular Block: Used for surgery on elbow, forearm, and hand. "Blockade occurs at the **distal trunk-proximal division level**."
- Axillary Block: "[V]ersatile block [for] surgical anesthesia of the distal upper arm, elbow, and hand." Works at the **level of the terminal nerves/branches**. Axillary blocks often supplemented with blocks to musculocutaneous nerve (branch of lateral cord), medial brachial cutaneous (branch of medial cord) and the intercostobrachial nerve (a branch of T2). (Miller 10th Ed, Ch 42)

Brachial plexus image: Public domain, via Wikimedia Commons (https://commons.wikimedia.org/wiki/File:Brachial_plexus_2.svg)

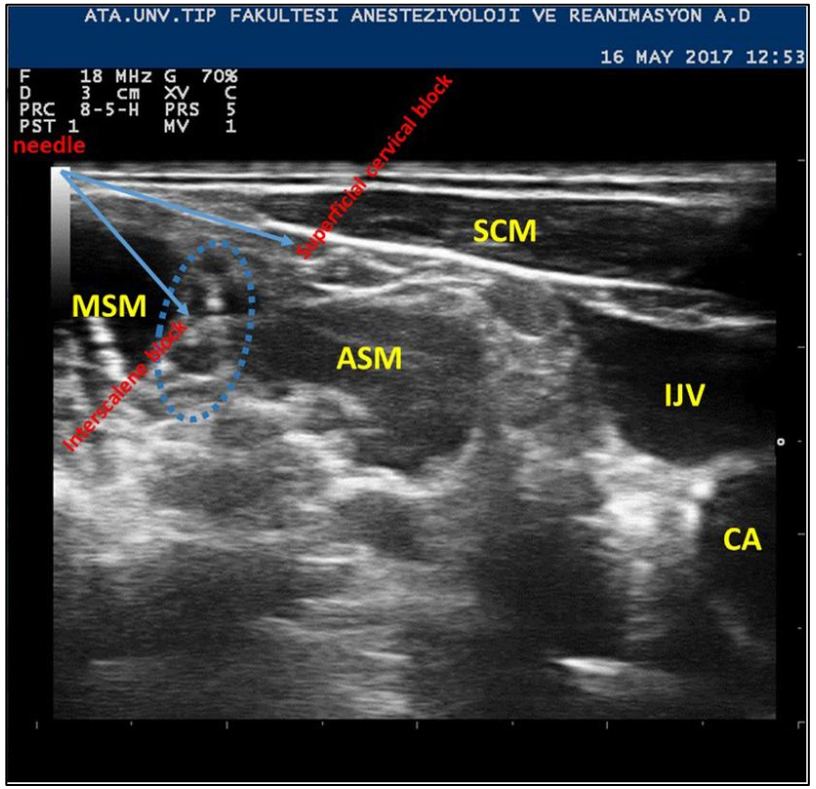
Room for notes

Interscalene & Superficial Cervical Plexus Block Anatomy

Anatomy



Ultrasound Anatomy



<u>Interscalene Block</u>:

- Often done for shoulder surgery in patients without major pulmonary disease.
- Blockade of inferior trunk (C8, T1 → ulnar nerve) can be incomplete. (Miller 10th Ed, Ch 42)

MSM: middle scalene muscle; ASM: anterior scalene muscle; SCM: sternocleidomastoid muscle; IJV: internal jugular vein; CA: carotid artery

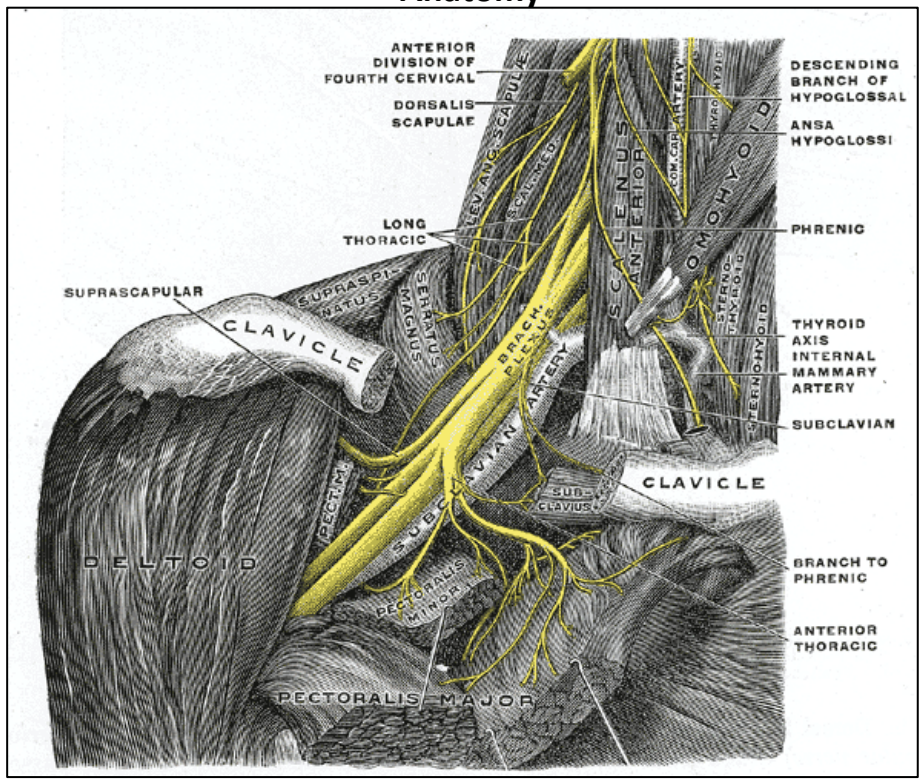
Anatomy image: Henry Vandyke Carter, https://commons.wikimedia.org/wiki/File:Gray808.png, Public domain, via Wikimedia Commons // Ultrasound Image: Kaciroglu et al. Kaciroglu, A. et al. Ultrasound-guided combined interscalene and superficial cervical plexus blocks for anesthesia management during clavicle fracture surgery. Ain-Shams J Anesthesiol 11, 28 (2019). https://doi.org/10.1186/s42077-019-0039-5. Creative Commons CC-BY-4.0.

Room for notes

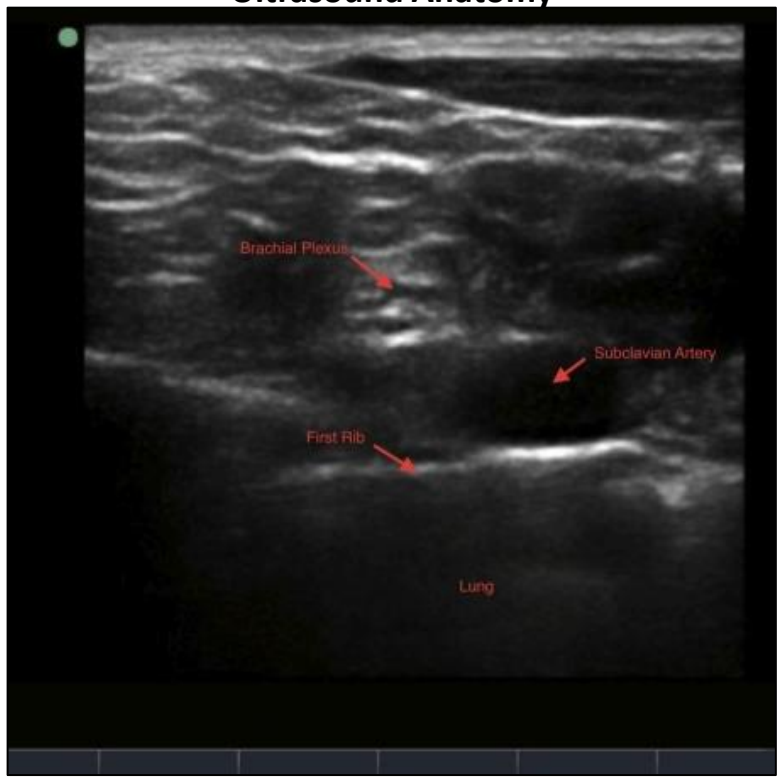
Supraclavicular Block Anatomy

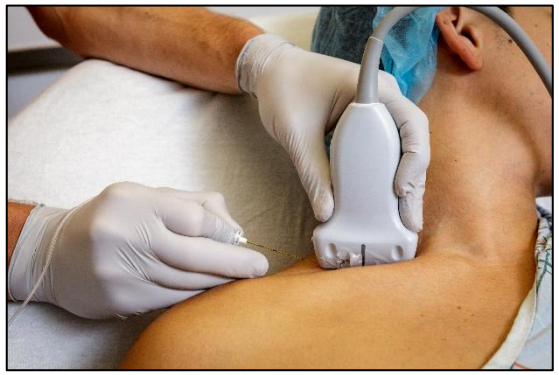
Room for notes

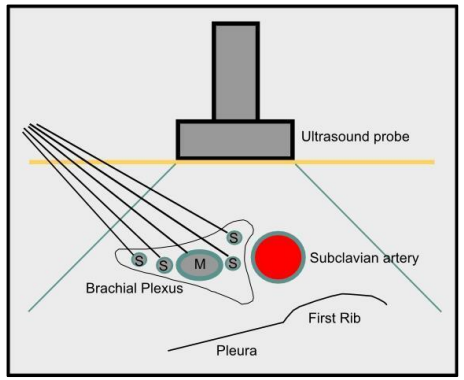
Anatomy



Ultrasound Anatomy







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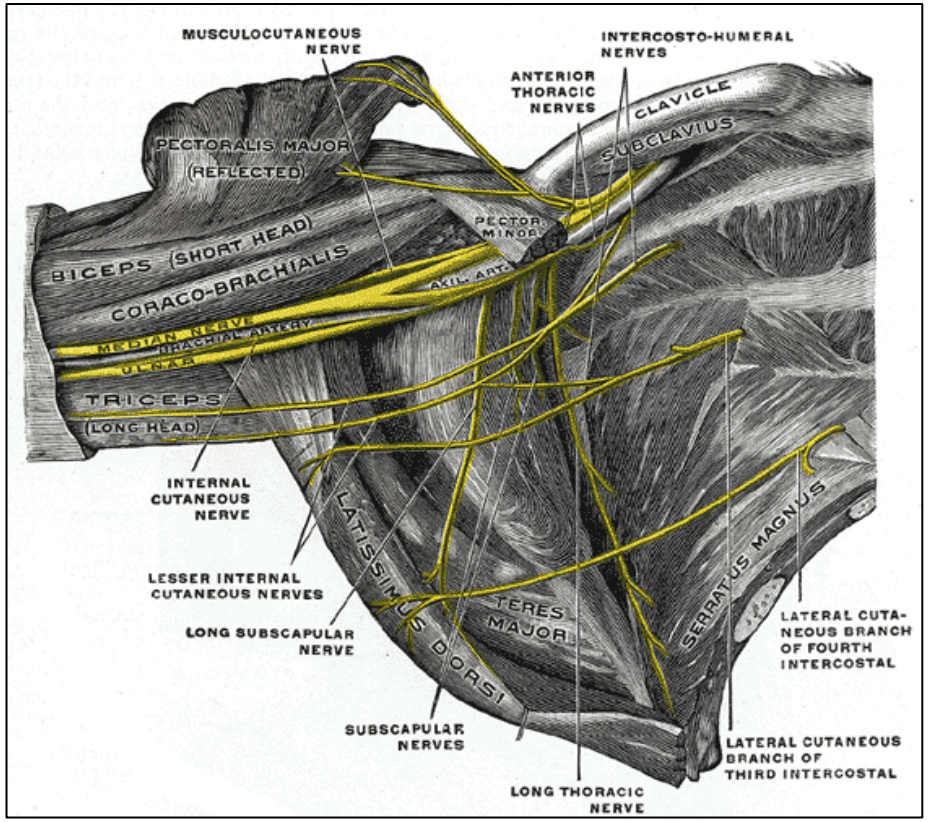
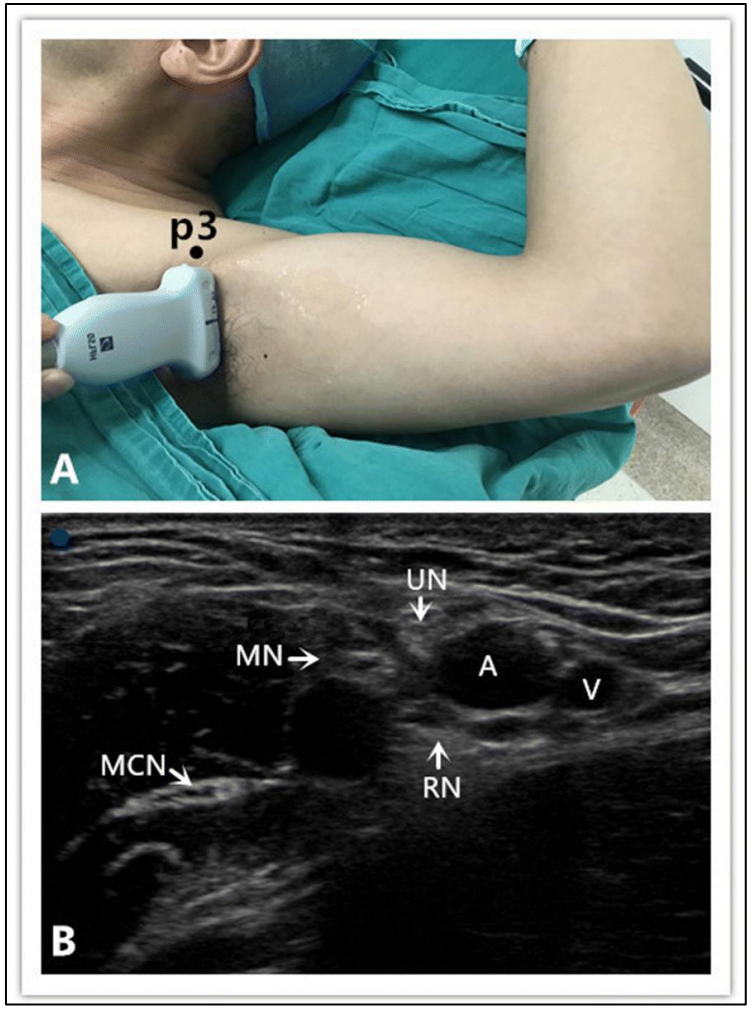
Axillary/Musculocutaneous Block Anatomy

Anatomy



"Relative to the third part of axillary artery, the usual course of the terminal nerves is as follows: the median nerve lies anterior and medial, the ulnar nerve lies posterior and medial, the musculocutaneous nerve lies anterior and lateral, and the radial nerve lies posterior and lateral."[1]

Ultrasound Anatomy



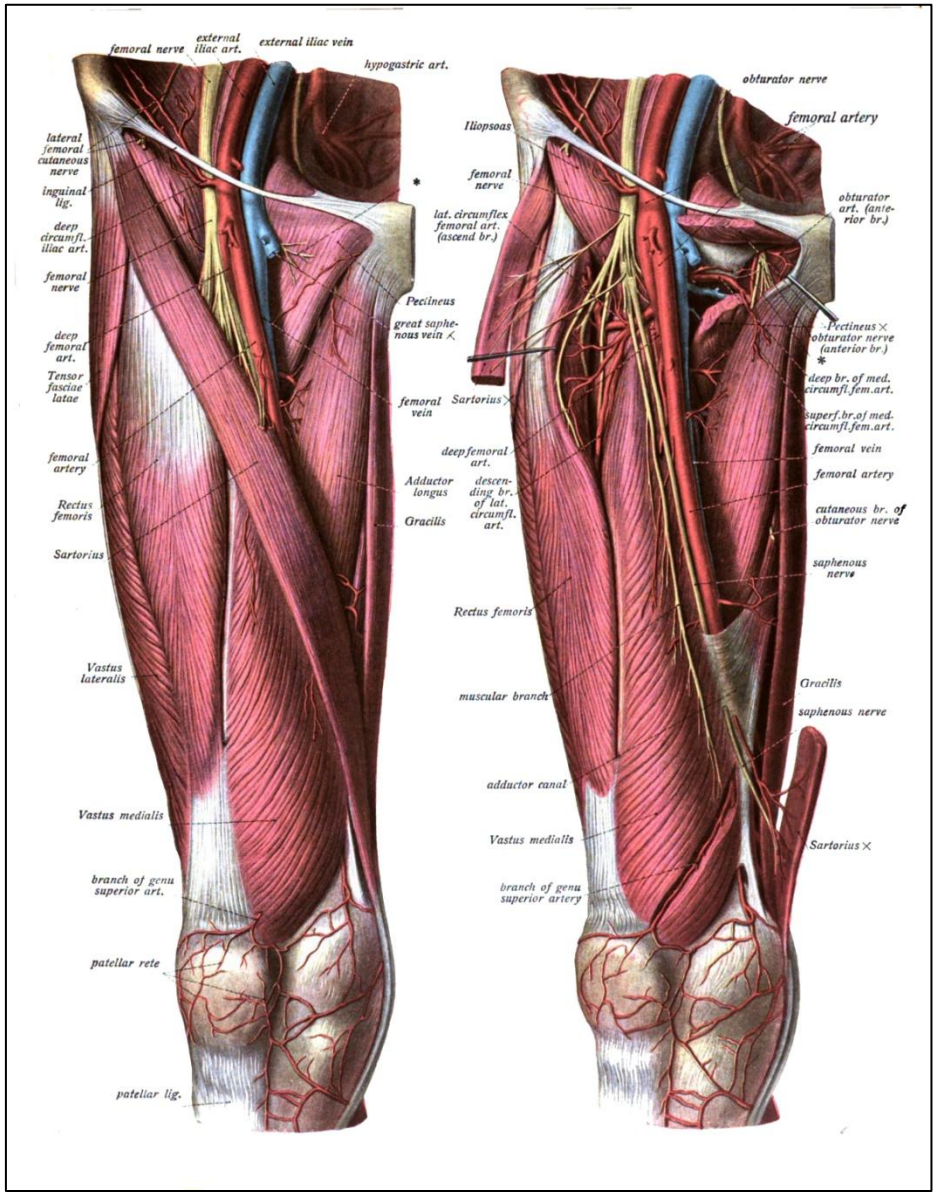
MCN: musculocutaneous nerve; MN: median nerve; UN: ulnar nerve; RN: radial nerve; A: axillary artery; V: axillary vein

Anatomy image: Henry Vandyke Carter, Public domain, via Wikimedia Commons; https://commons.wikimedia.org/wiki/File:Gray809.png // Ultrasound anatomy: Zhu et al. PMID: 30340524; Creative Commons CC-BY-4.0 // 1. Barash 9th Ed Ch 36

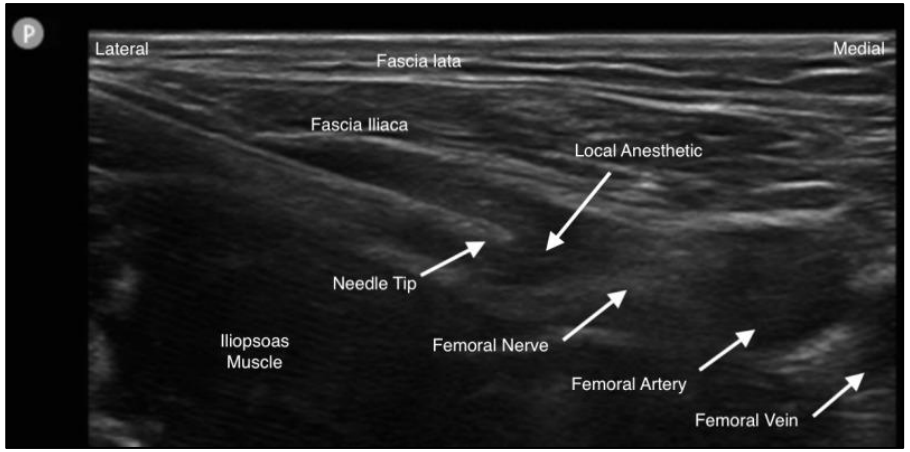
Room for notes

Femoral Nerve Block & Fascia Iliaca Block Anatomy

Lower extremity anatomy



Ultrasound Anatomy



Femoral Nerve: Formed from the posterior divisions of L2, L3, and L4. **Motor innervation:** quadriceps, sartorius, and pectineus muscles. "**Sensory branches** include the anterior cutaneous nerve of the thigh, the infrapatellar nerve, and the saphenous nerve. These nerves innervate the anterior thigh, the patella, and the medial leg and foot, respectively."[1,2]

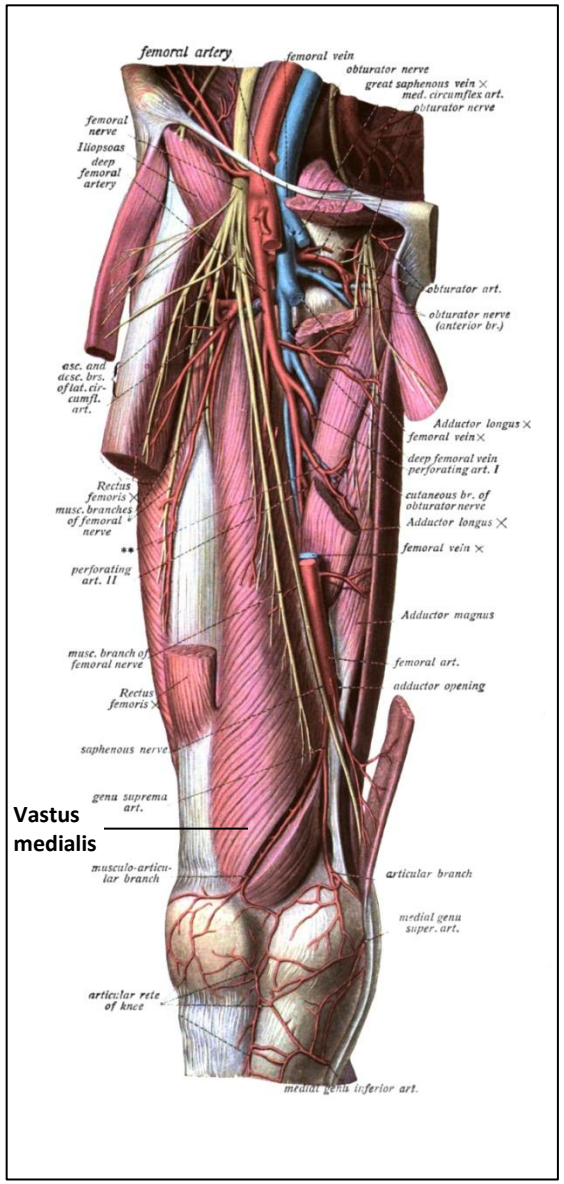
Room for notes

Ultrasound anatomy: Sykes et al. PMID: 31536310. Creative Commons CC-BY-4.0 // Lower extremity anatomy: Dr. Johannes Sobotta, Public domain, via Wikimedia Commons https://commons.wikimedia.org/wiki/File:Sobo_1909_573-574.png // 1. Atlas of Ultrasound-Guided Regional Anesthesia, 2nd Ed // 2. Miller 10th Ed Ch 42

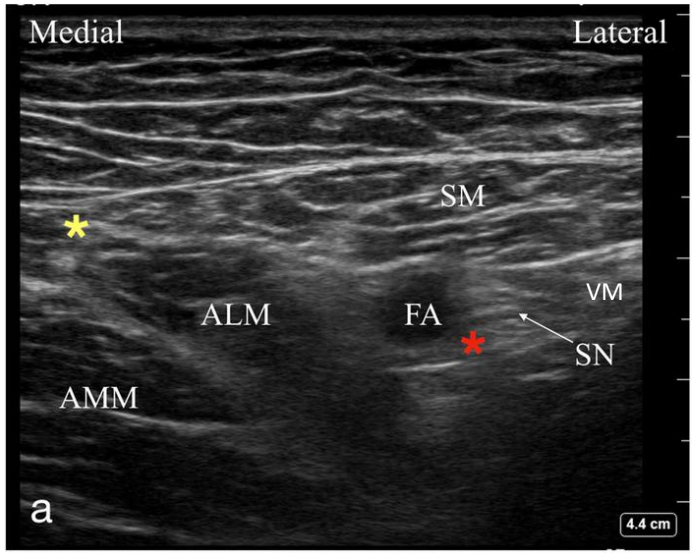
Adductor Canal Block Anatomy

Room for notes

More Lower extremity anatomy

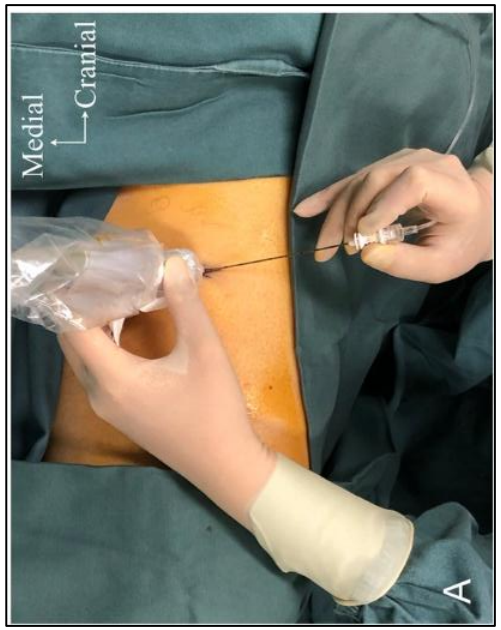


Ultrasound Anatomy



AMM: adductor magnus muscle; ALM: adductor longus muscle; SM: sartorius muscle; FA: femoral artery; VM: vastus medialis; *: proposed target of needle tip; yellow *: alignment of SM and ALM medial borders.

In-plane approach, needle direction lateral to medial

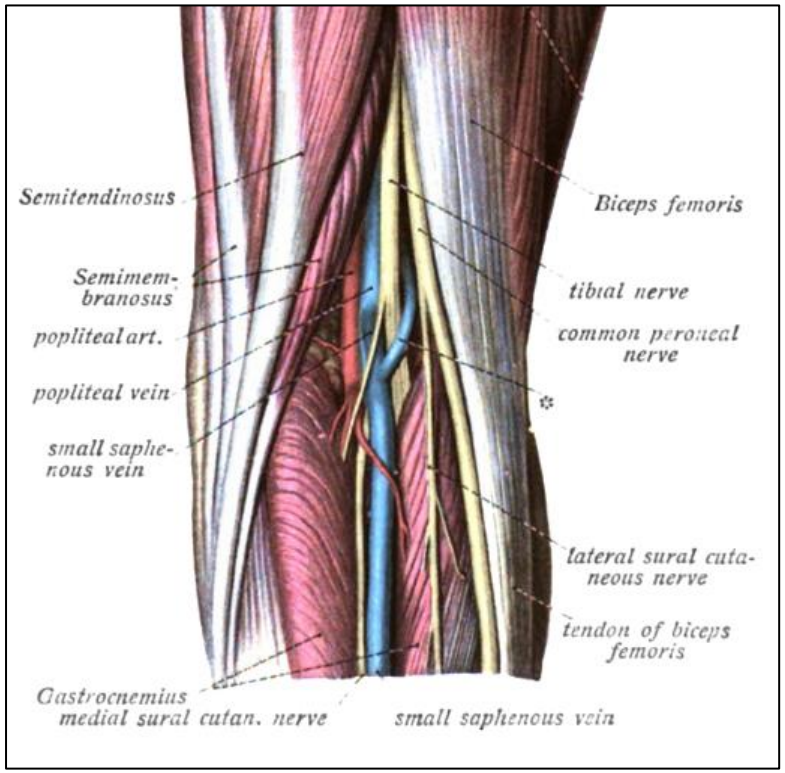


<u>Saphenous Nerve</u>: "terminal branch of the posterior division of the femoral nerve…**sensory innervation** to the medial, anteromedial, and posteromedial aspects of the lower extremity from the distal thigh to the medial malleolus."[1]

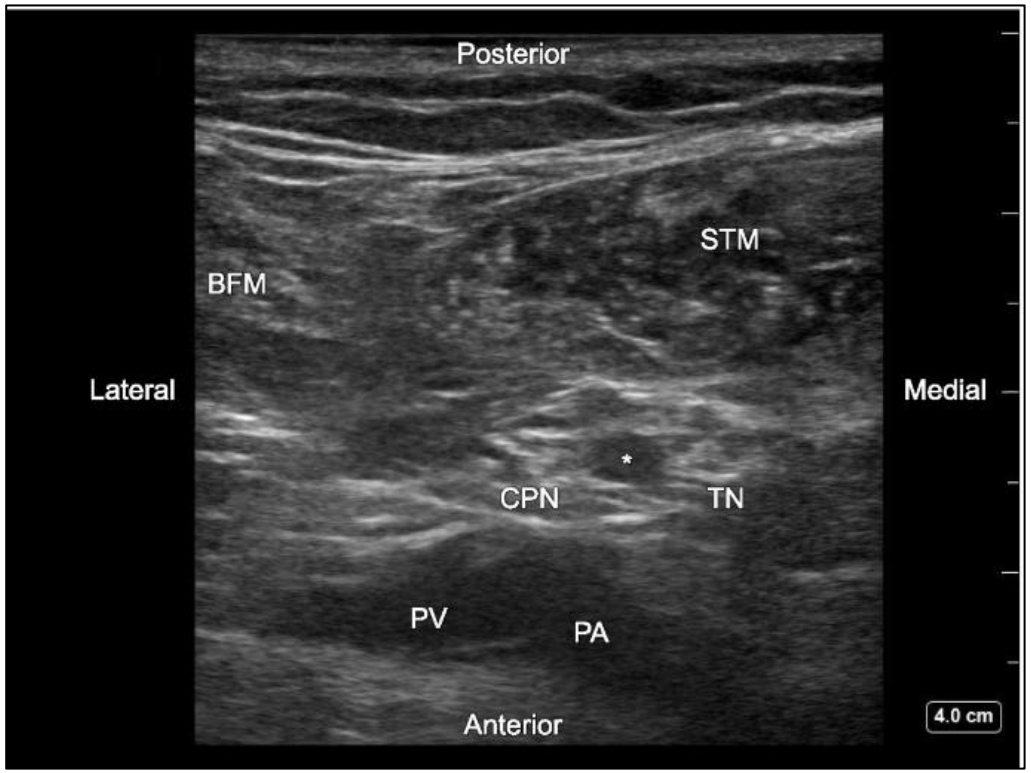
<u>Nerve to the Vastus Medialis</u>: "also a branch of the posterior division of the femoral nerve. It travels lateral to the superficial femoral artery within the adductor canal and sends multiple branches to the vastus medialis and supplies the anteromedial portion of the knee capsule."

Popliteal Fossa Block Anatomy

Anatomy



Ultrasound Anatomy

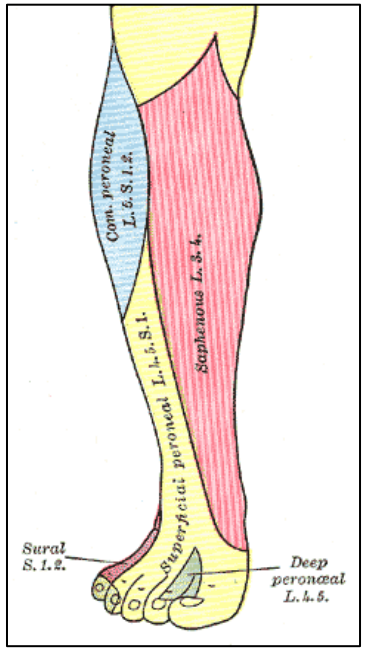


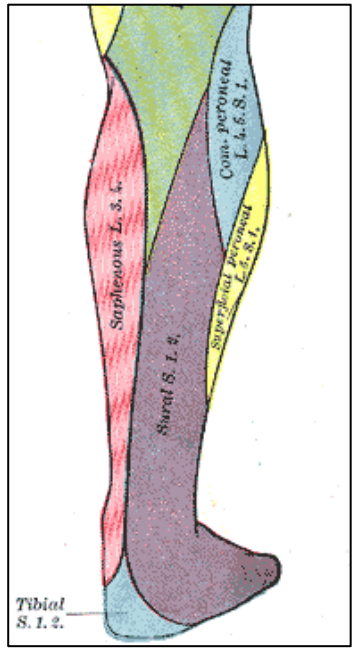
"Near the upper border of the popliteal fossa, the two components of the sciatic nerve separate. The peroneal nerve diverges laterally, and the larger tibial branch descends almost straight down through the fossa. The tibial nerve and popliteal vessels then disappear deep to the converging heads of the gastrocnemius muscle." "This block is chiefly used for foot and ankle surgery. "[1]

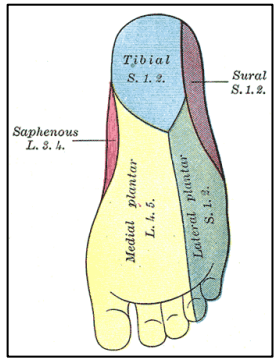
BFM: biceps femoris muscle; STM: semitendinosus muscle; TN: tibial nerve; CPN: common peroneal nerve; PA: popliteal artery; PV: popliteal vein (Note: asterisk depicts an anomalous vessel within the sheath around the TN and the CPN)

Room for notes

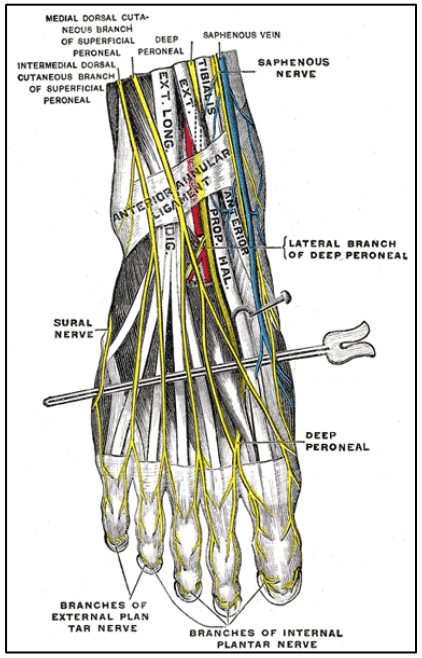
Ankle Block Anatomy



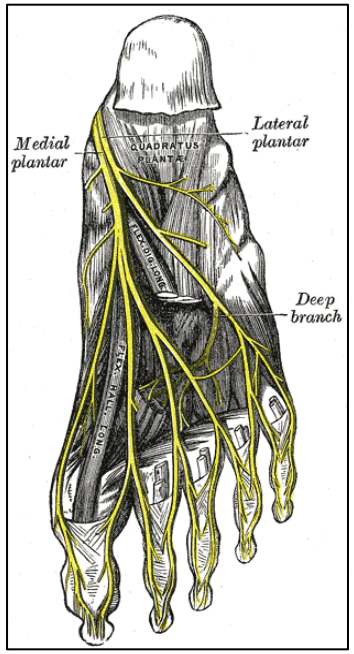




Dorsal side of foot



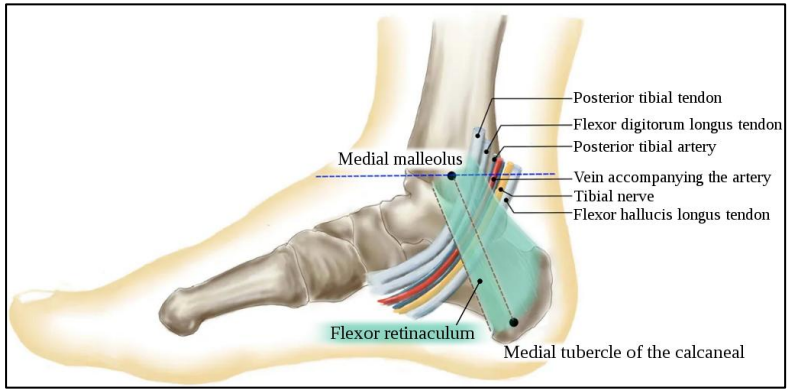
Plantar side of foot



Nerves to block at ankle:
1. Saphenous nerve

<u>Four branches of the sciatic nerve</u>:

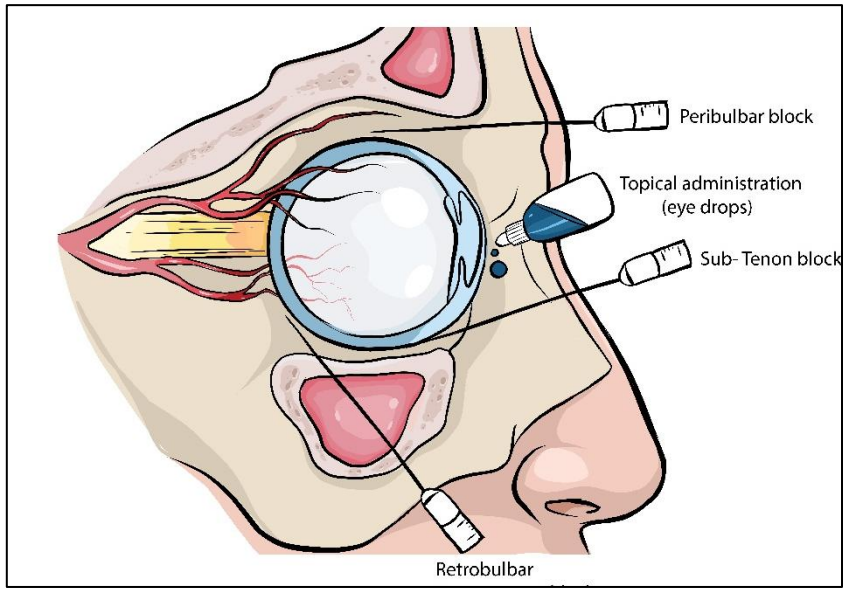
2. Posterior tibial (lateral plantar and medial plantar nerves are branches of posterior tibial nerve)
3. Sural
4. Superficial peroneal
5. Deep peroneal

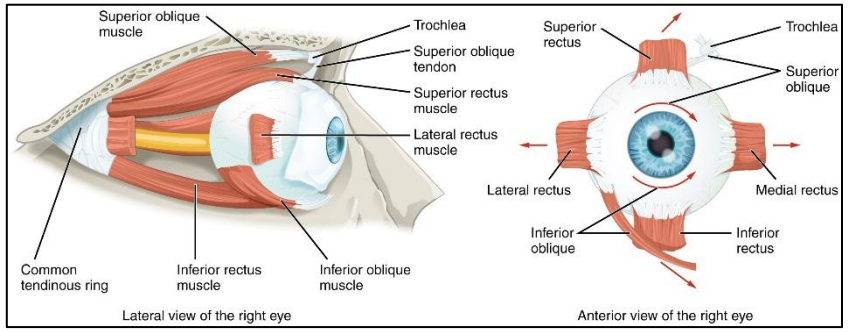


Sensory distribution images: Excerpt from Henry Vandyke Carter, Public domain, via Wikimedia Commons; https://commons.wikimedia.org/wiki/File:Gray826.png, https://commons.wikimedia.org/wiki/File:Gray831.png, https://commons.wikimedia.org/wiki/File:Gray834.png // Structures within tarsal tunnel: Y. Yang, M. L. Du, Y. S. Fu, W. Liu, Q. Xu, X. Chen, Y. J. Hao, Z. Liu & M. J. Gao, CC BY 4.0 <https://creativecommons.org/licenses/by/4.0>, via Wikimedia Commons https://commons.wikimedia.org/wiki/File:Structures_within_the_tarsal_tunnel_-_with_text.svg

Room for notes

Peribulbar and Retrobulbar Block Anatomy





"Routine preoperative laboratory testing is not necessary for cataract surgery and has not been shown to reduce adverse perioperative events."[1] Avoiding over-testing in this population is an active area of research.[5-7]

Many modifications to these blocks have been described.

Retrobulbar (intraconal) Block: Needle tip inserted behind the globe through the cone formed by the four rectus muscles ("muscle cone"). Onset typically faster with a retrobulbar block.[1-3] **Peribulbar (extraconal) Block**: Needle tip outside the muscle cone.[3] Might provide better akinesia of orbicularis oculi (muscle that closes eyelids).[4] Theoretically less serious complications (but see Cochrane review below).

- *Potential serious complications include*: intravascular injection (possible seizure if intraarterial); retrograde passage of local anesthesia via optic nerve causing partial or total brainstem anesthesia; severe oculocardiac reflex.[1,3,4] "Optic nerve damage, or globe perforation with retinal detachment and vitreous hemorrhage, are devastating complications of retrobulbar block. Risk factors include physician inexperience and a highly myopic eye."[1]

Sub-Tenon Block: Local anesthesia inserted under Tenon's capsule ("membrane which envelops the eyeball from the optic nerve posteriorly to the sclera anteriorly"). Can be done with blunt cannula instead of needle. Compared to retrobulbar/peribulbar blocks: akinesia onset might be slower (or depend on volume); chemosis [conjunctival swelling/edema] & minor subconjunctival hemorrhage might be more frequent (chemosis possibly mitigated via small volumes & long cannula).[3,4]

Cochrane Review (2015) comparing peribulbar vs retrobulbar block for cataract surgery: "There was no evidence of any difference in complete akinesia or the need for further injections of local anaesthetic. Conjunctival chemosis was more common after peribulbar block (relative risk (RR) 2.11, 95% confidence interval (CI) 1.46 to 3.05) and lid haematoma was more common after retrobulbar block (RR 0.36, 95% CI 0.15 to 0.88). Retrobulbar haemorrhage was uncommon and occurred only once, in a patient who had a retrobulbar block."

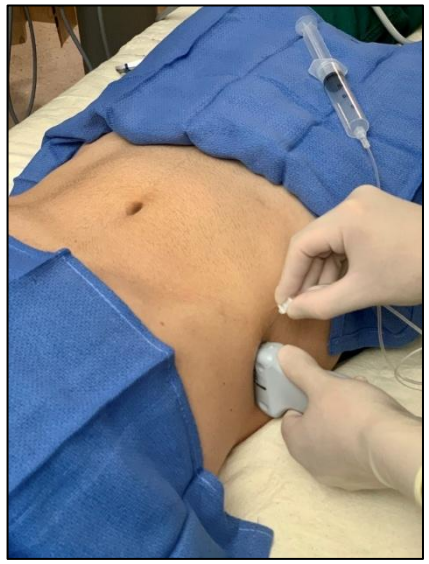
Room for notes

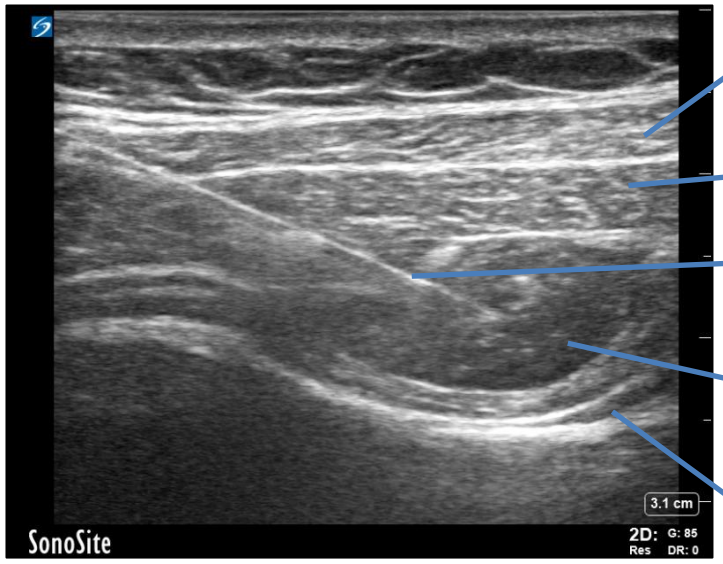
1. Miller 10th Ed Ch 65 // 2. Brown's Atlas of regional anesthesia, 6th Ed Ch 22 // 3. Smith and Aitkenhead's Textbook of Anaesthesia, 7th Ed, Ch 38 // 4. UpToDate: Anesthesia for elective eye surgery // 5. PMID: 25875258 // 6. PMID: 36190717 // 7. PMID: 32926912 // Block Image: ID: 1841033011, used via shutterstock.com license // Eye muscles: OpenStax College, via Wikimedia Commons; CC BY 3.0 https://commons.wikimedia.org/wiki/File:1412_Extraocular_Muscles.jpg

Transversus Abdominis Plane (TAP) Block Anatomy

ASRA-ESRA Consensus Anatomical Descriptions (note: images from separate sources):[1]

- TAP Block: "injection in the plane between the internal oblique and transversus abdominis muscles.
- Midaxillary TAP block: "injection in the plane between the internal oblique and transversus abdominis muscles at the mid-axillary line."





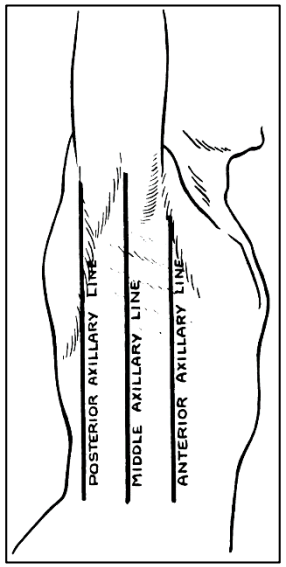
External oblique (EO) muscle

Internal oblique (IO) muscle

Needle

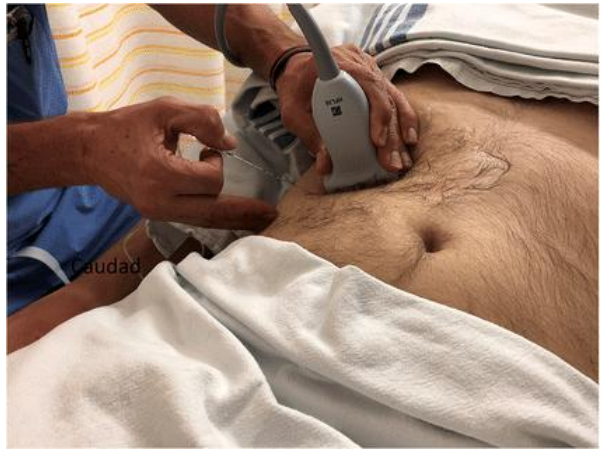
Local anesthetic hydrodissecting plane between the IO and TAM

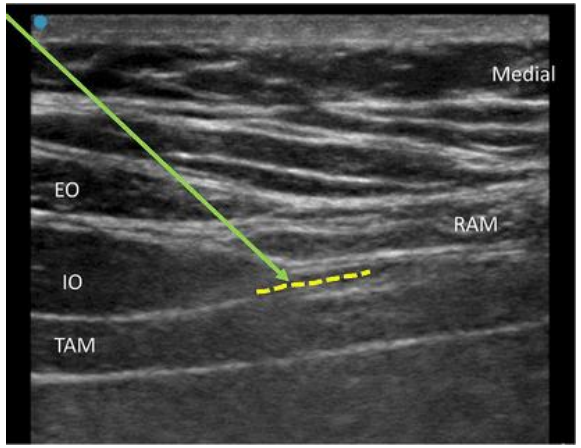
Transversus abdominis (TAM)

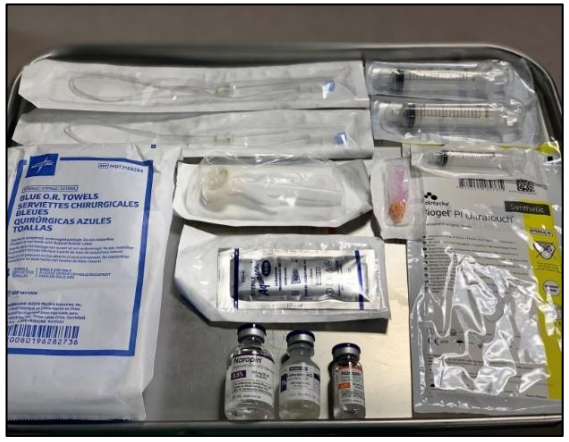


The midaxillary TAP block was classically reported for analgesia for lower abdominal surgical procedures.[2,4]

- Subcostal TAP Block: "injection in the plane between the internal oblique and transversus abdominis muscles along the medial costal margin in the upper quadrants of the anterior abdominal wall" (RAM: Rectus abdominis muscle)





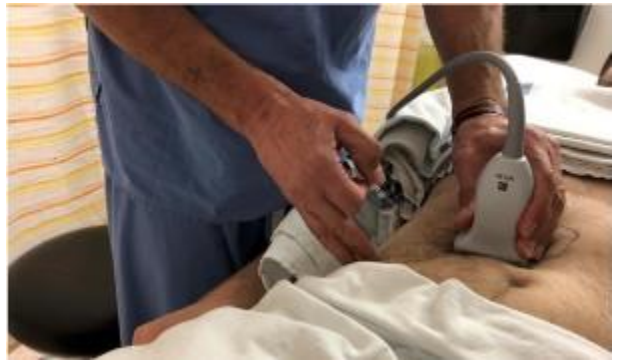


The subcostal TAP block has been reported to provide analgesia for upper abdominal surgical procedures.[3,5]

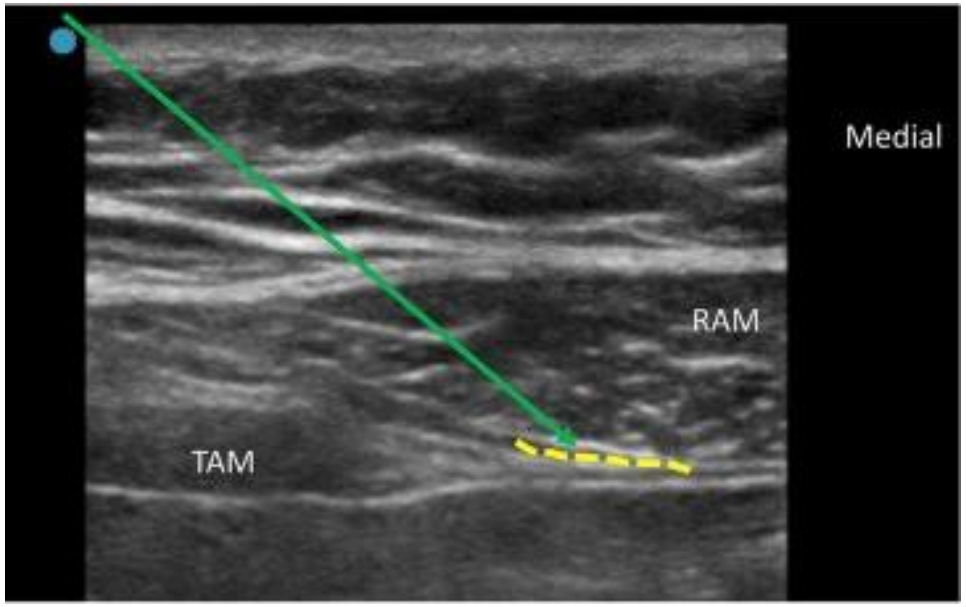
1. PMID 34145070 // 2. Brown's Atlas of Regional Anesthesia, 6th Ed, Ch 36 (ref#2) and 37 (ref#3) // 4. Miller 10th Ed, Ch 42 // 5. PMID: 29696110 // Axillary lines: Brantigan, Otto C., Public domain, https://commons.wikimedia.org/wiki/File:Brantigan_1963_1-53.png // Midaxillary TAP & supplies images: PMID: 32809362. Creative Commons CC-BY-4.0 // Subcostal TAP images: Curr Anesthesiol Rep 2019; 9: 479-87. https://doi.org/10.1007/s40140-019-00351-y. Creative Commons CC-BY-4.0.

Room for notes

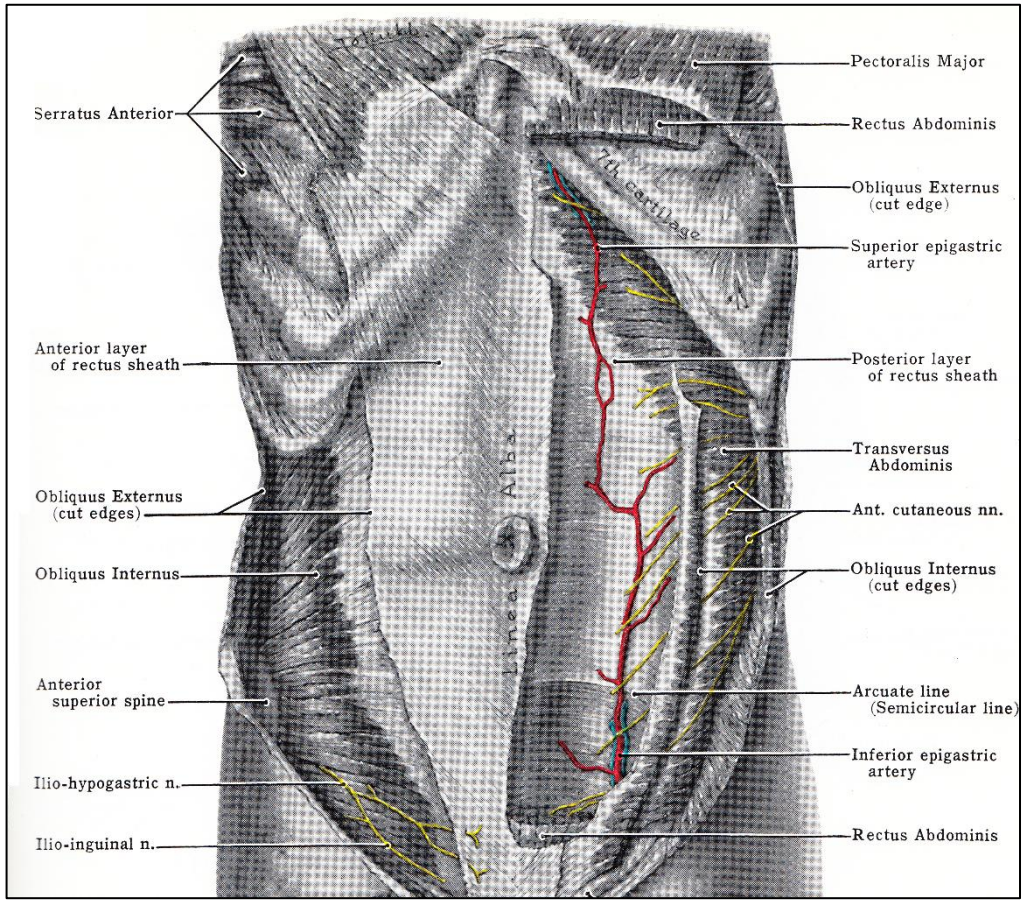
Rectus Sheath Block Anatomy



- "The rectus sheath block provides periumbilical somatic analgesia from the levels T9-T11."[1] Broader levels of coverage have also been described.[2]
- "The goal is to have the injected local anesthetic layer underneath the rectus abdominis muscle where the anterior […] nerves enter the rectus sheath."[3]



TAM: transversus abdominis muscle; RAM: rectus abdominis muscle. Green arrow depicts needle path; dotted yellow line depicts area of local anesthetic deposition.



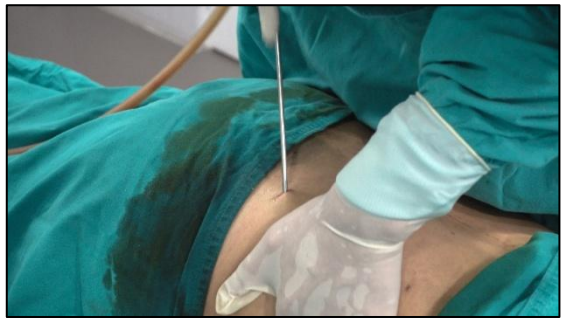
1. Brown's Atlas of Regional Anesthesia, 6th Ed, Ch 35. // 2. UpToDate: Abdominal nerve block techniques // 3. Atlas of Ultrasound-Guided Regional Anesthesia, 3rd Ed, Ch 57 // Ultrasound & Probe Images: Curr Anesthesiol Rep 2019; 9: 479-87. https://doi.org/10.1007/s40140-019-00351-y. Creative Commons CC-BY-4.0 // Grant's Anatomy image: Grant, John Charles Boileua, Public domain, via Wikimedia Commons https://commons.wikimedia.org/wiki/File:Grant_1962_106.png //

Room for notes

Tumescent Anesthesia

14X

Room for notes



- Total Dose of lidocaine: can range from 35-55mg/kg. Peak serum level of lidocaine: 12-14 hours after injection, w/decline over next 6-14 hours.[1]
  - "35 to 55 mg/kg doses have been used safely because the tumescent technique results in a single compartment clearance similar to that of a sustained-release medication. […] An office liposuction should be limited to 5L of total aspirant [including fluid and supernatant fat]."[1]
- "There have been several cases of cardiac arrest and death during plastic surgery procedures…multiple risk factors… [based on 2000 surgery of aesthetic plastic surgeons] high local anesthetic concentrations and concomitant use of sedatives may have contributed…."[1-3]
- 2002 survey of the American Society of Dermatologic Surgery: no mortality among 66,570 procedures; serious adverse events more frequent in hospitals & ASC's than offices (hospitals & ASC's may see sicker pts & remove more fat); morbidity had better correlation with area of body suctioned (more morbidity from abdomen and buttocks than extremities) than facility where procedure took place.[1,4]
- 2017 database study of over 31,000 liposuction procedures (surgical centers, hospitals, and office-based): independent predictors of major complications (including surgical site infection, DVT, and pulmonary complications): age, BMI, combination of liposuction w/other procedures, & location of procedure in a hospital. Liposuction performed alone had lower risk of major complications (0.7%).[1,5]
- 2019 systematic review of liposuction safety studies: factors associated w/serious complications included procedures requiring sedation beyond anxiolysis, procedure location in an operating room, specialty of physician performing the procedure (plastic surgeon greater than dermatologist/other), use of wet/superwet techniques (uses less infiltration of fluid [with or without local anesthetic] into the fat than tumescent anesthesia and requires sedation beyond anxiolysis), & combination of liposuction with other procedures.[1,6]

1. Barash 9th Ed, Ch 32 // 2. Miller 10th Ed, Ch 25 // 3. PMID 10627013 // 4. PMID 12460288 // 5. PMID 28430878 // 6. PMID 30702445 // Image: 642254683, used under license from Shutterstock.com

Anatomy & Airway

Room for notes

Difficult Airway

18X, incl next slide

07 Failed Airway

INDEX

2 unsuccessful intubation attempts by an airway expert in a patient under general anesthesia

START

1. **Call for help and a code cart**
   - **Ask:** *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Get difficult airway cart**
3. **Monitor elapsed TIME, intubation ATTEMPTS, and SpO_2**
   - Limit attempts to 3 by initial provider plus 1 attempt by other airway expert (**"3+1"**)
4. **Bag-mask ventilate with 100% Oxygen**
   - Is ventilation adequate?
     - Maintaining adequate SpO_2?
     - Capnographic evidence of adequate ventilation?

← *Switch if status changes* →

Ventilation NOT ADEQUATE

- Consider/attempt supraglottic airway
  - Optimize patient position
- If unsuccessful, attempt alternative intubation approaches as you **prepare** for emergency invasive airway
  - Limit to **"3+1"**
- If you remain unable to intubate and unable to ventilate, **implement** emergency invasive airway

Ventilation ADEQUATE

- Attempt alternative intubation techniques
  - Limit to **"3+1"**
- Consider doing procedure with a supraglottic or mask airway
- Optimize ventilation/intubating conditions
- Consider invasive airway
- Consider awakening patient
- If awakening patient, consider:
  - Awake intubation
  - Complete procedure under local or regional
  - Cancel the procedure

DRUG DOSES & treatments

Sugammadex	8 - 16 mg/kg IV
Naloxone	0.4 mg IV
Flumazenil	0.2 mg IV May repeat up to 1 mg

AVOID in chronic benzodiazepine use or seizure history

Alternative INTUBATION TECHNIQUES

Video laryngoscope
Intubation via supraglottic device
Different blades
Intubating stylet
Gum elastic bougie
Flexible bronchoscope
Lightwand
Retrograde intubation
Blind oral or nasal intubation

07

2022 ASA Guidelines for Management of Difficult Airway (includes pediatric algorithm):

NEJM Cricothyroidotomy video: https://www.nejm.org/doi/full/10.1056/NEJMvcm0706755 // https://youtu.be/Fb_EdieQet8

Room for notes

Difficult Airway Predictors

Room for notes

Predictors of difficult intubation and/or difficult mask ventilation:

Langeron et al. Predictors of difficult mask ventilation. Anesthesiology 2000; 92: 1229-36.

Multivariate risk factors for difficult mask ventilation: **Beard (Odds Ratio 3.18** [95% CI 1.39-7.27; p=0.006]), BMI 26 or greater (OR 2.75 [1.64-4.62; p<0.001]), Lack of teeth (OR 2.28 [1.26-4.10; p=0.006]), Age 55 or greater (OR 2.26 [1.34-3.81; p=0.002]), Snoring history (OR 1.84 [1.09-3.10; p=0.02]).

Shiga T et al. Predicting difficult intubation in apparently normal patients: A meta-analysis of bedside screening test performance. Anesthesiology 2005; 103: 429-37.

"The most useful bedside test for prediction was found to be a **combination of the Mallampati classification and thyromental distance**….combinations of tests add some incremental diagnostic value in comparison to the value of each test alone."

Kheterpal et al. Incidence and predictors of difficult and impossible mask ventilation. Anesthesiology 2006; 105: 885-91.

"**Limited or severely limited mandibular protrusion**[**p<0.0001**], abnormal neck anatomy [thick/obese: p=0.019], sleep apnea [p=0.036], snoring [p=0.049], and body mass index of 30 kg/m or greater [p=0.053] were independent predictors of grade 3 [inadequate, unstable, or requiring two providers] or 4 [impossible to ventilate] mask ventilation and difficult intubation."

Kheterpal et al. Prediction and outcomes of impossible mask ventilation: A review of 50,000 anesthetics. Anesthesiology 2009; 110: 891-7.

"**Neck radiation changes** [**Adjusted Hazard Ratio 7.1** (95% Confidence Interval 2.1-24.2; p=0.002)] , male sex [Adjusted HR 3.3 (1.8-6.3; p<0.001)], sleep apnea [Adjusted HR 2.4 (1.3-4.3; p=0.005)], Mallampati III or IV [Adjusted HR 2.0 (1.1-3.4; p=0.014)], and presence of beard [Adjusted HR 1.9 (1.1-3.3; p=0.024)] were identified as independent predictors."

Kheterpal et al. Incidence, predictors, and outcomes of difficult mask ventilation combined with difficult laryngoscopy. Anesthesiology 2013; 119: 1360-1369

Risk Index Classification System: Class I (0-3 risk factors; reference), Class II (4 risk factors; OR 2.56), Class III (5 risk factors; OR 4.18), Class IV (6 risk factors; OR 9.23), Class V (7-11 risk factors; OR 18.4). Risk Factors: Mallampati III or IV (Adjusted Odds Ratio 3.21 [95% CI 2.45-4.22; p<0.001]), Neck radiation changes or neck mass (2.57 [1.18-5.60; p=0.017]), Male sex (2.46 [1.80-3.36; p<0.001]), Limited thyromental distance (2.40 [1.68-3.44; p<0.001]), Presence of teeth (2.38 [1.50-3.79; p<0.001]), Body mass index 30 or more (2.16 [1.58-2.94; p<0.001]), Age 46 or more (1.93 [1.35-2.76; p<0.001]), Presence of beard (1.64 [1.21-2.24; p0.002]), Thick neck (1.53 [1.13-2.07; p=0.006]), Sleep apnea (1.59 [1.12-2.27; p=0.010]), Unstable cervical spine or limited neck extension (1.47 [1.05-2.05; p=0.024]), and Limited or severely limited jaw protrusion (1.47 [1.05-2.05; p=0.028]).

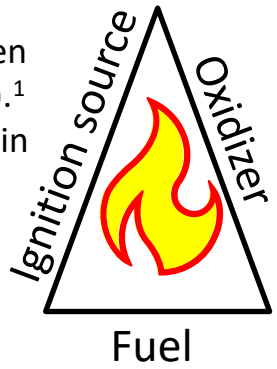
Garcia-Marcinkiewicz et al. Difficult or impossible facemask ventilation in children with difficult tracheal intubation: a retrospective analysis of the PeDI registry. Br J Anaesth 2023; 131: 178-87

Study of multicenter registry for children. "Infants and patients having increased weight, being less than 5th percentile in weight for age, or having Treacher-Collins syndrome, glossoptosis, or limited mouth opening were more likely to have difficult mask ventilation. [Mask induction and induction using] opioids was associated with decreased risk of difficult mask ventilation. […] Administration of neuromuscular blocking agents was more frequently associated with improvement or no change in quality of ventilation than with worsening."

Airway & Operating Room Fire

13X

- Fire Triad: (1) fuel (e.g., ETT, drapes), (2) oxidizer, (3) ignition source (Miller 9th Ed, Ch 70).
- Silverstein Fire Risk Assessment Tool: One point for each: 1. Surgical site above xiphoid, 2. Open oxygen source (e.g., facemask, nasal cannula), 3. Ignition source (electrocautery, laser, fiberoptic light source).[1] Some add additional point based on prepping agent (e.g., alcohol-based – acetone as well as other skin prep/adhesive agents are flammable).
- ASA 2013 Practice Advisory: (1) Use ETT resistant to laser being used; (2) Fill tracheal cuff with saline and indicator dye (e.g., methylene blue, indocyanine green); (3) Reduce FiO2 to "minimum required to avoid hypoxia (and stop nitrous oxide)." **For Airway/Breathing Circuit Fire**: Remove ETT, stop flow of airway gases, remove flammable/burning materials from airway, pour saline/water into airway.

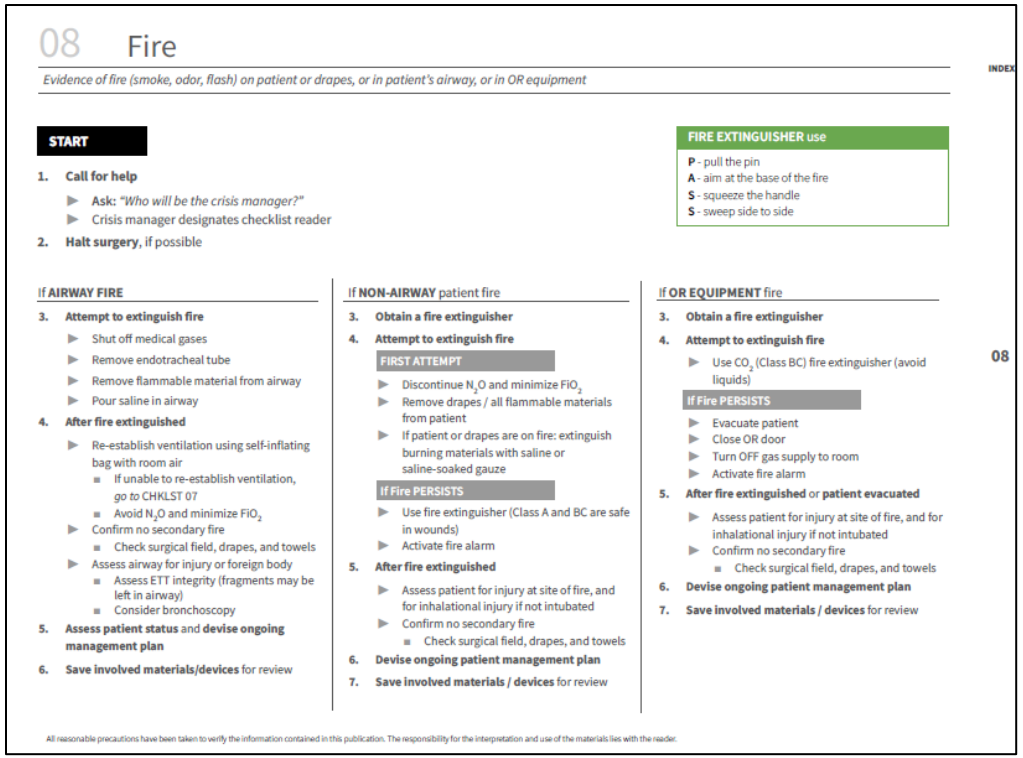


Potential ETT Options for Airway Laser Surgery
**** Preoperatively discuss with surgeon, including laser used and ETT preference ****

CO2 or KTP (potassium titanyl phosphate) lasers:
- Stainless steel corrugated spiral ETT
- Red rubber ETT wrapped with aluminum or copper foil
- Silicone ETT wrapped in aluminum foil

Nd/YAG, Argon, and CO2 lasers:
- Soft/flexible white rubber ETT covered with copper foil.

QR Code: Table from APSF Article on Common Prep Solutions and Their Alcohol Content



08 Fire

Evidence of fire (smoke, odor, flash) on patient or drapes, or in patient's airway, or in OR equipment

INDEX

START

1. **Call for help**
   - Ask: *"Who will be the crisis manager?"*
   - Crisis manager designates checklist reader
2. **Halt surgery**, if possible

FIRE EXTINGUISHER use

P - pull the pin
A - aim at the base of the fire
S - squeeze the handle
S - sweep side to side

If AIRWAY FIRE

3. **Attempt to extinguish fire**
   - Shut off medical gases
   - Remove endotracheal tube
   - Remove flammable material from airway
   - Pour saline in airway
4. **After fire extinguished**
   - Re-establish ventilation using self-inflating bag with room air
     - If unable to re-establish ventilation, *go to* CHKLST 07
     - Avoid N_2O and minimize FiO_2
   - Confirm no secondary fire
     - Check surgical field, drapes, and towels
   - Assess airway for injury or foreign body
     - Assess ETT integrity (fragments may be left in airway)
     - Consider bronchoscopy
5. **Assess patient status** and **devise ongoing management plan**
6. **Save involved materials/devices** for review

If NON-AIRWAY patient fire

3. **Obtain a fire extinguisher**
4. **Attempt to extinguish fire**

FIRST ATTEMPT
- Discontinue N_2O and minimize FiO_2
- Remove drapes / all flammable materials from patient
- If patient or drapes are on fire: extinguish burning materials with saline or saline-soaked gauze

If Fire PERSISTS
- Use fire extinguisher (Class A and BC are safe in wounds)
- Activate fire alarm

5. **After fire extinguished**
   - Assess patient for injury at site of fire, and for inhalational injury if not intubated
   - Confirm no secondary fire
     - Check surgical field, drapes, and towels
6. **Devise ongoing patient management plan**
7. **Save involved materials / devices** for review

If OR EQUIPMENT fire

3. **Obtain a fire extinguisher**
4. **Attempt to extinguish fire**
   - Use CO_2 (Class BC) fire extinguisher (avoid liquids)

If Fire PERSISTS
- Evacuate patient
- Close OR door
- Turn OFF gas supply to room
- Activate fire alarm

5. **After fire extinguished** or **patient evacuated**
   - Assess patient for injury at site of fire, and for inhalational injury if not intubated
   - Confirm no secondary fire
     - Check surgical field, drapes, and towels
6. **Devise ongoing patient management plan**
7. **Save involved materials / devices** for review

08

All reasonable precautions have been taken to verify the information contained in this publication. The responsibility for the interpretation and use of the materials lies with the reader.

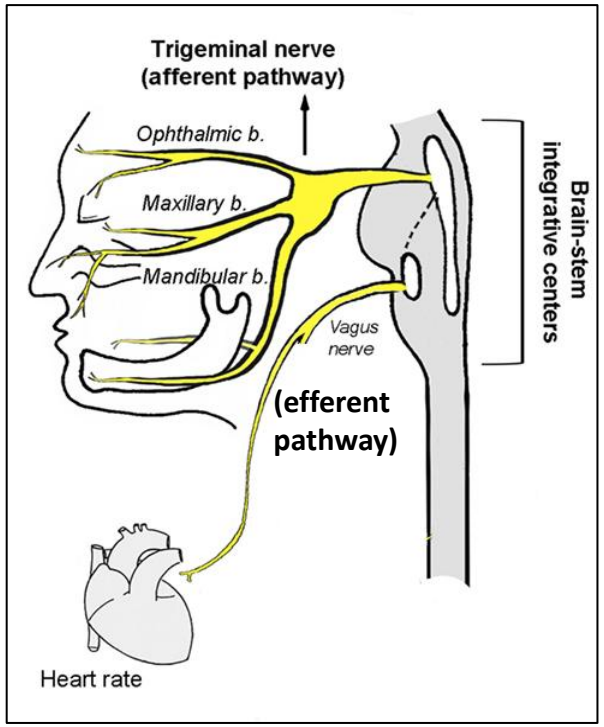
1. Mathias JM. Scoring fire risk for surgical patients. OR manager. 2006 Jan;22(1):19 // Miller 10th Ed, Ch 66. // Airway for Laser Surgery; PMID: 33232076 // Fire Checklist: From Ariadne Labs Operating Room Crisis Checklists. Revision September 2024. See https://orcc.ariadnelabs.net/ for latest version. With permission via Creative Commons BY-NC-SA (https://creativecommons.org/licenses/by-nc-sa/4.0/).

Room for notes

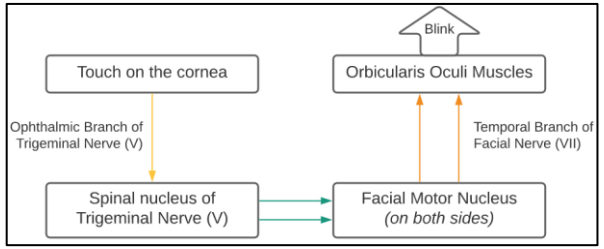
"Image/Buzzwords Co-slides":
Anatomy: Oculocardiac and other Reflexes

Room for notes

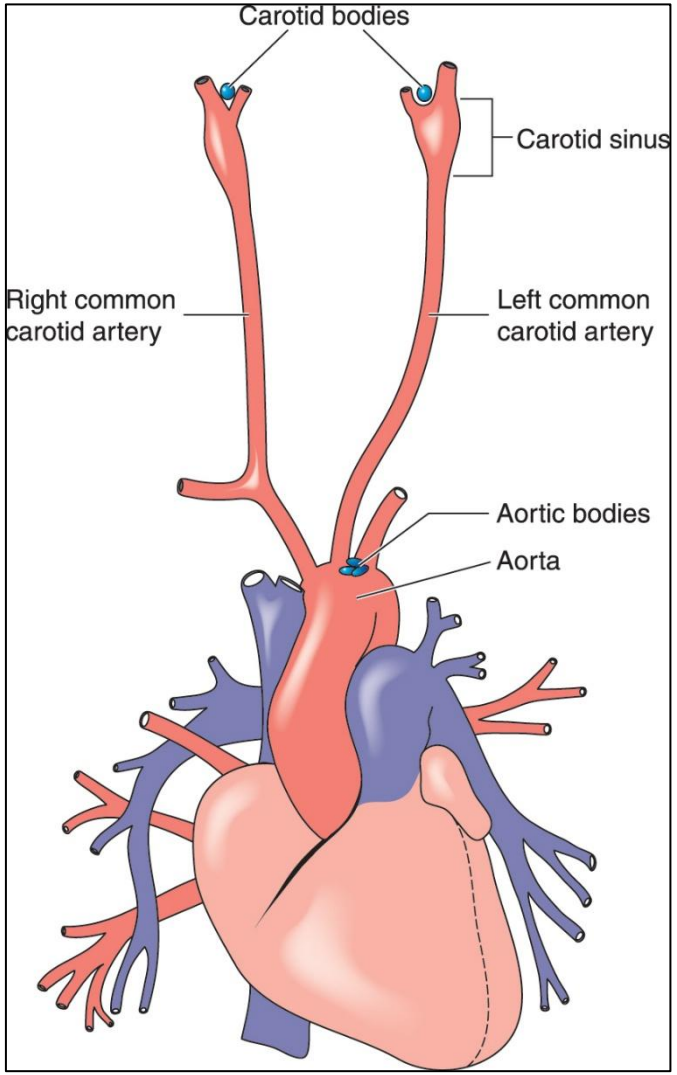
Oculocardiac Reflex

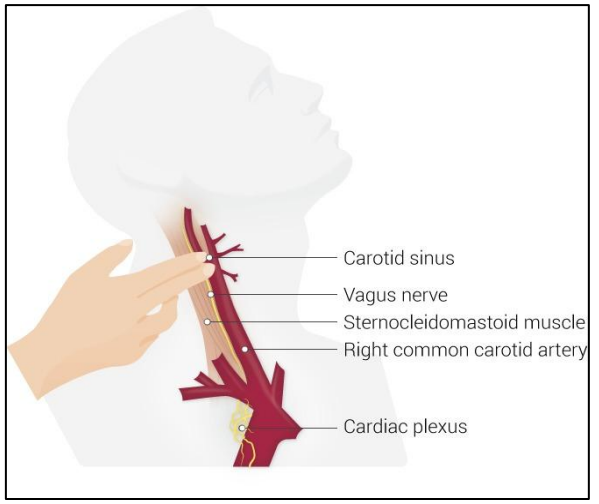


Corneal Reflex



Carotid Body (peripheral chemoreceptors) and Carotid Sinus (baroreceptors)





Khan Academy Videos related to carotid body and carotid sinus (Dr. Rishi Desai):

1. Peripheral chemoreceptors: https://youtu.be/cJXY3Cywrnc
2. Regulation of blood pressure with baroreceptors: https://youtu.be/ajLgwCygHsc
3. The respiratory center: https://youtu.be/_BFDgTci0ck
4. Central chemoreceptors: https://youtu.be/lVacrVMmJX8

"Image/Buzzwords Co-slides": Anatomy: Oculocardiac and other Reflexes

23X

Room for notes

Oculocardiac reflex: can be triggered by traction on extraocular muscles or external pressure to globe

- Afferent limb: long and short ciliary nerves -> ciliary ganglion → **ophthalmic branch of trigeminal nerve (cranial nerve V1)** → Gasserian (trigeminal) ganglion → brainstem. Efferent limb: Vagus nerve (CN X) → bradycardia, other dysrhythmias
- Intraop Tx: Tell surgeon to remove stimulation; consider atropine and/or glycopyrrolate.

Carotid Body vs. Carotid Sinus:

- Peripheral chemoreceptors in carotid bodies and aortic body: cells respond to mostly to hypoxemia/O2 tension (Some sensitivity to hypercarbia [pH], but mostly hypoxemia driven) -> glossopharyngeal nerve (CN IX) & vagal nerve (CN X) → medulla → change in ventilatory drive.
  - Some sympathetic component, but largely considered a ventilatory response.
  - Carotid endarterectomy patients may be sensitive to respiratory depressant effects of opioids.
- Baroreceptors in walls of carotid sinus and aortic arch: hypertension, vagal maneuver, surgical stimulation, or carotid angioplasty/stent → carotid sinus baroreceptors → CN IX & CNX → medulla → decreased sympathetic tone and parasympathetic activation (bradycardia, decreased cardiac contractility, decreased vascular tone).
  - "Vagal maneuver" can be attempted to stimulate the carotid sinus for a patient in SVT.
  - Some surgeons infiltrate carotid sinus w/local during carotid endarterectomy to blunt reflex.

Venous baroreceptor reflex (sometimes referred to as a "Bainbridge reflex"): "Stretch of the venous receptors produces changes in HR opposite to those produced when the arterial pressures decline": Examples: (1) Increased heart rate when right atrium/great veins stretched by volume; (2) bradycardia from spinal anesthesia (due to both decreased venous return and blockade of the T1-T4 cardiac accelerator nerves [which also leads to unopposed vagus nerve activity]).[1]

Triad of Bradycardia, Respiratory depression, & HTN due to increased ICP (sometimes referred to as Cushing triad, Cushing reflex, or Cushing response): theories to pathophysiology include: increased ICP → ischemia at medullary vasomotor center → respiratory depression & sympathetic activation → HTN & increased myocardial contractility → reflex bradycardia

Corneal reflex: see diagram on previous slide. May be a component of neuroprognostication after cardiac arrest. Sedation can inhibit this reflex. Different cranial nerves than pupillary light reflex (which involves CN2&3).

1. Barash 9th Ed, Ch 14 // Cote's A Practice of Anesthesia for Infants and Children, 6th Ed, Ch 34 // Miller 10th Ed Ch 13 // OpenAnesthesia: corneal reflex: anatomy (Caldwell S and Dabreo E) & carotid body: hypoxic drive // PMID's: 30664547, 31919808 // UpToDate: Evaluation and management of elevated intracranial pressure in adults.

Perioperative Medicine

Room for notes

ACC/AHA et al Guidelines: Periop CV Management for Noncardiac Surgery

28X including next slide

Room for notes

2024 Guidelines [1]

- **Main algorithm: Fig 1**
- **Severe Aortic Stenosis: Fig 2**
- **CIED's (PPM/ICD): Fig 3 & 4**
- **PCI/stents/DAPT & Timing: Fig 5***
- **Abnormal postop troponin: Fig 6**

Revised Cardiac Risk Index (RCRI)[1,2]

RCRI risk factors: *Greater than 1 factor*: elevated risk (≥ 1%) for major adverse cardiac event (MACE)
High-risk surgery (intrathoracic, intraperitoneal, or suprainguinal vascular)
CAD (history of ischemic heart disease)
CHF
CVA or TIA history
Diabetes mellitus requiring insulin
Preop serum creatinine ≥ 2mg/dL

ACC/AHA Guidelines: Risk Modifiers to consider in addition to MACE risk calculator:[1]

1. Severe valvular heart disease
2. Severe pulmonary HTN
3. Elevated-risk congenital heart disease (CHD) (single ventricle, unrepaired or palliated cyanotic CHD, double outlet right ventricle, pulmonary atresia, truncus arteriosus, transposition of the great arteries, interrupted aortic arch)
4. Prior coronary stents/CABG
5. Recent stroke (particularly ≤ 3 months)
6. Pacemaker/ICD (CIED)
7. Frailty

ACC/AHA et al Guidelines & Frailty:[1,3,4] "using a validated tool can be useful" to assess/manage frailty if (1) pt ≥ 65 yrs (or younger if perceived frailty); & (2) elevated risk noncardiac surgery.

Example: FRAIL Scale (each 1 point; 0=Nonfrail; 1-2: Intermediate; 3-5: Frail)

F: Fatigue (most of time over past month)
R: Resistance (can't walk up 10 steps)
A: Ambulation (can't do several hundred yards)
I: Illnesses (≥ 5 of 11 major illnesses)
L: Loss of weight (>5% over past year)

→ List of More Frailty Scales: https://frailtyscience.org/frailty-assessment-instruments/

Duke Activity Status Index (DASI): ACC/AHA et al Guidelines note "DASI ≤ 34" or "METS < 4" as "poor" functional capacity:[1,5,6]

1. "Can you take care of yourself (eating, dressing, bathing or using the toilet)? [2.75 pts]
2. Can you walk indoors, such as around your house? [1.75 pts]
3. Can you walk a block or two on level ground? [2.75 pts]
4. Can you climb a flight of stairs or walk up a hill? [5.5 pts]
5. Can you run a short distance? [8 pts]
6. Can you do light work around the house such as dusting or washing dishes? [2.7 pts]
7. Can you do moderate work around the house such as vacuuming, sweeping floors or carrying in groceries? [3.50 pts]
8. Can you do heavy work around the house such as scrubbing floors, or lifting and moving heavy furniture? [8.00 pts]
9. Can you do yard work such as raking leaves, weeding or pushing a power mower? [4.50 pts]
10. Can you have sexual relations? [5.25 pts]
11. Can you participate in moderate recreational activities such as golf, bowling, dancing, doubles tennis, or throwing a baseball or football? [6 pts]
12. Can you participate in strenuous sports such as swimming, singles tennis, football, basketball or skiing? [7.50 pts]"

ACC/AHA et al Guidelines & Biomarkers:[1]

1. B-type natriuretic peptide (BNP), N-terminal pro–B-type natriuretic peptide (NT-proBNP), or cardiac troponin (cTn) "is reasonable to measure" preop if (1) known cardiovascular dz (CVD); or (2) age ≥ 65 yrs; or (3) age ≥ 45 yrs w/symptoms suggestive of CVD & having elevated-risk noncardiac surgery.

2. cTn "may be reasonable to measure" at 24 & 48 hrs postop if (1) known CVD; or (2) symptoms of CVD; or (3) age ≥ 65 yrs w/CVD risk factors & had elevated-risk noncardiac surgery.

1. Thompson A et al 2024 PMID 39316661 // 2. Lee TH et al 1999 PMID 10477528 // 3. https://frailtyscience.org // 4. Morley et al 2012 PMID 22836700 // 5. Excerpt of DASI quoted from Silvapulle E et al BJA Educ 2022 PMID 35754857 // 6. Hlatky et al 1989 PMID 2782256 // * Note: Newer drug-eluting stent types w/potentially shorter dual antiplatelet therapy times is active area of study (NEJM 2020 PMID 32050061 // UpToDate: Intracoronary stents: Stent types // UpToDate: High bleeding risk patients undergoing percutaneous coronary intervention)

Additional Preoperative Medicine/Assessment

Room for notes

Obstructive Sleep Apnea (OSA) Diagnostic Criteria (institutional variation):[1] ≥ 5 events per hr (apneic, hypopneic, or respiratory-effort related arousals), each associated w/O2 desaturation, & daytime symptoms (unless ≥ 15 events/hr).

ACC/AHA Guidelines (for Periop CV Management for Noncardiac Surgery) and Obstructive Sleep Apnea:[2] "In patients scheduled for NCS, obstructive sleep apnea (OSA) screening using validated questionnaires is reasonable to assess the risk of perioperative complications."

STOP-BANG OSA risk factors:[3] Snoring, Tired, Observed apnea, blood Pressure (HTN), BMI>35, Age>50, Neck circumference >40cm, Sex = male.

AHA/ACC Guidelines (for Management of Patients with Valvular Heart Disease): Infective endocarditis (IE) pre-procedure antibiotic prophylaxis for patients with valvular heart disease (VHD):[5]

"Antibiotic prophylaxis is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa in patients with VHD who have any of the following:

1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts.
2. Prosthetic material used for cardiac valve repair, such as annuloplasty rings, chords, or clips.
3. Previous IE.
4. Unrepaired cyanotic congenital heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or prosthetic device.
5. Cardiac transplant with valve regurgitation due to a structurally abnormal valve."

"In patients with VHD who are at high risk of IE, antibiotic prophylaxis is not recommended for nondental procedures (e.g., TEE, esophagogastroduodenoscopy, colonoscopy, or cystoscopy) in the absence of active infection."

1. Kapur et al 2017 PMID 28162150 //2. Thompson A et al 2024 PMID 39316661 // 3. Chung et al 2012 PMID 22401881 // 4. Otto et al 2021 PMID 33332150

Cardiac Implantable Electronic Devices (CIED)

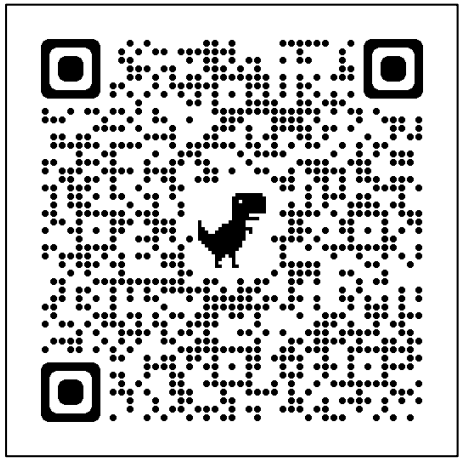
10X

Generic Pacemaker codes:*

Position I (Paced Chamber)	Position II (Sensed Chamber)	Position III Response to Sensing	Position IV Programmability	Position V Multisite Pacing
A= Atrium V= Ventricle O = None D=Dual (A&V)	A= Atrium V= Ventricle O = None D=Dual (A&V)	I= Inhibited T= Triggered O=None D=Dual (I&T)	R= Rate modulation O=None	A= Atrium V= Ventricle O = None D=Dual (A&V)

- Common items to look for in interrogation report: (1) Interrogation date; (2) manufacturer; (3) type of device (e.g., pacemaker, ICD); (4) device settings; (5) pacemaker dependence // underlying rhythm; (6) battery life.
- Interrogation note timing: "For patients with a **pacemaker**, they should have an interrogation report within the last **12 months**; patients with an **ICD** or CRT should have a report within the previous **6 months**." (Miller 10th Ed, Ch 34 [citing ACCF/AHA/HRS guidelines & consistent with 2024 ACC/AHA et al guidelines[1]]).
    - ASA 2020 Practice Advisory: consultants and ASA members agree that "a cardiac implantable electronic device should be interrogated within 3 to 6 months before a procedure."
- If the device is in close proximity to surgical field (e.g., some thoracic surgical procedures), the team may also consider whether a sterile magnet could be available for placement over the device as needed.

Summary Recommendations (Appendix 1) from ASA Practice Advisory on Cardiac Implantable Electronic Device Management



* Generic codes from the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology group (BPEG): References: Miller 10th Ed Ch 34 // ASA Practice Advisory for the Perioperative Management of Patients with Cardiac Implantable Electronic Devices. // 1. Thompson A et al 2024 PMID 39316661

Room for notes

ASA Physical Status, NPO Guidelines, Monitoring Standards, Sedation Continuum

35X

ASA Physical Status Classification System

ASA Standards for Basic Anesthesia Monitoring

ASA Continuum of Depth of Sedation

ASA Guidelines for Preoperative Fasting

2017 Guidelines

2023 Focused Update

ASA Physical Status classification system includes examples for general adult, pediatric, and obstetric populations.

2020 BASIC Exam Gaps in Knowledge: *"The ASA Standards for Basic Anesthesia Monitoring require audible alarm alerts only for certain monitoring parameters."*

From ASA Standards:

- "When the **pulse oximeter** is utilized, the **variable pitch pulse tone and the low threshold alarm** shall be audible to the anesthesiologist or the anesthesia care team personnel."
- "When **capnography or capnometry** is utilized, the **end tidal CO2 alarm** shall be audible to the anesthesiologist or the anesthesia care team personnel."
- "When **ventilation is controlled by a mechanical ventilator**, there shall be in continuous use a **device that is capable of detecting disconnection of components of the breathing system**. The device must give an audible signal when its alarm threshold is exceeded."

URL for ongoing updates to ASA Guidelines, Statements and related documents: https://www.asahq.org/standards-and-practice-parameters

Room for notes

Miscellaneous

Room for notes

Homeopathic Meds and Herbals

- Echinacea (cold supplement): decreased effectiveness of immunosuppressant medications and steroids; may cause hepatotoxicity.
- Ephedra (increases HR/BP/sympathetic tone): tachycardia, hypertension (risk of MI, stroke); may cause arrhythmias; can deplete natural catecholamines; life-threatening interaction with MAO inhibitors.
- Garlic, Ginger, Ginkgo (inhibits platelet aggregation): increased bleeding; can potentiate effect of anticoagulant/antiplatelet agents.
- Ginseng (inhibits platelet aggregation and can cause hypoglycemia): increased bleeding, altered mental status. Can potentiate effects of MAO inhibitors and digoxin.
- Kava (anxiolytic): may change MAC requirements
- Saw Palmetto (inhibits cyclooxygenase): increased bleeding; can cause hypertension
- St John's Wort (inhibits neurotransmitter uptake): induces cytochrome P450 enzymes; may have toxicity interaction with meperidine and MAO inhibitors.
- Valerian (sedative): may change MAC requirements

"The use of ginseng and garlic as herbal supplements does not represent a contraindication to spinal anesthesia." [2019 ITE Gaps in Knowledge]

Barash 9th Ed, Appdx 6 // Miller 9th Ed, Ch 33

Room for notes

High-Yield Formulas: M5 Board Review Public URL

Public URL for M5 Board Review Equations (via Google search):

https://m5boardreview.com/wp-content/uploads/M5_equations.pdf

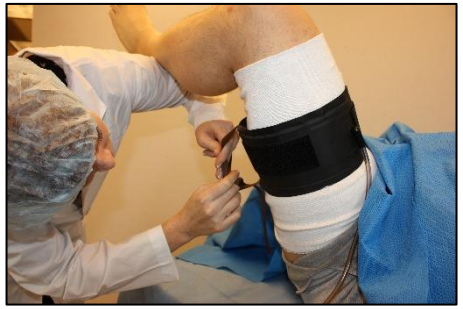
Exceptionally High Yield:

1. Allowable blood loss; Estimated blood volume
2. Volume/Pressure Oxygen-availability from E-cylinder gas tank.
3. Poiseuille's law for IV flow rate.
4. Systemic vascular resistance and cardiac output formula.
5. Arterial content of oxygen including understanding of contribution from hemoglobin saturation and PaO2; Oxygen delivery
6. Alveolar gas equation.

Room for notes

Tourniquet Management for Orthopedic Surgery (i.e., not Bier Blocks)

15X



- Tourniquet usually inflated 100mmHg over patient's systolic BP for thigh (50mmHg for the arm) for up to 2 hours (+/- perfusion break if more time needed).[1]

- <u>Complications after deflation</u>:[2]
  1. Bleeding
  2. Nerve injury/ischemia, especially after extended inflation (greater than 2 hours – deflating tourniquet for 30 minutes may reduce risk);
  3. Pain (may manifest as increased BP/heart rate; thought to be from firing of C-fibers)
  4. Hypotension (from release of acidic metabolites from ischemic limb).
  5. "Transient systemic metabolic acidosis, increased arterial CO2 levels, and decreased systolic BP can be expected with tourniquet deflation and are generally well tolerated in healthy patients."[1]

Room for notes

1. Barash 9th Ed, Ch 51. // 2. Miller's Basics of Anesthesia, 8th Ed, Ch 32 // Image: By Wikiwcetl - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=63113472

MRI Safety

17X

Room for notes

- MRI Compatibility of supplies/implants: “Certain metals such as nickel and cobalt are dangerous because they are magnetic, whereas other metals such as aluminum, titanium, copper, and silver do not pose a missile danger. These metals are used to make MRI-compatible intravenous poles, fixation devices, and nonmagnetic anesthesia workstations.” [Miller/Basics 8th Ed, Ch 38]
- Thermal burns: Monitoring lines should not form a loop or cross. Tattoos/cosmetics are not contraindicated but may contain iron or other metals that can cause heat/burns/image artifact (consider cold compress). MRI pulse oximeters should not physically connect patient to monitoring equipment (to prevent “**Antenna effect**,” where wires of certain lengths can interact with RF coil pulses to generate heat).
- MRI artifact to monitors: “The radiofrequency pulse from an MRI can cause a pressure transducer, and the pulse oximeter, to generate artifacts that can be misleading. Fortunately, visual inspection of the waveforms allows rapid recognition.” [Miller/Basics 8th Ed, Ch 38] Also, ECG interpretation may be limited. [ASA Pract Advis 2015]
- MRI and resuscitation: “Immediately remove patient from zone IV while initiating CPR, if indicated.” [ASA Pract Advis 2015]
- Gadolinium and acute or severe renal insufficiency: can cause nephrogenic systemic fibrosis.
- Other: MRI generates high-level acoustic noise. A quench can both displace oxygen in Zone IV and generate high-pressure from escaping gases and trap those inside.

MRI Zone Definitions and Summary of Recommendations from ASA MRI Practice Advisory

Image: Sung et al. Full-thickness burn on finger due to pulse oximetry during magnetic resonance imaging in a conscious patient. Arch Plas Surg 2016; 43: 612-3.

Radiology/Radiation (cont'd)

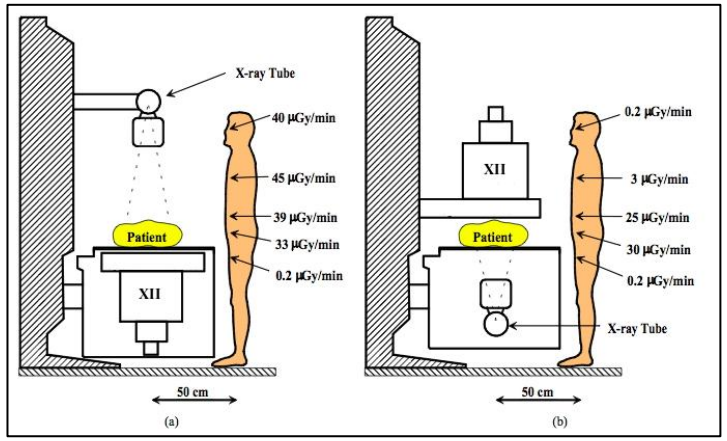
7X

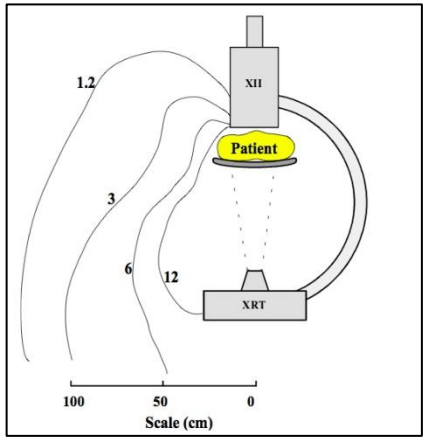
Room for notes

- Occupational eye injury from lasers or radiation: Hazards include direct exposure and reflected/scattered radiation. Occupational x-ray exposure to eye can cause cataracts. "[Laser] injuries include corneal and retinal burns, destruction of the macula or optic nerve, and cataract formation."[1]

  - "[C]lear plastic lenses block the far-infrared (10,600 nm) radiation from carbon dioxide lasers but provide no protection against the near-infrared (1064nm) radiation emitted by Nd:YAG lasers."[1]
  - "For KTP and argon lasers, all OR personnel require protective amber-colored eyeglasses"[2]
  - OSHA: "Opaque goggles are to be worn if in the direct x-ray field."[3] Different forms of lead glasses with side shields/goggles exist.

- Radiation exposure and distance: Radiation exposure is inversely proportional to the square of the distance from the source. "Six feet of air provides protection the equivalent of 9 inches of concrete or 2.5mm of lead."[1]





Left image: Occupational skin absorbed dose near fluoroscopic equipment without protective equipment (a) over-couch; (b) under-couch X-ray tube. Right image: Isodose curves (in microGy/min) for mobile C-arm.

1. Miller 10th Ed, Ch 84. // 2. Hagberg & Benumof's Airway Management 4th Ed Ch 39. // 3. OSHA: https://www.osha.gov/otm/section-6-health-care-facilities/chapter-1 // Left Image: By Kieranmaher - Own work, Public Domain, https://commons.wikimedia.org/wiki/File:OverUnderCouchDoses.jpg // Goggles: By Han-Kwang, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=8424277 Right Image: By Kieranmaher - Own work, Public Domain, https://commons.wikimedia.org/wiki/File:CArmDoseProfiles.jpg //PMID: 21285864, 29729877

Substance Use Disorder/ Anesthesiologist

16X

Room for notes

- Risk Factors for substance use disorder (SUD): "No study has clearly identified individual factors, and those often cited are not specific to the practice of anesthesiology. Risk factors for SUDs may be biologic, psychological, or occupational." [Miller 9th Ed, Ch 88]
- Signs/manifestations of SUD within anesthesia practice include [see also Miller 10th Ed, Ch 84 & Barash 9th Ed, Ch 3]: increasing quantities of narcotics dispensed, behavioral changes, recurrent documentation errors or sloppy charting, unexplained absences, being difficult to locate when on-call, unusual willingness for activities that could mask drug diversion while alone. Physical and other signs may include those of use or withdrawal (pinpoint pupils, tremors/diaphoresis, alcohol odor on breath, weight loss), long sleeves hiding needle marks, witnessed use, sudden death from use.
- Most common drugs misused by anesthesia personnel:
  - JAMA 2013 study on substance use disorder among anesthesiology residents, 1975-2009 (Warner et al, PMID: 24302092): "The most common substance category was intravenous opioids [fentanyl with highest frequency], followed by alcohol, marijuana or cocaine, anesthetics/hypnotics, and oral opioids."
  - Miller 10th Ed Ch 84: "The most common substance misused by anesthesia personnel has traditionally been opioids…Over the past several years there has been an increase in the abuse of other drugs, including propofol, ketamine, and remifentanil, as well as volatile anesthetics."
  - Barash 9th Ed Ch 3: "The most common substance abused by the general physician population remains alcohol […] among anesthesiologists, Warner found that the most commonly abused substances were opiates, followed by alcohol, followed by anesthetics/hypnotics." (Warner et al, Anesthesiology 2020, PMID 32282430)
- High Relapse rates among anesthesia providers: different studies cited in Miller 10th Ed, Ch 84 include: 16% , 25%, and 40.6%. "[R]elapse…highest in physicians who become addicted to potent narcotics early in their career."
- Death Rate: "…more than twice as high in anesthesiologists as internists." "The death rate for anesthesiologists with substance use disorders is 9% to 15%." [Mill 10thEd/Ch84]
- Treatment Lessons from Physician Health Programs [Miller 10th Ed, Ch 84]: (1) zero-tolerance policies; (2) individualized evaluation/treatment; (3) frequent random drug testing; (4) leverage medical boards, hospitals, and medical groups to deter relapse, (5) clear definition of "relapse" with meaningful consequences; (6) 12-step programs such as Alcoholics/Narcotics Anonymous.
- Naltrexone may reduce relapse.

Statistics and Mathematics

Excellent Review Article:
Guller U, Delong E. Interpreting statistics in medical literature: a *vade mecum* for surgeons. J Am Coll Surg 2004; 198: 441-458. PMID 14992748.

Vade mecum: "a handbook or guide that is kept constantly at hand for consultation." - Oxford English Dictionary

Room for notes

Types of Data: Interval Data

Data Type	Examples
Continuous Interval (some refer to as “interval” or “continuous”)	Age, Temperature
Discrete Interval (limited to integer values only)	Parity, Number of first-start cases.

- Continuous and discrete data are both examples of ***interval data*** (variables with equal distance between successive intervals).

- Common terms associated with continuous variables:
  - Mean: (sum of all observed values)/(number of observed values)
  - Median: middle value (or average of middle value and the one after it if even number of observations)
  - Mode: most frequently occurring value
  - Standard deviation (SD): refers to a formula that measures the variability/scatter of the distribution of the data. **SD can still be high with large sample size** if the data is highly scattered.
  - Standard error of the mean (SEM): approximated by (SD)/√n , where n represents the sample size. **SEM gets smaller with increasing sample size** and gives a more precise estimate of the population mean you are sampling from.

Room for notes

Rosner B. Fundamentals of Biostatistics, 8th Ed, pg 167-70. // Guller U et al. J Am Coll Surg 2004; 198: 441-58.

The Normal Distribution

The normal distribution for a random continuous variable refers to a mathematical formula where the distribution of the variable follows a symmetric bell-shaped curve around an average μ (“mu”) with changes in slope around a standard deviation σ (“sigma”).

In a normal distribution, the mean, median, and mode are equal.

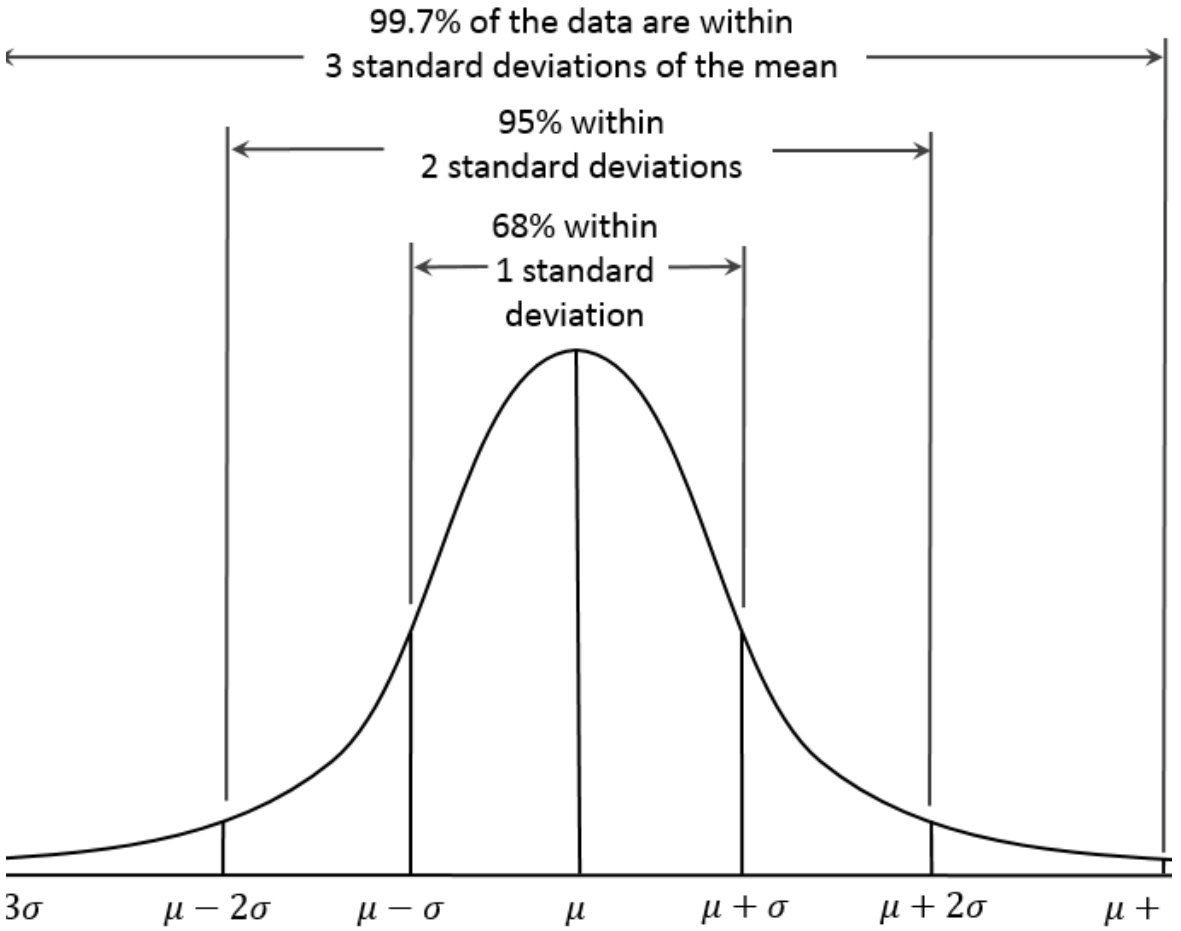


Figure: Empirical rule based on the normal distribution, by Dan Kernler. https://commons.wikimedia.org/wiki/File:Empirical_Rule.PNG. Creative Commons CC BY-SA 4.0 License. April 28, 2020. Rosner B. Fundamentals of Biostatistics, 8th Ed, pg 171-173.

Room for notes

Why is the Normal Distribution Important in Statistics?

- Continuous variables that are ***normally distributed*** can be tested with popular parametric statistical tests.
- ***Parametric Statistical Tests*** require the variable being tested to be assumed to follow a known distribution with known *parameters*.
  - For example: a continuous variable with a mean and standard deviation that follows a normal distribution.
- ***Nonparametric Statistical Tests*** don't require these assumptions and usually involve ranking/ordering the observations and making comparisons. They may have less statistical power.

Popular Parametric Statistical Tests for Normally Distributed Continuous Variables

T-test & its variations

- Paired t-test
- Unpaired t-test
  - Equal variances unpaired t-test
  - Unpaired t-test for unequal variances

Analysis of Variance (ANOVA) & its variations

- One-way ANOVA
  - Comparison of more than two means against one outcome variable of primary interest.
- One-way Analysis of Covariance (ANCOVA)
  - One-way ANOVA while controlling for confounders/covariates.
- Two-way ANOVA/ANCOVA
- Multivariate analysis of variance (MANOVA)

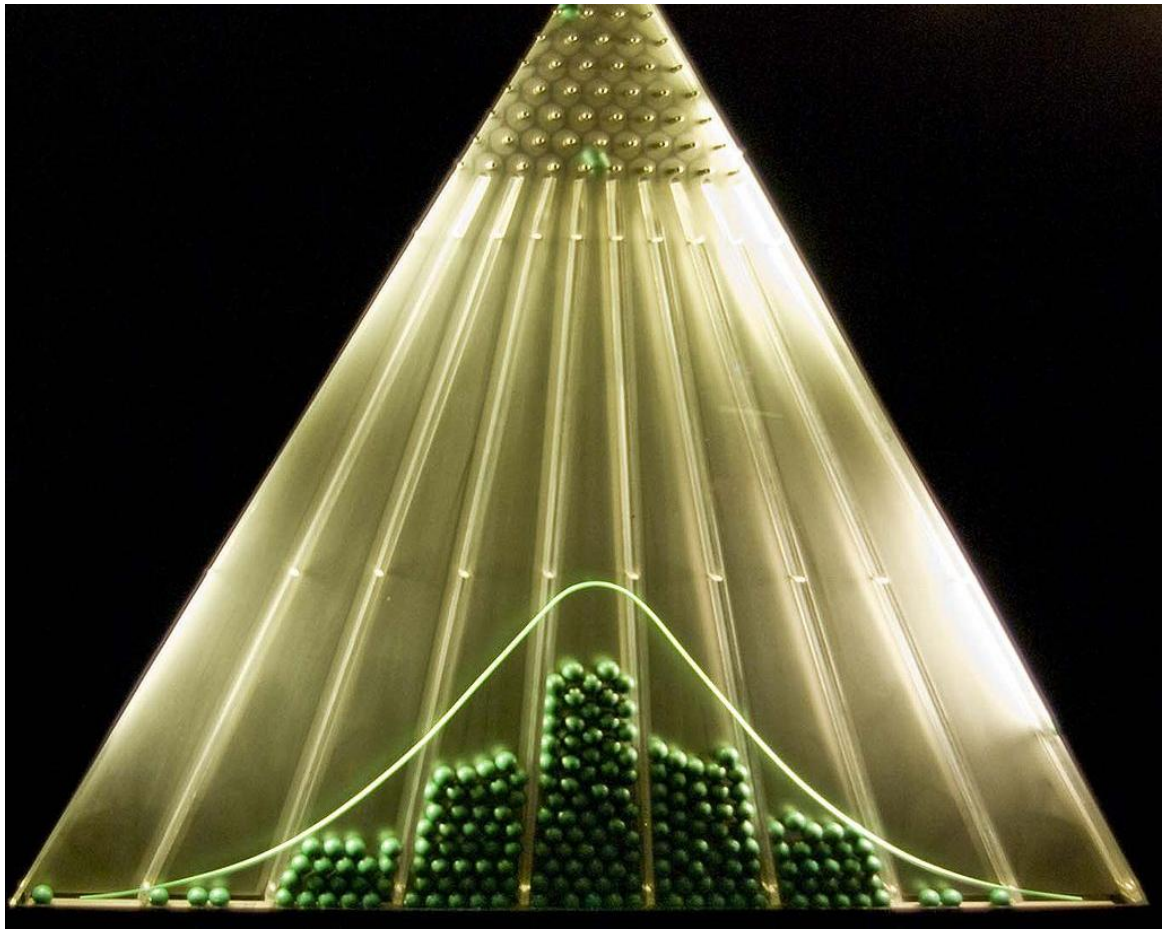
Rosner B. Fundamentals of Biostatistics, 8th Ed, pg 119, 338, 364.

Room for notes

The Central Limit Theorem

According to the **central limit theorem**, a continuous variable with any random distribution approaches a normal distribution if the sample size is sufficiently large.

In this image, a binomial distribution (at each peg, the ball can drop to the left or right) approaches a normal distribution with a large enough sample size.



Top: Galton Box (demonstrates normal distribution) by Antoine Taveneaux. Creative Commons CC BY-SA 3.0 License. April 28, 2020. https://commons.wikimedia.org/wiki/File:Planche_de_Galton.jpg. April 28, 2020. // Rosner B. Fundamentals of Biostatistics, 8th Ed, pg 119.

Room for notes

Types of Data: Binary and Categorical Data

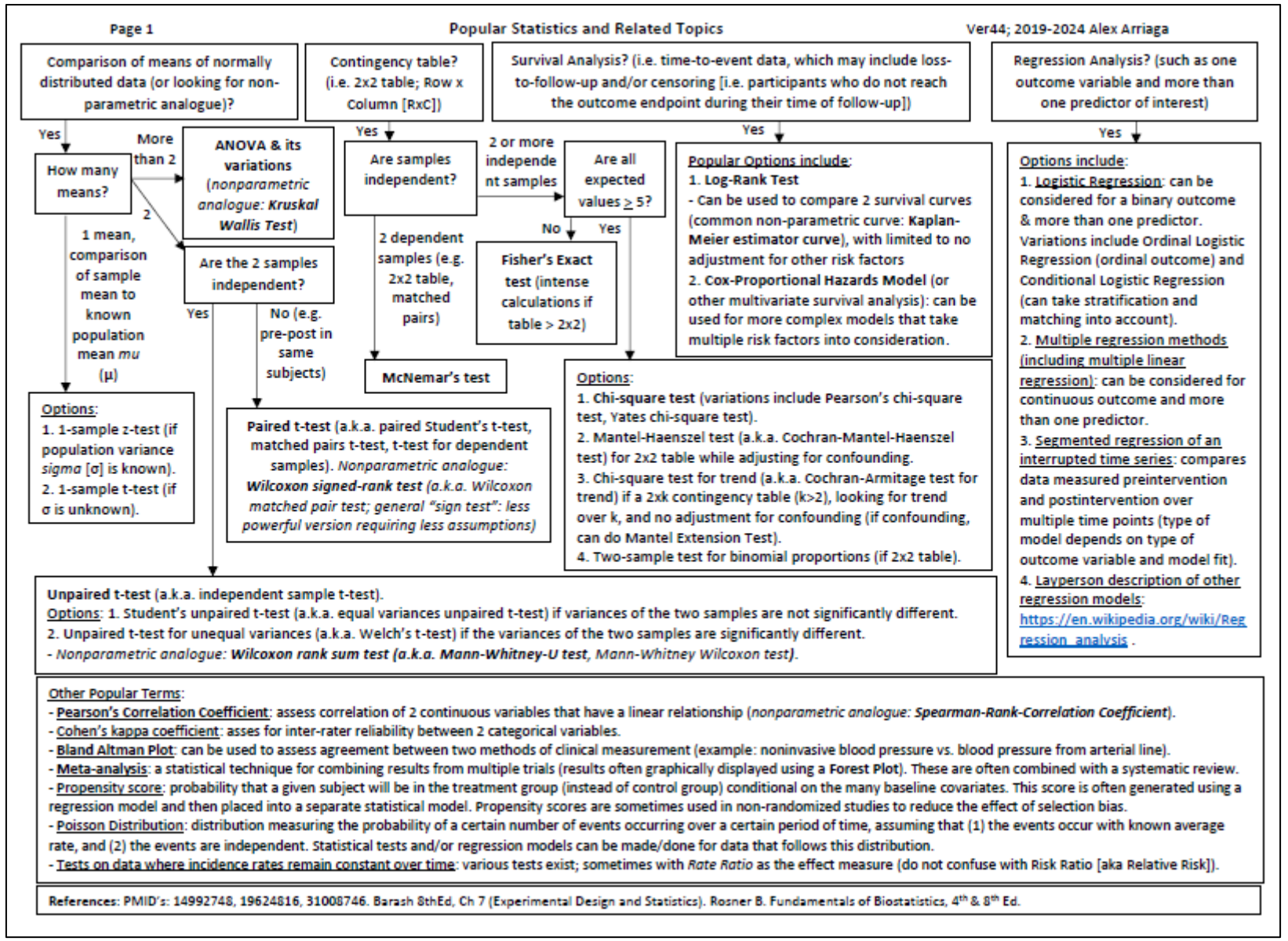
Data Type	Examples
Binary	Dead/Alive; Pregnant/Not-Pregnant; Chip falling to the left or right on a Plinko board
Categorical	
--- Ordinal Categorical	ASA-1, ASA-1E, ASA-2, ASA-2E, ASA-3, ASA-3E, ASA-4, ASA-4E
--- Nominal Categorical	Red, Blue, Green, Purple, Yellow

- Many statistical tests comparing binary or categorical variables to each other can be expressed using **contingency tables** placed in a Row x Column [RxC] format (such as a 2x2 table).
- Table to the right bottom: Example of contingency table with unpaired data (i.e., those getting antibiotics are different patients from those not getting it; the sample of patients who received pre-incision antibiotics are independent of patients who did not receive pre-incision antibiotics).

		Postoperative Surgical Site Infection	
		Yes	No
Pre-incision antibiotics	Yes	a	b
	No	c	d

Room for notes

High-Yield Mathematics/Statistics Handout (1 of 4)



Room for notes

High-Yield Mathematics/Statistics Handout (2 of 4)

Selected Example Studies of Popular Statistical Tests:

Statistical Test	Reference & Title of Example Study	Summary Relevant to the Statistical Test
1-sample t-test	Agarwal et al. A longitudinal survey of adult spine and peripheral nerve case entries during neurosurgery residency training. J Neurosurg Spine 2018; 29: 442-7.	Analysis of ACGME case logs for national sample of graduating neurosurgical residents (n=877) compared to ACGME minimum requirements (considered a proxy for the population mean). Among other results, the authors found a national average of 125.7 lumbar discectomies compared to the ACGME required minimum of 25 (one-sample t-test p<0.0001).
Unpaired t-test	Min et al. Randomized trial comparing early and late administration of rocuronium before and after checking mask ventilation in patients with normal airways. Anes Analg 2019; 129: 380-6.	Randomized trial of 114 patients with normal airways receiving IV rocuronium either before ("early"; n=58) or after ("late"; n=56) checking mask ventilation. The average mask expiratory tidal volume after apnea was larger in the early (552mL) rocuronium group than the late (393mL) group: "mean difference, 160mL/breath; 95% CI, 98-221 mL/breath; p<0.001, unpaired t test."
Analysis of Variance (ANOVA)	Christiansen et al. Volume of ropivacaine 0.2% and common peroneal nerve block duration: a randomized, double-blind cohort trial in healthy volunteers. Anaesthesia 2018; 73: 1361-1367.	Randomized trial of 60 volunteers allocated to receive one of five volumes of ropivacaine 0.2% (2.5, 5, 10, 15, or 20mL) for ultrasound-guided block of the common peroneal nerve. Differences of mean duration of sensory block (in hours) between the five groups were assessed via the one-way ANOVA test. Mean sensory block durations were 9.2h (2.5mL), 12.5h (5mL), 15.5h (10mL), 17.3h (15mL), and 17.3h (20mL); one-way ANOVA p<0.0001.
Fisher's Exact Test	Ferschl et al. A comparison of spinal anesthesia versus monitored anesthesia care with local anesthesia in minimally invasive fetal surgery. Anesth Analg 2020; 130: 409-15.	Retrospective observational study of anesthetic characteristics of 136 pregnant patients undergoing minimally invasive fetal surgery under spinal anesthesia (n=56) or monitored anesthesia care (n=80) over 6 years (2011-2016). One of the findings: the authors observed that remifentanil was given in 0/56 spinal anesthesia patients and 5/80 monitored anesthesia care patients (Fisher's Exact test p=0.08).
McNemar's Test	Ramsingh et al. Auscultation versus point-of-care ultrasound to determine endotracheal versus bronchial intubation: A diagnostic accuracy study. Anesthesiology 2016; 124: 1012-20.	Randomized study of 42 patients allocated to have their ETT intentionally placed via fiberoptic guidance into one of the mainstem bronchi or trachea. A blinded anesthesiologist assessed location of the ETT by auscultation. Each assessment was matched to a second blinded anesthesiologist who assessed the ETT location of the same patient via an ultrasound exam of the pulmonary tree and lung expansion. The four matched combinations were as follows: (1) Auscultation correct and ultrasound correct: 26/42; (2) Auscultation correct and ultrasound incorrect: 0/42; (3) Ultrasound correct and auscultation incorrect: 14/42; (4) Ultrasound incorrect and auscultation incorrect: 2/42. McNemar's test p<0.0001.
Conditional Logistic Regression	Clifford et al. Risk factors and clinical outcomes associated with perioperative transfusion-associated circulatory overload. Anesthesiology 2017; 126: 409-18.	Case-control study of 163 adults undergoing noncardiac surgery who developed perioperative transfusion-associated circulatory overload (matched to 726 transfused controls who did not develop respiratory complications). A conditional logistic regression multivariable model revealed the following predictors of the binary outcome of transfusion-associated circulatory overload: emergency surgery (p<0.001), chronic kidney disease (p=0.007), left ventricular dysfunction (p=0.028), previous beta-adrenergic receptor antagonist use (p=0.027), blood product type (p=0.011), and increasing intraoperative fluid administration (p<0.001).
Survival Analysis: Kaplan Meier estimator curve and Log-rank test.	Sharpe et al. Intrathecal morphine versus intrathecal hydromorphone for analgesia after cesarean delivery: A randomized trial. Anesthesiology 2020; 132: 1382-1391.	Randomized trial of 138 parturients undergoing scheduled cesarean delivery allocated to receive intrathecal morphine (150 micrograms) or intrathecal hydromorphone (75 micrograms) as part of a spinal anesthetic. Median time to first request for postoperative opioid was displayed using a Kaplan Meier estimator curve with data censored at 24 hours for patients who did not request opioids by 24 hours postop. The median time to first opioid request was 5.4 hours for hydromorphone and 12.1 hours for morphine (log-rank test p=0.2).

Room for notes

High-Yield Mathematics/Statistics Handout (3 of 4)

Odds Ratio, Risk Ratio, Absolute Risk Reduction, Number Needed to Treat:

Reference Terms: Risk: "the probability that an event will occur within a stated period of time."[1] Some refer to this probability using the letter "p." Odds = a numerical expression of relative probabilities. Formula for Odds: p/(1-p), or risk/(1-risk). Example: for **10:1** odds, **p=10/11**, and **1-p= 1/11** → p/(1-p) = (10/11)/(1/11) = 10/1

Classic 2 x 2 table:

		Outcome: Yes	Outcome: No
Exposed	Yes	a	b
	No	c	d

Note that a,b,c, and d are arranged as if you were reading left → right, then top row → bottom row.

- Risk of the exposed group experiencing the outcome: a/(a+b). Risk of the unexposed group experiencing the outcome: c/(c+d)
- **Risk Ratio (i.e. relative risk)** = [a/(a+b)]/[c/(c+d)]. Reporting a risk ratio in words: The risk of developing the outcome for exposed subjects is XX times that of unexposed subjects.
- Absolute risk reduction (ARR): [a/(a+b)] – [c/(c+d)]. In words: ARR: proportion of patients who didn't have the outcome due to lack of exposure.
- Number needed to treat: 1/(ARR). In words: Number of subjects who need to be treated (or have the exposure removed) in order to prevent one case from occurring.
- **Odds ratio**: [(a/b)]/[(c/d)]. This formula can be derived by taking the ratio of odds in the exposed versus unexposed, where odds = risk/(1-risk). In words: The odds of the outcome in the exposed group are XX times that of the unexposed group.
- **Note**: Odds ratio is approximately the same as the risk ratio for a rare outcome (i.e. if risk is very low, the "risk" in "1-risk" approaches zero). Conversely, the odds ratio can substantially differ from the risk ratio when the outcome is common.[1,2]

Type I Error, Type II Error, Power, and Sample Size:

		Reality/Truth: No difference exists	Reality/Truth: A true difference exists
Study Finding	Statistically significant result (null hypothesis rejected)	Type I error (a.k.a. alpha error)	Correct
	No statistically significant difference found (null hypothesis not rejected)	Correct	Type II error (a.k.a. beta error)

- **p-value**: "the alpha level at which we would be indifferent between accepting or rejecting the null hypothesis."[3] For an alpha level of 0.05, a p-value less than 0.05 would be considered statistically significant. There would be a 5% chance of an alpha error.
- **One-tailed vs. two-tailed p-value**: Assuming the null hypothesis is true (with the p-value set as the threshold to reject the null hypothesis): Two-tailed (or two-sided) p value: "the probability that the difference between two treatments…is as large or larger than observed, with either treatment being superior to the other. One-tailed p value: "the probability that the difference observed would have occurred by chance alone, with one treatment being superior to the other as specified in the alternative hypothesis."[2]
- **Confidence interval**: An XX% confidence interval (95% being common) "represents a range of values that will include the true population parameter in [XX%] of all cases."[2] The p=0.05 threshold is an arbitrary convention,[4] and there has been a growing movement to reduce the number of p-values reported in a manuscript and replace this with 95% confidence intervals.[5]

- **Power** = 1 – (beta error) = the probability of a statistically significant difference being detected, based on a sample size *n*, if a true difference exists.[3,4]
  - Alternatives that may increase power, for a given alpha level, if you are unable to increase sample size: (1) Use continuous instead of binary endpoints; (2) Use a paired data analysis instead of an unpaired one; (3) use a more common outcome or composite outcome (example: "death or major complication" as the outcome instead of just "death."[6]

References: 1. Montreuil et al. PMID: 16248140. 2. Guller et al. PMID: 14992748. 3. Rosner B. Fundamentals of Biostatistics, 8th Ed. 4. Ridgway et al. PMID: 19476801. 5. Harrington et al. PMID: 31314974. 6. Guller et al. PMID: 15834629.

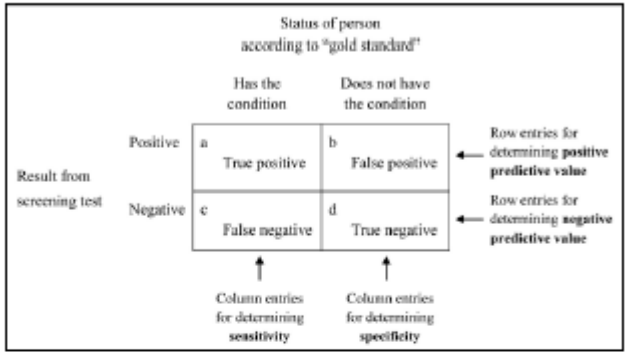
- Other basic statistical terms: Mean: (sum of all observed values)/(number of observed values). Median: middle value (or average of middle value and the one after it if even number of observations). Mode: most frequently occurring value. Standard Deviation (SD) vs. Standard Error of the Mean (SEM): "The SD is a measure of the variability (scatter) of a data distribution. It is a measure of the degree to which the individual values deviate from the population mean….Regardless of sample size, the SD will be large if the data are highly scattered. The SEM reflects the variability in the distribution of sample means from the population mean….Contrary to the SD, the SEM is an inferential statistic strongly dependent on sample size. The larger the sample size, the smaller the SEM, and the more precisely the sample mean estimates the overall population mean….The SEM can be obtained by dividing the SD by the square root of the number of patients in the sample (SEM= SD/√n)." [Guller U et al. J Am Coll Surg 2004; 198: 441-458]

Room for notes

High-Yield Mathematics/Statistics Handout (4 of 4)

Diagnostic Testing and Screening Tests: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Prevalence:

- "Gold standard": definitive indicator of person having (or not having) the target condition (ref: Trevethan). Some instead say **Reference Standard** given the potential imperfection of a "gold standard." Sensitivity and specificity assess the screening test against the reference standard.
- Sensitivity (i.e. of the people who have the condition, what proportion test positive on the screening test?): [a/(a+c)]
  - A highly sensitive test is capturing the vast majority of people who have the condition and has a low proportion of false negatives. If you test negative with a highly sensitive test, it is unlikely you have the condition. Hence, a highly SENSITIVE test (assuming that specificity is not overly low) is good to RULE OUT a disease (mnemonic "SNOUT").
- Specificity (i.e. of the people who do not have the condition, what proportion test negative on the screening test?): [d/(b+d)]
  - A highly specific test is capturing the vast majority of people who DO NOT have the condition and has a low proportion of false positives. If you test positive with a highly specific test, it is likely you have the disease. Hence, a highly SPECIFIC test (assuming sensitivity is not overly low) is good to RULE IN a disease ("SPIN").
- Positive Predictive Value (PPV): [a/(a+b)] • Negative Predictive Value (NPV): [d/(c+d)]
  - PPV and NPV assess whether the actual patient being tested is predicted to have the disease. In order to use the PPV and NPV formulas for a 2x2 table, the prevalence of disease for your patient (in terms of medical history and risk factors) has to be representative of the prevalence of disease in the 2x2 table. This is referred to as determining your patient's *pre-test probability*. PPV and NPV are metrics of *post-test probability*. **As prevalence increases, PPV increases and NPV decreases (and vice versa).**
- Likelihood ratio positive (LR+) = sensitivity/(1-specificity). Likelihood ratio negative (LR-) = (1-sensitivity)/specificity.
  - If you know a patient's pre-test probability (by looking at the prevalence of the condition in patients with risk factors similar to your patient) and the likelihood ratio, there are normograms to mathematically convert this into the patient's post-test probability.



Trevethan R. Sensitivity, Specificity, and Predictive Values: Foundations, Pliabilities, and Pitfalls in Research and Practice. Front Public Health 2017; 20: 5: 307. Open Access article; Figure 1 used via Creative Commons License CC BY 4.0: https://creativecommons.org/licenses/by/4.0/. Other references: Tenny S, Hoffman MR. Prevalence. StatPearls/NCBI Bookshelf; https://www.ncbi.nlm.nih.gov/books/NBK430867/. Hunick M et al. Decision making in health and medicine: Integrating evidence and values. Cambridge University Press, 2009.

Other Basic Math and Statistical Terms:

- Logarithms: $\log_x Y=z \rightarrow x^z=Y$ (in words: "log base x of Y equals z"). Example: $\log_2 16=x \rightarrow 2^x=16 \rightarrow x=4$. Second example: log 1,000 = $\log_{10}1{,}000=3$ (note: there are 3 zeros in 1,000; when the base number is not provided, it is implied to be 10). Third example: $\log_x 1=? \rightarrow \log_x 1=0$ (any base number x raised to the 0 power will equal 1). Fourth example: ln 1 = $\log_e 1$. $\log_e 1=? \rightarrow e^x=1 \rightarrow x=0 \rightarrow$ ln 1 = 0. Khan Academy intro video on logarithms: "Intro to logarithms": https://youtu.be/Z5myJ8dg_rM. Additional popular intro video on logarithms: "Logarithms…How?": https://youtu.be/Zw5t6BTQYRU.
  - *Anesthesiolgy example using logarithms:* Henderson-Hasselbalch equation: pH = 6.1 + log[(HCO_3^-)/(PCO_2 x 0.03)]. HCO_3^-: plasma bicarbonate (mmol/L); PCO2: partial pressure CO_2 (mmHg). [Miller 9thEd/Ch48] If PCO_2=66 and HCO_3^-=20, pH = 6.1 + log [20/(66 x 0.03)] ≈ 6.1 + log [20/2] = 6.1 + log [10] = 6.1 + 1 = 7.1.
- Graph of simple equations and Common Biologic Curves: Khan Academy video linear, quadratic, and exponential models: https://youtu.be/CxEFOozrMSE. Other common curves: Sigmoidal (the sigmoidal curve of the oxygen-hemoglobin dissociation curve has a section that appears exponential, and another section that appears linear), and Quadratic.
- *2024 ITE Gaps in Knowledge:* "The terminal half-life is the smallest exponent on a semilogarithmic graph." (Topic elaborated on in Miller 10th Ed, Ch 16).

Room for notes

Popular Statistics and Related Topics

Comparison of means of normally distributed data (or looking for non-parametric analogue)?

Yes

How many means?

More than 2

ANOVA & its variations (*nonparametric analogue: **Kruskal Wallis Test***)

2

Are the 2 samples independent?

Yes

No (e.g. pre-post in same subjects)

Paired t-test (a.k.a. paired Student's t-test, matched pairs t-test, t-test for dependent samples). *Nonparametric analogue: **Wilcoxon signed-rank test** (a.k.a. Wilcoxon matched pair test; general "sign test": less powerful version requiring less assumptions)*

1 mean, comparison of sample mean to known population mean *mu* (μ)

Options:
1. 1-sample z-test (if population variance *sigma* [σ] is known).
2. 1-sample t-test (if σ is unknown).

Unpaired t-test (a.k.a. independent sample t-test).
Options: 1. Student's unpaired t-test (a.k.a. equal variances unpaired t-test) if variances of the two samples are not significantly different.
2. Unpaired t-test for unequal variances (a.k.a. Welch's t-test) if the variances of the two samples are significantly different.
- *Nonparametric analogue: **Wilcoxon rank sum test (a.k.a. Mann-Whitney-U test**, Mann-Whitney Wilcoxon test**)**.*

Contingency table? (i.e. 2x2 table; Row x Column [RxC])

Yes

Are samples independent?

2 dependent samples (e.g. 2x2 table, matched pairs)

McNemar's test

2 or more independent samples

Are all expected values ≥ 5?

No

Fisher's Exact test (intense calculations if table > 2x2)

Yes

Options:
1. **Chi-square test** (variations include Pearson's chi-square test, Yates chi-square test).
2. Mantel-Haenszel test (a.k.a. Cochran-Mantel-Haenszel test) for 2x2 table while adjusting for confounding.
3. Chi-square test for trend (a.k.a. Cochran-Armitage test for trend) if a 2xk contingency table (k>2), looking for trend over k, and no adjustment for confounding (if confounding, can do Mantel Extension Test).
4. Two-sample test for binomial proportions (if 2x2 table).

Survival Analysis? (i.e. time-to-event data, which may include loss-to-follow-up and/or censoring [i.e. participants who do not reach the outcome endpoint during their time of follow-up])

Yes

Popular Options include:
1. **Log-Rank Test**
- Can be used to compare 2 survival curves (common non-parametric curve: **Kaplan-Meier estimator curve**), with limited to no adjustment for other risk factors
2. **Cox-Proportional Hazards Model** (or other multivariate survival analysis): can be used for more complex models that take multiple risk factors into consideration.

Regression Analysis? (such as one outcome variable and more than one predictor of interest)

Yes

Options include:
1. Logistic Regression: can be considered for a binary outcome & more than one predictor. Variations include Ordinal Logistic Regression (ordinal outcome) and Conditional Logistic Regression (can take stratification and matching into account).
2. Multiple regression methods (including multiple linear regression): can be considered for continuous outcome and more than one predictor.
3. Segmented regression of an interrupted time series: compares data measured preintervention and postintervention over multiple time points (type of model depends on type of outcome variable and model fit).
4. Layperson description of other regression models: https://en.wikipedia.org/wiki/Regression_analysis .

Other Popular Terms:
- **Pearson's Correlation Coefficient**: assess correlation of 2 continuous variables that have a linear relationship (*nonparametric analogue: **Spearman-Rank-Correlation Coefficient***).
- Cohen's kappa coefficient: asses for inter-rater reliability between 2 categorical variables.
- **Bland Altman Plot**: can be used to assess agreement between two methods of clinical measurement (example: noninvasive blood pressure vs. blood pressure from arterial line).
- **Meta-analysis**: a statistical technique for combining results from multiple trials (results often graphically displayed using a **Forest Plot**). These are often combined with a systematic review.
- Propensity score: probability that a given subject will be in the treatment group (instead of control group) conditional on the many baseline covariates. This score is often generated using a regression model and then placed into a separate statistical model. Propensity scores are sometimes used in non-randomized studies to reduce the effect of selection bias.
- Poisson Distribution: distribution measuring the probability of a certain number of events occurring over a certain period of time, assuming that (1) the events occur with known average rate, and (2) the events are independent. Statistical tests and/or regression models can be made/done for data that follows this distribution.
- Tests on data where incidence rates remain constant over time: various tests exist; sometimes with *Rate Ratio* as the effect measure (do not confuse with Risk Ratio [aka Relative Risk]).

References: PMID's: 14992748, 19624816, 31008746. Barash 8thEd, Ch 7 (Experimental Design and Statistics). Rosner B. Fundamentals of Biostatistics, 4th & 8th Ed.

Selected Example Studies of Popular Statistical Tests:

Statistical Test	Reference & Title of Example Study	Summary Relevant to the Statistical Test
1-sample t-test	Agarwal et al. A longitudinal survey of adult spine and peripheral nerve case entries during neurosurgery residency training. J Neurosurg Spine 2018; 29: 442-7.	Analysis of ACGME case logs for national sample of graduating neurosurgical residents (n=877) compared to ACGME minimum requirements (considered a proxy for the population mean). Among other results, the authors found a national average of 125.7 lumbar discectomies compared to the ACGME required minimum of 25 (one-sample t-test p<0.0001).
Unpaired t-test	Min et al. Randomized trial comparing early and late administration of rocuronium before and after checking mask ventilation in patients with normal airways. Anes Analg 2019; 129: 380-6.	Randomized trial of 114 patients with normal airways receiving IV rocuronium either before ("early"; n=58) or after ("late"; n=56) checking mask ventilation. The average mask expiratory tidal volume after apnea was larger in the early (552mL) rocuronium group than the late (393mL) group: "mean difference, 160mL/breath; 95% CI, 98-221 mL/breath; p<0.001, unpaired t test."
Analysis of Variance (ANOVA)	Christiansen et al. Volume of ropivacaine 0.2% and common peroneal nerve block duration: a randomized, double-blind cohort trial in healthy volunteers. Anaesthesia 2018; 73: 1361-1367.	Randomized trial of 60 volunteers allocated to receive one of five volumes of ropivacaine 0.2% (2.5, 5, 10, 15, or 20mL) for ultrasound-guided block of the common peroneal nerve. Differences of mean duration of sensory block (in hours) between the five groups were assessed via the one-way ANOVA test. Mean sensory block durations were 9.2h (2.5mL), 12.5h (5mL), 15.5h (10mL), 17.3h (15mL), and 17.3h (20mL); one-way ANOVA p<0.0001.
Fisher's Exact Test	Ferschl et al. A comparison of spinal anesthesia versus monitored anesthesia care with local anesthesia in minimally invasive fetal surgery. Anesth Analg 2020; 130: 409-15.	Retrospective observational study of anesthetic characteristics of 136 pregnant patients undergoing minimally invasive fetal surgery under spinal anesthesia (n=56) or monitored anesthesia care (n=80) over 6 years (2011-2016). One of the findings: the authors observed that remifentanil was given in 0/56 spinal anesthesia patients and 5/80 monitored anesthesia care patients (Fisher's Exact test p=0.08).
McNemar's Test	Ramsingh et al. Auscultation versus point-of-care ultrasound to determine endotracheal versus bronchial intubation: A diagnostic accuracy study. Anesthesiology 2016; 124: 1012-20.	Randomized study of 42 patients allocated to have their ETT intentionally placed via fiberoptic guidance into one of the mainstem bronchi or trachea. A blinded anesthesiologist assessed location of the ETT by auscultation. Each assessment was matched to a second blinded anesthesiologist who assessed the ETT location of the same patient via an ultrasound exam of the pulmonary tree and lung expansion. The four matched combinations were as follows: (1) Auscultation correct and ultrasound correct: 26/42; (2) Auscultation correct and ultrasound incorrect: 0/42; (3) Ultrasound correct and auscultation incorrect: 14/42; (4) Ultrasound incorrect and auscultation incorrect: 2/42. McNemar's test p<0.0001.
Conditional Logistic Regression	Clifford et al. Risk factors and clinical outcomes associated with perioperative transfusion-associated circulatory overload. Anesthesiology 2017; 126: 409-18.	Case-control study of 163 adults undergoing noncardiac surgery who developed perioperative transfusion-associated circulatory overload (matched to 726 transfused controls who did not develop respiratory complications). A conditional logistic regression multivariable model revealed the following predictors of the binary outcome of transfusion-associated circulatory overload: emergency surgery (p<0.001), chronic kidney disease (p=0.007), left ventricular dysfunction (p=0.028), previous beta-adrenergic receptor antagonist use (p=0.027), blood product type (p=0.011), and increasing intraoperative fluid administration (p<0.001).
Survival Analysis: Kaplan Meier estimator curve and Log-rank test.	Sharpe et al. Intrathecal morphine versus intrathecal hydromorphone for analgesia after cesarean delivery: A randomized trial. Anesthesiology 2020; 132: 1382-1391.	Randomized trial of 138 parturients undergoing scheduled cesarean delivery allocated to receive intrathecal morphine (150 micrograms) or intrathecal hydromorphone (75 micrograms) as part of a spinal anesthetic. Median time to first request for postoperative opioid was displayed using a Kaplan Meier estimator curve with data censored at 24 hours for patients who did not request opioids by 24 hours postop. The median time to first opioid request was 5.4 hours for hydromorphone and 12.1 hours for morphine (log-rank test p=0.2).

Odds Ratio, Risk Ratio, Absolute Risk Reduction, Number Needed to Treat:

Reference Terms: Risk: "the probability that an event will occur within a stated period of time."[1] Some refer to this probability using the letter "p." Odds = a numerical expression of relative probabilities. Formula for Odds: p/(1-p), or risk/(1-risk). Example: for **10:1** odds, p=**10**/11, and 1-p= **1**/11 → p/(1-p) = (10/11)/(1/11) = 10/1

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		Outcome Yes	No
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- Absolute risk reduction (ARR): [a/(a+b)] – [c/(c+d)]. In words: ARR: proportion of patients who didn't have the outcome due to lack of exposure.
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Type I Error, Type II Error, Power, and Sample Size:

		Reality/Truth No difference exists	A true difference exists
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	No statistically significant difference found (null hypothesis not rejected)	Correct	Type II error (a.k.a. beta error)

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- **One-tailed vs. two-tailed p-value**: Assuming the null hypothesis is true (with the p-value set as the threshold to reject the null hypothesis): Two-tailed (or two-sided) p value: "the probability that the difference between two treatments…is as large or larger than observed, with either treatment being superior to the other. One-tailed p value: "the probability that the difference observed would have occurred by chance alone, with one treatment being superior to the other as specified in the alternative hypothesis."[2]
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Diagnostic Testing and Screening Tests: Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Prevalence:

- "Gold standard": definitive indicator of person having (or not having) the target condition (ref: Trevethan). Some instead say **Reference Standard** given the potential imperfection of a "gold standard." Sensitivity and specificity assess the screening test against the reference standard.
- Sensitivity (i.e. of the people who have the condition, what proportion test positive on the screening test?): [a/(a+c)]
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- Specificity (i.e. of the people who do not have the condition, what proportion test negative on the screening test?): [d/(b+d)]
  - A highly specific test is capturing the vast majority of people who DO NOT have the condition and has a low proportion of false positives. If you test positive with a highly specific test, it is likely you have the disease. Hence, a highly SPECIFIC test (assuming sensitivity is not overly low) is good to RULE IN a disease ("SPIN").
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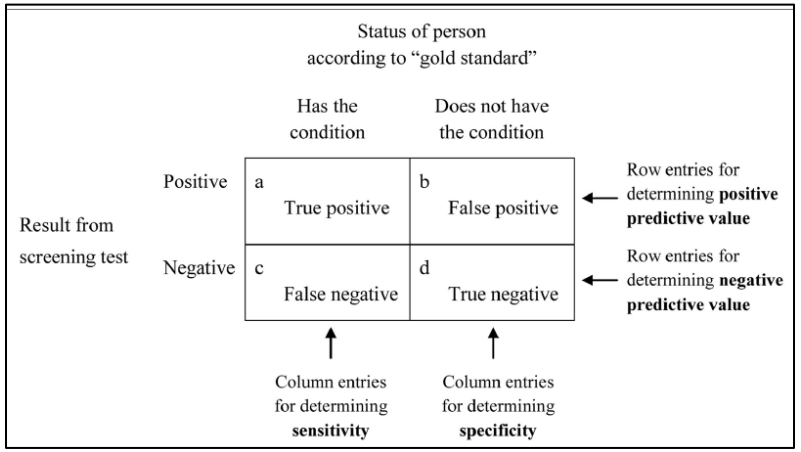
  - PPV and NPV assess whether the actual patient being tested is predicted to have the disease. In order to use the PPV and NPV formulas for a 2x2 table, the prevalence of disease for your patient (in terms of medical history and risk factors) has to be representative of the prevalence of disease in the 2x2 table. This is referred to as determining your patient's *pre-test probability*. PPV and NPV are metrics of *post-test probability*. **As prevalence increases, PPV increases and NPV decreases (and vice versa).**



Trevethan R. Sensitivity, Specificity, and Predictive Values: Foundations, Pliabilities, and Pitfalls in Research and Practice. Front Public Health 2017; 20: 5: 307. Open Access article; Figure 1 used via Creative Commons License CC BY 4.0: https://creativecommons.org/licenses/by/4.0/. Other references: Tenny S, Hoffman MR. Prevalence. StatPearls/NCBI Bookshelf; https://www.ncbi.nlm.nih.gov/books/NBK430867/. Hunick M et al. Decision making in health and medicine: Integrating evidence and values. Cambridge University Press, 2009.

- Likelihood ratio positive (LR+) = sensitivity/(1-specificity). Likelihood ratio negative (LR-) = (1-sensitivity)/specificity.
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Other Basic Math and Statistical Terms:

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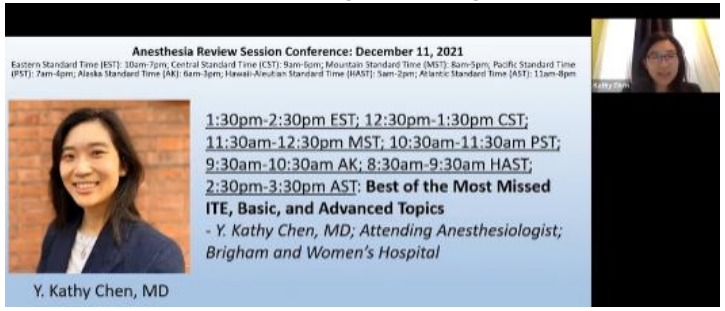
- *2024 ITE Gaps in Knowledge:* "The terminal half-life is the smallest exponent on a semilogarithmic graph." (Topic elaborated on in Miller 10th Ed, Ch 16).

ITE Gaps in Knowledge Reports

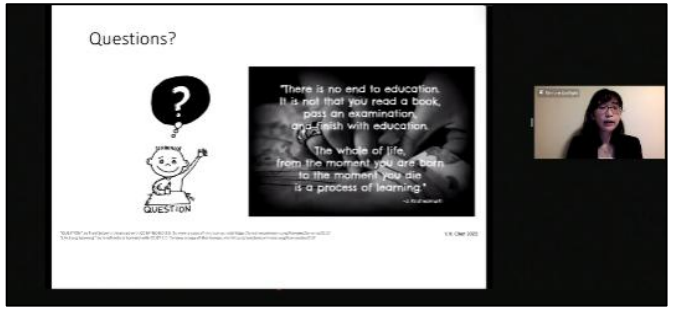
Video Lectures of Gaps in Knowledge reports from University of Kentucky Anesthesia:	
2020: https://youtu.be/X9NEntK89fE	2019: https://youtu.be/fpseLaUtDDE
2017/18: https://youtu.be/vAvLdl20orY	2016: https://youtu.be/qecGo1NyUBg
2015: https://youtu.be/qD_ch5_Z3tE	2014: https://youtu.be/OqonxKcSEs4

2021, 2022, 2023, and 2024 Best of Most Missed ITE, Basic, & Advanced Topics (Dr. Chen): www.datadrivendidactics.org

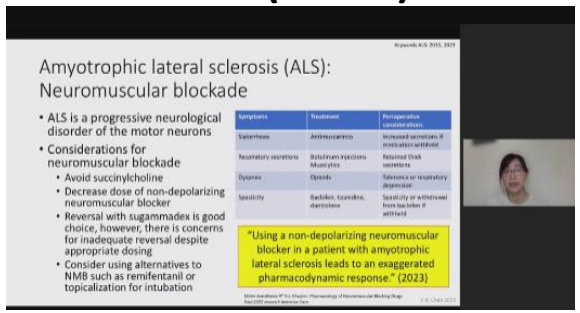
2021 (Part 1)



2022 (Part 2)



2023 (Part 3)



2024 (Part 4)

See this year's conference

Latest ABA ITE Gaps in Knowledge Report (2022-2024):

ABA ITE Gaps in Knowledge Reports. Latest update available at http://www.theaba.org

Room for notes

End

Room for notes

End of Anesthesia Review Session Conference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Thanks for coming! See you next time.