Name:_____

2017 CA-1 TUTORIAL TEXTBOOK 11th Edition

STANFORD UNIVERSITY MEDICAL CENTER DEPARTMENT OF ANESTHESIOLOGY

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STANFORD SCHOOL OF MEDICINE
Stanford University Medical Center

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INTRODUCTION TO THE CA-1 TUTORIAL MONTH

We want to welcome you as the newest members of the Department of Anesthesia at Stanford! Your first weeks and months as an anesthesia resident are exciting, challenging, stressful, and rewarding. Regardless how much or how little experience you have in the field of anesthesiology, the learning curve for the next few months will be very steep. In addition to structured lectures and independent study, you will be primarily responsible for patients as they undergo anesthesia and surgery.

Several years ago, before the development of this mentoring and tutorial system, CA-1's 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-1's worked with different attendings every 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 that independent study is a must. Teaching in the OR is lost without a foundation of knowledge. Afternoon lectures are more meaningful if you have already read or discussed the material. 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.

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 skill-set 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 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.

ACKNOWLEDGEMENTS

Thanks to Janine Roberts and Kathrina De La Cruz for their 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. If you ever feel like you're staying too late, know that Dr. Pearl is probably still working in his office when you leave the OR.

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 of 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. Also, 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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1st Edition (2007)

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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_2 absorbers.
c. Set up appropriate equipment and medications necessary for administration of anesthesia.
d. Conduct a focused history with emphasis on co-existing diseases that are of importance to anesthesia.
e. Perform a physical examination with special attention to the airway and cardiopulmonary systems.
f. Understand the proper use of laboratory testing and how abnormalities could impact overall anesthetic management.
g. Discuss appropriate anesthetic plan with patient and obtain an informed consent.
h. Write a pre-operative History & Physical with Assessment & Plan in the chart.

II. Anesthetic Management

a. Placement of intravenous cannulae. 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
    iii. Neuromuscular blocking agents: Succinylcholine and at least one non-depolarizing agent
    iv. Anticholinesterase and Anticholinergic reversal agents: Neostigmine and Glycopyrrolate
    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
July 5-7	_____ Discuss etiquette in the OR
	_____ Discuss proper documentation
	_____ Discuss proper sign out
	_____ Discuss post-op orders
	_____ Machine check
Week One	_____ Standard Monitors
July 10-14	_____ Inhalational Agents
	_____ MAC & Awareness
	_____ IV Anesthetic Agents
	_____ Rational Opioid Use
	_____ Intra-operative Hypotension & Hypertension
	_____ Neuromuscular Blocking Agents
Week Two	_____ Difficult Airway Algorithm
July 17-21	_____ Fluid Management
	_____ Transfusion Therapy
	_____ Hypoxemia
	_____ Electrolyte Abnormalities
	_____ PONV
	_____ Extubation Criteria & Delayed Emergence
Week Three	_____ Laryngospasm & Aspiration
July 24-28	_____ Oxygen Failure in the OR
	_____ Anaphylaxis
	_____ Local Anesthetics
	_____ ACLS
	_____ Malignant Hyperthermia
	_____ Perioperative Antibiotics

CA-1 INTRODUCTORY LECTURES – JULY 2017

Date	Time	Lecture	Chapter
7/5/2017	4:00PM	Introduction | Dr. Adriano	
	4:15PM	Introduction to Libero Lecture App | Dr. Tanaka	
	4:45PM	Ethics and Professionalism | Dr. Brock-Utne	
7/6/2017	4:00 pm	ASA Monitoring | Dr. Jaffe	
7/10/2017	4:00 pm	Basic Anesthesia Machines | Dr. Jaffe	
7/11/2017	4:00 pm	Pharmacology of Inhalational Agents | Dr. Painter	25, 26
	5:00 pm	Chief Resident Rounds 1	
7/12/2017	4:00 - 6:30 pm	Central Line Workshop | Dr. Mihm **(located at LKSC, LK005)**	
7/13/2017	4:00 pm	Principles of Pharmacology | Dr. Ingrande	24
	5:00 pm	Chief Resident Rounds 2	
7/17/2017	4:00 pm	Pharmacology of Intravenous Agents | Dr. Painter	30
	5:00 pm	Chief Resident Rounds 3	
7/18/2017	4:00 pm	Devising an Anesthetic Plan | Dr. Schmiesing	38
	5:00 pm	Chief Resident Rounds 4	
7/19/2017	4:00 pm	Positioning and Associated Risks | Dr. Drover	41
	5:00 pm	Chief Resident Rounds 5	
7/20/2017	4:00 pm	Respiratory Physiology | Dr. Lorenzo	19
	5:00 pm	Chief Resident Rounds 6	
7/24/2017	4:00 - 4:15 pm	Wellness Retreat | Dr. Hasan-Hill	
	4:15 pm	The Drugs in the Drawer | Dr. Heifets	
	5:00 pm	Chief Resident Rounds 7	
7/25/2017	4:00-4:20PM	Introduction to Nurse Colleagues | Dr. Hasan-Hill	
	4:20 - 5:00 pm	Orientation Items | Janine	
	5:00 pm	Chief Resident Rounds 8	
7/26/2017	4:00 pm	Pharmacology of Neuromuscular Blockade | Dr. Joseph	34
	5:00 pm	Chief Resident Rounds 9	
7/27/2017	4:00 pm	SAB/Epidural Regional Anesthesia | Dr. Basarab-Tung	
	5:00 pm	Chief Resident Rounds 10	
7/31/2017	4:00 pm	Airway Management | Dr. Collins	55
	5:00 pm	Chief Resident Rounds 11	

*Miller's Anesthesia is the reference text for these lectures.

**All lectures are held in the Anesthesia Conference Room unless otherwise noted.

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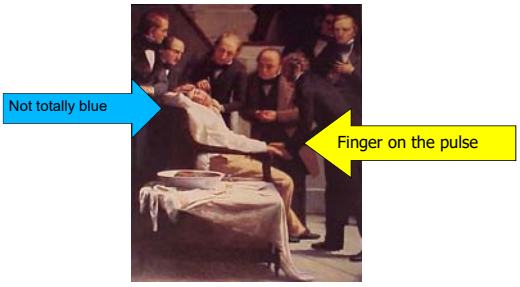
Monitoring in the Past



Basic Anesthetic Monitoring

ASA Standards for Basic Anesthetic Monitoring

STANDARD I

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

STANDARD II

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

OXYGENATION
- -Inspired gas
  - -FiO2 analyzer + low O2 concentration alarm
- -Blood oxygenation
  - -Pulse oximetry with variable pitch tone

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

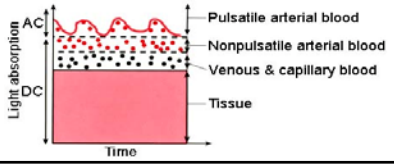
CIRCULATION
- EKG
  - Min 3 lead, consider 5 lead if any cardiac concerns
- Blood pressure
  - Minimum cycle q5 minutes
- Other continuous assessment
  - Pulse ox tracing, a line tracing, palpable pulse, auscultation, doppler

TEMPERATURE
- temperature probe

Pulse Oximetry

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

Fundamentals
- The probe emits light at 660 nm (red, for Hb) and 940 nm (infrared, for O_2Hb); sensors detect the light 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_pO_2 (S = 1:1 ratio = S_aO_2 85% → why a pulse ox not connected to the patient reads usually 85%).



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

Pulse Oximetry

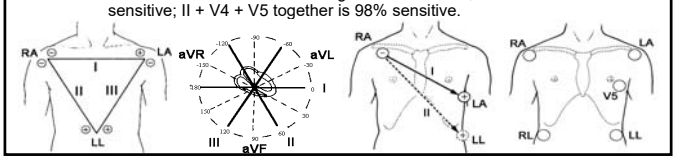
Pearls
- Methemoglobin (MetHb) - Similar light absorption at 660 nm and 940 nm (1:1 ratio); at high levels, S_pO_2 approaches 85%. When SaO2 is >85%, you will get a falsely low pulseox reading with MetHb. If SaO2 is actually <85%, you will get a falsely high reading.
- Carboxyhemoglobin (COHb) - Similar absorbance to O_2Hb. At 50% COHb, S_aO_2 = 50% on ABG, but S_pO_2 may be 95%, thus producing a falsely HIGH S_pO_2.
- Other factors producing a falsely LOW S_pO_2 = dyes (methylene blue > indocyanine green > indigo carmine), blue nail polish, shivering/other motion, ambient light, low perfusion (low cardiac output, profound anemia, hypothermia, elevated SVR), malpositioned sensor.
- Factors with NO EFFECT on S_pO_2 = bilirubin, HbF, HbS, SuHb, acrylic nails, flourescein dye.
- Cyanosis - clinically apparent with 5 g/dl desaturated Hb. At Hb = 15 g/dl, cyanosis occurs at S_aO_2 = 80%; at Hb = 9 g/dl (i.e. anemia), cyanosis occurs at S_aO_2 = 66%.

EKG

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

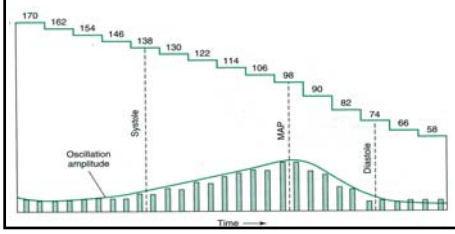
Modified 3-Electrode System
- If you have concerns for anterior wall ischemia, move L arm lead to V5 position, and monitor Lead I for ischemia.

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



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 >50% of extremity; width should be 20-50% greater than diameter of extremity.
- Cuff too small = falsely HIGH BP. Cuff too big = falsely LOW BP.



FYI:

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

Arterial Blood Pressure

Indications

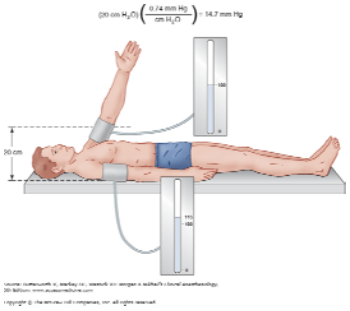
- Moment-to-moment BP changes anticipated and rapid detection is vital.
- Planned pharmacologic or mechanical manipulation.
- Repeated blood sampling.
- Failure of NIBP.
- Supplementary diagnostic information (e.g. perfusion of dysrhythmic activity, volume status, IABP).

Transducer Setup

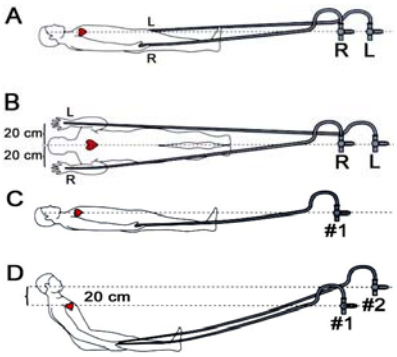
- Zeroing = exposes the transducer to air-fluid interface at any stopcock, thus establishing P_{atm} as the "zero" reference pressure.
- Leveling = assigns the zero reference point to a specific point on the patient; by convention, the transducer is "leveled" at the right atrium, but can level at any area of interest (eg in neurosurgery, level at circle of willis to know BP at surgical site)

Blood pressure, cont

- More distal sites have higher BP since wave reflection distorts the waveform, resulting in exaggerated systolic BP and pulse pressure at more distal sites (radial SBP > aortic SBP)
- BP varies by position: The difference in blood pressure (mm Hg) at two different sites of measurement equals the height of an interposed column of water (cm H2O) multiplied by a conversion factor (1 cm H2O = 0.74 mm Hg, or 15 cm height = 10 mm Hg)
  - Example: Beach chair position, cuff on leg --> cuff pressure will read much higher than actual MAP at brain



Effect of Patient & Transducer Position on BP Measurement



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

		#1	#2
C	ABP	120/80	
D	ABP	120/80	105/65

FYI:

10 cm H_2O = 7.4 mm Hg

Capnography

- Both the number and tracing provide much physiologic information

  -bronchospasm (upsloping trace)

  -inadequate circulation resulting from hypotension indicating BP is too low for pt (number decreasing)

  -pulmonary embolism (decreased number and increased gradient between ETCO2 and PaCO2)

  -adequacy of CPR eliminating need for pulse checks and compression interruption (ETCO2>10; if sudden increase in ETCO2, then likely have ROSC)

  -pt breathing spontaneously (more rounded trace)

  -esophageal intubation, circuit disconnect (no ETCO2 tracing)

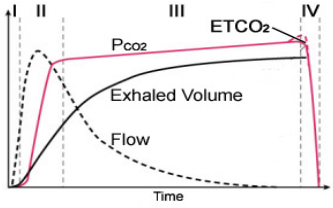
  -exhausted CO2 absorbent (ETCO2 does not return to 0-5)

Clinical pearl:

when apneic: expect ETCO2 to increase by 6 after 1 minute, and to increase by 3 every minute thereafter

Capnography

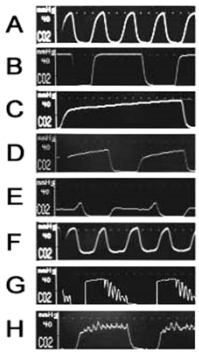
- Measures exhaled CO_2 (and other gases).
- Time delay exists due to length and volume of sample tube as well as sampling rate (50-500 ml/min).
- Anything distal to your Y-piece increases dead space



Capnogram Phases

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

Capnography



Example Traces

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

For more example tracings visit:
http://www.capnography.com/find.htm

Temperature

Monitoring is required if any anticipated change in temperature

Sites

- Pulmonary artery = "Core" temperature (gold standard)
- Tympanic membrane - correlates well with core; approximates brain/hypothalamic temperature
- Esophagus - correlates well with core (avoid w esophageal varices)
- Nasopharyngeal - correlates well with core and brain temperature (careful with coagulopathy, can get refractory epistaxis)
- Rectal - not accurate (temp affected by LE venous return, enteric organisms, and stool insulation)
- 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
- Skin - inaccurate; varies by site
- Oropharynx – good estimate of core temperature; recent studies show correlation with tympanic and esophageal temperatures

*Anticipate heat loss with GA as vasodilation causes blood redistribution from core to periphery

Causes of heat loss:
Radiation (*most common cause in OR), conduction, convection, evaporation

Other Monitors/Adjuncts to Consider

- Foley
- OG tube
- CVC
- Esophageal stethoscope
- ICP
- Pulmonary Artery catheter +/- continuous cardiac output
- BIS monitor/Sedline
- Precordial doppler (if risk of air embolus high)
- Transesophageal echo
- Cerebral oximetry (NIRS)

I just intubated, now what?!

- **Remember your A's**

-Adjust (vent settings, volatile)
-A temp probe
-Acid (OG tube)
-Antibiotics
-Air (Forced Air, aka Bair Hugger)
-Another IV
-A line

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Inhalational Agents

Historical Facts

- Several accounts of various forms of anesthesia in the BCE era using everything from cannabis and other herbs to carotid compression.

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

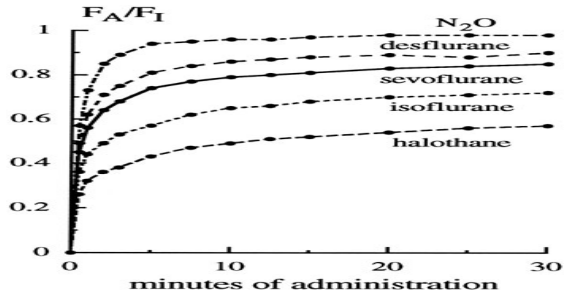
Pharmacokinetics

- Mechanism of action is complex, likely involving numerous membrane proteins and ion channels
- The pharmacokinetics of inhalational agents is divided into four phases
  - Absorption
  - Distribution (to the CNS/brain = site of action)
  - Metabolism (minimal)
  - Excretion (minimal)
- Goal is to produce a partial pressure of gas in the alveolus that will equilibrate with the CNS to render anesthesia
  - ***It is the PARTIAL PRESSURE that yields the effect, not the concentration
  - As higher altitudes where barometric is <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

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

Uptake and Distribution

- Fi (inspiratory concentration) = fresh gas leaving the anesthesia machine mixed with gas in circuit
  - Actual inspired concentration is closer to set inspired concentration when:
    - Higher fresh gas flows, smaller circuit, and small circuit absorption
- P_A (alveolar partial pressure) is determined by input (delivery) minus uptake (loss)
  - Input: inspired partial pressure, alveolar ventilation, breathing system
  - Uptake: gas taken up by the pulmonary circulation. Solubility in blood (defined by the blood gas partition coefficient), cardiac output, alveolar-to-venous partial pressure difference
    - 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
- F_A lags behind Fi due to uptake by the pulmonary circulation. How fast the ratio F_A/F_I rises equates to how speed of onset. Remember F_A = Arterial partial pressure = CNS partial pressure
- The greater the uptake (in blood), the slower the rate of rise of F_A/F_I
  - The gases with the lowest solubilities in blood (i.e. desflurane) will have the fastest rise in F_A/F_I (Nitrous Oxide has a higher solubility than desflurane but has a faster onset due to "concentration effect")
  - They also have the fastest elimination



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 Coeffecient	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% N2O then 1ml of blood will contain 0.47x0.5 ml's of N20 or 0.235 ml's #Jaffe

Fat:Blood partition coefficient is >1 therefore things that increase fat in the blood like postpradial lipidemia will increase the overall blood:gas partition coefficient. Anemia will decrease it (less lipid bilayer and fat etc.

Uptake and Distribution Continued

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

** 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 - > 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:
- Increases rate of rise of Fa/Fi by the "concentration effect"
  - the higher the concentration of gas administered, the faster the alveolar concentration approaches the inspired concentration
  - only clinically relevant for nitrous (MAC of others is much lower concentration)

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 increases relative concentration of second gas

Pharmacodynamics

- All inhalational agents decrease $CMRO_2$ and increase CBF (except nitrous - increases CMRO2 and CBF)
- Sevo/Des/Iso
  - 0.5 MAC (dec CMRO2 contracts vasodilation, CBF does not increase)
  - 1 MAC (vasodilatory effects more prominent, CBF increases)
- All agents cause a dose-related decrease in blood pressure by decreasing SVR (but maintaining CO)
- All agents produce muscle relaxation (except N2O)
- The older inhalational agents (halothane, enflurane) cause decreases in myocardial contractility
  - The newer agents have little to no effect
- All inhalational agents produce a dose-dependent depression of the ventilatory response to hypercarbia and hypoxia
- Increase RR (via direct activation of respiratory center in CNS) + decrease tidal volume = preserved minute ventilation

Theory of Mechanism

- No clear mechanism
- Produce immobility via actions on the spinal cord
- Likely enhance inhibitory channels and attenuate excitatory channels; unclear if by direct binding or membrane alterations
- Anesthetic gases have been shown to affect many different ion channels, second messengers, and metabolic processes.
- GABA, NMDA, glycine receptor subunits have all been shown to be affected.
- Potency of anesthetic has been roughly linked to lipid solubility.
  - Part of mechanism may involve anesthetic gases dissolving in lipophilic sites on cells.

Nitrous Oxide

- Low potency (MAC 104% - can never reach 1 MAC!)
- Insoluble in blood
  - Facilitates rapid uptake and elimination
- Commonly administered as an anesthetic adjuvant
- Does not produce skeletal muscle relaxation
- Increases CBF and CMO2
- Can potentially contribute to PONV (but can be controlled with antiemetic ppx as shown by the ENIGMA II trial.
- 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
- 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)
- Often used as adjuvant to volatile if hypotensive
- Should periodically let air out of the ETT cuff if using nitrous to avoid tracheal injury

Isoflurane

- Highly pungent
- Second most potent of the clinically used inhalational agents (MAC 1.2%)
- Preserves flow-metabolism coupling in the brain (i.e. CMO2 to CBF)
  - Highly popular for neuroanesthesia
- 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 2.15%)
- Rapid uptake and elimination
- Sweet smelling, non-pungent
  - Quick uptake and sweet smell make this agent very popular for inhalational induction
- Potent bronchodilator
- Can form CO in desiccated CO_2 absorbent
  - Can cause fires
- Forms Compound A in CO_2 absorbent (nephrotoxic in rats)
  - 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_2O)
- Very fast uptake and elimination
- 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).
  - **Remember that the anesthetic affect correlates to the partial pressure, NOT the concentration. You will get questions about administering des and sevo in Denver or having iso in a sevo vaporizer and how you should set the vaporizer concentration
- Very pungent
  - Can cause breath-holding, bronchospasm, laryngospasm, coughing, salivation when administered to an awake patient via face mask
- Can form CO in desiccated CO_2 absorbent (more so than other volatiles)
- Can cause an increased sympathetic response (tachycardia, hypertension) when inspired concentration is increased rapidly

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5. Yasuda N, Lockhart SH, Eger E *et al*: Kinetics of desflurane, isoflurane, and halothane in humans. Anesthesiology 74:489, 1991

It was the first case in the morning. I checked the gases and they were all filled up to the top. 10 minutes into the case, half the sevo was gone and I was running low flows. I was like what the heck! My med student starts coughing, I had a big headache, the surgeons didn't say a word, which was weird because that surgeon usually says a lot. The med student also had asthma and said something was making her cough. I checked for a leak in my circuit, checked my numbers, everything was fine. I called for an anesthesia tech and they checked the caps. Turns out that the anesthesia tech the day before hadn't screwed the cap back on tightly where you refill the stuff. The room was gassed.

MAC & Awareness

Minimum Alveolar Concentration

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

Important Points

- Remarkably consistent across species
- MAC mirrors the brain partial pressure of an agent
  - At equilibrium, brain anesthetic partial pressure = alveolar partial pressure
- MAC is a population average; not a true predictor of an individual's response (MAC is an $\mathbf{ED_{50}}$ concentration)
  - the $\mathbf{ED_{95}}$ is ±25% - so at 1.3 MAC, 95% of patients will not respond to incision
- MAC values are **additive** (e.g. 0.5 MAC isoflurane + 0.5 MAC N_2O = 1 MAC)
- MAC is inversely related to anesthetic potency (lipid solubility)
  - Potency (and lipid solubility are determined by the oil:gas partition coefficient (AND NOT blood:gas partition coefficient)

MAC of Inhaled Anesthetics

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

*MAC values for adults 36-49 years old

- MAC is an indicator of **gas potency**.
  - **Oil:gas partition coefficient** is an indicator of anesthetic potency
- The blood:gas partition coefficient is an indicator of **solubility**, which affects the rate of induction and emergence; it is NOT related to MAC.

More MAC Definitions

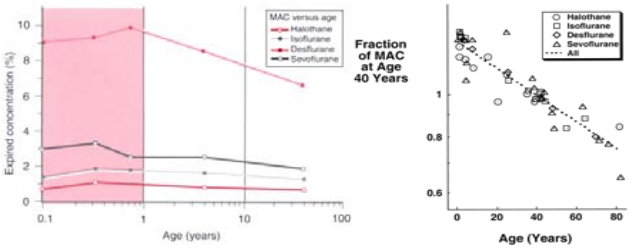
MAC_{Awake} (a.k.a. MAC-Aware)
- The MAC necessary to prevent response to verbal/tactile stimulation.
- Volatiles: ~0.4 MAC; N_2O: ~0.6 MAC

$MAC_{Movement}$
- 1.0 MAC

MAC_{EI} (a.k.a. LS, IT, or LMI = laryngoscopy, intubation, LMA insertion)
- The MAC necessary to prevent laryngeal response to "endotracheal intubation"
- Prevents movement in 99% of patients (ED_{99})
- ~1.3 MAC

MAC_{BAR}
- The MAC necessary to "blunt the autonomic response" to a noxious stimulus
- Opiates (even small amounts) and N20 often added to achieve this level and thus spare the requirement of high concentrations of halogenated anesthetics (and associated hypotension)
- ~1.6 MAC

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 an 80 year old is about 0.75 that of a 40 year old)

	Medications	**Alcohol**	**Physiologic Conditions**	**Pathophysiologic Conditions**	**Genetic Factors**
Factors Decreasing MAC	Opiates Benzodiazepines Barbituates Propofol Ketamine alpha-2 Agonists Chronic meth use Verapamil IV administered local anesthetic agents	Acute ethanol ingestion	Increasing age for patients >1 year of age pregnancy	Hypothermia Severe hypotension Severe hypoxemia Severe anemia Acute metabolic acidosis Sepsis	None established
Factors Increasing MAC	Inhibition of catecholamine reuptake (amphetamines, ephedrine, L-dopa, TCA)	Chronic ethanol abuse	First months of life for infants <6mo of age	Hyperthermia Hyperthyroidism Increased extracellular Na+ in CNS (hyperNa)	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
- Dreaming can also occur and be confused for awareness if it is disturbing to the patient; dreaming is not related to anesthetic depth

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 consciouness on EEG monitor (Bispectral Index or Sedline)

Preventing Awareness

- Consider administering an amnestic premed
- 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 (ie BIS or SedLine) if using TIVA
- Consider different treatment for hypotension other than decreasing anesthetic concentration
- Redose IV anesthetic when delivery of inhalational agent is difficult (ie during long intubation or rigid bronchoscopy)

BIS & Sedline

- Both use EEG monitoring and algorithms 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 and some studies argue that it is not more effective than monitoring end tidal gases alone.
  - Interpatient variability exists
  - Changes in EEG with medications (e.g. NDMB, ephedrine, ketamine), conditions (elderly with low amplitude), and other events (ischemia)
- Both have a roughly 2 min 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)

Management

If you suspect your patient may be aware:

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

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IV Anesthetic Agents

Mechanism of Action

- It is widely believed that most IV anesthetics exert their sedative and hypnotic effects via interaction with GABA receptors
  - GABA is the primary inhibitory neurotransmitter in the CNS
  - Activation of receptor causes increased chloride conductance, and therefore hyperpolarization (promotion of inhibition)
  - Other IV anesthetics exert effect via NMDA receptors (*Ketamine*) or alpha-2 receptors (*Dexmedetomidine*)
- *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

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

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

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

‡↓ = decrease; ↑ = increase.

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

Pharmacokinetic Values for the Currently Available Intravenous Sedative-Hypnotic Drugs

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

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

Pharmacodynamics

- The principle pharmacologic effect of IV anesthetics is to produce increasing sedation and eventually hypnosis. They can be used to induce loss of consciousness at the beginning of an anesthetic or used as infusions to maintain general anesthesia
- All hypnotics also effect other major organ systems
  - They produce a dose-dependent respiratory depression (exception: *Ketamine*)
  - They produce hypotension and cardiac depression (*Etomidate* causes the least cardiac depression)
- Profound hemodynamic effects can be seen with hypovolemia as a higher drug concentration is achieved within the central compartment
  - A large hemodynamic depressant effect can be seen in the elderly and those with pre-existing cardiovascular disease
    - These patients often exhibit decreased dose requirement

Drug	Induction Dose (mg/kg)	Effects	Pearls
Propofol	1.5-2.5	**Neuro:** Decreases cerebral metabolic O2 requirements, cerebral blood flow, intracranial pressure **CV**: Decreases SVR, direct myocardial depressant **Pulm:** Dose-dependent respiratory depression (apnea in 25-35% of patients)	-Pain on injection (32-67%) -can be attenuated with lidocaine and with injection into larger veins -Antiemetic properties -Anticonvulsant properties
Etomidate	0.2-0.3	**Neuro:** Decreases CMRO2, CBF, ICP **CV**: Maintains hemodynamic stability (minimal cardiac depression) **Pulm:** Minimal respiratory depression (no histamine release)	-Pain on injection -High incidence of PONV -Myoclonus -Inhibits adrenocortical axis
Thiopental	3-5	**Neuro:** Decreases CMRO2, CBF, ICP **CV**: Decreases SVR, direct myocardial depressant **Pulm:** Dose-dependent respiratory depression	-Anticonvulsant properties -Can precipitate when injected with acidic fluids (i.e LR)
Ketamine	1-2	**Neuro:** Increases CMRO2, CBF, ICP **CV**: Cardio-stimulating effects (negatively effects myocardial supply-demand) **Pulm:** Minimal respiratory depression; bronchodilation; most likely of all to protect airway reflexes	-Analgesic effects -Intrinsic myocardial depressant effects which may be unmasked with depleted catecholamines

Propofol

- Produced in an egg lecithin emulsion (egg yolk--not egg white--which is relevant to patient allergies, which is typically to the egg white protein) because of its high lipid solubility
- Pain on injection occurs in 32-67% of subjects; attenuated with IV lidocaine or administering the drug in a larger vein
- Induction dose 1.5-2.5 mg/kg
  - Children require higher doses (larger Vd and higher clearance)
  - Elderly require lower doses (smaller Vd and decreased clearance)
- Infusion doses ~100-200 mcg/kg/min for hypnosis and ~25-75 mcg/kg/min for sedation (depends on desired level of consciousness and infusion duration)
- Decreases $CMRO_2$, CBF, and ICP; CPP may decrease depending on effect on SBP
- 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 a background infusion for patients with PONV
- Formulations support growth of bacteria, good sterile technique and labeling of expiration times (typically 12 hours) is critical
- *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

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 CMRO2, 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

Thiopental

- Highly alkaline (pH 9)
- Can precipitate in acidic solutions (DO NOT MIX with Rocuronium or LR)
- 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 (accounts for short duration of action)
- Larger doses can saturate the peripheral compartments resulting in a prolonged duration of action
- Decreases CMRO2, CBF, ICP
  - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
- Anticonvulsant activity
  - 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

Ketamine

- Produces a dissociative anesthetic state
  - Profound analgesia and amnesia despite maintenance of consciousness
  - High incidence of psychomimetic reactions (attenuated by co-administration of midazolam)
- Induction dose 1-2 mg/kg
- NMDA antagonist (implications in prevention/treatment of chronic pain)
- Increases $CMRO_2$, CBF, ICP
  - 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)

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 CMRO2, 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 is a 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 α_2 adrenergic agonist (primarily central-acting)
- Hypnotic and analgesic
- Opioid-sparing effect and does not significantly depress respiratory drive
- Usually an infusion at a 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 2hr
- 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

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.

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 tatooed 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 (periaquaductal gray matter) and spinal cord (substantia gelatinosa)
- Well-known side effect profile:
  - Sedation, respiratory depression
  - Itching, nausea, ileus, urinary retention
  - Bradycardia, hypotension
  - Miosis (useful to assess patients under GA)
  - Chest wall rigidity
- Opioids are hemodynamically stable when given alone, but cause ↓CO, SV, and BP in combination with other anesthetics
- Reduces MAC of volatile anesthetics

Opioid Receptor Subtypes and Their Effects

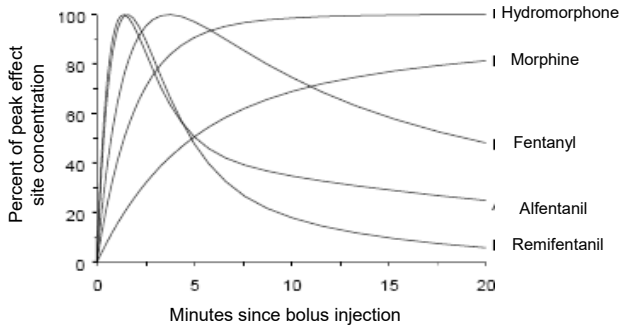
Receptor	Clinical effect	Agonists
μ	Supraspinal (μ1) Respiratory depression (μ2) Physical dependence Muscle rigidity	Morphine Met-enkephalin B-Endorphin Fentanyl
κ	Sedation Spinal analgesia	Morphine Nalbuphine Butorphanol Dynorphin Oxycodone
δ	Analgesia Behavioral Epileptogenic	Leu-enkephalin B-Endorphin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

Opioid comparison

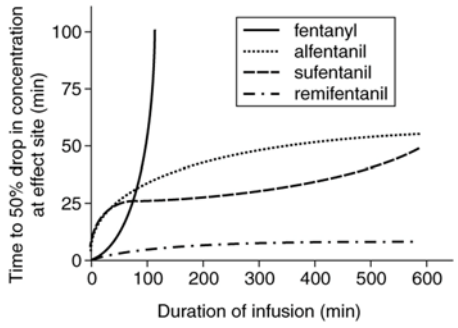
Drug	Approximate analgesic equivalent	Peak onset	Duration of action (single bolus only!)	Used as infusion
Alfentanil	500 mcg	1 – 2 min	5 – 10 min	Not common
Fentanyl	50 mcg	3 – 5 min	30 – 60 min	Use with caution*
Hydromorphone	0.75 mg	5 – 15 min	2 – 4 hours	ICU
Meperidine	37.5 mg	5 – 15 min	2 – 4 hours	No
Morphine	5 mg	10 – 20 min	4 – 5 hours	ICU (comfort care)
Remifentanil	50 mcg	3 – 5 min	5 – 10 min	OR
Sufentanil	5 mcg	3 – 5 min	20 – 45 min	OR

*Infrequently used given long context-sensitive half-life

Single bolus pharmacokinetics



Infusion pharmacokinetics



Special considerations

Fentanyl

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

Special considerations

Hydromorphone

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

Special considerations

Remifentanil

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

Special considerations

Remifentanil

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

Special considerations

Sufentanil

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

Opioids

Alfentanil

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

Opioids

Morphine

- Slower peak time and long duration of action often less desirable in acute surgical setting
- Active metabolite, 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)

- Most commonly used to treat shivering upon emergence
- Originally discovered as a local anesthetic ("pethidine")
- Active metabolite (normeperidine) lowers the seizure threshold; renally excreted
- Anticholinergic side effects: tachycardia
- Avoid using with MAOIs; can cause CNS excitation (agitation, hyperpyrexia, rigidity) and/or CNS depression (hypotension, hypoventilation, coma)
- Causes histamine release
- Has a euphoric effect with less respiratory depression than other opioids

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 caused by DL and intubation
- 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

- 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;
  - Adjuncts may be helpful (tylenol, lidocaine, ketamine, gabapentin, etc)
- Use morphine and meperidine cautiously in renal patients (renal excretion of active metabolites)!

Strategies for Opioid Use

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

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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 1) cardiac output and 2) vascular tone (SVR)

Cardiac Output (CO)
- **CO = HR x SV**

Heart Rate (HR)
- Dependent on the interplay between the sympathetic and parasympathetic nervous systems.
- In infants, SV is fixed, so CO is dependent on HR.
- In adults, SV plays a much more important role, particularly when increasing HR is not favorable (i.e. CAD)

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 = 80([MAP-CVP]/CO)**

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 Blood Pressure (SBP)
- Highest arterial pressure in the cardiac cycle.
- Dicrotic notch = a small notch in the invasive arterial pressure curve that represents closure of the aortic valve, producing a brief period of retrograde flow.

Diastolic Blood Pressure (DBP)
- Lowest arterial pressure in the cardiac cycle

Mean Arterial Pressure (MAP)
- **MAP = 2/3 DBP + 1/3 SBP, or (2xDBP + SBP) ⎪3**

Components of Blood Pressure

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.
- Readings may be affected by external pressure on cuff.

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

- "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 (e.g. "Roc-inephrine")
- Hypercarbia

Treatment of Hypertension

- Temporize with fast-onset, short-acting drugs
- Diagnose and treat the underlying cause.
- Pharmacologic Interventions:
  - Propofol or volatile anesthetics (deepen anesthesia, vasodilate)
  - Opioids (increase analgesia, histamine release causes hypotension)
  - Short-acting vasodilators
    - Clevidipine
      - Calcium-channel blocker.
      - In lipid emulsion (like propofol)
    - Nitroglycerin (venous > artierial)
    - Nitroprusside (artieral > venous) – very expensive
  - 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 mg/**hr**
Nitroglycerin	10 – 50 mcg	1 min	1 – 3 min	3 – 5 min	0.1 – 1 mcg/kg/min
Nitroprusside	10 – 50 mcg	<1 min	1 min	1 – 10 min	0.1 – 1 mcg/kg/min
Labetalol	5 – 10 mg	2 – 5 min	10 – 15 min	45 min – 6 hours	N/A
Esmolol	10 – 20 mg	1 min	2 min	10 min	50 – 300 mcg/kg/min
Hydralazine	5 mg	5 – 20 min	15 – 30 min	2 – 6 hours	N/A

Intraoperative Hypotension

- **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 lateral displacement during pregnancy
- **Surgical Events**: Vagal reflexes, obstructed venous return, pneumoperitoneum, retractors and positioning
  - Ensure: Surgeon 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
  - Call for help. Inform surgeons
- **Drugs**
  - Vasoconstrictors: phenylephrine, vasopressin, norepinephrine
  - + Inotropes: ephedrine, epinephrine
- **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

Antihypotensive 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	0.5 – 32 mg/**hr**
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

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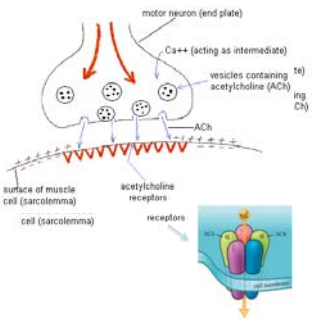
Neuromuscular Blocking Agents

Introduction

- Neuromuscular blocking agents (NMBA) are used to facilitate intubation and mechanical ventilation and improve operating conditions (e.g. laparotomy, orthopedic surgery).
- There are two categories of NMBAs with distinct properties: A) depolarizing (succinylcholine) versus B) nondepolarizing (eg. rocuronium, vecuronium, cisatracurium).
- Postoperative residual paralysis occurs frequently. Monitoring of neuromuscular blockade and pharmacological reversal are the standard of care.[1]
- NMBAs should be used judiciously as they carry their own risks. There are also many surgical- and patient-specific contraindications. Read yourtext book chapter on NMBAs several times during residency!

Neuromuscular Transmission



- Action potential depolarizes motor neuron→ Ca++ influx→ vesicles fuse and release ACh→ Ach across synaptic cleft and binds nicotinic receptors
- When ACh binds both α subunits, receptor ion channel opens with ion movement of Na+ and Ca++ in, K+ out

Depolarizing NMBA: Succinylcholine

- **Structure**: two ACh molecules joined by methyl groups
- **Mechanism of action**: ACh receptor agonist and prolonged muscle depolarization
- **Intubating Dose**: 1 – 1.5 mg/kg
- If you use a **defasciculating dose of roc** (0.03mg/kg), intubating dose of sux is higher (1.5 – 2mg/kg)
- **Onset**: within 30-60 sec; duration ~10 min depending on dose (often used for **rapid sequence induction and intubation**)
- Diffuses away to extracellular fluid → then rapidly metabolized by pseudocholinesterase = plasma cholinesterase = butyrylcholinesterase)
- ~1:3000 individuals are homozygous for an abnormal plasma cholinesterase, and paralysis can last 3-8 hours. Consider checking twitches before giving nondepolarizing NMBA after sux.
- **Dibucaine** (local anesthetic) inhibits 80% normal pseudocholinesterase activity, but 20% abnormal pseudocholinesterase activity.

Contraindications to Sux

- Hyperkalemia: Induction dose *typically* causes an increase in K^+ of 0.5 mEq/L. Normokalemic renal failure is NOT a contraindication.
- Conditions with upregulated junctional and extrajunctional cholinergic receptors: using sux can result in hyperK+ arrest. This includes burn injury (after 24-48hrs), muscular dystrophy, myotonias, prolonged immobility, crush injury, upper motor neuron insults from stroke and tumors.
- History of malignant hyperthermia and/or asociated diseases.

Additional Side Effects

- Fasciculations. Particularly painful in muscular patients. (can be decreased with **defasciculating dose of rocuronium** = 0.03 mg/kg 3 minutes prior to sux)
- Bradycardia (especially in children -- often given with atropine).
- Tachycardia
- Anaphylaxis (approx. 1:5000 – 1:10,000)
- Myalgia
- Trismus
- Increased ICP, IOP. **N.B.** Benefits of securing the airway quickly often take precedent over small increases in ICP or IOP.
- Increased intragastric pressure and lower esophageal sphincter pressure.

Nondepolarizing NMBA

- **Mechanism of action**: competitive inhibition of nicotinic Ach receptor (nAChR) at the NMJ.
- There are presynaptic nAChR which mobilize ACh containing vesicles. These presynaptic nAChR have a slightly different structure than postsynaptic nAChR. Some nondepolarizing agents block both pre- and postsynaptic nAChR.
- Two structural classes:
  1. **Benzylisoquinolinium** = "-urium"
     - Cisatracurium, Doxacurium, Atracurium, Mivacurium, d-Tubocurarine
     - Some can cause histamine release (d-Tubocurarine >> Atracurium and Mivacurium)
  2. **Aminosteroid** = "-onium"
     - Pancuronium, Vecuronium, Rocuronium, Pipecuronium
     - Vagolytic effects (Pancuronium > Rocuronium > Vecuronium)
- The most used nondepolarizing agents are the intermediate duration agents rocuronium, cisatracurium, and vecuronium.

Nondepolarizing NMBA (cont.)

- Intubating doses are **2 x ED $_{95}$** (ED_{95} = average dose required to produce 95% suppression of the twitch height in 50% of population).
- A larger intubating dose speeds onset time but lengthens duration of block.
- **Priming dose:** to increase speed of onset, can give 10% of intubating dose 3-5 minutes prior to administering actual intubating dose (efficacy debatable).
- Wide interindividual response to nondepolarizing agents. Monitor twitches and adjust doses accordingly.
- **Rocuronium can be used for rapid sequence inductions** when sux cannot, although roc is still slower. However, the increased 1 – 1.2mg/kg rocuronium necessary for RSI causes prolonged relaxation.
- Cisatracurium is degraded via **Hoffman elimination**. It can be useful for patients with hepatic or renal dysfunction.

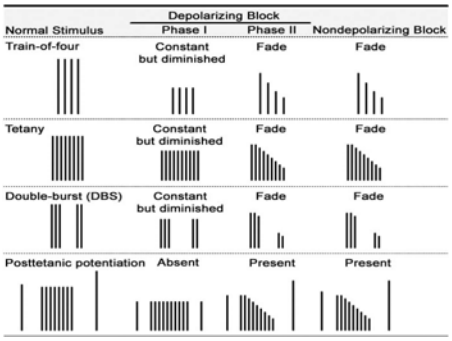
Agent	ED95 (mg/kg)	Intubating Dose (mg/kg)	Onset (min)	Duration to 25% recovery (min)	Intra-op Mainenance	Metabolism / Excretion
Succinylcholine	0.3	1	1-1.5	6-8	Rarely done	plasma cholin-esterase
Rocuronium	0.3	0.6	1.5-2	30-40	0.1 -0.2 mg/kg prn	Liver
		RSI 1.2	1	>60 min		Bile + Urine
Vecuronium	0.05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

Adopted from Table 20-2, Ch 20, Barash Clincial Anesthesia 6th edition

NMBA Monitoring

- The **train-of-four (TOF) ratio** is the common modality of monitoring nondepolarizing NMBA. The number of twitches and the ratio between the 4th and 1st twitch are measured with the TOF.
- In the OR, we often monitor twitch # and twitch height with sight or feel – which is not nearly as accurate as mechanomyography or accelerometry.
- A patient with "four strong twitches" can still misleadingly have significant weakness.
- A **TOF of 0.9** (when comparing 4th to 1st twitch) is considered fully strong. Similarly, 5 seconds of **sustained tetanus** at 50-100 Hz indicates full recovery.
- Surgical relaxation can be achieved when the patient has 2-3 twitches though this depends on the surgical site and the nerve being monitored. NMBA with the goal to achieve beyond zero twitching (i.e. "negative twitches") is controversial.

Depolarizing vs Nondepolarizing NMBA Monitoring



An aside about sux:

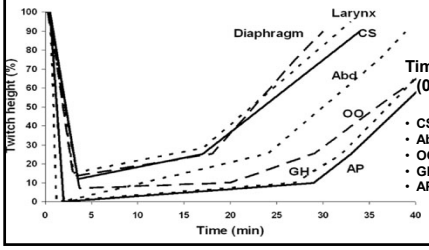
Phase I block is typical for a single bolus of sux.

Sux can cause a **Phase II** block at high or repeated doses and with with prolonged infusions.

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.

Variability in NMBA Monitoring

- Variability in muscle blockade (most resistant ➔ most sensitive): vocal cords > diaphragm > corrugator supercilii > abdominal muscles > adductor pollicis > pharyngeal muscles
- N.B. pharyngeal muscles are one of the last muscle groups to recover. Inadequate reversal leads to airway obstruction and aspiration. It also causes atelectasis and decreased pulmonary reserve.
- If placing electrodes on the face, you may stimulate facial muscles directly and may be fooled.



Time course after Rocuronium (0.6 mg/kg) at different muscles

- **CS** = corrugator supercilii (eyebrow)
- **Abd** = Abdomen
- **OO** = orbicularis oculi (eyelid)
- **GH** = geniohyoid (upper airway)
- **AP** = adductor pollicis (thumb)

Nondepolarizing NMBA Reversal

- Use acetylcholinesterase inhibitors as"reversal agents": less acetylcholinesterase working => more Ach in NMJ => stronger muscle firing.
- ACh inhibitor-based reversal should not be given until spontaneous recovery has started. Anticholinesterases can paradoxically slow recovery if given too early. Many authors advocate waiting until 4 twitches are visible before giving reversal.
- Acetylcholinesterase inhibitors can cause vagal side effects (eg. bradycardia, GI stimulation, bronchospasm) due to increasing ACh activity at parasympathetic **muscarinic** receptors. **Always administer with anticholinergics.**
- 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 is seems complete (4 equal twitches), 15-20mcg/kg of neostigmine is probably sufficient (attendings will have differing opinions).
  - **Dose of glycopyrrolate is 20% of the neostigmine dose** (eg. 3mg neostigmine with 0.6mg glyco). Adjust glycopyrrolate dose as needed if patient is already particularly tachycardic.

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:
  - 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, Sessler DI, Apfel CC. Does neostigmine administration produce a clinically important increase in postoperative nausea and vomiting? Anesth Analg 2005;101:1349-55.

Sugammadex

- Reverses neuromuscular blockade induced by rocuronium or vecuronium.
- 2 and 5 mL vials in a concentration of 100 mg/mL
- Examples of indications to use sugammadex:
  - "cannot intubate, cannot ventilate"
  - Failure to intubate ventilation without airway protection is contra-indicated e.g. the full stomach.
  - Neuromuscular blockade is too deep or inadequately reversed by neostigmine
  - For surgery during pregnancy it may be preferable to use sugammadex rather than neostigmine as sugammadex does not cross the placenta.
  - Gaining increased use as routine reversal agent given less side effects and cheaper cost than neostigmine + glycopyrrolate

Sugammadex (Cont.)

- Per the Committee on Quality, Efficiency and Patient Satisfaction (QEP) in our department:

Recommended Dosages

Indication	Dose
Cannot intubate, cannot ventilate	16 mg/kg
Deep reversal (zero twitches, if recovery has reached at least post tetanic count of 1-2)	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.
  - APTT and PT will be prolonged by ~ 25% for up to 60 minutes.
  - Do not mix in line with ondansetron, verapamil, and ranitidine.
  - Anaphylaxis reported as 0.3%
    - Seen in 1 healthy volunteer with study N=375

Important Facts to Know

- Diseases **SENSITIVE** to succinylcholine:
  - SLE, myositises
- Diseases **RESISTANT** to nondepolarizing NMBA:
  - Burns, Spinal cord injury, CVA, Prolonged immobility, Multiple sclerosis, cerebral palsy, tetanus/botulism
- Diseases **SENSITIVE** to nondepolarizing NMBA:
  - Myasthenia gravis (fewer AChR), Lambert-Eaton Syndrome (less ACh release), amyotrophic lateral sclerosis, SLE, myositises, guillain-Barre, muscular dystrophy (at least Duchenne), +/- myotonia
- Factors **ENHANCING** block by NMBA:
  - Volatile anesthetics, aminoglycosides, tetracycline, clinda, Mg (watch on OB), IV local anesthetics, CCBs, Lasix, Dantrolene, Lithium, anticonvulsants, sux, hypokalemia, hypothermia, ketamine
- Common surgeries to **avoid** NMBA
  - Axillary node dissection, ENT cases near nerves, neuromonitoring

Intra-op Discussion Topics

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

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- Sokół-Kobielska, E. Sugammadex — indications and clinical use. *Anaesthesiol Intensive Ther*. 2013 Apr-Jun;45(2):106-10.
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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

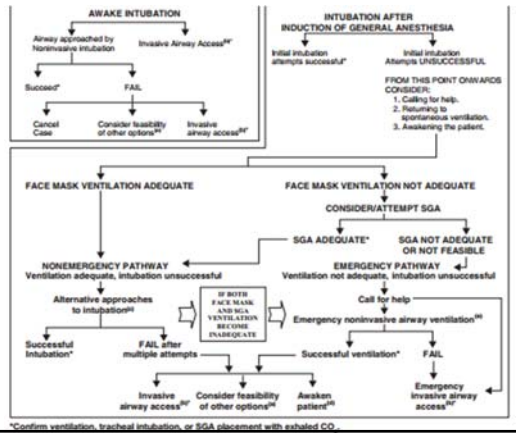
A difficult airway is a clinical situation wherein a conventionally trained anesthesiologist has difficulty with face mask ventilation, tracheal intubation, or both.

A difficult airway arises from a complex interaction between patient specific factors, the clinical environment, and the skills of the anesthesiologist.

American Society of Anesthesiologists®

DIFFICULT AIRWAY ALGORITHM

1. **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
2. **Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management.**
3. **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
4. **Develop primary and alternative strategies:**



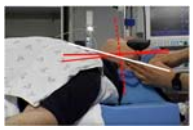
Be Prepared

Ventilation is arguably the most important job of the anesthesiologist.

Difficult mask ventilation is more of a concern than difficult intubation. **If you can mask, you have all day to intubate.**

Preparation is key – Do a thorough airway exam. Ensure that the equipment you want is available. Take time to position the patient correctly (look at the patient from the side). Poor positioning can make an easy airway very difficult.

VS



STEP 1

Assess the likelihood of airway management problems:

A) *Predictors of Difficult / Impossible Face Mask Ventilation*

≥3 of the following risk factors

Difficult Mask Ventilation:

"MaMaBOATS"
- **Ma**llampati III or IV
- **Ma**ndibular protrusion decreased
- **B**eard
- **O**besity (BMI > 30 kg/m^2)
- **A**ge >57-58
- **T**eeth (Lack of)
- **S**noring

Impossible Mask Ventilation:

"MaMaBORa"
- **Ma**llampati III or IV
- **Ma**les
- **B**eard
- **O**SA (mod-to-severe; on CPAP/BiPAP, or hx upper airway surgery)
- **Ra**diation changes (Neck)

And always… History of prior difficulty

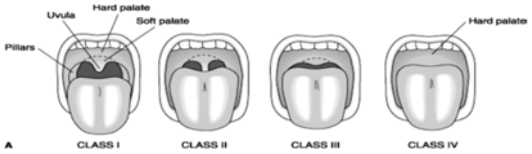
STEP 1

B) *Predictors of Difficult Intubation*

- History of prior difficulty
- Mallampati III-IV
- Thyromental distance: <3 finger breadths (6cm)
- Long incisors
- Interincisor distance (small mouth opening) <3 cm
- Prominent "overbite"
- Decreased TMJ mobility: inability to bring mandibular incisors anterior to maxillary incisors
- Neck range of motion: can't touch chin to chest or extend neck (c-collar)
- Short, thick neck
- Underlying pathology (e.g. laryngeal/tracheal stenosis, epiglottitis, tumors)
- Highly arched or very narrow palate
- Decreased submandibular compliance (stiff, indurated, occupied by mass)

STEP 1

Mallampati Score Assessment



C) *Difficulty with patient cooperation*

- Age
- Mental capacity
- Level of consciousness

D) *Difficulty with tracheostomy*

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

STEP 2

Actively pursue opportunities to deliver supplemental O_2 throughout the process of difficult airway management:

- Face mask
- LMA
- FOB swivel adaptor ETT connector
- Patil-Syracuse mask (mask with fiberoptic port)
- FOB side port
- Rigid bronchoscope side port
- Nasal cannula (apneic oxygenation during intubation attempt)
- Jet ventilation – usually very low on the list

STEP 3

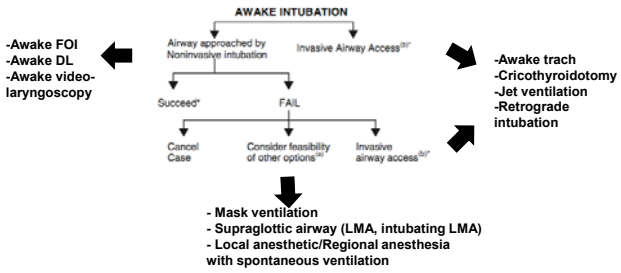
Consider the relative merits and feasibility of basic management choices/branch points:

A	Awake intubation	vs.	Intubation attempt after induction of GA
B	Non-invasive technique for initial approach to intubation	vs.	Invasive technique for initial approach to intubation
C	Video-assisted laryngoscopy as an initial approach to intubation		
D	Preservation of spontaneous ventilation	vs.	Ablation of spontaneous ventilation

STEP 4

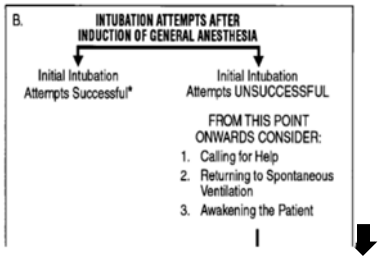
Develop primary and alternative strategies:

Algorithm A: Awake Techniques



STEP 4

Algorithm B: Intubation After Induction of GA

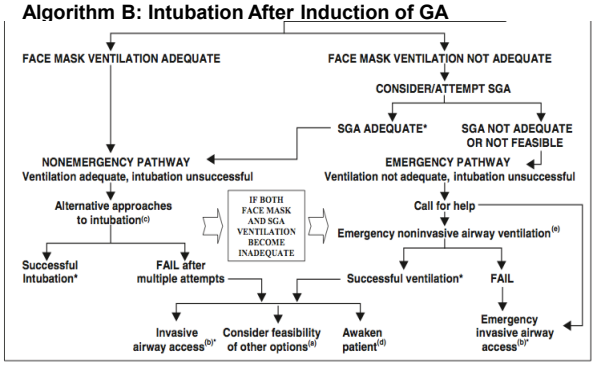


***If you used Rocuronium or Vecuronium, consider giving 16mg/kg of sugammadex to reverse muscle blockade and restore spontaneous ventilation**

Continue to next slide

STEP 4

Algorithm B: Intubation After Induction of GA



If feasible, consider sources of apneic oxygenation

Algorithm B

Non-Emergent Pathway

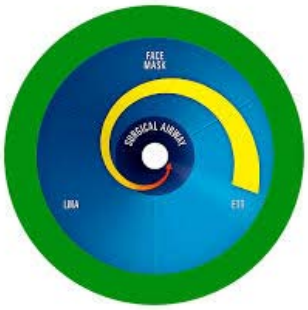
- CALL FOR HELP
- Mask ventilate with cricoid pressure
- Ensure optimal positioning
- Re-attempt DL with different blade (change something every attempt)
- Consider alternative techniques to secure airway
  - Gum elastic Bougie
  - Supraglottic device: LMA or intubating LMA
  - Video laryngoscope
  - Light wand
  - Fiberoptic intubation
  - Retrograde intubation

Algorithm B

Emergent Pathway

- "Can't intubate, can't ventilate"
- CALL FOR HELP
- <u>Emergency Non-Invasive Airway Ventilation</u>
  - Supraglottic airway: LMA, iLMA (intubating LMA)
  - Rigid bronchoscopy
  - Combitube
- <u>Emergency Invasive Airway Ventilation</u>
  - Cricothyroidotomy
  - Surgical tracheostomy
  - Transtracheal Jet Ventilation

The Vortex Approach



- Multidisciplinary approach to the difficult airway
- No more than 3 attempts of each technique (facemask, LMA, ETT), at least one by the most experienced clinician, then proceed to surgical airway
- Do something differently each attempt to optimize (airways, positioning, devices)

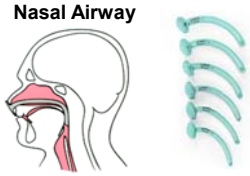
<u>KEY POINTS:</u>
PLAN AHEAD
CALL FOR HELP EARLY

If you're even thinking about a cric kit, call for one early. Better to have it and not need it than wish you had it.

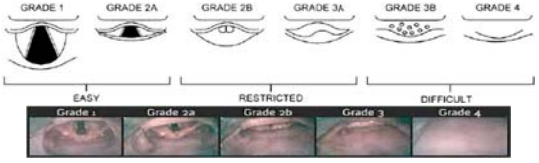
Basics of Airway Management

Oral Airway

Nasal Airway



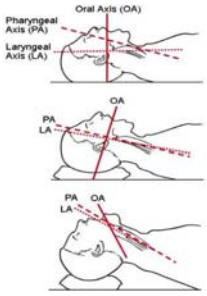
Cormack Lehane Laryngoscopy Views



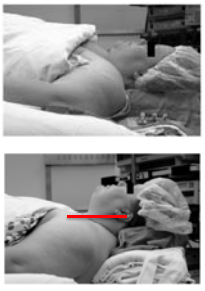
*Note a 3a view is when the epiglottis is lifted off the pharynx – Can still use bougie

Airway Axis: "Sniffing" Position

Sniffing position = flexion at C7 and extension C5/6



<u>Head elevation</u> helps to align PA & LA before DL



Ramp <u>obese</u> patients until tragus is aligned with sternum

*Just because they are "ramped" and tragus is aligned with sternum does not mean they will always be in good position. Make sure the neck can still be extended and they are still in sniffing position.

Pearls

- PREPARE
- CALL FOR HELP
- Always take the time to pre-oxygenate (de-nitrogenate) – goal expired O2 >80%
  - A pre-oxygenated patient can be apneic for 8-10 minutes until desaturation occurs
    - For average adult O2 consumption ~250cc/min. FRC is ~ 2000cc. 2000/250 = 8 minutes.
- The first attempt at DL is the best attempt
- Move to other airway options after 2 attempts at DL (More DL's = more edema, blood, etc)
- Know airway anatomy
- Know pharmacology of anesthetic agents

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The first time I had a patient with HIV, I was really nervous about putting in the IV. When I met him in preop, I was relieved that he had really great veins, and I knew he would be really easy. However, I kept missing IV after IV. After the third failed attempt, I finally paged my attending to come over. When he put on the tourniquet, I suddenly realized that that's what I had neglected to do in my previous attempts!

5 minutes after manipulating an NGT that the surgeon insisted wasn't in the stomach (they always say this) when I knew it was because I was getting gastric contents (you always say this), the surgeon complains about a periodic whiff of a foul odor. We all started to notice it. I explained it was probably the gastric contents that leaked out when I was fiddling with the NGT. By the end of the 10 hour case, we pretty much all had some kind of pediatric face mask scent on our masks and everyone that came into our room complained of the smell out in the hall. Then off the came drapes and the horrible truth stared us in the face: The lower body bair hugger was making jerky out of a code brown so massive that it completely filled the void between the patient's legs.

First week of CA1 year making my first sufentanil infusion. I have my 250mcg vial of sufentanil on the anesthesia cart. I get a 50cc syringe and attached one of the pink 19 gauge needles to draw up some saline from a 1 liter bag. I gently insert the needle into the port but I get a little resistance so I reposition the needle and still have some resistance. This time I decide to just push a little harder and then bam! Out pops the needle from the side of the port right into my thumb. My arm reflexively pulls back and then I knock the sufentanil vial off the cart and it shatters on the ground. I then grab some 4x4's for my thumb and collect the glass shards off the floor and put them into a kidney basin. I then proceed on the walk of shame to pharmacy for a bloody them and basin full of glass to explain what happened and promise them I wasn't stealing sufentanil.

Fluid Management

Evaluation of Intravascular Volume

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

Physical Exam
- *Hypovolemia*: skin turgor, 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
- *Hypervolemia*: increased pulm vascular markings on CXR

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)

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

Arterial Line
- Serial ABGs (pH, Hct, electrolytes)
- Pulse Pressure Variation to assess volume responsiveness
  - Requires sinus rhythm & positive pressure ventilation
- Commonly used when blood loss, fluid shifts, or prolonged OR time anticipated

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 is meaningful
- Catheter serves as additional central IV access for medications and fluids

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

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

Body Fluid Compartments

Males = 60% H_2O by weight
Females = 50% H_2O by weight

	Fluid as % of TBW (%)	Fluid as % of body weight (%)	Volume, in 70 kg male (L)
Intracellular	67	40	28
Extracellular			
- Interstitial	25	13	9
- Intravascular	8	7	5
TOTAL	100%	60%	42 L

TBW = Total Body Water

Q: What is the intravascular volume of a 90 kg male?
A: 90 kg x 7% = 6.3 L

Physiologic Regulation of Extracellular Fluid Volume

Aldosterone
- Enhances sodium reabsorption
- Increases intravascular volume

Antidiuretic Hormone/Vasopressin
- Enhances water reabsorption

Atrial Natriuretic Peptide
- Enhances sodium and water excretion

Crystalloids

	Osm (mOsm/L)	Na^+ (mEq/L)	Cl^- (mEq/L)	K^+ (mEq/L)	Ca^{2+} (mEq/L)	Buffer (mEq/L)	pH
NS	308	154	154	0	0	0	5.0
LR	273	130	109	4	3	28 (lactate)	6.6
Normosol*	294	140	98	5	0	27 (acetate)	6.6

*Normosol used almost exclusively in Cardiac surgery

	Advantages	Disadvantages
NS	• Preferred for diluting pRBCs • Preferred in brain injury	• In large volumes produces **hyperchloremic metabolic acidosis** • Hyperchloremia ➔ low GFR
LR	• More physiologic • Lactate is converted to HCO_3^- by liver	• Watch K+ in renal patients • Ca^{2+} may cause clotting with pRBCs

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**
- Hespan (in NS) and Hextend (in LR) solutions
- Solution of highly branched glucose chains (average MW 450 kD)
- Degraded by amylase, eliminated by kidney
- Maximum Dose: 15-20 ml/kg/day
- Side effects:
  - Can increase PTT (via factor VIII/vWF inhibition) and clotting times
  - Anaphylactoid reactions with wheezing and urticaria may occur
  - May interfere with platelet function
- Contraindications: coagulopathy, heart failure, renal failure

Colloids

Use
- Initial intravascular volume resuscitation with crystalloid administration inadequate
- Concern that continued crystalloid may cause volume overload in certain clinical situations (ie. CHF, pulmonary edema, bowel edema)
- Patients with large protein losses and decreased oncotic pressure (ie burns)

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

Crystalloid or Colloid?

	Advantages	Disadvantages
Crystalloid	• Lower cost • Readily available	• Requires more volume for the same hemodynamic effect • Short IV $t_{1/2}$ (20-30 min) • Dilutes plasma proteins ➔ peripheral/pulmonary edema
Colloid	• Restores IV volume and HD with less volume, less time • Longer IV $t_{1/2}$ • Maintains plasma oncotic pressure • Less cerebral edema (in healthy brain tissue) • Less intestinal edema	• Expensive • Coagulopathy (dextran > HES) • Potential renal complications • May cause cerebral edema (in areas of injured brain)

"Classical" Fluid Management

Maintenance
- "4-2-1 Rule" = 4 ml/kg/hr for the 1st 10 kg, 2 ml/kg/hr for the next 10-20 kg, and 1 ml/kg/hr for each additional kg above 20 kg

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

Ongoing Losses

Evaporative and Interstitial Losses (capillary leak)
- Minimal tissue trauma (e.g. hernia repair) = 0-2 ml/kg/hr
- Moderate tissue trauma (e.g. cholecystectomy) = 2-4 ml/kg/hr
- Severe tissue trauma (e.g. bowel resection) = 4-8 ml/kg/hr

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

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

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

Suggestions for Fluid Management

Tailor management to patient, surgery, and clinical scenario

Use a balanced approach
- Typically start with NS or LR
- Consider switch to LR, except in neuro cases (because of decreased osmolality) or patients with hyperkalemia, or ongoing blood transfusions
- Consider colloid for persistent hypotension despite adequate crystalloid administration

- Type and Cross for pBRC and other blood products prior to surgery if anticipating significant blood loss (ie. trauma, coagulopathy)
  - Consider that rapid volume resuscitation may worsen coagulopathy, in general if giving >2 units pRBCs, have FFP available as well

Liberal vs. Restrictive Management

Consequences of Volume Overload

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

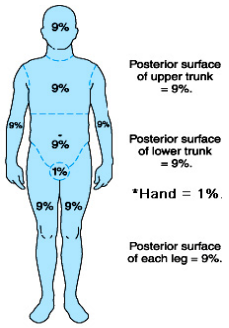
Suggestions for Rational Fluid Management

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

Burns

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

- Volume = %BSA x 4 ml/kg x kg
- Give 1/2 over the 1st 8 hours
- Give 1/2 over the next 16 hours
- Replace with LR
- %BSA is determined by the "Rule of Nines"



Intraoperative Oliguria

Pre-renal (decreased renal perfusion)

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

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

Fluid Management Words of Wisdom:

When emptying urine from Foley catheter, do not stare into the spout when releasing the clamp

The proper way to remove gloves:

1) Remove left glove into palm of right hand

2) Using left thumb, peel right glove off right hand starting at the wrist wrapping left glove into right glove

3) Create slingshot by stretching right glove between left thumb and right fingers

4) Shoot wherever (preferably in direction of Urology surgeon)

Never spike a bag of fluid that is already hanging on an IV pole, take it down to avoid giving yourself an NS bath

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Transfusion Therapy

Type and Screen

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

- ABO-Rh typing
  - Recipient RBCs tested with anti-A, B, and Rh antibodies
- Antibody screen
  - Recipient serum + type O RBCs for presence of A or B antibodies - no agglutination = negative screen
  - If antibody screen is positive: the serum is tested further
- *Use when case may require blood, but there is a low likelihood of transfusion*

Type and Crossmatch

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

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

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 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 (Ranger if OK to run in slowly, Belmont or Level 1 to run in fast)
- CPDA:
  - Citrate (anticoagulant) - also binds iCa – why you can see hypoCa with transfusions
  - 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_2
     - Example: myocardial ischemia

Platelets

Definition, Use, & Storage

- Platelet Concentrate (PC)
  - Platelets from one donated unit, vol = 50-70 ml; ↑ plt ~5,000-10,000
  - "6-pack" = 6 pooled PCs (rarely used anymore)
- Apheresis Unit
  - Platelets from a single donor; vol = 200-400 ml; **↑ plt ~50,000**
  - Document as 250ml (no exact number written on unit)
- Can give ABO-incompatible platelets, Rh tested only
- Stored at room temperature for ≤5 days.
- Hang separately (on blood pump with NS) – **Do not** run through fluid warmer, Level 1, or Belmont

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)

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
- 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

Cryoprecipitate

Definition, Use, & Storage

- Fraction of plasma that precipitates when FFP is thawed
- Contains Factors VIII, XIII, I (fibrinogen), and vWF
- 1 unit contains ~5X more fibrinogen than 1 unit FFP
- 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

Equations

Arterial O_2 Content

$C_aO_2 = O_2$-Hb + Dissolved O_2

$= (Hb \times 1.36 \times S_aO_2/100) + (P_aO_2 \times 0.003)$

$= (15 \times 1.36 \times 100\%) + (100 \times 0.003)$

≈ 20 cc O_2/dl (normal)

Allowable Blood Loss

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

Volume to Transfuse

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

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

Ordering Products

- Consider special needs of the patient:
  - 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 reducted, 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

Massive Transfusion

Definition and Use

•Administration of greater than 1 blood volume (~10 units) in 24 hours

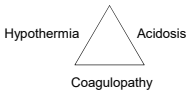
•At Stanford, calling the blood bank for the Massive Transfusion Guideline (MTG) will get you **6 pRBCs, 4 FFP, and 1 unit of platelets**

•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

Lethal Triad of Trauma:



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
   a. Dilutional thrombocytopenia
      - Platelet count likely <100,000 after ~10 units pRBCs
   b. Dilutional coagulopathies
      - ↓ Factors V & VIII ("labile factors") in stored blood
3. Citrate Toxicity
   - Citrate is in CPDA storage solution as a Ca^{2+} chelator (why you often give Ca^{2+} with transfusion)
   - Massive transfusion can cause an acute hypocalcemia
   - Citrate also binds magnesium causing hypomagnesemia

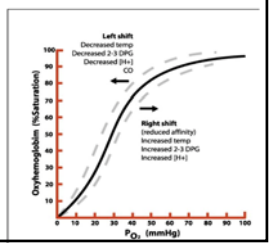
Massive Transfusion

Complications, cont

4. Acid-Base Abnormalities
   - At 21 days, stored blood has pH <7.0, due mostly to CO_2 production, which can be rapidly eliminated with respiration
   - Acidosis more commonly occurs due to ↓ tissue perfusion
5. Hyperkalemia
   - K^+ moves out of pRBCs during storage
   - If EKG changes occur,

   stop transfusion and treat hyperkalemia
6. Impaired O_2-Carrying Capacity
   - 2,3-DPG decreases in stored blood,

   causing a left-shifted O_2-Hb dissociation curve



Transfusion-Related Infections

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

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

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

Transfusion Reactions

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

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

Anaphylactic Reaction
- Occurs within minutes; life-threatening
- Usually associated with **IgA deficiency**
- Signs/Symptoms: shock, angioedema, ARDS
- Treatment:
  - 1) Stop blood
  - 2) Give fluids, Epi, antihistamines, ACLS

Transfusion Reactions

- **Acute Hemolytic Reaction**
  - Due to ABO incompatibility
  - Symptoms: fever, chills, flank pain usually masked by GA; watch for hypotension, diffuse oozing and brown urine; monitor for ARF and DIC
  - Treatment:
    - 1) Stop Blood products
    - 2) Maintain alkaline UOP (bicard, mannitol, lasix), supportive care
- **Summary of Transfusion Reactions**

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

Transfusion-Related Acute Lung Injury (TRALI)

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

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Hypoxemia

Causes of Hypoxemia

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

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

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

Equations

Alveolar-arterial (A-a) Gradient

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

Alveolar Gas Equation

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

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

$\approx$ <u>100 mm Hg</u>

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

<u>Normal P_aO_2</u>:
- 103 - age/3

Causes of Hypoxemia

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

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

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

Causes of Hypoxemia

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

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

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

Hypoxemia in the OR

Take a systematic approach to the diagnosis and treatment of hypoxemia in the OR!

<u>Suggestion</u>: *Alveoli ☻Machine*

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

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

Hypoxemia in the OR

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

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

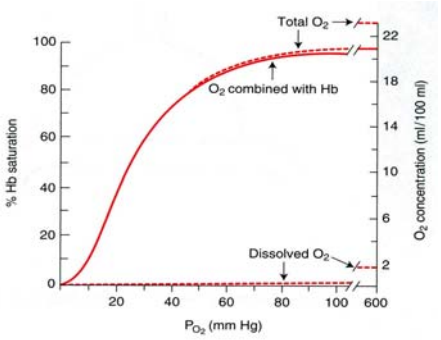
5. Check monitors to confirm (you will probably do this 1st!)
- – Pulse oximeter waveform
- – Look at the patient! - are they cyanotic? mottled?
- – Gas analyzer

Management of Hypoxemia

Assuming proper oximeter function, placement, and waveform:

- Place patient on 100% O_2.
- Perform recruitment maneuver (30 sec at 30mmHg *if pt can tolerate hemodynamically*), then add or increase PEEP.
- Confirm ETT placement by auscultation, bilateral chest rise, and FOB if necessary.
- Suction airway and ETT
- Consider cardiovascular causes and restore volume, RBCs and/or cardiac output
- Send ABG/VBG

O_2-Hb Dissociation Curve



Useful "anchor" points:

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

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

O_2-Hb Curve Shifts

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

Right Shift
(hemoglobin has lower affinity for O_2 = increased unloading at tissues)
- Acidosis
- Hyperthermia
- Hypercarbia
- Increased 2,3-DPG
- Sickle Cell Hb
- Pregnancy
- Volatile anesthetics
- Chronic anemia

Factors Affecting Tissue Oxygenation

- Hb concentration
- O_2 Saturation
- Cardiac Output
- O_2 Consumption
- O_2-Hb Affinity (P_{50})
- Dissolved O_2 in plasma (little effect)

See "Equations" for a mathematical explanation of these factors.

Equations

Arterial O_2 Content

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

Mixed Venous O_2 Content

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

Equations

O_2 Delivery

$DO_2 = CO \times C_aO_2$
$= 5$ L/min x 20 cc O_2/dl
$\approx$ 1 L O_2/min

O_2 Consumption (Fick Equation)

$VO_2 = CO \times (C_aO_2 - C_vO_2)$
$= 5$ L/min x 5 cc O_2/dl
$\approx$ 250 cc O_2/min

O_2 Extraction Ratio

$ER_{O2} = (VO_2 / DO_2) \times 100$
$= 250 / 1000$
$\approx$ 25% (normal 22-30%)

Other Concepts

Diffusion Hypoxia = when using N_2O — low P_AO_2 as a result of hypoventilation in combination with the washout of N_2O from blood into the alveoli (dilutes the O_2 molecules decreasing P_AO_2)

Absorption Atelectasis = the tendency for airways to collapse if proximally obstructed or poorly ventilated; poorly soluble N_2 normally stents alveoli open, but patients on 100% O_2 have greater tendency toward atelectasis.

Bohr Effect = a property of Hb in which increasing CO_2, temperature, and acidosis promote decreased O_2-Hb affinity and unloading of O_2 at periphery (i.e. right-shift of O_2-Hb curve).

Haldane Effect = a property of Hb in which O_2 binding promotes dissociation of CO_2 from Hb to the plasma (e.g. as when venous blood enters the lungs).

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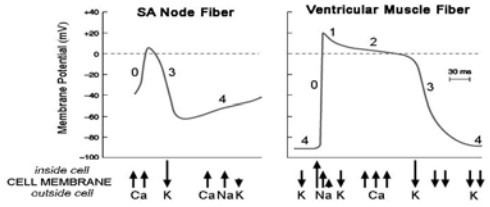
In one of my first days of residency (I was at the Valley, where there are 5 or 6 different kinds of anesthesia machines), it took me about 10 minutes in the morning to find the power button for the ventilator. I felt pretty dumb. The problem ended up being that I had a towel draped over the tray and 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	–	Slow inward I_{Ca} = Outward I_K
3	Final Rapid Repolarization	Outward I_K	Inward I_{Ca} < Outward I_K
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^+ = 6.5-8 mEq/L
- Severe K^+ > 8 mEq/L

Contributing Factors

- Renal disease
- Drugs (ACEI, NSAIDs, K-sparing diuretics, Digoxin, ß-blockers)
- Succinylcholine: acute, transient increase of 0.5-1 mEq/L
- Acidosis
- Transfusions
- Hemolysis
- Rhabdomyolysis (tourniquet), trauma
- Administration of Dantrolene to patients on Verapamil or concurrent administration of both drugs
- Hyponatremia, hypocalcemia
- Old packed red blood cells (can have [K+] of 50 or greater!)

Hyperkalemia

Signs and Symptoms

- Cardiac conducting system abnormalities including dysrhythmias, conduction abnormalities, and cardiac arrest.
  - Classically associated with administration of succinylcholine to paralyzed, immobilized (ICU), neuro disease (MS, ALS, etc.) or burn patients.
  - If plasma [K^+] is <6.0 mEq/L, cardiac effects are generally negligible.
  - As the concentration increases, may see tall, peaked T waves, especially in the precordial leads.
  - With further increases, the PR interval becomes prolonged, followed by a decrease in the amplitude of the P wave.
  - Finally, the QRS complex widens into a pattern resembling a sine wave and eventually culminates in VF arrest and asystole
- At plasma [K^+] 7.0 mEq/L, may have ascending paralysis that progresses to flaccid paralysis, inability to phonate, and respiratory arrest.
- Hyperkalemia may also accompany Malignant Hyperthermia.

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, 6th ed.* Philadephila: Lippincott Williams & Wilkins, 2009.

Hyperkalemia

Treatment

- **Reverse membrane effects**
  - Ca gluconate (peripheral IV)
  - Ca chloride (central line)
- **Transfer extracellular [K+] into cells**
  - Bicarbonate ($NaHCO_3$) - 50-100 mEq over 5-10 minutes
  - Insulin (10-15 units) w/ Glucose (25 g = 50 mL of D50)
  - Beta-2 agonists (Albuterol)
- **Remove potassium from body**
  - Kayexalate (PO/PR)
  - Diuretics (proximal or loop)
  - Dialysis

Hyperkalemia

Anesthetic Considerations

– Consider cancelling elective cases if $K^+ > 5.5$
– Consider alternative to succinylcholine
– EKG monitoring
– Avoid hypoventilation (respiratory acidosis)
– Treat acidosis
– Consider NS instead of LR or Normosol
– Monitor for increased sensitivity to muscle relaxants

Hypokalemia

Definition

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

Contributing Factors

Preoperative
– GI losses (NGT, N/V, Diarrhea)
– Lasix, RTA
– Magnesium deficiency

Intraoperative
– Alkalosis (both metabolic and respiratory)
– Insulin therapy
– Hypothermia

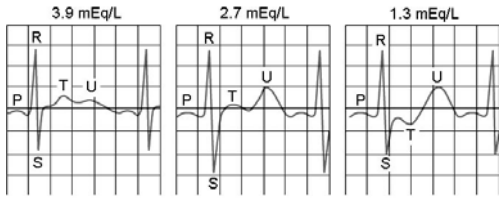
Hypokalemia

Signs & Symptoms

- Acute hypokalemia causes hyperpolarization of the cardiac cell and may lead to ventricular escape activity, re-entrant phenomena, ectopic tachycardias, and delayed conduction.
- Arrhythmias
  – PACs, PVCs
  – SVTs (esp. A Fib/A flutter)
- Metabolic alkalosis
- Autonomic lability
- Weakness, ↓DTRs
- Ileus
- Digoxin toxicity
- Enhanced response to muscle relaxants

EKG Progression of Hypokalemia

1. Flattened/ inverted T wave
2. U waves
ST depression



Hypokalemia

Treatment

– Chronic hypokalemia = total body K^+ depletion (1 mEq/L decrease = 300-600 mEq total body deficit)
  - Peripheral IV - 10 mEq/hr
  - Central IV - 10-20 mEq/hr
  - Life-threatening - 5-6 mEq bolus
– Acute hypokalemia = likely a redistribution phenomenon
  - Reverse underlying cause (e.g. alkalemia secondary to mechanical hyperventilation)

Hypokalemia

Anesthetic Considerations

– Consider cancelling elective cases if $K^+ < 3$-3.5 mEq/L (based on chronicity of deficit).
– EKG monitoring
– KCl replacement if arrhythmias develop
– Avoid hyperventilation (respiratory alkalosis)
– Consider reducing dose of muscle relaxant 25-50%

Hypercalcemia

Contributing Factors
- Hyperparathyroidism
- Malignancy (especially lung, ENT, GU, GYN, and multiple myeloma)
- Immobilization
- ARF
- Drugs (thiazide Ca^{2+} sparing 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 (reduces Ca^{2+}-albumin binding)
- Check serial K^+ and Mg^{2+}

Hypocalcemia

Contributing Factors

Preoperative
- Hypoparathyroidism
- Renal failure (decreased Vitamin D)
- Sepsis
- Magnesium deficiency (decresed end-organ response to PTH)

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

Signs & Symptoms
- EKG (prolonged QT, bradycardia)
- Hemodynamics (vasodilation, hypotension, decreased myocardial contractility, LV failure)
- 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 elemental Ca^{2+} (give via peripheral or central IV)
- Calcium chloride - 1 g = 13.6 mEq elemental Ca^{2+} (give via central IV)
- Do NOT give Ca^{2+} and $NaHCO_3$ together in the same IV - it will precipitate!
- Replace magnesium

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

Hypermagnesemia

Contributing Factors
- Renal failure
- Hypothyroidism
- Iatrogenic (tocolysis)

Signs & Symptoms
- EKG (widened QRS, prolonged PR interval, bradycardia)
- Hemodynamics (vasodilation, hypotension, myocardial depression)
- Neuro (↓DTRs, sedation, weakness, enhanced neuromuscular blockade)

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

Anesthetic Considerations
- EKG monitoring
- Consider reducing dose of muscle relaxants 25-50%

Hypomagnesemia

Contributing Factors
- GI/Renal losses
- ß-agonists (cause intracellular shift)
- Drugs (diuretics, theophylline, aminoglycosides, ampho B, cyclosporin A)

Signs & Symptoms
- Usually asymptomatic alone, but symptomatic in combination with induced hypokalemia, hypocalcemia, and hypophosphatemia
- EKG (prolonged QT, PACs, PVCs, and A Fib)
- Neuro (neuromuscular excitability, AMS, seizures)

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

Anesthetic Considerations
- EKG monitoring
- Check for coexistent electrolyte deficiencies.

Summary of EKG Changes

	PR interval	QRS complex	QT interval	T waves
Hypocalcemia	short	narrow	prolonged	Inversion
Hypercalcemia	prolonged	widened	shortened	--
Hypomagnesemia	short	narrow	prolonged	--
Hypermagnesemia	prolonged	widened	--	--
Hypokalemia	short	narrow	prolonged	Flat, u-waves
Hyperkalemia	prolonged	widened	--	Peaked

HypO___ = short PR, narrow QRS, and prolonged QT

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

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

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

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

Hypothermia & Shivering

Definition and Measurement

- Hypothermia is defined as a core body temperature less than 36 degrees C
- Temperature is measured from:
  - Nasopharynx (accurately reflects core temp, but can cause epistaxis)
  - Tympanic Membrane (reflects brain temp, but can cause perforation of ear drum)
  - Esophagus
  - Bladder (lags behind core temperature if low urine flow/output)
  - Rectum (slow response to changes in core temp, inaccurate with stool in rectum, contraindicated in neutropenic pt, fistula, etc.)
  - Skin (variable accuracy depending on skin perfusion)
  - Thermistor of Pulmonary Artery Catheter (gold standard)

Thermoregulation

Afferent Thermal Sensing

- Thermal inputs travel along A-delta (cold) and C fibers (warm) via the spinothalamic tract.
- Input comes from the skin, deep abdominal & thoracic tissues, spinal cord, brain, and hypothalamus (roughly 20% each).

Central Control

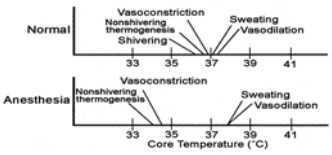
- Thermal inputs are "preprocessed" at numerous levels within the spinal cord and brainstem.
- Modulated by NE, DA, 5-HT, ACh, PGE, and neuropeptides.
- The preoptic-anterior hypothalamus is the central autonomic thermoregulatory center.

Efferent Responses

- Behavioral responses (shelter, clothing, voluntary movement, etc) are most important and are determined by skin temperature.
- Autonomic responses (skin vasomotor activity, nonshivering thermogenesis, shivering, and sweating) are ~80% determined by core temperature.

Interthreshold Range

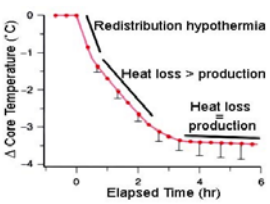
- Interthreshold Range = tight thermoregulatory range between cold-induced and warm-induced responses, usually ~0.2°C.
- General anesthesia inhibits thermoregulation and increases the interthreshold range ~20-fold, to ~4°C.
- Regional anesthesia inhibits thermoregulation to lower half of body, increasing the range ~4-fold, to ~0.8°C.



Development of Hypothermia

Anesthetic-impaired thermoregulation

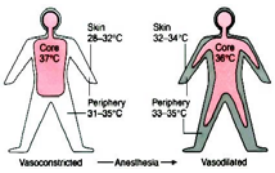
1. Redistribution hypothermia
2. Heat loss > heat production
3. Heat loss = heat production (steady-state heat balance)



Heat transfer to cold OR (in order of importance)

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

Redistribution Hypothermia



Benefits of Hypothermia

- Tissue metabolic rate decreases ~8% per 1˚C decrease in body temperature.
- CNS protection from ischemic and traumatic injuries.
- Improves neurologic outcomes after cardiac arrest.
- Some protection against malignant hyperthermia.
- Cardiac protection as decreased metabolic and O2 requirement.

Consequences of Hypothermia

- Increased myocardial morbidity (3x)
- Impaired coagulation (especially platelets), increased blood loss, & increased transfusion rates
- Increased infection rate (3x)
- Prolonged duration of drug action, delayed emergence
- Left-shifts O_2-Hb curve (increased Hgb affinity for oxygen)
- Increased SVR
- Difficulty monitoring patient (e.g. BP cuff, S_pO_2)
- Delays wound healing & jeopardizes grafts/flaps
- Altered mental status
- Increased sympathetic activity/stress response
- Increased postoperative shivering
- Prolonged PACU stay

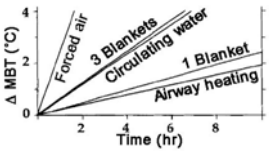
Warming Strategies

Prevention of hypothermia is more effective than treatment!

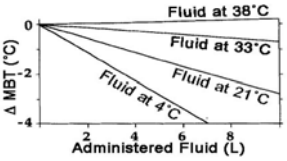
Active Warming
- Forced air (Bair Hugger)
- Circulating warm H_2O pad
- Radiant heat lamps
- IVF warmer
- Airway heating & humidification
- Warm the OR temperature

Passive Insulation (not as effective)
- Cotton blankets
- Surgical drapes
- Space blanket (silver plastic)

Effect of Warming Strategies



Effect of IVF Warming



Etiology of Postop Shivering

Intraoperative hypothermia (duh!)… *however*…
- Shivering does NOT always occur in hypothermic patients, and…
- Shivering DOES occur in normothermic patients

Other possible etiologies:
- Recovery from volatile anesthetics
- Pain may facilitate shivering-like tremor
- Fever increases the thermoregulatory set point causing shivering in normothermic patients.

Consequences of Shivering

- Increased O_2 consumption
  - Can be up to a 400-500% increase
- Increased CO2 production and V_E (minute ventilation)
- Increased incidental trauma
- Increased intraocular and intracranial pressures
- Uncomfortable and/or painful
- Stresses wound edges
- Disrupts monitoring (e.g. NIBP, EKG, S_pO_2)

Rates of MI do NOT correlate with shivering!

Treatment of Shivering

1. Skin surface warming and passive insulation
2. Pharmacologic:
   - Meperidine 12.5-25 mg IV (caution in renal and hepatic impairment)
   - Muscle relaxants (only in asleep, ventilated patients)

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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 (willing to pay $56-100 out-of-pocket for effective PONV control)
- 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

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

Major Risk Factors

Patient-Related

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

Anesthetic-Related

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

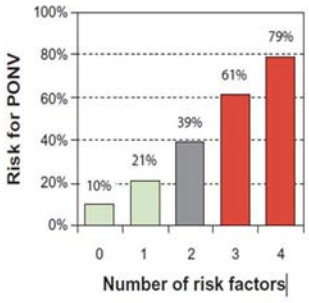
Surgery-Related

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

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

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

Steroids
- Cheap and effective
- Can be given anytime, for prolonged PONV relief
- Weigh risks/benefits in diabetics
- Decadron 4-10 mg IV anytime during case (given post-induction to avoid severe perineal itching)

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

Antiemetic Classes

Phenothiazines (e.g. Promethazine, Prochlorperazine)
- Dopamine antagonist
- Can cause sedation and extrapyramidal side effects
- Phenergan 12.5-25 mg at end of case

Anticholinergics (e.g. Scopolamine patch)
- Centrally acting
- Transdermal administration requires 2-4 hours for onset.
- 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

Butyrophenones (e.g. Droperidol, Haloperidol)
- Central dopamine antagonist
- Cheap and very effective, but a "black box" warning regarding QT prolongation has caused it to fall out of favor
- Contraindicated in Parkinson's patients
- Droperidol 0.625-1.25 mg IV at end of case.

Antiemetic Classes

Substance P antagonists (e.g. Aprepitant, fosaprepitant)
- NK1 receptor antagonist
- Expensive
- Typically used for 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

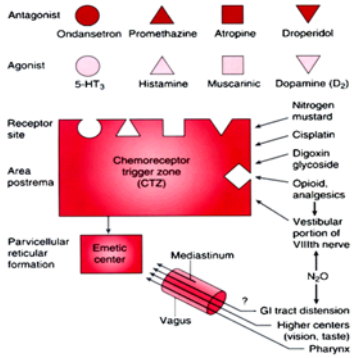
Other Antiemetic Agents

Vasopressors
- Ephedrine 50 mg IM
  - Prevents intestinal hypoperfusion

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

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

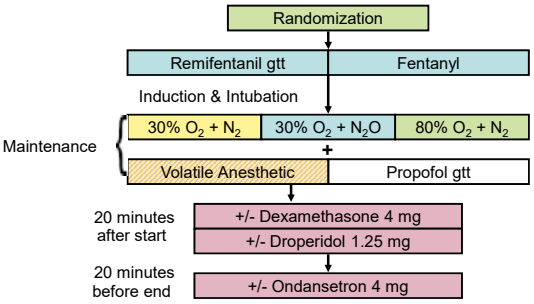
Chemoreceptor Trigger Zone



IMPACT Trial: Study Design

(Apfel et al., 2004)

5161 patients, 6 treatments (2^6 = 64 treatment groups)



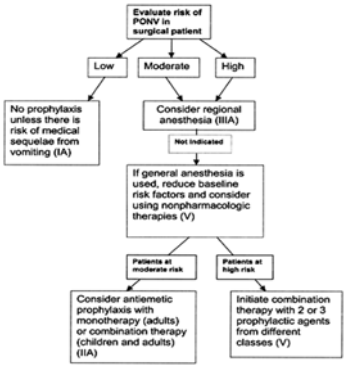
IMPACT Trial: Results

(Apfel et al., 2004)

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

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

Algorithm for PONV Treatment



Strategies to Reduce PONV

- Use regional anesthesia vs. GA
- Use propofol for induction and maintenance of anesthesia
- Avoid N_2O and/or volatile anesthetics
  - N_2O's role in PONV is controversial, possibly related to duration of exposure
- Minimize opioids (consider tylenol, NSAIDs, etc.)
- Minimize (<2.5 mg) or eliminate neostigmine
- Maintain euvolemia; 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)

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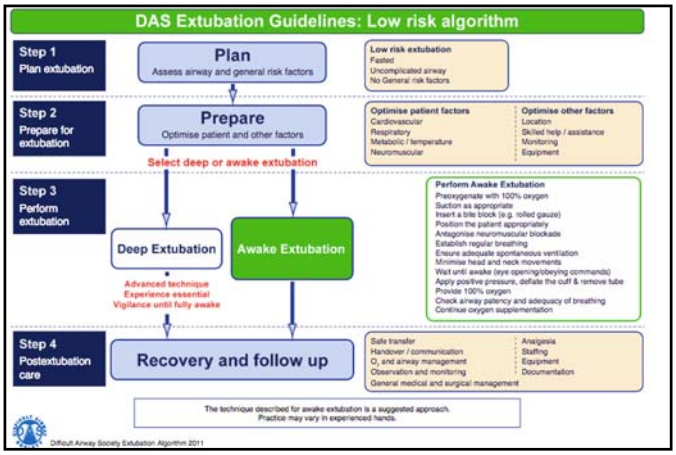
Extubation Criteria & Delayed Emergence

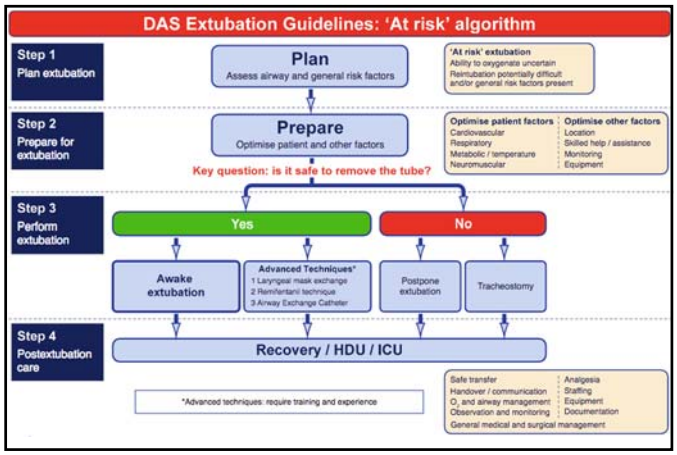
Extubation Overview

- 12% of the closed claim cases with perioperative difficult airway were from the time of extubation
- ASA Practice Guidelines for Management of the Difficult Airway: has *not* decreased the number of claims arising from injury at extubation
- As a result, Difficult Airway Society (DAS) published 2012 guidelines with low & high risk algorithm
  - Low Risk: awake vs. deep extubation (more advanced)
  - High Risk: awake (with possible AEC, LMA, or remifentanil technique) vs. postponing extubation vs. tracheostomy

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, SpO2 > 90%
2. **ABG "reasonable" with FiO2 ≤ 40%**
   - pH ≥7.30, PaO2 ≥60 mmHg, PaCO2 ≤50-60, normal lytes
3. **Adequate reversal or neuromuscular blockade**
   - TOF 4/4, TOF ratio >0.7-0.9, tetany >5 secs
   - Sustained head lift or hand grasp >5 secs
4. **Respiratory mechanics adequate**
   - Spontaneous V_T >5 mL/kg, Vital Capacity >15mL/kg
5. **Protective reflexes (gag, swallow, cough) returned**
6. **Awake, alert, able to follow commands**

Preparing to Extubate

- **Standard preparation any extubation**
  1. Ensure back-up airway / re-intubation equipment available
  2. Pre-oxygenate with 100% O_2; consider recruitment maneuver
  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
  7. Minimize touching pt during Stage 2 ("light") anesthesia
  8. Confirm that all "Routine Extubation Criteria" are met
- **Extubate**
  - Deflate cuff, remove tube with positive pressure
  - Provide 100% O2, ensure patent airway, adequate breathing

Failed Extubation

Causes	**Checklist prior to extubation (to help avoid failure)**
Failure to oxygenate	• TV >5cc/kg & VC > 15cc/kg • SpO_2 >90% with FiO_2 < 0.4
Failure to ventilate	• Same TV parameters above • NM Blockade appropriately reversed • RR >6 & <30? • No excessive hypercapnea ($EtCO_2$ < 50s-60)
Inadequate clearance of pulmonary secretions	• Nasopharynx suctioned? • Intact gag reflex? Able to cough? Alert/awake? • If aspiration risk, OG tube suction and consider emergence in lateral decubitus position
Loss of airway patency	• Soft bite block placed? • Alert? Following commands? • If edema a concern, is cuff leak >15.5% ** • Placed in optimal position (sniffing position, head up) • Reduced risk of laryngospasm? (not in stage 2, airway suctioned) • Airway exchange catheter for high risk patient?

**to calculate cuff leak: while on volume control, deflate cuff and occlude proximal end of ETT; measure before & after tidal volumes and calculate percent difference

Stages of Anesthesia

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

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

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

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

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

Causes of Delayed Emergence

Anesthesia Related	Residual anesthetic Excessive narcotics 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
  - 1.25 mg of physostigmine IV
- Consider benzodiazepine reversal
  - Start with 0.2mg flumazenil IV, repeat Q1 mins up to 1mg total
- Check blood glucose level & treat hypo or hyperglycemia
- Check ABG and electrolytes; rule out CO2 narcosis and hypo or hyponatremia
- 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 neurolgy follow up, frequent neuro exams, repeat head CT in 6-8hrs if no improvement

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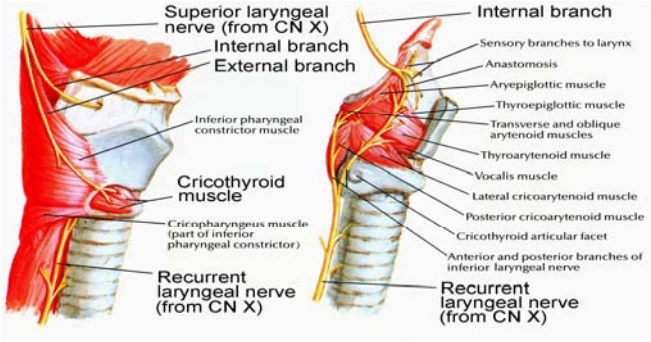
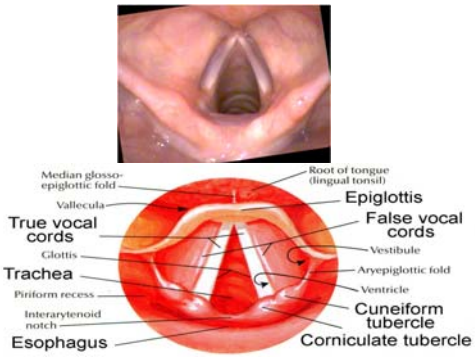
Laryngospasm & Aspiration

Larynx Anatomy



Larynx Anatomy



Larynx Anatomy: Innervation

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

Does bilateral recurrent laryngeal nerve injury produce the same defect as succinylcholine?

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
- Consequences include hypoxia, hypercapnia, and negative pressure pulmonary edema

Predisposing Factors

- Stage 2 of anesthesia (excitement/delirium)
- Light anesthesia relative to surgical stimulation
- Mechanical irritants to the airway
  - Blood or secretions
  - Airway suctioning or instrumentation
- GERD
- Upper respiratory tract infection (0.85-5% incidence)

Laryngospasm

Prevention

- Ensure adequate anesthetic depth before manipulation or movement of patient
- Clear secretions before extubation
- Topicalize larynx with local anesthetic
- Muscle relaxants

Management - *CALL FOR HELP EARLY!*

1. Jaw thrust, head tilt, oral or nasal airway
2. Deepen anesthesia with IV agent (e.g. Propofol)
3. CPAP via bag-mask ventilation with 100% O_2
4. Suction oropharynx
5. Succinylcholine 10-20 mg IV, maintain airway with bag-mask or ETT until spontaneously breathing
6. Prepare for surgical airway
7. Monitor for post-obstructive negative pressure pulmonary edema (NPPE)

Negative Pressure Pulmonary Edema

Causes
- Laryngospasm
- Upper airway obstruction/ETT obstruction
- Incidence: 0.1% of anesthetics

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

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

Negative Pressure Pulmonary Edema

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

Treatment
- Supportive care (O_2, IPPV, PEEP/CPAP)
- Conservative management until process reverses; consider volume and/or pressors PRN.
- Lasix is usually NOT helpful
- Does not typically require ETT

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)
- GE junction incompetence (GERD, hiatal hernia, scleroderma)
- Pregnancy, obesity
- Neuromuscular disease processes
- Difficult intubation and/or prolonged bag-mask ventilation

Pulmonary Aspiration

Prevention
- Follow NPO guidelines for routine elective cases
- Use metoclopramide, H_2-blockers, and antacids in high-risk patients
- Consider awake, regional anesthetic
- Consider awake, upright intubation and/or RSI
- If present, leave NGT to suction
- Apply cricoid pressure until ETT position confirmed
- Minimize bag-mask PPV and/or keep pressure <20 cmH_2O
- Extubate after recovery of protective reflexes

NPO Guidelines

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

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

Pulmonary Aspiration

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

Management
- Place patient in head-down position
- Immediately suction pharynx and trachea before PPV
- 100% O_2, intubate, 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

References

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Oxygen Failure in the OR

Etiology

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

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

Prevention

Pre-anesthesia Machine Check
- Check pipeline pressure ~50 psi.
- Check O_2 tanks >50% full.
- Calibrate O_2 analyzer.

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

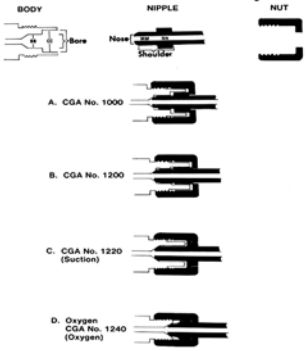
Anesthesia Machine Safety Features
- Flow-meter arrangement
- O_2:N_2O ratio controller
- Oxygen supply failure protection device ("fail-safe valve")

Gas Cylinders

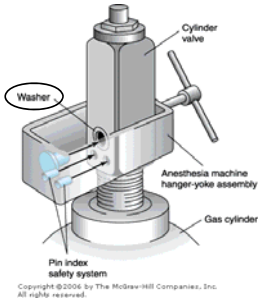
Gas	E-Cylinder Capacity (L)	Pressure (psi)	Color (USA)	Color (Int'l)	Form
O_2	660	1900	Green	White	Gas
Air	625	1900	Yellow	White & Black	Gas
N_2O	1590	745	Blue	Blue	Liquid + Gas
N_2	650	1900	Black	Black	Gas

How long can you use an O_2 tank starting at 430 psi running at 5 L/min?

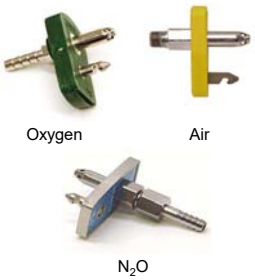
Diameter Index Safety System



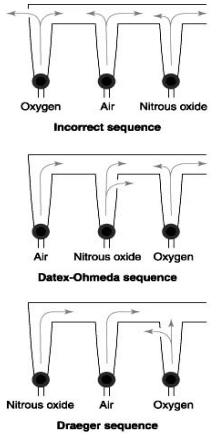
Pin Index Safety System



PISS for Gas Cylinders



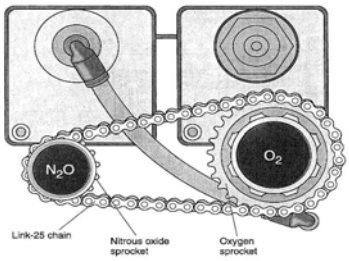
Quick Connects for Supply Lines



Flowmeter Arrangement

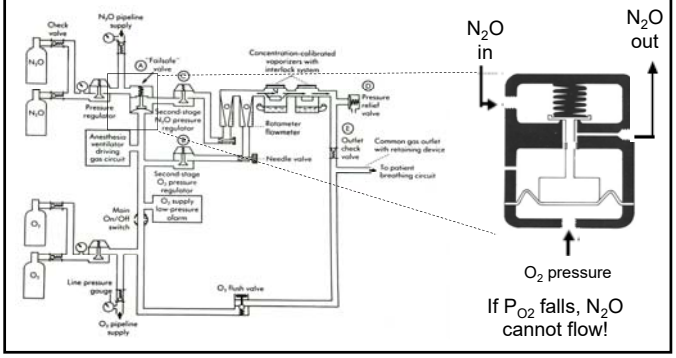
- A leak in the upstream O_2 flowmeter ("Incorrect sequence") results in a hypoxic gas mixture.
- A leak in the Datex-Ohmeda or Draeger flowmeter arrangements may deliver less Air or N_2O than expected, but the mixture will NOT by hypoxic because O_2 is closest to the FGF outlet.

O_2:N_2O Ratio Controller



Linkage mechanisms between flow valves can be either mechanical (above), pneumatic, or electronic.

Oxygen Failure Protection Device



Detection

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

Management

- Notify surgeon, call for help, use emergency manual.
- Verify problem.
- Disconnect patient from machine and ventilate with Ambu bag. Do not use auxiliary O_2 on machine as the source is the same. If patient needs higher FiO_2 call for E-cylinder.
- To keep patient connected to anesthesia machine, open O_2 cylinder on the back of the anesthesia machine and disconnect from pipeline O_2.
- Use manual ventilation to conserve O_2.
- D/C supply lines if crossed pipelines suspected.
- Call for backup O_2 tanks.
- Consider switching to TIVA until cause of failure is known.

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Anaphylaxis

Overview

- Allergic reactions are an important cause of intraoperative morbidity and mortality (3.4% mortality)
- Account for approximately 10% of all anesthetic complications
- More than 90% of reactions occur within 3 minutes, but can be delayed by hours with variable presentation
- Can be difficult to identify cause, as multiple drugs are given early in anesthetic
- 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:
  - Increase mucous membrane secretions
  - Increase bronchial smooth muscle tone
  - Decrease vascular smooth muscle tone and increase capillary permeability
- Anaphylactic and anaphylactoid reactions present similarly and are **treated IDENTICALLY**

Anaphylaxis vs. Anaphylactoid

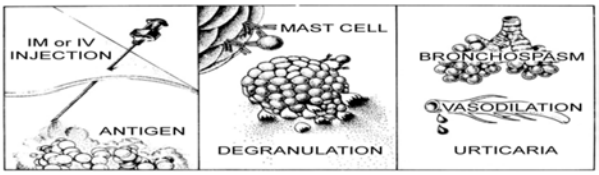
Anaphylaxis

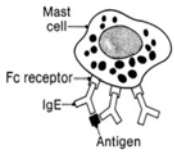
- IgE-mediated type I hypersensitivity reaction
- Sensitization happens with prior exposure to an antigen, which produces antigen-specific IgE antibodies that bind to Fc receptors on mast cells and basophils
- Upon re-exposure to the antigen, IgE antibodies then cross-link Fc receptors causing degranulation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

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

Sequence of Events





= Histamine, Leukotrienes, Kinins, Prostaglandins, Chemotactic factors, Tryptase

Sign and Symptoms

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

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

Common Precipitants

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 **(Roc > Vec > Cis > Sux)**
Natural rubber latex	12.1	Latex gloves, tourniquets, Foley catheters
Antibiotics	8	Penicillin and other β-lactams
Hypnotics	3.7	Propofol, thiopental
Colloids	2.7	Dextran, gelatin **>> Albumin > HES 6%**
Opioids	1.4	Morphine, meperidine
Other substances	2.9	Propacetamol, aprotinin, chymopapain, protamine, bupivacaine

Sugammadex

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 (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
- Prophylactic steroids and/ or H1-blockers (uncertain benefit)
- Prepare for the worst, hope for the best

Management

Acute Phase

1. Stop administration of offending antigen
2. Notify surgeon **AND** call for help
3. Maintain airway, give 100% O2
4. In cases of severe cardiovascular collapse, consider discontinuation of all agents that may augment hypotension such as inhaled anesthetics (via vasodilation) & narcotic infusions (via suppressing sympathetic response)
   - Give other amnestic agents (e.g. scopolamine, midazolam)
5. Fluids 2-4 L *or more!* (compensate for vasodilation, hypotension)
6. Epinephrine is drug of choice:
   (alpha-1→ supports BP; beta-2→ bronchial smooth muscle relaxation)
   1. Start **5-10 mcg IV boluses** for hypotension; **0.1-0.5 mg IV PRN** CV collapse. Escalate as needed.
   2. If no IV, give **0.3-0.5 mg IM** in anterolateral thigh, repeat q5-15 min
   3. ACLS doses (0.1-1 mg) for cardiovascular collapse

Management

Secondary Treatment

- Intubation
- Invasive lines: large-bore IVs, arterial line, central venous catheter, Foley catheter
- Drugs
  - H1-blocker - diphenhydramine 0.5-1 mg/kg IV
  - Steroids – decrease airway swelling, prevent recurrent sx in biphasic anaphylaxis
    - Hydrocortisone 0.25-1 g IV, or methylprednisolone 1-2 g IV
  - Epinephrine gtt - start 50-100 ng/kg/min (4-8 mcg/min)
    (Epi minidrip - 1 mg in 250 ml NS = 4 mcg/ml; run at 60 microdrips/min = 4 mcg/min; titrate to effect)
  - H2-blockers - not a first-line agent, but not harmful either!
  - Bicarbonate - 0.5-1 mEq/kg IV, as needed
  - Inhaled bronchodilator (Albuterol)

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

- At physiologic pH, local anesthetics are in equilibrium:

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

B (neutral) + H+ HB+

Lower pKa
Higher tissue pH

Higher pKa
Lower pH

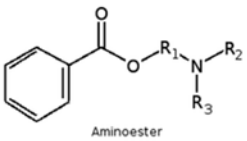
Mechanism of Action & Physiochemical Properties

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

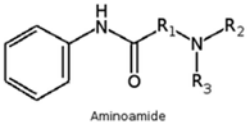
- Having a **pKa closer to physiologic pH** means a greater fraction of nonionized form (able to cross the neuronal membrane) for a **faster onset**
- Conversely, in an infected (acidic) environment, the pKa will be further from the environmental pH and have a slower onset

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

Local Anesthetic Structure



Aminoester



Aminoamide

- Three Major Chemical Moieties:
  - Lipophilic aromatic benzene ring
  - **Ester OR Amide** linkage
  - Hydrophilic tertiary amine
- Local anesthetics are weak bases
  pKa > 7.4

Categories

Category	Drugs	Metabolism
Esters	Cocaine 2-Chloroprocaine Procaine Tetracaine	Plasma **pseudocholinesterase** metabolism & RBC esterase (hydrolysis at ester linkage)
Amides (*i* before –caine)	Lidocaine Bupivacaine Ropivacaine Mepivacaine Etidocaine Levobupivacaine	**Liver metabolism:** Aromatic hydroxylation, N-dealkylation, Amide hydrolysis **p*-Aminobenzoic acid (PABA) metabolite can induce allergic-type reactions in a small percentage of patients

Routes of Delivery

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

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

*__Bupivacaine__ (Marcaine) is commonly used by surgeons for infiltration at 0.25% (2.5mg/ml), with max dose 2.5mg/kg
**__i.e. they can use a max volume of 1cc/kg__ (70kg pt gets max 70cc).

Toxicity

- Systemic absorption by injection site (vascularity):
  IV > tracheal > intercostal > caudal > epidural > brachial plexus > sciatic/femoral > subcutaneous
- Rate and extent of systemic absorption depends on:
  1) dose
  2) the drug's intrinsic pharmacokinetic properties
  3) the addition of a vasoactive agent (i.e. epinephrine)

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

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 especially has severe CV side effects
- 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 LA toxicity

- Initial management:
  - Stop local anesthetic
  - Give benzodiazepines for seizure, careful with propofol when there are signs of CV instability.
  - Begin ACLS: CPR, securing airway.
  - Reducing individual epinephrine doses to <1 mcg/kg. AVOID: vasopressin, Ca channel blockers, Beta blockers, and local anesthetics
- Initiate early intralipid (IL) therapy
  - Bolus IL 20% 1.5 ml/kg, followed by infusion of 0.25 ml/kg/min (up to 60min)
  - May repeat loading doses (max 3 total doses)
  - May increase infusion rate to 0.5 ml/kg/min if BP is still low. Not to exceed 10 ml/kg in the first 30 mins.
  - Consider early initiation of cardiopulmonary bypass

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Malignant Hyperthermia

Basics

Definition

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

Genetics

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

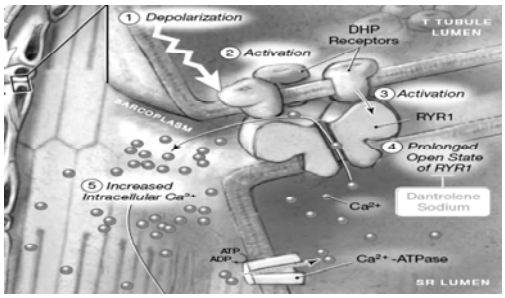
Basics (cont.)

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 >50yo
- The upper Midwest has highest incidence in US (geographic variation of gene prevalence)

- MH may occur on a patient's 2nd exposure to triggers
  - nearly 50% of MH episodes had at least one prior uneventful exposure to an anesthetic
- Risk factors include personal/family history of MH, pediatric age, comorbid myopathies (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 entry into cell from sarcoplasmic reticulum → sustained contraction → heat generation, CO_2 production, metabolic acidosis, and rhabdomyolysis

Sequence of Events

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

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

Sequence of Events

5. Secondary systemic manifestations
   - Arrhythmias
   - DIC
   - Hemorrhage
   - Cerebral Edema
   - Acute renal failure
   - Compartment syndrome
   - Death (due to DIC and organ failure as result of delayed

*****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.
•Look at your monitors – is there increased oxygen consumption? Tachycardia? Hypertension? Arrhythmias? Hyperthermia? Look at your patient – are they sweating? Rigid? Any combination of these findings should then make you want to rule out MH – consider an ABG (mixed metabolic and respiratory acidosis & hyperkalemia).

Differential Diagnosis

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

**Dantrolene can also treat both of these conditions

Treatment - Acute Phase

Immediate Actions	• Call for Help & obtain MH cart • D/C volatile agents and succinylcholine; switch to 100% O2 with high flows >10L/min • Notify surgeon; halt surgeon vs. finish ASAP with TIVA • Call MH hotline (1-800-MH-HYPER) • Check ABG and place foley
Dantrolene (interferes with RYR-1 Ca^{2+} channel)	• 2.5 mg/kg IV push q5min up to 10mg/kg (may need to exceed); prefer to give through large bore IV or central line (risk of phlebitis) • 1 vial = 20mg Dantrolene (dissolve in 60 cc sterile water); solution contains mannitol **New Ryanodex (250mg vial in 5cc sterile water) • Continue until decrease in EtCO2, rigidity, and tachycardia
Treat Acidosis	• Hyperventilate patient • If BE < -8, consider Bicarbonate 1-2 mEq/kg
Treat Temp	• Cool if temp >39 degrees C (cooling blankets, ice, cold NS, lavage stomach/bladder/rectrum)
Treat hyperkalemia & ARF	• $CaCl_2$ (10mg/kg) or Calcium gluconate (10-50mg/kg) • Bicarbonate, hyperventilate • Insulin and glucose (10 units in 50cc D50) • Diurese with mannitol 0.25g/kg (in dantrolene) or lasix 0.5-1mg/kg; goal > 1cc/kg/hr to help prevent pigment induced nephropathy/ARF
Treat dysrhythmias	• Avoid CCBs (may promote hyperkalemia and depress cardiac output) • Treat hyperkalemia and acidosis; if refractory, may need to add an antiarrhythmic
Continue monitoring	• Labs: ABG (BE, lactate, Ca^{2+}), Electrolytes (K^+), Coags, CK, Urine & serum myoglobin • EtCO2, temp, urine output/color

Treatment – Post Acute Phase

Admit to ICU	• ICU admission for at least 24 hrs (recrudescence rate 25%)
Continue Dantrolene	• 1 mg/kg IV q4-6hrs for at least 24-48 hrs • Note unpleasant side effects (nausea, malaise, muscle weakness) but is generally well tolerated)
Follow labs & watch for DIC & renal failure	• Serial ABGs, coags, electorlytes, CK, myoglobinuria • UOP and color
Counsel patient and family	• Future precautions • Refer to MHAUS • Refer patient and family to nearest Biopsy Center for follow-up

Who is Susceptible to MH?

- Autosomal dominance 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
    - Definitely avoid succinylcholine as can cause rhabdomyolysis, controversial whether to avoid volatile anesthetics; experts believe brief exposure should be small risk (i.e. inhalational induction in pediatric patients)
  - History of exertional heat stroke or exercise-induced rhabdomyolysis—some suggestion that these people may harbor genetic changes found in MH susceptible individuals

Susceptibility Testing

Caffeine-Halothane Contracture Test (CHCT)

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

Molecular Genetics

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

Prevention in Susceptible Patients

1. Machine

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

2. Monitors

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

3. Anesthetic

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

4. Emergency

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

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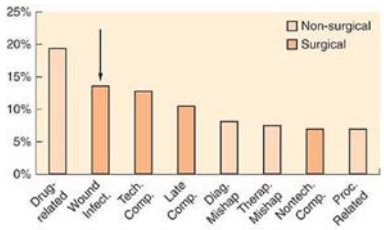
Perioperative Antibiotics

Why Antibiotics?



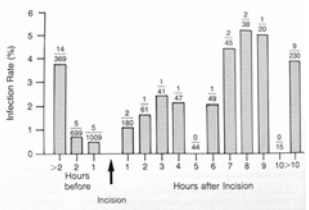
In 1984 a study including 51 acute care hospitals in New York State found that surgical site infection (SSI) was the **most common adverse surgical event** (and the second most common adverse event overall).

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.
- If a proximal tourniquet is used, the entire antibiotic dose should be administered before the tourniquet is inflated.
- Exceptions: Active ongoing antibiotic therapy (usually in-patients) or after a specimen is sent for culture.
- Epic tip: Click on “Patient Summary”, then the “Micro” tab. It will show you which antibiotics the patient is on and when they need to be redosed.

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

- Clean procedures (1.3 to 2.9% rate of surgical site infection)
  - Uninfected operative wound in which no inflammation is encountered and respiratory, GI, genital, or uninfected urinary tracts are not entered.
  - Common microbials are skin flora: staph 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 microbials are gram-negative rods and enterococci in addition to skin flora. If surgery involves a viscus, pathogens reflext 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 sterile technique, 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.

Preferred Empiric Agent by Surgery

Surgery	Preferred agent	Beta-lactam allergy
Cardiac Surgery / Vascular /Thoracic	Cefazolin	Vancomycin
Cardiac Surgery with prosthetic material	Cefazolin + Vancomycin	Vancomycin
Cardiac device insertion (e.g. pacemaker implantation)	Cefazolin	Vancomycin
Gastroduodenal	Cefazolin	Vancomycin
Biliary Tract	Cefazolin	Levofloxacin + Metronidazole
Colorectal, appendectomy	Cefazolin + Metronidazole (Ertapenem favored by Drs. Shelton and Rhoades)	Levofloxacin + Metronidazole
Other general surgery (e.g. hernia repair, breast)	Cefazolin	Vancomycin
Cesarean delivery	Cefazolin	Clindamycin + Gentamicin
Gynecological (e.g. hysterectomy)	Cefazolin	Clindamycin + Gentamicin

Per Stanford Pharmacy Guidelines (as of Aug 2016)

Preferred Empiric Agent by Surgery

Surgery	Preferred agent	Beta-lactam allergy
Head and Neck	Clean: Cefazolin Clean-contaminated: Ear/sinonasal: Cefazolin Oral mucosa breach: Cefazolin + metronidazole Contaminated: Cefazolin + metronidazole	Clindamycin
Neurosurgery	Cefazolin	Vancomycin
Orthopedics	Cefazolin	Vancomycin
Plastic Surgery	Cefazolin	Vancomycin
Urology (if no pre-op urine culture data is available or cultures were negative)	Cefazolin Open/laparoscopic involving intestine: Cefoxitin	Gentamicin + Clindamycin

Per Stanford Pharmacy Guidelines (as of Aug 2016)

Dosing and Re-dosing Guidelines

Antibiotic	Recommended dose	Re-dosing Interval
Cefazolin	≤120 kg = 2 gm >120 kg = 3 gm	4 hours
Clindamycin	900 mg	6 hours
Vancomycin	< 80 kg = 1 gm 80-99 kg = 1.25 gm 100-120 kg = 1.5 gm >120 kg = 2 gm	12 hours*

* Requires prolonged infusion time. Can be given 60-120 minutes prior to incision

Per Stanford Pharmacy Guidelines (as of Aug 2016)

Dosing and Re-dosing Guidelines

Antibiotic	Recommended dose	Re-dosing Interval
Ampicillin/Sulbactam	3 gm	2 hours
Aztreonam	2 gm	4 hours
Cefotetan	2 gm	6 hours
Cefoxitin	2 gm	2 hours
Ceftriaxone	2 gm	n/a (24 hours)
Cefuroxime	1.5 gm	4 hours
Ciprofloxacin	400 mg	8 hours*
Ertapenem	1 gm	n/a (24 hours)
Gentamicin	5 mg/kg (single dose) **	n/a (24 hours)
Levofloxacin	500 mg	n/a (24 hours)
Metronidazole	500 mg	12 hours
Tobramycin	5 mg/kg (single dose) **	n/a (24 hours)

* Requires prolonged infusion time. Can be given 60-120 minutes prior to incision
** If CrCl <20, give 2 mg/kg (single dose) or consult pharmacy

Per Stanford Pharmacy Guidelines (as of Aug 2016)

Administration and Common Side Effects

Administer via slow infusion (reconstitute in 100ml NS and give with microdripper)

- Vancomycin - over 30-60 mins
  - Side effect of Red Man Syndrome)
- Gentamicin - over 30-60 mins
  - Side effects of ototoxicity/nephrotoxicity
- Metronidazole (low pH) - over 60 mins
- Ciprofloxacin - over 30 mins
- Clindamycin - over 10-15 mins
  - Can cause QT prolongation if given too rapidly
  - Can also potentially potentiate neuromuscular blockers
- Ertapenem - over 30 mins

Allergies and Interactions

- Penicillins and cephalosporins have similar β-lactam ring
- 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.
- The cross-reaction rate between PCN and cephalosporins is substantially **less than 10%**
- History of PCN allergy is a general risk factor for allergic manifestations to antibiotic administration that may not be specific to cephalosporins
- Cross-reaction rate between 3rd generation cephalosporins and PCN approaches 0%!

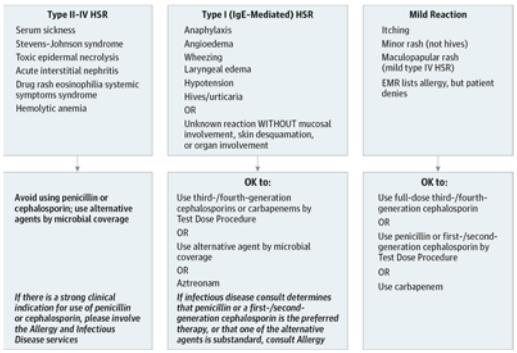
Allergies and Interactions

- Be sure to obtain a detailed history of patient's documented allergy to determine what type of reaction it is.
- Overuse of alternative antibiotics could result in adverse affects (e.g. C diff with clindamycin) and promote resistance.
- For suspected IgE-mediated reaction (anaphylaxis urticaria, angioedema), consider Vancomycin or Clindamycin ± one of the following for Gram neg coverage (ciprofloxacin, levofloxacin, gentamicin, or aztreonam)
- Type 1 anaphylactic reaction to antimicrobials occur 30-60 minutes after administration.

Allergies and Interactions

- If the allergic reaction to PCN is only “rash” or “hives,” many attendings would give a cephalosporin, but always ask your specific attending!
- However, hx of anaphylactic reaction to PCN is an absolute contraindication to cephalosporins.
- **Test dose**: Not always done. However, it may be prudent to give 1ml of the antibiotic first to see if the patient will have a reaction. This test dose only decreases the *anaphylactoid* reaction, not anaphylaxis.
- Allergic reactions are **more likely from neuromuscular blockers** than antibiotics.

Penicillin Allergy Pathway for Antibiotic Prescriptions



From Vaisman, et al. JAMA 2017

Special considerations

- The American Heart Association guidelines recommend prophylaxis for those with conditions that place them at increased risk for infective endocarditis AND for those at highest risk for adverse outcomes when endocarditis does occur. These are patients with:
  - 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
  - Congenital heart disease and completely repaired congenital heart defect if it’s within the first 6 months.
  - Cardiac transplant patients who develop cardiac valvulopathy
- 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
- For mitral valve prolapse, 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 this condition.
- Do not need prophylaxis for bronchoscopy without biopsy, vaginal delivery, hysterectomy, or GI/GU procedures, including colonoscopy.

Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 Guideline Update on Valvular Heart Disease: Focused Update on Infective Endocarditis: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol.* 2008;52(8):676-685. doi:10.1016/j.jacc.2008.05.008.

Hall Question

Each of the following drugs can enhance the neuromuscular blockade produced by nondepolarizing muscle relaxants EXCEPT

A. Calcium
B. Aminoglycoside antibiotics
C. Magnesium
D. Dantrolene
E. Intravenous lidocaine

- See next slide for answer.

Hall Answer

- (A) Many drugs can enhance the neuromuscular block produced by nondepolarizing muscle relaxants. These include volatile anesthetics, aminoglycoside antibiotics, magnesium, intravenous local anesthetics, furosemide, dantrolene, calcium channel blockers, and lithium. Calcium does not enhance neuromuscular blockade and, in fact, actually antagonizes the effects of magnesium. In patients with hyperparathyroidism and hypercalcemia there is a decreased sensitivity to nondepolarizing muscle relaxants and shorter durations of action (*Miller: Anesthesia, ed 6, pp 514-518; Stoelting: Pharmacology and Physiology in Anesthetic Practice, ed 4, pp 224-226, 395*).

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- Vaisman A, McCready J, Powis J. Clarifying a "Penicillin" Allergy: A Teachable Moment. JAMA Intern Med. 2017 Feb 1;177(2):269-270.
- 2016 SHC guidelines for Adult Patients- Antimicrobial Surgical Prophylaxis

I met my next patient in the VA preop area. I did my physical exam and was ready to place the IV. I had the lidocaine needle at his skin and announced, "Small prick!" He responded, "Honey, that's what my ex-wife used to tell me, too."

It was time to bring the patient to the OR, and I was pushing him on a gurney down the ASC hallway. I got lost along the way and took a wrong turn leading to a dead end. I tried to play it off that we had taken this round about way just to get a patient hat for the OR. Unfortunately, despite the Versed, I think he saw right through the subterfuge.

Wheeled the patient into the room for a hip fracture repair. Nurse on the computer. Myself, anesthesia attending and ortho resident move the patient to the OR bed at which point the pt chuckles and smiles. I ask "what's so funny?" He responds, " I just had about a million dollars worth of education move me from one bed to another."

I anesthetized a trauma patient with multiple fractures. We did his hip while he was still intubated and I gave him a fair amount of ketamine for multimodal analgesia. The surgeons told me that when they rounded on him after he was extubated, the patient said, “Thanks for fixing my hip, but what are you going to do about my hind legs?” The patient then proceeded to explain that his hind legs needed to be fixed because he was a “centaur.”” When I did his ankle fracture a few days later he told me that, “The last time I had anesthesia, I had a ‘bad trip.’”

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?