Name:_____

2022 CA-1 TUTORIAL TEXTBOOK 16th Edition

STANFORD UNIVERSITY MEDICAL CENTER
DEPARTMENT OF ANESTHESIOLOGY

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INTRODUCTION TO THE CA-1 TUTORIAL MONTH

We want to welcome you as the newest members of the Department of Anesthesia at Stanford! Your first weeks and months as an anesthesia resident are exciting, challenging, stressful, and rewarding. Regardless how much or how little experience you have in the field of anesthesiology, the learning curve for the next few months will be steep. Luckily, there are countless people and resources here in the department to help you succeed.

Years ago, before the development of this mentoring and tutorial system, CA-1s had little structure to their first month. While there were regular intra-operative and didactic lectures, the nuts and bolts of anesthesiology were taught with little continuity. CA-1s worked with different attendings each day and spent as much time adjusting to their particular styles as they did learning the basics of anesthesia practice. Starting in 2007, the first month of residency was overhauled to include mentors: each CA-1 at Stanford was matched with an attending or senior resident for a week at a time. In addition, a tutorial curriculum was refined to give structure to the intra-operative teaching and avoid redundancy in lectures. By all accounts, the system has been a great success!

There is so much material to cover in your first couple months of residency, and the number of resources available to you can be overwhelming. This booklet serves as a launching point for independent study. While you review the tutorial with your mentor, use each lecture as a starting point for conversations or questions. From there, senior residents and faculty will be happy to help point you in the direction of other useful resources and textbooks.

During your mentorship, we hope you can use your mentor as a role model for interacting with patients, surgeons, consultants, nurses and other OR personnel. This month, you will interact with most surgical specialties as well as nurses in the OR, PACU, and ICU. We suggest you introduce yourself to them and draw on their expertise as well.

Nobody expects you to be an independent anesthesia resident after just one month of training. You will spend the next three years at Stanford learning the finer points of anesthesia practice, subspecialty anesthesiology, ICU care, pre-operative and post-operative evaluation and management, etc. By the end of this month, we hope you attain a basic knowledge and skillset that will allow you to understand your environment, know when to ask for help, and determine how to direct self-study. Sprinkled throughout this book, you'll find some light-hearted resident anecdotes from all the good times you'll soon have, too.

CA-1 Introduction to Anesthesia Lecture Series:

The Introduction to Anesthesia Lecture series, given by attendings, is designed to introduce you to the basic concepts of anesthesia. Topics covered include basic pharmacology of anesthetics, basic physiology, and various clinical skills and topics. You will be relieved of all clinical duties to attend these lectures. You can find copies of all major Anesthesia textbooks in the anesthesia library or online through Lane Medical Library, and a wealth of subspecialty resources on the Stanford Ether website.

ACKNOWLEDGEMENTS

Thanks to Janine Roberts for her hard work and assistance in constructing the CA-1 Mentorship Textbook.

Thanks to our department chair Dr. Bateman for his support and assistance with this endeavor and our former chair Dr. Pearl for his guidance of generations of anesthesiologists. Their wisdom and encouragement are much appreciated by all.

Thanks to Dr. Macario, our Residency Program Director, who will be one of the first attendings to know each of you by your first name.

Special thanks to Dr. Ryan Green, Class of 2008, founder of the CA-1 mentorship program, and principal editor of the first edition of the CA-1 Mentorship Textbook.

Lastly, thanks to all of the resident and faculty mentors at Stanford University Medical Center, Palo Alto VA, and Santa Clara Valley Medical Center for all their time and effort spent teaching Stanford anesthesia residents.

As you start this July, don't be too hard on yourself if you miss an IV or an intubation. If it were that easy, no one would need residency. Just stay positive, embrace a growth mindset, and enjoy the incredible learning opportunities that are ahead of you. Try to go with the flow if plans change on you suddenly; flexibility is very important in this field. May your first month be a smooth transition to your anesthesia career.

Welcome to Stanford Anesthesia. We hope you love it as much as we do! Please do not hesitate to contact us with any questions or concerns.

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We also want to specifically thank all of the faculty and resident mentors who invest the extra amount of effort to train CA-1s in the month of July. Their designation as mentor is a rewarding and challenging opportunity. As Ralph Waldo Emerson said, "Our chief want in life is somebody who will make us do what we can." These mentors will serve a key role in the rapid transformation that takes place as you commence your career and obtain the knowledge and skills required to become a successful anesthesiologist.

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2009 MENTORS

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KEY POINTS AND EXPECTATIONS

Key Points:

- The program will last 4 weeks.
- Mentors will consist of faculty members and senior residents (CA-2s and CA-3s).
- CA-1s scheduled to start in the Stanford GOR will be assigned a different mentor each week (CA-1s scheduled to begin at the Palo Alto VAMC or Santa Clara Valley Medical Center will be mentored according to local program goals and objectives).
- Faculty will provide one-on-one mentoring while senior residents will provide one-on-one mentoring with oversight by a supervising faculty member.
- All CA-1s (including those starting at Stanford, VAMC, and SCVMC) will receive the syllabus of intra-operative mini-lecture topics to be covered with their mentors. These mini-lectures provide goal-directed intra-operative teaching during the first month. CA-1s will document the completion of each mini-lecture by obtaining their mentors' initials on the "Checklist for CA-1 Mentorship Intra-operative Didactics."
- CA-1s will receive verbal feedback from their mentors throughout the week, as appropriate, as well as at the end of each week. Mentors will communicate from week to week to improve longitudinal growth and mentorship of the CA-1.

Expectations of CA-1 Residents:

- Attend the afternoon CA-1 Introduction to Anesthesia Lecture Series.
- Participate in goal-directed learning by completing the CA-1 Mentorship Intra-operative Didactics with your mentors.
- Discuss cases with your mentor the night before.
- CA-1s at SUH are not expected to take weekend call with your mentor (for those at the Valley and VA, discuss with your mentor).

Expectations of Senior Resident Mentors:

- Senior mentors will take primary responsibility for discussing the case, formulating a plan, and carrying out the anesthetic with their CA-1; if concerns arise, the senior mentor will discuss the case with the covering faculty member.
- Instruct CA-1s in the hands-on technical aspects of delivering an anesthetic.
- Participate in goal-directed learning by completing the CA-1 Mentorship Intra-operative Didactics with your CA-1.
- Provide timely feedback to your CA-1 every day and at the end of the week.
- Provide continuity of teaching by communicating with the CA-1's other mentors.

Expectations of Faculty Mentors:

- Participate in goal-directed learning by completing the CA-1 Mentorship Intra-operative Didactics with your CA-1.
- Provide timely feedback to your CA-1 every day and at the end of the week.
- Provide continuity of teaching by communicating with the CA-1's other mentors.

GOALS OF THE CA-1 TUTORIAL MONTH

Anesthesia is a "hands-on" specialty. Acquiring the fundamental knowledge, as well as cognitive and technical skills necessary to provide safe anesthesia, are essential early on in your training. The CA-1 Mentorship Program and the CA-1 Introduction to Anesthesia Lecture Series will provide you with the opportunity to achieve these goals. The following are essential cognitive and technical skills that each CA-1 resident should acquire by the end of their first month.

I. Preoperative Preparation:

- a. Perform a complete safety check of the anesthesia machine.
- b. Understand the basics of the anesthesia machine including the gas delivery systems, vaporizers, and CO_2 absorbers.
- c. Set up appropriate equipment and medications necessary for administration of anesthesia.
- d. Conduct a focused history with emphasis on co-existing diseases that are of importance to anesthesia.
- e. Perform a physical examination with special attention to the airway and cardiopulmonary systems.
- f. Understand the proper use of laboratory testing and how abnormalities could impact overall anesthetic management.
- g. Discuss appropriate anesthetic plan with patient and obtain an informed consent.
- h. Write a pre-operative History & Physical with Assessment & Plan in the chart.

II. Anesthetic Management

- a. Placement of intravenous cannula. Central venous catheter and arterial catheter placement are optional.
- b. Understanding and proper use of appropriate monitoring systems (BP, EKG, capnography, temperature, and pulse oximeter).
- c. Demonstrate the knowledge and proper use of the following medications:
  - i. Pre-medication: Midazolam
  - ii. Induction agents: Propofol, Etomidate, Ketamine
  - iii. Neuromuscular blocking agents: Succinylcholine and at least one non-depolarizing agent
  - iv. NMBA reversal agents: Neostigmine/Glycopyrrolate & Sugammedex
  - v. Local anesthetics: Lidocaine
  - vi. Opioids: Fentanyl and at least one other opioid
  - vii. Inhalational anesthetics: Nitrous oxide and one other volatile anesthetic
  - viii. Vasoactive agents: Ephedrine and Phenylephrine
- d. Position the patient properly on the operating table.
- e. Perform successful mask ventilation, endotracheal intubation, and LMA placement.
- f. Recognize and manage cardiopulmonary instability.
- g. Spinal and epidural anesthesia are optional.
- h. Record intra-operative note and anesthetic data accurately, punctually, and honestly.

III. Post-operative Evaluation

- a. Transport a stable patient to the Post Anesthesia Care Unit (PACU)
- b. Provide a succinct anesthesia report to the PACU resident and nurse.
- c. Complete the anesthesia record with proper note.
- d. Leave the patient in a stable condition.
- e. Make a prompt post-operative visit and leave a note in the chart (optional but strongly encouraged).

SUGGESTED CHECKLIST FOR CA-1 MENTORSHIP
INTRAOPERATIVE DIDACTICS

Mentors ***initial*** completed lectures

First Days
_____ Discuss GOR Goals and Objectives for CA-1
_____ Discuss etiquette in the OR
_____ Discuss proper documentation
_____ Discuss proper sign out
_____ Discuss post-op orders
_____ Machine check

Week One
_____ Standard Monitors
_____ Inhalational Agents
_____ MAC & Awareness
_____ IV Anesthetic Agents
_____ Rational Opioid Use
_____ Intra-operative Hypotension & Hypertension
_____ Neuromuscular Blocking Agents

Week Two
_____ Difficult Airway Algorithm
_____ Fluid Management
_____ Transfusion Therapy
_____ Hypoxemia
_____ Electrolyte Abnormalities
_____ Hypothermia & Shivering
_____ PONV
_____ Extubation Criteria & Delayed Emergence

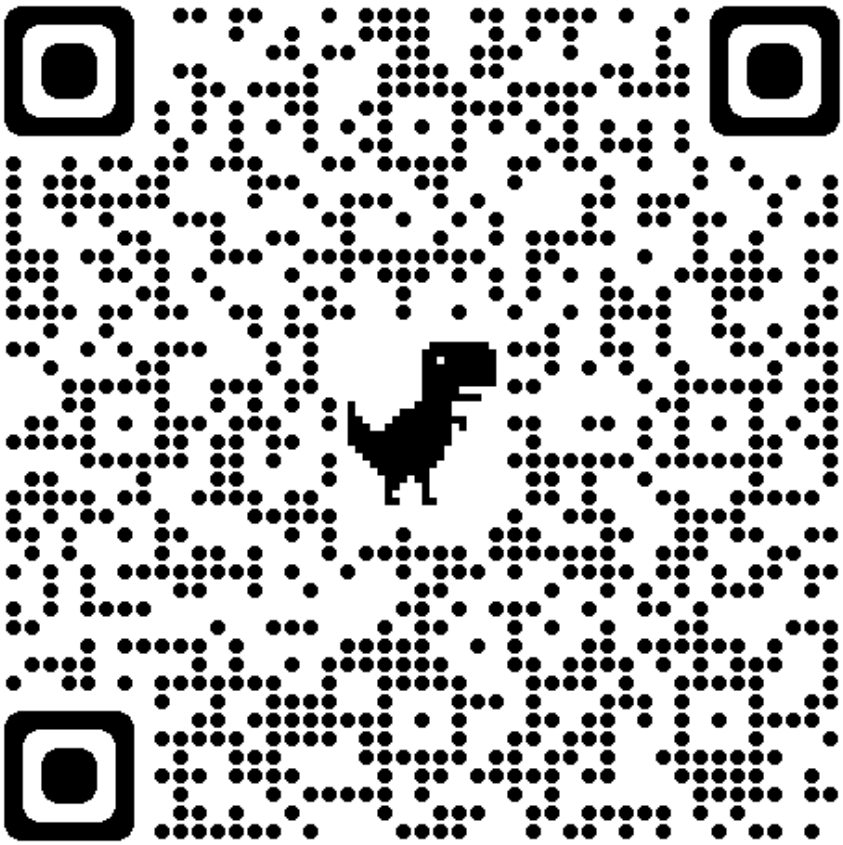
Week Three
_____ Laryngospasm & Aspiration
_____ Oxygen Failure in the OR
_____ Anaphylaxis
_____ Local Anesthetics
_____ ACLS
_____ Malignant Hyperthermia
_____ Perioperative Antibiotics

CA-1 Introductory Lectures July 2022

DATE	TIME	LECTURE*	CHAPTER**
7/7/22	4:00 PM	Tips and Tricks for the OR/Patient Care | Dr. Pam Flood	
	5:00 PM	Pharmacology of Intravenous Agents | Dr. Steven Shafer	9 (8)
7/11/22	4:00 PM	ASA Monitoring | Dr. Richard Jaffe	5/6 (20)
7/12/22	4:00 PM	Basic Anesthesia Machines | Dr. Richard Jaffe	2/3/4 (15)
7/13/22	4:00 PM	Positioning and Associated Risks | Dr. David Drover	(19)
	5:00 PM	Pharmacology of Neuromuscular Blockade | Dr. Amit Joseph	11/12 (11)
7/14/22	4:00 PM	The Drugs in the Drawer | Dr. Boris Heifets	10/13/14
	5:00 PM	Chief Resident Rounds 1	
7/18/22	4:00 PM	Devising an Anesthetic Plan | Dr. Cliff Schmiesing	18 (14)
	5:00 PM	Chief Resident Rounds 2	
7/19/22	4:00 PM	Respiratory Physiology | Dr. Javier Lorenzo	23 (5)
	5:00 PM	Chief Resident Rounds 3	
7/20/22	4:00 PM	Airway Management | Dr. Vicky Yin	19 (16)
	5:00 PM	Ethics and Professionalism | Dr. Alyssa Burgart	
7/21/22	4:00 PM	Intro to POCUS | Dr. Marianne Chen	
	5:00 PM	Wellness Program and Retreat | Dr. Hasan	
	5:15 PM	Chief Resident Rounds 4	
7/25/22	4:00 PM	Principles of Pharmacology | Dr. Steve Shafer	7 (4)
	5:00 PM	Pharmacology of Inhalational Agents | Dr. Steve Shafer	8 (7)
7/26/22	4:00 PM	SAB/Epidural Regional Anesthesia | Dr. Philip Wang	16/45 (17)
	5:00 PM	Chief Resident Rounds 5	
7/27/22	4:00 PM	Pearls and Pitfalls| Drs. Tracey Hong & Derrick Wu	
	5:00 PM	Chief Resident Rounds 6	
7/28/22	4:00 PM	Anesthesia Machine Round 2| Drs. Jason Batten & Meg Quinn	
	5:00 PM	Chief Resident Rounds 7	
8/1/22	4:00 PM	Central Line Workshop | Dr. Fred Mihm (Group 1)	LKSC ILC
	4:00 PM	iStat Training | Dr. Fiona Zeng (Group 1 & 2)	
8/2/22	4:00 PM	iStat Training | Dr. Fiona Zeng (Group 3 & 4)	
	4:30 PM	iStat Training | Dr. Fiona Zeng (Group 5 & 6)	
	5:00 PM	iStat Training | Dr. Fiona Zeng (Group 7 &8)	
8/3/22	4:00 PM	De Escalation Training	Zoom
	5:00 PM	Chief Resident Rounds 8	
8/4/22	4:00 - 6:00PM	Central Line Workshop | Dr. Fred Mihm (Group 2)	LKSC ILC
*Location is the Anesthesia Conference Room unless otherwise specified			
**Refers to corresponding chapter in Morgan & Mikhail's Clinical Anesthesiology 6e & (Basics of Anesthesia 7e)			

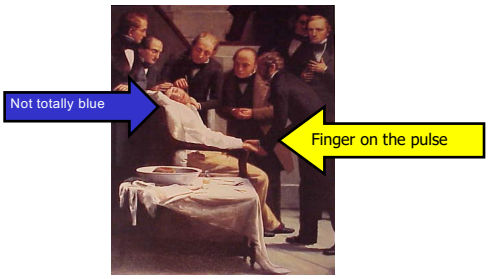
Anesthesia STAT: the Stanford Anesthesia Tutorial Companion Podcast

New for the 2022-2023 year is the Stanford Anesthesia Tutorial Companion Podcast with new episodes published throughout the year! The podcast will cover topics in the tutorial textbook in an audio format as well as other pertinent topics in anesthesia. Scan the QR code below.



Standard Monitors

Monitoring in the Past



Basic Anesthetic Monitoring

ASA Standards for Basic Anesthetic Monitoring

STANDARD I

"Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics and monitored anesthesia care."

STANDARD II

"During all anesthetics, the patient's ***oxygenation***, ***ventilation***, ***circulation***, and ***temperature*** shall be **continually** evaluated."

OXYGENATION
- -If using anesthesia machine: Inspired gas FiO2 analyzer + low O_2 concentration alarm
- -All anesthetics: quantitative method of assessing oxygenation (pulse oximetry with variable pitch tone)

CIRCULATION
- EKG: Minimum **3 lead**; 5 lead if any cardiac concern
- BP: Minimum cycle **q5** minutes
- At least one additional **continual** circulatory assessment: pulse ox tracing, a-line tracing, palpable pulse, auscultation, doppler

VENTILATION
- -Capnography (with expired Vt)
- -Disconnect alarm required if mechanically ventilated

TEMPERATURE
- Temperature probe if clinically significant changes in body temperature are anticipated

ITE tip: continuous vs. continual

- "**continual**" is defined as "repeated regularly and frequently in steady rapid succession"
  - Eg: the patient's blood pressure shall be *continually* evaluated q5 min
- "**continuous**" means "prolonged without any interruption at any time"
  - Anesthesia personnel shall be *continuously* present during an anesthetic
  - During mechanical ventilation *continuous* use of a device to detect disconnection shall be used
  - EKG monitoring shall be *continuously* displayed

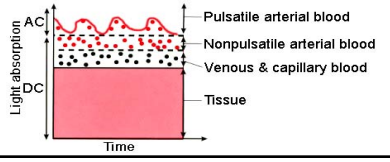
Pulse Oximetry

Terminology

- S_aO_2 (Fractional Oximetry) = O_2Hb / (O_2Hb + Hb + MetHb + COHb)
- S_pO_2 (Functional Oximetry/Pulse Oximetry) = O_2Hb / (O_2Hb + Hb)

Fundamentals

- The probe emits light at 660 nm (red, for Hb) and 940 nm (infrared, for O_2Hb); sensors detect the light that passes unabsorbed at each wavelength.
- Photoplethysmography is used to identify arterial flow (alternating current = AC) and cancels out the absorption during non-pulsatile flow (direct current = DC); the patient is their own control!
- The ratio (R) is used to derive the S_pO_2 (R = 1:1 ratio = S_pO_2 85% → why a pulse ox not connected to the patient reads usually 85%).



$$R = \frac{(AC/DC)_{660}}{(AC/DC)_{940}}$$

Pulse Oximetry Pearls

- Methemoglobin (MetHb) - Similar light absorption at 660 nm and 940 nm (R = 1:1 ratio) → at high levels **S_pO_2 approaches 85%**. PaO2 typically remains normal.
  - When true S_pO_2 is >85% you get a **falsely LOW** S_pO_2 reading
  - If the true S_pO_2 is actually <85%, S_pO_2 will be **falsely HIGH**
  - **Causes**: prilocaine/benzocaine topicalization, metoclopramide, dapsone, nitric oxide, nitroglycerine
  - **Treatments**: methylene blue, vitamin C (in G6PD deficiency)
- Carboxyhemoglobin (COHb) - Similar absorbance to O_2Hb. Higher affinity to Hgb than O2
  - At 50% COHb, S_pO_2 may be 95% despite a low S_aO_2 = 50% on ABG, thus producing a **falsely HIGH** S_pO_2
  - **Causes**: smoke inhalation, volatile anesthetic degradation, desiccated baralyme/soda lime
  - **Treatments**: 100% FiO2, hyperbaric O2
- Cyanide toxicity: Clinical cyanosis despite **HIGH** SpO_2. ABG and VBG will show similar PO2 values due to uncoupling of oxidative phosphorylation. Lactate will be very high.
  - **Hgb remains oxygenated**, but tissues cannot use it
  - **Causes**: sodium nitroprusside, smoke inhalation
  - **Treatment**: hydroxocobalamin (previously sodium/amyl nitrite)

Pulse Oximetry Pearls

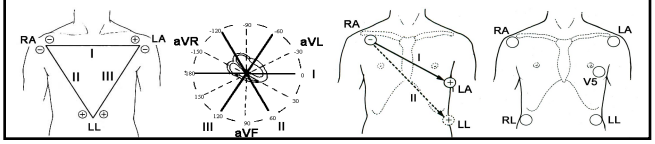
- Other factors producing a **falsely LOW** S_pO_2:
  - dyes (methylene blue > indocyanine green > indigo carmine)
  - blue nail polish
  - shivering/other motion,
  - ambient light
  - malpositioned sensor
  - low perfusion (low cardiac output, profound anemia, hypothermia, elevated SVR)
    - *Perfusion index (ratio of AC/DC) can give indication of quality of signal or pulsatility of site where sensor is applied. Ranges from .02% (very weak) to 20% (very strong)*
- Factors with **NO EFFECT** on S_pO_2 = bili, HbF, HbS, acrylic nails, fluorescein dye.
- **Cyanosis** - clinically apparent with **5 g/dl** desaturated Hb. Typically seen at an S_pO_2 below 85%.

EKG

3-Electrode System
- Allows monitoring of Leads I, II, and III
- but only one lead (i.e. electrode pair) can be examined at a time while the 3rd electrode serves as ground
- Lead II is best for detecting P waves and sinus rhythm

Modified 3-Electrode System
- If you have concerns for anterior wall ischemia, **move L arm lead to V5 position**, and monitor **Lead I** for ischemia

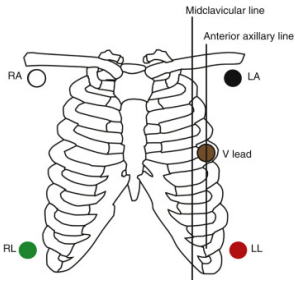
5-Electrode System
- Four limb leads + V5 (left anterior axillary line, 5th ICS)
- allows monitoring of **7 leads** simultaneously.
- V5 is **75%** sensitive for detecting ischemic events
- II + V5 is **80%** sensitive
- **II + V4 + V5** together is **98% sensitive**



Placement of EKG leads

3-Electrode System
- 3 Limb leads: RA (right arm - white lead), LA (left arm - black lead), and LL (left leg - red lead)
- Place on limbs, or in operating room if limbs inaccessible, on chest equidistant from the heart

5-Electrode System
- 3-electrode system PLUS RL (right leg – green lead) and V lead (brown lead)
- Brown lead – Anterior axillary line in 5th intercostal space
  - Anterior axillary line = line between the midpoint of clavicle and midpoint of axilla
- Green lead = reference point/ground, traditionally placed on RL, but can be placed anywhere on body away from other leads



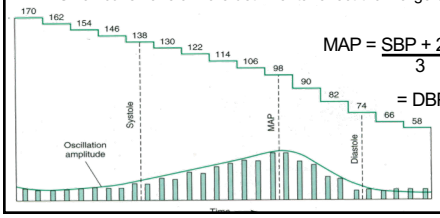
Mnemonic: "Smoke over fire, clouds over grass, white on the right"
(Black lead over red, white lead over green, white lead on the right)

ITE tip

- Which lead is most sensitive to atrial dysrhythmias?
  - Lead II, (V1 is second best)
- What are the benefits and drawbacks of a 3 lead EKG?
  - Poorly sensitive for ST segment changes, good for atrial arrhythmia detection (lead II) and R wave changes
- What are the benefits of a 5 lead EKG?
  - Addition of V1 enhances atrial dysrhythmia detection
  - Addition of V4, V5 improves detection of ischemic events

Noninvasive Blood Pressure

- Automated, microprocessor-assisted interpretation of oscillations in the NIBP cuff
- MAP is primary measurement; SBP and DBP are derived from algorithms
- Bladder should encircle >80% of extremity
  Bladder Width should be > 40% arm circumference
- Cuff too small = **falsely HIGH** BP
- Cuff too big = **falsely LOW** BP
  *Small cuffs have a more detrimental effect than large cuffs on BP accuracy



$$MAP = \frac{SBP + 2DBP}{3}$$

$$= DBP + 1/3*(\text{pulse pressure})$$

Invasive Blood Pressure

Indications
- Moment-to-moment BP changes anticipated and rapid detection is vital
- Planned pharmacologic or mechanical manipulation
- Repeated blood sampling
- Failure of NIBP (e.g. due to positioning with arms tucked or lateral positioning with up arm and down arm)
- Supplementary diagnostic information (e.g. pulse pressure variation to guide volume status)

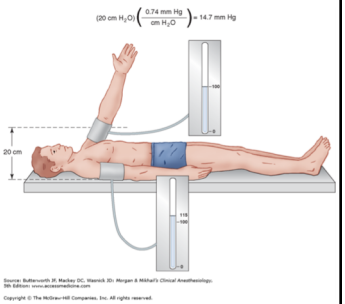
Transducer Setup
- Zeroing = exposes the transducer to air-fluid interface, thus establishing P_{atm} as the "zero" reference pressure
  - If you are zeroing at the transducer, **it does not matter what height/level the transducer is at** (there is little change in P_{atm} between the floor and the ceiling)
- Leveling = assigns the zero reference point to a specific point on the patient
  - by convention, the transducer is "leveled" at the right atrium
  - can level at any area of interest (e.g. in neurosurgical cases, level at circle of Willis to assess cerebral perfusion)

Blood pressure, cont

- **BP varies by position:**
- The difference in blood pressure (mm Hg) at two different sites of measurement equals the height of an interposed column of water (cm H2O) multiplied by a conversion factor (1 cm H2O = 0.74 mm Hg, or 15 cm height = 10 mm Hg)

Mnemonic: pH 7.410

A change in "p" pressure of 7.4 mm Hg coincides with "H" height change of 10 cm



ITE tip

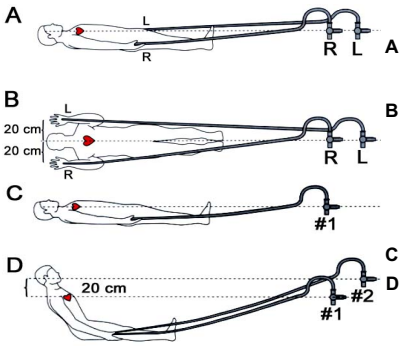
Question:

In the Beach chair position, the BP cuff on leg may read 120/80. But if the brain is 60cm vertically higher than the cuff, what is the BP in the brain?

Answer:

the BP in the brain would be closer to 75/35

Effect of Patient & Transducer Position on BP Measurement

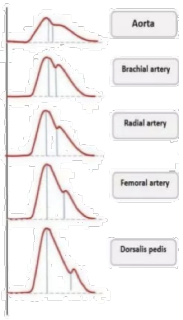


		R	L
A	ABP	120/80	120/80
	NIBP	120/80	120/80
B	ABP	120/80	120/80
	NIBP	135/95	105/65

		#1(RA)	#2(Brain)
C	ABP	120/80	
D	ABP	120/80	105/65

Remember "pH=7.410":
7.4 mm Hg = 10 cm H_2O

Arterial line tracings



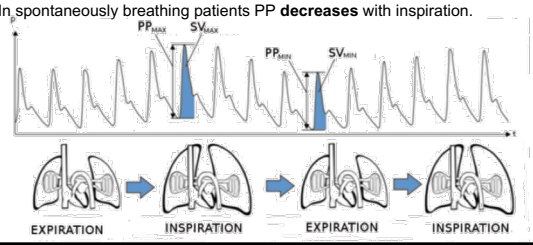
Systolic amplification: increase in peak systolic pressure as you move away from proximal aorta (caused by reflected waves) is offset by the narrowing of the systolic pressure wave, so the mean arterial pressure remains unchanged.

So the further from the aorta you are:

- Later dicrotic notch
- Higher systolic pressure, so pulse pressure widens
- MAP is unchanged

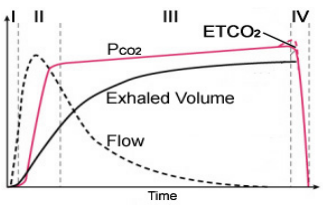
Pulse Pressure Variation

- Pulse pressure (PP) increases with **increased** stroke volume and **decreased** vessel wall compliance.
- The variation in PP seen on arterial line tracing can be used to guide volume resuscitation.
- Diagram below illustrates changes seen during positive pressure ventilation.
- In spontaneously breathing patients PP **decreases** with inspiration.



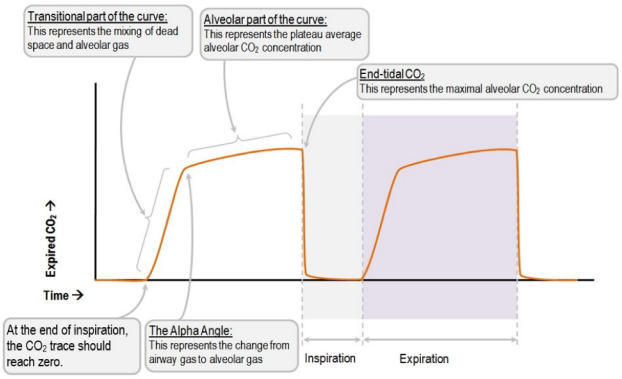
Capnography

- Measures exhaled CO_2
- Time delay exists due to length and volume of sample tube as well as sampling rate (50-500 ml/min)
- Anything distal to your Y-piece contributes to dead space



Capnography Phases

I. Dead space gas exhaled
II. Transition between dead space and alveolar gas
III. Alveolar plateau
IV. Inspiration



Capnography Pearls

Both the number and tracing provide much physiologic information

- Bronchospasm (upsloping trace)
- Significant hypotension can be associated with a drop in EtCO2
- Pulmonary embolism (decreased EtCO2 but increased A-a gradient between ETCO2 and PaCO2)
- Adequacy of CPR and indicator of ROSC (ETCO2 goal during CPR>10; if sudden increase in ETCO2, then likely have ROSC)
- Esophageal intubation, circuit disconnect (no ETCO2 tracing)
- Exhausted CO2 absorbent (ETCO2 does not return to 0-5)

Clinical pearl:

- When apneic: expect ETCO2 to increase by 6 mm Hg after 1 minute, and to increase by 3 mm Hg every minute thereafter

3 reasons for a drop in ETCO2

1. Decreased CO2 elimination:
   - Acute cardiovascular collapse (reduced cardiac index)
   - Massive venous air embolism (increased ET nitrogen)
   - Large PE (ECG showing S1,Q3,T3)
   - Kinked, dislodged, or esophageal ETT
2. Decreased CO2 production:
   - Hypothermia
   - Hypothyroidism
   - Neuromuscular blockade
3. Circuit sampling line disconnect

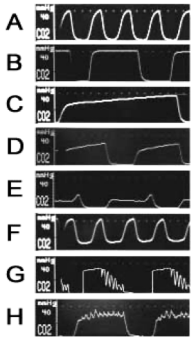
ITE tip

During diagnostic laparoscopy, an intubated and anesthetized patient is placed in Trendelenburg. Over the next 20 minutes SpO_2 decreases from 100% to 95%, and ETCO2 increases from 35 to 40 without changes in ventilator settings. The most likely reason is:

A. Decreased diaphragmatic excursion
B. Compression of vena cava
C. Carbon dioxide embolism
D. Pneumothorax

answer: A

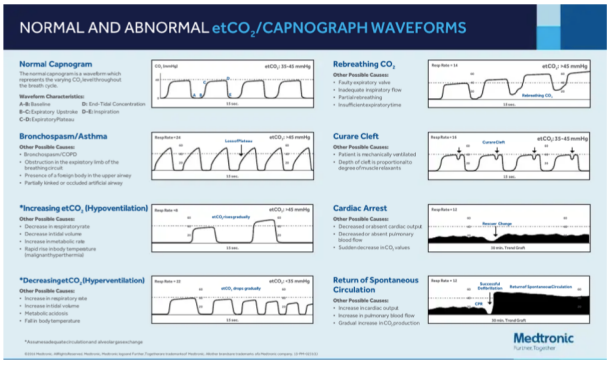
Capnography Pearls



Example Traces

A. Spontaneous ventilation
B. Mechanical ventilation
C. Prolonged exhalation (spontaneous)
D. Emphysema (notice upsloping plateau)
E. Sample line leak
F. Exhausted CO_2 absorbant
G. Cardiogenic oscillations
H. Electrical noise

Capnography Pearls



Temperature

Sites

- **Core temperature monitoring:**
  - **Pulmonary artery** = "Core" temperature (gold standard)
  - **Tympanic membrane** - correlates well with core; approximates brain/hypothalamic temperature
  - **Nasopharyngeal** - correlates well with core and brain temperature (careful with coagulopathy, can get refractory epistaxis)
  - **Oropharynx** – good estimate of core temperature; recent studies show correlation with tympanic and esophageal temperatures
  - **Esophagus** - correlates well with core (avoid w esophageal varices)
- **Temperature monitoring that less correlates with "core" temperature**
  - **Bladder** - approximates core when urine flow is high, may be significant delay between bladder temp reading and true temp
  - **Axillary** - inaccurate; varies by skin perfusion
  - **Rectal** - not accurate (temp affected by LE venous return, enteric organisms, and stool insulation)
  - **Skin** - inaccurate; varies by site

*Major mechanisms of heat loss with GA are redistribution as vasodilation causes blood to shift from core to periphery, then radiation (but other forms include conduction, convection, and evaporation)

Other Monitors/Adjuncts to Consider

Depth of anesthesia:

- BIS monitor/Sedline

Circulation/Fluids:

- PA catheter +/- Continuous Cardiac Output
- Central venous pressure (CVP)
- Intracranial Pressure (ICP)
- Transesophageal Echo (TEE)
- Precordial doppler (if risk of air embolus is high)
- Cerebral oximetry (NIRS)
- Esophageal stethoscope
- Foley
- OG tube

AAAHH!! I just intubated, now what?!

Remember your A's

- Airway (ETT secured, vent settings)
- Anesthesia (volatile, infusions)
- Access (a-line, PIV, CVC, etc.)
- Another thing in the mouth (OG tube, bite block, TEE probe)
- Arms (positioning okay?)
- Air (forced air, aka Bair Hugger + temp probe)
- ABG/ACT (check baseline ABG and/or ACT if applicable)
- Antibiotics
- Analgesia (redose pain med prior to incision?)

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Inhalational Agents

Historical Facts

- Several accounts of various forms of anesthesia in the BCE era using everything from cannabis and other herbs to carotid compression.
- **Modern anesthesia**
  - **1842** – Dr. Crawford Long had been using ether for fun with its exhilarating effects on what were known as ether frolics.
    - Dr. Long used ether to anesthetize a friend to excise some neck tumors (not reported until 1849)
  - **1845** – Dentist Horace Wells successfully uses nitrous oxide for dental extractions; however, public demonstration fails.
  - **1846** – First public demonstration of ether at MGH in what is now called the ether dome by Dr. Morton.
    - Dr. Warren (famous surgeon) was skeptical of Dr. Morton's offer to keep the patient from pain after Dr. Well's failed demonstration with nitrous. Dr. Warren called it "Humbug".
    - Dr. Morton stayed up all night with Dr. Gould (instrument maker) to construct a device to deliver ether that was more sophisticated than a rag. They arrived for the schedule vascular tumor removal on Mr. Abbot 15 minutes late. Dr. Warren remarked "Well, Sir, your patient is ready". After inducing anesthesia Dr. Morton fired back "Sir, *your* patient is ready!".
    - After the surgery Dr. Warren commented, "Gentlemen, this is no humbug"

Pharmacokinetics

- **Pharmacokinetics** of inhalational agents divided into four phases
  - Uptake
  - Distribution (to CNS = site of action)
  - Metabolism (minimal)
  - Elimination
- Goal: to produce **partial pressure** of gas in the **alveolus** that will **equilibrate** with **CNS** to render anesthesia
  - PARTIAL PRESSURE yields effect, **not** concentration
  - At higher altitudes where P_{atm} < 760 mmHg, the same concentration of inhalation agent will exert a lower partial pressure within alveolus and therefore a REDUCED anesthetic effect
- At equilibrium the following applies

  $P_{CNS}=P_{arterial\ blood}=P_{alveoli}$

PK: F_I, $F_{A,}$ and Uptake

- **F_I** (inspired concentration)
  - Determined by fresh gas flows, volume of breathing system, and absorption by machine/circuit
    - ↑ fresh gas flow, ↓ circuit, and ↓ circuit absorption allow actual Fi to be close to delivered Fi
- **F_A** (alveolar concentration)
  - Determined by uptake, alveolar ventilation, and concentration/second gas effects
  - **P_A** (alveolar partial pressure) is determined by input (delivery) minus uptake (loss)

» **Uptake**: gas taken up by the pulmonary circulation.
– Affected by blood solubility, alveolar blood flow (i.e. cardiac output), alveolar-to-venous partial pressure difference
  - ↓ blood solubility, ↓ CO, ↓ alveolar-venous partial pressure difference → ↓ uptake
    – ↓ uptake → ↑ F_A/F_I → faster induction
  - Highly soluble gases = more gas required to saturate blood before it is taken up by CNS
  - High CO = equivalent to a larger tank; have to fill the tank before it is taken up by CNS

» Rate of rise in **FA/FI ratio** is a marker of anesthetic uptake by the blood.
– More uptake means slower rise of F_A/F_I
– Gases with the lowest solubilities in blood (eg. Desflurane) will have fastest rise in F_A/F_I

PK: More on Uptake

Alveolar Blood Flow:
- In the absence of any shunt, alveolar blood flow = cardiac output
- *Poorly* soluble gases are *less* affected by CO (so little is taken up into blood)
- *Low cardiac output* states predispose patients to overdose of inhalational agents as *Fa/Fi will be faster* (esp. for soluble gases)

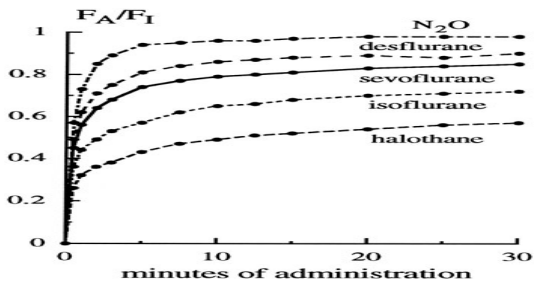
** Shunt States **

Right to Left Shunt (intracardiac or transpulmonary, i.e. mainstem intubation)
- Shunted blood (containing no volatile anesthetic) mixes with blood coming from ventilated alveoli (contains volatile), diluting the arterial anesthetic partial pressure → *slows onset of induction*
- will have *more significant* delay in onset of *poorly* soluble agents
- IV anesthetics = faster onset (if bypassing lungs, quicker to CNS)

Left to Right Shunt
- little effect on speed of induction for IV or volatile anesthetics

Concentration effect:
- ↑ F_I not only ↑ F_A, but also ↑ rate at which F_A approaches F_I (see following graph)

Second Gas Effect:
- concentration effect of one gas augments another gas (questionably clinically relevant with nitrous both during induction and emergence)
  - rapid intake of nitrous into blood → ↑ relative concentration of second gas



The rise in alveolar (*FA*) anesthetic concentration toward the inspired (*FI*) concentration is most rapid with the least soluble anesthetics (nitrous oxide, desflurane, and sevoflurane). It rises more slowly with the more soluble anesthetics (halothane). Nitrous (typically given in higher concentrations) has the greatest concentration effect, which is why *FA*/ *FI* rises the most quickly with nitrous even though desflurane has a slightly lower blood solubility. All data are from human studies.

(Adapted from Yasuda N, Lockhart SH, Eger EI II *et al*: Comparison of kinetics of sevoflurane and isoflurane in humans. Anesth Analg 72:316, 1991; and Yasuda N, Lockhart SH, Eger EI II *et al*: Kinetics of desflurane, isoflurane, and halothane in humans. Anesthesiology 74:489, 1991.)

Anesthetic Gas Properties

	Blood:Gas Partition Coeffecient	Vapor Pressure (mmHg) at 20°C	MAC
Nitrous Oxide	0.46	38,770	104%
Desflurane	0.45	669	6%
Sevoflurane	0.65	160	1.85%
Isoflurane	1.46	240	1.15%
Halothane	2.54	244	0.76%
Enflurane	1.9	172	1.63%

Example: Blood:gas partition coefficient of nitrous = 0.46 = at steady state 1ml of blood contains 0.46 as much nitrous oxide as does 1 ml of alveolar gas. In other words, at steady state if your fraction inspired gas is 50% N2O then 1ml of blood will contain 0.46x0.5 ml's of N2O or 0.23 ml (Jaffe)

Fat:blood partition coefficient is >1. Therefore, things that increase fat in the blood (e.g. postprandial lipidemia) will increase the overall blood:gas partition coefficient → slows induction

ITE tip

Things to Remember:

- Factors that **increase** the rate of rise of FA/FI
  - Relatively **low** blood:gas partition coefficient (solubility) for the volatile
  - **Low** cardiac output (affects *soluble* gasses more)
  - **High** minute ventilation
  - **Low** (Parterial – Pvenous), meaning less blood **uptake**

– *Increase* in cardiac output would *decrease* rate of rise in FA/FI for relatively *soluble* inhaled anesthetics (but would NOT produce much effect for insoluble agents)

– **Shunts** on the other hand, typically ***affect insoluble agents*** more than soluble agents

Which of the following is true about FA/FI when cardiac output is doubled?

- A. increasing cardiac output has no significant effect on anesthetic uptake.
- B. FA/FI ratio rises faster for soluble agents than insoluble agents.
- C. FA/FI ratio rises slower for soluble agents than insoluble agents.
- D. the rate of rise is the same for insoluble and soluble agents.

Answer: C

Pharmacodynamics

- No clear mechanism
- Direct binding to amphiphilic cavities in proteins, but unclear how this produces anesthesia
- Likely enhancement of inhibitory channels and attenuation of excitatory channels
  - **GABA**, **NMDA**, **glycine** receptor subunits have all been shown to be affected
- Potency of anesthetic has been roughly linked to lipid solubility

PD: Shared Properties

- Neuro: $CMRO_2$↓; cerebral vascular resistance ↓ → CBF ↑ → ICP ↑
  - ***except N2O :*** $CMRO_2$↑ and CBF ↑
  - Sevo/Des/Iso
    - 0.5 MAC: $CMRO_2$ ↓ counteracts cerebral vasodilatation on CBF → **CBF** ↔
    - 1 MAC: $CMRO_2$↓ maximal, so vasodilatory effects more prominent → **CBF** ↑
- CV: dose-related ↓ SVR → ↓ MAP (but CO maintained)
  - Halothane cause decreases in myocardial contractility
- Pulm
  - ↓ Vt, ↑ RR → preserved minute ventilation
  - Dose-dependent ↓ of ventilatory response to hypercapnia and hypoxemia
  - ↑ bronchodilation
- Renal: ↓ renal blood flow and ↓ GFR
- MSK: ↑ muscle relaxation (except N2O)

Nitrous Oxide

- Low potency (MAC 104% - can never reach 1 MAC!)
- Low solubility in blood facilitates rapid uptake and elimination
- Commonly administered as an anesthetic adjuvant
- Does not produce skeletal muscle relaxation
- Can potentially contribute to PONV (but can be controlled with antiemetics)
- Can diffuse into air filled cavities and cause expansion of these structures (pneumothorax, bowel, middle ear, ET tube balloons, pulmonary blebs, etc.)
  - Nitrous oxide can enter cavities faster than nitrous can leave
  - Often contraindicated in these settings
- Myocardial depression may be unmasked in CAD or severe hypotension
- Can cause pulmonary hypertension if used for prolonged period
- NMDA antagonist → may have analgesic effects
- Prolonged exposure can result in bone marrow depression and peripheral neuropathies
- NOT a trigger for MH (unlike volatile agents)
- Should periodically let air out of the ETT cuff if using nitrous to avoid tracheal injury

Isoflurane

- Highly pungent
- Least expensive among clinically used volatile anesthetics
- Second most potent of the clinically used inhalational agents (MAC 1.15%)
- Previously implicated for causing "**coronary steal**" (more recent studies have disputed this)
  - Dilation of "normal" coronary arteries causing blood to be diverted away from maximally dilated/stenotic vessels, to vessels with more adequate perfusion
- Causes vasodilation
  - Decreases BP
  - Increases CBF (usually seen at 1.6 MAC)
    - Minimal compared to halothane
  - Increases ICP (usually at above 1 MAC; short lived)
    - Minimal compared to halothane
- At 2 MAC produces electrically silent EEG

Sevoflurane

- 2/3rds as potent as isoflurane (MAC 1.85%)
- Rapid uptake and elimination
- Sweet smelling, non-pungent
  - Popular for inhalational induction (often used in pediatrics)
- When exposed to CO_2 absorbent, sevoflurane breaks down to **compound A** (nephrotoxic in rats, however no human clinical evidence of nephrotoxicity)
  - Some guidelines recommended to keep fresh gas flows **>2 L/min** to prevent rebreathing of Compound A (not formation of it), however this is disputed
  - Occurs in alkali such as barium hydroxide lime (Baralyme) or soda lime but **NOT** calcium hydroxide

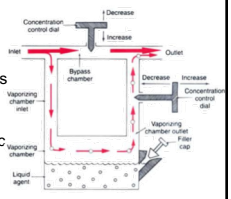
Desflurane

- Lowest blood:gas solubility coefficient (lower than N_2O)
- Low potency (MAC 6%)
- High vapor pressure (669 mmHg) is close to atmospheric pressure therefore boils at sea level
  - Must be stored in a heated, pressurized vaporizer so pressure stays constant (the vaporizer is set to 2 atm) and Desflurane vaporizers are set to deliver a *constant volume* of anesthetic.
  - **Remember that the anesthetic affect (MAC) correlates to the partial pressure, NOT the concentration.
- Very pungent
  - Can cause breath-holding, bronchospasm, laryngospasm, coughing, salivation when administered to an awake patient via face mask
- Can form CO in desiccated CO_2 absorbent (more so than other volatiles)
- Can cause an increased sympathetic response (tachycardia, hypertension) when inspired concentration is increased rapidly

Delivery of Volatile Anesthetics

- Modern anesthetic machines use **vaporizers** that take a reservoir of liquid anesthetic and create saturated vapor in equilibrium with the liquid.
  - A portion of the fresh gas flow or carrier gas then passes through the vaporizer chamber and becomes saturated with anesthetic vapor, which then is carried to the patient as a mix of fresh gas and anesthetic vapor.
  - Liquid anesthetic evaporates in chamber up to its **saturated vapor pressure (SVP).**
    - SVP: the partial pressure of anesthetic vapor at a given temp, where the anesthetic liquid and its vapor are in equilibrium.
    - **Partial pressure** of the anesthetic vapor in the carrier gas is equal to the SVP of the anesthetic

$$\frac{SVP}{P_T} = \frac{V_A}{V_C + V_A}$$



SVP = agent SVP, PT = total pressure (usually atmospheric pressure), VA *= agent vapor volume,* VC *= carrier gas volume*

Delivery of Volatile Anesthetics

- Using the SVP and total pressure, you can calculate the **volume of anesthetic** delivered in a volume of fresh gas to determine how much anesthetic you are delivering to a patient.
  - Rearrange previous equation to:

$$V_A = \frac{SVP}{P_T - SVP} \times V_C$$

- Once VA or volume of anesthetic is calculated , the **total % concentration** delivered can then be determined.

$$\%\ \text{Volatile anesthetic} = \frac{V_A}{FGF + V_A} \times 100$$

– It is worth knowing SVP of Sevoflurane and Isoflurane for your basic exam, as you may be asked to calculate anesthetic gas output.

ITE tip

There is a shortcut for calculating vaporizer output!

- If you can remember the ratio generated from the equation $SVP/(P_T - SVP)$, assuming $P_T = 760$, you can just multiply that ratio by the fresh gas flow through the vaporizer to get the volume of volatile anesthetic (this is just another way of thinking about the equation on the last slide!)… see fractions below.

AGENT	SVP (mm Hg)	SVP/(PT - SVP)
Sevoflurane	160	~1/4
Enflurane	172	~1/3
Isoflurane	240	~1/2
Halothane	244	~1/2
Desflurane	669	N/A

- So… if fresh gas flow is 3L/ min and of that 200 mL/min goes through the sevo vaporizer (¼ * 200 = 50) you can estimate that about 50 mL of sevo will be picked up by the carrier gas, and the volume concentration will then be: 50/(3000 + 50) x100 = 1.6% sevo

ITE tip

Anesthesia in Denver?

- For Sevo and Iso:
  - Remember modern vaporizer output is a function of saturated vapor pressure of the anesthetic in proportion to atmospheric pressure … so dropping atmospheric pressure will increase the output (volume) of your vaporizer, **but the partial pressure of your anesthetic gas remains the same**.
    - In terms of **volume,** altitude has significant effect on vaporizer output.
      - At higher altitude the volume (%) delivered will be higher than what the dial is set to
    - **But** the **partial pressure** will remain the same
      - Remember *partial pressure* of an anesthetic gas in the alveoli is what determines how anesthetized your patient is
      - Therefore, in Denver to give 1 MAC of Sevo you still turn the dial to 2% because the vaporizer compensates with more output (a higher % at a lower atmospheric pressure will give you the same partial pressure of volatile)
  - But also remember…
    - Desflurane uses a **DIFFERENT** heated vaporizer system that delivers anesthetic at a fixed *percent concentration* and **NOT** at a fixed *partial pressure* (like sevo and iso vaporizers do!).
    - At higher altitudes the partial pressure of Des is reduced due to lower barometric pressure. So: **Des required dial setting** = **desired %** x (**760** mmHg/ **current** atmospheric pressure)
      - To deliver the equivalent of 1 MAC of Des at 380 ATM, you must turn the dial to **12%.**

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During a robotic prostate case where the lights were dimmed, the anesthetic machine alarmed that the delivered MAC was low. I checked the circuit for leaks – nothing. I sniffed around – no smell of sevo. I checked the vaporizer – it was closed tight. Where was the sevo going?! I pushed bits of propofol to buy time while I called the anesthesia tech for help. He scanned the machine with a flashlight and focused on the vaporizer – the meniscus was super low. It was nearly empty. Turned out the sevo wasn't refilled between cases…

Never drive on an empty tank.

MAC & Awareness

Minimum Alveolar Concentration

Alveolar concentration of a gas at 1 atm at steady-state concentration *at which 50% of subjects do not respond to surgical incision*

Important Points

- Remarkably consistent across species
- MAC mirrors *brain partial pressure* of agent
  - At equilibrium, brain anesthetic partial pressure = alveolar partial pressure
- MAC is population average, thus not true predictor of individual response (MAC = $\mathbf{ED_{50}}$)
  - the $\mathbf{ED_{95}}$ is ± 20% - so at **1.2 MAC**, 95% of patients will not respond to incision
- MAC values are **additive** (e.g. 0.5 MAC iso + 0.5 MAC N_2O = 1 MAC)
- MAC is **inversely related** to anesthetic potency (lipid solubility)
  - Potency (and lipid solubility) are determined by **oil:gas partition coefficient** (*NOT blood:gas partition coefficient*)

MAC of Inhaled Anesthetics

Gas	Blood:Gas Partition Coefficient	Oil:Gas Partition Coefficient	MAC*
Halothane	2.5	197	0.75%
Enflurane	1.9	98.5	1.7%
Isoflurane	1.4	90.8	1.2%
Sevoflurane	0.65	50	2.0%
N_2O	0.47	**1.3**	**104%**
Desflurane	0.45	19	6.0%

*MAC values for adults 36-49 years old

- MAC is indicator of anesthetic **potency**, which is measured by a volatile's **Oil:gas partition coefficient** *(higher the coefficient, the more potent the agent)*
- **Blood:gas partition coefficient** is indicator of **solubility**, which affects rate of induction and emergence. It is NOT related to MAC.

ITE tip

The potency of an inhalational agent can be estimated by knowing its solubility in _____.

a. olive oil
b. deionized water
c. ethylene glycol
d. coconut water

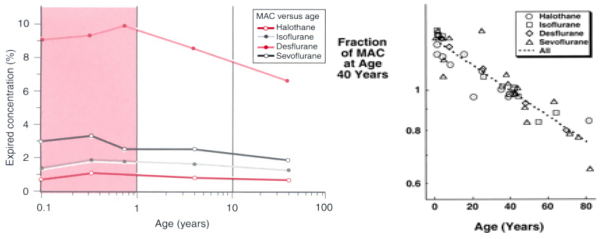
Answer: **a**, olive oil. This discovery was made in the 1800s, by Hans Meyer and Ernest Overton independently, also known as the Meyer-Overton correlation.

ITE tip

» True or False?

- Anesthetics with greater blood:gas partition coefficients have lower solubility in blood. – F
- Blood gas coefficient is an important determinant of speed of anesthetic induction and recovery. – T
- Oil gas partition coefficient has been correlated to anesthetic elimination. – F
- Tissue: blood partition coefficients are important to describe redistribution of a chemical in the body – T

Effect of Age on MAC



MAC is highest at 6 months old, then begins to decline

After age 40, MAC declines ~6% per decade
(i.e. MAC for 80 year old is about 75% that of 40 year old)

	Medications	Alcohol	Physiologic Conditions	Pathophysiologic Conditions	Genetic Factors
Factors Decreasing MAC	Opiates Benzodiazepines Barbiturates Propofol Ketamine Alpha-2 agonists Chronic meth use Verapamil Local anesthetics	Acute ethanol ingestion	Increasing age for patients >1 year of age pregnancy	Hypothermia Hypoxia Hypercarbia Severe anemia (Hb < 5) Sepsis Hyponatremia	None established
Factors Increasing MAC	Inhibition of catecholamine reuptake (amphetamines, ephedrine, L-dopa, TCA)	Chronic ethanol abuse	First months of life for infants <6mo of age	Hyperthermia Hypernatremia	Genotype related to red hair

More MAC Definitions

MAC_{Awake} (a.k.a. MAC-Aware)
- MAC necessary to prevent response to verbal/tactile stimulation
- Volatiles: ~0.4 MAC; N_2O: ~0.6 MAC

$MAC_{Movement}$
- 1.0 MAC

MAC_{EI} (a.k.a. LS, IT, or LMI = laryngoscopy, intubation, LMA insertion)
- MAC necessary to prevent laryngeal response to "endotracheal intubation"
- Prevents movement in 95% of patients (ED_{95})
- ~1.3 MAC

MAC_{BAR}
- MAC necessary to "**b**lunt **a**utonomic **r**esponse" to noxious stimulus
- Opiates (even small amounts) and N_2O often added to achieve this level and thus spare requirement of high concentrations of halogenated anesthetics
- ~1.6 MAC

Awareness

- Estimated to be 1-2 per 1000 GA cases
  - Higher incidence in pediatrics – up to 2.7% in kids over 6 years old but psychological sequelae are fewer
  - Twice as likely to happen when neuromuscular blockade is used
  - More common if chronically using alcohol, opiates, meth, cocaine
  - More common in high-risk surgeries where deep anesthesia may be dangerous to an unstable patient (e.g. trauma 11-43%, cardiac 1-1.5%, cesarean section 0.4%)
- Most common sensation is hearing voices
- Mostly occurs during induction or emergence
- Early counseling after an episode is very important (needed by 40-60%)
- Patient handout available at: www.asahq.org/patientEducation/Awarenessbrochure.pdf
- Dreaming can also occur and be confused for awareness if it is disturbing to the patient; dreaming is not related to anesthetic depth

ITE tip

Which of the following is LEAST likely to be associated with an increased risk of intraop awareness?

a. cesarean delivery under GA
b. emergency damage-control lap chole under GA
c. history of opioid abuse
d. red hair

Answer: d. Red hair is associated with distinct mutations on the melanocortin-1 receptor. MAC may be altered in these patients, however hair color has never been identified as a risk factor for intraoperative recall)

ITE tip

_____ causes the LEAST reduction in MAC of volatile anesthetics.

a. fentanyl
b. morphine
c. remifentanil
d. nalbuphine

Answer: **d.** Nalbuphine. Unlike volatile anesthetics and other IV induction agents such as propofol, opioids have ceiling effects that prevent them from being used as sole induction agents. This is evidenced by reports of recall and awareness in cases using high-dose fentanyl and even combinations of opioids and nitrous. Combining opioids with volatiles can significantly decrease MAC but there is a sub-MAC ceiling effect at which there is not further reduction in MAC despite increasing opioid doses.

Signs of Light Anesthesia

- Tearing
- Sympathetic activation: Dilated pupils, sweating
- Coughing or bucking
- Patient movement
- Increase in HR or BP by 20% above baseline (albeit these do not reliably predict awareness)
- Signs of consciousness on EEG monitor (Bispectral Index or Sedline, see below)

Preventing Awareness

- Consider administering an amnestic premedication
- Avoid or minimize muscle relaxants when able
- Choose potent inhalational agents rather than TIVA if possible -> use at least 0.5-0.7 MAC
- Monitor brain activity using BIS or SedLine if using TIVA
- Consider different treatment for hypotension other than decreasing anesthetic concentration
- Redose IV anesthetic when delivery of inhalational agent is difficult (ie during long intubation or rigid bronchoscopy)

BIS & Sedline

- Both use processed EEG signals to produce numbers (0-100) relating to depth of anesthesia.
  - BIS index ideally 40-60
  - Sedline (PSI) ideally 25-50
- Both have been shown to be fairly good predictors of loss and regaining consciousness. However, no monitoring device is 100% effective.
  - Significant variability based on age
  - Changes in EEG with medications (e.g. NDMB, ephedrine, ketamine), conditions (elderly with low amplitude), and other events (ischemia)
- Both have ~ 2 minute time lag
- It is possible to display the raw EEG in real time on either device, and be able to interpret on your own (highly encouraged - http://icetap.org/)

ITE tip

- Procedures associated with awareness
  - 1. Major trauma with significant blood loss
  - 2. Cardiac surgery
  - 3. Cesarean section under GA
  - 4. procedures done under pure TIVA
- Awareness facts:
  - Awareness is **twice** as likely when neuromuscular blocking drugs are used.
  - The **amount of volatile anesthetic** is what matters most.
    - MAC of 0.8 with mostly N2O is more likely to result in awareness than MAC of 0.7 of volatile alone.
  - Other risk factors for awareness
    - h/o substance abuse
    - h/o difficult intubation or anticipated difficult intubation
    - Chronic pain patients
  - Clinical pearl: **Red hair** is associated with higher MAC requirement but not increased risk of awareness.

Management

If you suspect your patient may be aware:

- Immediately deepen the anesthetic with fast-acting agents (e.g. propofol)
- Talk to the patient, reassure them that everything is OK (hearing is the last sense to be lost)
- Consider a benzodiazepine for amnesia
- Talk to the patient after the case to assess if they had any awareness
- Set up counseling if necessary
- Contact Patient Services and Risk Management (potential lawsuit?)

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IV Anesthetic Agents

CNS Targets of IV Anesthetics

- **GABA receptors** (most common target)
  - GABA is the primary **inhibitory** neurotransmitter in CNS
  - Activation causes **increase in chloride conductance**, and therefore **hyperpolarization** of neuron (inhibiting nerve transmission)
  - Propofol and Barbiturates decrease the rate of dissociation of GABA and its receptor (increasing the duration of chloride channel opening)
  - Benzodiazepines facilitate the attachment of GABA to its binding site on the receptor (increasing the frequency of chloride channel openings)
- **NMDA receptors**
  - NMDA receptors are glutamate, glycine, and D-serine activated excitatory ion channels
  - *Ketamine* is an uncompetitive antagonist
- **Alpha-2 receptors**
  - *Dexmedetomidine* is an alpha-2 agonist: inhibits NE release
    - 1. CNS inhibition via the **locus creuleus** (primary site for brain release of NE) in brain stem
    - 2. analgesia via decreased **substance P** release at the **dorsal horn** of the spinal cord.

Induction Characteristics and Dosage Requirements for the Currently Available Sedative–Hypnotic Drugs

DRUG NAME	INDUCTION DOSE (mg/kg)	ONSET (sec)	DURATION (min)	EXCITATORY ACTIVITY*	PAIN ON INJECTION*	HEART RATE†	BLOOD PRESSURE†
Thiopental	3–6	<30	5–10	+	0–+	↑	↓
Methohexital	1–3	<30	5–10	++	+	↑↑	↓
Propofol	1.5–2.5	15–45	5–10	+	++	0–↓	↓↓
Midazolam	0.2–0.4	30–90	10–30	0	0	0	0/↓
Diazepam	0.3–0.6	45–90	15–30	0	+/+++	0	0/↓
Lorazepam	0.03–0.06	60–120	60–120	0	++	0	0/↓
Etomidate	0.2–0.3	15–45	3–12	+++	+++	0	0
Ketamine	1–2	45–60	10–20	+	0	↑↑	↑↑

*0 = none; + = minimal; ++ = moderate; +++ = severe.

†↓ = decrease; ↑ = increase.

(Clinical Anesthesia 6th Edition; Barash, P.; Lippincott Williams and Wilkins; 2011)

Pharmacokinetic Values for the Currently Available Intravenous Sedative–Hypnotic Drugs

DRUG NAME	DISTRIBUTION HALF-LIFE (min)	PROTEIN BINDING (%)	DISTRIBUTION VOLUME AT STEADY STATE (L/kg)	CLEARANCE (mL/kg/min)	ELIMINATION HALF-LIFE (h)
Thiopental	2–4	85	2.5	3.4	11
Methohexital	5–6	85	2.2	11	4
Propofol	2–4	98	2–10	20–30	4–23
Midazolam	7–15	94	1.1–1.7	6.4–11	1.7–2.6
Diazepam	10–15	98	0.7–1.7	0.2–0.5	20–50
Lorazepam	3–10	98	0.8–1.3	0.8–1.8	11–22
Etomidate	2–4	75	2.5–4.5	18–25	2.9–5.3
Ketamine	11–16	12	2.5–3.5	12–17	2–4

(Clinical Anesthesia 6th Edition; Barash, P.; Lippincott Williams and Wilkins; 2011)

Pharmacodynamics

- All hypnotics also affect other major organ systems besides brain:
  - dose-dependent respiratory depression
    - (exception: *Ketamine*)
  - hypotension and cardiac depression
    - (*Etomidate* causes least cardiac depression)
- *Profound hemodynamic effects can be seen with **hypovolemia** since higher drug concentration is achieved within central compartment
  - Large hemodynamic depressant effect can be seen in elderly and those with pre-existing cardiovascular disease
    - These patients often exhibit **decreased dose requirement**

Propofol

- Produced in egg lecithin emulsion (egg yolk--not egg white--which is relevant to patient allergies, which is typically to egg white protein) because of high lipid solubility
  - Formulations support growth of bacteria, good sterile technique and labeling of expiration times (typically 12 hours) is critical
- Pain on injection occurs in 32-67% of subjects; attenuated with IV lidocaine or administering drug in larger vein
- **Induction dose 1.5-2.5 mg/kg**
  - Children require *higher* doses (larger V_d and higher clearance)
  - Elderly require *lower* doses (smaller V_d and decreased clearance)
- Infusion doses ~100-200 mcg/kg/min for hypnosis and ~25-75 mcg/kg/min for sedation (depends on desired level of consciousness and infusion duration)
- **Decreases $CMRO_2$, CBF, and ICP**; CPP may decrease depending on effect on SBP
  - *Counterintuitively a cerebral vasoconstrictor*!
- Anticonvulsant properties
- Decreases SVR (arterial and venous), direct myocardial depressant
- Dose-dependent respiratory depression
- Has anti-emetic properties – often used for TIVA cases and as background infusion for patients with PONV
- *Propofol infusion syndrome (**PRIS**)*: Risk in critically ill patients receiving high dose propofol infusions (>4mg/kg/hr) for prolonged periods of time. Causes severe metabolic acidosis, rhabdomyolysis, cardiac failure, renal failure, and hypertriglyceridemia. High mortality, especially in children. Treatment is supportive.

ITE tip

True or False regarding propofol:

- ➢Propofol can produce bronchodilation in patients with COPD.
- ➢Propofol inhibits pulmonary vasoconstriction.
- ➢Premedication does not affect the speed to apnea after administration of propofol.
- ➢Propofol produces depression of central respiratory drive that is dose-independent.

Answer: T, F, F, T

Etomidate

- High incidence of pain on injection
- Induction dose **0.2-0.3 mg/kg**
- Rapid onset due to high **lipid** solubility and large **non-ionized** fraction at physiologic pH
- Myoclonus, hiccups, thrombophlebitis
- **Decreases $CMRO_2$**, **CBF**, **ICP**; **CPP maintained** because less decrease in SBP
- Anticonvulsant properties; but **minimal effect on duration of ECT-induced** seizure activity
- Maintains **hemodynamic stability** (even in the presence of pre-existing disease)
  - Does not induce histamine release
- Inhibits adrenocortical synthetic function **(11-beta-hydroxylase**)
  - Inhibition for 4-8 hours even after a single induction dose; more prominent with infusions
- Increased incidence of PONV

ITE tip

True or False regarding Etomidate

- ➢ Etomidate is metabolized by hepatic ester hydrolysis to inactive metabolite, which is then renally secreted
- ➢ Reduced dose is required in renal insufficiency
- ➢ Etomidate reduces cerebral perfusion pressure
- ➢ Etomidate is a GABA(B) agonist

Answer: T, F(no need for renal dosing), F(Cerebral blood flow and cerebral metabolic rate are reduced resulting in a decrease in ICP. However, cerebral perfusion pressure is preserved), F(GABA-A agonist)

Thiopental

- Highly alkaline (pH 9)
- Can precipitate in acidic solutions (*DO NOT MIX* with Rocuronium)
- Intra-arterial injection can cause intense vasoconstriction, thrombosis and tissue necrosis; treat with papaverine and lidocaine or regional anesthesia-induced sympathectomy and heparinization
- Induction dose **3-5 mg/kg** in adults**, 5-6 mg/kg** in children, **6-8 mg/kg** in infants
- Rapidly redistributed into peripheral compartments
- Larger doses can saturate peripheral compartments → prolonged duration of action
- **Decreases $CMRO_2$, CBF, ICP**
  - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
- A barbiturate with anticonvulsant properties (typical for this class of meds)
  - Exception: Methohexital (reduces seizure threshold and prolongs seizure duration)
- Decreases SVR, direct myocardial depressant
- Dose-dependent respiratory depression
- Unlikely to use at Stanford (no longer produced in US) but may use internationally

ITE tip

_____is the most likely cause of the reduced induction dose of thiopental in the elderly.

a. Decreased initial volume of distribution
b. Enhanced brain sensitivity
c. Increased protein binding

Answer: A. The induction dose of barbiturates is reduced in the elderly due to a decreased initial Vd, the result of a 10-15% reduction in total body water. Based on multicompartment pharmacokinetic models, this reduction in total body water results in a decreased volume of the central compartment. Thus, initial plasma concentration of barbiturates will be increased following IV administration. Other pharmacokinetic changes in elderly include a decrease in lean body mass and an increase in total body fat. Considering the increase in total body fat and the lipophilic nature of thiopental, and elderly patient will take longer to wake up after a dose of thiopental due to its larger volume of distribution. Of note, there is no effect on brain sensitivity to barbiturates with aging. Medications to which elderly patients will have increased sensitivity include: propofol, midazolam, opioids, and inhaled agents.

Ketamine

- Produces a dissociative anesthetic state
  - Profound analgesia and amnesia despite maintenance of consciousness
  - High incidence of psychomimetic reactions (attenuated by co-administration of midazolam)
- Induction dose **1-2 mg/kg**
- **NMDA antagonist** (implications in prevention/treatment of chronic pain)
- **Increases $CMRO_2$, CBF, ICP**
- Most likely to **preserve airway reflexes** among the IV anesthetics
- Minimal respiratory depression
- Cardio-stimulating effects secondary to **direct sympathetic stimulation**
  - Produces increase in BP, HR and CO
  - Negatively effects myocardial oxygen supply-demand ratio
- Intrinsic myocardial depressant, may be significant in severely ill patients with depleted catecholamine reserves
- Causes **bronchodilation**
- Causes **increased oral secretions** (consider co-admin of glyco)
- Useful for chronic pain patients (common dose for intra-operative management is **0.5-1 mg/kg** prior to incision (after intubation, unless using for induction) and then **0.25 mg/kg each hour** (infusion or bolus)
- Common side effect is **nystagmus**

ITE tip

True or False regarding Ketamine

- ➢ Ketamine is a racemic mixture, and R(-) is more potent than S(+)
- ➢ Ketamine is secreted in the urine with a half-life of 2-3 hrs
- ➢ Ketamine is highly protein bound
- ➢ Norketamine is the metabolite of ketamine and has no clinical effect

Answer: F(S+ is more potent), T, F(highly lipid soluble), F(Norketamine is ⅓ as potent)

Midazolam

- All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant properties (but **not** analgesia!)
- Premedication dose 0.02-0.04 mg/kg IV/IM (typically 1-2 mg)
- Induction dose 0.1-0.2 mg/kg IV
- **Decreases $CMRO_2$** and **CBF**
- Does not produce EEG burst suppression
- **Can cause some SVR and BP depression** when used in large doses, but is generally considered a more hemodynamically stable induction agent
- Causes dose-dependent respiratory depression
  - Exaggerated when combined with opioids and in patients with chronic respiratory disease
- **Flumazenil** = specific antagonist
  - Very short acting
  - 45-90 minutes of action following 1-3 mg dose
    - May see **re-sedation** as benzodiazepine is eliminated more slowly compared to effects of flumazenil

ITE tip

After being given 0.2mg flumazenil, the patient becomes responsive and ready to leave, he should be observed for _____ hrs.

Answer: 2-3hrs. Flumazenil is a short acting **competitive antagonist** of benzos. It has the shortest half-life of all benzos (45mins-1hr) which means that anyone who has received it should be observed for recurrent sedation. Flumazenil has a high portion of free drug when injected with little protein binding. This leads to a very quick onset of action (peak effect in 1-3mins) and allows for quick clearance by the liver. The duration of action from shortest to longest are: flumazenil<midazolam<lorazepam<diazepam.

Dexmedetomidine

- Selective **α_2 adrenergic agonist** (primarily central-acting)
- Hypnotic and analgesic
- Opioid-sparing effect; does **not** significantly depress respiratory drive
- Usual infusion concentration is 4 mcg/ml
- Loading dose **0.5-1 mcg/kg** over **10 min**
- Infusion rate **0.4-1.2 mcg/kg/hr** (ask your attending)
- Rapid onset (<5 min) and terminal half-life of 2 hours
- Decrease dosage for patients with hepatic impairment
- Main side effects are bradycardia, heart block, hypotension
- Can be utilized for sedation during awake FOB intubations
- Useful when managing delirium in pediatric or ICU patients

ITE tip

- ❖ Dexmedetomidine is an a2 agonist with a2:a1 receptor selectivity of _____. In comparison, clonidine's a2:a1 receptor ratio is 220:1.
- ❖ Other key pharmacokinetic parameters include pKa of 7.1, 94% protein binding, and complete _____(hepatic/renal) biotransformation to inactive metabolites via _____, _____, and _____.
- ❖ The elimination half-life is _____hrs and the context-sensitive half-time is _____min after 10min infusion and _____min after an 8hr infusion. This medication has no CYP450 drug interactions.
- ❖ A 62yo male is undergoing a right ganglion cyst excision under local anesthesia with sedation. ABG is taken 30min after starting sedation and the PaCO2 is 38mmHg, unchanged from a preop baseline ABG. RR is 10, down from 12 bpm. _____(dexmedetomidine/midazolam/propofol/remifentanil) is most likely administered.

Answer: 1600:1, hepatic, glucuronidation, hydroxylation, N-methylation, 2-3hrs, 4min, 250min, dexmedetomidine

ITE tip

» IV anesthetics are easily titratable to your desired depth of anesthesia.

– For this reason (and for the boards) it is good to familiarize yourself with the specifics of sedation depth so you can run a smooth, safe, MAC.

	Minimal Sedation Anxiolysis	Moderate Sedation/ Analgesia ("Conscious Sedation")	Deep Sedation/ Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful** response to verbal or tactile stimulation	Purposeful** response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous Ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular Function	Unaffected	Usually maintained	Usually maintained	May be impaired

Summary

Drug	Induction Dose (mg/kg)	Effects	Pearls
Propofol	1.5-2.5	**Neuro:** Decreases cerebral metabolic O2 requirements, cerebral blood flow, intracranial pressure **CV:** Decreases SVR, direct myocardial depressant **Pulm:** Dose-dependent respiratory depression (apnea in 25-35% of patients)	-Pain on injection (32-67%) -can be attenuated with lidocaine and with injection into larger veins -Antiemetic properties -Anticonvulsant properties
Etomidate	0.2-0.3	**Neuro:** Decreases CMRO2, CBF, ICP **CV:** Maintains hemodynamic stability (minimal cardiac depression) **Pulm:** depresses airway reflexes/ventilation less than propofol or barbiturates	-Pain on injection -High incidence of PONV -Myoclonus -Inhibits adrenocortical axis
Thiopental	3-5	**Neuro:** Decreases CMRO2, CBF, ICP **CV:** Decreases SVR, direct myocardial depressant **Pulm:** Dose-dependent respiratory depression	-Anticonvulsant properties -Can precipitate when injected with acidic fluids (i.e LR)
Ketamine	1-2	**Neuro:** Increases CMRO2, CBF, ICP **CV:** Cardio-stimulating effects (negatively effects myocardial supply-demand) **Pulm:** Minimal respiratory depression; bronchodilation; most likely of all to protect airway reflexes	-Analgesic effects -Intrinsic myocardial depressant effects which may unmasked in those with depleted catecholamines

I was in the preop area at the VA, and introduced myself to the patient as Dr. Taylor. He quickly replied, "What was your name?", to which I said my first name, "Victoria". He looked at me amazed and said, "I can't believe it. I have your name tattooed on my a**." I asked if he was willing to show me. As he rolled over, the words "your name" appeared on his left butt cheek.*

** Names have been changed*

It was the 4th week of CA-1 year, and I knew I was going to need 2 PIVs for a relatively bloody case. That morning I prepared the fluid warmer with a blood pump, ready to go once I got the 2nd PIV inside the OR. In pre-op, I placed a PIV on the RIGHT side, then brought him in to the OR, connected the monitors and started giving fentanyl and propofol through the stop cocks on the LEFT blood pump. No change in the patient or vital signs-- my attending and I were puzzled. I came to realize that I was basically feeding meds into the fluid warmer (which had the capacity to absorb the meds without causing significant resistance or dripping onto the floor). Yeah, I remember my attending giving me a smile, shaking his head and saying, "Give me the blood pump and connect it over here." Regardless, the patient was induced and we played it off cool.

References

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Rational IV Opioid Use

Basic Opioid Pharmacology

- Analgesia produced by **mu (μ)** opioid receptor agonism
  - In the **brain** *(periaqueductal gray matter)*
  - In the **spinal cord** *(substantia gelatinosa)*
- Well-known side effect profile:
  - sedation
  - respiratory depression
  - muscle rigidity (especially with synthetic opioids - laryngeal structures, chest wall)
  - bradycardia
  - hypotension
  - itching, nausea, ileus, urinary retention
  - miosis (useful to assess patients under GA)
- Opioids are hemodynamically stable when given alone, but cause ↓**CO, SV and BP** in **combination** with other anesthetics
- Reduces MAC of volatile anesthetics

Opioid Receptor Subtypes and Their Effects

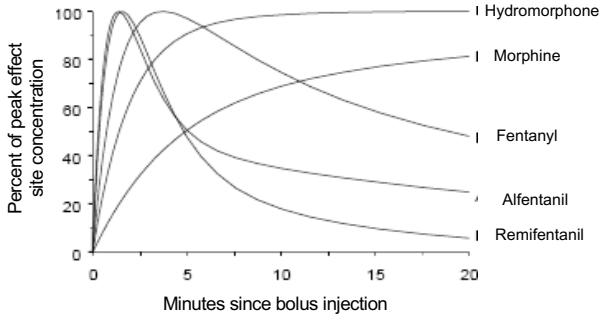
Receptor	Clinical effect	Agonists
μ	Supraspinal (μ1) Respiratory depression (μ2) Physical dependence Muscle rigidity	Morphine Met-enkephalin B-Endorphin Fentanyl
κ	Sedation Spinal analgesia	Morphine Nalbuphine Butorphanol Dynorphin Oxycodone
δ	Analgesia Behavioral Epileptogenic	Leu-enkephalin B-Endorphin
σ	Dysphoria Hallucinations	Pentazocine Nalorphine Ketamine

Opioid comparison

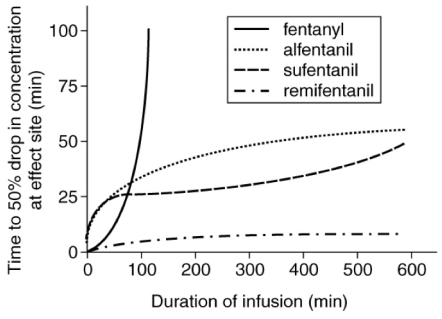
Drug	Approximate analgesic equivalent	Peak onset	Duration of action (single bolus only!)	Used as infusion
Alfentanil	150-250 mcg	1 – 2 min	5 – 10 min	Not common
Fentanyl	50 mcg	3 – 5 min	30 – 60 min	Use with caution*
Hydromorphone	0.75 mg	5 – 15 min	2 – 4 hours	ICU
Meperidine	37.5 mg	5 – 15 min	2 – 4 hours	No
Morphine	5 mg	10 – 20 min	4 – 5 hours	ICU (comfort care)
Methadone	2.5 mg	10 min	24 hours	No
Remifentanil	50 mcg	3 – 5 min	5 – 10 min	OR
Sufentanil	5 mcg	3 – 5 min	20 – 45 min	OR

*Infrequently used given long context-sensitive half-life

Single bolus pharmacokinetics



Infusion pharmacokinetics



Special considerations

Fentanyl

- Easily titratable given rapid onset and short duration of action of single bolus
- Frequently used during induction to blunt sympathetic response to laryngoscopy or LMA placement (*wait 3-5 min after administration for peak effect*)
- Shorter duration of action can be desirable for analgesia on emergence if concerns for airway protection, delirium, PONV, etc.
- However, **very long context-sensitive half-life** limits use as an infusion
  - Cut dose in half about every 2 hours
  - Can also lead to prolonged duration of action with repeated boluses intraoperatively

Special considerations

Hydromorphone

- Often used for post-op pain control due to **longer duration of action**
- Titrate near end of case for smooth wakeup and adequate pain control on emergence
  - Be patient since **peak effect can take 15 minutes**
- If expected surgical stimulation is relatively constant, can also be given early in case to provide stable analgesia
- Metabolite **hydromorphone-3-glucuronide** has no analgesic properties, but may cause neuroexcitation
- No histamine release

Special considerations

Remifentanil

- Most commonly used as infusion when significant intraoperative stimulation but minimal post-operative pain is expected (i.e. analgesic tail is **NOT** needed)
  - Rapid metabolism by **plasma esterases** causes no context-sensitivity of half-life
    - i.e. lasts 5 – 10 min regardless of infusion duration
- Typical infusion dosing
  - Start at **0.05 – 0.1 mcg/kg/min**
  - Titrate as needed (rarely need more than 0.3 mcg/kg/min)
  - Wean near end of surgery to assess if boluses of long-acting opioids are needed

**do not confuse with sufentanil dosing which is mcg/kg/HOUR!!!*

Special considerations

Remifentanil

- Also useful to prevent movement when neuromuscular blockade is contraindicated (i.e. during neuromonitoring)
- Bradycardia is common
  - If giving as bolus, have glycopyrrolate or atropine ready
- Sudden cessation at end of case can lead to acute opioid tolerance
  - Develops within minutes
  - Treatable with more opioid
- Long infusions of higher doses (>0.15 mcg/kg/min) also associated with opioid-induced hyperalgesia
  - Develops within hours/days, can last days-weeks+
  - Less responsive to additional opioid

ITE tip (a short tangent – Esterase metabolism)

» **Remifentanil** is an introduction to **esterase** metabolized medications

- Esterases are a group of enzymes that are found in plasma, NMJ, RBC and hepatic sinusoids
- In general all are non-organ dependent metabolic pathways (except that very severe hepatic disease decreases production of plasma cholinestersases)

- **RBC esterases**
  - Esmolol
  - *Remifentanil in small proportions
- **Plasma esterases**
  - Remifentanil – fixed and context independent metabolism
  - Etomidate (plasma and hepatic)
- **Pseudocholinesterase** *aka plasma cholinesterase or butyrylcholinesterase
  - Succinylcholine – fyi this occurs in the plasma (not at the NMJ)
  - Mivacurium
  - Ester local anesthetics
- **Hofmann elimination**
  - Atracurium/cisatracurium

Special considerations

Sufentanil

- Most commonly used as infusion when both significant intraoperative stimulation and post-operative pain are expected (i.e. **analgesic tail** is desirable)
  - Context-sensitive half-life allows some accumulation (in contrast to remifentanil), but is *much more forgiving than a fentanyl infusion*
- Typical infusion dosing
  - Divide expected case duration into 3rds
    - **0.3 mcg/kg/h → 0.2 → 0.1**
  - Turn off **15 – 30 minutes** prior to end of surgery

**don't confuse with Remifentanil dosing which is mcg/kg/MIN*

Opioids

Alfentanil

- Most commonly used as a bolus to treat brief periods of intense stimulation
  - E.g. immediately prior local injection by surgeon during MAC case
- **Fastest** onset time of all opioids (~90 seconds); **pKa = 6.5**, so it crosses the blood-brain barrier rapidly *despite high protein binding*
- Brief duration of action due to rapid redistribution
- Also causes more N/V, chest wall rigidity, and respiratory depression

Opioids

Morphine

- Slower peak time and long duration of action often less desirable in acute surgical setting
- **Active** metabolite (5-10%), **morphine-6-glucuronide**, has analgesic properties and is *renally excreted* (not clinically relevant unless patient has renal failure, but common boards question)
- Morphine-3-glucuronide (~60% of metabolites) – no analgesic action, but can cause neuroexcitability
- Can cause *histamine* release

Opioids

Methadone

- **Longest** terminal half-life (about 1 day)
- May see peak effect ~10 min after IV bolus dose
- May accumulate during titration to steady state
- Supplied as a racemic mixture
  - **L** methadone is an **opioid agonist**
  - **D** methadone is an **NMDA antagonist**
- Underutilized in anesthesia practice
- As a rule of thumb, many attendings will not give methadone as part of an anesthetic unless the patient will be monitored in the hospital for at least 1 night

Opioids

Meperidine (Demerol)

- Commonly used to treat **shivering** upon emergence
- Originally discovered as a local anesthetic ("pethidine")
- Toxic metabolite (**normeperidine**) lowers the seizure threshold; renally excreted
- Anticholinergic side effects: tachycardia
- Avoid using with **MAOIs**
  - can cause CNS excitation (agitation, hyperpyrexia, rigidity) or CNS depression (hypotension, hypoventilation, coma)
  - **Libby Zion Law: instituted resident physician work hour restrictions after the death of an 18-year-old patient due to serotonin syndrome caused by interaction of a MAOI and meperidine**
- Causes histamine release
- Has a **euphoric effect** with less respiratory depression than other opioids

ITE tip

Opioids with active metabolites

Morphine	Morphine-6-Glucuronide	100x higher affinity for u receptors than morphine, can cause resp depression due to delayed excretion in renal failure, can also cause neuroexcitation/seizures or sedation
	Morphine 3 glucuronide	Inactive but can cause seizures/neuroexcitation
Meperidine	Normeperidine	Reduces seizure threshold, renally excreted
Hydromorphone	Hydromorphone 3- glucuronide	inactive but can result in neuro excitation with accumulation in renal insufficiency
Codeine	Morphine	is an active metabolite of prodrug codeine (via CYP 2D6)
Oxycodone	oxymorphone	active metabolite
** fentanyl and methadone have no active metabolites		

Rational Opioid Use

Note: All anesthesiologists (attendings & residents alike) have different theories and opinions on the optimal choice and dose of opioids in different situations. The strategies presented here are simply suggestions, something to get you thinking rationally about how and when you use opioids for analgesia. Discuss the merits of these strategies with your attending before or during each case, but do not take these suggestions as firm guidelines for how all anesthetics should be done!

With that disclaimer in mind, continue reading…

Strategies for Opioid Use

- For a standard GETA induction, use fentanyl (1-2 mcg/kg) to blunt the stimulation and subsequent hemodynamic effects caused by DL and intubation
  - Fyi: esmolol is a reasonable alternative
- For brief, intense stimulation (e.g. retrobulbar block, Mayfield head pins, rigid bronchoscopy), consider a bolus of short-acting opioid like alfentanil or remifentanil
- For intra-op analgesia:
  - Fentanyl is rapidly titratable but requires frequent redosing; it may be more "forgiving" if overdosed. Repeated boluses will lead to long duration of action due to long context-sensitive half-life
  - Morphine has a long time to peak effect (90 min!), but gives prolonged analgesia during the case and into the post-op period
  - Hydromorphone is titratable (like fentanyl) with prolonged analgesia (like morphine)

Strategies for Opioid Use

- For ENT cases, consider an opioid infusion (e.g. remifentanil or sufentanil):
  - Stable level of analgesia
  - Induced hypotension
  - "Narcotic wakeup" reduces bucking on ETT
  - Smooth transition to post-op analgesia
- For chronic opioid users (e.g. methadone, MS Contin, OxyContin, etc.), continue the patient's chronic opioid dose intraoperatively PLUS expect higher opioid requirements for their acute pain
  - Preop suboxone use and dosing is debated
  - Adjuncts may be helpful (tylenol, lidocaine, ketamine, gabapentin, etc)
- Use morphine and meperidine cautiously in renal patients (renal excretion of active metabolites)!

Strategies for Opioid Use

- Meperidine is usually reserved for treatment/prevention of postoperative shivering
  - Common in younger patients
- For post-op pain control (i.e. PACU):
  - Consider fentanyl (rapid onset, easily titratable, cheap, and the nurses are familiar with its use)
  - Consider hydromorphone (rapid onset, easily titratable, prolonged effect, nurses are familiar with its use, and it is a good transition to PCA)
  - If surgery is ambulatory and/or patient is tolerating POs, give PO (i.e. oxycodone or hydrocodone)

Alternative analgesic strategies

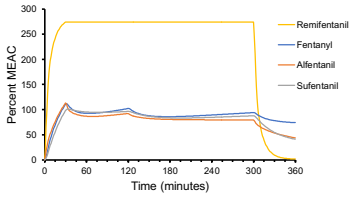
- Recommend **preop multimodal analgesics:**
  - Acetaminophen 1000mg PO (unless liver dz)
  - Gabapentin 600mg PO (reduce dose for impaired renal fxn)
  - One of:
    - Tramadol 100mg PO (unless codeine doesn't work for the patient, i.e. poor 2D6 metabolizer)
    - Oxycodone 10mg PO
- **Intraop opioid boluses** (comparable to fentanyl 150 µg for induction, then fentanyl* 50 µg Q 60 min)

	Induction	Hourly
Alfentanil (µg)	500	250*
Meperidine (mg)	100	25
Methadone (mg)	5	2.5

*for fentanyl and alfentanil: first dose at 30 min

Intraop opioid infusions

	Fentanyl (mcg/kg/h)	Alfentanil (mcg/kg/h)	Sufentanil (mcg/kg/h)	Remifentanil (mcg/kg/min)
Start rate	2.5	8	0.2	0.1
At 30 min	1	3	0.1	
At 120 min	0.5	2	0.075	



MEAC = minimum effective analgesic concentration

ITE tip: mixed opioid agonists and antagonists

- » Mu opioid **agonist** and kappa receptor **antagonist**
  - » Buprenorphine
- » Mu **agonist** and nmda **antagonist**
  - » Methadone
- » Partial mu **antagonist** and kappa opioid receptor **agonist**
  - » Nalbuphine
- » Mu opioid **agonist** and Ach receptor **antagonist**
  - » Meperidine
- » Mixed mu opioid receptor **agonism** and **antagonism** plus kappa receptor agonism
  - » Butorphanol
- » Mu, kappa, and delta agonists
  - » Most typical opioids: eg morphine

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Intraoperative Hypotension & Hypertension

Determinants of Blood Pressure

Blood Pressure (BP)
- BP represents the force exerted by circulating blood on the walls of blood vessels
- Determined by cardiac output and SVR:
  - **(MAP - CVP) = CO x SVR**

Cardiac Output (CO) = HR x SV
- CO / BSA = Cardiac Index (normal range **2.6–4.2 L/min/m²**)
- Dependent on the interplay between the sympathetic and parasympathetic nervous systems
- Infants: SV is relatively fixed; CO is depends mainly on HR
- Adults: SV plays a much more important role, particularly when increasing HR is not favorable (e.g. CAD, HOCM, aortic stenosis)

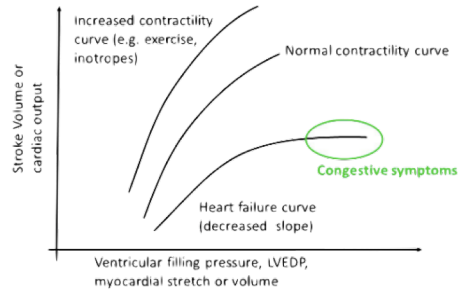
Determinants of Blood Pressure

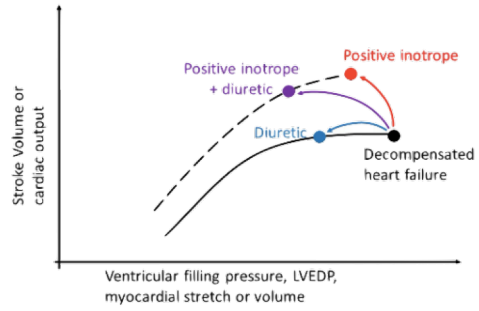
Stroke Volume (SV):
Dependent on 1) preload 2) afterload and 3) myocardial contractility

Preload
- Volume of blood in the ventricle at end-diastole (LVEDV)

Afterload
- Resistance to ejection of blood from the ventricle
- SVR accounts for 95% of the impedance to ejection
- **SVR** (Wood units) **= [MAP-CVP]/CO** (normal range 9-20)
  - Conversion to non-Wood units: **SVR** (Wood units) x 80 = dyn·s/cm^5 (normal range 900-1200)

Contractility
- The force and velocity of ventricular contraction when preload and afterload are held *constant*.
- Ejection fraction (EF) is one of the most clinically useful indices of contractility (normal left ventricle EF is ~60%).





Components of Blood Pressure

- **Systolic, Diastolic, and Mean Arterial Pressures**
- **Pulse Pressure**
  - **PP = SBP - DBP**
  - Normal PP is ~40 mm Hg at rest, and up to ~100 mm Hg with strenuous exercise.
  - **Narrow PP** (e.g. < 25 mm Hg) = may represent aortic stenosis, coarctation of the aorta, tension pneumothorax, myocardial failure, shock, or damping of the system.
  - **Wide PP** (e.g. > 40 mm Hg) = aortic regurgitation, atherosclerotic vessels, PDA, high output state (e.g. thyrotoxicosis, AVM, pregnancy, anxiety)

Blood Pressure Measurement

Non-Invasive Blood Pressure (NIBP)

- Oscillometric BP determination: oscillations in pressure are detected through the cuff as it deflates.
- MAP is measured as the largest oscillation; it is the *most accurate* number produced by NIBP.
- SBP and DBP are calculated by proprietary algorithms in the machine.
- Inaccurate in conditions with variable pulse pressure (e.g. **atrial fibrillation**) and noncompliant arteries (severe PVD)
- Readings may be affected by external pressure on cuff (e.g. surgeon leaning on arm, moving arm for positioning).

Invasive Arterial Blood Pressure (IABP)

- Most accurate method of measuring BP.
- If system is zeroed, leveled, and properly dampened, SBP, DBP, and MAP are very accurate.

Intraoperative Hypertension: DDx

- "Light" anesthesia
- "Pain" (i.e. sympathetic activation from surgical stimuli)
- Chronic hypertension
- Illicit drug use (e.g. cocaine, amphetamines)
- Hypermetabolic state (e.g. MH, thyrotoxicosis, NMS)
- Elevated ICP (Cushing's triad: HTN, bradycardia, irregular respirations)
- Autonomic hyperreflexia (spinal cord lesion higher than T5 = severe; lower than T10 = mild)
- Endocrine disorders (e.g. pheochromocytoma, hyperaldosteronism)
- Hypervolemia
- Drug contamination - intentional (e.g. local anesthetic + Epi) or unintentional
- Hypercarbia

Treatment of Hypertension

- **Temporize** with fast-onset, short-acting drugs
- Diagnose and treat the **underlying cause**.

- Pharmacologic Interventions:
  - Deepen anesthesia:
    - Propofol or volatile anesthetics
    - Opioids (increase analgesia, histamine release causes hypotension)
  - Short-acting vasodilators
    - **Clevidipine**
      - Calcium-channel blocker.
      - In a lipid emulsion (looks like propofol)
    - **Nitroglycerin** (venous > arterial dilatation)
    - **Nitroprusside** (arterial > venous); very expensive; risk for cyanide toxicity
      - Avoid both NTG and NTP in setting of intracerebral hemorrhage (cerebral vasodilator)
  - Beta-blockers
    - **Labetalol** (α:β ratio – 1:4 when given PO, 1:7 when given IV)
    - **Esmolol**, affects HR >> BP
  - Long-acting vasodilators
    - **Hydralazine** – Less predictable pharmacokinetics & pharmacodynamics

Antihypertensive comparison

Drug	Initial bolus dose	Onset	Time to peak	Duration of action	Infusion rate range
Clevidipine	50 – 100 mcg	1 min	2 – 4 min	5 – 15 min	0.5 – 32 mg/**hr**
Nitroglycerin	10 – 50 mcg	1 min	1 – 3 min	3 – 5 min	0.1 – 1 mcg/kg/min
Nitroprusside	10 – 50 mcg	<1 min	1 min	1 – 10 min	0.1 – 1 mcg/kg/min
Labetalol	5 – 10 mg	2 – 5 min	10 – 15 min	45 min – 6 hours	N/A
Esmolol	10 – 20 mg	1 min	2 min	10 min	50 – 300 mcg/kg/min
Hydralazine	5 mg	5 – 20 min	15 – 30 min	2 – 6 hours	N/A

Intraoperative Hypotension: DDx

- **Measurement error**: confirm cuff size and position, for invasive BP confirm transducer level, waveform, & correlate with non-invasive BP readings
- **Hypovolemia**: Blood loss, dehydration, diuresis, sepsis
  - Ensure: Adequate IV access, fluid replacement, cross match if necessary
- **Drugs**: Induction and volatile agents, opioids, anticholinesterases, local anesthetic toxicity, vancomycin, protamine, vasopressor/vasodilator infusion problem, syringe swap or drugs given by surgeon
- **Regional/Neuraxial Anesthesia**: Vasodilation, bradycardia, respiratory failure, local anesthetic toxicity, high spinal
  - Ensure: Volume loading, vasopressors, airway support, left uterine displacement during pregnancy
- **Surgical Events**: Vagal reflexes, obstructed venous return, pneumoperitoneum, retractors and positioning
  - Communicate with surgeon and ensure surgical team is aware
- **Cardiopulmonary Problems**: Tension PTX, hemothorax, tamponade, embolism (gas, amniotic fluid, or thrombotic), sepsis, myocardial depression (from drugs, ischemia, electrolytes, trauma)

Treatment of Hypotension

- **Temporize** with fast-onset, short-acting drugs, but ultimately diagnose and treat the **underlying cause**.
  - Turn down (sometimes turn off) the anesthetic—give versed if indicated
  - Call for help & inform surgical team
- **Drugs**
  - Vasoconstrictors: phenylephrine, vasopressin, norepinephrine
  - Postive Inotropes: ephedrine, epinephrine
  - HR control: glycopyrrolate, atropine, pacing?
- **Volume**
  - Reevaluate EBL; replace with crystalloid, colloid, or blood, as needed
  - Consider arterial line
  - Other monitoring options: CVP, PAC, or TEE
- **Ventilation**
  - Reduce PEEP to decrease intrathoracic pressure --> improve venous return
  - Decrease I:E ratio to shorten inspiratory time and improve venous return
  - Rule out PTX
- **Metabolic**
  - Treat acidosis and/or hypocalcemia
    - **Important:** Most vasoactive drugs will not work effectively if patient is acidotic or hypocalcemic; surviving sepsis guidelines recommend considering bicarbonate use if pH < 7.15

Pressor/Inotrope comparison

Drug	Initial bolus dose	Onset	Time to peak	Duration of action	Infusion rate range
Phenylephrine	50 – 100 mcg	<1 min	1 min	10 – 15 min	0.2 – 2 mcg/kg/min
Vasopressin	0.5 – 1 unit	<1 min	1 min	30 – 60 min	0.01 – 0.04 units/min
Norepinephrine	5 – 10 mcg	<1 min	1 min	1 – 2 min	0.02 – 0.3 mcg/kg/min
Ephedrine	5 – 10 mg	1 – 2 min	2 – 5 min	60 min	N/A
Epinephrine	5 – 10 mcg	<1 min	2 min	<5 min	0.02 – 0.3 mcg/kg/min

ITE tip:

Vasopressor receptors

Vasopressor / Inotrope	Receptor: alpha-1	beta-1	beta-2	Dopamine Receptor	Physiologic Effects
Norepinephrine	+ + +	+ +	0	0	↑↑ SVR +/- CO
Dobutamine	+/-	+ + +	+ +	0	↑ CO ↓ SVR
Epinephrine	+ + +	+ + +	+ +	0	↑↑ CO ↓ SVR (low dose) ↑ SVR (high dose)
Dopamine (mcg/kg/min)					
1 to 3	0	+	0	+ +	CO
5 to 10	+	+ +	0	+ +	↑ CO ↑ SVR
> 10	+ +	+ +	0	+ +	↑↑ SVR
Phenylephrine	+ + +	0	0	0	↑↑ SVR +/- CO

CO: Cardiac Output **SVR:** Systemic Vascular Resistence
+++ Strong effect ++ Moderate Effect + Weak Effect 0 No effect

ITE tip

A 56-year-old patient with a history of liver disease and osteomyelitis is anesthetized for tibial debridement. After induction and intubation, the wound is inspected and debrided with a total blood loss of 300 mL. The patient is transported intubated to the recovery room, at which time the systolic blood pressure falls to 50 mm Hg. HR is 120 bpm, ABG reads 7.3/45/103, with SpO2 97% on 100% FiO2. VBG reads 7.25/50/60. Which of the following diagnoses is MOST consistent with this clinical picture?

a. Hypovolemia
b. CHF
c. Cardiac tamponade
d. Sepsis with ARDS

Answer: d. The patient has an abnormally high mixed venous PO2 (50, versus a normal value of 40). This is consistent with a high cardiac output state, such as sepsis.

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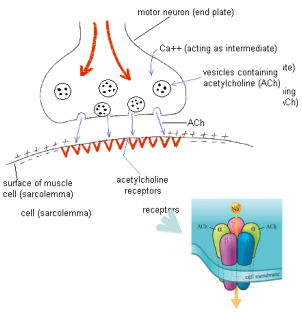
Neuromuscular Blocking Agents (NMBAs)

Introduction

- NMBAs facilitate intubation, mechanical ventilation, and surgical relaxation
- There are two categories of NMBAs with distinct properties:
  - **Depolarizing** (succinylcholine)
  - **Non-depolarizing** (eg. rocuronium, vecuronium, cisatracurium)
- Postoperative residual paralysis occurs frequently. Monitoring of neuromuscular blockade and pharmacological reversal are standard of care.
- NMBAs should be used carefully; there are also many surgical and patient-specific contraindications. Neuromuscular blocking agents play a prominent role in the incidence of **adverse reactions** that occur during anesthesia.
  - The Committee on Safety of Medicines in the United Kingdom reported that 10.8% (218 of 2014) of adverse drug reactions and 7.3% of deaths (21 of 286) were attributable to neuromuscular blocking drugs.
- **Nondepolarizing** agents account for >50% cases of intraoperative **anaphylaxis** (incidence <0.1%).
  - Cross-reactivity has been reported between neuromuscular blocking drugs and food, cosmetics, disinfectants, and industrial materials (anaphylaxis can happen on a patient's first exposure to the drug).

Neuromuscular Transmission



- Action potential depolarizes motor neuron→ Ca++ influx→ vesicles fuse and release Ach
- ACh diffuses across synaptic cleft → binds **α-subunit** of the **nicotinic** receptors
- When ACh binds both α subunits, receptor ion channel opens
  - Na+ and Ca++ influx
  - K+ efflux

Depolarizing NMBA: Succinylcholine

- **Structure**: two ACh molecules joined by methyl group
- **Mechanism of action**: nAChR agonist, prolonged muscle depolarization
- **Intubating Dose**: 1-1.5 mg/kg
  - 1.5-2 if using a defasciculating dose of rocuronium
- **Onset**: 30-60 sec
- **Duration:** ~10 min, depending on dose
- Diffuses away → rapidly metabolized by pseudocholinesterase (aka plasma cholinesterase, butyrylcholinesterase)
- **Pseudocholinesterase deficiency**
  - In reality, *abnormal* (nonfxn'l) pseudocholinesterase
  - Heterozygous: incidence ~1/480; paralysis extended 50-100%
  - Homozygous: ~1/3200; paralysis extended 4-8 hrs
  - Consider checking twitches after sux before nondepolarizers
- **Dibucaine number: % of *normal* pseudocholinesterase inhibited** by dibucaine (does not inhibit abnormal pseudocholinesterase)
  - Normal 80; Heterozygous 50; Homozygous 20

Contraindications to Succinylcholine

- Hyperkalemia → cardiac arrest
  - Induction dose *typically* ↑ K^+ 0.5 mEq/L
  - Normokalemic ESRD is NOT contraindication
- Upregulated junctional & extrajunctional AChR → hyperK
  - Burn injury >24 hrs, muscular dystrophy, myotonias, prolonged immobility, upper motor neuron dz (spinal cord injury, stroke, tumor, MS, GBS)
- Hx malignant hyperthermia
- Open globe (anterior chamber): transient increase IOP

Additional Side Effects

- Fasciculations. (can be decreased with **defasciculating dose of rocuronium** = 0.03 mg/kg, 3 minutes prior to sux)
- Myalgia: ***Less frequent*** in children, ages 50-60yo, those with good muscular training. ***More frequent*** in women and ambulatory patients
- Bradycardia (especially in children -- often given with atropine)
- Tachycardia
- Anaphylaxis (approx. 1:5000 – 1:10,000)
- Trismus
- Increased ICP & IOP
- Increased intragastric pressure and lower esophageal sphincter pressure

Nondepolarizing NMBA

- **Mechanism of action**: competitive inhibition of nAChR
  - NMBAs also block presynaptic nAChR, which help mobilize ACh-containing vesicles. Blockade results in the "fade" seen on train-of-four
  - May interact with nicotinic and muscarinic cholinergic receptors within the sympathetic and parasympathetic nervous systems when given at large doses = "autonomic margin of safety"
    - Rocuronium: ED_{50} >3-5 mg/kg to block vagal, >10 to block sympathetic
- Two structural classes:
  1. **Benzylisoquinolinium** = "-urium"
     - Cisatracurium, Doxacurium, Atracurium, Mivacurium, d-Tubocurarine
     - More likely to cause histamine release (d-Tubocurarine >> Atracurium and Mivacurium); can attenuate with slower administration
  2. **Aminosteroid** = "-onium"
     - Pancuronium, Vecuronium, Rocuronium, Pipecuronium
     - Vagolytic effects (Pancuronium > Rocuronium > Vecuronium)
- Most used nondepolarizing agents are of **intermediate duration**: rocuronium, cisatracurium, vecuronium

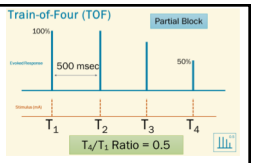
Nondepolarizing NMBA (cont.)

- Intubating doses **~2x ED_{95}**
  - ED_{95} = average dose to achieve 95% suppression of twitch height in 50% of population
- Larger intubating dose speeds onset time, lengthens duration
- **Priming dose:** increase speed of onset
  - 10% of intubating dose 3-5 minutes prior (efficacy debatable)
- Wide inter-individual response to nondepolarizing agents
  - Monitor twitches and adjust doses accordingly
- **Rocuronium can be used for RSI (1-1.2 mg/kg)** when sux cannot, though roc is still slower and has much longer duration

Agent	ED95 (mg/kg)	Intubating Dose (mg/kg)	Onset (min)	Duration to 25% recovery (min)	Intra-op Mainenance	Metabolism / Excretion
Succinylcholine	0.3	1	1-1.5 min	6-8 min	Rarely done	plasma cholin-esterase
Rocuronium	0.3	0.6	1.5-2	30-40	0.1 -0.2 mg/kg prn	>70% Liver
		RSI 1.2	1	>60		Bile + Urine
Vecuronium	0.05	0.1 -0.2	3-4	35-45	0.01 -0.02 mg/kg prn	50% Liver / Bile + Urine*
Cisatracurium	0.05	0.15-0.2	5-7	35-45	0.3 mg/kg q20min prn	Hoffman elimination

*Vecuronium's 3-OH metabolite (80% potency) accumulates in renal failure. Rocuronium however does not have any active metabolites
**Recovery of neuromuscular function takes place as plasma concentrations decline, and the greater part of this decrease initially occurs primarily because of distribution after initial drug administration. After a large or repeated dose, recovery relies more on elimination
**Rocuronium has lower molar potency (requires a larger mg/kg dose) and in effect has faster onset (i.e. it equilibrates faster from plasma to the neuromuscular junction)

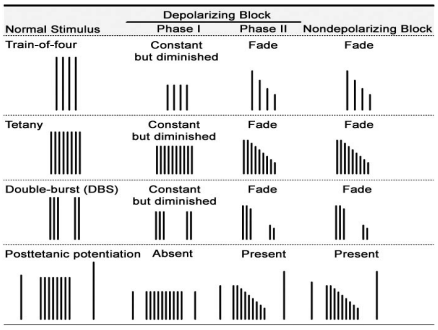
NMBA Monitoring



- **Train-of-four (TOF)**
  - Most common modality
  - TOF count = # of twitches (out of 4)
  - TOF ratio = height of 4th compared to 1st
- Intraop, often monitored subjectively (visual or tactile)
  - Can't distinguish TOF ratio >0.4
  - Much less accurate than mechanomyography or accelerometry
- Full recovery
  - **TOF ratio 0.9** (e.g. with accelerometer)
  - **5 seconds sustained tetany** at 50-100 Hz without fade

% ACh Receptors Blocked	T1 %	TOF Count	T4/T1
70-75	100	4	0.75-0.9
	95	4	0.7-0.75
	80-90	4	0.6-0.7
75-80	25	3	0
80-85	20	2	0
85-90	10	1	0
90-98	0	0	0

Phase I and Phase II blocks



An aside about sux:

Phase I block
- typical for single dose

Phase II block
- total dose >5 mg/kg
- repeated doses >60 min

N.B. Neostigmine will potentiate a phase I block but will reverse a phase II block if there is a low enough concentration of sux left.

Phase I and Phase II blocks

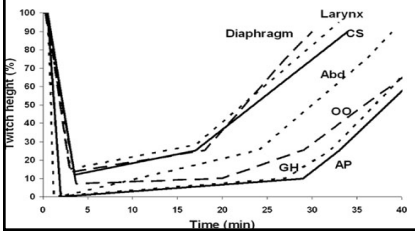
- **Phase I** – depolarization block
  - Often preceded by muscle fasciculation, and is result of pre-junctional action of succinylcholine stimulating receptors on the motor nerve and causing repetitive firing at neuron
  - Channels remain inactive until sux diffuses away to the plasma and is metabolized by plasma cholinesterase
- **Phase II** – desensitization block
  - Repeated or prolonged agonism of the Ach receptor causes it to no longer open and close to stimulation
  - Caused by repeated or high doses of sux
  - Continuous stimulation of the receptor leads to ongoing shifts of K and Na so the blockade effect is prolonged
  - Features of this block are similar to a non-depolarizing blockade, meaning there is fade on TOF, block is antagonized by anticholinesterases (unpredictable though)
  - Seen clinically at >4 mg/kg, but some features present at >0.3mg/kg

ITE tip

	Succinylcholine Phase I Block	Succinylcholine Phase II Block	Rocuronium
Administration of rocuronium	Antagonize	Augment	Augment
Administration of succinylcholine	Augment	Augment	Antagonize
Administration of neostigmine	Augment	Antagonize*	Antagonize
TOF ratio	> 0.7	< 0.3	< 0.3
Response to tetanus	Sustained	Unsustained	Unsustained
Post-tetanic fade	No	Yes	Yes

Variability in NMBA Monitoring

- Variability in muscle blockade (<u>most resistant → most sensitive</u>): vocal cords > diaphragm > corrugator supercilii > abdominal muscles > adductor pollicis > pharyngeal muscles
- To assess deep blockade (i.e. ablate diaphragmatic movement intraop): monitor **<u>corrugator supercilii</u>**
- To assess return of function of pharyngeal muscles (i.e. readiness for extubation): monitor **<u>adductor pollicis</u>**
- Caution: differentiate between nerve stimulation and direct muscle stimulation



Recovery after rocuronium (0.6 mg/kg)

- **CS** = corrugator supercilii
- **Abd** = Abdomen
- **OO** = orbicularis oculi
- **GH** = geniohyoid
- **AP** = adductor pollicis

Nondepolarizing NMBA Reversal

- Use acetylcholinesterase inhibitors as"reversal agents": less acetylcholinesterase working → **more Ach in NMJ** → overcomes the competitive inhibition by rocuronium & allows muscle firing
  - Acetylcholinesterase inhibitor-based reversal should <u>not</u> be given until spontaneous recovery has started (the patient should have 2 twitches before reversal)
    Anticholinesterases can theoretically ***paradoxically slow recovery if given too early***
- Acetylcholinesterase inhibitors can cause muscarinic <u>vagal side effects</u> (eg. bradycardia, GI stimulation, bronchospasm) due to increasing ACh activity at parasympathetic **muscarinic** receptors. **Always administer with anticholinergics to prevent bradycardia**
- Neostigmine with glycopyrrolate is most commonly used in the OR
  - 40-50 mcg/kg of neostigmine is appropriate for most instances
  - There is a **ceiling effect**. <u>*Do not give >70mcg/kg of neostigmine*</u>
  - If recovery is seems complete (4 equal twitches), 15-20mcg/kg of neostigmine is **probably sufficient (attendings will have differing opinions)**
  - **Dose of glycopyrrolate is 1/5 of the neostigmine dose** (eg. 3mg neostigmine with 0.6mg glyco). Adjust glycopyrrolate dose as needed for baseline bradycardia/tachycardia

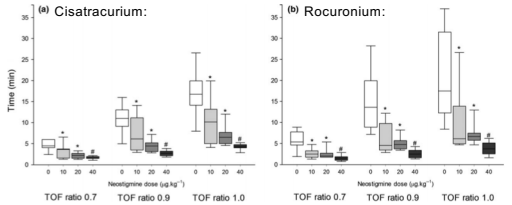


Figure 2 Times to reach the stated train-of-four (TOF) ratio of 0.7, 0.9 and 1.0 after receiving 0, 10, 20 or 40 μg.kg^{-1} of neostigmine at a TOF ratio of 0.5 after the use of cisatracurium (a) or rocuronium (b). Horizontal line = median; box = IQR; whiskers = 5th–95th percentile. *$p < 0.05$ vs saline, #$p < 0.05$ vs saline, 10 and 20 μg.kg^{-1} of neostigmine.

**Note that with a TOF 0.5, full reversal with 40 mcg/kg of neostigmine can take up to 5 minutes

Nondepolarizing NMBA Reversal

- Anticholinesterase inhibitors:
  - **Neostigmine, Pyridostigmine, Edrophonium**: do NOT cross BBB
  - **Physostigmine**: crosses BBB, can treat central anticholinergic syndrome/atropine toxicity
- Pair acetylcholinesterase inhibitor and anticholinergic based on speed of onset to appropriately block muscarinic effect:
  - Edrophonium (rapid) w/ Atropine
  - **<u>Neostigmine</u>** (intermediate) w/ **<u>Glycopyrrolate</u>**
  - Pyridostigmine (slow) w/ Glycopyrrolate
- Does reversal increase the risk of PONV? A metanalysis says no (Cheng CR, 2005).

ITE tip: Nondepolarizing NMBA Metabolism

- Has an active metabolite almost as potent as its parent drug, accumulates in renal failure and causes prolonged blockade
- This drug undergoes no clinically significant metabolism and is cleared primarily by the liver via bile excretion
- This drug is metabolized through Hofmann elimination and non-specific ester hydrolysis
- This drug has metabolite laudanosine that can cause neuroexcitation and seizures
- This drug causes sympathomimetic response by blocking Ach receptors

- Vecuronium
- Rocuronium
- Atracurium and cisatracurium
- Atracurium
- Pancuronium

Nondepolarizing NMBA Reversal: Sugammadex

- γ-cyclodextrin, directly traps NMBA to reverse its action
  - Designed specifically for rocuronium
  - Also works for vecuronium (though 2.5x stronger affinity for roc)
- Possible indications
  - "Cannot intubate, cannot ventilate": after rocuronium 1.2mg/kg, sugammadex 16mg/kg decreases time to full recovery, 122 min → <2 min
  - Blockade too deep or inadequately reversed by neostigmine
  - During pregnancy (unlike neostigmine, sugammadex does not cross the placenta)
  - Increasing popularity as routine reversal agent given less side effects, faster onset, ?cheaper cost (institution-dependent) than neostigmine + glycopyrrolate
  - Emerging evidence that reversal with sugammadex may reduce the risk of post-op pulmonary complications (STRONGER trial)

Sugammadex (cont.)

Recommended Dosages

Indication	**Dose** (Total body weight)
Cannot intubate, cannot ventilate	16 mg/kg
Deep reversal (1 twitch OR, if recovery has reached at least post tetanic count of 2)	4 mg/kg
Standard reversal (1-2 twitches in TOF)	2 mg/kg

After inadequate neostigmine reversal sugammadex dose depends on TOF (same as indicated in the above table).

- *Caution:*
  - Patients using **hormonal contraceptives** must use an additional, non-hormonal method of contraception for the next 7 days
  - Not recommended in patients with **severe renal insufficiency or dialysis** (theoretical risk of complex dissociating), though complex can be hemodialyzed using high-flow filter
  - **PTT and PT** will be prolonged by ~ 25% for up to 60 minutes (no change in coags clinically)
  - Precipitates if given with ondansetron, verapamil, or ranitidine
  - Anaphylaxis reported as 0.3% (seen in 1 healthy volunteer with study N=375)
    - During post-marketing use, reports of anaphylaxis occurred in ~0.01% cases

Clinical Pearls

- Conditions with nAChR upregulation (**SENSITIVE** to succinylcholine; **RESISITANT** to NMBA):
  - Spinal cord injury, stroke, burns, prolonged immobility, prolonged exposure to NMBA, multiple sclerosis, Guillain-Barré syndrome
- Conditions with nAChR downrgulation (**RESISTANT** to succinylcholine; **SENSITIVE** to NMBA):
  - Myasthenia gravis, Lambert-Eaton syndrome, anticholesterase poisoning, organophosphate poisoning
- Factors **ENHANCING** block by NMBA:
  - Volatile anesthetics, aminoglycosides, tetracycline, clindamycin, Mg (watch on OB), IV local anesthetics, CCBs, Lasix, Dantrolene, Lithium, anticonvulsants, sux, acidosis, hypokalemia, hypothermia, ketamine
- Common surgeries to **avoid** NMBA
  - Axillary node dissection, ENT cases near nerves (eg NIMS tube to monitor recurrent laryngeal nerve), neuromonitoring

Disorder	Acetylcholine Receptors	Depolarizing Muscle Relaxant	Non-depolarizing Muscle Relaxant (NDMR)	Comments
Stroke	Up-regulation	Do not use after 24 hours		Succinylcholine may cause hyperkalemia months after the stroke
Burns	Up-regulation	Do not use after 24-48 hours		Recovery of neuromuscular function to pre-burn level may take months to years
Prolonged Immobility	Up-regulation	Be cautious; no guidelines on minimal time patient has to be immobile before having hyperkalemic response		Risk of reaction increases significantly after 16 days
Multiple Sclerosis	Up-regulation	Careful: especially if flaccidity, spasticity or hyperreflexia	May show resistance or sensitivity	If using NDMR give small doses and monitor neuromuscular function: twitch monitor may not be accurate depending on site (orbicularis occuli underestimates muscle paralysis)
Amyotrophic lateral sclerosis (ALS)	Up-regulation	High risk for hyperkalemia	Sensitive	
Guillain-Barre	Up-regulation	Contraindicated	Sensitive	Risk of hyperkalemia may persist after symptomatic recovery

Disorder	Acetylcholine Receptors	Depolarizing Muscle Relaxant	Non-depolarizing Muscle Relaxant (NDMR)	Comments
Muscular Dystrophies (MD): Duchenne/ Becker	Up-regulation	Contraindicated	May be normal or sensitive due to muscle wasting and decreased contractile force	FDA warning against the use of succinylcholine in pediatric patients due to potential undiagnosed MD and hyperkalemic arrest
Myasthenia Gravis	Down-regulation	Resistant	Sensitive	Pyridostigmine will diminish the sensitivity to non-depolarizers, possibly prolong the response to succinylcholine and reversal may be ineffective (due to acetylcholinesterase inhibition from the pyridostigmine)
Lambert-Eaton syndrome	Disorder of prejunctional calcium auto-antibodies	Sensitive	Sensitive	Neostigmine is ineffective for reversal of NDMR
Anticholinesterase poisoning	Down-regulation	Prolonged response		Succinylcholine should be avoided as it is degraded by plasma cholinesterase - may result in prolonged paralysis: neostigmine should be avoided since it will worsen the primary problem
Organophosphate poisoning	Down-regulation			

Intra-op Discussion Topics

- How do you induce a patient with full stomach and open globe?
- Can you use sux with increased ICP?
- What degree of immobility can cause hyperkalemia with sux?
- Can you use rocuronium for a renal transplant?
- Does reversal cause PONV?
- You just gave reversal and there is a lap in the abdomen. How do you paralyze the patient?
- Why is repeated sux doses associated with bradycardia?
- Does a defasciculating dose of roc correspond to decreased myalgia in the setting of using sux?
- When do you use neostigmine vs. sugammadex to reverse NDMB?
- How do you decide what dose of reversal to administer?

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For a while, one of the surgery residents referred to me as Superman. Not because of anything good, but because I woke his patient up and he emerged a little goofy. He insisted on keeping his arms stretched perfectly straight out in front him, and despite many attempts to get him to relax, he wouldn't put them down. We sat the head of the bed up, thinking that might help, but it just made it more obvious to everyone we drove past on the way to the PACU, with this old guy holding his Superman pose.

Difficult Airway Algorithm

According to the ASA, "a difficult airway is defined as the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with **facemask ventilation** of the upper airway, difficulty with **tracheal intubation**, or both. The difficult airway represents a complex interaction between patient factors, the clinical setting, and the skills of the practitioner."

*Remember: patients do not die from an inability to intubate the trachea… *they die from a lack of oxygen*. If the pulse ox is dropping, fall back to whatever strategy allows you to **oxygenate your patient.**

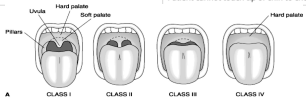
Difficult Airway Algorithm

Practical considerations/questions:

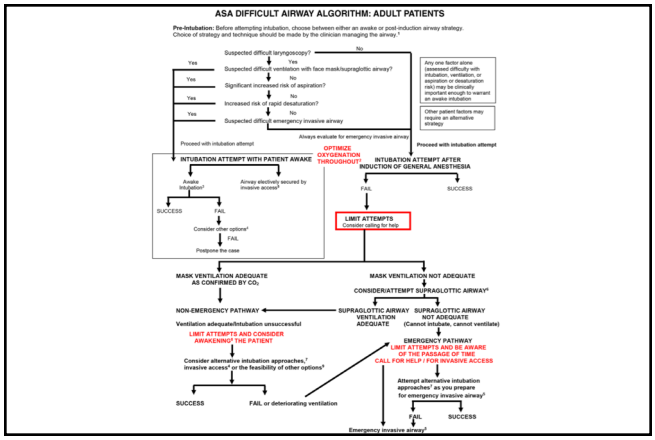
- Awake or Asleep?
- Spontaneous vs Positive pressure ventilation?
- Consider VL as initial approach to intubation
- Pursue attempts at oxygen delivery throughout
- Call for help after *INITIAL* unsuccessful intubation
- Place LMA immediately after unsuccessful intubation AND mask ventilation
- Do not postpone a life-saving surgical airway

Preoperative Airway Examination

Airway examination component	Nonreassuring findings
Length of upper incisors	Relatively long
Relationship of maxillary and mandibular incisors during normal jaw closure	Prominent "overbite" (maxillary incisors anterior to mandibular incisors)
Relationship of maxillary and mandibular incisors during voluntary protrusion of mandible*	Patient cannot bring mandibular incisors anterior to (in front of) maxillary incisors
Interincisor distance	Less than 3 cm
Visibility of uvula	Not visible when tongue is protruded with patient in sitting position (eg, Mallampati class >2)
Shape of palate	Highly arched or very narrow
Compliance of mandibular space	Stiff, indurated, occupied by mass, or non-resilient
Thyromental distance	Less than three ordinary finger-breadths
Length of neck	Short
Thickness of neck	Thick
Range of motion of head and neck	Patient cannot touch tip of chin to chest or cannot extend neck

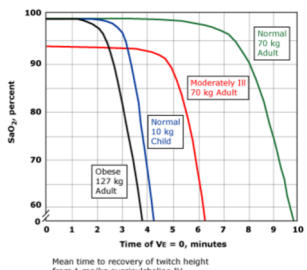


*Consider a preoperative endoscopic airway examination in all cases of a potentially difficult airway



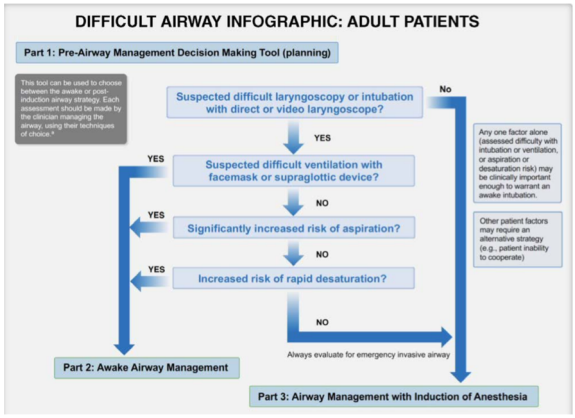
Attempt Oxygenation Throughout

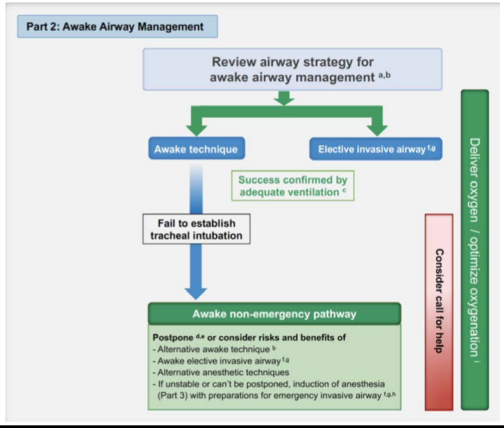
Time to oxygen desaturation

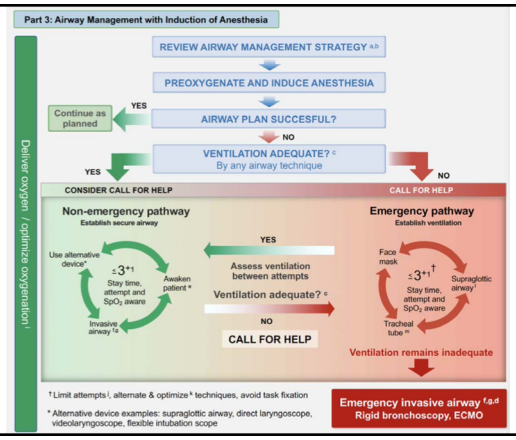


Mean time to recovery of twitch height from 1 mg/kg succinylcholine IV

- Mask ventilate in the sniffing position
- Place an oral airway or nasal trumpet
- Place an SGA
- Nasal cannula
  - Including high-flow (e.g. Optiflow, "THRIVE") apneic oxygenation
- When using a fiberoptic bronchoscope:
  - Use an endoscopic mask (e.g. Patil-Syracuse) to allow PPV with a face mask while using the bronchoscope
  - Use a swivel adapter to allow oxygenation via the ETT (if in place) while performing fiberoptic bronchoscopes
- Use the rigid bronchoscope's side port for oxygen delivery
- Jet ventilation

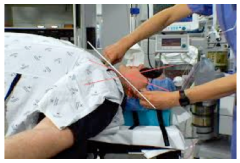






BE PREPARED!

- Oxygenation is paramount
- Difficult mask ventilation is more dangerous than difficult intubation
- **So long as you can mask, you can oxygenate the patient through almost any anesthetic**
- Preparation is key! Set yourself up for success.
  - Do a thorough airway exam
  - Ensure the airway equipment you need is readily available and tested.
  - Take the time to correctly position your patient. Poor positioning can turn a Cormack-Lehane grade 1 view into a grade 4 view.
    Proper positioning is worth your effort, even at the start of an emergent case.



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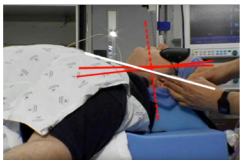


Proper: Align tragus to sternum, parallel to floor

Difficult Mask Ventilation

If at least 3 of the following predictors of **difficult or impossible face mask ventilation** are present, be wary…

DIFFICULT Mask Ventilation	IMPOSSIBLE Mask Ventilation
"MaMaBOATS"	**"MaMaBORa"**
• **Ma**llampati III or IV	- **Ma**llampati III-IV
• **Ma**ndibular protrusion decreased	- **Ma**les
• **B**eard	- **B**eard
• **O**besity (BMI >30 kg/m^2)	- **O**SA or Upper Airway Surgery
• **A**ge >57-58	- **Ra**diation changes (neck)
• **T**eeth (lack of)	
• **S**noring	

And of course… history of prior difficulty

Difficult Intubation

Successful direct laryngoscopy requires aligning the oral, pharyngeal, and laryngeal axes (see image). There are known predictors of **difficult laryngoscopy and intubation:**

- Mallampati III-IV
- Short, thick neck (>40 cm)*
- Interincisor distance <4 cm (i.e. small mouth opening)
- Thyromental distance <6 cm
- Sternomental distance <12cm*
- Prominent "overbite"
- Inadequate mandibular protrusion (Upper Lip Bite Test Class III)
- Limited cervical range of motion (<30 degrees from neutral)
- Highly arched or very narrow palate
- Poor submandibular compliance (stiff, indurated, occupied by a mass)*
- Underlying pathology (e.g. laryngeal stenosis, epiglottitis, tumor)

*Also predicts difficults video laryngoscopy

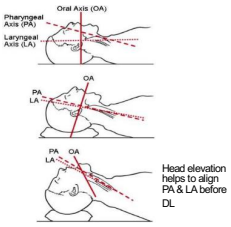
ITE TIP: highest PPV comes from a history of difficulty with intubation, or short TM distance, or decreased ROM

And of course… history of prior difficulty

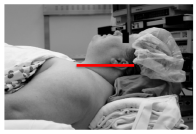
Optimize Positioning

Obtaining the Sniffing Position

- Requires flexion at C7 with extension at C5-C6
- Ramp obese patients until the line between the tragus and the sternal notch is parallel to the floor
- And then verify you are still in the sniffing position. If not, elevate the head



Head elevation helps to align PA & LA before DL



Ramp obese patients until tragus is aligned with sternum

Other Difficulties

Difficulty with Patient Cooperation

- Age
- Mental capacity
- Level of consciousness
- Intoxication

Difficult Surgical Airway Access

- Obesity
- Facial hair
- Prior ENT surgery
- Prior radiation to neck
- Goiter

Difficult Supraglottic Airway

"MR. ODDORR"

- **M**ale gender
- **R**estricted mouth opening
- **O**besity
- **D**entition (poor)
- **O**bstruction at or below larynx
- **R**educed neck ROM
- **R**adiation (to the neck)
- **D**istorted anatomy (tonsillar hypertrophy, glottic/hypopharyngeal/subglottic pathology)

Awake Options

Awake Intubation – key is topicalization

- Non-invasive options:
  - Conventional fiberoptic intubation
  - Also consider laryngoscopy (direct, video)
  - Topicalize airway with local anesthetic or perform select nerve blocks
  - A fully-awake patient can tolerate a Glidescope if the airway is properly topicalized!
- Invasive options:
  - Tracheostomy
  - Cricothyroidotomy
  - Retrograde intubation

Asleep

Post-Induction Intubation

- If your initial attempt is unsuccessful…
  - Call for help!
  - Attempt to mask ventilate
    - If you can mask, head down the non-emergency pathway
    - If you cannot mask, place an SGA
      If successful, head down the non-emergency pathway
  - If you cannot mask or place an SGA, head down the **Emergency Pathway**

Asleep: Non-Emergent

Post-Induction Intubation – Non-emergency Pathway

- Ventilation is adequate, so you may wake the patient up, or try alternatives
- Alternative approaches:
  - SGA (as bridge to ETT or destination throughout case)
  - Video laryngoscopy
  - Fiberoptic intubation
  - Light wand
  - Blind nasal intubation
- Limit direct laryngoscopy attempts.
  - Don't repeat same DL attempt – change blade, positioning, provider
- Be *very* careful to avoid causing airway trauma
  - Oropharynx and larynx are delicate
  - Bleeding and swelling can turn a maskable airway into a "Cannot Intubate, Cannot Oxygenate" emergency

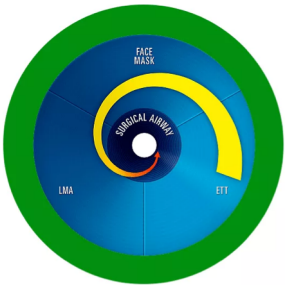
Asleep: Emergent

Post-Induction – EMERGENCY PATHWAY (CAN'T VENTILATE, CAN'T OXYGENATE)

- If at any time, ventilation becomes inadequate, you enter the Emergency Pathway:
  - You should already have called for help. If not, do so now.
- Perform emergency noninvasive airway ventilation
  - Different SGA (intubating LMA?)
  - Combitube
  - Apneic oxygenation (e.g. Optiflow)
  - Rigid bronchoscopy
- Perform emergency invasive airway access *before* SpO2 drops
  - Cricothyrotomy
  - Surgical tracheostomy
  - Trans-tracheal jet ventilation

The Vortex Approach

- Multidisciplinary approach to the difficult airway
- No more than 3 attempts for each technique (facemask, LMA, ETT)
  - At least one by most experienced clinician
- Then proceed to surgical airway
- **Do something differently each attempt** to optimize (airways, positioning, devices)
- **If you're even thinking about a cric kit, call for one early**!
  - Better to have it and not need it, than need it and not have it.



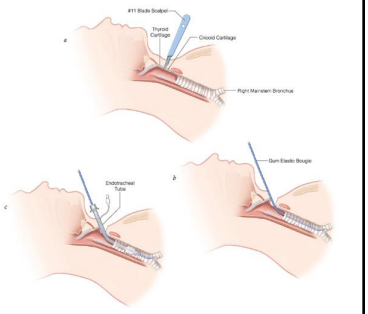
https://emcrit.org/emcrit/vortex-approach/

Surgical Airways

- From an ENT Chief Resident:
  - Even in an emergency, *always* invest 20 seconds to:
    - Identify someone to **assist**
    - Place a **shoulder roll** to expose the trachea
    - Direct a **light source** at the neck
- Cannula-based (aka percutaneous) techniques have a far higher failure rate than **surgical techniques**, which are successful >90% of the time
- Know how and where to get the tools you need
- Cricothyroidotomy can be performed in under 60 seconds:
  - Scalpel, #10 or #11 blade
  - +/- Trousseau dilator or Kelly clamp
  - Bougie introducer
  - 6.0 cuffed ETT
- You will get to practice the procedure on an animal model during your training!

Scalpel-Bougie Surgical Airway Technique

- Identify the cricothyroid membrane
- Make a vertical midline incision
- Palpate the cricothyroid membrane, make a horizontal stab incision and extend to the edge of the cricothyroid membrane
- Turn scalpel 180 degrees and extend incision to the opposite edge
- Use your finger to palpate the incision you just created, and pass the bougie through
- Railroad an endotracheal tube over the bougie, advancing until the balloon is in the trachea but being careful not to advance too deeply
- Confirm placement with end tidal CO2



https://deckerjo.wordpress.com/2016/07/25/use-a-bougie-when-performing-a-cricothyroidotomy/

Clinical Pearls

- Call for help early!
- Anticipate difficulties
- Be prepared in both equipment and mindset
- Always pre-oxygenate to buy yourself safe apneic time
- First DL attempt is the best attempt
- If two DL attempts fail, move on to a different approach
- Remember the pharmacokinetics of your induction and paralytic meds

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Fluid Management

Evaluation of Intravascular Volume

HPI

- *Hypovolemia*: vomiting, diarrhea, fever, sepsis, trauma
- *Hypervolemia*: weight gain, edema, acute renal failure, ascites

Physical Exam

- *Hypovolemia*: skin turgor, capillary refill, dry mucous membranes, tachycardia, orthostasis, decreased UOP
- *Hypervolemia*: pitting edema, rales, wheezing, elevated JVP

Labs/Studies

- *Hypovolemia*: rising Hct, contraction alkalosis then metabolic acidosis, Ur specific gravity > 1.010, hypernatremia, BUN:Cr > 10:1; bedside ultrasound (IVC <1.7cm OR 1.7cm with >50% IVCCI)
- *Hypervolemia*: increased pulmonary vascular markings on CXR, B-lines on Lung US

Intraoperative Intravascular Assessment

Monitor trends and compare multiple modalities to confirm clinical impressions

Vitals

- HR and BP trends, though consider the impact of positive pressure ventilation and anesthetics when interpreting these parameters
- Pulse Oximetry: waveform changes from baseline (assuming patient normothermic and not in shock)
  - Pulse pleth variability index (PVI): >12-16% volume responsive

Foley Catheter

- UOP: consider that ADH levels may be increased due to stress response (less reliable measure of volume status intraop)

Arterial Line

- Serial ABGs (pH, Hct, electrolytes)
- **Pulse Pressure Variation (PPV):** indicator of preload responsiveness; in essence it's a 'small fluid challenge' with each respiratory cycle from pooled blood in lungs going to left ventricle.
  - PPV = $\frac{\text{Pulse Pressure (Max) - Pulse pressure (Min)}}{\text{Pulse Pressure (Mean)}}$
  - PPV >10% suggests patient is volume responsive
  - Not reliable if not sinus rhythm, open chest, not on PPV, or if TV > 8cc/kg

Intraoperative Intravascular Assessment

Monitor trends and compare multiple modalities to confirm clinical impressions

Central Venous Catheter

- Absolute CVP unreliable measure of volume status, though trend can be meaningful (still debated)

Pulmonary Artery Catheter

- Most commonly used in RV dysfunction, pulmonary HTN, valvular pathology (AS, MR), LV dysfunction
- Consider risks/benefits of PAC placement

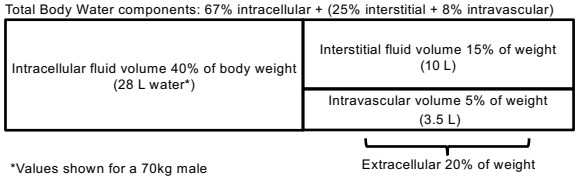
Transesophageal Echocardiogram

- Most commonly used in major cardiac surgeries and liver transplants
- Transgastric view gives most accurate assessment of volume status
- Valuable in narrowing differential of hemodynamic instability

Body Fluid Compartments

Males: Total Body Water = weight x 60%
Females: Total Body Water = weight x 50%

Total Body Water components: 67% intracellular + (25% interstitial + 8% intravascular)



*Values shown for a 70kg male

Remember the **5 – 15 – 40 Rule:**
5% weight is intravascular water, 15% is interstitial, 40% is intracellular
All other calculations can be extrapolated from this

Physiologic Regulation of Extracellular Fluid Volume

Aldosterone

- Enhances sodium reabsorption
- Increases intravascular volume

Antidiuretic Hormone/Vasopressin

- Enhances water reabsorption

Atrial Natriuretic Peptide

- Enhances sodium and water excretion

Crystalloids

	Osm (mOsm/L)	Na^+ (mEq/L)	Cl^- (mEq/L)	K^+ (mEq/L)	Ca^{2+} (mEq/L)	Buffer (mEq/L)	Glucose (g/L)
NS	308	154	154	0	0	0	0
LR	273	130	109	4	3	28 (lactate)	0
Normosol	294	140	98	5	0	27 (acetate)	0
D5W	253	0	0	0	0	0	50

	Advantages	Disadvantages
NS	• Preferred in brain injury/swelling (hyperosmolar) • Preferred for diluting pRBCs	• In large volumes produces **hyperchloremic metabolic acidosis** • Hyperchloremia → low GFR and risk AKI
LR	• More physiologic ("balanced crystalloid") • Lactate is converted to HCO_3^- by liver	• Watch K+ in renal patients • Ca^{2+} may interfere with citrate's chelating properties of pRBCs (debated if this is clinically relevant)

Colloids

Use

- Initial intravascular volume resuscitation with crystalloid administration inadequate or when you expect to give over 3-4L of crystalloid for fluid resuscitation
  - ½ life is 3-6 hrs vs 20-30 minutes for crystalloids
- Patients with large protein losses and decreased oncotic pressure (ie cirrhotic patients and burn patients)
- Fluid resuscitation in hemorrhagic shock when blood is not initially available - give 1cc colloid for every cc of blood lost
- Concern that continued crystalloid may cause volume overload in certain clinical situations (e.g. pulmonary edema, bowel edema)

Mechanism

- *When capillary membrane is intact*, fluids containing colloid, such as albumin, preferentially expand plasma volume rather than ICF volume from increased oncotic pressure

Colloids

Albumin (5% and 25%)

- Derived from pooled donated blood after cold ethanol extraction and ultra-filtration; heat-treated (60 degree C x 10 hrs)
- Use 5% for hypovolemia; 25% for hypovolemia in patients with restricted fluid and Na intake
- Minimal risk for viral infection (hepatitis or HIV); theoretical risk of prion transmission
- Expensive, occasional shortages

Hetastarch (6% hydroxyethyl starch, HES)

***Rarely used; may encounter on OB rotation at LPCH**

- Solution of highly branched glucose chains (average MW 450 kD)
- Degraded by amylase, eliminated by kidney
- Maximum Dose: 15-20 ml/kg/day
- Side effects:
  - Can increase PTT (via factor VIII/vWF inhibition) and clotting times
  - Anaphylactoid reactions with wheezing and urticaria may occur
  - May interfere with platelet function
- Contraindications: coagulopathy, heart failure, renal failure
- Newer starch formulations called tetrastarches are less likely to cause coagulopathy and anaphylaxis and can be given in larger doses. Maximum dose: 50ml/kg/day

Crystalloid or Colloid?

	Advantages	Disadvantages
Crystalloid	• Lower cost • Readily available	• Requires more volume for the same hemodynamic effect • Short IV $t_{1/2}$ (20-30 min) • Dilutes plasma proteins → peripheral/pulmonary edema
Colloid	• Restores IV volume and HD with less volume, less time • Longer IV $t_{1/2}$ • Maintains plasma oncotic pressure • Less cerebral edema (in healthy brain tissue) • Less intestinal edema	• Expensive • Coagulopathy (dextran > HES) • Potential renal complications • May cause cerebral edema (in areas of injured brain where BBB not intact)

"Classical" Fluid Management

Maintenance

- "4-2-1 Rule" = 4 ml/kg/hr for the 1st 10 kg, 2 ml/kg/hr for the next 10-20 kg, and 1 ml/kg/hr for each additional kg above 20 kg
  - To simplify this rule if patient is >20kg, **maintenance = 40 + weight**

Preexisting Fluid Deficits

- Multiply maintenance requirement by # of hours NPO.
- Give 1/2 over 1st hour, 1/4 over 2nd hour, and 1/4 over 3rd hour
- Patients no longer undergo bowel preparation, so deficit decreased

Ongoing Losses

Evaporative and Interstitial Losses (capillary leak)

- Minimal tissue trauma (e.g. hernia repair) = **0-2 ml/kg/hr**
- Moderate tissue trauma (e.g. cholecystectomy) = **2-4 ml/kg/hr**
- Severe tissue trauma (e.g. bowel resection) = **4-8 ml/kg/hr**

Blood Loss

- EBL = (suction canister - irrigation) + "laps" (**100-150** ml each) + 4x4 sponges (**10 ml** each) + field estimate (very approximate estimation)
- Replace with pRBCs, colloid, or crystalloid

Urine Output: Be aware of losses from increased urine output (diuretics, etc.)

Caveat: This is a general guide to help consider sources of volume loss and replacement, by no means the rule and not data driven as limited data exist

Suggestions for Fluid Management

Tailor management to patient, surgery, and clinical scenario

Use a balanced approach

- Typically start with normosol, NS or LR
- Consider switch from NS to LR, except in neuro cases (because of decreased osmolality)
  - Be wary of using too much NS in hyperkalemic patients as the hyperchloremic metabolic acidosis can increase serum potassium as well
- Type and Cross for pBRC and other blood products prior to surgery if anticipating significant blood loss (ie. trauma, coagulopathy)
  - Consider that rapid volume resuscitation with only RBC may still create dilutional coagulopathy
    - If receiving > 2 units RBC, consider FFP use

*1L of IVF at room temperature will decrease core body temp by 0.25 degrees Celsius

Liberal vs. Restrictive Management

Consequences of Volume Overload

- Increased mortality and length of ICU/hospital stay
- Increased myocardial morbidity
- Increased pulmonary, periorbital, and gut edema
- Decreased hematocrit and albumin
- Worsened wound healing/ increased anastomosis dehiscense due to edema

Suggestions for Rational Fluid Management

- Use good clinical judgment
- Tailor management to patient, surgery, and clinical picture
- Use balanced fluid therapy: use crystalloid for maintenance, consider use of colloid as discussed
- Consider conservative replacement of interstitial losses or UOP unless vital signs unstable or other signs of inadequate perfusion

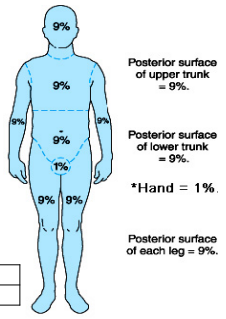
Burns

- Increased evaporative losses
- H_2O, electrolytes, and protein shift from normal to burned tissue causing intravascular hypovolemia
- Volume to infuse is calculated by the Parkland Formula:

Volume = **%BSA x 4 ml/kg x kg**

- Give 1/2 over the 1st 8 hours
- Give 1/2 over the next 16 hours
- Replace with **Lactated Ringers**
- %BSA is determined by the "Rule of Nines"

First 8 hours	Next 16 hrs
2cc/kg x (weight) x (%BSA)	2cc/kg x (weight) x (%BSA)



ITE Tip: burn injuries cause upregulation of extrajunctional acetylcholine receptors, so avoid using succinylcholine >24h after a burn injury due to risk of hyperkalemia

Intraoperative Oliguria

Pre-renal (decreased renal perfusion)

- Hypovolemia
- Decreased CO (LV dysfunction, valvular disease)
- Decreased MAP
- Perfusion is compromised with increased intra-abdominal pressure (e.g. laparoscopy & pneumoperitoneum)

Post-renal (post-renal obstruction)

- Foley kinked, clogged, displaced, or disconnected
- Surgical manipulation of kidneys, ureters, bladder, or urethra

Renal

- Neuroendocrine response to surgery (i.e. activation of renin-angiotensin-aldosterone system with increased ADH), is age dependent
- Baroreceptor response to PPV also activates neuroendocrine response

Treatments

1. Relieve obstruction: check Foley; consider IV dyes (e.g. indigo carmine, methylene blue) to check for patency of ureters (i.e. Urology cases)
2. Increase renal perfusion: fluids (bolus vs increased maintenance rate), vasopressors/inotropes, or furosemide

*In general UOP is a poor marker of renal/organ perfusion

IVF Components

	Osmolarity (mOsm/L)	Na (mEq/L)	Cl (mEq/L)	K (mEq/L)	Ca (mEq/L)	Mg (mEq/L)	Glucose (g/L)	HCO3 (mEq/L)	Lactate (mEq/L)	Acetate (mEq/L)	Gluconate (mEq/L)	pH
Plasma	285	140	100	4	4.4	2	-	24	1	-	-	7
D5W	253			-	-	-	50	-	-	-	-	4.5
D5 1/4 NS	355	38.5	38.5	-	-	-	50	-	-	-	-	
D5 1/2 NS	420	77	77	-	-	-	50	-	-	-	-	4
D5NS	586	154	154	-	-	-	50	-	-	-	-	
NS	308	154	154	-	-	-	-	-	-	-	-	6
1/2 NS	154	77	77	-	-	-	-	-	-	-	-	6
1/4 NS	77	38.5	38.5	-	-	-	-	-	-	-	-	
3% HTS	1026	513	513	-	-	-	-	-	-	-	-	5
LR	273	130	109	4	3	-	-	-	28	-	-	6.5
D5LR	525	120	109	4	-	-	50	-	28	-	-	5
Plasmalyte	294	140	98	5	-	3	-	-	-	27	23	7.4
HES 6%	308	154	154	-	-	-	-	-	-	-	-	5.9
7.5% NaHCO3	1786	893	-	-	-	-	-	893	-	-	-	8
Albumin 5%	330	145	-	<2	-	-	-	-	-	-	-	7.4

ITE tip

Fluid resuscitation during major abdominal surgery with which of the following agents is associated with the BEST survival data?

a. 5% albumin
b. 6% Hydroxyethyl starch
c. Dextran 70
d. None of the above

Answer: d. There is controversy not only as to which intravenous fluid is the best but also how much to give. Most would suggest that isotonic crystalloids should be the initial resuscitative fluids to any trauma patients, and they are certainly less expensive than 5% albumin, 6% hydroxyethyl starch and dextran 70. Clear advantages of one fluid over another are hard to find.

Catheter Basics

Poiseuille's Law:

$$Q = \frac{\pi \Pr^4}{8\eta l}$$

French = catheter outer diameter / 0.33 in mm
- roughly approximates the circumference in mm
- French x 0.33 = OD in mm

Gauge: refers needle outer diameter but not directly correlated in mm
16G ~ 1.65mm ~ 5Fr

- 14G: 250-300ml/min, 1L=4min, 2.1mm OD, Orange
- 16G: 180-200ml/min, 1L=5.5min, 1.65mm OD, Grey
- 18G: 75-120ml/in, 1L=11min, 1.27mm OD, Green
- 20G: 40-80ml/min, 1L=17min, 0.9mm OD, Pink
- 22G: 36-55ml/min, 1L=28min, 0.71mm OD, Blue
- 24G: 20-35ml/min, 1L=50min, 0.56mm OD, Yellow

- MAC: 14Fr (4.7mm) OD x 11.5cm
  - 9Fr Lumen (Distal)
  - 12G Lumen (Proximal)
- PSI Kit "Cordis Introducer": 9Fr x 10cm
- Triple Lumen CVC: 7Fr (2.4mm) OD x 16 or 20cm
  - Distal 16G
  - Medial 18G
  - Proximal 18G

*refer to the iGuide for information on placement of these catheters

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Transfusion Therapy

Type and Screen

Type and Screen (takes 30-120 min, lasts 72 hr)

- Type: test ABO-Rh antigens on RBC
  - Recipient RBCs tested with anti-A&B and anti-D (Rh) antibodies
- Screen: indirect Coomb's test to assess for antibodies in recipient's serum
  - Recipient serum mixed with RBCs of known antigens
    - no agglutination = negative screen
  - If antibody screen is positive: the serum is tested further
- Antigens not represented in screen cells are unlikely to cause clinically significant hemolytic reactions
  - can be safely transfused with negative Type-specific blood if negative screen
    - If only a type and screen is used, the risk of transfusion reaction is approximately 0.2%

Type and Crossmatch

Type and Crossmatch (if T&S negative, takes 30-60 min)

- Immediate phase (5min)
  - checks against ABO typing errors & incompatibilities caused by naturally occurring antibodies to the MN, P, and Lewis systems
- Incubation phase (45min)
  - Immediate phase reaction products incubated to detect incomplete abs to the Rh system that do not cause agglutination in the first phase
- Indirect Antiglobulin test
  - Antiglobulin serum added to products of first two tests to look for incomplete recipient antibodies to Rh, Kell, Duffy, and Kidd
- Use when it is very likely you will transfuse (this actually reserves blood products)

*At Stanford, an electronic crossmatch is used instead of a physical crossmatch if ABO compatible and Ab negative

Packed Red Blood Cells

Definition, Use, & Storage

- Single donor; volume 250-300 ml with Hct ~60-70%
- 1 unit pRBCs: **increases adult Hgb ~1 g/dl or Hct ~3%**
  - 10 ml/kg pRBC increases Hct 10%
- Always run in with bag of NS or normosol on blood pump
- Solutions not compatible with pRBC:
  - LR (theoretical clot formation due to calcium)
  - D5W, hypotonic solutions (RBC hemolysis)
- Stored at 4˚C in CPD (lasts 21 days), CPDA (lasts 35 days), or Adsol (lasts 42 days)
  - Run through a warmer (Slow rates: Ranger; Fast rates: Belmont or Level 1)
- CPDA:
  - Citrate (anticoagulant): metabolized by liver to bicarb; at high transfusion rates, excess citrate binds to calcium (resulting in hypocalcemia)
  - Phosphate (buffer)
  - Dextrose (energy source)
  - Adenine (precursor to ATP synthesis)

Packed Red Blood Cells

Indications:

1. Hg < 7 in *young, healthy patients*
2. Usually unnecessary when Hg >10
3. At Hgb 6-10 g/dl, the decision to transfuse is based on:
   - Ongoing indications of organ ischemia
   - Potential for ongoing blood loss
   - Volume status
   - Risk factors for complications of inadequate O_2
     - *Example: myocardial ischemia*

Fresh Frozen Plasma

Definition, Use, & Storage

- *contains all clotting factors, fibrinogen, plasma proteins (particularly albumin), electrolytes, physiologic anticoagulants (protein C, protein S, antithrombin), and added anticoagulants (citrate)*
- 10-20ml/kg will raise factors by 20-30% (2.5-4.5 units for 70kg patient)
- Use ABO-compatible; Rh-incompatible is OK
  - AB blood type is the universal donor
- Stored frozen up to 1yr; takes 30min to thaw; use within 24hrs of thawing

Indications (ASA Guidelines)

1. Correction of excessive microvascular bleeding with INR > 2
2. During massive transfusion (before lab results available)
3. Urgent reversal of warfarin (or can use Prothrombin Complex Concentrate)
4. Correction of known factor deficiency, when specific factor concentrates are unavailable
5. Heparin resistance (i.e. antithrombin III deficiency) in patients requiring heparinization

Starting INR	FFP Units Needed To Reach INR 1.5
2.5	4
2.0	3
1.8	2

*FFP has an INR of 1.6-1.8, hence think about whether it really makes sense to "correct" your particular pts. INR before giving…

Platelets

Definition, Use, & Storage

- Platelet Concentrate (PC)
  - Platelets from one donated unit, vol = 50-70 ml; ↑ plt ~5,000-10,000
  - "6-pack" = 6 pooled PCs from different donors (rarely used anymore)
- Apheresis Unit
  - Platelets from a single donor; vol = 200-400 ml; **↑ plt ~30-50,000**
  - Document as 250ml (no exact number written on unit)
- Can give ABO-incompatible platelets, Rh tested only
  - However, contain a small amount of RBCs so Rh sensitization can occur for some
- Stored at room temperature for ≤5 days.
- Hang separately (on blood pump with NS) – Do not run through fluid warmer, Level 1, or Belmont (heating can injure the platelets but studies have challenged this theory)

Indications (ASA Guidelines)

1. Rarely when plt > 100K
2. Usually when plt < 50K and undergoing surgery/procedure (spontaneous bleed at < 10K)
3. When plt 50K, based on risk of bleeding; often <100K if concern for CNS bleeding
4. With platelet dysfunction (e.g. CPB, plt inhibitors, renal dysfunction)

Cryoprecipitate

Definition, Use, & Storage

- Fraction of plasma that precipitates when FFP is thawed
- Contains Factors I (fibrinogen), VIII, XIII and vWF
  - 1 unit contains ~5X more fibrinogen than 1 unit FFP
- Contains 200-250mg of Fibrinogen/unit: 10 units = 2g
  - 10units will raise a 70kg patient's fibrinogen by 70mg/dL (60-100)
- 0.1u/kg raises fibrinogen by 100mg/dL
- Once thawed must be stored at room temp and given w/in 6hrs
  - can be stored -18-20 degrees celsius for 1yr
- Not screened for ABO incompatibility d/t limited Ab concentration

Indications (ASA Guidelines)

1. Rarely when fibrinogen >150 mg/dl
2. When fibrinogen **<100 mg/dl** with microvascular bleeding
3. During massive transfusion when fibrinogen level not available
4. Bleeding patients with von Willebrand Disease
5. Congenital fibrinogen deficiency

Prothrombin Complex Concentrate

Unactivated prothrombin complex concentrates (PCCs)	
4 factor: ▪ Kcentra	Contains inactive forms of 4 factors: Factors II, VII, IX, and X Also contains heparin
3 factor: ▪ Profilnine	Contains inactive forms of 3 factors: Factors II, IX, and X Contains little or no factor VII Does not contain heparin
Activated prothrombin complex concentrate (aPCC)	
4 factor: ▪ FEIBA	Contains 4 factors: Factors II, VII, IX, and X. Of these, only factor VII is mostly the activated form Does not contain heparin

Anticoagulant	Reversal agent (all are given intravenously)
Dabigatran (Pradaxa; oral thrombin inhibitor)	▪ Idarucizumab (Praxbind). Dose: 5 grams*
Oral factor Xa inhibitors: ▪ Apixaban (Eliquis) ▪ Edoxaban (Lixiana, Savaysa) ▪ Rivaroxaban (Xarelto)	▪ Andexanet alfa (AndexXa). Dosing for the initial bolus and subsequent infusion depend on the dose level of the factor Xa inhibitor and the interval since it was last taken. **-OR-** ▪ 4-factor PCC (Kcentra, Beriplex P/N, Octaplex). Dosing can be done with a fixed dose of 2000 units **OR** a weight-based dose of 25 to 50 units per kg.

ITE Tip

The administration of FFP in patients on warfarin is MOST appropriate in which of the following scenarios?
a. Elective cataract surgery with INR of 3.0
b. Urgent ruptured appendectomy with INR of 1.8
c. Emergent ex lap with INR of 1.3
d. Femur fracture ORIF that needs to proceed within 48hrs with INR 2.5

Answer is B.
•Warfarin Reversal, Urgent Surgery:
INR 1.5-1.9: treat with FFP
INR 1.9-5: FFP + 1-3 mg of IV vitamin K
INR 5-9: FFP + 2-5 mg IV vitamin K
•Warfarin Reversal, Surgery 24-48 Hours Later:
INR 1.5-1.9: 1 mg PO vitamin K
INR 1.9-5: 1 - 2.5 mg PO vitamin K, if INR still elevated 24 hours after dose give 1 - 2 mg PO vitamin K
INR 5-9: 2.5 - 5 mg PO vitamin K, if INR still elevated 24 hours after dose give 1 - 2 mg PO vitamin K
•For non-surgical patients, the use of FFP for warfarin reversal is based on bleeding. FFP is not used in non-surgical patients to reverse warfarin if there is no bleeding, even for an INR > 9. Further, FFP is used only to supplement after vitamin K administration in non-surgical patients with bleeding and a supratherapeutic INR.

ITE Tip

Which of the following is NOT an indication for cryoprecipitate administration?
a. Factor VII deficiency
b. Factor XIII deficiency
c. Factor VIII deficiency
d. Surgical bleeding in patients with vWD

Answer is A, cryoprecipitate does not contain factor VII.

Equations

Arterial O_2 Content

$C_aO_2 = O_2\text{-Hb} + \text{Dissolved } O_2$
$= (Hb \times 1.36 \times S_aO_2/100) + (P_aO_2 \times 0.003)$
$= (15 \times 1.36 \times 100\%) + (100 \times 0.003)$
≈ 20 cc O_2/dl (normal)

Allowable Blood Loss

$$ABL = \frac{[\text{Hct (start)} - \text{Hct (allowed)}] \times \text{EBV}}{\text{Hct (start)}}$$

Volume to Transfuse

$$\text{Volume} = \frac{[\text{Hct (desired)} - \text{Hct (current)}] \times \text{EBV}}{\text{Hct (transfused blood)}}$$

Estimated Blood Volume (ml/kg)	
Preemie	100
Term	90
< 1 year	80
1-6 years	75
Male	70
Female	65
Obese	≤60

Ordering Products

- Consider special needs of the patient:
  - Irradiated: BMT (GVHD), cellular immunodeficiency, donated by first or second degree relative (not needed for solid organ transplant)
  - Leukoreduced: chronically transfused pts, CMV seronegative pts and at-risk (HIV, transplant), post-transplant pts, **previous febrile non-hemolytic rxn**, immunosuppressed, reducing FNHTR, HLA-alloimmunization
    - **(Standard at Stanford)**
  - Washed: IgA deficiency, complement dependent autoimmune hemolytic anemia, continued allergic rxn despite pretreatment with antihistamines
    - only 1 in 100 patients with IgA deficiency and anti-IgA antibodies develop anaphylaxis
- If you anticipate the patient may require a transfusion, ask them if they will accept blood products during your pre-op discussion
- For intraoperative questions or concerns pager: 12027 is Transfusion Services MD, x36445 is charge tech

Massive Transfusion

Definition and Use

- Administration of greater than 1 blood volume (~10 units) in 24 hours
- At Stanford, calling the blood bank for the Massive Transfusion Guideline (MTG) will get you **6 pRBCs, 4 FFP, and 1 unit of platelets**
- May take *up to 30 minutes* to have blood prepared and picked up for OR use. Plan ahead and use closed-loop communication with support staff.
- Also consider location, getting blood in the ASC or OB department takes much longer than the MOR
- Typically, will utilize Belmont, Level 1, or both for rapid infusion
- Emergency release blood is the same process as an MTG but used when you don't need a full MTG
  - if no screen on file you will get universal products
- Sometimes will start giving (getting) Rh(D) + blood after 10 units have been transfused to conserve Rh(D) – blood

*In general, when preparing to give blood both place the order AND let your circulator know so they can coordinate delivery/pick-up with the blood bank

Massive Transfusion

Complications

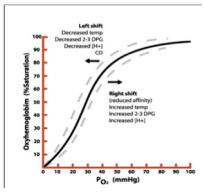
Lethal Triad of Trauma:

1. Hypothermia
   - Blood products are stored cold!
   - This worsens coagulopathy and is why you need to run blood through a warming device
2. Coagulopathy
   a. Dilutional thrombocytopenia
      - Platelet count likely <100,000 after ~10 units pRBCs
   b. Dilutional coagulopathies
      - ↓ Factors V & VIII ("labile factors") in stored blood
3. Acid-Base Abnormalities
   - At 21 days, stored blood has pH <7.0, due mostly to CO_2 production, which can be rapidly eliminated with respiration
   - Acidosis more commonly occurs due to ↓ tissue perfusion

Massive Transfusion

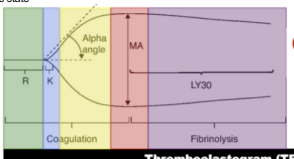
Complications

4. Citrate Toxicity
   - Citrate is in CPDA storage solution as a Ca^{2+} chelator (why you give Ca^{2+} with transfusion)
   - Rapid transfusion (>65cc/min in a healthy adult with healthy liver) can cause an acute hypocalcemia
   - Citrate also binds magnesium causing hypomagnesemia
5. Hyperkalemia
   - K^+ moves out of pRBCs during storage
   - If EKG changes occur, stop transfusion and treat hyperkalemia
6. Impaired O_2-Delivery Capacity
   - 2,3-DPG decreases in stored blood, causing a left-shifted O_2-Hb dissociation curve rendering Hgb to hold on to & not release as much oxygen at target sites



Transfusion Diagnostics

Thromboelastography (TEG) measures the dynamics of clot development, stabilization/strength, and dissolution. Assuming the body's ability to achieve hemostasis is a function of these clot properties, TEG provides specific, real-time indicators of a patient's in vitro hemostatic state



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rebelem.com

Thromboelastogram (TEG)

Components	Definition	Normal Values	Problem with...	Treatment
R Time	Time to start forming clot	5 – 10 minutes	Coagulation Factors	FFP
K Time	Time until clot reaches a fixed strength	1 – 3 minutes	Fibrinogen	Cryoprecipitate
Alpha angle	Speed of fibrin accumulation	53 – 72 degrees	Fibrinogen	Cryoprecipitate
Maximum Amplitude (MA)	Highest vertical amplitude of the TEG	50 – 70 mm	Platelets	Platelets and/or DDAVP
Lysis at 30 Minutes (LY30)	Percentage of amplitude reduction 30 minutes after maximum amplitude	0 – 8%	Excess Fibrinolysis	Tranexemic Acid and/or Aminocaproic Acid

Transfusion Reactions

**Whenever you suspect a transfusion reaction, STOP THE TRANSFUSION IMMEDIATELY and alert attending, surgeon, and blood bank*

- **Febrile Non-Hemolytic Reaction**
  - recipient abs stimulate donor WBCs to release cytokines and/or WBCs in plasma release cytokines during storage
    - Most common with platelets
  - Benign; occurs with 0.5-1% of transfusions
  - Treatment: Tylenol, Benadryl, slow transfusion, prevention by giving a patient leukoreduced blood
- **Anaphylactic Reaction**
  - Occurs within minutes; life-threatening
  - Usually associated with **IgA deficiency**- they have IgA antibodies
  - Signs/Symptoms: shock, angioedema, ARDS
  - Treatment:
    1) Stop blood
    2) Give fluids, Epi, antihistamines, ACLS
  - In a patient with known IgA deficiency, get washed blood (it reduces the amount of plasma proteins and immunoglobins)

Transfusion Reactions

- **Acute Hemolytic Reaction**
  - Due to ABO incompatibility
  - Symptoms: fever, chills, flank pain usually masked by GA; watch for unexplained tachycardia and hypotension, diffuse oozing and brown urine; monitor for ARF and DIC
  - Treatment:
    1) Stop blood products
    2) Maintain alkaline UOP (bicarb, mannitol, lasix/crystalloid), supportive care
- **Delayed Hemolytic Reaction**
  - Due to antibodies (not anti-A or anti-B) to antigens on donor RBCs
  - More insidious, develops on day 2-21
- **TACO (Transfusion Associated Circulatory Overload)**
  - Can order volume reduced blood for those with severe CHF

Transfusion-Related Acute Lung Injury (TRALI)

- Occurs 4-6 hours after transfusion
- Due to plasma-containing products (platelets and FFP > pRBCs)
- **Usually donor antibodies reacting to recipient leukocytes**
- Incidence: 1:1100 (but likely under-reported)
- Mortality 5-10% - Leading cause of transfusion-related mortality
- Signs & symptoms
  - Dyspnea, hypoxemia, hypotension, fever, pulmonary edema
- Diagnosis of exclusion
  - First rule out sepsis, volume overload, and cardiogenic pulmonary edema
- Treatment
  - Supportive care, similar to ARDS (O_2, mechanical ventilation, tidal volume 6-8 cc/kg)
  - Diuretics are not indicated (etiology = microvascular leak, not fluid overload)

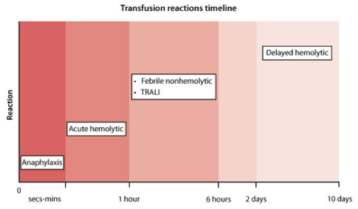
Transfusion Reactions

Presenting *With* Fever	
Acute	**Delayed**
Acute Hemolytic	Delayed Hemolytic
Febrile Non-hemolytic	TA-GVHD
Transfusion-related Sepsis	
TRALI	
Presenting *Without* Fever	
Acute	**Delayed**
Allergic	Delayed Serologic
Hypotensive	Post-transfusion Purpura
Tx-associated Dyspnea	Iron Overload
TACO	

ITE Tip

What is the primary mechanism behind delayed hemolytic transfusion reaction?

a. ABO incompatibility
b. Cytokines and Ab to HLA
c. Donor lymphocytes reacting against recipient
d. Donor RBC Ag



Answer: D

ITE Tip

A 30 year-old male undergoes an exploratory laparotomy. He receives 4 RBC, 2 FFP and 2 hours after the surgery, he becomes hypoxemic and hypotensive. A CXR shows bilateral pulmonary edema and PCWP is 8 mmHg (normal is 6-12). Which of the following is the most appropriate management of this patient?

a. Corticosteroids to reduce inflammation
b. Diuresis with lasix
c. IV fluid bolus
d. Start a course of antibiotics

Answer is C. The treatment of TRALI is very similar to that of ARDS, which is mainly supportive.

- **Oxygenation** can be maintained using non-invasive or invasive methods. Those that are on mechanical ventilation should have "lung protective" low tidal volumes settings.
- **Counterintuitively, patients with TRALI are typically hypovolemic** with resultant hypotension. Intravenous fluids can be used to resuscitate without worsening the pulmonary status. However, fluids should not be aggressively replaced and vasopressors are another option.
- Since TRALI patients are not volume overloaded, the benefit of diuretics is questionable and their use should be avoided.
- **The use of corticosteroid is avoided** just as it is in ARDS.
- **TRALI is not due to infectious sources** and the use of antibiotics treatment is not recommended.

ITE tip: Differentiating TACO vs. TRALI

TRALI	TACO
Criteria: 1) Acute lung injury (ALI) - Acute onset - Hypoxemia ($PaO_2/FiO_2 \leq 300$ mm Hg or $SpO_2 < 90\%$ on room air, or other clinical evidence of hypoxemia - Bilateral infiltrates on frontal chest radiograph - No evidence of left atrial hypertension as the sole explanation for the clinical findings 2) No pre-existing ALI before transfusion 3) Onset during or within 6 hours of transfusion 4) No temporal relationship to an alternative risk factor for ALI	New onset or exacerbation of three or more of the following within 6 hours of transfusion: - Acute respiratory distress (dyspnea, cough, orthopnea) - Increased brain natriuretic peptide (BNP) - Increased central venous pressure (CVP) - Evidence of left heart failure - Evidence of positive fluid balance - Radiographic evidence of pulmonary edema

Transfusion-Related Infections

Risk factor/infectious agent		Risk of TTI in blood products released
Virus		
CMV		**> 1 in 100**
HIV		1 in 2,135,000
HCV		1 in 1,930,000
HBV		1 in 277,000
HTLV-II		1 in 2,993,000
Bacteria		
Bacterial contamination*	RBC	1 in 38,500
	Platelets	***1 in 5,000**

*Bacterial contamination is most common with platelets due to their storage in dextrose at room temperature, pRBCs are less common cause due to their storage at 4˚C, but *Yersinia* is most likely organism

Blood is screened for HCV, HBV core Ab, HIV-1, HIV-2, HTLV, syphilis, and zika

Alternative Strategies for Management of Blood Loss During Surgery

- Autologous transfusion
  - Blood can be taken and self-donated if a patient's Hct is >34
  - Should be taken 4-5 week prior to surgery
  - Reduces the risk of infection and transfusion reactions
- Cell saver
  - Blood that is shed during the operation is aspirated into a reservoir, mixed with heparin, concentrated, and removed of debris
  - Useful if there are blood losses **>1000-1500mL**
  - Relative contraindications: **septic wound, cancer**
  - Heparinized, and provides packed RBCs only, so remember that patients may still require transfusion of other products for coagulopathy
- Normovolemic hemodilution
  - 1-2 units of a patient's blood are removed and stored in a CPD bag and replaced with crystalloid for goal Hct 20-25%
  - Blood is given back after blood loss

It was my first week of anesthesia residency and my mentor asked me to hang some blood to transfuse. I reached up and removed the spike from the bag of fluid that was already hanging…I was immediately soaked by the open IV fluid bag. My mentor later told me that he knew that would happen, but let me do it anyway so that I would always remember to bring the bag down first. I haven't forgotten.

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Hypoxemia

Causes of Hypoxemia

	P_aCO_2	A-a Gradient	DLCO	Corrects w/ supplemental O_2?
Low inspired O_2	Normal	Normal	Normal	Yes
Hypoventilation	↑	Normal	Normal	Yes
Diffusion Impairment	Normal	↑	↓	Yes
Shunt	Normal	↑	Normal	No
V/Q Mismatch	Normal / ↑	↑	Normal	Yes

Shunt: perfusion without ventilaton (V/Q=0); see ↓pO2. No increase in pCO_2 (2/2 chemoreceptor mediated hyperventilation) until shunt fraction→50%

Dead Space: ventilation without perfusion (V/Q=∞); see ↑pCO2

Equations

Alveolar-arterial (A-a) Gradient

$P_{(A\text{-}a)}O_2 = P_AO_2 - P_aO_2$

Alveolar Gas Equation

$P_AO_2 = F_iO_2 (P_{atm} - P_{H2O}) - (P_aCO_2 / 0.8)$

$= 0.21 (760 - 47) - (40 / 0.8)$

$\approx$ 100 mm Hg

Normal A-a Gradient:
- < 10 mm Hg ($F_iO_2 = 0.21$)
- < 60 mm Hg ($F_iO_2 = 1.00$)
- < (age / 4) + 4
- a/A ratio > 0.75

Normal PaO_2:
- 103 - age/3

Causes of Hypoxemia

1. Low inspired O_2
- Altitude (normal F_iO_2, decreased barometric pressure)
- Hypoxic F_iO_2 gas mixture (crossed gas lines, loss of pipeline pressure)

2. Hypoventilation
- Drugs (opioids, benzodiazepines, barbiturates), chest wall damage (e.g. splinting from rib fx, neuromuscular diseases, obstruction (e.g. OSA, upper airway compression)
- Very responsive to supplemental O_2 - (PaCO2/0.8) term of alveolar gas equation becomes insignificant at higher FiO2 even with relatively high PaCO2.
  - FiO2 21%
    - PaCO2 40 → PAO2 = 0.21(760-47) - 40/0.8 ≈ **100mmHg —> SpO2 100%**
    - PaCO2 80 → PAO2 = 0.21(760-47) - 80/0.8 ≈ **50mmHg —> SpO2 80%**
  - FiO2 30%
    - PaCO2 40→ PAO2 = 0.3(760-47) - 40/0.8 ≈ **160mmHg —> SpO2 100%**
    - PaCO2 80 → PAO2 = 0.3(760-47) - 80/0.8 ≈ **115mmHg —> SpO2 100%**

3. Diffusion Impairment
- Increased diffusion pathway (e.g. pulmonary edema, fibrosis)
- Decreased surface area (e.g. emphysema, pneumonectomy)
- Decreased rate of O_2-Hb association (e.g. high CO, anemia, PE)

Causes of Hypoxemia

4. R —> L Shunt (i.e. perfusion w/o ventilation; V/Q = 0)
- Congenital (e.g. TOF, TA, ASD/VSD/PDA w/ Eisenmengers)
- AVM (AVF, congenital)
- Pulmonary fluid (pneumonia, CHF, ARDS, NPPE, TACO, TRALI)
- Atelectasis (mucus plugging, GA)
- Endobronchial intubation (ETT is "mainstemmed")

5. V/Q Mismatch
- Often multifactorial
- COPD, ILD
- Dead space (V > Q ie PE, surgical clamping)
- Decreased CO (V > Q ie MI, CHF)

6. Mixed Process
- Hypoxemia is often due to multiple causes.
- Example: A tourist with COPD is visiting Denver, overdoses on heroin, now s/p MVA with chest wall trauma, pulmonary hemorrhage, Hct = 15%, and LV contusion. What is the cause of hypoxemia?

Hypoxemia in the OR

Use a systematic approach to the Dx/Rx of intra-op hypoxemia

Suggestion: trace a path from the alveoli to the anesthesia machine

1. Listen to the lungs
- Atelectasis (rales)
- Pulmonary edema (rales, decreased BS)
- Bronchoconstriction (wheezes, shark-fin end-tidal CO2 tracing, ↓TV)
- Mucus plug or secretions (↑PAP, ↓TV, mucus in ETT, rhonchi)
- Right mainstem ETT (SpO2 ~90%, ↑PAP, ↓TV, unilateral BS. Caused by repositioning, insufflation with laparoscopic procedures)
- Pneumothorax (unilateral BS, ↑PAP, ↓TV. HD instability, tracheal deviation if tension physiology)
- Esophageal intubation (no end-tidal CO2 tracing, BS in stomach & not lungs)

2. Check ETT
- Cuff deflation
- Kinked/bitten or detached ETT
- Extubation (ENT/Neuro cases when bed turned 180, surgeons near head, leaning on ETT/circuit)

Hypoxemia in the OR

3. Check circuit
- ETT disconnect
- Circuit disconnect (check inspiratory/expiratory limbs at machine, connection near ETT, gas sampling line)

4. Check machine
- Inspiratory & expiratory valves
- Bellows
- Minute ventilation
- F_iO_2
- Pipeline & cylinder pressures

5. Check monitors to confirm (you will probably do this 1st!)
- Pulse oximeter waveform
- Look at the patient! Are they cyanotic? mottled?
- Gas analyzer

Management of Hypoxemia

Assuming accurate SpO2/pulse oximetry:
- 100% FiO_2, high flow
- Manual ventilation: assess compliance, leaks
  - Recruitment maneuver if suspected atelectasis & hemodynamics can tolerate
- Auscultate: lung sounds, ETT position
  - Bronchodilators if bronchospasm
  - Fiberoptic bronchoscopy to further eval ETT position
- Suction airway and ETT
- Consider cardiovascular causes
  - Restore volume, RBCs and/or cardiac output
- Send ABG/VBG
- Consider CXR

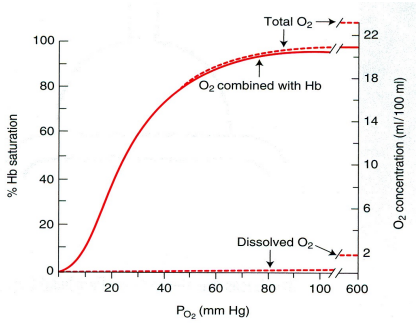
ITE tip

Differentiating intraoperative Hypoxemia causing changes in ventilator pressures:

Airway Resistance	Pulmonary Compliance (Elastic Resistance)
Increased P_{IP}, Unchanged Pplateau	Increased P_{IP}, Increased $P_{plateau}$
Airway compression Bronchospasm Foreign body Kinked endotracheal tube Mucus plug Secretions	Abdominal insufflation Ascites Intrinsic lung disease Obesity Pulmonary edema Tension pneumothorax Trendelenburg position?

P_{IP} = peak inspiratory pressure
$P_{plateau}$ = plateau pressure

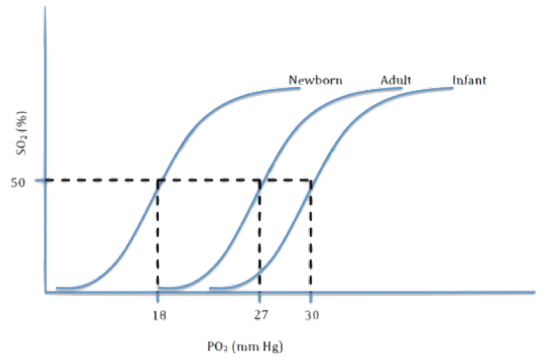
O_2-Hb Dissociation Curve



Useful "anchor" points:

S_{O2}	P_{O2} (mm Hg)
50%	27
75%	40
97%	100

Note:
$P_{50} \approx 27$ mm Hg



P50 is lowest in newborns (18) and highest in children over 12mo of age (30). After 10 years of age, P50 decreases to adult level ~27

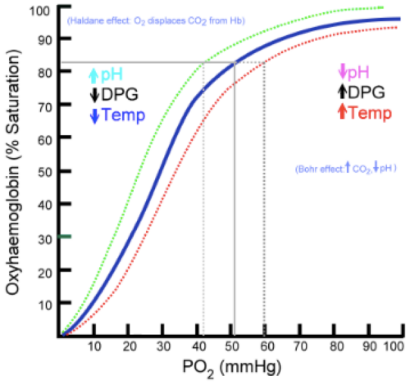
O_2-Hb Curve Shifts

Left Shift

(Hb has higher affinity for O_2 = decreased unloading at tissues)
- Alkalosis
- Hypothermia
- Hypocarbia
- Decreased 2,3-DPG
- CO-Hb
- Met-Hb
- Sulf-Hb
- Fetal Hb
- Myoglobin

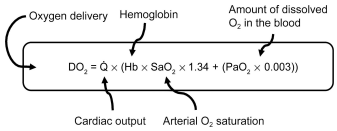
Right Shift

(Hb has lower affinity for O_2 = increased unloading at tissues)
- Acidosis
- Hyperthermia
- Hypercarbia ("Bohr Effect")
- Increased 2,3-DPG
- Sickle cell
- Pregnancy
- Volatile anesthetics
- Chronic anemia



Factors Affecting Tissue Oxygenation

- O_2 delivery
  - Cardiac output
  - Hb (concentration & O_2-Hb dissociation)
  - O_2 saturation
  - Dissolved O_2 in plasma (little effect)
- O_2 consumption



Equations

Arterial O_2 Content

CaO_2 = O_2-Hb + Dissolved O_2

= (Hb x 1.36 x SaO_2/100) + (PaO_2 x 0.003)

= (15 x 1.36 x 100%) + (100 x 0.003)

≈ 20 cc O_2/dl

Mixed Venous O_2 Content

CvO_2 = O_2-Hb + Dissolved O_2

= (Hb x 1.36 x SvO_2/100) + (PvO_2 x 0.003)

= (15 x 1.36 x 75%) + (40 x 0.003)

≈ 15 cc O_2/dl

Equations

O_2 Delivery

DO_2 = CO x CaO_2

= 5 L/min x 20 cc O_2/dl

≈ 1 L O_2/min

O_2 Consumption (Fick Equation)

VO_2 = CO x (CaO_2 - CvO_2)

= 5 L/min x 5 cc O_2/dl

≈ 250 cc O_2/min

O_2 Extraction Ratio

ERO_2 = (VO_2 / DO_2) x 100

= 250 / 1000

≈ 25% (normal 22-30%)

Other Concepts

Diffusion Hypoxia (usually with N_2O, due to high inspired % needed)

- Hypoventilation + diffusion of N_2O from blood to alveoli → displaces O_2 → ↓P_AO_2

Absorption Atelectasis

- Poorly soluble N_2 normally stents alveoli open
- O_2 readily absorbed; 100% FiO_2 predisposes toward atelectasis

Bohr Effect

- ↑PCO_2 → ↓pH → right shift of O_2-Hb dissociation curve (↓O_2-Hb affinity) → ↑ O_2 release (e.g. at peripheral tissue)

Haldane Effect

- ↑PO_2 → ↓CO_2-Hb affinity
- i.e. O_2-Hb binding → CO_2-Hb dissociation (e.g. when blood enters the lungs)

ITE tip

Which of the following mechanisms is most frequently responsible for hypoxia in the recovery room?

a. Ventilation/perfusion mismatch
b. Hypoventilation
c. Hypoxic gas mixture
d. Intracardiac shunt

Answer: a. The most common cause is uneven V/Q distribution caused by loss of lung volume and atelectasis.

References

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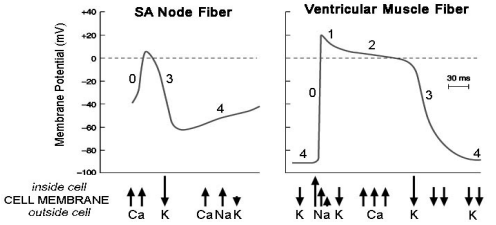
In one of my first days of residency (I was at the Valley, where there are 5 or 6 different kinds of anesthesia machines), it took me about 10 minutes in the morning to find the power button for the ventilator. I felt pretty dumb. The problem ended up being that I had a towel draped over the tray and it was obscuring the otherwise direct view of the right button. But it's a humbling reminder that our job is a mix of complex physiology / pharmacology / etc. and very practical, mundane details. You can master all the ventilator physiology you want, but it won't do you much good if you can't turn the ventilator on.

Electrolyte Abnormalities

Cardiac Action Potentials



Phase	Phase Name	SA Node Fiber	Ventricular Muscle Fiber
0	Rapid Upstroke	Slow inward I_{Ca}	Fast inward I_{Na}
1	Early Rapid Repolarization	–	Inactivation of I_{Na} Start Outward I_K
2	Plateau	–	Outward I_K = Slow Inward I_{Ca}
3	Final Rapid Repolarization	Outward I_K	Outward I_K > Inward I_{Ca}
4	Diastolic Depolarization/ Resting Potential	Slow inward I_{Ca} Slow inward I_{Na} Outward I_K (minimal)	Outward I_K

Hyperkalemia

Definition

- Mild K^+ = 5.5-6.5 mEq/L
- Moderate K^+ = 6.6-7.5 mEq/L
- Severe K^+ > 7.5 mEq/L

Contributing Factors

- Renal disease (esp GFR <15)
- Drugs (ACEI/ARBs, NSAIDs, K-sparing diuretics, digoxin, ß-blockers)
- Acidosis
- Hyponatremia, hypocalcemia
- Hemolysis, transfusions (esp old PRBCs -- [K^+] of 50 or greater!)
- Release from muscle
  - Succinylcholine: acute, transient ↑ 0.5-1 mEq/L (*may be greater in certain diseases)
  - Tourniquet, trauma, rhabdomyolysis
  - Malignant hyperthermia (do not administer verapamil with dantrolene)

Hyperkalemia

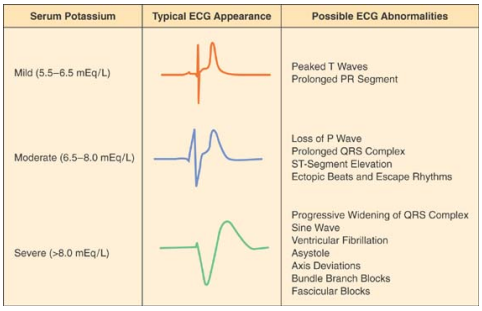
Signs and Symptoms

• Cardiac: dysrhythmias, conduction abnormalities, cardiac arrest

- Classically associated with giving succinylcholine to immobilized (ICU), spinal cord injury, neurological diseases (e.g. MS, ALS), burn patients – upregulated extrajunctional AChR (fetal AChR)
- Usually with [K^+] >6.0 mEq/L
- Progression with increasing K concentration:
  1. Tall peaked T waves, esp precordial leads
  2. Long PR interval, low P wave amplitude
  3. Wide QRS complex → sine wave → VF arrest, asystole

• [K^+] >7.0 mEq/L: ascending flaccid paralysis, inability to phonate, respiratory arrest

EKG Progression of Hyperkalemia



Barash PG et al. *Clinical Anesthesiology, 6th ed.* Philadephila: Lippincott Williams & Wilkins, 2009.

Hyperkalemia

Treatment

- **Stabilize cardiomyocyte membrane**
  - Ca gluconate (peripheral IV): 10% calcium gluconate (10cc over 5 min; repeat q5min prn)
  - Ca chloride (central line)
    *Do not use calcium for digitalis toxicity
- **Shift K intracellular (temporary)**
  - Sodium bicarbonate: 50-100 mEq over 5-10 minutes
  - Regular insulin: bolus 10 units with D50 (25 g = 50 mL)
  - Albuterol
- **Remove potassium from body**
  - Diuretics (proximal or loop)
  - Kayexalate (PO/PR): oral 30g in 20% sorbitol (50cc); rectal 50g in 20% sorbitol (200cc)
  - Dialysis

Hyperkalemia

Anesthetic Considerations

- Consider cancelling elective cases if K >5.5
- Avoid succinylcholine
- EKG monitoring
- Avoid hypoventilation (respiratory acidosis)
- Treat acidosis
- Monitor for increased sensitivity to neuromuscular blockers

	K (mEq/L)	pH
0.9% NaCl	0	5.5
Lactated Ringer's	4	6.5
Normosol, Plasma-Lyte	5	7.0

- Classical teaching favors NS (no $[K^+]$), but hyperchloremic metabolic acidosis worsens hyperkalemia. Negligible $[K^+]$ in other crystalloids (e.g. LR) would bring serum K closer to 4

Hypokalemia

Definition

- Mild K^+ = 3.1-3.5 mEq/L
- Moderate $K^+ \leq 3$ mEq/L with PACs
- Severe $K^+ < 3$ mEq/L with PVCs

Contributing Factors

Preoperative

- GI losses (NGT, N/V, diarrhea)
- Lasix, RTA
- Magnesium deficiency

Intraoperative

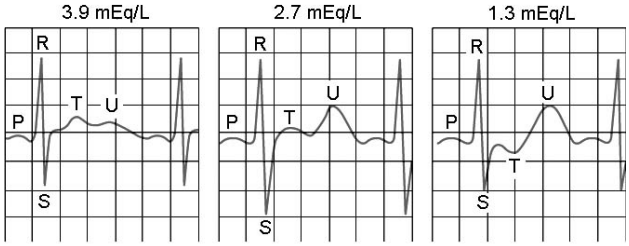
- Alkalosis (metabolic or respiratory)
- Insulin
- Hypothermia

Hypokalemia

Signs & Symptoms

- Cardiac: hyperpolarization → ventricular escape, re-entrant phenomena, ectopic tachycardias, conduction delay
  - PACs, PVCs
  - SVTs (esp afib, aflutter)
- Metabolic alkalosis
- Autonomic lability
- Weakness, ↓DTRs
- Ileus
- Digoxin toxicity
- Increased sensitivity to neuromuscular blockers

EKG Progression of Hypokalemia



Flattened/inverted T wave → U waves, ST depression

Hypokalemia

Treatment

Acute hypokalemia = likely from cellular shifts

- Reverse underlying cause (e.g. alkalosis from mechanical hyperventilation)

Chronic hypokalemia = total body K^+ depletion
(1 mEq/L = 175-350 mEq total body deficit)

- Peripheral IV: 10 mEq/hr
- Central line: 10-20 mEq/hr
- Life-threatening: 5-6 mEq bolus

Hypokalemia

Anesthetic Considerations

- Consider cancelling elective cases if K^+ <3-3.5 (based on chronicity of deficit)
- EKG monitoring
- If arrhythmias develop, check/replete K
- Avoid hyperventilation (respiratory alkalosis)
- Consider reduce dose of neuromuscular blocker by 25-50%

Hypercalcemia

Contributing Factors

- Hyperparathyroidism
- Malignancy (esp lung, ENT, GU, GYN, multiple myeloma)
- Immobilization
- AKI
- Drugs (thiazide diuretics, lithium)

Signs & Symptoms

- EKG changes (short QT)
- Hypertension
- Polyuria

Treatment

- Hydration (bolus crystalloid) + Lasix diuresis
- Dialysis

Hypercalcemia

Anesthetic Considerations

- Consider cancelling elective cases
- Avoid acidosis (Increased H^+-albumin binding reduces Ca^{2+}-albumin binding)
- Check serial K^+ and Mg^{2+}

Hypocalcemia

Contributing Factors

Preoperative

- Hypoparathyroidism
- Renal failure (decreased vitamin D activation)
- Sepsis
- Magnesium deficiency (decreased end-organ response to PTH)

Intraoperative

- Alkalosis (increased Ca^{2+}-albumin binding)
- Massive PRBC transfusion (due to citrate binding)
- Drugs (heparin, protamine, glucagon)

Signs & Symptoms

- EKG (prolonged QT, bradycardia)
- Hypotension (vasodilation, decreased contractility, LV failure); usually when iCa <0.65
- Respiratory (laryngospasm, stridor, bronchospasm, respiratory arrest)
- Neuro (cramps, tetany, ↑DTRs, perioral numbness, seizures, Chvostek's sign, Trousseau's sign)

Hypocalcemia

Treatment

- Calcium gluconate (PIV or central line) 1 g = 4.5 mEq Ca^{2+}
- Calcium chloride (central line only) 1 g = 13.6 mEq Ca^{2+}
- Do NOT give Ca^{2+} and $NaHCO_3$ together in the same IV - it will precipitate!
- Replace magnesium

Anesthetic Considerations

- EKG monitoring
- Avoid alkalosis
- Monitor paralysis with muscle relaxants
- Monitor iCa with transfusions

Hypermagnesemia

Contributing Factors

- Renal failure
- Hypothyroidism
- Iatrogenic (OB tocolysis)

Signs & Symptoms

- EKG (wide QRS, long PR interval, bradycardia)
- Hypotension (vasodilation, myocardial depression)
- Neuro (↓DTRs, sedation, weakness, enhanced neuromuscular blockade)

Treatment

- Hydration (bolus crystalloid) + Lasix diuresis
- Ca^{2+} administration
- Diuresis

Anesthetic Considerations

- EKG monitoring
- Consider reducing dose of neuromuscular blocker by 25-50%

Hypomagnesemia

Contributing Factors

- GI/renal losses
- ß-agonists (intracellular shift)
- Drugs (diuretics, theophylline, aminoglycosides, ampho B, cyclosporin A)

Signs & Symptoms

- Usually asymptomatic alone, but contributes to other electrolyte abnormalities (e.g. hypokalemia, hypocalcemia, hypophosphatemia)
- EKG (long QT; PACs, PVCs, afib)
- Neuro (neuromuscular excitability, AMS, seizures)

Treatment

- Replete with $MgSO_4$ to $[Mg^{2+}] > 2$ mg/dl
- Watch for hypotension & arrhythmias with rapid administration!

Anesthetic Considerations

- EKG monitoring
- Check for coexistent electrolyte deficiencies

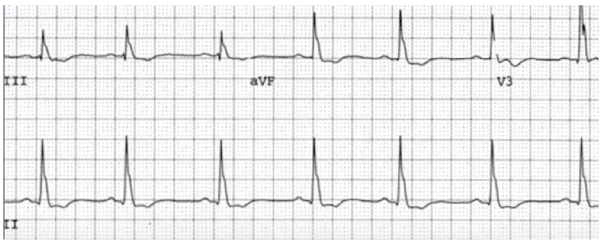
Summary of EKG Changes

	PR interval	QRS	QT interval	T waves
↓ Ca	short	narrow	prolonged	inversion
↑ Ca	prolonged	widened	shortened	--
↓ Mg	short	narrow	prolonged	--
↑ Mg	prolonged	widened	--	--
↓ K	short	narrow	prolonged	flat, U waves
↑ K	prolonged	widened	--	peaked

Rule of thumb: ↓ electrolyte → short PR, narrow QRS, prolonged QT

ITE tip

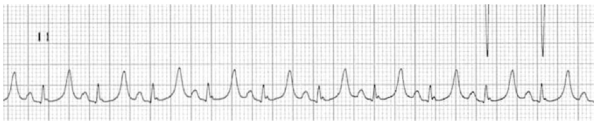
What is the suspected electrolyte abnormality?



Answer: hypercalcemia (short QT and J wave within QRS)

ITE tip

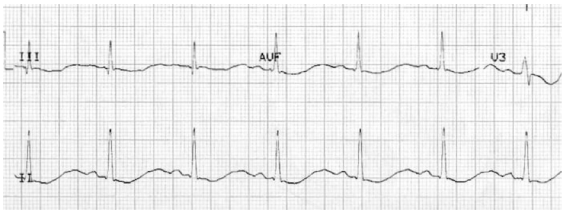
What is the suspected electrolyte abnormality?



Answer: hyperkalemia (super peaked Twaves)

ITE tip

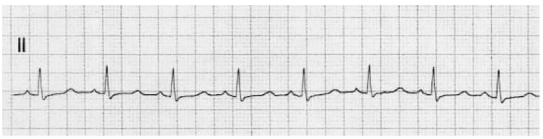
What is the suspected electrolyte abnormality?



Answer: hypokalemia (inverted T waves and prominent U wave)

ITE tip

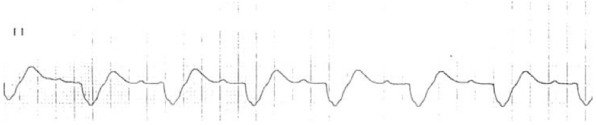
What is the suspected electrolyte abnormality?



Answer: hypocalcemia (prolonged QT interval)

ITE tip

What is the suspected electrolyte abnormality?



Answer: worsening hyperkalemia – wide bizarre QRS and prolonged PR

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I was in the middle of a long, stable but tedious endometriosis case in the ASC. I tried to open my next vial of dilaudid and blam! It shattered in my hand and I had 2mg of dilaudid dripping down my fingers. Not wanting to be pegged as a CA-1 with a drug problem, I quietly called the pharmacy to ask them how to document the incident. The discussion took about a minute or so, and when I hung up, I realized the attending surgeon had stopped the case and was staring at me, as was everyone else in the room. He told me he gets "easily distracted" and so he was patiently waiting until I was off the phone!

During the middle of a straightforward case I was drawing up my drugs for the next case. I dropped the propofol vial but after inspection nothing was damaged. I proceeded to inject air into the vial making it easier to draw up. Needless to say it exploded on me.....and the sterile operative field. Bummer.

CSI tip: In July, keep your eyes peeled for distinctive splatter patterns of white stuff on new residents' scrubs, badges, or other paraphernalia. It is a sign that they, too, have been sprayed with either Propofol or Kefzol while trying to draw up a syringe. The needle tip has to stay inside the vial.

CSI tip: Don't believe it if another CA1 has a BandAid on their finger or hand and they tell you they cut themself in the kitchen or have a paper cut. Odds are they stabbed themself with a needle drawing up drugs in the morning.

Hypothermia & Shivering

Definition and Measurement

- **Hypothermia**: a core body temperature less than 36 degrees Celsius
- Many places to measure temperature…
  - Some accurately reflect core temperature:
    - Nasopharynx- risk cause epistaxis
    - Distal Esophagus- strictures and varices are a relative contraindication
    - Tympanic Membrane- lead may perforate the ear drum
    - Thermistor of a Pulmonary Artery Catheter- the gold standard
  - Some lag behind core temperature during thermal perturbations:
    - Bladder- especially when urine output is low
    - Rectum- inaccurate with stool in rectum; contraindicated with neutropenia
  - Skin is generally much cooler than core temperature

Pathways of Thermoregulation

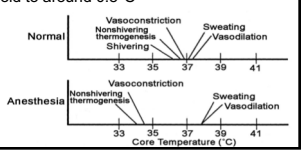
- **Afferent Sensing**
  - Nerve endings are found in the the skin, deep abdominal and thoracic tissues, spinal cord, brain matter, and the hypothalamus
  - These thermal inputs travel along A-delta fibers (cold sensation) and C fibers (warm sensation) to the brain via the spinothalamic tracts
- **Central Control**
  - Thermal inputs are pre-processed within the spinal cord and brainstem.
  - Ultimately, the preoptic-anterior hypothalamus is the central autonomic thermoregulatory center that sums these various inputs.
- **Efferent Responses**
  - Behavioral responses are triggered by skin temperature.
  - Autonomic responses are triggered by core temperature.

Mechanisms to Control Body Temperature

- **Behavioral Responses**
  1. Seeking shelter or clothing
  2. Voluntary movement
- **Autonomic Responses – there are only 3 things the body can do:**
  1. Shivering
  2. Sweating
  3. Modulating vascular tone to redirect blood flow

Interthreshold Range

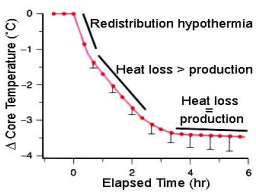
- **Interthreshold Range:** the core temperature range between cold-induced and warm-induced responses, usually as narrow as 0.2°C
- **General anesthesia**
  - inhibits thermoregulation globally
  - increases the interthreshold range 20-fold to around 4°C
- **Regional anesthesia**
  - inhibits thermoregulation to the lower half of body
  - increases the interthreshold range 4-fold to around 0.8°C



Development of Hypothermia

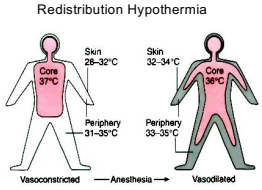
Phases of Anesthetic-impaired thermoregulation

1. Redistribution hypothermia
2. Heat loss > heat production
3. Heat loss = heat production
   - heat balance is at steady state



Heat transfer in an Icy Operating Room
(in order of importance)

1. Radiation
2. Convection
3. Evaporation
4. Conduction



Benefits of Hypothermia

- Metabolic rate decreases by 8% per 1˚C decrease in temperature
  - Confers myocardial protection as a lower total body metabolic rate requires less oxygen delivery to tissues, leading to lower demands on the heart to provide cardiac output
- The CNS has partial protection from ischemic and traumatic injuries
  - Targeted cooling improves neurologic outcomes after cardiac arrest, and allows deep hypothermic circulatory arrest (i.e., all blood flow ceases) to be induced for certain cardiac surgeries e.g. complex aortic arch repairs
- Possibly provides some protection against malignant hyperthermia

Drawbacks of Hypothermia

- Increases infection rates up to 3-fold
- Delays wound healing and increases risk of surgical graft failure
- Induces a coagulopathy as platelet function fails and coagulation factor function slows (part of the trauma's "lethal triad")
  - Leads to increased surgical blood loss and greater transfusion rates
- Delays emergence from general anesthesia
  - Prolongs the activity of many anesthetic drugs
  - Consider rewarming the patient prior to emergence
- Left-shifts the oxygen-hemoglobin dissociation curve, which impairs delivery of O_2 delivery
- While it decreases cardiac output requirements, hypothermia has a negative effect on inotropy and chronotropy, increases EKG intervals, leads to dysrhythmias, and increases systemic vascular resistance.
- Increases the systemic stress response
- Increases postoperative shivering rates
- Prolongs PACU stays

Warming Strategies

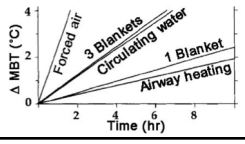
Prevention of hypothermia is much more effective than treatment!

Active Warming
- Forced air (e.g. Bair Hugger)
- Heating pad with circulating water
- Breathing circuit heating & humidification
- IV Fluid warmer (e.g. Ranger)
- Bladder irrigation with warm fluids
- Heating lamp or raising room temp

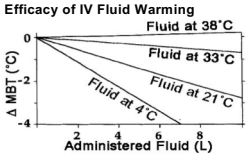
Passive Insulation
(not as effective)
- Cotton blankets
- Surgical drapes
- Heat-reflective "space" blanket

Also…
- Preoperative skin warming is excellent prophylaxis!

Efficacy of Warming Strategies



Efficacy of IV Fluid Warming



Rhythmic Muscular Activity

- **Shivering in the PACU**
  - Generally due to *hypothermia*
    - Lack of shivering does not mean patient is not hypothermic; recall the aforementioned effects of opioids and general/regional anesthetics on the interthreshold range!
  - Shivering may occur in normothermic patients
    - e.g.: uncontrolled *pain* can cause non-thermoregulatory driven shivering
- **Pure clonic movements**
  - Seen in patients as volatile MAC drops to the 0.15 – 0.3 range, regardless of temperature
- **Fevers**
- **Seizures**

Consequences of Shivering

- Dramatic increase in O_2 consumption
  - Up to 500% in some studies
- Increased CO2 production
  - Can greatly increase minute ventilation requirement
- Not all patients can tolerate the increased metabolic and respiratory demands!
- Also associated with shivering:
  - Trauma
  - Elevated intraocular pressure
  - Elevated intracranial pressures
- Distressing or even painful
- Disrupts monitoring, especially oscillometric blood pressure measurements and pulse oximetry

Treatment of Shivering

- Prevention is *by far* the most important step you can take!
- Warm the patient aggressively
  - Typically, forced air and blankets suffice
- Pharmacologic interventions:
  - **Meperidine** 12.5-25 mg IV
    - Caution as normeperidine accumulates in renal insufficiency, which then leads to **seizures**
  - Non-depolarizing muscle relaxants
    - Obviously, only in anesthetized, mechanically ventilated patients
- And be mindful of the differential of rhythmic muscular activity…
  - e.g. ensure pain is well controlled, patient is not seizing, etc.

ITE tip

What is the most effective way to reduce amount of heat lost due to redistribution from core to periphery during the first 30 min after induction?

Answer: preoperative forced air warming to torso and legs 30 min before induction.

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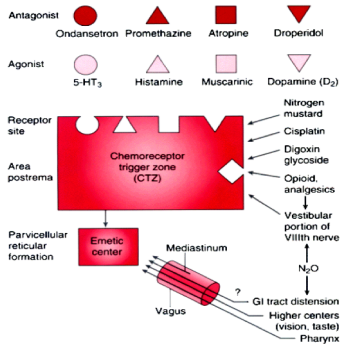
Postoperative Nausea & Vomiting (PONV)

Why do we care about PONV?

- Up to 1/3 of patients without prophylaxis will experience PONV (up to 80% among high-risk pts)
- Causes patient discomfort - patients report avoidance of PONV as a greater concern than post-op pain
- Leading cause of delay of discharge from PACU
- Causes unanticipated hospital admission
- Possible aspiration risk and airway compromise
- Can lead to dehydration and electrolyte changes
- Can cause increased CVP, ICP, suture or mesh disruption, venous HTN and bleeding, or wound dehiscence

Chemoreceptor Trigger Zone



Major Risk Factors

Patient-Related

- Female > male
- History of PONV or motion sickness
- Young > old
- Non-smoker > Smoker

Anesthetic-Related

- Volatile anesthetics including N_2O
- Drugs (postoperative narcotics, neostigmine)
- Aggressive hydration (gut edema)

Surgery-Related

- Duration of surgery – higher risk if > 2 hours
- Type of surgery shown to have **MINIMAL** effect (laparoscopic, ENT, neuro, breast, plastics, strabismus)
- **laparoscopic, bariatric, gynecological surgery, and cholecystectomy**

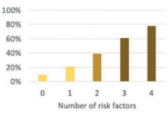
Evidence Based Risk Factors (Apfel et al., 2012)

- Christian Apfel (UCSF PONV guru) meta-analysis of 22 PONV studies (>95,000 pts)
- Highest risk factors:

Risk Factor	OR (versus not having risk factor)	P value
Female Gender	2.57 (2.32-2.84)	<0.001
History of PONV/Motion Sickness	2.09 (1.90-2.29)	<0.001
Non-smoking Status	1.82 (1.68-1.98)	<0.001
Younger Age	0.88 per decade	<0.001
Use of Volatile Anesthetics	1.82 (1.56-2.13)	<0.001
Post-op Opioids	1.39 (1.20-1.60)	<0.001

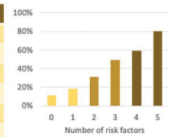
PONV Risk Scores

Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV and/or Motion Sickness	1
Postoperative Opioids	1
Sum of points	0-4



Simplified Apfel

Risk Factors	Points
Female Gender	1
History of PONV	1
Age <50	1
Use of opioids in PACU	1
Nausea in PACU	1
Sum of points	0-5



Koivuranta

Gan TJ, et al. 2020

PONV Prophylaxis Based on Apfel Score

Risk Score	Prevalence PONV	Prophylaxis: No of Anti-emetics	Examples*
0	9%	0-1	± Ondansetron 4 mg
1	20%	1	Ondansetron 4 mg ± Dexamethasone 4mg
2	39%	2	Ondansetron 4 mg +Dexamethasone 4mg ± Propofol infusion
3	60%	3	Ondansetron 4 mg + Dexamethasone 4 mg + Propofol infusion ± Scopolamine patch
4	78%	4	Ondansetron 4 mg + Dexamethasone 4 mg + Propofol infusion + Scopolamine patch

- Current recommendation is at least 2 prophylactic drugs in patients with at least one risk factor
- Combinations should be with drugs that have a different mechanism of action
- Try not to order agents for treatment in PACU that have already been used for ppx (e.g. Re-administration of Zofran in PACU not as effective as first dose used for ppx)

Antiemetic Classes

5-HT$_3$ Antagonists (e.g. Ondansetron, Granisetron)
- Serotonin receptor antagonist
- More effective at preventing emesis than preventing just nausea
- Zofran 4-8 mg IV or Kytril 0.1-1 mg IV before end of case (usually given ~30 minutes before emergence)
- Side effects: Headache, QT prolongation

Steroids
- Cheap and effective; for prolonged PONV relief
- Uncertain mechanism of action
- Even in the presence of diabetes, there is minimal evidence to support a clinically significant increase in blood glucose levels with low dose
- Antiemetic single dose has not been found to cause a clinically significant increase in bleeding, infection or cancer recurrence based on current studies
- Decadron 4-10 mg IV after induction
- Avoid in awake patients as can cause severe perineal itching or discomfort

Induction agents
- Propofol 10-20 mg IV bolus in PACU vs low-dose infusion during case
- Consider volatile sparing TIVA

Antiemetic Classes

Anticholinergics (e.g. Scopolamine patch)
- Centrally acting
- Transdermal administration requires 2-4 hours for onset. (give pre-op)
- Anticholinergic side effects ("mad as a hatter", "blind as a bat", "dry as a bone", "red as a beet") - potentially worse than N/V for some patients
- Scopolamine patch 1.5 mg TD q72hr, place posterior to ear lobe
- Warn patients not to touch patch and wipe eyes → dilate affected pupil
- Avoid in elderly as it can contribute to post-op confusion/ delirium

Phenothiazines (e.g. Promethazine, Prochlorperazine)
- Dopamine antagonist (promethazine also exhibits H$_1$ antagonism as well)
- Given IV or IM
- Can cause sedation and extrapyramidal side effects
- Phenergan 12.5-25 mg at end of case

Gastrokinetic (e.g. Metoclopramide)
- Dopamine antagonist; can cause extrapyramidal SEs
- Increases GI motility and LES tone, avoid in patients with bowel obstruction
- Reglan 10mg may not be effective, doses require may exceed 25 mg which can increase risk of EPS symptoms
- Contraindicated in Parkinson's patients

Antiemetic Classes

Butyrophenones (e.g. Droperidol, Haloperidol)
- Central dopamine antagonist
- Droperidol cheap and very effective, but a "black box" warning regarding QT prolongation has caused it to fall out of favor (based on data when given at doses 50-100x than standard dosing – 25 mg vs 0.625-1.25 mg used for PONV)
- Haloperidol at antiemetic doses ~1mg has similar effectiveness as 5-HT3 antagonists and similar side effect profiles (including QT prolongation)
- Contraindicated in Parkinson's patients

Substance P antagonists (e.g. Aprepitant, fosaprepitant)
- NK1 receptor antagonist; more effective when given with Zofran ATC
- Expensive: typically for posterior fossa neurosurgical cases & chemotherapy-related nausea and vomiting. PO is preferred as more cost effective
- Also useful for patients with refractory PONV
- Can be given IV or PO (PO should be given 3 hours before induction)
- Must be ordered from pharmacy

Other Antiemetic Agents

Vasopressors
- Ephedrine 50 mg IM
  - Prevents intestinal hypoperfusion

Antihistamines (H_2-blockers)
- Cimetidine 300 mg IV
- Ranitidine 50 mg IV
  - Often given pre-operatively

Gabapentin
- 600-800 mg preoperatively

Midazolam
- Effective if given at end of case but less favorable because of sedation

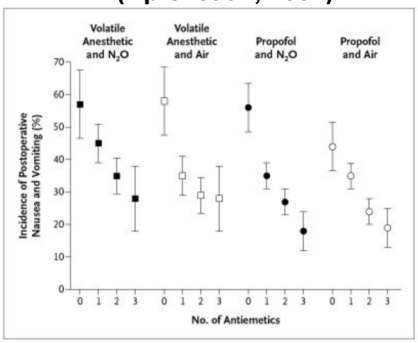
IMPACT Trial: Results
(Apfel et al., 2004)

Intervention	RR Reduction	P value
Dexamethasone (vs. none)	26.4%	<0.001
Ondansetron (vs. none)	26.0%	<0.001
Droperidol (vs. none)	24.5%	<0.001
Nitrogen carrier (vs. N_2O)	12.1%	0.003
Propofol gtt (vs. volatiles)	18.9%	<0.001
Remifentanil gtt (vs. fentanyl)	-5.2%	0.21

- Interventions acted independently of each other; relative risk reduction (RRR) of combined therapy can be estimated by multiplying individual RRRs
- Average PONV = 34% (59% with volatile + N_2O + remi + no antiemetics; 17% with propofol + N_2 + fentanyl + antiemetics x 3)
- Use the safest and cheapest antiemetic first; use combined therapy only in moderate or high-risk patients

IMPACT Trial: Results

(Apfel et al., 2004)



Strategies to Reduce PONV

- Use regional anesthesia vs. GA
- Use propofol for induction and maintenance of anesthesia (TIVA)
- Avoid N_2O and/or volatile anesthetics
  - N_2O's role in PONV is controversial, possibly related to duration of exposure
- Minimize intraoperative and postoperative opioids (consider Tylenol, NSAIDs, etc.)
- Avoid hypotension and cerebral hypoxia
- Use a combination of antiemetics in different classes
- Consider acupuncture, acupressure, or transcutaneous electrical nerve stimulation (rarely used)
- Use sugammadex instead of neostigmine for reversal
- Adequate hydration

ITE tip

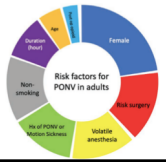
PONV Risk Factors in Adults	PONV Risk Factors in Children
Age < 50 years old Female gender History of PONV or motion sickness Non-smoker	Age > 3 years old History of nausea/vomiting (in the child or relative) Strabismus surgery Surgery > 30 minutes

Increases Incidence of PONV	Decreases Incidence of PONV
Duration of anesthesia Opioid use (especially post-operatively) Surgery (laparoscopic, cholecystectomy, gynecological) Use of nitrous oxide/volatile agents	Adequate hydration Avoid nitrous oxide/volatile agents Minimize opioid use Regional anesthesia (avoid general anesthesia) Use of propofol

ITE tip

Which of the factors in adults listed below is the strongest independent predictor of PONV in most adults?

a. Female gender
b. History of PONV
c. History of migraines
d. History of cigarette smoking



Answer: a

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Extubation Criteria & Delayed Emergence

Extubation Overview

- 12% of the closed claim cases with perioperative difficult airway were from the time of extubation
- ASA Practice Guidelines for Management of the Difficult Airway: has *not* decreased the number of claims arising from injury at extubation
- Incidence of respiratory complications *may be higher with extubation* than intubation.
  - Most common complications with extubation: coughing, difficult ventilation through facemask, desaturations.
- Extubations are almost always elective with adequate time to methodically plan, organize, and communicate essential interventions.

Extubation Overview (cont)

- As a result, Difficult Airway Society (DAS) published 2012 guidelines with low & high risk algorithm
  - Low Risk: awake vs. deep extubation
    - *Awake: usual way of extubating*
    - *Deep: more advanced, ask your attending, usually has specific indications, others may use it to expedite transfer to PACU and room turnover*
  - High Risk: awake (with possible Airway Exchange Catheter (AEC), LMA, or remifentanil technique) vs. postponing extubation vs. tracheostomy
    - *AEC: hollow catheters similar in shape to bougie. Can be placed through an ETT in an intubated patient and left in place while the patient is extubated. This allows you to both ventilate through the AEC and easily reintubate if needed by railroading an ETT over the AEC*

Extubation Risk Stratification:

- **Airway Risk Factors**
  - Known difficult airway
  - Airway deterioration:
    - consider bleeding, trauma, edema (surgical site, prone or Trendelenberg positioning, large volume resuscitation)
  - Restricted airway access
  - Obesity and OSA
  - Aspiration Risk
- **General Risk factors**
  - Cardiovascular, Respiratory, & Neuromuscular diseases
  - Metabolic derangements
  - Special surgical requirements

Deep Extubation

- Deep extubation can be performed when the patient demonstrates adequate depth of anesthesia (e.g. no response to pharyngeal suctioning or jaw thrust, breath holding, etc.)
- Compared to an awake extubation, a deep extubation does not result in tachycardia, hypertension, or coughing and can reduce the risk of wound dehiscence, bleeding and bronchospasm
- However, patients extubated deeply remain at risk for laryngospasm as they emerge from anesthesia, which can occur during transport or in the PACU

"Routine Extubation Criteria"

1. **Vital signs stable**
   - BP/HR stable within acceptable ranges (on minimal pressors)
   - T > 35.5C
   - Spontaneous RR >6 and <30, SpO_2 > 90%
2. **ABG "reasonable" with $FiO_2 \leq 40\%$**
   - pH ≥7.30, PaO_2 ≥60 mmHg, $PaCO_2$ ≤50-60, normal lytes
   - As a surrogate, $ETCO_2$ can be used and should be <60
3. **Adequate reversal of neuromuscular blockade**
   - TOF ratio >0.9, tetany >5 secs
     - The "direct palpation" method cannot determine if the TOF ratio is > 0.9.
   - Sustained head lift or hand grasp >5 secs (sensitive but not specific)
     - Not adequate to rule out residual paralysis or incomplete reversal
4. **Respiratory mechanics adequate**
   - Spontaneous VT >5 mL/kg, Vital Capacity >15mL/kg
5. **Protective reflexes (gag, swallow, cough) returned***
6. **Awake, alert, able to follow commands***
7. **Optimize the patient :** 100% O_2, consider positioning in slight reverse trendelenberg, suction oropharynx, consider small dose of lidocaine to reduce coughing

***These need not be present in the case of a deep extubation**

Causes of Failed Extubation

Causes	Checklist prior to extubation (to help avoid failure)
Failure to oxygenate	• TV >5cc/kg & VC > 15cc/kg • SpO_2 >90% with FiO_2 < 0.4
Failure to ventilate	• Same TV parameters above • NM Blockade appropriately reversed • RR >6 & <30? • No excessive hypercapnea ($EtCO_2$ < 50s-60)
Inadequate clearance of pulmonary secretions	• Oropharynx suctioned? • Intact gag reflex? Able to cough? Alert/awake? • If aspiration risk, OG tube suction and consider emergence in lateral decubitus position
Loss of airway patency	• Soft bite block or oral airway placed? • Alert? Following commands? • If edema a concern, is cuff leak >10-15%** • Placed in optimal position (sniffing position, head up) • Reduced risk of laryngospasm? (not in stage 2, airway suctioned) • Airway exchange catheter for high risk patient?

Cuff Leak Test

- While the patient is ventilated on volume control mode, deflate the ETT cuff
- In the absence of significant airway edema, a leak should be present
- Calculate the difference between your programmed tidal volume and the observed expiratory tidal volume. This is your cuff leak.
- Suggested cutoff for an adequate cuff leak is at least 10-15% of your tidal volume

Standard preparation any extubation

1. Ensure back-up airway / re-intubation equipment available
   - LMA, bougie, Mac/Miller blade nearby on hand
2. Pre-oxygenate with 100% O_2; consider recruitment maneuver to reduce atelectasis
3. Reverse neuromuscular blockade
4. Turn off primary anesthetic agent
5. Insert a soft bite block (rolled gauze); suction as appropriate
6. Position patient and bed appropriately
   - Is the patient still turned 180 degrees? Lithotomy position?
   - Consider reverse Trendelenburg positioning to improve ventilation
7. Minimize touching patient during Stage 2 ("light") anesthesia
8. Confirm that all "Routine Extubation Criteria" are met
9. **Extubate:**
   - Deflate cuff, remove tube with positive pressure
   - Provide 100% O2, ensure patent airway, adequate breathing
     - Use an oral airway or nasal trumpet as needed
10. Transport to PACU on continuous oxygen

Stages of Anesthesia

Described by Guedel in 1937 to describe depth of anesthesia, originally from ether. Classification still used today despite newer agents and delivery techniques.

Stage 1 – Amnesia
- Ranges from awake to loss of consciousness, amnestic throughout

Stage 2 – Delirium/Excitement *
- Potential for vomiting, laryngospasm, breath-holding
- Hypertension, tachycardia, dilated/non-conjugate pupils
- Uncontrolled, non-purposeful movement, unable to follow commands

Stage 3 – Surgical Anesthesia
- Absence of movement
- Constricted pupils, regular respiration, cardiovascular stability (e.g. prevention of tachycardia and/or hypotension)

Stage 4 – Overdose
- Shallow or no respiration, dilated/non-reactive pupils, cardiovascular collapse (e.g. hypotension)

* Avoid extubation during Stage 2 to reduce risk of laryngospasm

Causes of Delayed Emergence

Anesthesia Related	Residual anesthetic • Rapid shallow breaths? MAC still showing? • Time since propofol turned off? Excessive narcotics • Recent administration? Pinpoint pupils? Residual muscle relaxant, pseudocholinesterase deficiency.
Metabolic	Hypothermia (T<34°C) Hypoxemia Hypercarbia/hyponatremia/hypocalcemia/ hypoglycemia Renal/hepatic failure
Intracranial event	Stroke/CVA (2.5-5% in high risk patients) Seizure Intracranial HTN

Diagnosis and Treatment

Stanford Protocol for Delayed Emergence

- Confirm that all **anesthetic** agents (inhalational/IV) are off
- Check for **residual NMB** paralysis, reverse as appropriate
- Consider **opiate** reversal (medications delivered, evaluate pupils & respiratory rate)
  - Start with ***40mcg naloxone IV***, repeat Q2 mins up to 200mcg total
- Consider **inhalational** anesthetic reversal (rare)
  - 1.25 mg of physostigmine IV
- Consider **benzodiazepine** reversal
  - Start with ***0.2mg flumazenil IV***, repeat Q1 min up to 1mg total
- Check blood **glucose** level & treat hypo or hyperglycemia
- Check **ABG** and **electrolytes**
  - rule out ***CO2*** narcosis and ***hypo or hypernatremia***
- Check patient **temperature** and actively warm if <34 degrees C
- Perform **neuro exam** if possible: examine pupils, symmetric motor movements, gag reflex/cough
- Obtain **stat head CT** and consult neurology/neurosurgery to rule out possible CVA
- If residual sedation/coma persists despite the evaluating all possible causes, ICU admit with neurology follow up, frequent neuro exams, repeat head CT in 6-8hrs if no improvement

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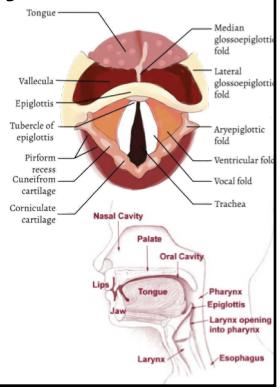
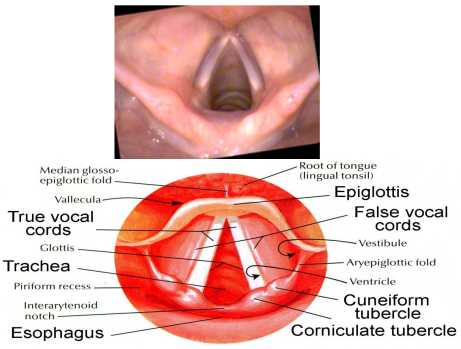
Laryngospasm & Aspiration

Airway Anatomy Review

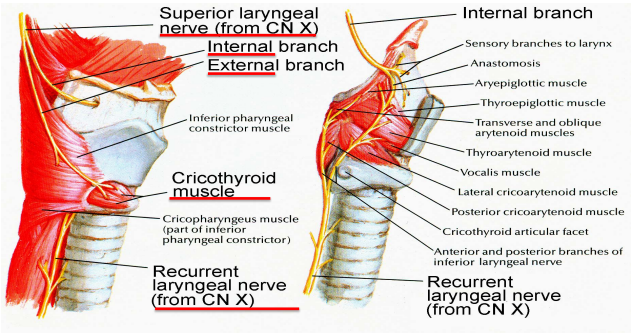
- Pharynx - passage that connects posterior nasal and oral cavities to the larynx and esophagus.
  - Nasopharynx
  - Oropharynx
  - Laryngopharynx – starts at epiglottis and extends to cricoid cartilage at the level of C6 vertebrae



Laryngeal Anatomy



Laryngeal Anatomy



Airway Innervation Review

Larynx is innervated by CNX – RLN and SLN are branches of the vagus nerve (CNX)

- Recurrent Laryngeal Nerve
  - Provides sensation to pharynx, middle ear, posterior one third of the tongue and the carotid body/sinus
  - Provides sensation to larynx from the glottis (vocal cords) and below
  - Provides motor innervation on all intrinsic muscles of the larynx **except the cricothyroid muscle*
- Superior Laryngeal Nerve
  - Internal branch
    - **Sensory** nerve innervating *larynx above the glottis* (vocal cords) up to the epiglottis.
    - Afferent sensory input between epiglottis and vocal cords
  - External branch
    - **Motor** nerve to **cricothyroid muscle** which *tenses and adducts the vocal cords*

Glossopharyngeal nerve does **not innervate the larynx

Laryngeal Anatomy: Innervation

Nerve	Motor	Sensory
Recurrent Laryngeal (from CN X)	Thyroarytenoid (tensor) Lateral Cricoarytenoid (adductor) Transverse Arytenoid (adductor) Posterior Cricoarytenoid (abductor, tensor)	Subglottic mucosa
Superior Laryngeal (from CN X)		
• Internal branch	None	Epiglottis/Tongue Base Supraglottic mucosa
• External branch	**Cricothyroid (adductor)**	Anterior subglottic mucosa

Note: The RLN innervates all of the intrinsic muscles of the larynx except for the cricothyroid muscle (innervated by the external branch of SLN). RLN injury produces unopposed superior laryngeal n. activity (adduction) on the vocal cord

Laryngospasm

What is laryngospasm?
- Closure of the true vocal cords (+/- the false vocal cords) from the action of laryngeal muscles → occlusion of the glottis/laryngeal inlet
- Mediated by Superior Laryngeal Nerve
- Consequences include hypoxia, hypercapnia, and negative pressure pulmonary edema (NPPE)

Predisposing Factors
- Stage 2 of anesthesia (excitement/delirium)
- Light anesthesia relative to surgical stimulation
- Mechanical irritants to the airway
  - Blood, mucous, vomit, secretions
  - ETT (RR 12) > LMA (RR 7) > facemask
  - Suctioning
- Reactive airway disease, eczema, asthma, rhinitis, smoking exposure
- Recent upper respiratory tract infection (< 1 month); (RR 3.4)
- Pediatrics ~3x more likely than adults

Laryngospasm

Prevention
- Ensure adequate anesthetic depth before manipulation or movement of patient
- Clear secretions before extubation- suction
- Topicalize larynx with local anesthetic (LTA)
- Adequate reversal of muscle relaxants to assist in secretion management

Detection
- Inspiratory stridor/ airway obstruction
- Increased inspiratory effort/tracheal tug
- Paradoxical chest/abdominal movements
- Auscultate with stethoscope over trachea to listen for degree of obstruction & airway patency
- Poor $EtCO_2$ tracing, desaturation, bradycardia, central cyanosis

Laryngospasm

Management - *CALL FOR HELP EARLY!*
1. Jaw thrust, head tilt, oral or nasal airway
   - Larson's Maneuver: a jaw thrust with bilateral pressure on the body of the mandible anterior to the mastoid process
2. Suction oropharynx
3. CPAP via bag-mask ventilation with 100% O_2 May need pressure ~40 mmHg
4. Deepen anesthesia with IV agent (e.g. Propofol)
   - Consider IV lidocaine, as well
5. Succinylcholine 10-20 mg IV, maintain airway with bag-mask or ETT until spontaneously breathing
   - May also give succinylcholine via IM route
6. Reintubation vs. prepare for surgical airway
7. Monitor for post-obstructive negative pressure pulmonary edema (NPPE)

Negative Pressure Pulmonary Edema

Causes
- Laryngospasm
- Upper airway obstruction/ETT obstruction (e.g. biting on tube)
- Incidence: 0.1% of anesthetics

Risk Factors
- Laryngospasm
- Young (20-40 years), healthy (ASA I-II), male (80%)

Presentation
- Laryngospasm, chest wall retraction
- Frothy, serosanguinous or bloody airway secretions
- ↓S_pO_2, ↑ET_{CO2}, hypotension, large $P_{(A-a)}$ gradient
- CXR with pulmonary edema

Negative Pressure Pulmonary Edema

Pathogenesis
- Negative intrathoracic pressure (up to -100 cmH_2O)
- ↑RV preload → ↑pulmonary hydrostatic pressure
- ↑RV preload → interventricular septum shift → LV diastolic dysfunction → ↑PCWP
- Hypoxia, hypercapnea, acidosis → Hypoxic Pulmonary Vasoconstriction (HPV) & ↑PVR
- Stress response → ↑SVR and ↑LV afterload
- Alveolar-capillary membrane leak → protein loss

Treatment
- Supportive care (O_2, IPPV, PEEP/CPAP)
- Conservative management until process reverses (usually quickly); consider volume and/or pressors PRN.
- Lasix is usually NOT helpful
- Severe cases may require reintubation or ECMO

Pulmonary Aspiration

Predisposing Conditions
- Full stomach or unknown NPO status (e.g. trauma)
- Intra-abdominal process (bowel obstruction, ileus, inflammation)
- Gastroparesis (narcotics, DM, uremia, EtOH, infection, severe pain/trauma)
- GE junction incompetence (GERD, hiatal hernia, scleroderma)
- Pregnancy, obesity
- Neuromuscular disease processes
- Difficult intubation and/or prolonged bag-mask ventilation

Pulmonary Aspiration

Prevention

- Follow NPO guidelines for routine elective cases
- Use metoclopramide, H_2-blockers, and antacids in high-risk patients
- Consider awake, regional anesthetic (e.g. spinal or epidural for c-sections)
- Consider awake, upright intubation and/or RSI
- If present, leave NGT to suction
- Apply cricoid pressure until ETT position confirmed
  - Although this practice is debated, one could contend it is considered the 'standard of care.'
- Minimize bag-mask PPV and/or keep pressure <20 cmH_2O
- Extubate after recovery of protective reflexes
- Remain vigilant: aspiration occurs during emergence and maintenance and not just during induction

NPO Guidelines

Ingested Material	Minimum Fasting Period
Clears	2 hours
Breast Milk	4 hours
Formula	6 hours
Non-human Milk	6 hours
Light Meal	6 hours
Fatty Meal	6-8 hours

- There is no evidence for the routine use of metoclopramide, H_2-blockers, proton pump inhibitors, antiemetics, or anticholinergics in preventing aspiration or in reducing its morbidity/mortality.
- If given preoperatively, only nonparticulate antacids (Sodium Citrate) should be used.

Pulmonary Aspiration

Aspiration Pneumonitis

- Sterile, chemical pneumonitis caused by aspiration of acidic and particulate material
- Highest risk in patients with gastric volume >25 ml and pH <2.5.
- Aspiration does NOT always cause pneumonia

Management

- Place patient in head-down position (allow to drain from lungs)
- Immediately suction pharynx and trachea before PPV
- 100% O_2, intubate (if needed), apply PEEP or CPAP
- Supportive care - monitor for chemical PNA/ARDS
- Possible bronchoscopy for removal of particulate matter, if suspected
- Antibiotics are not necessary unless subsequent infection develops (or, as happens more commonly in pediatrics, fecal matter is aspirated)
- Steroids are not indicated

ITE tips

- Pt has hoarsness and weak voice after extubation, which nerve is injured?
  - Unilateral RLN injury
    - Cords assume a paramedian position and cannot move laterally on the affected side
    - Can still move air usually
- Which nerve is the afferent limb of laryngospasm reflex?
  - SLN
- Pt has aphonia and airway obstruction after extubation, which nerve/nerves are injured?
  - Bilateral RLN injury

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Oxygen Failure in the OR

Etiology

Loss of Pipeline Oxygen
- Exhaustion of central O_2 supply.
- Obstruction of central O_2 supply line to OR.
- O_2 shutoff valve in OR is off.
- Obstruction or disconnection of O_2 hose in the OR.
- Failure of O_2 regulator in the anesthesia machine.

Faulty Oxygen Supply
- Crossing of pipelines during construction/repairs.
- Incorrect connection of gas hoses.
- Non-O_2 cylinder at the O_2 yoke.
- Wrong gas in the O_2 cylinder.
- Broken flowmeter.

Prevention of O2 Failure is KEY

Selected Daily Pre-anesthesia Machine Checks
- Verify Auxiliary Oxygen Cylinder (with regulator) and Self-Inflating Manual Ventilation Device (ie AMBU) are Available and Functioning
- Verify pipeline gas pressure ≥50 psi.
- Verify that pressure is adequate (>50%) on the spare oxygen cylinder mounted on the anesthesia machine
- Verify calibration of O_2 analyzer and that the low O_2 alarm is audible
  - Self calibrating O_2 monitors should read 21% when sampling room air

Supply-Side Safety Features
- Color-coded gas tanks
- DISS, PISS, and Quick Connects

Anesthesia Machine Safety Features
- Flow-meter arrangement
- O_2:N_2O ratio controller
- Oxygen supply failure protection device ("fail-safe valve")

Medical Gas Cylinders

- Designations A (smallest) through H (largest)
- E-cylinders most common in the OR (portable)
- H-cylinders most common in central pipeline
- O_2 E-cylinders are used as backup in case of pipeline supply failure (2200 psi)
  - Attached to anesthesia machine via **pin index safety system (PISS)** and must be checked prior to delivering anesthetics (maintain in closed position unless needed to avoid depletion)

Gas Cylinders

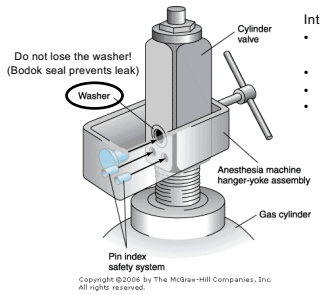
Gas	E-Cylinder Capacity (L)	Pressure (psi)	Color (USA)	Color (Int'l)	Form
O_2	660	1900	Green	White	Gas
Air	625	1900	Yellow	White & Black	Gas
N_2O	1590	745	Blue	Blue	Liquid + Gas*
N_2	650	1900	Black	Black	Gas

*Because N2O is stored as a liquid, the psi of 745 will not decrease until the tank is at 1/4 capacity (400 L); you must weight the tank to know how full it is.

How long can you use an O_2 tank starting at 430 psi running at 5 L/min? (remember 3 psi = 1 Liter for oxygen)

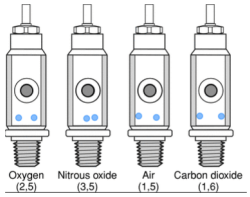
Answer = PSI ÷ 3 ÷ Flow rate.
430 ÷ 3 ÷ 5 = 29 minutes

Pin Index Safety System



PISS for Gas Cylinders

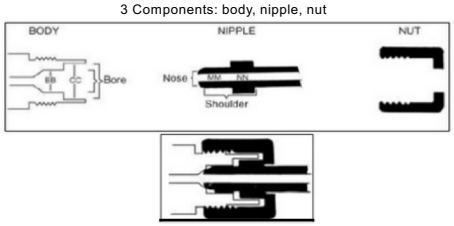
International Standard:
- Physical Barrier to ensures that the correct gas is connected to the correct cylinder type
- Pin positions for each gas is unique
- Do not break or force pins to connect
- Possible to bypass safety check if pins are eroded, damaged, or corroded

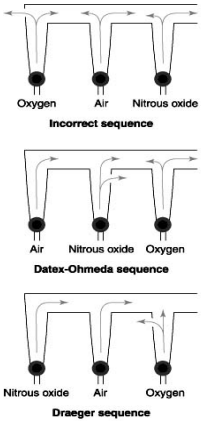


Diameter Index Safety System

Standard for non-interchangeable, removable connections where color-coded gas hoses at pressures of ≤200psi connect to the wall outlet of each gas with different diameter threaded connectors (tighter connection than Quick Connect)

3 Components: body, nipple, nut





Flowmeter Arrangement

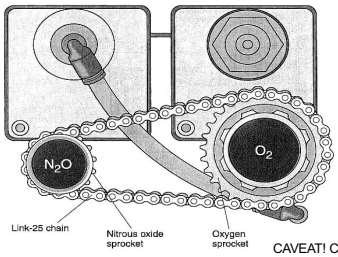
- A leak in the upstream O_2 flowmeter ("Incorrect sequence") results in a hypoxic gas mixture.
- A leak in the Datex-Ohmeda or Draeger flowmeter arrangements may deliver less Air or N_2O than expected, but the mixture will NOT be hypoxic because **O_2 is closest to the FGF outlet**.

Note: Flowmeter governed by viscosity at low "laminar" flows (Poiseuille's law); **density** at high "**turbulent**" flows

Q	Flow rate
P	Pressure
r	Radius
η	Fluid viscosity
l	Length of tubing

$$Q = \frac{\pi \Pr^4}{8\eta l}$$

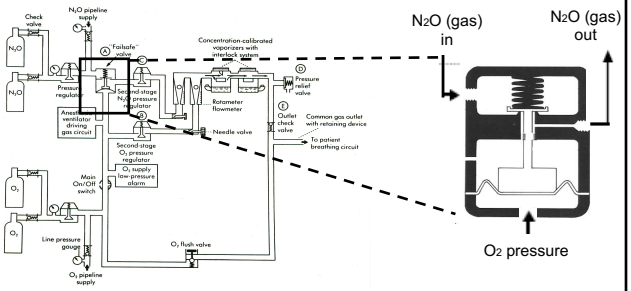
O_2:N_2O Proportioning System "hypoxic guard"



Linkage mechanisms between flow valves can be either mechanical (above), pneumatic, or electronic to prevent FiO2 <25% when N_2O is used.

CAVEAT! Can still deliver hypoxic mixtures IF there are:
- Incorrect supply gas connections
- Errors in or defective components/links
- Downstream leaks
- Introduction of third inert gas like helium

Oxygen Failure Protection Device



Fail-safe Valve: If P_{O2} falls <30 psi, N_2O cannot flow AND alarm sounds (Datex-Ohmeda)
Note: Does not prevent 100% N_2O delivery! (this is accomplished by the proportioning system)

Detection

- Pressure gauges fall (pipeline, tanks)
- Low O_2 alarms (O_2 supply failure, F_iO_2 analyzer)
- Flowmeters fall (O_2 and other gases)
- O_2 flush inoperative
- Bellows inoperative
- Apnea alarms (spirometer, capnograph)
- Increasing O_2 flow makes the problem worse
- Hypoxemia, hypercarbia
- Arrhythmias, bradycardia, cardiac arrest

Management

- Notify surgeon, call for help, use emergency manual.
- Verify problem
- Disconnect patient from machine and ventilate with Ambu bag. **Do not use auxiliary O_2 on machine as the source is the same**. If patient needs higher FiO_2 call for extra E-cylinders early.
- To keep patient connected to anesthesia machine, open O_2 cylinder on the back of the anesthesia machine and disconnect from pipeline O_2.
- Use manual ventilation to conserve O_2.
- D/C supply lines if crossed pipelines suspected.
- Check pipeline gas supply content prior to restarting
- Consider switching to TIVA/maintain low gas flows to avoid awareness until cause of failure is known.

Management of O_2 Pipeline Failure

Table 1 Anaesthetists' management of oxygen failure.

Category	Description	*n* (%)
Pre-op machine check	Checks rotameters and circuit	15 (75%)
	Identifies empty oxygen cylinder before case	6 (30%)
	Checks self-inflating bag present	5 (25%)
Immediate response to pipeline failure	Turns on machine cylinder	20 (100%)
	Requests more oxygen cylinders	20 (100%)
Conserves oxygen	Voices need to conserve oxygen	3 (15%)
	Reduces gas flows	7 (35%)
Uses oxygen above essential requirements	Uses ventilator during failure	12 (60%)
	Uses self-inflating bag with high flow oxygen during failure	8 (40%)
Reconnection	Used untested pipeline gas supply	20 (100%)
Anaesthesia during pipeline failure	Volatile or TIVA	12 (60%)
	Relies on sedative infusion alone	6 (30%)
	No anaesthesia or sedation	2 (10%)

Commonly missed steps:

- Identifying empty O2 E-cylinder before case start
- Identifying easily accessible self-inflating bag prior to every case
- Conservation of O2 (use lowest gas flows required and use manual ventilation)
  - Electrically powered ventilators do not consume O_2, Pneumatic powered may use O_2!
- Re-test pipeline gas supply if central failure prior to administration to patient

ITE tip

How long can you deliver oxygen at 4L/min flow if the E-cylinder reads 1500 psi?

Answer: about 2 hours

- A full E-cylinder is approximately 1900 psi or 660 liters of oxygen
- An E-cylinder that reads 1500 psi is about 78.9% full, containing about 521 liters of oxygen
- 521 liters/4L/min = 130 minutes (or roughly 2 hours)

ITE tip

The device on anesthesia machines that most reliably detects delivery of hypoxic gas mixtures is the:

a. Fail-safe valve
b. O2 analyzer
c. Second-stage O2 pressure regulator
d. Proportion-limiting control system

Answer: b. The O2 analyzer is located in the inspiratory limb of the breathing circuit to provide maximum safety. Because the O2 concentration in the fresh-gas supply lune may be different from that of the patient's breathing circuit, the O2 analyzer should not be located in the fresh-gas supply line.

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Anaphylaxis

Overview

- Allergic reactions are an important cause of intraoperative morbidity and mortality (3.4% mortality)
- Account for approximately 10% of all anesthetic complications
- More than 90% of reactions occur within 3 minutes, but can be delayed by hours with variable presentation
- Can be difficult to identify cause, as multiple drugs are given early in anesthetic (e.g. antibiotics often given soon after rocuronium)
- Usually the faster the reaction, the more severe the course
- Anaphylaxis involves a combination of systemic (pulmonary, CV, GI) and dermal signs & symptoms, all due to release of vasoactive mediators, which:
  - ↑ mucous membrane secretions
  - ↑ bronchial smooth muscle tone
  - ↑ capillary permeability
  - ↓ vascular smooth muscle tone
- Anaphylactic & anaphylactoid reactions present similarly and are **treated IDENTICALLY.**

Anaphylaxis vs. Anaphylactoid

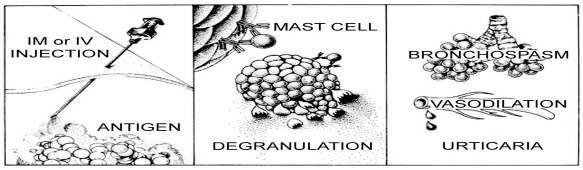
Anaphylaxis

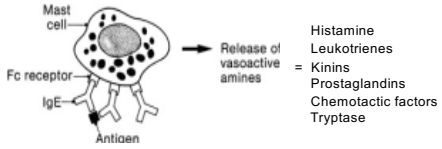
- **IgE-mediated** type I hypersensitivity reaction
- Sensitization happens with **prior exposure** to an antigen, which produces antigen-specific IgE antibodies that bind to Fc receptors on mast cells and basophils
- Upon re-exposure to the antigen, IgE antibodies then cross-links Fc receptors causing degranulation and release of stored mediators (vasoactive)
- Reaction is *independent of dose*

Anaphylactoid

- **Direct activation** of mast cells and basophils by non-IgE mechanisms, or activation of the complement system
- **May occur on first exposure** to an antigen
- Reaction is *dose-dependent*

Sequence of Events





Signs and Symptoms

System	Symptoms (e.g. MAC/Regional)	Signs (e.g. General or Regional)
Respiratory	Dyspnea Chest tightness	Hypoxia Wheezing Laryngeal edema Pulmonary edema ↓ Compliance ↑ PIPs
Cardiovascular	Dizziness ↓ LOC	Hypotension Dysrhythmias Pulmonary HTN Tachycardia Cardiac arrest
Cutaneous	Itching	Perioral edema Periorbital edema Flushing Hives
Renal		↓ urine output
Gastrointestinal	Nausea, vomiting, diarrhea	
Hematologic		DIC

Can have variable presentations with some or all of these signs & symptoms

Common Triggering Agents

Table 1. Drugs Involved in Perioperative Anaphylaxis

Substance	Incidence of perioperative anaphylaxis (%)	Most commonly associated with perioperative anaphylaxis
Muscle relaxants	69.2	Succinylcholine, rocuronium, atracurium
Natural rubber latex	12.1	Latex gloves, tourniquets, Foley catheters
Antibiotics	8	Penicillin and other β-lactams
Hypnotics	3.7	Propofol, thiopental
Colloids	2.7	Dextran, gelatin **>> Albumin > HES 6%**
Opioids	1.4	Morphine, meperidine
Other substances	2.9	Propacetamol, aprotinin, chymopapain, protamine, bupivacaine

*There is a wide variation in the reported incidence of anaphylaxis amongst common precipitants.
- **Rocuronium's** incidence of anaphylaxis is quoted anywhere from 1/3,500 to 1/445,000
- **Sugammadex**: quoted around 1/35,000

Latex Allergy

- Obtain a careful history:
  - Healthcare workers (frequent exposure)
  - Children with spina bifida (multiple prior medical procedures/exposures)
  - Urogenital abnormalities (h/o multiple urogenital catheters)
  - Food allergies (tropical fruits [mango, kiwi, avocado, passion fruit, bananas], fig, chestnut)
- Establish a latex-free environment:
  - Schedule patient as first case of the day
  - **Most equipment & supplies are latex-free**; if available, have a cart of latex-free alternatives available
  - Remove tops of multi-dose vials when drawing up drugsl with significant latex allergy
- Prophylactic steroids and/ or H1-blockers (uncertain benefit)
- Prepare for the worst, hope for the best

Management

Acute Phase

1. Stop administration of offending antigen (muscle relaxants, latex, antibiotics, colloids, blood, contrast, etc.)
2. Notify surgeon **AND** call for help
3. Increase FiO_2 to 100%
4. In hypotensive, consider discontinuation of agents that may augment hypotension. Give other amnestic agent (e.g. midazolam, ketamine)
   1. inhaled anesthetics causes vasodilation
   2. narcotic infusions suppress sympathetic response
5. Give **IV fluid** bolus
   1. May require many liters, 2-4 L *or more!* (compensate for vasodilation, hypotension)
6. Give **Epinephrine** (α-1→ supports BP; β-2→ bronchial smooth muscle relaxation)
   1. Start **10-100 mcg IV boluses** for hypotension; escalate as needed
   2. Start early epinephrine infusion (0.02-0.3 mcg/kg/min)
   3. If no IV, give **0.3-0.5 mg IM** in anterolateral thigh, repeat q5-15 min
   4. ACLS doses (0.1-1 mg) for cardiovascular collapse
7. Consider vasopressin bolus or norepinephrine infusion
8. Treat bronchospasm with **albuterol** and epinephrine (if severe)

Management

Secondary Treatment

- **Intubation**, especially if signs of angioedema
- **Invasive lines**: large-bore IVs, arterial line, central venous catheter, foley catheter
- Drugs to consider after stable
  - **H_1-blocker**: diphenhydramine 0.5-1 mg/kg IV
  - **H_2-blocker**: ranitidine; not a first-line agent, but low risk of harm
  - **Steroids:** decrease airway swelling, **prevent recurrent symptoms** in biphasic anaphylaxis
    - Hydrocortisone 0.25-1 g IV, or methylprednisolone 1-2 g IV

Post event

- Send labs
  - Serum **tryptase** (peaks < 60min post event)
  - Serum **histamine** (peaks < 30 min post event)
- Biphasic anaphylaxis is known phenomenon
  - Consider monitoring patient for 24 hours post-recovery
  - Consider keeping intubated and sedated
- Refer for postoperative allergic testing

Prevention

- Obtain a careful history:
  - Previous allergic reactions?
  - Atopy or asthma?
  - Food allergies?
- Give a test dose, followed by slow administration
  - reduces *anaphylactoid*, but not anaphylactic reactions
- Use blood products judiciously
- Use prophylactic steroids and/ or H1-blockers
  - H1-blockers: no clear benefit; may blunt early signs before presenting as full-blown episode
- If no alternative agent, may pursue desensitization
- Obtain consultation from an allergist if necessary

ITE tip

Evidence of an anaphylactic reaction to atracurium 1 to 2 hours after the episode could be best established by measuring blood levels of:

a. Tryptase
b. Laudanosine
c. Histamine
d. Bradykinin

Answer: a.

Testing for an Allergy

- Testing may not be necessary if there is a clear temporal association between drug and reaction
- Measurement of serum mast cell tryptase levels can help establish the diagnosis in uncertain cases of anaphylaxis (although can be negative in ~35% of pts)
- Follow up with an allergist may be useful for establishing a diagnosis (e.g. skin testing)

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Local Anesthetics

Local Anesthetics (LA)

- Provide anesthesia and analgesia by disrupting the conduction of impulses along nerve fibers
- LAs block voltage-gated sodium channels
  - Reversibly bind intracellular alpha subunit
  - Inhibit the influx of sodium, thus preventing an action potential from being reached
  - Resting membrane and threshold potentials are not affected

Physiochemical Properties

- Local anesthetics are weak bases in equilibrium:

Nonionized (lipid-soluble) ⇄ ***Ionized (water-soluble)***

B (neutral) + H^+ ⇄ HB^+

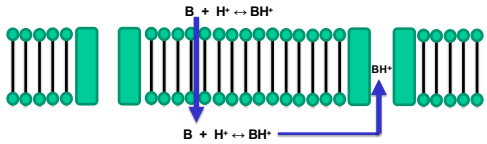
Lower pKa
Higher tissue pH

Higher pKa
Lower pH

$$\text{pK}a = pH - log\frac{[B][H^+]}{[BH^+]}$$

Mechanism of Action & Physiochemical Properties

1) Nonionized (base, lipid-soluble) form crosses neuronal membrane
2) Re-equilibration in axoplasm between the 2 forms
3) Ionized (cationic, water-soluble) form binds to the Na^+ channel



Nonionized local anesthetic (B) diffuses through axonal lipid bilayer.
Ionized form (BH+) reversibly binds alpha subunit of Na channel.

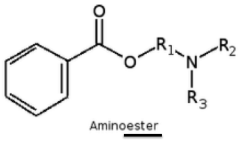
- Having a **pKa closer to physiologic pH** means a greater fraction of nonionized form (able to cross the neuronal membrane) for a **faster onset**
- Conversely, in an infected (acidic) environment, the pKa will be further from the environmental pH and have a slower onset

Characteristic	Association
Speed of onset	1. pKa (degree of ionization) 2. Concentration *procaine and chlorprocaine have a high pKA but quick onset due to concentration effect
Potency	Lipid solubility
Duration of action	Protein binding (alpha-1 amino glycoprotein binds drug and carries it away for metabolism)

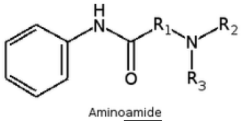
Amides	pKa	Esters	pKa
Lidocaine	7.9	Procaine	8.9
Mepivicaine	7.6	Chloroprocaine	8.7
Prilocaine	7.9	Tetracaine	8.5
Bupivacaine	8.1		
Ropivacaine	8.1		

Note: chloroprocaine is unique in that it has a fast onset NOT because of its pKa but because its low systemic toxicity (due to rapid metabolism by pseudocholinesterase) allows us to use relatively high concentrations

Local Anesthetic Structure



Aminoester



Aminoamide

3 Major Chemical Moieties
1. Lipophilic aromatic benzene ring
2. **Ester OR Amide** linkage
3. Hydrophilic tertiary amine

Local anesthetics are weak bases
pKa > 7.4

Categories

Category	Drugs	Metabolism
Esters	Cocaine 2-Chloroprocaine Procaine Tetracaine	Plasma **pseudocholinesterase** metabolism & RBC esterase (hydrolysis at ester linkage)
Amides (*i* before –caine) *Am**i**de anesthetics have 2 **i**'s	L**i**docaine Bup**i**vacaine Rop**i**vacaine Mep**i**vacaine Et**i**docaine Levobup**i**vacaine	**Liver metabolism:** Aromatic hydroxylation, N-dealkylation, Amide hydrolysis *methylparaben preservative is metabolized to *p*-Aminobenzoic acid (PABA), which can induce allergic-type reactions in a small percentage of patients

Routes of Delivery

- Topical
- IV
  - Systemic local anesthetics inhibit inflammation
  - Decrease the hemodynamic response to laryngoscopy
  - Decrease postoperative pain and opioid consumption
  - Can reduce MAC requirements by 40%
- Epidural
- Intrathecal (Spinal)
- Perineural (Regional)
  - Small diameter (A delta) and myelinated nerves (more concentrated effect at nodes of Ranvier) are most susceptible, thus sensory loss precedes motor weakness

Drug	Onset	Max dose (mg/kg)	Max dose with Epi (mg/kg)
Lidocaine	Rapid	4.5	7
Mepivacaine	Medium	5	7
Bupivacaine*	Slow	2.5	3
Ropivacaine (S-racemate)	Slow	4	N/A
Tetracaine	Slow	1.5	N/A
Chloroprocaine	Rapid	10	15

***Bupivacaine** (Marcaine) is commonly used by surgeons for infiltration at 0.25% (2.5mg/ml), with max dose 2.5mg/kg
***i.e. <u>can use a max volume of 1cc/kg</u>** (70kg patient gets max 70cc)

LAST (Local Anesthetic Toxicity)

Systemic absorption by injection site (vascularity)

- IV > tracheal > **I**ntercostal > **C**audal > **E**pidural > **B**rachial plexus > **A**xillary > **L**ower extremity (sciatic/femoral) > **S**ubcutaneous

  *mnemonic: ICEBALLS

Rate and extent of systemic absorption depends on:

1) dose
2) the drug's intrinsic pharmacokinetic properties
3) the addition of a vasoactive agent (i.e. epinephrine)

*Bupivacaine is **more cardiotoxic** (high binding to resting or inactivated Na+ channels; also slower dissociation from channels during diastole)

<u>CNS toxicity</u>

- Local anesthetics readily cross the blood brain barrier
- Clinical manifestations: lightheadedness, tinnitus, tongue numbness, metallic taste → CNS excitation (block inhibitory pathways) → CNS depression, seizure → coma

<u>Cardiovascular toxicity</u>

- Dose dependent blockade of Na channels → disruptions of cardiac conduction system → bradycardia, ventricular dysrhythmias, decreased contractility, cardiovascular collapse/circulatory arrest
- Bupivacaine has higher risk of CV toxicity
- Approximately 3x the amount of local anesthetics are required to produce cardiovascular toxicity than CNS toxicity
- Addition of epi allows for early detection of intravascular injection and also increases the max allowable dose

Treatment of LAST

- Initial management:
  - Call for intralipid kit
  - ABCs: do you need to support circulation/airway?
  - Stop local anesthetic
  - Give benzodiazepines for seizure
  - Reduce individual epinephrine doses to <1 mcg/kg
  - **AVOID**: vasopressin, Ca channel blockers, Beta blockers, local anesthetics, and propofol (can further decrease cardiac contractility)
- Initiate early intralipid (IL) therapy
  - Rapidly give **1.5 cc/kg bolus** of 20% intralipid IV (*max 3 doses)
  - Start infusion at 0.25 cc/kg/min (*max rate 0.5 cc/kg/min)

    *if patient remains unstable, may repeat bolus and increase infusion rate

ITE tip

Nerves in order of sensitivity to local anesthetics:

Most sensitive → least sensitive:

B fibers > A fibers > C fibers

Small myelinated fibers (B) are easiest to block, and have least surface area. Unmyelinated nerves (C) are the most resistant because surface area of available channels to block is largest.

ITE tip

The correct arrangement of local anesthetics in order of their ability to produce cardiotoxicity from most to least is:

a. Bupivacaine, lidocaine, ropivacaine
b. Bupivacaine, ropivacaine, lidocaine
c. Ropivacaine, bupivacaine, lidocaine
d. Lidocaine, ropivacaine, bupivacaine

Answer: b.

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Malignant Hyperthermia

Basics

Definition

- A **hypermetabolic** crisis that occurs when susceptible patients are exposed to a triggering anesthetic agent (halogenated anesthetics or succinylcholine)
  - Underlying defect is abnormally increased Ca^{2+} levels in skeletal muscle resulting in sustained muscle contraction
- Calcium pump attempts clearance → increased ATP usage
- Results of hypermetabolic rate
  - increase O2 consumption, CO2 production, severe lactic acidosis, hyperthermia, risk of rhabdomyolysis, hyperkalemia, and arrhythmia

Genetics

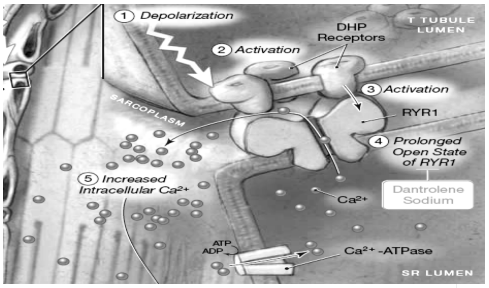
- Genetic hypermetabolic muscle disease
- 80% of cases: RYR-1 receptor mutation (affects calcium release channel in sarcoplasmic reticulum)
  - **Autosomal dominant** inheritance **with variable penetrance and expression**, but autosomal recessive forms also described (especially that associated with King-Denborough syndrome)
- At least 6 chromosomal loci identified, but >80 genetic defects associated with MH

Basics

Incidence

- Rare, see in 1:15,000 pediatric vs. 1: 40,000 adult patients
- Most common in young males
  - Almost no cases in infants; few in adults >50 years old
- The upper Midwest has highest incidence in US (geographic variation of gene prevalence)
- MH may occur on a patient's 2nd exposure to triggers
  - nearly 50% of MH episodes had at least one prior uneventful exposure to an anesthetic
- Risk factors include personal/family history of MH, pediatric age, comorbid myopathies, caffeine intolerance, history of unexplained fevers/cramps/weakness, h/o exercise induced rhabdomyolysis, trismus on induction (precedes 15-30% of MH)
  - Associated Disorders: Central Core disease, Multi-minicore Disease and King Denborough Syndrome

Excitation-Contraction Coupling



MH: Depolarization → **mutant RYR-1 receptor *remains* open** → unregulated calcium from SR into intracellular space → sustained contraction & increased activity of Ca-ATPase to remove Ca → heat generation, CO_2 production, metabolic acidosis, and rhabdomyolysis/hyperkalemia

Sequence of Events

1. Triggers
   - All halogenated **inhalational agents** (not N_2O)
   - **Succinylcholine**
2. Increased Cytoplasmic Free Ca^{2+}
   - Masseter muscle rigidity (**trismus**)*; more common if succinylcholine used
     - If there is rigidity of other muscles in addition to trismus, the association with MH is absolute
   - Total body rigidity
3. Hypermetabolism
   - Increased CO_2 production (most sensitive and specific sign of MH!) and metabolic acidosis
     - Note sympathetic surge of **increased HR and BP**
   - Increased O_2 consumption (decreased ScvO2)
     - Body will compensate with **tachypnea**
   - Increased heat production
     - A **late** sign of MH; **temperature** can rise 1-2˚C every 5 minutes
   - Increased utilization of ATP to clear calcium: metabolic acidosis
4. Cell Damage & Rhabdomyolysis
   - Leakage of K^+, myoglobin, CK *(may see dark-colored urine)*

**not all patients with trismus will go on to have MH, and not all MH cases will be heralded by trismus*
Earliest recognized signs of MH= **muscle rigidity, tachycardia, and hypercarbia*

Sequence of Events (2)

5. Secondary systemic manifestations
   - Rhabdomyolysis→
     - Acute renal failure
     - Hyperkalemia/Arrhythmias
     - DIC / Hemorrhage / Compartment syndrome
   - Metabolic exhaustion: increased cellular permeability→
     - Whole body edema & Cerebral Edema
   - Death (due to DIC and organ failure); previously 70% mortality, now 5% with dantrolene

*****The signs & symptoms of MH are seen often in the OR and are non-specific*****

Clinically, you may first see **trismus**, but often **hypercarbia** will be your first sign
- Without another reasonable explanation for this (hypoventilation, pneumoperitoneum), you should start looking for other signs.
  - Any increased oxygen consumption? (decreased SpO_2 or $ScvO_2$?)
  - Increased metabolic & sympathetic activity? (increased $etCO_2$, HR, temperature, **lactate**)
  - Signs of rhabdo or any electrolyte abnormalities? (Hyperkalemia/arrhythmias, CKMB, urine myoglobin/blood tinged urine)

Differential Diagnosis

Neuroleptic Malignant Syndrome (NMS)*	More common in patients receiving antidopaminergic agents or in withdrawal from dopamine agents as in Parkinson's, usually develops over days rather than minutes to hours
Thyroid Storm*	Usually associated with hypokalemia
Sepsis	fever, tachypnea, tachycardia, metabolic acidosis
Pheochromocytoma	↑HR, ↑ BP, but normal $EtCO_2$ and Temp
Drug-induced	e.g. ecstasy, cocaine, amphetamines, PCP, LSD
Serotonin Syndrome	associated drugs interactions MAOIs + merperidine or MAOIs+ SSRIs
Iatrogenic Hyperthermia	
Hypercarbia from CO2 insufflation for laparoscopy	see ↑$EtCO_2$ with tachycardia

*Dantrolene can also treat both of these conditions

Treatment - Acute Phase

Immediate Actions	• **Call for Help & obtain MH cart**; inform team and start preparing **dantrolene or ryanodex** • **D/C volatile agents and succinylcholine** (no need to change machine or circuit) **Switch to 100% O2 with high flows >10L/min; increase minute ventilation • Halt surgery vs. finish ASAP with TIVA; arrange for ICU bed • Call MH hotline (1-800-MH-HYPER) • **Labs**: ABG, lactate, K+/electrolytes, CK, Coags; place foley to monitor UOP
Dantrolene (interferes with RYR-1 Ca^{2+} channel)	• **2.5 mg/kg IV push q5min;** patient may need >10mg/kg; continue giving until stable. Give through large bore IV or central line (risk of phlebitis); assign several people to prepare this • 1 vial = 20mg Dantrolene (dissolve in 60 cc sterile water); solution has mannitol **New Ryanodex (250mg vial in 5cc sterile water) • Continue until stable (decrease in EtCO2, rigidity, and tachycardia); continue dantrolene infusion **0.25mg/kg/hr for at least 24 hrs**
Treat Acidosis	• Hyperventilate patient • **Sodium Bicarbonate** 1-2 mEq/kg
Treat hyperkalemia & ARF	• **$CaCl_2$** (10mg/kg) or Calcium gluconate (30mg/kg); Bicarbonate, hyperventilate • **Insulin and glucose** (10 units in 50cc D50) • **Sodium bicarbonate** (1-2 mEq/kg) • Diuresis; **urine output goal > 1-2cc/kg/hr** to help prevent pigment induced nephropathy/ARF and reduce hyperkalemia; consider IV fluids, diuretics, and alkalinize urine
Treat dysrhythmias	• Avoid CCBs (may promote hyperkalemia and depress cardiac output) • Treat hyperkalemia and acidosis; if refractory, may need to add an antiarrhythmic
Treat temp	• Cool if temp >39 degrees C (cooling blankets, ice, cold NS, lavage stomach/bladder/rectum)
Labs	• ABG, lactate, K+/electrolytes, CK, urine myoglobin, Coagulation studies

Treatment – Post Acute Phase

Admit to ICU	• ICU admission for at least 24 hrs (recrudescence rate 25%)
Continue monitoring	• Labs: serial ABG, lactate, Electrolytes (K^+, Ca^{2+}), CK/serum myoglobin, Urine myoglobin, Coags • $EtCO_2$, temp, urine output/color • *Watch for DIC and renal failure*
Counsel patient and family	• Future precautions • Refer to MHAUS • Refer patient and family to nearest Biopsy Center for follow-up

Who is Susceptible to MH?

- Autosomal dominant inheritance pattern
  - All closely related family members considered susceptible in absence of testing (even if they had prior uneventful anesthetics)
- Several rare musculoskeletal disorders linked to MH
  - **Central Core Disease**
  - **King Denborough Syndrome**
  - **Multi-minicore myopathy**
- Other disorders:
  - Muscular dystrophy and other neuromuscular diseases, upon exposure to triggering agents, have weak associations with MH-like events
    - Avoid succinylcholine as can cause rhabdomyolysis; controversial whether to avoid volatile anesthetics
    - Experts believe brief exposure is a small risk (i.e. inhalational induction in pediatric patients)
  - History of exertional heat stroke or exercise-induced rhabdomyolysis - some suggestion that these people may harbor genetic changes found in MH-susceptible individuals

Susceptibility Testing

Caffeine-Halothane Contracture Test (CHCT)

- Takes fresh muscle biopsy and exposes to triggers
- Gold Standard; used to rule-out MH
  - **High Sensitivity >97%**
  - Specificity 80-93%
  - 10-20% false positive rate but zero false negative rate
- Available at 9 U.S. testing centers

Molecular Genetics

- *RYR1* mutation screening
- **Low sensitivity**, but **high specificity** (rule-in criteria)
  - **Only screens for 20% of recognized mutations**
- Typically reserved for patients with a positive CHCT, relatives of known MH susceptibility, or patients with highly suspicious MH episode

Prevention in Susceptible Patients

1. Machine

- Change circuit and CO_2 absorbent
- Remove or disable vaporizers
- Can use activated charcoal filters on both inflow and outflow of circuit
- Refer to anesthetic machine regarding time required to flush machine (FGF of 10 L/min for ≥20 minutes)
  - During case, keep flows > 10L/min to avoid "rebound phenomenon" (release of dissolved residual volatile anesthetic agent)

2. Monitors

- Standard ASA monitors, especially temperature and ET_{CO2}

3. Anesthetic

- Avoid succinylcholine and volatiles
- All other non-triggering agents are okay (including N_2O)

4. Emergency

- Know where to find the MH cart
- Have dantrolene or rhyanodex available

ITE tip

Which of the following findings is NOT consistent with a diagnosis of malignant hyperthermia?

a. PaCO2 150 mm Hg
b. MVO2 50 mm Hg
c. pH 6.9
d. Onset of symptoms an hour after end of operation

Answer: b. MH reflects a hypermetabolic state. Clinical signs include tachycardia, tachypnea, arterial hypoxemia, hypercarbia, metabolic acidosis, hyperkalemia, hypotension, muscle rigidity, trismus after succinylcholine administration, and increased temperature. Mixed venous oxygen tension would be very low (normal MVO2 is 30-35, so an elevated MVO2 of 50 would not be consistent with MH, and answer b is incorrect).

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- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 5th ed.* New York: McGraw-Hill Companies, Inc., 2013.
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- UCLA Department of Anesthesiology (http://www.anes.ucla.edu/dept/mh.html)

Pre-operative Evaluation

Chart Review

- A pre-op template can be found and downloaded at http://ether.stanford.edu/ca1_new/ca1_preop_new1.html
- Link includes a useful guide for chart review and how to assess relevant comorbidities

Pre-op Tips

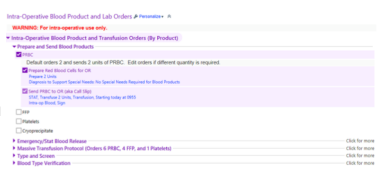
- Don't forget to include other pertinent studies, such as PFTs, TTE or stress echo results, Holter or Zio patch results, device interrogations, etc.
- Check the media and care everywhere tabs for outside studies
- Review the Anesthesia sub-tab under the chart review tab to see prior anesthetics and airway/procedure notes
- Add the "Pre-Admission/Pre-op Orders" set to your favorites
  - You can use this order set for day-of-surgery labs, rapid COVID-19 testing, pre-op IV placement if appropriate, ordering blood products to be available in blood bank, and medications (e.g. PO analgesics) to be given in pre-op

Anesthetic Plan

- To start, consider referring to Jaffe's *Anesthesiologist's Manual of Surgical Procedures,* or talk with a senior resident
- Who is the surgeon? What is the expected procedure duration?
- Patient positioning
  - This may affect your line and monitor placement
  - May also have hemodynamic implications (e.g. steep Trendelenburg or reverse Trendelenburg)
- Is special monitoring required?
  - Is there an indication for an arterial or central line?
  - Is there an indication for an EEG monitor (Sedline, BIS)?
  - Is neuromonitoring part of the procedure plan?

Anesthetic Plan

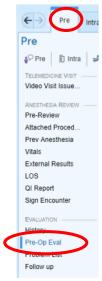
- Blood products
  - Based on anticipated blood loss and patient's pre-operative CBC, consider ordering blood products
  - Add order set "Intra-Operative Blood Product and Lab Orders" to favorites
  - Separate orders to prepare products and send to OR (aka call slip)



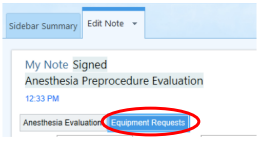
Anesthetic Plan

- Induction
  - Choice of induction agent
  - RSI vs standard
  - Any relevant comorbidities that may change your induction plan (most commonly cardiac or pulmonary comorbidities)
- Have a well-thought-out airway plan, as well as a backup plan
- Maintenance
  - Inhalational agent vs TIVA
  - Analgesia
  - Anticipate need for pressors, fluid resuscitation, frequent labs
- Emergence
  - Anticipate need for a more controlled emergence (e.g. high risk for bleeding into an enclosed space)
  - Consider the need for post-op intubation or monitoring in the ICU

Ordering Extra Equipment



- Pre-op navigator → Pre-op eval → Equipment requests
- Equipment requests placed by 10 pm the night before for first cases will be seen by anesthesia techs and equipment will be ready in the OR for your AM setup



Device Management

- Patients with PPMs and AICDs present unique management challenges
- Important questions to ask about managing AICDs and pacemakers intra-operatively:
  - What is the site of surgery? If above the umbilicus, there is a risk of interference
  - Is the patient pacemaker dependent?
  - What type of device does the patient have, and what were the results of the last interrogation?
  - What effect will placing a magnet over the device have?
  - Does the patient's device need to be interrogated or reprogrammed before or after surgery?
- When in doubt, best to contact the device rep
- As a backup, you can also page the "Pacemaker Inpatient Service" through Smartpage

Day of surgery

Ask

- Verify name and procedure
- Verify allergies and assess for severity/reaction - for example, you might still use cefazolin if a patient has a mild penicillin allergy but not if they had anaphylaxis
- Ask about NPO status
- Ask about personal history of problems with anesthesia or family history if first anesthetic
- Go through relevant medical problems that you read about the night before, fill in gaps in knowledge and verify what you already know
  - Ask all patients about activity level (Assess METS), chest pain/trouble breathing, GERD symptoms
- Verify that they took the medications they should or held the ones they should not

Day of surgery continued

Exam

- Do an airway exam: Mallampati, thyromental distance, cervical ROM, loose/missing teeth, ask about denture/removable devices
- Do a cardiac and pulmonary exam
- Do a neurological assessment if they have known deficits or the surgery could impact their neurologic status such as invasive spine surgery
- Note any clubbing, deformities, bruising, and gauge level of difficulty for IV access
- *Any other relevant examination for their history or procedure*
- Make sure their existing IV is running well or help the nurses place one if they have difficulty

Day of surgery continued

Consent and Planning

- **You may have a plan but your patient still has a say!** You may want to do a MAC but they may really want to do a GA. They may refuse the epidural you recommend. If you are planning for any procedures, they need to be consented. Walk them through the risks and benefits of the plan.
- Make sure they are consented for blood if you anticipate needing it intra-op
- ***Anesthesia is scary.*** Please help your patient understand what to expect when they go to the OR. I talk my patient through the roll back, moving to the other bed, the monitors, the mask, how the medications will feel going into the IV etc. I also let them know what will happen after they sleep, i.e putting in a breathing tube that comes out before they wake up and any more lines they may wake up with.
- Inform all patients about risks of anesthesia: sore throat, risk to teeth/gums, PONV etc. When patients are at elevated cardiac risk or other risk such as ocular injury during prone positioning, they should be educated on this.
- Your patient should be both comforted by you and appropriately informed!

Pre-operative Testing and Medication Management

Ordering Tests

Probability of an abnormal screening test result

Number of independent tests	Probability of abnormal test
1	5 percent
2	10 percent
4	19 percent
6	26 percent
10	40 percent
20	64 percent
50	92 percent

Before ordering any testing, consider what you will do with the result, the likelihood that it will be positive/negative and whether or not it will actually change your anesthetic management

Basic Labs

- CBC:
  - >65yo and major surgery
  - <65yo and major surgery w/expected significant blood loss
  - Neuraxial technique
- BMP:
  - >50yo and intermediate or major surgery
    - For creatinine (renal function)
  - Diabetics
- HbA1c: only for cardiac/vascular surgery
  - Diabetics
    - Fasting glucose <300- okay to proceed, >300 case by case basis
    - HbA1c <9- okay to proceed, >9 case by case basis
- LFTs: rarely indicated in absence of specific hx/exam findings
- Coags: not routinely recommended for routine surgery in the absence of risk factors
- TSH: should be normalized in patients with moderate-severe hypothyroidism undergoing elective surgery
  - mild/subclinical- may proceed
- Urinalysis: not routinely recommended
- Pregnancy: all women of child-bearing age

Studies

- EKG:
  - Asymptomatic and low risk surgery: No
  - Risk factors: may be reasonable
    - May omit if low risk surgery
  - Symptoms: Yes
  - High risk surgery: Yes
- CXR: indicated >50yo and cardiopulmonary disease and AAA/upper abdominal/thoracic surgery
  - BMI >40: may be reasonable (to detect underlying disease)
- PFTs: only to aid in diagnosis of patients with unexplained dyspnea
- Echo: only obtain if would order anyway in the absence of surgery
  - patients with dyspnea of unknown origin
  - suspected HF
  - HF with changed clinical status (worsening dyspnea)
  - HF without prior TTE or >1yr since last echo
  - suspected asymptomatic LV dysfunction
  - other specific indications for echocardiography, such as suspected valve disease

Medication Management

Diabetes:

- Stop orals, continue basal insulin (1/2 or full dose); schedule in AM
  - Applies to well-controlled BG, if poorly controlled may need to give closer to usual dose
  - reasonable to continue Metformin if low risk (d/c day of surgery)
    - if renal dz d/c 24-48hrs prior
- SGLT-2: stop 3-4 days prior to surgery
- restart orals when eating regularly

Estrogens:

- OCPs, Postmenopausal replacement, SERMs: continue if low VTE risk, if high VTE risk stop 4 weeks, 2 weeks, and 2 weeks (3 days if raloxifene) before surgery
  - continue SERMs if for CA tx, but consult with oncology recommended

GI:

- Continue PPIs, H2RBs
  - Cimetidine may have drug-drug interactions

Hypertension:

- Continue BB, CCB, alpha-2 agonists
  - Stop ACE/ARB/Diuretic on day of surgery
    - failure to restart ARBs within 48 hours after surgery has been associated with increased 30-day mortality

Hypolipidemic:

- Statin: continue
- Hold others 1 day before surgery

Medication Management Continued

- Aspirin: should be held prior to intracranial neurosurgical procedures, middle ear surgery, posterior eye surgery, intramedullary spine surgeries, and possibly prostate surgeries
- NSAIDS: hold 5 days prior to surgery
  - Salsalate has no anti-platelet activity (non-acetylated NSAID)
- Perioperative management of anticoagulants/antiplatelets is nuanced and beyond the scope of this guide

Beta-Blockers:

- BBs started on the day of surgery decrease nonfatal MI but increase risks of stroke, death, hypotension, and bradycardia; even if the POISE-1 is excluded
- Continue in those taking them chronically (class I)
- Start in:
  - Pts. w/moderate-severe myocardial ischemia noted in preoperative risk stratification tests (class IIb)
  - Pts. w/3 or more RCRI risk factors (class IIb)
- Begin > 1 day before surgery (class IIb); >2-7 days ideal
  - target HR 60-70
- Do not start on the day of surgery (class III)

Medication Management Continued

Pulmonary:

- Continue all inhalers
- Discontinue theophylline day before surgery (narrow therapeutic range)

Psych:

- Continue most psychiatric medications
  - may need to avoid Meperidine/Tramadol and Ephedrine (MAOIs)
  - continue TCAs but obtain EKG (QT prolongation)
    - patients on low doses or in whom the risk of perioperative arrhythmia is increased, the agents should be tapered off over a period of 7 to 14 days before surgery
  - SSRIs can increase the risk of bleeding (NSGY); may discontinue 3wks before if high-risk

Vitamins/Supplements:

- Discontinue 1wk prior

Steroids

- Do NOT need stress dosing:
  - any dose <3wks
  - 5mg Prednisone/day or equivalent
  - 10mg Prednisone every other day or equivalent
- Presumed to have suppressed HPA axis:
  - >20mg Prednisone/day or equivalent for >3wks
  - Any patient with clinical Cushing's syndrome
- HPA axis testing indicated for intermediate risk (5-20mg >3wks)
  - *rarely happens at Stanford
- Continue usual dose for minor procedures or procedures under local anesthesia
- Sources very for optimal dose of "stress dose steroid" but often 50-100mg Hydrocortisone can be given with induction if there is concern
  - Continue stress dosing perioperatively should be done with Endocrinology assistance (often 25-50mg q8hrs x24hrs)

In general, patients are probably given stress dose steroids more often than is needed. (4mg Decadron = 27mg Prednisone = 107mg Hydrocortisone)

Preoperative Risk Assessment

*2014 ACC/AHA Algorithm

Preoperative Risk Assessment

Step 1: Determine Urgency to Proceed

- Emergent (or not): <6hrs ← STOP, proceed to surgery
- Urgent: <24hrs
- Time sensitive: <6wks (Onc)
- Elective: w/in 1yr

Step 2: Determine if ACS (or not)

- Active Cardiac Conditions: (should be stabilized before surgery)
  - Unstable coronary syndromes: Unstable angina (class III or IV), Active myocardial infarction (occurring within the last 7 days), Recent myocardial infarction (occurring within the past 8 to 30 days)
  - Decompensated congestive heart failure: New York Heart Association (NYHA) class IV, new onset or worsening dyspnea
  - Significant arrhythmias: High-grade atrioventricular block, symptomatic ventricular arrhythmias, uncontrolled supraventricular tachycardia including atrial fibrillation, symptomatic bradycardia, new ventricular tachycardia
  - Severe valvular disease: Severe aortic stenosis or symptomatic aortic stenosis, symptomatic mitral stenosis

Preoperative Risk Assessment

Step 3: Estimate Risk

- RCRI
  - Hx of ischemic heart disease (do not count PCI for stable CAD)
  - Hx of heart failure
    - HF (9% risk) is 3x higher risk than CAD
      - Symptomatic heart failure morbidity is 49% for major surgery
      - Asymptomatic systolic heart failure morbidity is 23%
      - Asymptomatic diastolic heart failure morbidity is 18%
  - Hx of stroke or TIA
  - DM which requires insulin
  - CKD (creatinine > 2.0)
  - High-risk surgery (intrathoracic, intraperitoneal, or suprainguinal vascular)
- Rate of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest
  - 0 factors: 0.4%
  - 1 factor: 1.0%
  - 2 factors: 2.4%
  - ≥ 3 factors: 5.4%
  - if MI in last 3mo, risk is 37%
    - 94% of PMIs occur by POD2
  - does not capture risk factors for noncardiac causes of perioperative mortality and only one-third of perioperative deaths are due to cardiac causes

Preoperative Risk Assessment

Step 3: Estimate Risk, alternative risk calculators

- ACS-SRC: riskcalculator.facs.org/RiskCalculator
- NSQIP (MICA)
  - Type of surgery
  - Dependent functional status
  - Abnormal creatinine
  - ASA Class
  - Increased age
    - patients who have fallen 3 or more times in the previous 6mo have a 100% chance of perioperative complication
- VQI: for vascular surgery
- Risk of particular surgery
  - High risk: aortic and vascular surgery
    - ≥ 5% risk of MI or cardiac death
  - Intermediate risk: intraperitoneal, intrathoracic, head/neck, orthopedic, prostate
    - 1-5% risk
  - Low risk: endoscopic, ambulatory, breast, cataract
    - < 1% risk
- BNP >92 and NT-proBNP >300 are independent risk predictors for post-op MI or death within 30 days

Preoperative Risk Assessment

Step 4: If low risk, proceed to surgery

- low risk = <1%
- high risk = ≥ 1%
- low risk patients or patients with good functional capacity (≥ 4 mets) require no further testing, proceed to surgery

Preoperative Risk Assessment

Step 5: Assess exercise capacity in high risk patients

- Ability to perform 4 mets: walk up a flight of stairs or walk on level ground at 3-4mph, walk up a hill, perform heavy work around the house
  - 1 MET is defined as 3.5 mL O2 uptake/kg per min, which is the resting oxygen uptake in a sitting position
- DASI (Duke Activity Status Index) is the most sensitive non-invasive estimate of functional capacity

Preoperative Risk Assessment

Step 6: Determine Need for Further Testing

- Patients with poor functional capacity:
  - 0 risk factors: no further testing--> proceed to surgery
  - ≥ 1 risk factor and poor functional capacity--> do stress test if otherwise indicated or will impact perioperative care
    - no study has shown that stress testing improves perioperative outcomes
- There are few circumstances in which testing should be performed solely because the patient has upcoming surgery
- Perioperative implications of coronary revascularization are nuanced and beyond the scope of this guide

References

- Ether (Resources for Anesthesia Research and Education). The Preoperative Evaluation. http://ether.stanford.edu/ca1_new/ca1_preop_new1.html, 2020.
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OR Setup

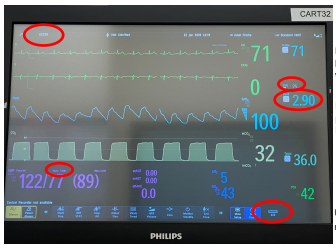
Monitors

- Setup:
  - Make sure BP cuff is set to cycle automatically Q1min for induction
  - Add or remove waveforms to your monitor if needed for Art line, CVP, etc.
  - Make sure vitals are populating into EPIC
    - If not, it is much easier to fix ahead of time rather than after the fact
- You can route video from the Cmac in each 500p OR to the room monitors for intubation

Monitor Tips

If your monitor does not automatically transfer vitals to Epic record, you can manually enter the device name, which is found here in the top left corner of the monitor

Remember to check that your BP cuff is set to cycle at the desired frequency



PVI (or PPV if using an A line) can be used as a surrogate marker of volume status

Perfusion index is the ratio of pulsatile to non-pulsatile flow. If low, may indicate poor perfusion

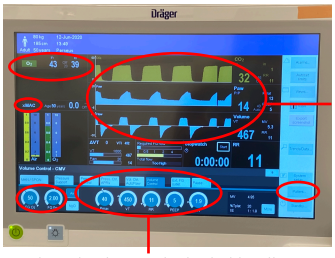
Use this icon to troubleshoot monitor/cable setup

Monitor Tips

Fraction inspired and end-tidal gases appear here

The anesthesia machine will calculate MAC based on the age you have entered

Set your FiO2 and total fresh gas flows here



Waveforms for:
- end-tidal CO2
- peak airway pressures
- flows (tidal volume)

Set patient age and weight here

Ventilator modes and settings can be selected and changed here

Alaris pumps

- Power on → options → anesthesia mode → enable
- To set up channels:
  - You will use either a syringe on a syringe pump with primed microbore tubing, or if using a drip (such as propofol or pressors), you will spike the medication and run it through an Alaris infusion set
  - Once tubing is primed and placed into the channel, hit channel select → guardrails drugs (most commonly used medications can be found here) → then finish the setup by entering patient weight and starting infusion rate
  - If the medication you're looking for isn't under guardrails drugs, you should be able to find it by name under "all drugs"
  - If your patient has a high BMI, consider whether to dose your drips by lean body weight

    Ideal body weight = 22 x height (in m)^2

    Lean body weight = Ideal body weight x 1.2

Alaris pumps, cont.

- Hit pause to leave drips on standby
- If you anticipate running at least 2 drips during a case, consider asking the anesthesia techs for a fluid carrier
- To setup the fluid carrier, place the primed tubing into the channel, select basic infusion, and set your carrier fluid rate

Anesthetic Drug Dosing

Please contact us with edits/revisions/suggestions

Airway Equipment

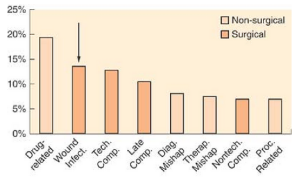
- At a minimum, always have an ETT with stylet and 10 mL syringe, either video or standard laryngoscope, and appropriately sized oral airway
- Always have a backup airway plan, with supplies available
  - Bougie is available in all ORs
  - LMAs may also be useful for airway rescue and are stocked in the anesthesia machines
  - Video laryngoscopy is always available with a Cmac in each 500p OR (also consider whether you need a Glidescope available)
  - If you anticipate a difficult airway, talk with your attending about other airway adjuncts and management
  - Ambu bag available for anesthesia machine failure
- For any cases you plan to spin 180 or flip prone, the patient should have a soft bite block in place and you should have an accordion and straight connector ready for your circuit

Drugs

- Standard setup:
  - 1-2 20cc syringes of Propofol 10mg/ml
  - Rocuronium 10mg/ml prefilled syringe or Succinylcholine 20mg/ml
  - +/- 2mg Midazolam, 1mg/kg 1-2% Lidocaine, 100-250mcg Fentanyl
  - Rescue drugs:
    - Phenylephrine & Ephedrine come in pre-filled syringes
    - Lidocaine, atropine, and code-dose epinephrine (100 mcg/ml or 1 mg in 10 ml) come in ready-to-assemble syringes
  - Antibiotic: depends on case (most commonly 2-3g Cefazolin)
  - PONV PPx: most patients will get 4mg Ondansetron +/- 4-8mg Dexamethasone +/- other
  - Drips: depends on case, most commonly propofol infusion and/or phenylephrine infusion
- If you anticipate needing to give other pressors or antihypertensives, discuss with your attending what to have drawn up and available

Perioperative Antibiotics

Why Antibiotics?



In 1984 a study including 51 acute care hospitals in New York State found that surgical site infection (SSI) was the **most common adverse surgical event** (and the second most common adverse event overall).

Perioperative antibiotic prophylaxis – administration of abx prior to surgery to prevent surgical site infections, **but best practice also includes sterility (surgeon and instruments), skin prep (clipping hair, allowing skin antiseptic to dry)**

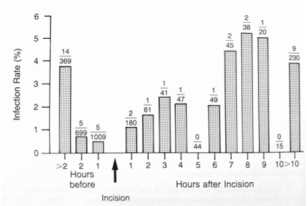
SSIs- now a marker of quality of care in the US, Medicare no longer reimburses for certain SSIs (ie mediastinitis after cardiac surgery, SSIs post-bariatric surgery & some orthopedic procedures)

Barash, Paul G. *Clinical Anesthesia*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009. Print.

Timing of prophylaxis

- Antibiotic therapy should be given **within 60 min** (ideally: 15-45 mins) prior to surgical incision for **adequate serum drug tissue levels** at incision.
  - Exception IV vanco/cipro (requires longer infusion)
- If a proximal tourniquet is used, the entire antibiotic dose should be administered **before** the tourniquet is inflated.
- Exceptions to pre-incision antibiotics:
  - check for active ongoing antibiotic therapy, may not be indicated for surgery, surgeon declined, or delay until after a specimen is sent for culture.

Timing of prophylaxis



Rates of Surgical-Wound Infection Corresponding to the Temporal Relation between Antibiotic Administration and the Start of Surgery

- The number of infections and the number of patients for each hourly interval appear as the numerator and denominator, respectively, of the fraction for that interval. The trend toward higher rates of infection for each hour that antibiotic administration was delayed after the surgical incision was significant (z score = 2.00; P<0.05 by the Wilcoxon test).

Classen DC, et. Al. (1992) The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *The New England Journal of Medicine* 326:281-286.

Types of Wounds (per CDC/NHSN)

- Clean procedures (1.3 to 2.9% rate of surgical site infection)
  - Uninfected operative wound closed primarily in which no inflammation is encountered and respiratory, GI, genital, or uninfected urinary tracts are not entered.
  - Common skin flora: CoNS, MSSA/MRSA and strep
- Clean-contaminated procedures (2.4 to 7.7% rate of SSI)
  - Operative wounds in which the respiratory, GI, genital, or urinary tracts are entered under controlled conditions and without unusual contamination.
  - Common bugs are skin flora, gram-negative rods, *Enterococci*. If surgery involves a viscus, pathogens reflect endogenous flora of the viscus or nearby mucosa
- Contaminated procedures (6.4 to 15.2% rate of SSI)
  - Open fresh, accidental wounds. Also, operations with major breaks in sterility, gross spillage from the GI tract, and incisions in which acute non-purulent inflammation is encountered
- Dirty or infected (7.1 to 40.0% rate of SSI)
  - Includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera.

2017 SHC Surgical Antimicrobial Prophylaxis Guidelines*

Surgery	Preferred Agent	Beta-lactam allergy
Cardiac Surgery/Vascular/Thoracic Cardiac device insertion (PM implant) Other General Surgery (hernia, breast) Neurosurgery Orthopedics Plastic Surgery	Cefazolin	Vancomycin (preferred) *Clindamycin can be used as an alternative. Based on 2015 SHC Antibiogram, 81% MSSA susc to clinda vs 100% MSSA susc to vanc*
Cardiac Surgery w/ prosthetic material	Cefazolin + Vancomycin	Vancomycin
Gastroduodenal	Cefazolin	Vancomycin + Gentamicin
Biliary Tract	Cefazolin	Metronidazole + Levofloxacin
Colorectal, Appendectomy	Cefazolin + Metronidazole	Metronidazole + Levofloxacin
Gynecological (hysterectomy/Cesarean)	Cefazolin	Clindamycin + Gentamicin
Urology *These are EMPIRIC abx recs when no preoperative urine cx available or culture negative. Ask urology team for recs.*	*If clean:* Cefazolin *If clean contaminated (eg open or lap with ileal conduit)- cefoxitin* *If prosthetic material involved, should add gentamicin x1 dose*	Gentamicin + Clindamycin[1] *If clean: (skin incision only)- clinda[1]* *If clean-contaminated:* metronidazole + *levofloxacin* [1]sub vanc for clinda if MRSA due to clinda poor urinary penetration
Head & Neck	Clean or ear/sinonasal: Cefazolin *If contaminated (include oral mucosa breach)- Cefazolin+ Metronidazole*	Clindamycin

*Based on 2013 consensus guidelines from American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS) and the Society for Healthcare Epidemiology of America (SHEA)

Selected 2017 SHC Dosing and Re-dosing Guidelines

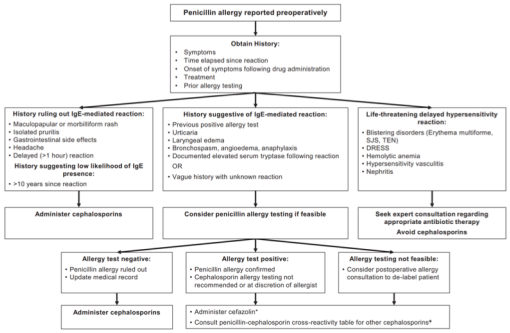
Antimicrobial	Recommended Dose	Re-dosing (hrs)	Notes
Cefazolin	**<120kg- 2g** **>120kg- 3g** **Peds: 30mg/kg, max 2g**	**4**	Can bolus over 3 minutes**
Clindamycin	**900mg**	**6**	**Give over 30 minutes**
Vancomycin	**<80kg – 1g** **80-99kg- 1.25g** **100-120kg- 1.5g** **>120kg- 2g** **Adult and Peds 15mg/kg**	**12**	**Give over 30-60 minutes**, or <10mg/min; whichever is longer) Can be given 60-120min prior to incision (long half life)
Ampicillin-Sulbactam	3g	2	**Give over 15-30 minutes**
Aztreonam	2g	4	
Cefoxitin	2g	2	
Ceftriaxone	2g	24	
Ciprofloxacin	400mg	8	**Give over 60 minutes** Contraindicated in pregnancy
Ertapenem	1g	24	Give over 30 minutes
Gentamicin	5 mg/kg (single dose) If CrCl<20, 2mg/kg (single dose or consult Rx)	24	Dilute to <1mg/cc **Give over 30-120 minutes** (risk of ototo/nephrotoxicity with bolus)
Levofloxacin	500mg	24	
Metronidazole	500mg	12	**Give over 20-60 minutes**

*As a general rule, for drugs with a greater therapeutic index, you can administer them faster

Allergies and Interactions

- Penicillins and 1st & 2nd generation cephalosporins have similar side change with some risk of cross-reactivity
  - Cephalothin (1st cephalosporin) marketed in 1964; cross-reactivity with penicillin allergy noted to be 5-10%. This over-generalization of cross-reactivity has resulted in the avoidance of all cephalosporins, not just cephalothin, in patients labeled as penicillin allergic
  - Some of this cross-reactivity is historically thought to be due to cross-contamination during manufacturing
- True incidence of allergy in patients with a reported history of PCN allergy is less than 10%.
  - Only *IgE-mediated* reaction (type I, immediate hypersensitivity reactions) are true allergic reactions.
  - Encourage skin testing to simplify future antibiotic choices
- The cross-reaction rate between PCN and 1st & 2nd cephalosporins is 1-10%
  - Cross-reaction rate between 3rd generation cephalosporins and PCN approaches 0%!
- History of PCN allergy is a general risk factor for allergic manifestations to antibiotic administration that may not be specific to cephalosporins

Perioperative Antibiotic Decision Algorithm

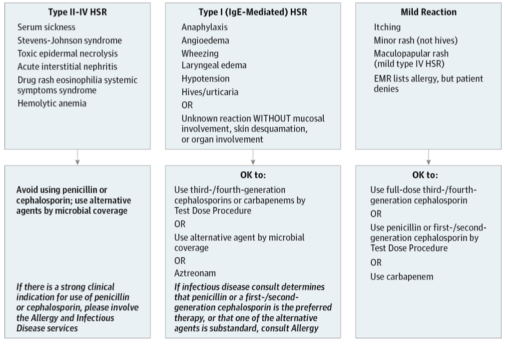


From Vorobeichik, et. al. Anesthesia & Analgesia, 2018

Allergies and Interactions

- If the allergic reaction to PCN is only erythema or pruritis, many attendings still give a cephalosporin, but always check with your attending
  - However, hx of anaphylactic reaction to PCN is an absolute contraindication to cephalosporins.
- Type 1 anaphylactic reaction to antimicrobials occur 30-60 minutes after administration
- **Test dose**: Not always done. However, it may be prudent to give 1ml of the antibiotic first to see if the patient will have a reaction. This test dose only decreases the *anaphylactoid* reaction, not anaphylaxis
- Allergic reactions are **more likely from neuromuscular blockers** than antibiotics

Penicillin Allergy Pathway for Antibiotic Prescriptions



From Vaisman, et al. JAMA 2017

Endocarditis Prophylaxis

- Patients at increased risk:
  - Prosthetic cardiac valve (including transcatheter-implanted prostheses and homografts)
  - Prosthetic material used for cardiac valve repair, including annuloplasty rings and chords
  - Previous history of infective endocarditis
  - Unrepaired cyanotic congenital heart disease or completely repaired congenital heart defect within the first 6 months.
  - Cardiac transplant patients who develop cardiac valvulopathy
- Procedures at risk
  - Dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa (not all dental procedures)
  - Upper respiratory tract: only if it is incised or biopsied
  - Procedures on infected skin, skin structure, or musculocutaneous tissue
  - GI/GU: prophylaxis no longer recommended
- **Bacterial Endocarditis prophylaxis**
  - **Ampicillin** 1-2gm IV, 30min prior to surgery AND **Gentamicin** 1.5mg/kg IV, 30min prior to surgery
    - IF PCN allergic, use cefazolin or ceftriaxone 1gm IV, or clindamycin 600mg IV
- Mitral valve prolapse/HoCM/Bicuspid AV **do not** need prophylaxis because while there is increased risk for IE, the most serious adverse outcomes of IE do not usually occur in patients with these conditions.

ITE tip

Which of the following antibiotics does NOT augment neuromuscular blockade?

a. Clindamycin
b. Neomycin
c. Streptomycin
d. Erythromycin

Answer: d. Cephalosporins also do not affect neuromuscular blockade.

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- 2017 SHC guidelines for Adult Patients- Antimicrobial Surgical Prophylaxis

Topics for Discussion

1. Your IV infiltrates during induction. What are your options?
2. You get stuck with a needle. How do you protect yourself and the patient?
3. You can't deliver positive pressure. What are your next steps?
4. You witness an unprofessional exchange between a surgeon and a nurse/med student/resident/etc. Who should you talk to?
5. You encounter an unanticipated difficult airway. You know you're supposed to CALL FOR HELP. Who do you call and what do you ask for?
6. You inadvertently administer the wrong medication. What should you do and who should you tell?
7. Your patient tells you that he wants only the attending to perform invasive procedures. How do you respond?
8. The surgeon insists that the patient is not relaxed enough, even though you just re-dosed a NDMB 5 minutes ago. What are your options?
9. You administer antibiotics after induction. An hour later, incision has still not been made. What should you do?
10. The surgeon appears to be struggling and the patient is rapidly losing blood. The surgeon insists that he does not need help. What should you do?

Anesthesia Exams & Dates

ABA In-Training Exam (ITE)	February each year	Percentile scoring; important for fellowship programs. *Financial incentive CA-2 and CA-3 years: department awards half the cost of the ABA Advanced Written exam for each year you score >70th percentile*
ABA BASIC Exam	June of CA-1 year	Pass/Fail. No percentile reported. Award for top 10%
ABA ADVANCED Written	Post-training (July & January)	You must pass the Advanced written exam to be eligible to take Applied.
ABA Applied Exams (Oral Boards & OSCE)*	Post-training (9 sessions offered per year)	

*To help better prepare residents for the ABA Oral Boards & OSCE:
- Mock Orals are held in November & May of each year
- Mock OSCEs are held in April of CA3 year

What to study?

For the first 1-2 months of CA1 year, it is common to be exhausted after each workday. For this initial period, these resources may provide a lighter study material or reference:

- CA-1 Tutorial Textbook ← Main resource for early CA1
- Stanford Anesthesia EMERGENCY MANUAL
  - http://emergencymanual.stanford.edu/
  - Handheld pocket manuals are also available
- Jaffe's Anesthesiologist's Manual of Surgical Procedures
  - Source of clinically relevant information regarding common and not-so-common surgical procedures. It's a great reference to read the pertinent sections in preparation for your upcoming cases.
- Stanford Anesthesiology iGuide

What to study?

After you have transitioned into CA-1 year, there are many study resources available to prepare for your exams, increase your fund of knowledge, and strengthen your skills in anesthesia. Here are some recommendations to get you started:

- Question Banks
  - Truelearn (https://truelearn.com/) - subscription paid for by the department, you will receive an e-mail to activate ← **HIGHLY RECOMMENDED**
  - *Hall's Anesthesia: A Comprehensive Review*
- Textbooks
  - Core: often useful to read corresponding chapter before starting a specific rotation
    - *Morgan & Mikhail's Clinical Anesthesiology* (more readable/less detailed than Baby Miller) ← **HIGHLY RECOMMENDED**
    - *Basics of Anesthesia* (Baby Miller- many residents have found to be less readable after a long day)
  - More comprehensive: *Miller's Anesthesiology; Clinical Anesthesia (Barash)*
  - *Anesthesiology (Yao & Artusio)*
  - *Faust's Anesthesia Review* (concise short chapters to cover ITE topics) ← **HIGHLY RECOMMENDED**
- Online resources
  - Open Anesthesia: http://openanesthesia.org.
  - Learnly: https://learnly.org.
- Podcasts
  - ACCRaC: http://accrac.com/ ← **HIGHLY RECOMMENDED**
  - Stanford Anesthesia CA-1 companion podcast (coming soon!!)
- Online library
  - Lane Library: https://lane.stanford.edu/index.html (access to UpToDate, PubMed, and all major journals)

Useful Apps

- **Epic Haiku-** looking up patients, checking status of cases
- **Ether-** links to call schedule and directory
- **UpToDate**
- **ASRA Coags-** for regional anesthesia guidelines
- **Regional Anesthesia Reference, AnSo-** useful to review/refresh before blocks
- **ACGME Case Logs**
- **HospitalTree-** links to Stanford phone #s/pagers
- **Zoom**
- **Pacemaker-** IDs make and model of PPMs/ICDs
- **EchoCalc, EchoTools-** helpful to quickly lookup POCUS calculations/measurements

Other useful documents

- Rishi Kumar, MD (Cardiac/Critical Care Anesthesiologist) perioperative and critical care reference: https://rk.md/wp-content/uploads/2021/12/rk-perioperative-critical-care-sheet-dec-2021.pdf
- UCSF pediatric anesthesia reference card for weight-based dosing/ped equipment sizing: https://anesthesia.ucsf.edu/sites/anesthesia.ucsf.edu/files/wysiwyg/pdfs/PediRefCard.pdf

Subspecialty Anesthesia: Basic Sciences

Appendix

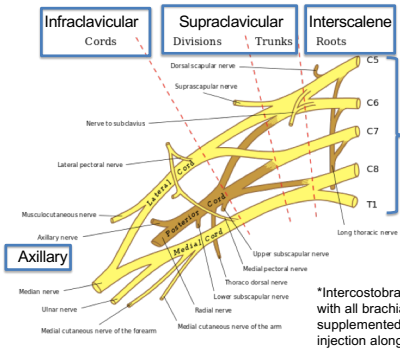
REGIONAL

Techniques

- Ultrasound-guided
  - **Primary modality** for majority of peripheral nerve localization
    - May be combined with other techniques PRN
  - High frequency sounds waves 1-20MHz
  - Hypoechoic: structures which sound waves pass through easily (appear dark)
  - Hyperechoic: structures which reflect sound waves (appear white)
  - Higher frequency transducer= high-res picture, poor tissue penetration (better for superficial nerves)
- Nerve Stimulation
  - Insulated needle concentrates electrical current at tip
  - Poor evidence to support, but classically:
    - <0.2mA current with muscle contraction = **intraneural** needle location
    - <0.5mA current with muscle contraction = proximity to motor nerve
- Field Block
  - Targets terminal cutaneous nerves
    - Ex: intercostobrachial nerve block, superficial cervical plexus block, ankle block

REGIONAL

Brachial Plexus Anatomy



*Intercostobrachial Nerve (T2) is spared with all brachial plexus blocks but can be supplemented with a subcutaneous injection along the axillary crease for procedures involving the upper arm

REGIONAL

Anatomy Tidbits

- Interscalene
  - **Phrenic nerve (C3-5) is ANTERIOR** to anterior scalene muscle
  - Dorsal scapular nerve and Long thoracic nerve travels through belly of middle scalene
  - Vertebral artery is medial and deep to anterior scalene muscle
  - Nerve roots are hypoechoic on ultrasound: **"traffic light sign"**
- Supraclavicular
  - **Subclavian artery** rests on first rib in ideal view
  - Watch out for pleura deep to ribs
- Infraclavicular
  - Axillary artery is cephalad to axillary vein
  - Cords are hyperechoic on ultrasound
  - Superficial to vessels are Pec Major and Pec Minor
- Axillary
  - Musculocutaneous (most lateral) is missed because it traverses between biceps brachii m. and coracobrachialis m.
  - **Median nerve is lateral to both radial and ulnar nerves**
    - superficial and lateral to axillary artery (10 o'clock)
  - Ulnar nerve is superficial and medial to axillary artery (around 2 o'clock)
  - Radial nerve is posterior to axillary artery (6 o'clock)
  - Axillary artery is lateral to axillary vein

REGIONAL

Upper Extremity Blocks

Approach	Sensory Block	Complications	Other
Interscalene	Roots C5-C7, shoulder, upper arm	100% phrenic nerve palsy; Horner's syndrome (myosis, ptosis, anhydrosis); RLN palsy (hoarseness); pneumothorax; avoid vertebral artery and intrathecal/epidural space	Ulnar nerve sparing + catheter
Supraclavicular	Trunks/divisions, forearm	Pneumothorax (rates improved with ultrasound); ~50% ipsilateral phrenic nerve palsy; Horner's; RLN palsy	"spinal of the arm" (single shot)
Infraclavicular	Cords, forearm, hand	Pneumothorax (less common than supraclavicular block), vascular puncture	+ catheter
Axillary	Terminal branches	Vascular uptake (LAST)	Musculocutaneous nerve sparing
Intercostobrachial	T2		Field block

Intravenous Regional Anesthesia (aka **Bier Block**, first use in 1908)

- Mechanism of Action: diffusion of local anesthetic extravascularly
- May provide dense surgical block for short (45-60 min) procedures if done correctly
- Safer for upper extremity blocks than lower extremity
- Uses a double pneumatic tourniquet system inflated in order: distal then proximal
- Risk of Local Anesthetic Systemic Toxicity if cuff deflated within 30min
- Typically use lidocaine 0.5-1% +/- adjuncts

REGIONAL

Lumbosacral plexus anatomy

- Lumbar Plexus (L1-L4, occasionally T12)
  - Lateral Femoral Cutaneous nerve (L1-L3) – sensory only
  - Femoral nerve (L2-4) – sensory and motor
    - Branches medially into saphenous nerve (sensory only)
  - Obturator nerve (L2-4) – sensory and motor
    - Sensation of medial thigh, motor of ADductors of leg
- Sacral Plexus (L5-S4)
  - Sciatic nerve (L5-S4) – sensory and motor
    - Branches into tibial and peroneal nerve PROXIMAL to popliteal crease
  - Posterior femoral cutaneous nerve (S1-S3)- sensory only
    - Sensation to posterior thigh, travels with sciatic nerve near piriformis muscle

REGIONAL

Common Lower Extremity Blocks

Approach	Anatomy/Sensory/Motor	Other
Femoral	Hip flexors; knee extensors Sensation of hip, anterior thigh, medial leg, medial ankle	Better for postop analgesia than surgical analgesia
Fascia Iliaca	Typically affects femoral and lateral femoral cutaneous nerves (lateral thigh sensation)	Two "pops" through fascia lata and fascia iliaca proximal to femoral art bifurcation
Adductor Canal	Sensation of anterior thigh, medial leg, medial ankle; underlying sartorius muscle	Less motor block than femoral
Sciatic	L4-S3 roots, posterior hip/thigh/knee/lower leg/foot	Avoids sympathectomy associated with lumbar plexus block
Popliteal	Foot and ankle sensation Medially: semimembranous, semitendinous m Laterally: biceps femoris m.	Less motor block of hamstrings
Ankle	Deep: deep peroneal, tibial Superficial: superficial peroneal, sural, saphenous nerves	Avoid epi in local anesthestic

REGIONAL

Other common blocks

- Paravertebral
  - Borders:
    - Costotransverse ligament posteriorly
    - Parietal pleura anterolaterally
    - Vertebrae and intervertebrae foramina medially
    - Ribs inferiorly and superiorly
  - Side effects: pneumothorax, hypotension, bradycardia due to **sympathectomy**
  - Common to leave catheters for post-op analgesia
  - Anticoagulation guidelines per epidural guidelines
- Intercostal
  - Arise from dorsal and ventral rami of thoracic spinal nerves
  - Run along underside of ribs with artery and vein
  - **High vascular uptake of local anesthetic**
  - Watch out for LAST, pneumothorax
- Transversus Abdominis Plane (TAP)
  - Targets **subcostal n (T12), ilioinguinal n (L1), and iliohypogastric n (L1)**
  - Fascial plane block between internal oblique and transversus abdominis plane
  - Amenable to single shot or catheter placement
- Erector Spinae
  - Paraspinal fasical plane block -> **volume dependent for analgesia**
  - Safer than paravertebral due to increased distance from pleura and spinal cord
  - Novel approach for rib fracture pain, amenable to catheter

ACUTE AND CHRONIC PAIN

Pain Basics

- Pain = an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
- Nociceptive pain – result of tissue damage to non-neural tissue
  - Due to activation of normally functioning nociceptors
  - Somatic:
    - Originates from skin, muscle, joints, bone, connective tissue
    - Sharp, throbbing and easily localizable if superficial
    - Via Aδ/C fibers
  - Visceral:
    - Originates from solid or hollow visceral organs
    - Dull, diffuse pain
    - Via visceral nociceptive afferent fibers that travel with the sympathetic efferent fibers
- Neuropathic pain
  - Damage or dysfunction of PNS or CNS nerves themselves
  - Dysesthetic (ex: burning, pricking) or paroxysmal (ex: stabbing, shooting, electric shock)
  - Includes deafferentation pain (ex: phantom limb pain), CRPS
  - Polyneuropathies and mononeuropathies
  - Less likely responds to pharmacologic treatments like opioids

ACUTE AND CHRONIC PAIN

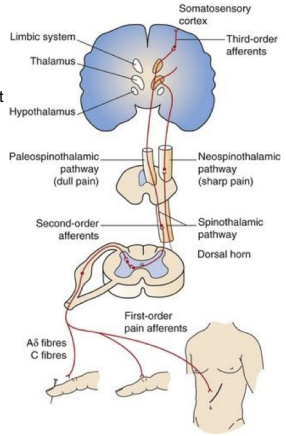
Pain Terminology

- **Allodynia**- pain due to a stimulus that does not normally provoke pain
- **Hyperalgesia**- increased pain from a stimulus that normally provokes pain
- **Hyperesthesia**- increased sensitivity to stimulation, excluding the special senses
- **Dysesthesia**- an unpleasant abnormal sensation, whether spontaneous or evoked
- **Paresthesia**- an abnormal sensation, whether spontaneous or evoked (aka not unpleasant)
- **Central sensitization**- increased responsiveness of nociceptive neurons in the CNS to their normal or subthrehold afferent input
- **Peripheral sensitization**- increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields

ACUTE AND CHRONIC PAIN

PAIN PATHWAY:

- 1st order neuron
  - Cell bodies located in dorsal root ganglia
  - Primary afferents with single axon the bifurcated (one to periphery and one to central)
  - Synapses with 2nd order neuron
- 2nd order neuron
  - Axon crosses midline and ascends in contralateral spinothalamic tract to thalamus
  - Synapses with 3rd order neuron
- 3rd order neuron
  - Sends projections via internal capsule and corona radiata to the postcentral gyrus of the cerebral cortex



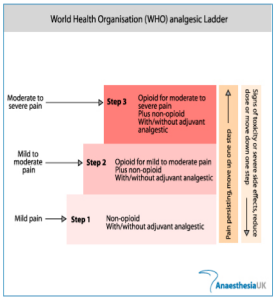
ACUTE AND CHRONIC PAIN

Pain Pathways

- Nociceptors:
  - Primarily free nerve endings of Aδ and C fibers transmitting nociception
    - Aδ – thin, myelinated, fast conduction = RAPID, SHARP, localized pain
    - C – very thin, unmyelinated, slower conduction = SLOW, DIFFUSE, DULL pain
- Dorsal Horn of Spinal Cord
  - 10 layers of Rexed laminae, esp laminae I, II, III, V in pain
  - Excitatory Neurotransmitters: Glutamate, Substance P
  - Inhibitory Neurotransmitters: Glycine, GABA
- Ascending Tracts
  - Spinothalamic- decussates and ultimately ends in somatosensoary cortex (localization of pain)
  - Spinoreticular – decussates and ends in reticular formation (affective aspect of pain)
- Descending Inhibitory Pain Modulation
  - Periaqueductal gray in midbrain and Ventromedial medulla
    - Both contain opioid receptors and endogenous opioids to inhibit pain transmission
    - Also uses norepinephrine and serotonin to modulate

ACUTE AND CHRONIC PAIN

- Neuraxial blockade of nociceptive stimuli via epidural or spinal anesthetics may blunt the metabolic and neuroendocrine stress response to surgery if it is established BEFORE incision and continued post-op
- Lidocaine bolus + infusion has analgesic, antihyperalgesic, and antiinflammatory properties (data strongest in colorectal and prostate surgeries)
- Patient-controlled analgesia (PCA) – provides better pain control, greater patient satisfaction, and fewer opioid side effects compared to PRN IV opioids



Tolerance vs Dependence

- **Opioid Tolerance** - requirement of increasing doses of opioids to maintain same analgesic effect
  - May result in less sedation, nausea, or respiratory depression
  - Constipation does not develop tolerance
  - Common issue with chronic intrathecal opioids
- **Opioid Dependence** - manifests as withdrawal when the medication is either abruptly discontinued or significantly decreased
  - May be precipitated by opioid antagonists

PEDIATRICS

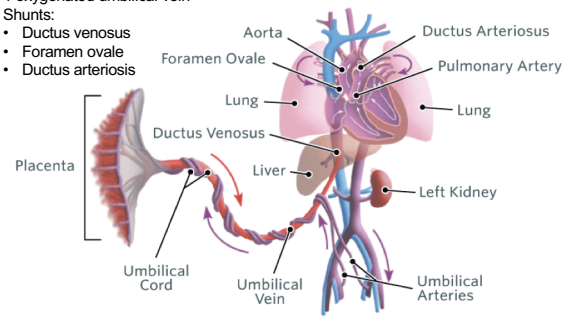
Pediatric Airway

Anatomy	Pediatric	Adult
Tongue	Large	Normal
Epiglottis shape	Floppy, omega shaped	Firm, flatter
Epiglottis level	C2-C3	C4-C5 (by 3 yo)
Trachea	Shorter (higher carina)	Longer
Larynx shape	Funnel shaped	Column
Larynx position	Angles posteriorly away from glottis	Straight up and down
Narrowest point	Cricoid cartilage	At level of vocal cords
Lung volume	250 ml at birth	6000 ml as adult

PEDIATRICS

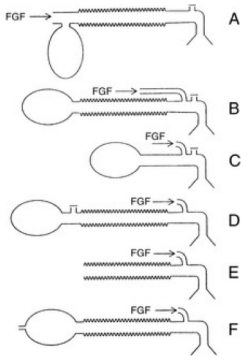
Fetal Circulation

2 deoxygenated umbilical arteries
1 oxygenated umbilical vein
Shunts:
- Ductus venosus
- Foramen ovale
- Ductus arteriosis



PEDIATRICS

Pediatric Breathing Circuits



- Lack unidirectional valves
- No CO2 absorber
- Lower airflow resistance better for peds
- Increased venting
- Efficiency determined by amount of FGF needed to prevent rebreathing:
  - Spontaneous : Mapleson A most efficient
  - Controlled: Mapleson D most efficient

OB

Maternal Physiology of Pregnancy

- CNS
  - **Decreased MAC** (40%) for all general anesthetics
  - MAC returns to normal by 3rd day postpartum
    - Likely in part due to progesterone (sedating at high doses!) and β-endorphins
  - MLAC: minimum local analgesic concentration
    - Concentration of LA leading to analgesia in 50% pts
    - **Pregnancy increases sensitivity to local anesthetics**
  - Increased epidural blood volume (engorgement due to gravid uterus obstruction of IVC)
  - Decreased CSF volume
  - Increased epidural space pressures

OB

Maternal Physiology of Pregnancy

- Respiratory
  - **Decreased FRC, Increase O2 consumption** leads to poor oxygen reserve and rapid desaturation
    - **Sharp decrease in ERV**
    - FRC returns to baseline by 48h postpartum
  - Increased minute ventilation (50%)
    - Increased Tidal Volume and Increased RR
  - Decreased PaCO2 due to hyperventilation
    - Respiratory alkalosis compensation with LOWER bicarb
  - Elevated diaphragm but larger AP diameter of chest
  - **NO CHANGE in vital capacity** and closing capacity
  - Increased upper airway edema

OB

Maternal Physiology of Pregnancy

- Cardiovascular
  - Increase cardiac output (40%), Increase SV (30%)
    - **Peak CO during active labor and immediately after delivery**
    - 2 weeks for CO to return to baseline
  - Increase HR (20%)
  - Decrease SBP (5%), Decrease SVR and DBP (15%)
  - **Cardiomyopathy** and myocardial hypertrophy
  - Normal to have Left Axis Deviation and T wave changes on EKG
  - Normal to have Systolic flow murmur and **Split S1/S3** on exam
  - NO CHANGE in PA pressure, CVP, PCWP
  - Gravid uterus compresses venous return
    - Maintain Left Uterine Displacement if hypotensive

OB

Maternal Physiology of Pregnancy

- Hematologic
  - Increase plasma volume (55%)
  - Increase RBC mass (45%)
  - Net **dilutional anemia** and lower blood viscosity
  - "hypercoagulable" due to
    - LARGE increase in fibrinogen
    - Increase factors VII, VIII, IX, X, XII
    - Decrease only in factor XI
  - Mild thrombocytopenia (10%) drop expected
  - Iron and folate deficiency
- Renal
  - Increase RPF and GFR
  - **Decrease Creatinine** (aka Cr 1.0 is ABNORMAL)
  - Decreased BUN
- GI
  - Delayed gastric emptying (**during labor only**)
  - Incompetent lower esophageal sphincter

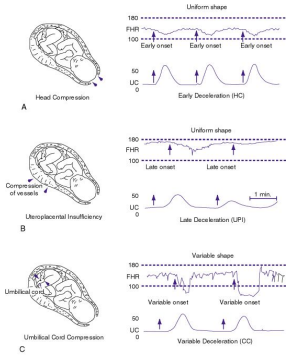
OB

Fetal Heart Tracings

- Accelerations
  - Increase HR >15bpm from baseline for >15sec
- Early deceleration
  - Head compression (activates vagal response)
- Variable deceleration
  - Cord compression
- Late deceleration
  - Uteroplacental insufficiency

- Bradycardia: mean FHR <110 bpm
- Tachycardia: mean FHR >160 bpm
- Variability: normally 6-25bpm

Fetal Heart Tracings



OB

Uterine Blood Flow

- 10% of cardiac output
- Uterine vasculature is maximally dilated, limiting autoregulation available
  - Sensitive to alpha-adrenergic agonism
- Blood flow depends on Uterine vascular resistance and pressure gradient from artery to veins
- Factors that DECREASE uterine blood flow
  - Hypotension
  - Uterine vasoconstriction
  - Uterine contractions

CARDIAC

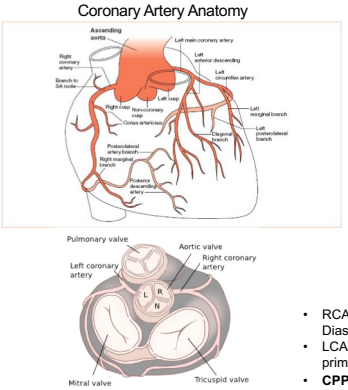
Common Cardiac Equations

- Cardiac Output (CO) = HR x SV
- Stroke Volume (SV) = EDV – ESV
- Ejection Fraction (EF) = SV/EDV
- Mean Arterial Pressure (MAP) = (2xDBP + SBP)/3
- Systemic Vascular Resistance (SVR) = {(MAP-CVP)/CO} x 80*
- Pulmonary Vascular Resistance (PVR) = {(PAP-PCWP)/CO} x 80*
- Coronary Perfusion Pressure (CPP) = AoDP – LVEDP

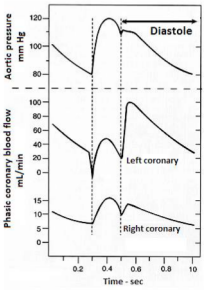
*Multiply by 80 to convert SVR/PVR units to dynes/sec/cm^{-5}

CARDIAC

Coronary Artery Anatomy



Coronary Blood Flow

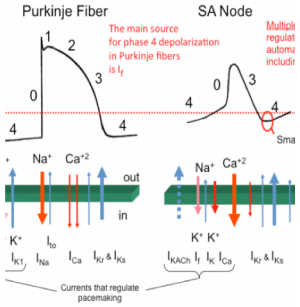


- RCA receives flow in both Systole and Diastole
- LCA and hence LV receives perfusion primarily in Diastole
- **CPP = DBP- LVEDP (perfusion in diastole!)**

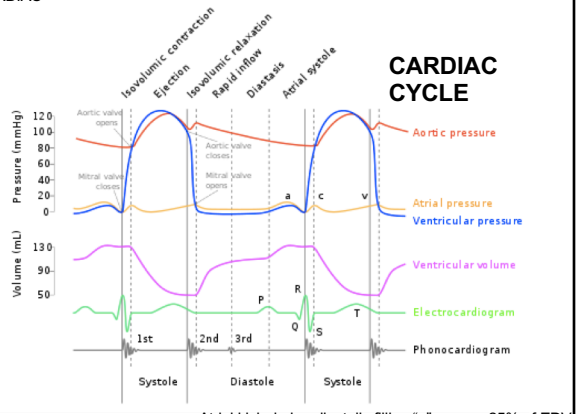
CARDIAC

Electrophysiology

- Cardiac muscle cells resting potential -90mV
- K+ is major determinant of resting potential
  - Gradient determined by Na/K ATPase
- Cardiac ventricular myocytes are FAST:
  - Phase 0 – Na+ channels open cause depolarization
  - Phase 1 – Na+ close, K+ diffuses out causes slight repolarization
  - Phase 2 – K+ outflow balanced by Ca+ inflow
  - Phase 3 – Ca+ close, only K+ open
- SA and AV node myocytes are SLOW:
  - No phase 1 or 2 components
  - Phase 4 is Na+ and Ca+ open slow depolarization
  - Phase 0 is Ca+ open



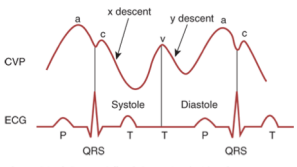
CARDIAC



Atrial kick during diastolic filling "a" wave = 25% of EDV

CARDIAC

CVP waveforms



Source: Brian S. Freeman, Jeffrey S. Berger: Anesthesiology Core Review: Part 2, Advanced Exam, www.accessanesthesiology.com
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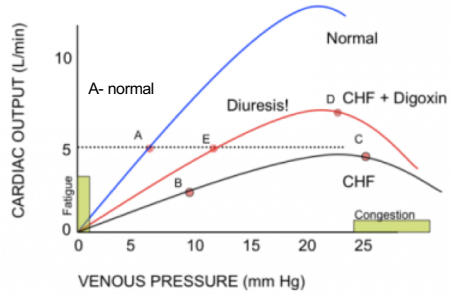
Waveform Component	Phase of Cardiac Cycle	Mechanical Event
a wave	End diastole	Atrial contraction
c wave	Early systole	Tricuspid bulging (IVC)
v wave	Late systole	Systolic filling of the atrium
x descent	Mid systole	Atrial relaxation
y descent	Early diastole	Early ventricular filling

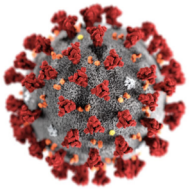
CARDIAC

Effect of CHF & Digoxin on Frank-Starling Curve

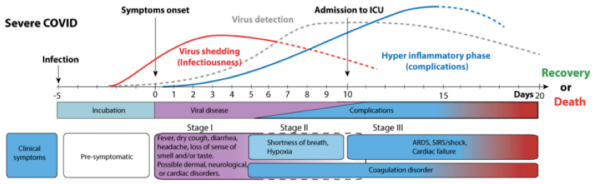


***CONTRACTILITY CHANGES = slope of Frank-Starling curve changes**
***VOLUME CHANGES (ex: diuresis) = move along curve (ex: D to E)**

COVID RESOURCES



COVID-19 Timeline of Symptoms



Where do I get a N95?

500p OR front desk
or
any anesthesia tech room

Who do I call if I have symptoms?

COVID-19 **H**ealthcare workforce **R**esponse **T**eam (HRT):

650-497-9595

Available 24/7*

For assistance with:
- *Exposure questions*
- *Test scheduling*
- *Symptoms questions*
- *Contact tracing/exposure management*

**after hours calls answered by clinical advice services, who can page on-call HRT provider if needed to arrange urgent testing in ED*

COVID-19 HRT Employee Testing Locations

Location	Address	Hours
HRT (300P)	300 Pasteur Dr 1st Floor, ED Extension	Monday – Saturday 0800-1800
HRT (Emeryville)	Garage: 5818 Peladeau St Emeryville, CA 94608	Monday, Tuesday, Wednesday, Friday 0800-1530
HRT (CCSB)	Garage: 2585 Samaritan Dr San Jose, CA 95124	Monday – Friday 0700-1600
SHC – Valley Care Occupational Health Call 925-534-0211 for appointments	Effective 06/09/2021 4000 Dublin Blvd #150 Dublin, CA 94568	Effective 06/09/2021 Monday – Friday 0800-1630 SX: by appt only (0800-1100 and 1300-1630) ASX: Walk-in basis

Color Self-Swab Testing Program

- All Stanford employees are encouraged to test weekly using this Color Genomics self-swab testing program
- Register here: https://home.color.com/create-account?next=%2Fcovid%2Factivation (use Stanford email)
- Pick up kits and drop off your sample at work!
  - Check https://shcconnect.stanfordmed.org for latest on pick up and drop off locations (click on "Latest updates on Novel Coronavirus" and search for "color")
- More info: https://healthalerts.stanford.edu/covid-19/prevention-care/employee-postdoc-testing/#winterquarter-hours

Other Resources

- Latest COVID-19 updates: https://shcconnect.stanfordmed.org
- Stanford COVID ICU Task Force: https://sites.google.com/view/stanford-covid/home (highly recommend for all things ICU)
- Dept of Anesthesia specific information: https://ether.stanford.edu/covid-19/index.html
  - Information on PPE use
  - OR protocols
  - Airway management
  - COVID airway call coverage schedule

RNA Negative Strand Test

- SARS-CoV-2 is a **PLUS (POSITIVE)** single stranded RNA virus
- After entering a host cell, the virus generates a complementary **MINUS (NEGATIVE)** strand
- The **MINUS (NEGATIVE)** strand is a critical part of the replication process and is used to create more **PLUS (POSITIVE)** RNA

RNA Negative Strand Test

Why does this matter?

- When patients test positive for SARS-CoV-2 but are asymptomatic and have a documented history of recent COVID-19, a **negative strand test** is ordered
- This test can be ordered as an **add-on** using the already collected sample
- The lab runs this test on **Mondays**, **Wednesdays**, and **Fridays** (under special circumstances you can call the lab and request a test be run on a Saturday)
- The lab needs the order and sample **the night before** in order to guarantee that the sample will be processed the following day
- Do not expect to get a result back that same day (processing time is variable and sometimes they run the samples at night)

COVID REGULAR SWAB Detects: PLUS and/or MINUS STRAND (any viral particles)	RNA STRAND TEST Detects: MINUS STRAND
First Positive Detection: patient is considered **infectious**	Any Positive Detection: patient is considered **infectious**
Positive Detection After Initial Test: patient **might** be infectious Patient can be "positive" on the test for weeks and no longer be infectious	Not Detected: **not** infectious
Not Detected: **not** infectious	No RNA strand test needed if regular swab is negative

RNA Negative Strand Test

MINUS STRAND detected = **active infection**

Only **PLUS STRAND** detected = inactive (not replicating) virus