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# 2020 CA-1 TUTORIAL TEXTBOOK 14th Edition

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STANFORD UNIVERSITY MEDICAL CENTER  
DEPARTMENT OF ANESTHESIOLOGY

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### CA-1 Mentorship Intraoperative Didactic Lectures

1. Standard Monitors
2. Inhalational Agents
3. MAC and Awareness
4. IV Anesthetic Agents
5. Rational Opioid Use
6. Intraoperative Hypotension & Hypertension
7. Neuromuscular Blocking Agents
8. Difficult Airway Algorithm
9. Fluid Management
10. Transfusion Therapy
11. Hypoxemia
12. Electrolyte Abnormalities
13. Hypothermia & Shivering
14. PONV
15. Extubation Criteria & Delayed Emergence
16. Laryngospasm & Aspiration
17. Oxygen Failure in the OR
18. Anaphylaxis
19. Local Anesthetics
20. Malignant Hyperthermia
21. Pre-Operative Evaluation
22. OR Setup
23. Perioperative Antibiotics
24. Topics for Discussion
25. CA-1 Exams, Dates & Preparation
26. Subspecialty Appendix

## **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.

Several 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. The department has purchased Miller's *Basics of Anesthesia* for use as a reference for these lectures. You can also find copies of all other major Anesthesia textbooks in the anesthesia 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 Dr. Pearl for his support and assistance with this endeavor. His guidance is 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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## **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.
- Mentors (both faculty and residents) and CA-1s will take weekday call together. CA-1s will take call with their mentor, but only in a shadowing capacity; both mentor and CA-1 take DAC (day-off after call) together. CA-1s will be expected to attend scheduled daily afternoon lecture on their DAC days.
- 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.
- Take weekday call with your mentor. You will be expected to stay as long as the ongoing cases are of high learning value. You will take DAC day off with your mentor.
- 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.
- Take weekday call with your CA-1. When you go home, your CA-1 goes home. When you have a DAC, your CA-1 has a DAC.
- 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.
- Take weekday call with your CA-1. When you go home, your CA-1 goes home. When you have a DAC, your CA-1 has a DAC.
- 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<sub>2</sub> 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 & Sugammadex
  - 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**

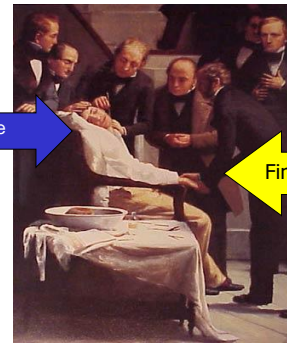
Mentors *initial* completed lectures

- 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



# Monitoring in the Past

## Standard Monitors



Not totally blue

Finger on the pulse

## 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<sub>2</sub> concentration alarm
- All anesthetics: **continual** blood 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 **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: continual 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

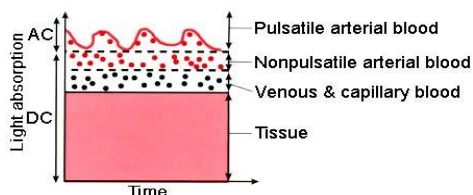
## Pulse Oximetry

### Terminology

- S<sub>a</sub>O<sub>2</sub> (Fractional Oximetry) = O<sub>2</sub>Hb / (O<sub>2</sub>Hb + Hb + MetHb + COHb)
- S<sub>p</sub>O<sub>2</sub> (Functional Oximetry/Pulse Oximetry) = O<sub>2</sub>Hb / (O<sub>2</sub>Hb + Hb)

### Fundamentals

- The probe emits light at **660 nm** (red, for Hb) and **940 nm** (infrared, for O<sub>2</sub>Hb); sensors detect the light absorbed 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 S value is used to derive the S<sub>p</sub>O<sub>2</sub> (S = 1:1 ratio = S<sub>p</sub>O<sub>2</sub> 85% → why a pulse ox not connected to the patient reads usually 85%).



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

## Pulse Oximetry Pearls

- **Methemoglobin (MetHb)** - Similar light absorption at 660 nm and 940 nm (1:1 ratio); at high levels, S<sub>p</sub>O<sub>2</sub> **approaches 85%**
  - Commonly, paO<sub>2</sub> remains normal, when SaO<sub>2</sub> is >85% you get a **falsely LOW** S<sub>p</sub>O<sub>2</sub>
  - If the true SaO<sub>2</sub> is actually <85%, spo<sub>2</sub> will be **falsely HIGH**
  - **Causes:** prilocaine/benzocaine topicalization, metoclopramide, dapsone, nitric oxide, nitroglycerine
  - **Treatments:** methylene blue, vitamin c (only in G6PD deficiency)
- **Carboxyhemoglobin (COHb)** - Similar absorbance to O<sub>2</sub>Hb. Higher affinity to Hgb than O<sub>2</sub>
  - At 50% COHb S<sub>p</sub>O<sub>2</sub> may be 95% despite a low S<sub>a</sub>O<sub>2</sub> = 50% on ABG, thus producing a **falsely HIGH** S<sub>p</sub>O<sub>2</sub>
  - **Causes:** smoke inhalation, volatile anesthetic degradation, desiccated baralyme/soda lime
  - **Treatments:** 100% fio<sub>2</sub>, hyperbaric O<sub>2</sub>
- **Cyanide toxicity:** also causes **falsely HIGH** SpO<sub>2</sub>. ABG and VBG will show similar PO<sub>2</sub> 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:** hydroxocobalamine (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)
- Factors with **NO EFFECT** on  $S_pO_2$  = bili, HbF, HbS, SuHb, acrylic nails, fluorescein dye.
- Cyanosis** - clinically apparent with **5 g/dl** desaturated Hb. Typically seen clinically at an  $S_pO_2$  around 85%.

## 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

# EKG

## 3-Electrode System

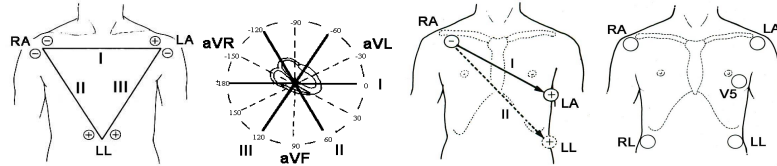
- Allows monitoring of Leads I, II, and III
- but only one lead (i.e. electrode pair) can be examined at a time while the 3<sup>rd</sup> electrode serves as ground
- Lead II is best for detecting **P waves** and sinus rhythm

## 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

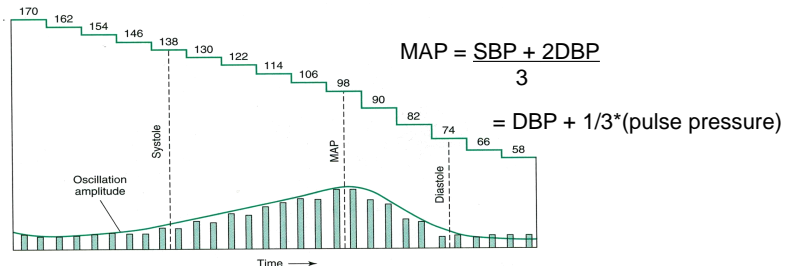
## 5-Electrode System

- 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**



# 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



# Invasive Blood Pressure

## Indications

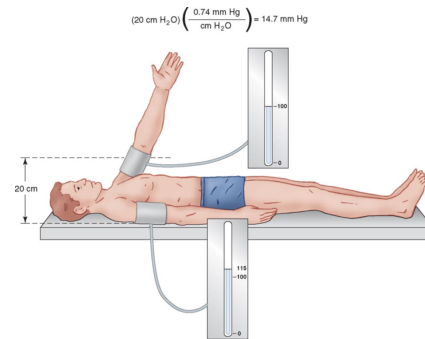
- Moment-to-moment BP changes anticipated and rapid detection is vital
- Planned pharmacologic or mechanical manipulation
- Repeated blood sampling
- Failure of NIBP (e.g. due to positioning with arms tucked or lateral positioning with up arm and down arm)
- Supplementary diagnostic information (e.g.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

## Transducer Setup

- Zeroing** = exposes the transducer to air-fluid interface at any stopcock, thus establishing  $P_{atm}$  as the "zero" reference pressure
  - One should zero the transducer while also **at the appropriate height/level**
- 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 H<sub>2</sub>O) multiplied by a conversion factor (1 cm H<sub>2</sub>O = 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

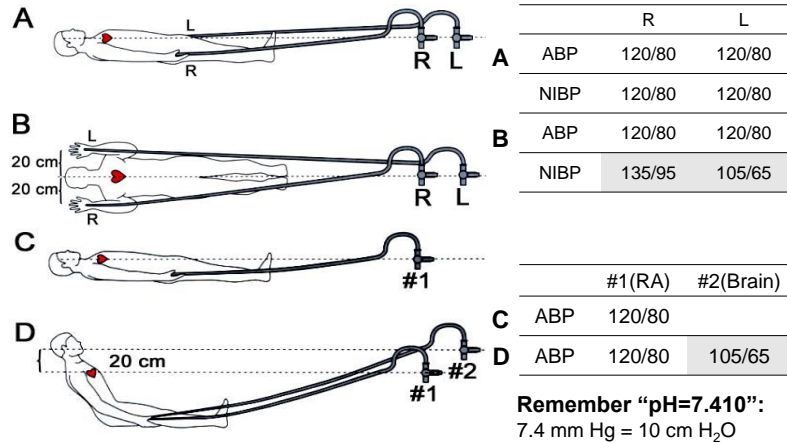
## ITE tip

Question:

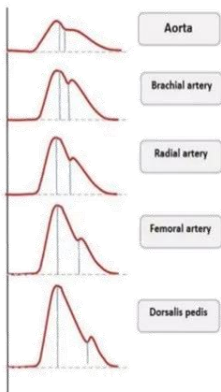
In the Beach chair position, the BP cuff on leg may read 120/80. But if the brain is 60cm vertically higher than the cuff, what is the BP in the brain?

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

## Effect of Patient & Transducer Position on BP Measurement



## Arterial line tracings



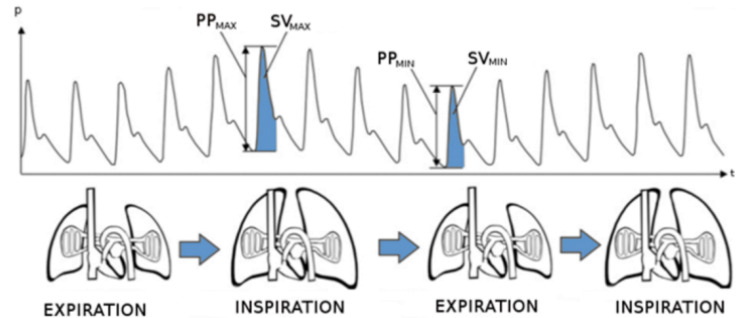
**Systolic amplification:** increase in peak systolic pressure as you move away from proximal aorta (caused by reflected waves) is offset by the narrowing of the systolic pressure wave, so the mean arterial pressure remains unchanged.

So the further from the aorta you are:

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

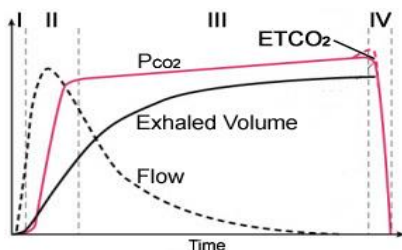
## Pulse Pressure and Stroke Volume Variation

Other useful data can be gathered from arterial lines and used to guide volume resuscitation



## Capnography

- Measures exhaled CO<sub>2</sub>
- 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



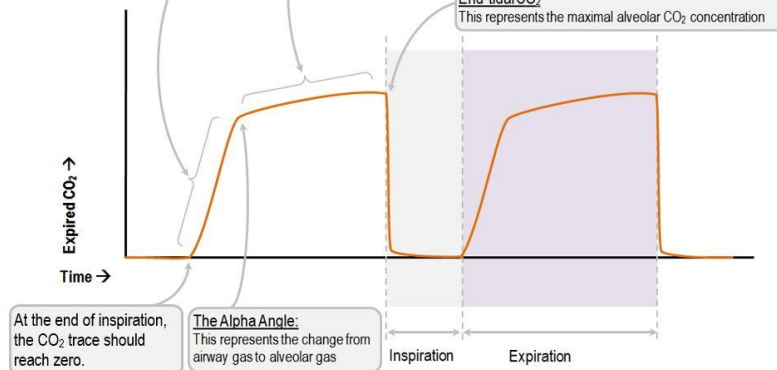
### Capnography Phases

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

**Transitional part of the curve:**  
This represents the mixing of dead space and alveolar gas

**Alveolar part of the curve:**  
This represents the plateau average alveolar CO<sub>2</sub> concentration

**End-tidal CO<sub>2</sub>:**  
This represents the maximal alveolar CO<sub>2</sub> concentration



# Capnography Pearls

Both the number and tracing provide much physiologic information

- Bronchospasm (upsloping trace)
- Significant hypotension can be associated with a drop in EtCO<sub>2</sub>
- Pulmonary embolism (decreased EtCO<sub>2</sub> but increased A-a gradient between ETCO<sub>2</sub> and PaCO<sub>2</sub>)
- Adequacy of CPR and indicator of ROSC (ETCO<sub>2</sub> goal during CPR >10; if sudden increase in ETCO<sub>2</sub>, then likely have ROSC)
- Esophageal intubation, circuit disconnect (no ETCO<sub>2</sub> tracing)
- Exhausted CO<sub>2</sub> absorbent (ETCO<sub>2</sub> does not return to 0-5)

Clinical pearl:

- When apneic: expect ETCO<sub>2</sub> 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 ETCO<sub>2</sub>

1. Decreased CO<sub>2</sub> 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 CO<sub>2</sub> production:
  - Hypothermia
  - Hypothyroidism
  - Neuromuscular blockade
3. Circuit sampling line disconnect

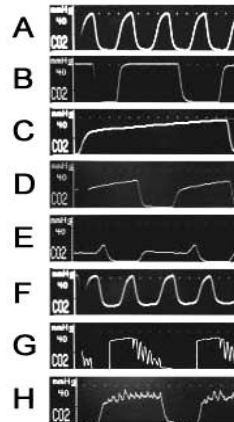
## ITE tip

During diagnostic laparoscopy, an intubated anesthetized patient is placed in Trendelenburg, over the next 20 minutes, pulse oximeter decreases from 100% to 95%, ETCO<sub>2</sub> increases from 35 to 40 without changes in ventilator settings, most likely reason is:

- Decreased diaphragmatic excursion
- Compression of vena cava
- Carbon dioxide embolism
- Pneumothorax

answer: A

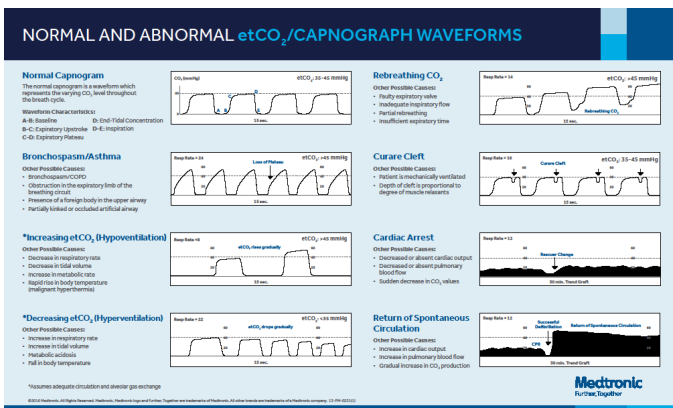
# Capnography Pearls



## Example Traces

- Spontaneous ventilation
- Mechanical ventilation
- Prolonged exhalation (spontaneous)
- Emphysema (notice upsloping plateau)
- Sample line leak
- Exhausted CO<sub>2</sub> absorbant
- Cardiogenic oscillations
- Electrical noise

# Capnography Pearls



# Temperature

Monitoring is required if clinically significant changes in body temperature are anticipated

Sites

- **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)
- **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)

\*Clinical pearl: using low fresh gas flows during anesthesia helps maintain body temperature and reduce water loss



## 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**

- Anesthesia (vent settings, volatile)
- Analgesia (redose pain med prior to incision?)
- Air (Forced Air, aka Bair Hugger), plus a temp probe
- Another thing in the mouth – OG tube? Bite block?
- Antibiotics
- Access adequate? another IV / A line?
- Arms/Legs – positioning OK?
- Acid/Base – check Baseline ABG (if applicable)

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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 scheduled 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
    - $\uparrow$  fresh gas flow,  $\downarrow$  circuit, and  $\downarrow$  circuit absorption allow actual  $F_I$  to be close to delivered  $F_I$
- $F_A$  (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
    - $\downarrow$  blood solubility,  $\downarrow$  CO,  $\downarrow$  alveolar-venous partial pressure difference  $\rightarrow$   $\downarrow$  uptake
    - $\downarrow$  uptake  $\rightarrow$   $\uparrow$   $F_A/F_I \rightarrow$  **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 taken up by CNS
- » Rate of rise in  **$F_A/F_I$  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  $F_A/F_I$  will be faster (esp. for soluble gases)

## \*\* Shunt States \*\*

### Right to Left Shunt (intracardiac or transpulmonary, i.e. mainstem intubation)

- increases alveolar partial pressure, decreases arteriolar partial pressure; dilution from non-ventilated alveoli  $\rightarrow$  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

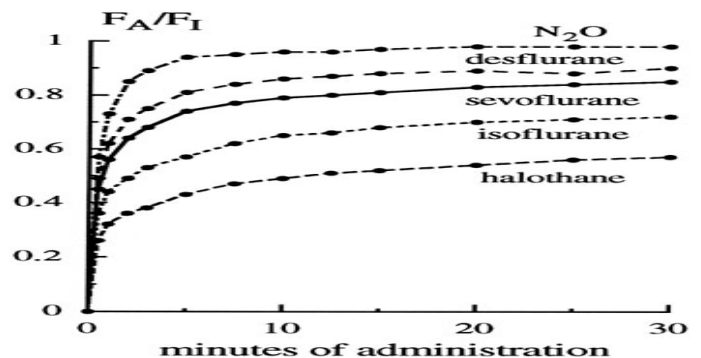
- little effect on speed of induction for IV or inhalation anesthetics

## Concentration effect:

- $\uparrow F_I$  not only  $\uparrow F_A$ , but also  $\uparrow$  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  $\rightarrow$   $\uparrow$  relative concentration of second gas



The rise in alveolar ( $F_A$ ) anesthetic concentration toward the inspired ( $F_I$ ) concentration is most rapid with the least soluble anesthetics, nitrous oxide, desflurane, and sevoflurane. It rises most slowly with the more soluble anesthetics, for example, halothane. 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 Coefficient	Partial Pressure (mmHg) at 20°C	MAC
Nitrous Oxide	0.47	~39000	104%
Desflurane	0.42	681	6%
Sevoflurane	0.69	160	2.15%
Isoflurane	1.40	240	1.2%
Halothane	2.3	243	0.75%
Enflurane	1.8	175	1.68%

Example: Blood:gas partition coefficient of nitrous = 0.47 = at steady state 1ml of blood contains 0.47 as much nitrous oxide as does 1 ml of alveolar gas. In other words, at steady state if your fraction inspired gas is 50% N<sub>2</sub>O then 1ml of blood will contain 0.47x0.5 ml's of N<sub>2</sub>O or 0.235 ml (Jaffe)

Fat: blood partition coefficient is >1. Therefore, things that increase fat in the blood (e.g. postprandial lipemia) 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 anesthetic
  - **Low** cardiac output (affects *soluble* gasses more)
  - **High** minute ventilation
  - **Low** (Arterial – Venous), 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<sub>2</sub> ↓; cerebral vascular resistance ↓ → CBF ↑ → ICP ↑
  - **\*except N<sub>2</sub>O**: CMRO<sub>2</sub> ↑ and CBF ↑
  - Sevo/Des/Iso
    - 0.5 MAC: CMRO<sub>2</sub> ↓ counteracts cerebral vasodilatation on CBF → **CBF ↔**
    - 1 MAC: CMRO<sub>2</sub> ↓ maximal, so vasodilatory effects more prominent → **CBF ↑**
- CV: dose-related ↓ SVR → ↓ MAP (but CO maintained)
  - Halothane cause decreases in myocardial contractility
- Pulm
  - ↓ V<sub>t</sub>, ↑ RR → preserved minute ventilation
  - Dose-dependent ↓ of ventilatory response to hypercapnia and hypoxemia
  - ↑ bronchodilation
- Renal: ↓ renal blood flow and ↓ GFR
- MSK: ↑ muscle relaxation (except N<sub>2</sub>O)

## 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 air filled 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 1.2%)
- Has been implicated for causing “**coronary steal**”
  - 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

- Half as potent as isoflurane (MAC 2%)
- Rapid uptake and elimination
- Sweet smelling, non-pungent
  - Popular for inhalational induction
- Can form CO in desiccated CO<sub>2</sub> absorbent
  - Can cause fires
- Forms **Compound A** in CO<sub>2</sub> absorbent (nephrotoxic in rats, however no human clinical evidence of nephrotoxicity)
  - Guidelines recommended to keep fresh gas flows >2 L/min to prevent rebreathing of Compound A (not formation of it)
  - Occurs in alkali such as barium hydroxide lime or soda lime but **NOT** calcium hydroxide

# Desflurane

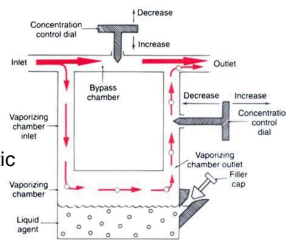
- Lowest blood:gas solubility coefficient (lower than N<sub>2</sub>O)
- Low potency (MAC 6.6%)
- High vapor pressure (669 mmHg) is close to atmospheric pressure therefore boils at sea level
  - Must be stored in a heated, pressurized vaporizer so pressure stays constant (the vaporizer is set to 2 atm) 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<sub>2</sub> 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 gas, which then is carried to the patient as a mix of fresh gas and anesthetic gas.
  - Liquid anesthetic evaporates in chamber up to its **saturated vapor pressure (SVP)**.

- SVP: partial pressure at a given temp where the liquid and vapor are in equilibrium.
- **Partial pressure** of the anesthetic gas in the carrier gas is equal to the SVP of the anesthetic

$$\frac{SVP}{PT} = \frac{VA}{VC + VA}$$



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

## ITE tip

There is a shortcut for calculating vaporizer output!

- If you can remember the PP fraction for each gas (which is calculated from the gas SVP divided atmospheric pressure), you can just multiply that fraction by the fresh gas flow to get the anesthetic volume ... see fractions below.

AGENT	SVP (mm Hg)	PP/ (ATM - PP)
Sevoflurane	160	~ 1/4
Enflurane	175	~ 1/3
Isoflurane	238	~ 1/2
Halothane	241	~ 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, you can estimate that ~ 1/4<sup>th</sup> of that 200 mL flow will be sevo (about 50 mL), and the volume concentration will then be (50/3000 + 50) x100 = 1.6% sevo

## 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:

$$VA = \frac{SVP \times VC}{PT - SVP}$$

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

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

- 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

Anesthesia in Denver?

- For Sevo and Iso:
  - Remember modern vaporizer output is a function of partial pressure of the anesthetic in proportion to atmospheric pressure ... so dropping atmospheric pressure will increase the output of your vaporizer in order to **keep the partial pressure of your anesthetic gas the same**.
    - In terms of **volume**: altitude has significant effect on vaporizer output.
      - There must be increased volume when atmospheric pressure is reduced.
    - **But** in terms of **partial pressure**, altitude has **little effect** on modern vaporizers
      - Remember *partial pressure* of an anesthetic gas in the alveoli is what determines MAC, (and there fore 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.
  - 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 1 MAC of Des at 380 ATM, you must turn the dial to **12%**.

## References

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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.*

# 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 = ED<sub>50</sub>)
  - the ED<sub>95</sub> 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<sub>2</sub>O = 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 & Awareness

## 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	<b>90.8</b>	<b>1.2%</b>
Sevoflurane	0.65	50	2.0%
N <sub>2</sub> O	0.47	<b>1.3</b>	<b>104%</b>
Desflurane	0.45	<b>19</b>	<b>6.0%</b>

\*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 \_\_\_\_\_.

- olive oil
- deionized water
- ethylene glycol
- 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.

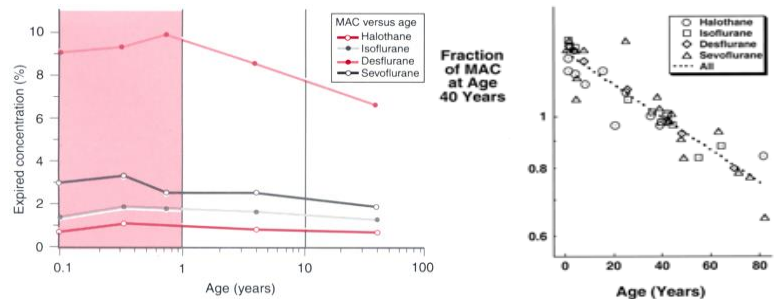
## ITE tip

» True or False?

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

- F
- T
- F
- 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)

## More MAC Definitions

### MAC<sub>Awake</sub> (a.k.a. MAC-Aware)

- MAC necessary to prevent response to verbal/tactile stimulation
- Volatiles: ~0.4 MAC; N<sub>2</sub>O: ~0.6 MAC

### MAC<sub>Movement</sub>

- 1.0 MAC

### MAC<sub>EI</sub> (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<sub>95</sub>)
- ~1.3 MAC

### MAC<sub>BAR</sub>

- MAC necessary to "blunt autonomic response" to noxious stimulus
- Opiates (even small amounts) and N<sub>2</sub>O often added to achieve this level and thus spare requirement of high concentrations of halogenated anesthetics
- ~1.6 MAC

	Medications	Alcohol	Physiologic Conditions	Pathophysiologic Conditions	Genetic Factors
<b>Factors Decreasing MAC</b>	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
<b>Factors Increasing MAC</b>	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

## 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](http://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

\_\_\_\_\_ causes the LEAST reduction in MAC of volatile anesthetics.

- fenentanyl
- morphine
- remifentanyl
- 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.

### ITE tip

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

- cesarean delivery under GA
- emergency damage-control lap chole under GA
- history of opioid abuse
- 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)

## 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)

### 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.

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## 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/>)

## 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?)



# IV Anesthetic Agents

# CNS Targets of IV anesthetics

- **GABA receptors** (most common target)
  - GABA is primary **inhibitory** neurotransmitter in CNS
  - Activation causes **increase in chloride conductance**, and therefore **hyperpolarization** (promotion of inhibition)
  - Propofol and Barbiturates decrease the rate of dissociation of GABA and its receptor
  - Benzodiazepines increase the efficiency of GABA-receptor and chloride ion channel coupling
- **NMDA receptors**
  - NMDA receptors are glutamate and glycine activated ion channels
  - *Ketamine* is an uncompetitive antagonist
- **Alpha-2 receptors**
  - *Dexmedetomidine* is an  $\alpha$ -2 agonist: inhibits NE release which results in 1. CNS inhibition via the **locus coeruleus** in brain stem and 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 <sub>1</sub>	PAIN ON INJECTION <sub>2</sub>	HEART RATE <sub>2</sub>	BLOOD PRESSURE <sub>2</sub>
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	↑↑	↑↑

<sup>0</sup> = none; + = minimal; ++ = moderate; +++ = severe.

<sup>↓</sup> = decrease; <sup>↑</sup> = increase.

(Clinical Anesthesia 6<sup>th</sup> 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 6<sup>th</sup> 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<sub>2</sub>, 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, hypertriglyceridemia, with 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<sub>2</sub>, 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<sub>2</sub>, CBF, ICP**
  - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
- Anticonvulsant properties
  - Exception: Methohexital
- 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.

- decreased initial volume of distribution
- enhanced brain sensitivity
- increased protein binding

Answer: A. The induction dose of barbiturates is reduced in the elderly due to a decreased initial Vd/2 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 with 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<sub>2</sub>, CBF, ICP**
  - Contraindicated in neurosurgical procedures
- Most likely to **preserve airway reflexes** among the IV anesthetics
- Minimal respiratory depression
- Cardio-stimulating effects secondary to **direct sympathetic stimulation**
  - Can be unmasked in patients with increased sympathetic outflow
  - Negatively effects myocardial oxygen supply-demand ratio
- Intrinsic myocardial depressant, may be significant in severely ill patients with depleted catecholamine reserves
- **Increases PVR**
- 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))

## 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 1/3 as potent)

## 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.

## ITE tip

- ❖ Dexmedetomidine is an  $\alpha_2$  agonist with  $\alpha_2:\alpha_1$  receptor selectivity of \_\_\_\_\_. In comparison, clonidine's  $\alpha_2:\alpha_1$  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 PaCO<sub>2</sub> is 38mmHg, unchanged from a preop baseline ABG. RR is 10, down from 12 bpm. \_\_\_\_\_(dexmedetomidine/midazolam/propofol/remifentanyl) is most likely administered.

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

## Midazolam

- All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant properties (but **not** analgesia!)
- Premedication dose 0.04-0.08 mg/kg IV (typically 1-2 mg)
- Induction dose 0.1-0.2 mg/kg IV
- **Decreases CMRO<sub>2</sub>, CBF, ICP**
  - Does not produce EEG burst suppression
- **Decrease SVR and BP** when used as induction dose
- 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

## Dexmedetomidine

- Selective  $\alpha_2$  **adrenergic agonist** (primarily central-acting)
- Hypnotic and analgesic
- Opioid-sparing effect; does **not** significantly depress respiratory drive
- Usually infusion at concentration of 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 and terminal half-life of 2 hours
- Decrease dosage for patients with renal insufficiency or hepatic impairment
- Main side effects are bradycardia, heart block, hypotension
- Can be utilized for sedation during awake FOB intubations

## 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
<b>Responsiveness</b>	Normal response to verbal stimulation	Purposeful** response to verbal or tactile stimulation	Purposeful** response following repeated or painful stimulation	Unarousable even with painful stimulus
<b>Airway</b>	Unaffected	No intervention required	Intervention may be required	Intervention often required
<b>Spontaneous Ventilation</b>	Unaffected	Adequate	May be inadequate	Frequently inadequate
<b>Cardiovascular Function</b>	Unaffected	Usually maintained	Usually maintained	May be impaired

## Summary

Drug	Induction Dose (mg/kg)	Effects	Pearls
Propofol	1.5-2.5	<b>Neuro:</b> Decreases cerebral metabolic O2 requirements, cerebral blood flow, intracranial pressure <b>CV:</b> Decreases SVR, direct myocardial depressant <b>Pulm:</b> 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	<b>Neuro:</b> Decreases CMRO2, CBF, ICP <b>CV:</b> Maintains hemodynamic stability (minimal cardiac depression) <b>Pulm:</b> Minimal respiratory depression (no histamine release)	-Pain on injection -High incidence of PONV -Myoclonus -Inhibits adrenocortical axis
Thiopental	3-5	<b>Neuro:</b> Decreases CMRO2, CBF, ICP <b>CV:</b> Decreases SVR, direct myocardial depressant <b>Pulm:</b> Dose-dependent respiratory depression	-Anticonvulsant properties -Can precipitate when injected with acidic fluids (i.e LR)
Ketamine	1-2	<b>Neuro:</b> Increases CMRO2, CBF, ICP <b>CV:</b> Cardio-stimulating effects (negatively effects myocardial supply-demand) <b>Pulm:</b> Minimal respiratory depression; bronchodilation; most likely of all to protect airway reflexes	-Analgesic effects -Intrinsic myocardial depressant effects which may be unmasked 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.*

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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
  - chest wall rigidity
  - 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)	Morphine
	Respiratory depression (μ2)	Met-enkephalin
	Physical dependence	B-Endorphin
	Muscle rigidity	Fentanyl
κ	Sedation	Morphine
	Spinal analgesia	Nalbuphine
		Butorphanol
		Dynorphin
		Oxycodone
δ	Analgesia	Leu-enkephalin
	Behavioral	B-Endorphin
	Epileptogenic	
σ	Dysphoria	Pentazocine
	Hallucinations	Nalorphine

## Opioid comparison

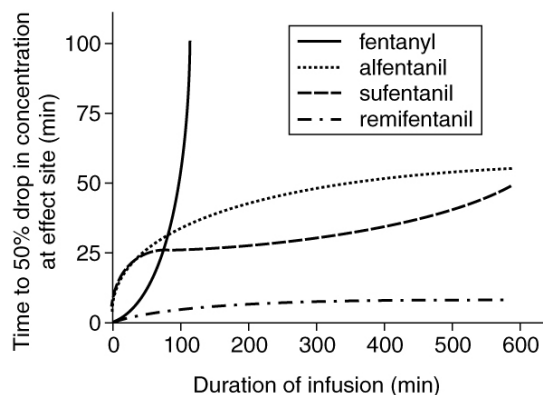
Drug	Approximate analgesic equivalent	Peak onset	Duration of action (single bolus only!)	Used as infusion
Alfentanil	150-250 mcg	1 – 2 min	5 – 10 min	Not common
Fentanyl	50 mcg	3 – 5 min	30 – 60 min	Use with caution*
Hydromorphone	0.75 mg	5 – 15 min	2 – 4 hours	ICU
Meperidine	37.5 mg	5 – 15 min	2 – 4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

### Remifentanyl

- 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!!!*

## ITE tip (a short tangent – Esterase metabolism)

- » **Remifentanyl** 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 cholinesterases)
- **RBC esterases**
  - Esmolol
  - \*Remifentanyl in small proportions
- **Plasma esterases**
  - Remifentanyl – fixed and context independent metabolism
  - Atracurium/cisatracurium
  - 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

## 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

### Remifentanyl

- 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

## 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 remifentanyl), 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 Remifentanyl 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

## Methadone

- **Longest** terminal half-life (about 1 day)
- 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

## Morphine

- Slower peak time and long duration of action often less desirable in acute surgical setting
- **Active** metabolite, **morphine-6-glucuronide**, has analgesic properties and is *renally excreted* (not clinically relevant unless patient has renal failure, but common boards question)
- Can cause *histamine* release

# 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 an 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 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 onset time to peak effect, but gives prolonged analgesia during the case and into the post-op period
  - Hydromorphone is titratable (like fentanyl) with prolonged analgesia (like morphine)

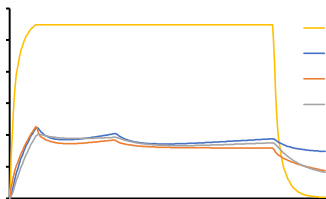
## Strategies for Opioid Use

- 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 Vicodin or Percocet

## Strategies for Opioid Shortages

- Intraop opioid infusions

	Fentanyl (mcg/kg/h)	Alfentanil (mcg/kg/h)	Sufentanil (mcg/kg/h)	Remifentanil (mg/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	



## 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 is debated and more complicated for the level of this discussion
  - 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 Shortages

- 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*	*for fentanyl and alfentanil: first dose at 30 min
Meperidine (mg)	100	25	
Methadone (mg)	5	2.5	

## 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



## ITE tip: anticholinergic side effects

Which of the following opioid-receptor agonists has anticholinergic properties?

- a. Morphine
- b. Hydromorphone
- c. Sufentanil
- d. Meperidine

Answer: d, Meperidine

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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:
  - $(MAP - CVP) = CO \times SVR$

### Cardiac Output (CO) = HR x SV

- $CO / BSA = \text{Cardiac Index}$  (normal range **2.6–4.2 L/min/m<sup>2</sup>**)
- 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

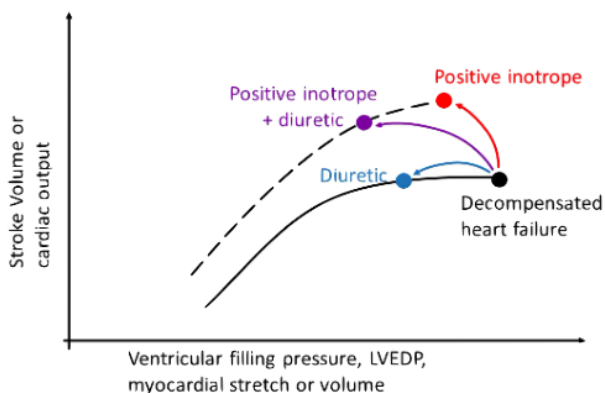
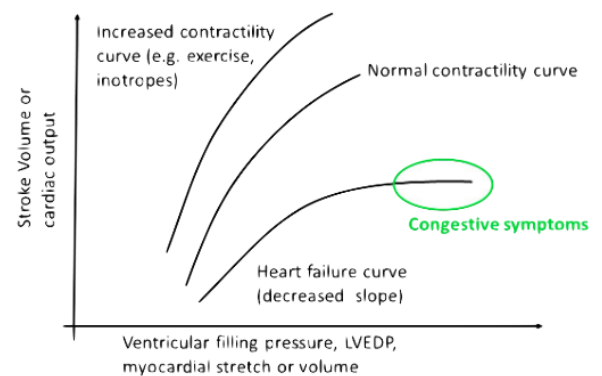
- Volume of blood in the ventricle at end-diastole (LVEDV)

#### Afterload

- Resistance to ejection of blood from the ventricle
- SVR accounts for 95% of the impedance to ejection
- **SVR** (Wood units) =  $[MAP - CVP] / CO$  (reference range 9-20)
  - $SVR \times 80 = \text{dyn}\cdot\text{s}/\text{cm}^5$  (reference range 70-160)

#### 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**
    - **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 <b>mg/hr</b>
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 & 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 improve venous return
  - Decrease I:E ratio to shorten inspiratory time
  - 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				Physiologic Effects
	alpha-1	beta-1	beta-2	Dopamine Receptor	
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  
 +++ 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?

- Hypovolemia
- CHF
- Cardiac tamponade
- 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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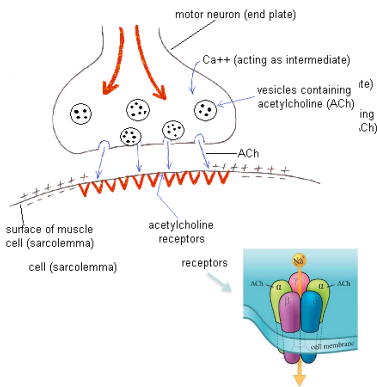
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# Neuromuscular Blocking Agents (NMBAs)

## 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<sup>++</sup> 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<sup>+</sup> and Ca<sup>++</sup> influx
  - K<sup>+</sup> 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<sup>+</sup> 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<sub>50</sub> >3-5 mg/kg to block vagal, >10 to block sympathetic
- Two structural classes:
  - Benzyliisoquinolinium** = "-urium"
    - Cisatracurium**, Doxacurium, Atracurium, Mivacurium, d-Tubocurarine
    - More likely to cause histamine release (d-Tubocurarine >> Atracurium and Mivacurium); can attenuate with slower administration
  - Aminosteroid** = "-onium"
    - Pancuronium, **Vecuronium**, **Rocuronium**, Pipecuronium
    - Vagolytic effects (Pancuronium > Rocuronium > Vecuronium)
- Most used nondepolarizing agents are of **intermediate duration**: rocuronium, cisatracurium, vecuronium

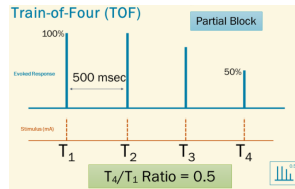
## Nondepolarizing NMBA (cont.)

- Intubating doses ~2x ED<sub>95</sub>
  - ED<sub>95</sub> = 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 Maintenance	Metabolism Excretion
Succinylcholine	0.3	1	1-1.5 min	6-8 min	Rarely done	plasma cholinesterase
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)

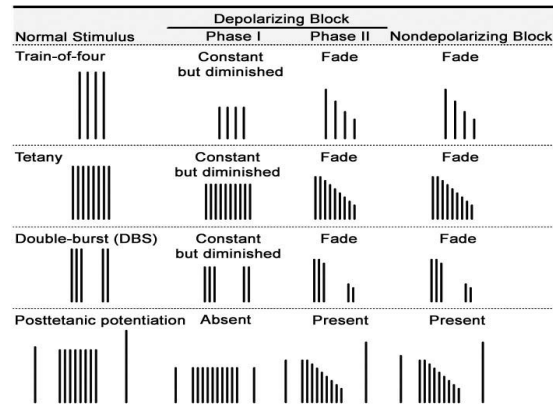
## NMBA Monitoring



- **Train-of-four (TOF)**
  - Most common modality
  - TOF count = # of twitches (out of 4)
  - TOF ratio = height of 4<sup>th</sup> compared to 1<sup>st</sup>
- 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	95	4	0.7-0.75
80-90	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

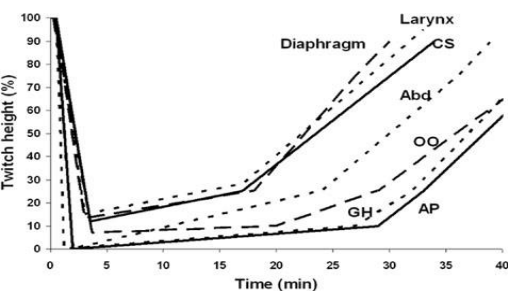
- **Phase I** – depolarization block
  - Often preceded by muscle fasciculation, and is result of pre-junctional action of succinylcholine stimulating receptors on the motor nerve and causing repetitive firing at neuron
  - Channels remain inactive until sux diffuses away to the plasma and is metabolized 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 (most resistant → most sensitive):  
vocal cords > diaphragm > corrugator supercilii > abdominal muscles > adductor pollicis > pharyngeal muscles
- To assess deep blockade (i.e. ablate diaphragmatic movement intraop):  
monitor **corrugator supercilii**
- To assess return of function of pharyngeal muscles (i.e. readiness for extubation):  
monitor **adductor pollicis**
- 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 not 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 **vagal side effects** (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**. *Do not give >70mcg/kg of neostigmine*
  - If recovery 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

## 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
  - Neostigmine** (intermediate) w/ **Glycopyrrolate**
  - Pyridostigmine (slow) w/ Glycopyrrolate
- Does reversal increase the risk of PONV? A metanalysis says no (Cheng CR, 2005).

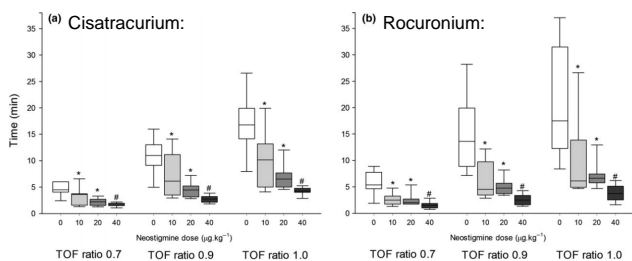


Figure 2 Times to reach the stated train-of-four (TOF) ratio of 0.7, 0.9 and 1.0 after receiving 0, 10, 20 or 40  $\mu\text{g}\cdot\text{kg}^{-1}$  of neostigmine at a TOF ratio of 0.5 after the use of cisatracurium (a) or rocuronium (b). Horizontal line = median; box = IQR; whiskers = 5th-95th percentile.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

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

## Nondepolarizing NMBA Reversal: Sugammadex

### 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

- $\gamma$ -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.)

# Clinical Pearls

## 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

- Conditions with nAChR upregulation (**SENSITIVE** to succinylcholine; **RESISTANT** to NMBA):
  - Spinal cord injury, stroke, burns, prolonged immobility, prolonged exposure to NMBA, multiple sclerosis, Guillain-Barré syndrome
- Conditions with nAChR downregulation (**RESISTANT** to succinylcholine; **SENSITIVE** to NMBA):
  - Myasthenia gravis, Lambert-Eaton syndrome, anticholinesterase 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 oculi 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

## References

- 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

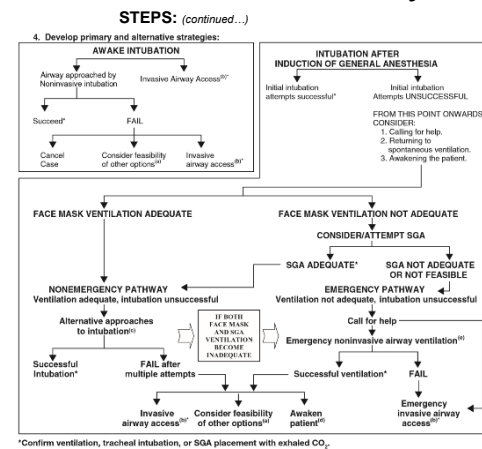
According to the ASA, "a difficult airway is defined as the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with **facemask ventilation** of the upper airway, difficulty with **tracheal intubation**, or both. The difficult airway represents a complex interaction 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 oxygenation*. If the pulse ox is dropping, fall back to whatever strategy allows you to **oxygenate your patient**.

## STEPS: (verbatim from the 2013 ASA Practice Guidelines)

- Assess the likelihood and clinical impact of basic management problems:
  - Difficulty with patient cooperation or consent
  - Difficult mask ventilation
  - Difficult supraglottic airway placement
  - Difficult laryngoscopy
  - Difficult intubation
  - Difficult surgical airway access
- Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management.
- Consider the relative merits and feasibility of basic management choices:
  - Awake intubation vs. intubation after induction of general anesthesia
  - Non-invasive technique vs. invasive techniques for the initial approach to intubation
  - Video-assisted laryngoscopy as an initial approach to intubation
  - Preservation vs. ablation of spontaneous ventilation
- Develop primary and alternative strategies (continued...)

# Difficult Airway Algorithm



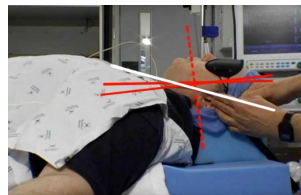
- Please note:
- First decide: awake or asleep?
  - Call for help after initial unsuccessful intubation
  - Use SGA after intubation and facemask unsuccessful
  - Emergency invasive airway access is listed last; but do not postpone this possible life-saving procedure when indicated.

## 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.



VS



Proper: Align tragus to sternum, parallel to floor

# Difficult Airway Algorithm

## STEP 1: Assess the Likelihood of Airway Management Problems:

### Any possible difficulty with:

- Patient cooperation (awake vs. asleep)
- Mask ventilation
- Laryngoscopy or intubation
- Supraglottic airway placement
- Difficulty with surgical airway access

# Difficult Mask Ventilation

## STEP 1: Assess the Likelihood of Airway Management Problems

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

### DIFFICULT Mask Ventilation

#### "MaMaBOATS"

- Mallampati III or IV
- Mandibular protrusion decreased
- Beard
- Obesity (BMI >30 kg/m<sup>2</sup>)
- Age >57-58
- Teeth (lack of)
- Snoring

### IMPOSSIBLE Mask Ventilation

#### "MaMaBORa"

- Mallampati III-IV
- Males
- Beard
- OSA or Upper Airway Surgery
- Radiation changes (neck)

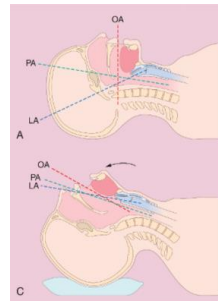
And of course... history of prior difficulty

# Difficult Intubation

## STEP 1: Assess the Likelihood of Airway Management Problems

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
- Thyromental distance < 3 (patient's) finger breadths
- Long incisors, inter-incisor distance < 3 cm (i.e. small mouth opening)
- Prominent "overbite"
- Decreased TMJ mobility; inability to prognath
- Limited cervical range of motion
- Highly arched or very narrow palate
- Poor submandibular compliance (stiff, indurated, occupied by a mass)
- Underlying pathology (e.g. laryngeal stenosis, epiglottitis, tumor)



And of course... history of prior difficulty

# Other Difficulties

## STEP 1: Assess the Likelihood of Airway Management Problems

### Difficulty with Patient Cooperation

- Age
- Mental capacity
- Level of consciousness
- Intoxication

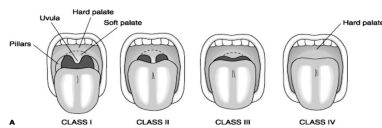
### Predictors of Supraglottic Airway Failure

- Restricted mouth opening
- Obstruction at or below larynx
- Distorted anatomy
- Stiff lungs

### Difficult Surgical Airway Access

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

### Mallampati Score Assessment



# Oxygenation Options

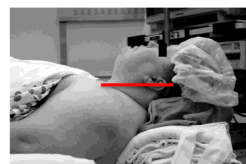
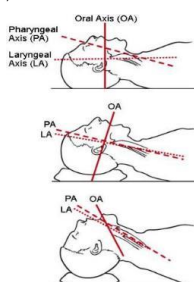
## STEP 2 on the algorithm: Attempt to Oxygenate the Patient throughout the Process

- Mask ventilate in the sniffing position (*see next slide*)
- 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

# Optimize Positioning

## Obtaining the Sniffing Position

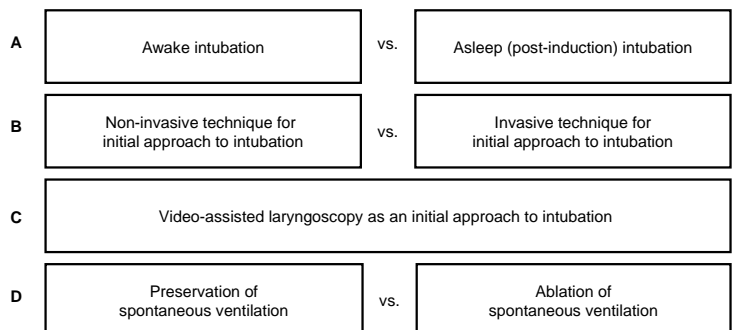
- Requires flexion at C7 with extension at C5-C6
- Ramp obese patients until the line between the tragus and the sternal notch is parallel to the floor
- And then verify you are still in the sniffing position. If not, elevate the head



Ramp obese patients until tragus is aligned with sternum

# Options

## STEP 3: Think Broadly About Your Management Options

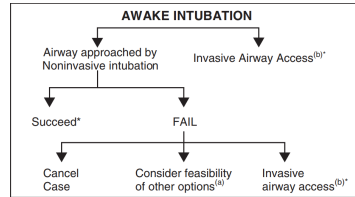


# Awake Options

## STEP 4: Awake vs. Post-induction Algorithms

### Awake Intubation – key is topicalization

- Non-invasive options:
  - Conventionally, 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



# Airway topicalization

- There are many ways to topicalize the airway. Whichever method you choose, make sure to take your time and that your patient is thoroughly topicalized before you attempt the awake intubation
- Atomizer
- Viscous lidocaine swish and spit
- Lidocaine nebulizer
- “Lollipop” method
- PICS

# Asleep

## STEP 4: Awake vs. Post-induction Algorithms

### 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

## STEP 4: Awake vs. Post-induction Algorithms

### 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

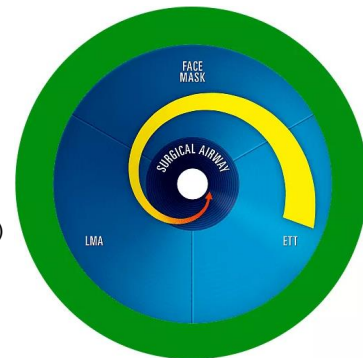
## STEP 4: Awake vs. Post-induction Algorithms

### 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
  - 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.

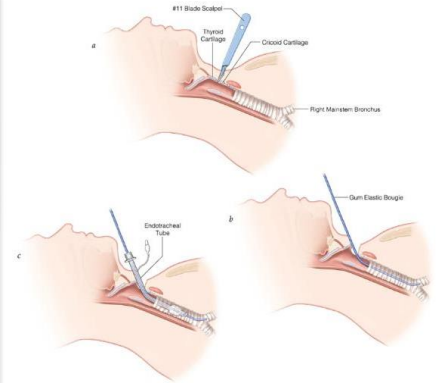


# Surgical Airways

- 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 CO<sub>2</sub>



<https://deckerip.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

# References

- Difficult/Impossible Mask Ventilation Acronyms courtesy of Dr. Vladimir Nekhendzy
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- Rosenblatt WH, Wagner PJ, Ovassapian A, et al. 1998. Practice patterns in managing the difficult airway by anesthesiologists in the United States. *Anesth Analg*, **87**: 153-7.
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# Fluid Management



## 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.
  - $PPV = \frac{\text{Pulse Pressure (Max)} - \text{Pulse pressure (Min)}}{\text{Pulse Pressure (Mean)}}$
  - PPV >10% suggests patient is volume responsive
  - Not reliable if not sinus rhythm, open chest, not on PPV, or if TV > 8cc/kg

## 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)

Intracellular fluid volume 40% of body weight (28 L water*)	Interstitial fluid volume 15% of weight (10 L)
	Intravascular volume 5% of weight (3.5 L)

Extracellular 20% of weight

\*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

## Evaluation of Intravascular Volume

### HPI

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

### Physical Exam

- *Hypovolemia:* skin turgor, thready pulse, 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, Urine Na < 10, Urine Osm > 450, hypernatremia, BUN:Cr > 10:1; bedside ultrasound (IVC <1.7cm OR 1.7cm with >50% IVCCI)
- *Hypervolemia:* increased pulmonary vascular markings on CXR

## 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

## 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 <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Ca <sup>2+</sup> (mEq/L)	Buffer (mEq/L)	Glucose (g/L)
<b>NS</b>	308	154	154	0	0	0	0
<b>LR</b>	273	130	109	4	3	28 (lactate)	0
<b>Normosol</b>	294	140	98	5	0	27 (acetate)	0
<b>D5W</b>	253	0	0	0	0	0	50

## Advantages

## Disadvantages

<b>NS</b>	<ul style="list-style-type: none"> <li>Preferred in brain injury/swelling (hyperosmolar)</li> <li>Preferred for diluting pRBCs</li> </ul>	<ul style="list-style-type: none"> <li>In large volumes produces <b>hyperchloremic metabolic acidosis</b></li> <li>Hyperchloremia → low GFR and risk AKI</li> </ul>
<b>LR</b>	<ul style="list-style-type: none"> <li>More physiologic ("<u>balanced crystalloid</u>")</li> <li>Lactate is converted to HCO<sub>3</sub><sup>-</sup> by liver</li> </ul>	<ul style="list-style-type: none"> <li>Watch K<sup>+</sup> in renal patients</li> <li>Ca<sup>2+</sup> may interfere with citrate's chelating properties of pRBCs (debated if this is clinically relevant)</li> </ul>

# 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/WWF 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 tetraastarches 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

<b>Crystalloid</b>	<ul style="list-style-type: none"> <li>Lower cost</li> <li>Readily available</li> </ul>	<ul style="list-style-type: none"> <li>Requires more volume for the same hemodynamic effect</li> <li>Short IV t<sub>1/2</sub> (20-30 min)</li> <li>Dilutes plasma proteins → peripheral/pulmonary edema</li> </ul>
	<b>Colloid</b>	<ul style="list-style-type: none"> <li>Restores IV volume and HD with less volume, less time</li> <li>Longer IV t<sub>1/2</sub></li> <li>Maintains plasma oncotic pressure</li> <li>Less cerebral edema (in healthy brain tissue)</li> <li>Less intestinal edema</li> </ul>

# "Classical" Fluid Management

## Maintenance

- "4-2-1 Rule" = 4 ml/kg/hr for the 1<sup>st</sup> 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 1<sup>st</sup> hour, 1/4 over 2<sup>nd</sup> hour, and 1/4 over 3<sup>rd</sup> 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) and hyperkalemic patients
  - 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 pRBC 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

# 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 dehiscence 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

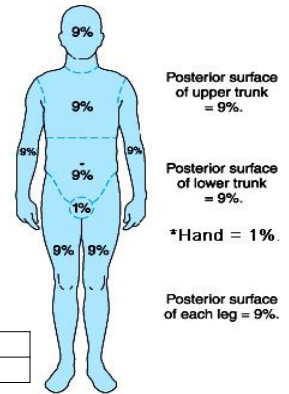
# Burns

- Increased evaporative losses
- H<sub>2</sub>O, electrolytes, and protein shift from normal to burned tissue causing intravascular hypovolemia
- Volume to infuse is calculated by the Parkland Formula:

$$\text{Volume} = \%BSA \times 4 \text{ ml/kg} \times \text{kg}$$

- Give 1/2 over the 1<sup>st</sup> 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

## ITE tip

### IVF components

	Osmolarity (mOsm/L)	Sodium (mEq/L)	Chloride (mEq/L)	Potassium (mEq/L)	Glucose (g/L)	Lactate (mEq/L)
D5W	253	-	-	-	50	-
D5 1/4 NS	355	38.5	38.5	-	50	-
D5 1/2 NS	432	77	77	-	50	-
D5NS	586	154	154	-	50	-
NS	308	154	154	-	-	-
1/2 NS	154	77	77	-	-	-
1/4 NS	77	38.5	38.5	-	-	-
3% HS	1026	513	513	-	-	-
LR	273	130	109	4	-	28
D5LR	525	130	109	4	50	28
Plasmalyte	294	140	98	5	-	-

D5 = dextrose 5%, NS = normal saline, HS = hypertonic saline, LR = lactated Ringer

Plasmalyte also contains 3mEq/L of magnesium, 27 mEq/L acetate, and 23 mEq/L gluconate.

## 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.

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# Transfusion Therapy

## Packed Red Blood Cells

### Definition, Use, & Storage

- Single donor; volume 250-300 ml with Hct ~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 citrate; at high transfusion rates, excess citrate binds to calcium (resulting in hypocalcemia)
  - Phosphate (buffer)
  - Dextrose (energy source)
  - Adenosine (precursor to ATP synthesis)

## Packed Red Blood Cells

### Indications (ASA Guidelines)

1. Hg < 6 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<sub>2</sub>
    - Example: myocardial ischemia

## Fresh Frozen Plasma

### Definition, Use, & Storage

- Fluid portion from whole blood
- Contains all coagulation factors (except platelets)
- 1 unit increases clotting factors 2-3%
- Use ABO-compatible; Rh-incompatible is OK
  - AB blood type is the universal donor
- Stored frozen; takes 30 min to thaw; use within 24 hrs 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

## Platelets

### Definition, Use, & Storage

- Platelet Concentrate (PC)
  - Platelets from one donated unit, vol = 50-70 ml;  $\uparrow$  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;  $\uparrow$  plt ~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  $\leq 5$  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 > 100,000
2. Usually when plt < 50,000 (spontaneous bleed at < 20K)
3. When plt 50-100,000, based on risk of 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
- Typically, **0.1 units/kg** would be expected to increase the fibrinogen concentration by **100 mg/dL**
- Use within 4-6 hours after thawed if you want to replace Factor VIII

### 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

## ITE Tip

The administration of FFP in patients on warfarin is MOST appropriate in which of the following scenarios?

- Elective cataract surgery with INR of 3.0
- Urgent ruptured appendectomy with INR of 1.8
- Emergent ex lap with INR of 1.3
- 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?

- Factor VII deficiency
- Factor XIII deficiency
- Factor VIII deficiency
- Surgical bleeding in patients with vWD

Answer is A, cryoprecipitate does not contain factor VII.

## Equations

### Arterial O<sub>2</sub> Content

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

### Allowable Blood Loss

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

### 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:
  - Special populations to consider:
    - Cancer patients, BMT recipients, pregnant patients, solid organ transplant patients, those at risk of volume overload, patients with immunodeficiencies
- Examples of special requests of blood products with certain populations:
  - CMV tested, Irradiated, leukocyte reduced, washed, fresh, volume reduced
- If you anticipate the patient may require a transfusion, ask them if they will accept blood products during your pre-op discussion
  - If patients refuse transfusion they must sign a special form before going to the OR

## 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
- Use when there is a low likelihood of transfusion. If you give blood in an emergency situation (only a T&S and no crossmatch available), risk of a serious hemolytic reaction is <1%

## Type and Crossmatch

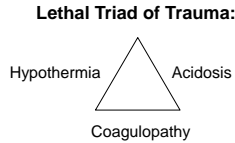
### Type and Crossmatch (if T&S negative, takes 30-60 min)

- Immediate phase
  - Recipient serum + donor cells test for recipient antibodies to donor
  - Takes 5 minutes
- Incubation phase
  - Incubate products from first test to look for incomplete recipient antibodies to donor (i.e. Rh system)
- Indirect Antiglobulin test
  - Antiglobulin serum to products of first two tests to look for incomplete recipient antibodies to Rh, Kell, Duffy, and Kidd
- At Stanford, an electronic crossmatch is used instead of a physical crossmatch
- Use when it is very likely you will transfuse (this actually reserves blood products)

# 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



# Massive Transfusion

## Complications

### 4. Acid-Base Abnormalities

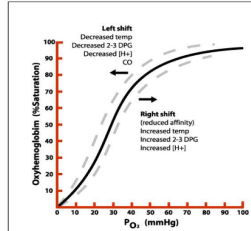
- At 21 days, stored blood has pH <7.0, due mostly to CO<sub>2</sub> production, which can be rapidly eliminated with respiration
- Acidosis more commonly occurs due to ↓ tissue perfusion

### 5. Hyperkalemia

- K<sup>+</sup> moves out of pRBCs during storage
- If EKG changes occur, stop transfusion and treat hyperkalemia

### 6. Impaired O<sub>2</sub>-Delivery Capacity

- 2,3-DPG decreases in stored blood, causing a left-shifted O<sub>2</sub>-Hb dissociation curve rendering Hgb to hold on to & not release as much oxygen at target sites



# Massive Transfusion

## Complications

### 1. Hypothermia

- Blood products are stored cold!
- This worsens coagulopathy and is why you need to run blood through a warming device

### 2. Coagulopathy

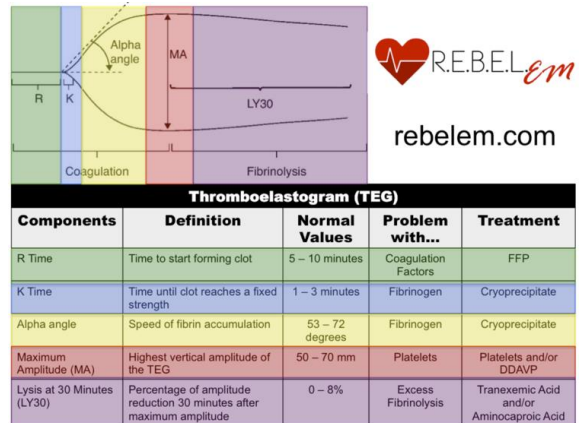
- Dilutional thrombocytopenia
  - Platelet count likely <100,000 after ~10 units pRBCs
- Dilutional coagulopathies
  - ↓ Factors V & VIII ("labile factors") in stored blood

### 3. Citrate Toxicity

- Citrate is in CPDA storage solution as a Ca<sup>2+</sup> chelator (why you often give Ca<sup>2+</sup> with transfusion)
- Rapid transfusion (>65cc/min in a healthy adult with healthy liver) can cause an acute hypocalcemia
- Citrate also binds magnesium causing hypomagnesemia

# 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



# Transfusion Reactions

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

### • Febrile Non-Hemolytic Reaction

- Due to recipient reaction to residual donor WBCs or 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 (bicard, 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<sub>2</sub>, mechanical ventilation, tidal volume 6-8 cc/kg)
  - Diuretics are not indicated (etiology = microvascular leak, not fluid overload)

# Transfusion Reactions

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

## ITE Tip

What is the primary mechanism behind delayed hemolytic transfusion reaction?

- ABO incompatibility
- Cytokines and Ab to HLA
- Donor lymphocytes reacting against recipient
- Donor RBC Ag

## 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?

- Corticosteroids to reduce inflammation
- Diuresis with lasix
- IV fluid bolus
- 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.

Answer: D

## ITE tip: Differentiating TACO vs. TRALI

TRALI	TACO
Criteria: 1) Acute lung injury (ALI) - Acute onset - Hypoxemia (PaO <sub>2</sub> :FiO <sub>2</sub> ≤ 300 mm Hg or SpO <sub>2</sub> < 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
<b>Virus</b>		
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
<b>Bacteria</b>		
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

## Equations

### Alveolar-arterial (A-a) Gradient

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

### Alveolar Gas Equation

$$P_AO_2 = F_iO_2 (P_{atm} - P_{H_2O}) - (P_aCO_2 / 0.8)$$

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

$$\approx \underline{100 \text{ mm Hg}}$$

#### 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 $P_aO_2$ :

- 103 - age/3

## 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?

## 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 ventilation (V/Q=0); see  $P_aO_2$ . No increase in  $pCO_2$  (2/2 chemoreceptor mediated hyperventilation) until shunt fraction 50%

Dead Space: ventilation without perfusion (V/Q=∞); see  $P_aCO_2$

## 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  $O_2$  - ( $PaCO_2/0.8$ ) term of alveolar gas equation becomes insignificant at higher  $F_iO_2$  even with relatively high  $PaCO_2$ .
  - $F_iO_2$  21%
    - $PaCO_2$  40 →  $PAO_2 = 0.21(760-47) - 40/0.8 \approx 100\text{mmHg} \rightarrow SpO_2$  100%
    - $PaCO_2$  80 →  $PAO_2 = 0.21(760-47) - 80/0.8 \approx 50\text{mmHg} \rightarrow SpO_2$  80%
  - $F_iO_2$  30%
    - $PaCO_2$  40 →  $PAO_2 = 0.3(760-47) - 40/0.8 \approx 160\text{mmHg} \rightarrow SpO_2$  100%
    - $PaCO_2$  80 →  $PAO_2 = 0.3(760-47) - 80/0.8 \approx 115\text{mmHg} \rightarrow SpO_2$  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)

## 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  $CO_2$  tracing, ↓TV)
- Mucus plug or secretions (↑PAP, ↓TV, mucus in ETT, rhonchi)
- Right mainstem ETT ( $SpO_2$  ~90%, ↑PAP, ↓TV, unilateral BS. Repositioning, insufflation with laparoscopic procedures)
- Pneumothorax (unilateral BS, ↑PAP, ↓TV. HD instability, tracheal deviation if tension physiology)
- Esophageal intubation (no end-tidal  $CO_2$  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 1<sup>st</sup>!)

- Pulse oximeter waveform
- Look at the patient! Are they cyanotic? mottled?
- Gas analyzer

# Management of Hypoxemia

## Assuming accurate SpO<sub>2</sub>/pulse oximetry:

- 100% FiO<sub>2</sub>, 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

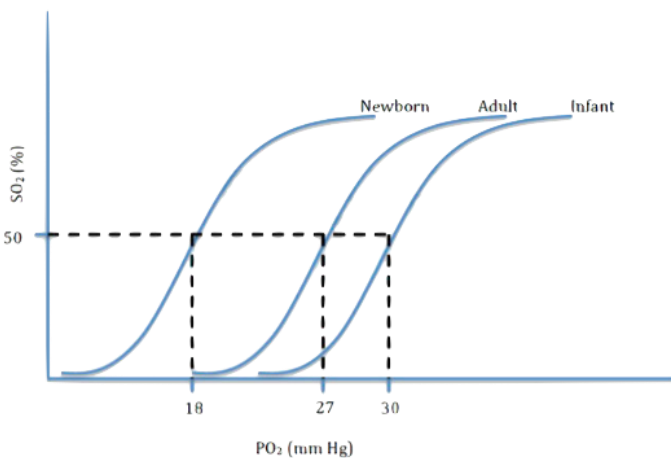
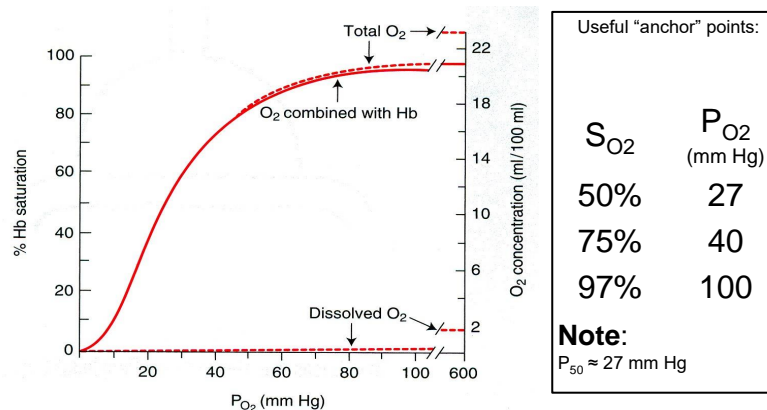
## ITE tip

Differentiating intraoperative Hypoxemia causing changes in ventilator pressures:

Airway Resistance	Pulmonary Compliance (Elastic Resistance)
Increased P <sub>IP</sub> , Unchanged P <sub>plateau</sub>	Increased P <sub>IP</sub> , Increased P <sub>plateau</sub>
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<sub>IP</sub> = peak inspiratory pressure  
P<sub>plateau</sub> = plateau pressure

## O<sub>2</sub>-Hb Dissociation Curve



P<sub>50</sub> is lowest in newborns (18) and highest in children over 12mo of age (30). After 10 years of age, P<sub>50</sub> decreases to adult level ~27

## O<sub>2</sub>-Hb Curve Shifts

### Left Shift

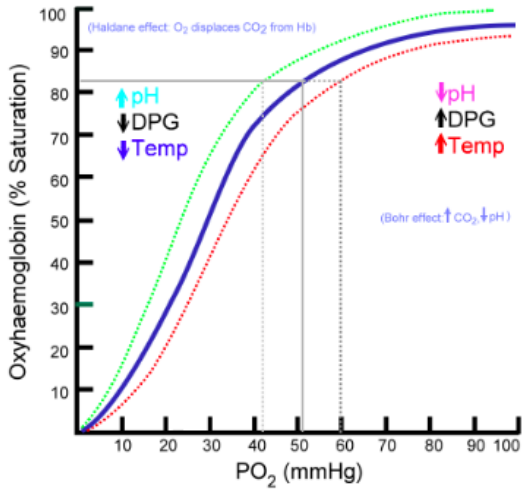
(Hb has higher affinity for O<sub>2</sub> = decreased unloading at tissues)

- Alkalosis
- Hypothermia
- Hypocarbica
- Decreased 2,3-DPG
- CO-Hb
- Met-Hb
- Sulf-Hb
- Fetal Hb
- Myoglobin

### Right Shift

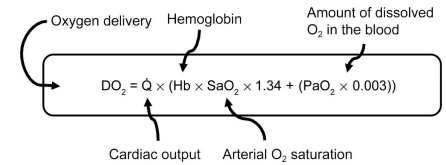
(Hb has lower affinity for O<sub>2</sub> = increased unloading at tissues)

- Acidosis
- Hyperthermia
- Hypercarbica ("Bohr Effect")
- Increased 2,3-DPG
- Sickle cell
- Pregnancy
- Volatile anesthetics
- Chronic anemia



## Factors Affecting Tissue Oxygenation

- O<sub>2</sub> delivery
  - Cardiac output
  - Hb (concentration & O<sub>2</sub>-Hb dissociation)
  - O<sub>2</sub> saturation
  - Dissolved O<sub>2</sub> in plasma (little effect)
- O<sub>2</sub> consumption



## Equations

### Arterial O<sub>2</sub> Content

$$\begin{aligned}
 C_aO_2 &= O_2\text{-Hb} + \text{Dissolved } O_2 \\
 &= (Hb \times 1.36 \times S_aO_2 / 100) + (P_aO_2 \times 0.003) \\
 &= (15 \times 1.36 \times 100\%) + (100 \times 0.003) \\
 &\approx \underline{20 \text{ cc } O_2/\text{dl}}
 \end{aligned}$$

### Mixed Venous O<sub>2</sub> Content

$$\begin{aligned}
 C_vO_2 &= O_2\text{-Hb} + \text{Dissolved } O_2 \\
 &= (Hb \times 1.36 \times S_vO_2 / 100) + (P_vO_2 \times 0.003) \\
 &= (15 \times 1.36 \times 75\%) + (40 \times 0.003) \\
 &\approx \underline{15 \text{ cc } O_2/\text{dl}}
 \end{aligned}$$

## Equations

### O<sub>2</sub> Delivery

$$\begin{aligned}
 DO_2 &= CO \times C_aO_2 \\
 &= 5 \text{ L/min} \times 20 \text{ cc } O_2/\text{dl} \\
 &\approx \underline{1 \text{ L } O_2/\text{min}}
 \end{aligned}$$

### O<sub>2</sub> Consumption (Fick Equation)

$$\begin{aligned}
 VO_2 &= CO \times (C_aO_2 - C_vO_2) \\
 &= 5 \text{ L/min} \times 5 \text{ cc } O_2/\text{dl} \\
 &\approx \underline{250 \text{ cc } O_2/\text{min}}
 \end{aligned}$$

### O<sub>2</sub> Extraction Ratio

$$\begin{aligned}
 ER_{O_2} &= (VO_2 / DO_2) \times 100 \\
 &= 250 / 1000 \\
 &\approx \underline{25\% \text{ (normal 22-30\%)}}
 \end{aligned}$$

## Other Concepts

**Diffusion Hypoxia** (usually with N<sub>2</sub>O, due to high inspired % needed)

- Hypoventilation + diffusion of N<sub>2</sub>O from blood to alveoli → displaces O<sub>2</sub> → ↓P<sub>A</sub>O<sub>2</sub>

### Absorption Atelectasis

- Poorly soluble N<sub>2</sub> normally stents alveoli open
- O<sub>2</sub> readily absorbed; 100% FiO<sub>2</sub> predisposes toward atelectasis

### Bohr Effect

- ↑PCO<sub>2</sub> → ↓pH → right shift of O<sub>2</sub>-Hb dissociation curve (↓O<sub>2</sub>-Hb affinity) → ↑O<sub>2</sub> release (e.g. at peripheral tissue)

### Haldane Effect

- ↑PO<sub>2</sub> → ↓CO<sub>2</sub>-Hb affinity
- i.e. O<sub>2</sub>-Hb binding → CO<sub>2</sub>-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?

- Ventilation/perfusion mismatch
- Hypoventilation
- Hypoxic gas mixture
- Intracardiac shunt

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



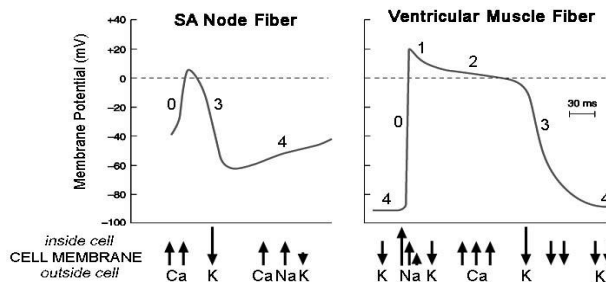
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*In one of my first days of residency (I was at the Valley, where there are 5 or 6 different kinds of anesthesia machines), it took me about 10 minutes in the morning to find the power button for the ventilator. I felt pretty dumb. The problem ended 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,  $\beta$ -blockers)
- Acidosis
- Hyponatremia, hypocalcemia
- Hemolysis, transfusions (esp old PRBCs --  $[K^+]$  of 50 or greater!)
- Release from muscle
  - Succinylcholine: acute, transient  $\uparrow$  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  $\rightarrow$  sine wave  $\rightarrow$  VF arrest, asystole
- $[K^+] > 7.0$  mEq/L: ascending flaccid paralysis, inability to phonate, respiratory arrest

## EKG Progression of Hyperkalemia

Serum Potassium	Typical ECG Appearance	Possible ECG Abnormalities
Mild (5.5–6.5 mEq/L)		Peaked T Waves Prolonged PR Segment
Moderate (6.5–8.0 mEq/L)		Loss of P Wave Prolonged QRS Complex ST-Segment Elevation Ectopic Beats and Escape Rhythms
Severe (>8.0 mEq/L)		Progressive Widening of QRS Complex Sine Wave Ventricular Fibrillation Asystole Axis Deviations Bundle Branch Blocks Fascicular Blocks

Barash PG et al. *Clinical Anesthesiology*, 6<sup>th</sup> ed. Philadelphia: 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<sup>+</sup>]), but hyperchloremic metabolic acidosis worsens hyperkalemia. Negligible [K<sup>+</sup>] in other crystalloids (e.g. LR) would bring serum K closer to 4

# Hypokalemia

## Definition

- Mild K<sup>+</sup> = 3.1-3.5 mEq/L
- Moderate K<sup>+</sup> ≤ 3 mEq/L with PACs
- Severe K<sup>+</sup> < 3 mEq/L with PVCs

## Contributing Factors

### Preoperative

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

### Intraoperative

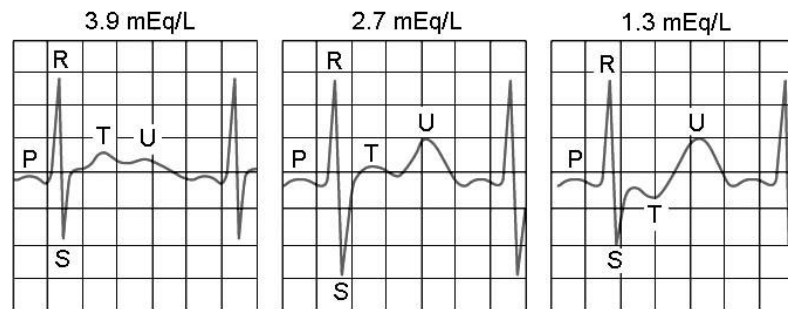
- Alkalosis (metabolic or respiratory)
- Insulin
- Hypothermia

# 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<sup>+</sup> 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<sup>+</sup> < 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<sup>+</sup>-albumin binding reduces Ca<sup>2+</sup>-albumin binding)
- Check serial K<sup>+</sup> and Mg<sup>2+</sup>

# Hypocalcemia

## Contributing Factors

### Preoperative

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

### Intraoperative

- Alkalosis (increased Ca<sup>2+</sup>-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 1 g = 4.5 mEq Ca<sup>2+</sup> (PIV or central line)
- Calcium chloride 1 g = 13.6 mEq Ca<sup>2+</sup> (central line only)
- Do NOT give Ca<sup>2+</sup> and NaHCO<sub>3</sub> 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<sup>2+</sup> administration
- Diuresis

## Anesthetic Considerations

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

# Hypomagnesemia

## Contributing Factors

- GI/renal losses
- β-agonists (intracellular shift)
- Drugs (diuretics, theophylline, aminoglycosides, amphotericin 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<sub>4</sub> to [Mg<sup>2+</sup>] > 2 mg/dl
- Watch for hypotension & arrhythmias with rapid administration!

## Anesthetic Considerations

- EKG monitoring
- Check for coexistent electrolyte deficiencies

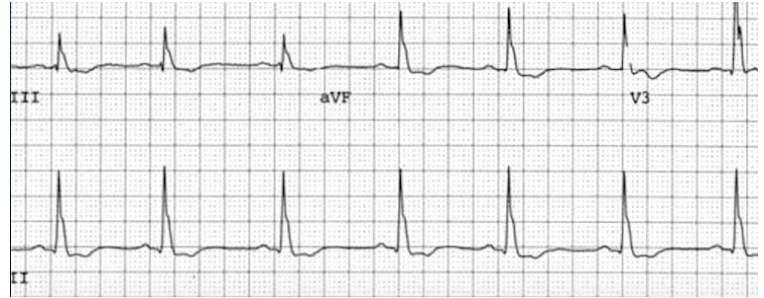
# Summary of EKG Changes

	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

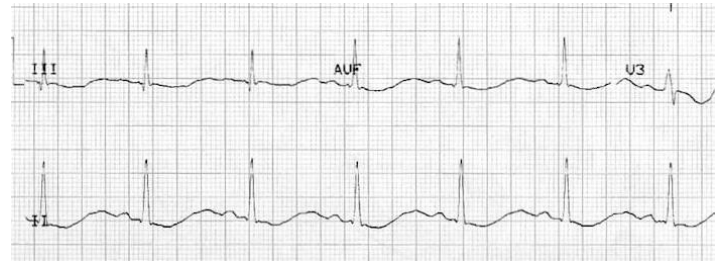
What is the suspected electrolyte abnormality?



Answer: hyperkalemia (super peaked Twaves)

## ITE tip

What is the suspected electrolyte abnormality?



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

## ITE tip

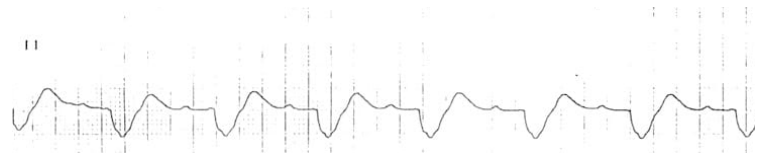
What is the suspected electrolyte abnormality?



Answer: hypocalcemia (prolonged QT interval)

## ITE tip

What is the suspected electrolyte abnormality?



Answer: worsening hyperkalemia – wide bizarre QRS and prolonged PR

## References

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*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.*

*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 bam! 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!*

*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 themselves in the kitchen or have a paper cut. Odds are they stabbed themselves 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

# Mechanisms to Control Body Temperature

- **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.

- **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

# Development of Hypothermia

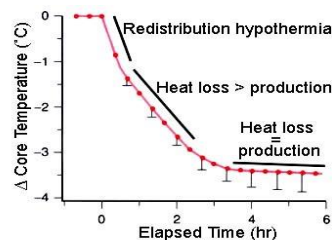
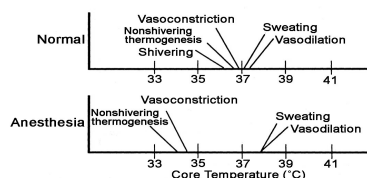
- **Interthreshold Range:** the core temperature range between cold-induced and warm-induced responses, usually as narrow as 0.2°C
- **General anesthesia**
  - inhibits thermoregulation globally
  - increases the interthreshold range 20-fold to around 4°C
- **Regional anesthesia**
  - inhibits thermoregulation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

## Phases of Anesthetic-impaired thermoregulation

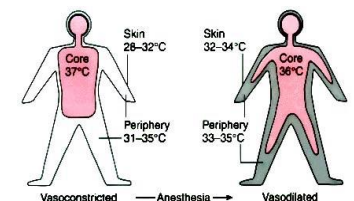
1. Redistribution hypothermia
2. Heat loss > heat production
3. Heat loss = heat production
  - heat balance is at steady state

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

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



## Redistribution Hypothermia



## 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<sub>2</sub> 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

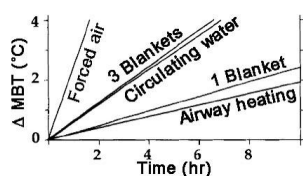
(not as effective)

- Cotton blankets
- Surgical drapes
- Heat-reflective "space" blanket

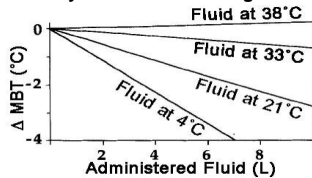
### Also...

- 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<sub>2</sub> consumption
  - Up to 500% in some studies
- Increased CO<sub>2</sub> 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.

## References

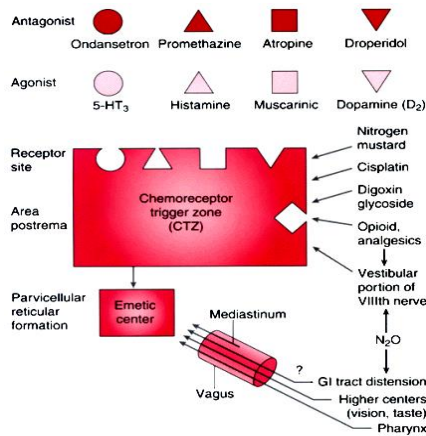
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# Postoperative Nausea & Vomiting (PONV)

## 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<sub>2</sub>O
- 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)

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

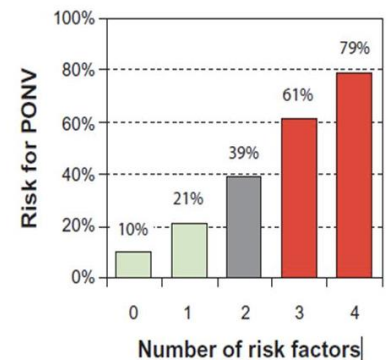
- Christian Apfel (UCSF PONV guru) meta-analysis of 22 PONV studies (>95,000 pts)
- Highest risk factors:

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

## Simplified Apfel Score

Risk factors	Points
Female gender	1
Nonsmoker	1
History of PONV and/or motion sickness	1
Postoperative opioids	1
Sum =	0 ... 4

Apfel CC et al. *Anesthesiology*. 1999;91:693.



## 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

- 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

### 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<sub>1</sub> 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 10-20 mg IV before end of case
- Contraindicated in Parkinson's patients

## Other Antiemetic Agents

### Vasopressors

- Ephedrine 50 mg IM
  - Prevents intestinal hypoperfusion

### Antihistamines (H<sub>2</sub>-blockers)

- Cimetidine 300 mg IV
- Ranitidine 50 mg IV
  - Often given pre-operatively

## Antiemetic Classes

### 5-HT<sub>3</sub> 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
- Weigh risks/benefits in diabetics and sepsis
- Decadron 4-10 mg IV anytime during case (give post-induction and not when awake: s/e at time of administration is severe perineal itching)

### Induction agents

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

## 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)
- Contraindicated in Parkinson's patients
- Droperidol 0.625-1.25 mg IV at end of case.

### Substance P antagonists (e.g. Aprepitant, fosaprepitant)

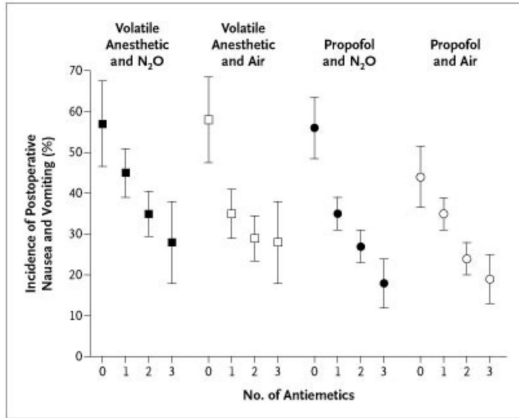
- NK1 receptor antagonist; more effective when given with Zofran ATC
- Expensive: typically for posterior fossa neurosurgical cases & chemotherapy-related nausea and vomiting
- Also useful for patients with refractory PONV
- Can be given IV or PO (PO should be given 3 hours before induction)
- Must be ordered from pharmacy

## 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 <sub>2</sub> O)	12.1%	0.003
Propofol gtt (vs. volatiles)	18.9%	<0.001
Remifentanyl 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<sub>2</sub>O + remi + no antiemetics; 17% with propofol + N<sub>2</sub> + 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<sub>2</sub>O and/or volatile anesthetics
  - N<sub>2</sub>O's role in PONV is controversial, possibly related to duration of exposure
- Minimize opioids (consider Tylenol, NSAIDs, etc.)
- Maintain euvoolemia; avoid hypervolemia (gut edema)
- Avoid hypotension and cerebral hypoxia
- Use a combination of antiemetics in different classes
- Consider acupuncture, acupressure, or transcutaneous electrical nerve stimulation (rarely used)

## 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?

- Female gender
- History of PONV
- History of migraines
- History of cigarette smoking

Answer: a

## References

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# Extubation Overview

## Extubation Criteria & Delayed Emergence

- 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 remifentanyl 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*

## 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

## 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

## “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<sub>2</sub> > 90%
2. **ABG “reasonable” with FIO<sub>2</sub> ≤ 40%**
  - pH ≥7.30, PaO<sub>2</sub> ≥60 mmHg, PaCO<sub>2</sub> ≤50-60, normal lytes
  - As a surrogate, ET/CO<sub>2</sub> can be used and should be <60
3. **Adequate reversal or neuromuscular blockade**
  - TOF 4/4, TOF ratio >0.7-0.9, 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<sub>2</sub>, 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	<ul style="list-style-type: none"> <li>• TV &gt;5cc/kg &amp; VC &gt; 15cc/kg</li> <li>• SpO<sub>2</sub> &gt;90% with FiO<sub>2</sub> &lt; 0.4</li> </ul>
Failure to ventilate	<ul style="list-style-type: none"> <li>• Same TV parameters above</li> <li>• NM Blockade appropriately reversed</li> <li>• RR &gt;6 &amp; &lt;30?</li> <li>• No excessive hypercapnea (EtCO<sub>2</sub> &lt; 50s-60)</li> </ul>
Inadequate clearance of pulmonary secretions	<ul style="list-style-type: none"> <li>• Oropharynx suctioned?</li> <li>• Intact gag reflex? Able to cough? Alert/awake?</li> <li>• If aspiration risk, OG tube suction and consider emergence in lateral decubitus position</li> </ul>
Loss of airway patency	<ul style="list-style-type: none"> <li>• Soft bite block or oral airway placed?</li> <li>• Alert? Following commands?</li> <li>• If edema a concern, is cuff leak &gt;10-15%**</li> <li>• Placed in optimal position (sniffing position, head up)</li> <li>• Reduced risk of laryngospasm? (not in stage 2, airway suctioned)</li> <li>• Airway exchange catheter for high risk patient?</li> </ul>

# 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<sub>2</sub>; 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% O<sub>2</sub>, 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, amnesic 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 <ul style="list-style-type: none"> <li>• Rapid shallow breaths? MAC still showing?</li> <li>• Time since propofol turned off?</li> </ul> Excessive narcotics <ul style="list-style-type: none"> <li>• Recent administration? Pinpoint pupils?</li> </ul> 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

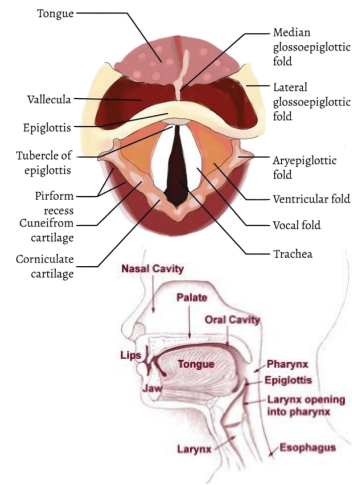
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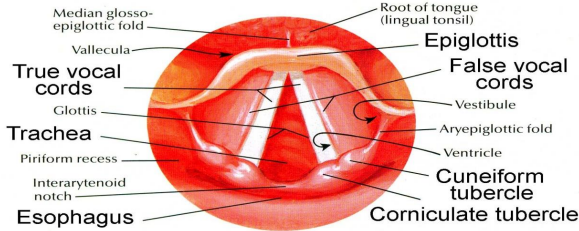
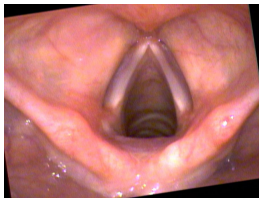
# Airway Anatomy Review

## Laryngospasm & Aspiration

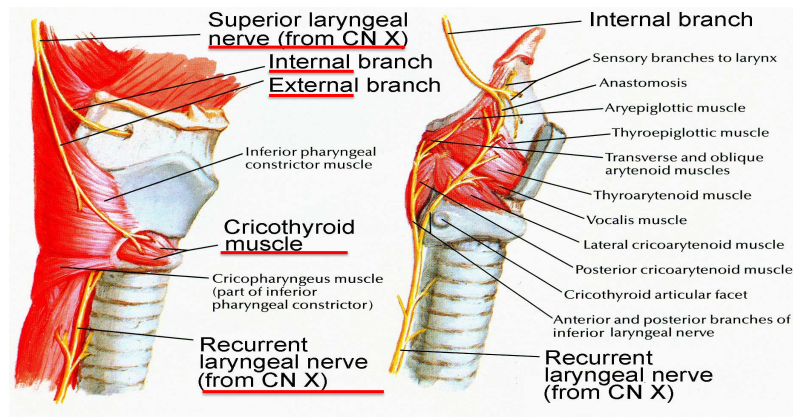
- Pharynx - passage that connects posterior nasal and oral cavities to the larynx and esophagus.
  - Nasopharynx
  - Oropharynx
  - Laryngopharynx – starts at epiglottis and extends to cricoid cartilage at the level of C6 vertebrae



## 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
<b>Recurrent Laryngeal</b> (from CN X)	Thyroarytenoid (tensor) Lateral Cricoarytenoid (adductor) Transverse Arytenoid (adductor) Posterior Cricoarytenoid (abductor, tensor)	Subglottic mucosa
<b>Superior Laryngeal</b> (from CN X)		
• Internal branch	None	Epiglottis/Tongue Base Supraglottic mucosa
• External branch	<b>Cricothyroid (adductor)</b>	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

## 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<sub>2</sub> 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

## Pathogenesis

- Negative intrathoracic pressure (up to -100 cmH<sub>2</sub>O)
- ↑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<sub>2</sub>, 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

# 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<sub>2</sub> tracing, desaturation, bradycardia, central cyanosis

# 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<sub>p</sub>O<sub>2</sub>, ↑ET<sub>CO2</sub>, hypotension, large P<sub>(A-a)</sub> gradient
- CXR with pulmonary edema

# 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<sub>2</sub>-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<sub>2</sub>O
- 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<sub>2</sub>-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<sub>2</sub>, 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<sub>2</sub> supply.
- Obstruction of central O<sub>2</sub> supply line to OR.
- O<sub>2</sub> shutoff valve in OR is off.
- Obstruction or disconnection of O<sub>2</sub> hose in the OR.
- Failure of O<sub>2</sub> regulator in the anesthesia machine.

### Faulty Oxygen Supply

- Crossing of pipelines during construction/repairs.
- Incorrect connection of gas hoses.
- Non-O<sub>2</sub> cylinder at the O<sub>2</sub> yoke.
- Wrong gas in the O<sub>2</sub> 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<sub>2</sub> analyzer and that the low O<sub>2</sub> alarm is audible
  - Self calibrating O<sub>2</sub> 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<sub>2</sub>:N<sub>2</sub>O 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<sub>2</sub> 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 <sub>2</sub>	660	1900	Green	White	Gas
Air	625	1900	Yellow	White & Black	Gas
N <sub>2</sub> O	1590	745	Blue	Blue	Liquid + Gas*
N <sub>2</sub>	650	1900	Black	Black	Gas

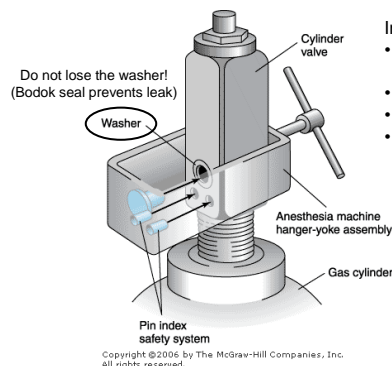
\*Because N<sub>2</sub>O is stored as a liquid, the psi of 745 will not decrease until the tank is at 1/4 capacity (400 L); you must weight the tank to know how full it is.

How long can you use an O<sub>2</sub> tank starting at 430 psi running at 5 L/min? (remember 3 psi = 1 Liter for oxygen)

$$\text{Answer} = \text{PSI} \div 3 \div \text{Flow rate.}$$

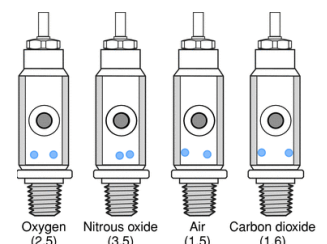
$$430 \div 3 \div 5 = 29 \text{ minutes}$$

## Pin Index Safety System



International Standard:

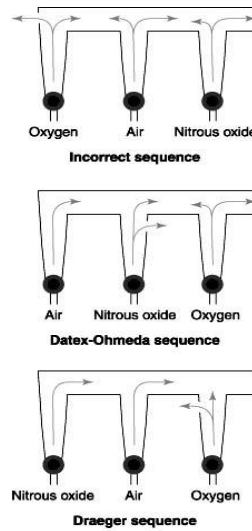
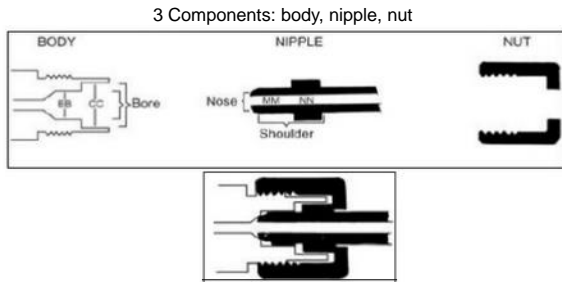
- Physical Barrier to ensures that the correct gas is connected to the correct cylinder type
- Pin positions for each gas is unique
- Do not break or force pins to connect
- Possible to bypass safety check if pins are eroded, damaged, or corroded



PISS for Gas Cylinders

# 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)



# Flowmeter Arrangement

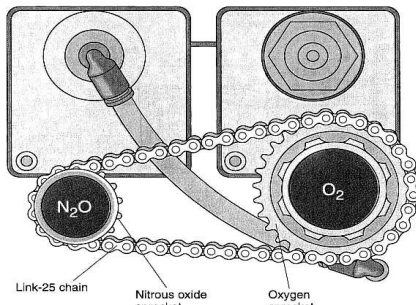
- A leak in the upstream O<sub>2</sub> flowmeter (“Incorrect sequence”) results in a hypoxic gas mixture.
- A leak in the Datex-Ohmeda or Draeger flowmeter arrangements may deliver less Air or N<sub>2</sub>O than expected, but the mixture will NOT be hypoxic because O<sub>2</sub> is closest to the FGF outlet.

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

Note: Flowmeter governed by viscosity at low “laminar” flows (Poiseuille’s law); density at high “turbulent” flows

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

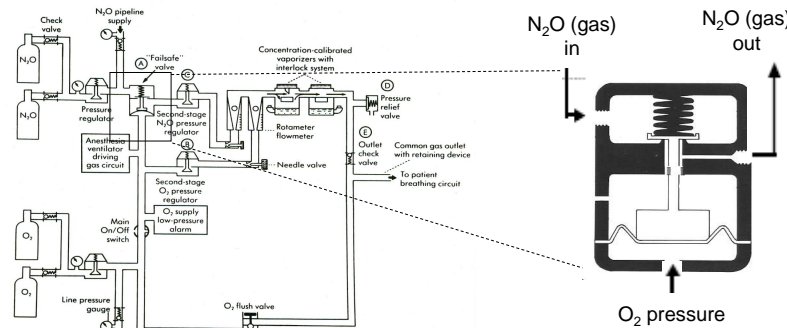
# O<sub>2</sub>:N<sub>2</sub>O Proportioning System “hypoxic guard”



Linkage mechanisms between flow valves can be either mechanical (above), pneumatic, or electronic to prevent FiO<sub>2</sub> <25% when N<sub>2</sub>O 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<sub>O<sub>2</sub></sub> falls <30 psi, N<sub>2</sub>O cannot flow AND alarm sounds (Datex-Ohmeda)  
 Note: Does not prevent 100% N<sub>2</sub>O delivery! (this is accomplished by the proportioning system)

# Detection

- Pressure gauges fall (pipeline, tanks)
- Low O<sub>2</sub> alarms (O<sub>2</sub> supply failure, F<sub>i</sub>O<sub>2</sub> analyzer)
- Flowmeters fall (O<sub>2</sub> and other gases)
- O<sub>2</sub> flush inoperative
- Bellows inoperative
- Apnea alarms (spirometer, capnograph)
- Increasing O<sub>2</sub> 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<sub>2</sub> on machine as the source is the same.** If patient needs higher FiO<sub>2</sub> call for extra E-cylinders early.
- To keep patient connected to anesthesia machine, open O<sub>2</sub> cylinder on the back of the anesthesia machine and disconnect from pipeline O<sub>2</sub>.
- Use manual ventilation to conserve O<sub>2</sub>.
- 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<sub>2</sub> Pipeline Failure

J. Weller et al. • Management of oxygen pipeline failure

Anaesthesia, 2007, 62, pages 122-126

Category	Description	n (%)
Pre-op machine check	Checks rotameters and circuit	15 (75%)
	Identifies empty oxygen cylinder before case	6 (30%)
Immediate response to pipeline failure	Checks self-inflating bag present	5 (25%)
	Turns on machine cylinder	20 (100%)
Conserves oxygen	Requests more oxygen cylinders	20 (100%)
	Voices need to conserve oxygen	3 (15%)
Uses oxygen above essential requirements	Reduces gas flows	7 (35%)
	Uses ventilator during failure	12 (60%)
Reconnection	Uses self-inflating bag with high flow oxygen during failure	8 (40%)
	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%)

Table 1 Anaesthetists' management of oxygen failure.

## Commonly missed steps:

- Identifying empty O<sub>2</sub> E-cylinder before case start
- Identifying easily accessible self-inflating bag prior to every case
- Conservation of O<sub>2</sub> (use lowest gas flows required and use manual ventilation)
  - Electrically powered ventilators do not consume O<sub>2</sub>, Pneumatic powered may use O<sub>2</sub>!
- Re-test pipeline gas supply if central failure prior to administration to patient

## ITE tip

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

- Fail-safe valve
- O<sub>2</sub> analyzer
- Second-stage O<sub>2</sub> pressure regulator
- Proportion-limiting control system

Answer: b. The O<sub>2</sub> analyzer is located in the inspiratory limb of the breathing circuit to provide maximum safety. Because the O<sub>2</sub> concentration in the fresh-gas supply lumen may be different from that of the patient's breathing circuit, the O<sub>2</sub> analyzer should not be located in the fresh-gas supply line.

## 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)

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# Overview

## Anaphylaxis

- 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

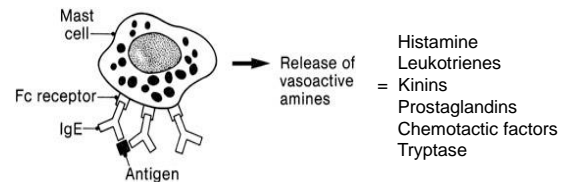
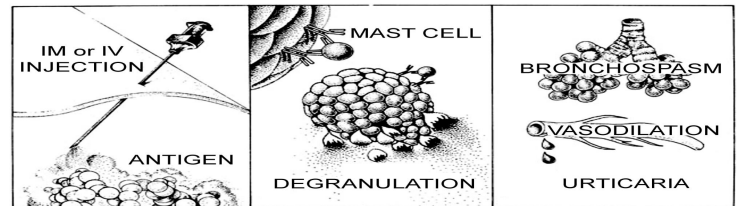
### Anaphylaxis

- **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 Pulmonary edema Wheezing ↓ Compliance Laryngeal edema ↑ PIPs
Cardiovascular	Dizziness ↓ LOC	Hypotension Tachycardia Dysrhythmias Cardiac arrest Pulmonary HTN
Cutaneous	Itching	Perioral edema Flushing Periorbital edema 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 >> <b>Albumin &gt; HES 6%</b>
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 drugs with significant latex allergy
- Prophylactic steroids and/ or H1-blockers (uncertain benefit)
- Prepare for the worst, hope for the best

# 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<sub>1</sub>-blocker**: diphenhydramine 0.5-1 mg/kg IV
  - **H<sub>2</sub>-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

## 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.

# 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<sub>2</sub> 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)

# 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

# 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

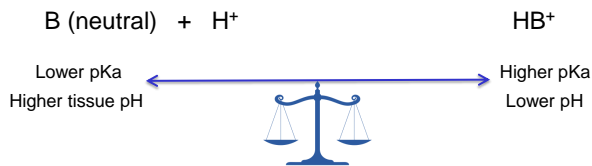
## Local Anesthetics (LA)

- 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)**



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

- 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

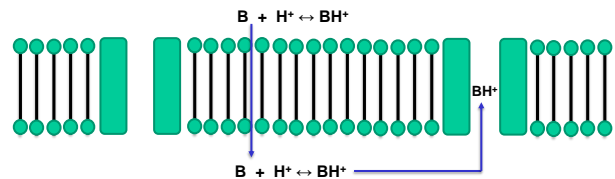
Characteristic	Association
Speed of onset	1. pKa (degree of ionization) 2. Concentration *procaine and chlorprocaine have a high pKa but quick onset due to concentration effect
Potency	Lipid solubility
Duration of action	Protein binding (alpha-1 amino glycoprotein binds drug and carries it away for metabolism)

Amides	pKa	Esters	pKa
Lidocaine	7.9	Procaine	8.9
Mepivacaine	7.6	Chlorprocaine	8.7
Prilocaine	7.9	Tetracaine	8.5
Bupivacaine	8.1		
Ropivacaine	8.1		

Note: chlorprocaine 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

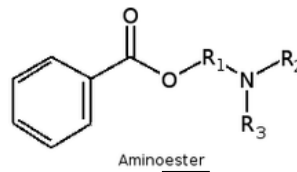
## Mechanism of Action & Physiochemical Properties

- 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<sup>+</sup> channel



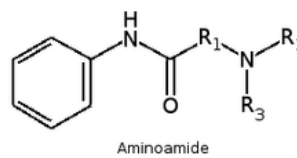
Nonionized local anesthetic (B) diffuses through axonal lipid bilayer. Ionized form (BH<sup>+</sup>) reversibly binds alpha subunit of Na channel.

## Local Anesthetic Structure



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 <b>pseudocholinesterase</b> metabolism & RBC esterase (hydrolysis at ester linkage)
Amides (i before -caine)  *Amide anesthetics have 2 I's	Lidocaine Bupivacaine Ropivacaine Mepivacaine Etidocaine Levobupivacaine	<b>Liver metabolism:</b> Aromatic hydroxylation, N-dealkylation, Amide hydrolysis  *methylparaben preservative is metabolized to <i>p</i> -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

## LAST (Local Anesthetic Toxicity)

Systemic absorption by injection site (vascularity)

- IV > tracheal > Intercostal > Caudal > Epidural > Brachial plexus > Axillary > Lower extremity (sciatic/femoral) > Subcutaneous

\*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<sup>+</sup> channels; also slower dissociation from channels during diastole)

### CNS toxicity

- 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

### Cardiovascular toxicity

- 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:

- Bupivacaine, lidocaine, ropivacaine
- Bupivacaine, ropivacaine, lidocaine
- Ropivacaine, bupivacaine, lidocaine
- Lidocaine, ropivacaine, bupivacaine

Answer: b.

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# 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  $O_2$  consumption,  $CO_2$  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

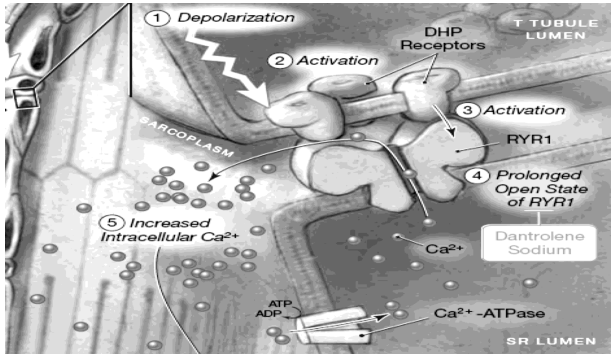
# Malignant Hyperthermia

## 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 2<sup>nd</sup> 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 (Central Core disease and King Denborough Syndrome), caffeine intolerance, history of unexplained fevers/cramps/weakness, h/o exercise induced rhabdomyolysis, trismus on induction (precedes 15-30% of MH)

## 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 ScvO<sub>2</sub>)
    - 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<sub>2</sub>?)
    - 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 <sub>2</sub> 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 CO <sub>2</sub> insufflation for laparoscopy	see ↑EtCO <sub>2</sub> with tachycardia

\*Dantrolene can also treat both of these conditions

# Treatment - Acute Phase

<b>Immediate Actions</b>	<ul style="list-style-type: none"> <li>• <b>Call for Help &amp; obtain MH cart:</b> inform team and start preparing dantrolene or ryanodex</li> <li>• <b>D/C volatile agents and succinylcholine</b> (no need to change machine or circuit) **Switch to 100% O<sub>2</sub> with high flows &gt;10L/min; increase minute ventilation</li> <li>• Halt surgery vs. finish ASAP with TIVA; arrange for ICU bed</li> <li>• Call MH hotline (1-800-MH-HYPER)</li> <li>• <b>Labs:</b> ABG, lactate, K+/electrolytes, CK, Coags; place foley to monitor UOP</li> </ul>
<b>Dantrolene</b> (interferes with RYR-1 Ca <sup>2+</sup> channel)	<ul style="list-style-type: none"> <li>• <b>2.5 mg/kg IV push q5min;</b> patient may need &gt;10mg/kg; continue giving until stable. Give through large bore IV or central line (risk of phlebitis); assign several people to prepare this</li> <li>• 1 vial = 20mg Dantrolene (dissolve in 60 cc sterile water); solution has mannitol</li> <li>• **New Ryanodex (250mg vial in 5cc sterile water)</li> <li>• Continue until stable (decrease in EtCO<sub>2</sub>, rigidity, and tachycardia); continue dantrolene infusion <b>0.25mg/kg/hr for at least 24 hrs</b></li> </ul>
<b>Treat Acidosis</b>	<ul style="list-style-type: none"> <li>• Hyperventilate patient</li> <li>• <b>Sodium Bicarbonate</b> 1-2 mEq/kg</li> </ul>
<b>Treat hyperkalemia &amp; ARF</b>	<ul style="list-style-type: none"> <li>• <b>CaCl<sub>2</sub></b> (10mg/kg) or Calcium gluconate (30mg/kg); Bicarbonate, hyperventilate</li> <li>• <b>Insulin and glucose</b> (10 units in 50cc D50)</li> <li>• <b>Sodium bicarbonate</b> (1-2 mEq/kg)</li> <li>• Diuresis; <b>urine output goal &gt; 1-2cc/kg/hr</b> to help prevent pigment induced nephropathy/ARF and reduce hyperkalemia; consider IV fluids, diuretics, and alkalize urine</li> </ul>
<b>Treat dysrhythmias</b>	<ul style="list-style-type: none"> <li>• Avoid CCBs (may promote hyperkalemia and depress cardiac output)</li> <li>• Treat hyperkalemia and acidosis; if refractory, may need to add an antiarrhythmic</li> </ul>
<b>Treat temp</b>	<ul style="list-style-type: none"> <li>• Cool if temp &gt;39 degrees C (cooling blankets, ice, cold NS, lavage stomach/bladder/rectum)</li> </ul>
<b>Labs</b>	<ul style="list-style-type: none"> <li>• ABG, lactate, K+/electrolytes, CK, urine myoglobin, Coagulation studies</li> </ul>

# Treatment – Post Acute Phase

<b>Admit to ICU</b>	<ul style="list-style-type: none"> <li>• ICU admission for at least 24 hrs (recrudescence rate 25%)</li> </ul>
<b>Continue monitoring</b>	<ul style="list-style-type: none"> <li>• Labs: serial ABG, lactate, Electrolytes (K<sup>+</sup>, Ca<sup>2+</sup>), CK/serum myoglobin, Urine myoglobin, Coags</li> <li>• EtCO<sub>2</sub>, temp, urine output/color</li> <li>• *Watch for DIC and renal failure*</li> </ul>
<b>Counsel patient and family</b>	<ul style="list-style-type: none"> <li>• Future precautions</li> <li>• Refer to MHAUS</li> <li>• Refer patient and family to nearest Biopsy Center for follow-up</li> </ul>

# 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**
  - **Multiminicore 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<sub>2</sub> absorbent
- Remove or disable vaporizers
- 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<sub>CO2</sub>

## 3. Anesthetic

- Avoid succinylcholine and volatiles
- All other non-triggering agents are okay (including N<sub>2</sub>O)

## 4. Emergency

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

## ITE tip

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

- a. PaCO<sub>2</sub> 150 mm Hg
- b. MVO<sub>2</sub> 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 MVO<sub>2</sub> is 30-35, so an elevated MVO<sub>2</sub> of 50 would not be consistent with MH, and answer b is incorrect).

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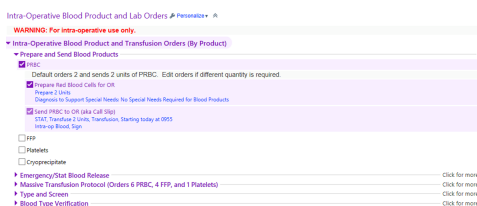
# Pre-operative Evaluation

## 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 tab and care everywhere for outside studies
- Review the Anesthesia tab in chart review 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 you can order PO analgesics to be given in pre-op

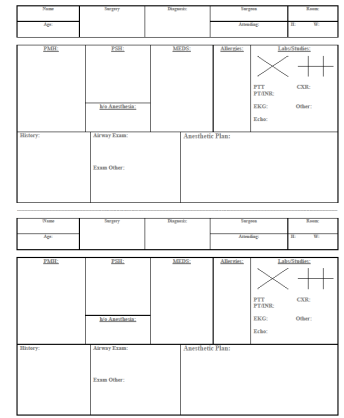
## Anesthetic Plan

- 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)



## Chart Review

- A pre-op template can be found and downloaded at [http://ether.stanford.edu/ca1\\_new/ca1\\_preop\\_new1.html](http://ether.stanford.edu/ca1_new/ca1_preop_new1.html)
- Link includes a useful guide for chart review and how to assess relevant comorbidities



## 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

- 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

Navigation menu with 'Pre' highlighted and 'Pre-Op Eval' circled in red.

- Pre
- Summary
- Chart Review
- Care Everywh...
- Results Review
- Notes
- Open Orders
- Orders
- Pre
- Intra
- Post
- Log Navigator
- Admit

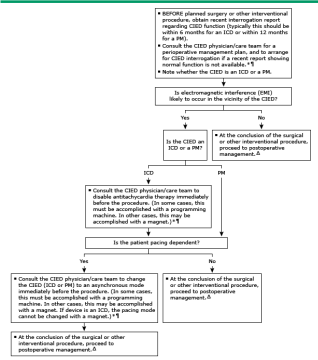
- Pre-op navigator → Pre-op eval → Equipment requests
- Equipment requests placed by 10 pm for first cases or 90 minutes ahead of time for subsequent cases will be seen by anesthesia techs and equipment will be ready in the OR for your AM setup

Screenshot of NoteWriter showing 'Equipment Requests' tab with a circled red box around the heading.

# 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

## Pre- and intraoperative management of patients with a pacemaker or implantable cardioverter-defibrillator\*



**Preoperative evaluation for patients with a cardiac implantable electronic device (CIED)**

**A. CIED information needed at time of preoperative evaluation**

- Model/Manufacturer
- Device location (epicardial or endocardial PM, transvenous or subcutaneous ICD)
- Reseeding history (single)
- Program/Mode
- Modes
  - Single PM and CDD
  - High-energy ICD mode
  - Maximum heart rate (bpm) or F (burst/short burst mode) 100, 1000
  - Max. ICD
  - ICD off
  - If off, will it stay on?
  - ICD not tested
- Does programming (mode, rate, delay, etc.) prevent supra-ventricular tachycardia?
- Interactions that require an anesthesiologist to be present (cardiac anesthesia, anesthesia induction)
- Interactions that require an anesthesiologist to be present (cardiac anesthesia, anesthesia induction)
  1. Anesthesia induction: ensure the patient is awake before the CIED will pace for heart in the absence of AVN or SVT
  2. Anesthesia maintenance: ensure the patient is awake before the CIED will pace for heart in the absence of AVN or SVT
  3. Rate that requires high rate pacing: usually 100 bpm for 1:1:10 minutes - interrupted for a 10 minute break to prevent neurovascular compromise
- Is pacing and/or defibrillation
  - essential to the patient's well-being?
  - Is Sub-Model "ventricular sense and/or defibrillation" or "defibrillation only" mode?
  - Is the CIED in "synchronous" mode?
  - Is the CIED in "asynchronous" mode?
  - Is the CIED in "ventricular sense and/or defibrillation" mode?
  - Is the CIED in "asynchronous" mode?
  - Is the CIED in "ventricular sense and/or defibrillation" mode?
- High-rate pacing (usually 100-120 bpm) and AV delay (and settings on, off)
- Is the CIED in "synchronous" mode?
- Is the CIED in "asynchronous" mode?
- Is the CIED in "ventricular sense and/or defibrillation" mode?
- Is the CIED in "asynchronous" mode?

**B. Patient information**

- Medical history
  - Existing rhythm (sinus, atrial, ventricular, or unknown)
  - History of syncope (transient loss of consciousness)
  - History of arrhythmias and pharmacologic or electrical treatments (ICD)
  - History of structural heart disease (dilated cardiomyopathy, hypertrophic cardiomyopathy, aortic stenosis)
  - Family history of sudden cardiac death
  - Drug allergy
- Current medications
  - Anti-arrhythmic drugs
  - Beta-blockers
  - Calcium channel blockers
  - Diuretics
  - Digoxin
  - Sedatives
  - Anticoagulants
  - Anti-infectives
  - Insulin
  - Chemotherapy
  - Anti-epileptics
  - Anti-platelet/anti-thrombotic
  - Anti-hypertensives
  - Anti-diabetics
  - Immunosuppressants
  - Hormones
  - Vitamins
  - Herbal supplements
  - Alcohol
  - Tobacco
  - Other
- Procedure information
  - Name of procedure
  - Reason for procedure
  - Patient position during the procedure
  - Need for sedation/analgesia
  - Need for anesthesia
  - Need for ventilation
  - Need for defibrillation
  - Need for continuous resuscitation
  - Need for cardiac arrest simulation
  - Need for cardiac arrest simulation
  - Need for cardiac arrest simulation
  - Need for cardiac arrest simulation

## Reprogramming of the cardiac implantable electronic device (CIED) likely to be necessary to:

- Disable anti-tachyarrhythmia therapy (shock[s] and antibradycardia pacing) in an ICD when EMI is expected.
  - Disable anti-tachyarrhythmia therapy where movement from shock might create a hazard (eg, intraocular surgery).
  - Disable asynchronous pacing in a pacing-dependent patient when EMI is expected.
  - Increase the paced heart rate in a patient with sinus node incompetence to augment perioperative cardiac output and oxygen delivery.
  - Disable a minute ventilation sensor to prevent inappropriate high rate pacing in the presence of any monopolar radiofrequency instruments.
  - Disable a mechanical rate sensor where surgery will likely produce mechanical stimulation near the pulse generator (eg, breast surgery).
- Magnet use may be an acceptable alternative to reprogramming with a programming machine if:**
- Response to magnet is known and effect is desirable
  - Patient is supine
  - Access to magnet is adequate
  - Magnet can be observed
  - Magnet can be easily removed in case of arrhythmia

## Postoperative management of patients with a pacemaker or implantable cardioverter-defibrillator\*

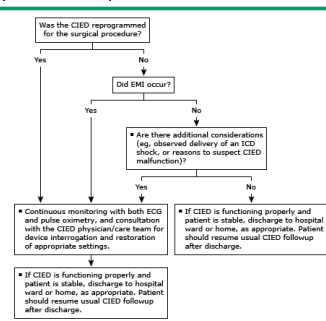


Table with multiple columns detailing various clinical scenarios and management steps for CIED patients.

ICD response to magnet placement

ICD manufacturer	Magnet mode designation	Effect on tachy therapy	Effect on brady therapy (regular pacing)	Magnet mode confirmation
Medtronic		Disables	No effect	None
Boston Scientific (Ouster Medical, etc)	Transvenous "BSC" all "BSC" (except 119, 210) or "BSC"	ON (DEFAULT)	Disables	No effect
	OFF	No effect	No effect	None
	Transvenous "TPT", "TCL", "BOS 119", "BOS 207"	ON (DEFAULT)	Disables	No effect
	OFF	No effect	No effect	None
	Subcutaneous	Disables	No effect	None
	Disables	No effect	No effect	None
Medtronic	AT 300*	Disables	No effect	None
	All others	Disables	No effect	None
Pacemaker and St. Jude Medical	NORMAL (DEFAULT)	Disables	No effect	None
	SINCE	No effect	No effect	None
Siemens (see ILA Medical)		Disables	No effect	None

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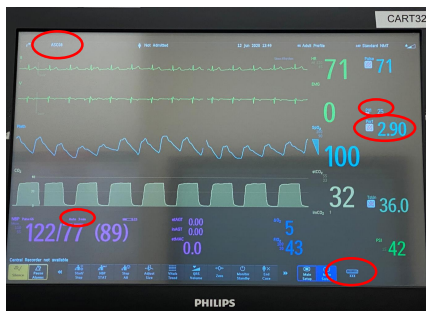
# OR Setup

## 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.
- 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



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

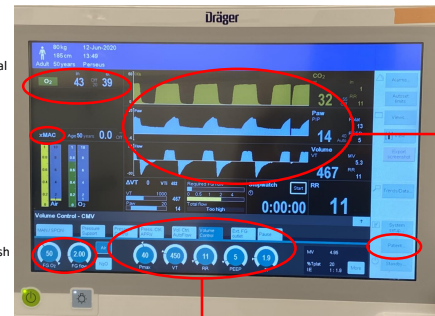
Remember to check that your BP cuff is set to cycle at the desired frequency

## 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 =  $22 \times \text{height (in m)}^2$
    - Lean body weight = Ideal body weight  $\times 1.2$

## 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

## Drips – Opioids

Medication	Dilution	Typical infusion rate
Remifentanyl	1 mg into 20 mL OR 2 mg into 40 mL = 50 mcg/mL	0.05-0.2 mcg/kg/min
Sufentanyl	250 mcg into 50 mL = 5 mcg/mL	0.1-0.5 mcg/kg/hr  Typically started at 0.3 mcg/kg/hr and decreased to 0.2 and then 0.1 mcg/kg/hr about 1/3 and 2/3 of the way through the case, respectively

## Drips – Analgesics and Anxiolytics

Medication	Dilution	Typical infusion rate
Dexmedetomidine	0.2 mg into 50 mL = 4 mcg/mL	Loading dose 1 mcg/kg over 10 min  Then run at 0.2-1 mcg/kg/hr
Lidocaine	500 mg (50 mL of 1% lidocaine) comes in a vial available in the Omnicell drawer  Draw up into 50 mL syringe	1 mg/kg/hr  Check plasma levels Q8h

## Drips – Pressors and Inotropes

Medication	Dilution	Typical infusion rate
Phenylephrine	40 mg in 250 mL = 160 mcg/mL  If no drip available from pharmacy, you can also place one 10 mg vial into a 100 mL saline bag for a concentration of 100 mcg/mL	0.2-1 mcg/kg/min
Norepinephrine	4 mg in 250 mL = 16 mcg/mL	0.02-0.1 mcg/kg/min
Vasopressin	60 units in 100 mL = 0.6 units/mL  For a bolus syringe, always dilute to 1 unit/mL (one 20 unit vial into 20 mL of saline)	0.01-0.04 units/min
Epinephrine	4 mg in 250 mL = 16 mcg/mL	0.02-0.1 mcg/kg/min
Dopamine	400 mg in 250 mL = 1600 mcg/mL	1-10 mcg/kg/min
Milrinone	20 mg in 100 mL = 200 mcg/mL	Loading dose 50 mcg/kg over 10 min  Then run at 0.125-0.5 mcg/kg/min

## Drips - Antihypertensives

Medication	Dilution	Typical infusion rate
Clevidipine	25 mg in 50 mL vial = 0.5 mg/mL  If giving as a bolus, draw up into TB syringe and give 0.1 mL (0.05 mg) at a time	1-20 mg/hr
Esmolol	2500 mg in 250 mL = 10 mg/mL	50-300 mcg/kg/min
Nicardipine	25 mg into 250 mL = 0.1 mg/mL  If giving as a bolus, draw into a syringe and give 0.5-1 mL (50-100 mcg) at a time	1-15 mg/hr
Nitroglycerin	50 mg into 250 mL = 200 mcg/mL	0.1-1 mcg/kg/min
Nitroprusside	50 mg into 250 mL = 200 mcg/mL	0.1-1 mcg/kg/min

## Airway Equipment

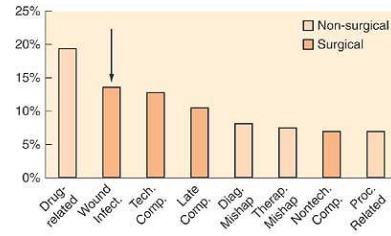
- At a minimum, always have an ETT with stylet and 10 mL syringe, either video or standard laryngoscope, and appropriately sized oral airway
- Always have a backup airway plan, with supplies available
  - Bougie is available in all ORs
  - LMAs may also be useful for airway rescue and are stocked in 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
- 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

- For a standard setup, have rescue drugs immediately available
  - Phenylephrine, ephedrine, and glycopyrrolate 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
  - If you anticipate needing to give other pressors or antihypertensives, discuss with your attending what to have drawn up and available
- Have induction medications (anxiolytic, opioid, induction agent, and muscle relaxant) and any other meds that need to be given soon after induction (antibiotics, steroids) drawn up and ready

# 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)**

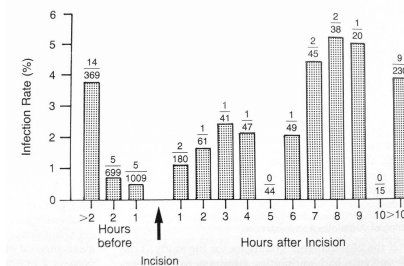
SSIs- now a marker of quality of care in the US, Medicare no longer reimburses for certain SSIs (ie mediastinitis after cardiac surgery, SSIs post-bariatric surgery & some orthopedic procedures)

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)  <i>Clindamycin can be used as an alternative. Based on 2015 SHC Antibiogram, 81% MSSA susc to clinda vs 100% MSSA susc to vanc</i>
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
<b>Urology</b>  <i>These are EMPIRIC abx recs when no preoperative urine cx available or culture negative. Ask urology team for recs.</i>	<i>If clean:</i> Cefazolin  <i>If clean contaminated (eg open or lap with ileal conduit)- cefoxitin</i>  <i>If prosthetic material involved, should add gentamicin x1 dose</i>	Gentamicin + Clindamycin <sup>1</sup> <i>If clean: (skin incision only)- clinda!</i> <i>If clean-contaminated: metronidazole + levofloxacin</i>  <sup>1</sup> sub vanc for clinda if MRSA due to clinda poor urinary penetration
Head & Neck	Clean or ear/sinonasal: Cefazolin  <i>If contaminated (include oral mucosa breach)- Cefazolin+ Metronidazole</i>	Clindamycin

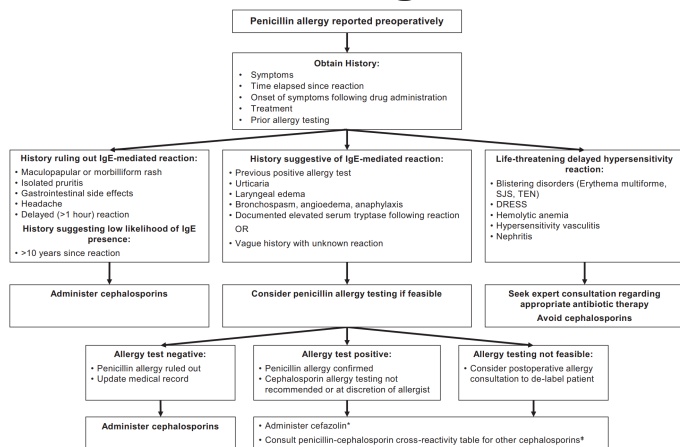
\*Based on 2013 consensus guidelines from American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS) and the Society for Healthcare Epidemiology of America (SHEA)

## 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

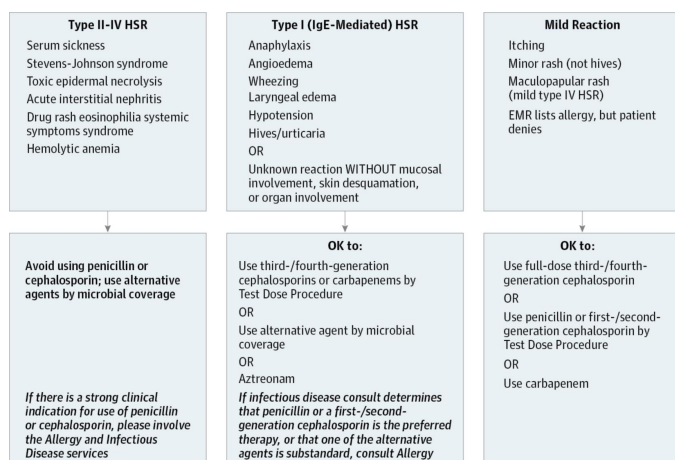
\*As a general rule, for drugs with a greater therapeutic index, you can administer them faster

## Perioperative Antibiotic Decision Algorithm



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

## Penicillin Allergy Pathway for Antibiotic Prescriptions



From Vaisman, et al. JAMA 2017

## Allergies and Interactions

- Penicillins and 1<sup>st</sup> & 2<sup>nd</sup> generation cephalosporins have similar side change with some risk of cross-reactivity
  - Cephalothin (1<sup>st</sup> 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 1<sup>st</sup> & 2<sup>nd</sup> cephalosporins is 1-10%
  - Cross-reaction rate between 3<sup>rd</sup> 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

## 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

## 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 musculoskeletal 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.

# References

## 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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- Vorobeichik, L; Weber, EA; Tarshis, J. Misconceptions Surrounding Penicillin Allergy: Implications for Anesthesiologists. *Anesthesia & Analgesia*: September 2018 - Volume 127 - Issue 3 - p 642-649 doi: 10.1213/ANE.0000000000003419.
- 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 >70 <sup>th</sup> percentile
ABA BASIC Exam	June of CA-1 year	Pass/Fail. No percentile reported.
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

\*\*Exam dates for 2020 have been affected by the COVID-19 pandemic and future exam dates may be subject to change

## What to study?

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

- CA-1 Tutorial Textbook
- 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
  - *Hall's Anesthesia: A Comprehensive Review*
- Online resources
  - Open Anesthesia: <http://openanesthesia.org>
  - Learnly: <https://learnly.org>
- Podcasts
  - ACCRaC: <http://accrac.com/>
- Online library
  - Stanford Anesthesia: <http://inkling.com/read> - (\*ask others for the username and password)
  - Lane Library: <https://lane.stanford.edu/index.html> (access to UpToDate, PubMed, and all major journals)
- Textbooks
  - *Faust's Anesthesia Review* (concise short chapters to cover ITE topics)
  - Available through Lane Library: *Basics of Anesthesia* (Miller), *Clinical Anesthesiology* (Morgan & Mikhail), *Clinical Anesthesia* (Barash), *Anesthesiology* (Yao & Artusio)



# Techniques

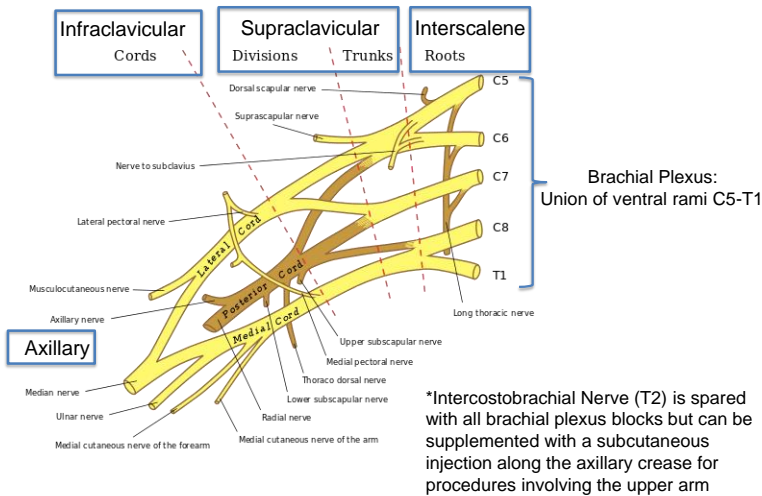
## Subspecialty Anesthesia: Basic Sciences

### Appendix

- Ultrasound-guided
  - **Primary modality** for majority of peripheral nerve localization
    - May be combined with other techniques PRN
  - High frequency sounds waves 1-20MHz
  - Hypochoic: 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 = **intra-neural** 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



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 hypochoic 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

# 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 anesthetic

## ACUTE AND CHRONIC PAIN

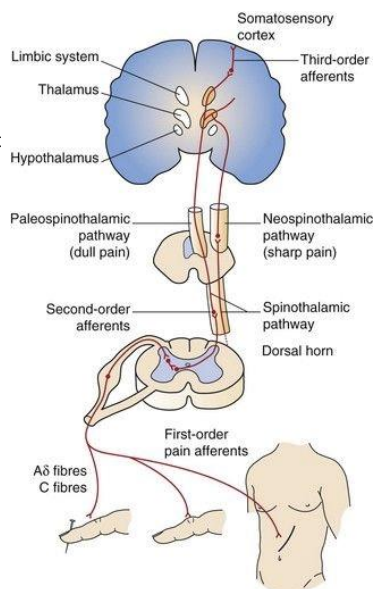
## Pain Basics

- 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
  - Polynuropathies and mononeuropathies
  - Less likely responds to pharmacologic treatments like opioids

## ACUTE AND CHRONIC PAIN

### PAIN PATHWAY:

- 1<sup>st</sup> 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 2<sup>nd</sup> order neuron
- 2<sup>nd</sup> order neuron
  - Axon crosses midline and ascends in contralateral spinothalamic tract to thalamus
  - Synapses with 3<sup>rd</sup> order neuron
- 3<sup>rd</sup> order neuron
  - Sends projections via internal capsule and corona radiata to the postcentral gyrus of the cerebral cortex



# 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 fascial 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 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 subthreshold afferent input
- Peripheral sensitization**- increased responsiveness and reduced threshold of nociceptive neurons in the periphery to the stimulation of their receptive fields

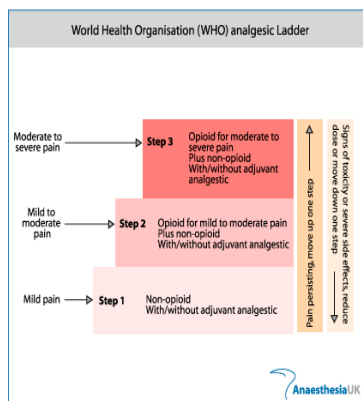
## ACUTE AND CHRONIC PAIN

## Pain 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 somatosensory 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
Eiglottis Shape	Floppy, omega shaped	Firm, flatter
Epiglottis Level	Level of C3 - C4	Level of C5 - C6
Trachea	Smaller, shorter	Wider, longer
Larynx Shape	Funnel shaped	Column
Larynx Position	Angles posteriorly away from glottis	Straight up and down
Narrowest Point	Sub-glottic region	At level of Vocal cords
Lung Volume	250ml at birth	6000 ml as adult

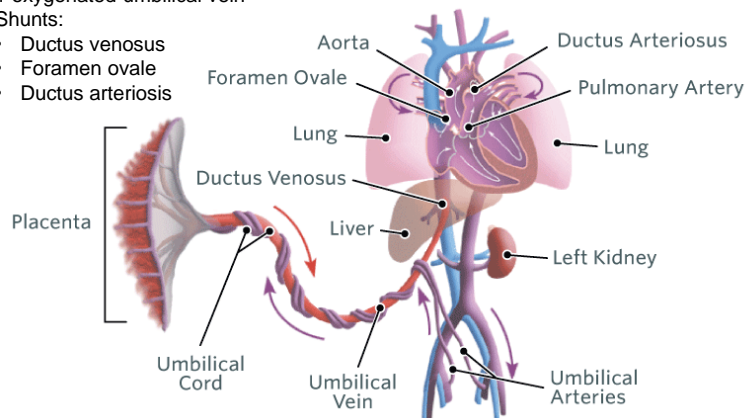
## PEDIATRICS

### Fetal Circulation

2 deoxygenated umbilical arteries  
1 oxygenated umbilical vein

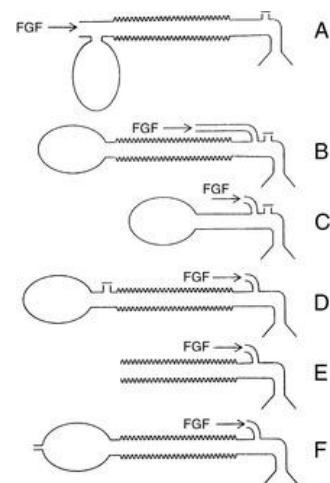
Shunts:

- Ductus venosus
- Foramen ovale
- Ductus arteriosus



## PEDIATRICS

### Pediatric Breathing Circuits



- Lack unidirectional valves
- No CO<sub>2</sub> 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 3<sup>rd</sup> day postpartum
    - Likely in part due to progesterone (sedating at high doses!) and  $\beta$ -endorphins
  - **MLAC**: minimum local anesthetic 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

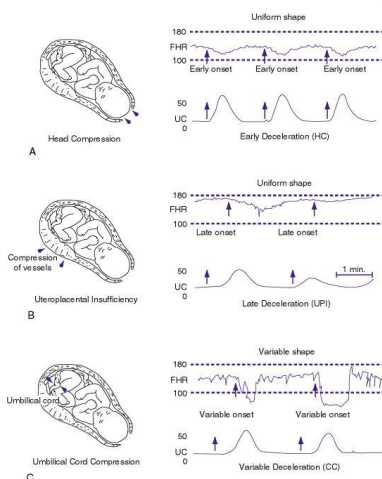
## Maternal Physiology of Pregnancy

- 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 PaCO<sub>2</sub> 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

## 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

## Fetal Heart Tracings



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## 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

## 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

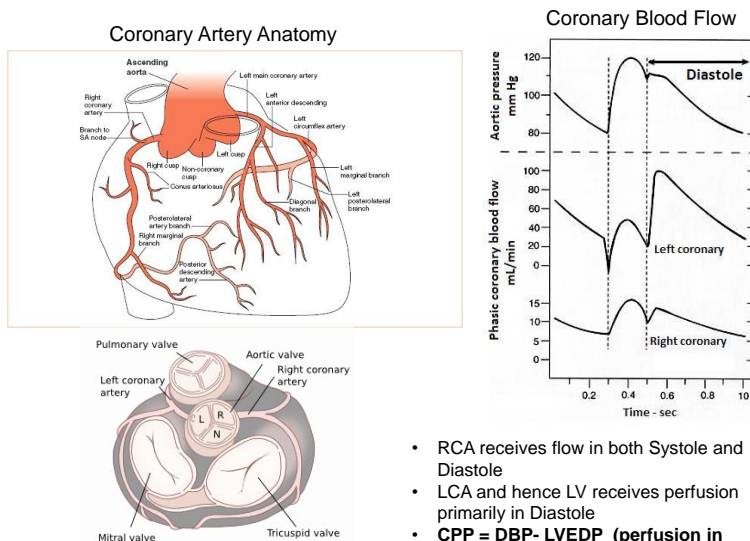
## Uterine Blood Flow

- 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

# Common Cardiac Equations

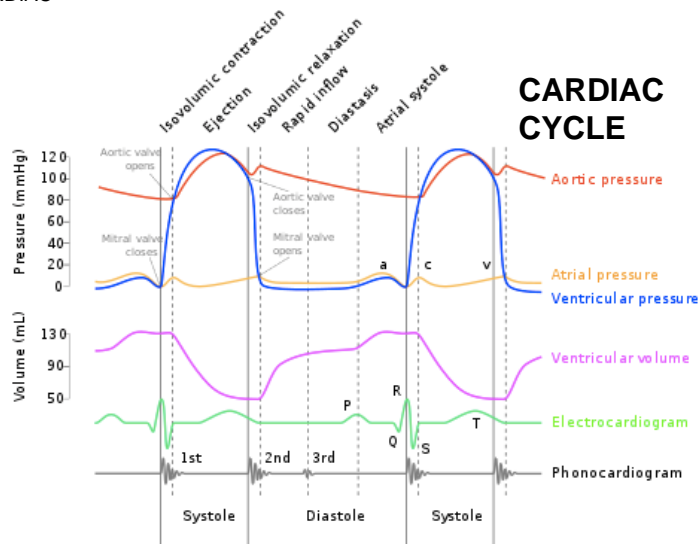
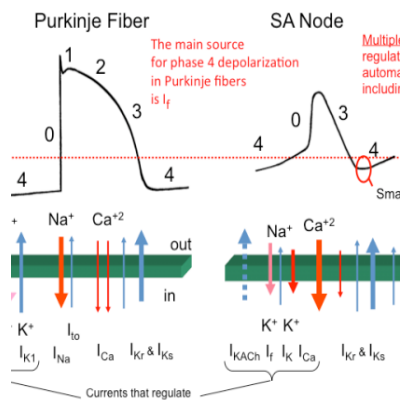
- Cardiac Output (CO) = HR x SV
- Stroke Volume (SV) = EDV - ESV
- Ejection Fraction (EF) = SV/EDV
- Mean Arterial Pressure (MAP) = (2xDBP + SBP)/3
- Systemic Vascular Resistance (SVR) =  $\frac{(MAP-CVP)}{CO} \times 80^*$
- Pulmonary Vascular Resistance (PVR) =  $\frac{(PAP-PCWP)}{CO} \times 80^*$
-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

\*Multiply by 80 to convert SVR/PVR units to dynes/sec/cm<sup>-5</sup>

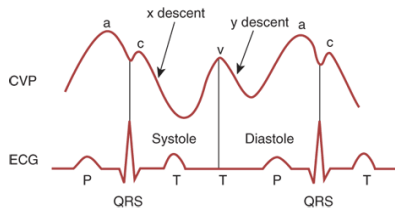


# Electrophysiology

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

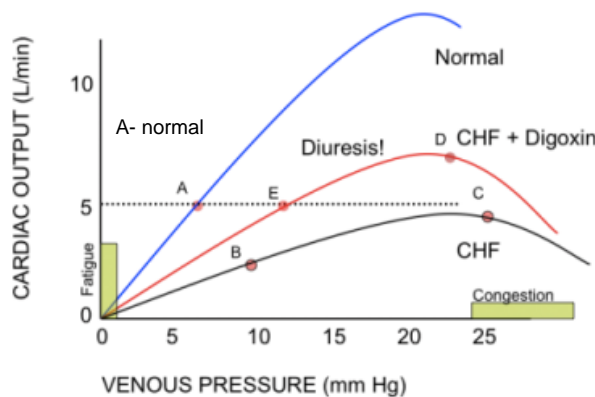


Atrial kick during diastolic filling "a" wave = 25% of EDV



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

## 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)