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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 conversation 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. This lecture series starts on July 6th at 4pm in the Anesthesia Conference room. You should receive a schedule of lectures separate from this book. The last lecture is July 31st. 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 Melissa Cuen 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 either one of us with questions or concerns.

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KEY POINTS AND EXPECTATIONS

Key Points:

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

Expectations of CA-1 Residents:

• Attend the afternoon CA-1 Introduction to Anesthesia Lecture Series.
• Participate in goal-directed learning by completing the CA-1 Mentorship Intra-operative Didactics with your mentors.
• Discuss cases with your mentor the night before.
• Take weekday call with your mentor. You will be expected to stay as long as the ongoing cases are of high learning value. You will take DAC day off with your mentor.
• CA-1s at SUH are not expected to take weekend call with your mentor (for those at the Valley and VA, discuss with your mentor).

Expectations of Senior Resident Mentors:

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

Expectations of Faculty Mentors:

• Participate in goal-directed learning by completing the CA-1 Mentorship Intra-operative Didactics with your CA-1.
• Take weekday call with your CA-1. When you go home, your CA-1 goes home. When you have a DAC, your CA-1 has a DAC.
• Provide timely feedback to your CA-1 every day and at the end of the week.
• Provide continuity of teaching by communicating with the CA-1’s other mentors.
GOALS OF THE CA-1 TUTORIAL MONTH

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

I. Preoperative Preparation:
   a. Perform a complete safety check of the anesthesia machine.
   b. Understand the basics of the anesthesia machine including the gas delivery systems, vaporizers, and CO\textsubscript{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

<table>
<thead>
<tr>
<th>First Day</th>
<th>July 7</th>
<th>Discuss GOR Goals and Objectives for CA-1</th>
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<td>Discuss etiquette in the OR</td>
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<td>Discuss proper documentation</td>
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<td>Malignant Hyperthermia</td>
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<td>Perioperative Antibiotics</td>
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Monitoring in the Past

Finger on the pulse

Standard Monitors

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
- FIO2 Analyzer
- Pulse Oximetry
- Low O2 Concentration Alarm

VENTILATION
- Capnography (with expired VT)
- Disconnect alarm

CIRCULATION
- EKG
- Blood Pressure
- Pulse Oximetry

TEMPERATURE
- Temperature Probe

Pulse Oximetry

Terminology
- SaO2 (Fractional Oximetry) = O2Hb / (O2Hb + Hb + MeHb + COHb)
- SpO2 (Functional Oximetry/Pulse Oximetry) = O2Hb / (O2Hb + Hb)

Fundamentals
- The probe emits light at 660 nm (red, for Hb) and 940 nm (infrared, for O2Hb); sensors detect the light absorbed at each wavelength.
- Photoplethysmography is used to identify arterial flow (alternating current = AC) and cancel out the absorption during non-pulsatile flow (direct current = DC); the patient is their own control!
- The S value is used to derive the SpO2 (S = 1:1 ratio = SpO2 85%).

Pearls
- Methemoglobin (MetHb) - Similar light absorption at 660 nm and 940 nm (1:1 ratio); at high levels, SaO2 approaches 85%.
- Carboxyhemoglobin (COHb) - Similar absorbance to O2Hb. At 50% COHb, SaO2 = 50% on ABG, but SpO2 may be 95%, thus producing a falsely high SpO2.
- Other factors producing a falsely low SpO2 = dyes (methylene blue > indocyanine green > indigo carmine), blue nail polish, shivering, ambient light.
- Cyanosis - clinically apparent with 3 g/dl desaturated Hb. At Hb = 15 g/dl, cyanosis occurs at SaO2 = 80%; at Hb = 9 g/dl (i.e. anemia), cyanosis occurs at SaO2 = 96%.

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.

**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.

**Effect of Patient & Transducer Position on BP Measurement**

**Capnography**
- Gives you tons of information (both number & tracing):
  - bronchospasm (upsloping trace)
  - inadequate circulation resulting from hypotension indicating BP is too low for pt (number decreasing)
  - pulmonary embolism (decreased number and increased different 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 absorbant (ETCO2 does not return to 0-5)

For example tracings visit: [http://www.capnography.com/find.htm](http://www.capnography.com/find.htm)

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

**Example Traces**
A. Spontaneous ventilation
B. Mechanical ventilation
C. Prolonged exhalation (spontaneous)
D. Emphysema
E. Sample line leak
F. Exhausted CO2 absorbant
G. Cardiogenic oscillations
H. Electrical noise
# Temperature

Monitoring is now required (previously recommended)

## Sites
- **Pulmonary artery**: = "Core" temperature (gold standard)
- **Tympanic membrane**: correlates well with core; approximates brain/ hypothalamic temperature
- **Esophagus**: correlates well with core
- **Nasopharyngeal**: correlates well with core and brain temperature
- **Rectal**: not accurate (temp affected by LE venous return, enteric organisms, and stool insulation)
- **Bladder**: approximates core when urine flow is high
- **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

## Other Monitors/Adjuncts to Consider
- **Foley**
- **A-line**
- **CVC**
- **Esophageal stethoscope**
- **ICP**
- **Pulmonary Artery catheter +/- continuous mixed venous SpO2/cardiac output**
- **BIS monitor/Sedline**
- **Precordial Doppler (if risk of air embolism high)**
- **Transesophageal Echo**
- **Cerebral Oximetry (NIRS)**

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## References

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## 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
Inhalational Agents

Pharmacokinetics

- The pharmacokinetics of inhalational agents is divided into four phases
  - Absorption
  - Distribution (to the CNS; brain = site of action)
  - Metabolism (minimal)
  - Excretion (minimal)
- The ultimate goal is to establish a particular partial pressure of an agent in the alveoli \( P_A \)
- This partial pressure will equilibrate with the CNS tissue to produce an anesthetized state
- At equilibrium the following applies
  \[ P_A = P_{Alv} \]
- At higher altitudes where barometric is <760 mmHg, the same concentration of inhalation agent will exert a lower partial pressure within alveoli and therefore a REDUCED anesthetic effect

Uptake and Distribution

- \( P_A \) is determined by input (delivery) minus uptake (loss)
  - Input: inspired partial pressure, alveolar ventilation, breathing system
  - Uptake: solubility in blood (defined as blood gas partition coefficient, \( k_a \)), cardiac output \( Q \), alveolar-to-venous partial pressure difference \( \left( P_A - P_v \right) \), minute ventilation \( Q/V \)
- Inhalational anesthetic uptake is commonly followed by the ratio of pulmonary arterial and venous blood partial pressure. (Clinical Anesthesia 5th Edition; Barash, P.; Lippincott Williams and Wilkins, 2006)
- Parameters as described in Equation 15–16: \( P, Q, V \)
- All inhalational agents produce a dose-dependent depression of the cardiovasculature (except N2O) 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

Factors That Increase or Decrease the Rate of Rise of \( F_A/F_I \)

<table>
<thead>
<tr>
<th>INCREASE</th>
<th>DECREASE</th>
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<tbody>
<tr>
<td>Low ( k_a )</td>
<td>High ( k_a )</td>
</tr>
<tr>
<td>Low ( Q )</td>
<td>High ( Q )</td>
</tr>
<tr>
<td>High ( V )</td>
<td>Low ( V )</td>
</tr>
<tr>
<td>High ( P_A - P_v )</td>
<td>Low ( P_A - P_v )</td>
</tr>
</tbody>
</table>
**Time Constant**

- For volatile anesthetic, time constant = volume (L) / flow (L/min)
- For the anesthesia circuit, time constant = volume of circuit (L)/ fresh gas flow rate (L/min)
- Calculation of washout for VOLATILES requires use of the TIME CONSTANT
  - 1 time constant for 63% washout of volatile agent
  - 2 time constants for 84% washout of volatile agent
  - 3 time constants for 95% washout of volatile agent

**Nitrous Oxide**

- Low potency (MAC 104% - can never reach 1 MAC!)
- Relatively insoluble in blood
  - Facilitates rapid uptake and elimination
- Does not produce skeletal muscle relaxation
- Increases CBF and CMRO2
- Can potentially contribute to PONV
- 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)

**Isoflurane**

- Highly pungent
- Second most potent of the clinically used inhalational agents (MAC 1.2%)
- Preserves flow-metabolism coupling in the brain
  - 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 at above 1 MAC; short lived)
  - Minimal compared to halothane
- At 2 MAC produces electrically silent EEG

**Sevoflurane**

- Half as potent as isoflurane (MAC 1.8%)
- 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 CO2 absorbent
  - Can cause fires
  - Forms Compound A in CO2 absorbent (nephrotoxic)
  - 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 N2O)
- Very fast uptake and elimination
- Low potency (MAC 6.6%)
- High vapor pressure (699 mmHg) is close to atmospheric pressure therefore boils at sea level
  - Must be stored in a heated, pressurized vaporizer so pressure stays constant
- Very pungent
  - Can cause breath-holding, bronchospasm, laryngospasm, coughing, salivation when administered to an awake patient via facemask
- Can form CO in desiccated CO2 absorbent (more so than other volatiles)
- Can cause an increased sympathetic response (tachycardia, hypertension) when inspired concentration is increased rapidly

**References**

2. Miller’s Anesthesia 6th edition; Miller R.; Churchill Livingstone, 2005
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
- MAC is a population average, not a true predictor of an individual's response.
- MAC is an ED50 concentration. The ED95 is ±25%, so at 1.3 MAC, 99% of patients will not respond to incision.
- MAC values are additive (e.g. 0.5 MAC isoflurane + 0.5 MAC N2O = 1 MAC)
- MAC is inversely related to anesthetic potency & therefore its lipid solubility

MAC of Inhaled Anesthetics

<table>
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<tr>
<th>Gas</th>
<th>Blood Gas Partition Coefficient</th>
<th>MAC*</th>
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<tbody>
<tr>
<td>Halothane</td>
<td>2.4</td>
<td>0.75%</td>
</tr>
<tr>
<td>Enflurane</td>
<td>1.9</td>
<td>1.7%</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>1.4</td>
<td>1.2%</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>0.85</td>
<td>2.0%</td>
</tr>
<tr>
<td>N2O</td>
<td>0.47</td>
<td>104%</td>
</tr>
<tr>
<td>Desflurane</td>
<td>0.42</td>
<td>6.0%</td>
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*MAC values for adults 36-49 years old

- MAC is an indicator of gas 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.
- Oil gas partition coefficient is an indicator of anesthetic potency

More MAC Definitions

MAC-Awake (a.k.a. MAC-Aware)
- The MAC necessary to prevent response to verbal/tactile stimulation.
- Volatiles: ~0.4 MAC; N2O: ~0.6 MAC

MAC-BAR
- The MAC necessary to "blunt the autonomic response" to a noxious stimulus
- ~1.6 MAC

MAC-EI
- The MAC necessary to prevent laryngeal response to "endotracheal intubation"
- ~1.3 MAC

Effect of Age on MAC

MAC is highest at 6 months, then begins to decline. After age 40, MAC declines ~6% per decade. MAC for an 80 year old is about 0.75 that of a 40 year old

Factors Increasing MAC

- Drugs increasing central catecholamines:
  - MAOIs, TCAs
  - Acute cocaine and amphetamine use
  - Ephedrine
  - Levodopa
- Factors that increase metabolic function of brain, i.e. hyperthermia (over 42C)
- Hypoventilation
- Chronic EtOH abuse
- Genetic factors
  - Redheaded females may have a 19% increased MAC requirement compared to brunettes.
- Highest MAC for infants is at 1-6 months old (except sevoflurane which has highest MAC in neonates age 0-30 days)
Factors Decreasing MAC

- Drugs decreasing central catecholamines:
  - Reserpine, α-methyldopa
  - Chronic amphetamine abuse
- Other drugs:
  - Opioids, benzodiazepines, barbiturates, α₂-agonists (clonidine, dexmedetomidine), ketamine, lidocaine, lithium, verapamil, hydroxyzine.
- Acute EtOH intoxication
- Pregnancy (1/3 after 12 weeks, normal by 72h post-partum)
- Hypothermia (50% per 10˚C)
- Hypotension (MAP<40 in adult)
- Hypoxemia (PₐO₂ < 38 mm Hg)
- Hypercarbia (PₐCO₂ > 95 mm Hg)
- Hyponatremia
- Metabolic acidosis
- Anemia (Hct < 10%)

Factors that do NOT Influence MAC

- Duration of anesthesia
- Hypocapnea or Hypercapnea (unless >95mmHg)
- Arterial blood pressure >50mmHg
- Sex
- Patient size

Awareness

- Very rare
- Most common sensation is hearing voices
- Mostly occurs during induction or emergence
- More common in high-risk surgeries where deep anesthesia may be dangerous to an unstable patient (e.g. trauma, cardiac, cesarean section)
- Early counseling after an episode is very important
- Patient handout available at: www.asahq.org/patientEducation/Awarenessbrochure.pdf

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)

Signs of Light Anesthesia

- Increase in HR or BP by 20% above baseline
- Tearing
- Dilated pupils
- Coughing or bucking
- Patient movement
- Signs of consciousness on EEG monitor (Bispectral Index or Sedline)

BIS & Sedline

- Both use EEG monitoring and algorithms to produce numbers (0-100) relating to depth of anesthesia.
  - 65-85 = sedation
  - 30-65 = general anesthesia
  - <30 = too deep
- Both have been shown to be fairly good predictors of loss and regaining consciousness
- Interpatient variability exists
- Both have a noticeable time lag (~2min)
- It is possible to display the raw EEG in real time on either device and interpret on your own.
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?)

References

**IV Anesthetic Agents**

Mechanism of Action

- It is widely believed that most IV anesthetics exert their sedative and hypnotic effects via their interaction with GABA
  - GABA is the primary inhibitory neurotransmitter in the CNS
  - Activation of receptor causes increased chloride conductance and therefore hyperpolarization
- 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

**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 affect 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

**Pharmacokinetic Values for the Currently Available Intravenous Sedative-Hypnotic Drugs**

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

**Drug** | **Dose (mg/kg)** | **Effects** | **Pearls**
--- | --- | --- | ---
**Propofol** | 1.5-2.5 | Decreases cerebral metabolism; ICU extubation; central venous line, arterial line, endotracheal tube insertion | - Intrinsic myocardial depressant effects which may be unmasked with depleted catecholamines
- Can precipitate when injected with acidic fluids
- Increases CMRO2, CBF, ICP
- Myoclonus
- High incidence of PONV

**Etomidate** | 0.2-0.3 | Decreases cerebral metabolism; ICU extubation; rapid sequence induction | - Intrinsic myocardial depressant effects which may be unmasked with depleted catecholamines
- Can precipitate when injected with acidic fluids

**Thiopental** | 3-5 | Decreases cerebral metabolism; ICU extubation; rapid sequence induction | - Analgesic effects
- Minimal respiratory depression effects which may be unmasked with depleted catecholamines

**Ketamine** | 1-2 | Decreases cerebral metabolism; ICU extubation; rapid sequence induction | - Analgesic effects
- Minimal respiratory depression effects which may be unmasked with depleted catecholamines

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--- | --- | --- | ---
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- 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
## Propofol
- Produced in an egg lecithin emulsion (egg yolks—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<sub>2</sub>, CBF, and ICP; CPP maintained because less decrease in SBP
- Anticonvulsant activity
- Decreases CMRO<sub>2</sub>, CBF, ICP
  - 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 (especially for prolonged periods of time). Causes severe metabolic acidosis, rhabdomyolysis, cardiac failure, renal failure, hypertriglyceridemia, with high mortality, especially in children
- May see re-sedation as benzodiazepine is eliminated more slowly compared to effects of flumazenil
- Induction dose 1.5-2.5 mg/kg in adults, 2-3 mg/kg in children, 3-4 mg/kg in infants
- Rapidly redistributed into peripheral compartments (accounts for short duration of action)
- Induction dose 1.5-2.5 mg/kg in adults, 5-6 mg/kg in children, 6-8 mg/kg in infants
- Larger doses can saturate the peripheral compartments resulting in a prolonged duration of action
- Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
- Anticonvulsant activity
  - Exceptions: Methohexital
- Decreases SVR, direct myocardial depressant
- Antitussive activity
- Inefficient
- Does not induce histamine release
- Inhibition for 5-8 hours even after a single induction dose
- High incidence of PONV
- Propofol infusions (>4mg/kg/hr) for prolonged periods of time. Causes severe respiratory depression
- Induction dose 3-5 mg/kg in adults, 5-6 mg/kg in children, 6-8 mg/kg in infants
- Dose-dependent respiratory depression
- Larger doses can cause increased oral secretions
- Causes bronchodilation
- Increases PVR
- Intrinsic myocardial depressant, may be significant in severely ill patients with depleted catecholamine reserves
- Cardio-stimulating effects secondary to direct sympathetic stimulation
- Most likely to preserve airway reflexes among the IV anesthetics
- Does not induce histamine release
- Inhibition for 5-8 hours even after a single induction dose
- High incidence of PONV
- Produces a dissociative anesthetic state
  - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
  - Decreases SVR, direct myocardial depressant
- Hypnotic and analgesic
  - Selective α<sub>2</sub> adrenergic agonist (primarily central-acting)
  - May see re-sedation as benzodiazepine is eliminated more slowly compared to effects of flumazenil
  - 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
  - Opioid-sparing effect and does not significantly depress respiratory drive
  - Usually an infusion at a concentration of 4 mcg/ml
  - Loading dose 0.5-1mcg/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

## 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
- Myocardial depression
- Induction dose 0.2-0.3 mg/kg
- Decreases CMRO<sub>2</sub>, CBF, ICP
- 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
- Inhibition for 5-8 hours even after a single induction dose
- High incidence of PONV

## Thiopental
- Highly alkaline (pH 9)
- Can precipitate in acidic solutions (DO NOT MIX with Rocuronium or LR)
- Induction dose 0.1-0.2 mg/kg IV
- Premedication dose 0.04-0.08 mg/kg IV (typically 1-2 mg)
- Rapid onset and terminal half-life of 2hr
- Loading dose 0.5-1mcg/kg over 10 min
- Infusion rate 0.4-1.2 mcg/kg/hr (ask your attending)
- Opioid-sparing effect and does not significantly depress respiratory drive
- Usually an infusion at a concentration of 4 mcg/ml
- Loading dose 0.5-1mcg/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

## Ketamine
- Produces a dissociative anesthetic state
  - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
  - Decreases SVR, direct myocardial depressant
- Hypnotic and analgesic
  - Selective α<sub>2</sub> adrenergic agonist (primarily central-acting)
  - May see re-sedation as benzodiazepine is eliminated more slowly compared to effects of flumazenil
  - Opioid-sparing effect and does not significantly depress respiratory drive
  - Usually an infusion at a concentration of 4 mcg/ml
  - Loading dose 0.5-1mcg/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

## Midazolam
- All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant properties (but not analgesia!)
- Premedication dose 0.04-0.08 mg/kg IV (typically 1-2 mg)
- Induction dose 0.1-0.2 mg/kg IV
- Decreases CMRO<sub>2</sub>, CBF, ICP
  - Does not produce EEG burst suppression
  - Decrease SVR and BP when used as induction dose
- Causes dose-dependent respiratory depression
- Most likely to preserve airway reflexes among the IV anesthetics
- Does not induce histamine release
- Inhibition for 5-8 hours even after a single induction dose
- High incidence of PONV

## Dexmedetomidine
- Selective α<sub>2</sub> 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 0.5-1mcg/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 tattooed on my a**." I asked if he was willing to show me. As he rolled over, the words "your name" appeared on his left butt cheek.

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

References

*Names have been changed
Rational IV Opioid Use

Basic Opioid Pharmacology

- **Analgesia** produced by mu (µ) opioid receptor agonism in the brain (periaqueductal gray matter) and spinal cord (substantia gelatinosa).
- Well-known side effect profile:
  - Sedation, respiratory depression
  - Itching, nausea, ileus, urinary retention
  - Bradycardia, hypotension
  - Miosis, chest wall rigidity
- Opioids are hemodynamically stable when given alone, but cause \text{CO}, SV, and BP in combination with other anesthetics.
- Reduces MAC of volatile anesthetics.

### Opioid Receptor Subtypes and Their Effects

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Clinical effect</th>
<th>Agonists</th>
<th>Clinical effect</th>
<th>Agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>µ</td>
<td>Supraspinal (µ1)</td>
<td>Morphine</td>
<td>Respiratory depression (µ2)</td>
<td>Met-enkephalin</td>
</tr>
<tr>
<td></td>
<td>Physical dependence</td>
<td>B-Endorphin</td>
<td>Muscle rigidity</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>κ</td>
<td>Sedation</td>
<td>Morphine</td>
<td>Spinal analgesia</td>
<td>Nalbuphine</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Butorphanol</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Dynorphin</td>
</tr>
<tr>
<td>δ</td>
<td>Analgesia</td>
<td>Leu-enkephalin</td>
<td>Behavioral</td>
<td>B-Endorphin</td>
</tr>
<tr>
<td></td>
<td>Epileptogenic</td>
<td></td>
<td>Hallucinations</td>
<td>Pentazocine</td>
</tr>
<tr>
<td>σ</td>
<td>Dysphoria</td>
<td>Naltrexone</td>
<td></td>
<td>Ketamine</td>
</tr>
</tbody>
</table>

### Opioids

**Morphine**
- Slow peak time (~80% effect at 15 minutes, but peak analgesic effect is at ~90 minutes).
- Active metabolite, morphine-6-glucuronide, has analgesic properties and is renally excreted (not clinically relevant unless patient has renal failure).
- Can cause histamine release.

**Hydromorphone (Dilaudid)**
- “A rapid onset morphine” --> Peak effect in 5-10 minutes.
- About 8-fold more potent than morphine (i.e. 1 mg Dilaudid = 8 mg morphine).
- No active metabolites, no histamine release.
- Good choice for postop analgesia and PCA.

**Fentanyl**
- Fast onset & short duration of action (peak effect at 3-5 minutes; effect site half-life ~30 minutes).
- ~100-fold more potent than morphine.
- Very cheap.

**Sufentanil**
- Fast onset, but slightly slower than fentanyl
- 10-fold more potent than fentanyl (i.e. 5 mcg sufentanil = 50 mcg fentanyl).
- More rapid recovery than fentanyl.

**Alfentanil**
- Fastest onset time of all opioids (~90 seconds); pKa = 6.5, so it crosses the blood-brain barrier rapidly.
- Also causes more N/V, chest wall rigidity, and respiratory depression.
- Brief duration of action due to rapid redistribution.

**Remifentanil**
- Peak effect time ~90 seconds
- Unique pharmacokinetics - metabolized by plasma esterases.
- Short context-sensitive half-time after termination of infusion with predictable offset in ~5-10 minutes.
Opioids

Meperidine (Demerol)
- Originally discovered as a local anesthetic (“pethidine”)
- Peak effect in 15 minutes, lasts 2-4 hours.
- Active metabolite (normeperidine) lowers the seizure threshold; renally excreted.
- Use for treating shivering.
- 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 a short-acting opioid like remifentanil or alfentanil.
• For intraop analgesia:
  - Fentanyl is rapidly titratable, but requires frequent redosing; it may be more “forgiving” if overdosed.
  - Morphine has a long onset time to peak effect, but gives prolonged analgesia during the case and into the postop period.
  - Hydromorphone is rapidly titratable (like fentanyl) with prolonged analgesia (like morphine).

• For ENT cases, consider an opioid infusion (e.g. remifentanil, alfentanil, sufentanil, or fentanyl):
  - Stable level of analgesia
  - Induced hypotension
  - Narcotic wakeup reduces bucking on ETT
  - Smooth transition to postop 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.
• 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.
• For postop 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.
References

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

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)

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

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)

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%).

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
- 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

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, vaspressors, airway support, left lateral displacement during pregnancy
- Surgical Events: Vagal reflexes, obstructed venous return, pneumoperitoneum, retractor 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 Hypertension

- Temporize with fast-onset, short-acting drugs, but ultimately diagnose and treat the underlying cause.
- Pharmacologic Interventions:
  - Volatile anesthetics (cause vasodilation while deepening anesthetic)
  - Opioids (treat pain and deepen the anesthetic, histamine release causes hypotension)
  - Propofol (quickly sedates and vasodilates)
  - Beta-blockers (e.g. labetalol, esmolol - affects HR > BP)
  - Vasodilators (e.g. hydralazine - takes 20min for peak, NTG, SNP)

Treatment of Hypotension

- Temporize with fast-onset, short-acting drugs (e.g. ephedrine, phenylephrine), but ultimately diagnose and treat the underlying cause.
  - Turn down (sometimes turn off) the anesthetic
  - Call for help. Inform surgeons
- Volume
  - Reevaluate EBL; replace with crystalloid, colloid, or blood, as needed
  - Consider art line, 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

Treatment of Hypotension

Drugs (doses in parentheses are bolus starting doses)
- Phenylephrine (Neosynephrine) = α₁ agonist (start at 100mcg)
  - Direct vasoconstrictor
  - Use in vasodilated state with tachycardia
  - Will cause reflex bradycardia
- Ephedrine = α₁, β₁, and β₂ (less so) agonist (start at 5mg)
  - Direct and indirect adrenergic stimulation via NE release
  - Use in vasodilated, bradycardic, low CO states
- Epinephrine = β₁, α₁, α₂, and β₂ agonist (start at 5mcg)
  - Endogenous catecholamine
  - Causes vasoconstriction and increased CO
- Inotropes (in low CO states)
  - Epinephrine, Dopamine, Metimine, Dobutamine (the last 2 vasodilate)
- Stress-dose steroids – consider 100mg hydrocortisone if steroids taken in past 6 months

References

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 NMBA with distinct properties: depolarizing (succinylcholine) and nondepolarizing (e.g. rocuronium, vecuronium, cisatracurium).
- Postoperative residual paralysis occurs frequently. Monitoring of neuromuscular blockade and pharmacological reversal are the standard of care.
- NMBA have risks and there are a number of surgical and patient specific contraindications. NMBA should be used judiciously. Read your text book chapter on NMBA several times during residency!

Neuromuscular transmission

- Action potential depolarizes motor neuron → Ca²⁺ influx → vesicles fuse and release Ach across synaptic cleft and binds nicotinic receptors
- If Ach binds both α subunits, receptor ion channel opens and ions move: Na⁺ and Ca²⁺ in, K⁺ out

The Depolarizer: Succinylcholine

- Structure: 2 joined ACh molecules
- Mechanism of action: ACh receptor agonist and prolonged muscle depolarization
- Intubating Dose: 1 to 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
- Diffuses away then rapidly metabolized by pseudocholinesterase
- ~1:3000 individuals is homozygous for an abnormal plasma cholinesterase and paralysis can last 3-8 hours in such individuals.
- Consider checking twitches before giving nondepolarizing NMBA after sux.
- Dibucaine (local anesthetic) inhibits normal pseudocholinesterase 80%, but abn pseudocholinesterase 20%.

Contraindications to Sux

- Hyperkalemia. Sux causes an increase in K⁺ of 0.5 mEq/L. Normokalemic renal failure is NOT an contraindication.
- Giving sux to patient with conditions that cause upregulation of nAChR on muscle may result in hyperK⁺ arrest. This includes burn injury (after 24-48hrs), muscular dystrophy, myotonia, long immobility, stroke, upper motor neuron disease
- Malignant Hyperthermia (sux is a trigger)

Additional Side Effects

- Bradycardia, esp. in children. Often given with atropine.
- Tachycardia (catecholamine release)
- Anaphylaxis approx. 1:5000 – 1:10,000
- Fasciculations + myalgia. Possibly preventable with defasciculating dose of roc.
- Trismus
- Increased ICP, IOP, and intragastric pressure. N.B. Benefits of securing the airway quickly often take precedent over small increases in IOP or IOP.

Defasciculating Dose of Roc. (0.03mg/kg 3 minutes prior to sux)

- Can prevent myalgias and increased ICP
- Does NOT prevent hyperkalemia or increase IOP

Non-Depolarizing NMBA

- Mechanism of action: competitive inhibition of nicotinic ACh receptor (nAChR) at the NMJ.
- Fade with high-frequency nerve stimulation is characteristic. There are presynaptic nAChR which mobilize Ach containing vesicles. These presynaptic nAChR have a slightly different structure from post synaptic nAChR. Nondepolarizing agents block presynaptic nAChR and sux does not.
- Two structural classes:
  1. Benzylisoquinoliniums = "uriums"
     - Atracurium, Cisatracurium, Mivacurium, Doxacurium, d-Tubocurarine
     - Can cause histamine release (d-Tubocurarine >> Atracurium)
  2. Aminosteroids = "oniums"
     - Pancuronium, Vecuronium, Rocuronium, Pimecuroonium
     - No histamine release
     - Possible vagolytic effects (Pancuronium > Rocuronium > Vecuronium)
- The most used non-depolarizing agents are the intermediate duration agents cisatracurium, rocuronium and vecuronium.
Non-Depolarizing NMBA (cont.)

- Intubating doses are 2 x ED_{95}, average dose required to induce 95% suppression of the twitch height in half of the population. I.E. if you give 0.3mg/kg of roc, 50% of the population will have 95% suppression of a monitored twitch. A larger intubating dose speeds onset time but lengthens duration of block.
- To speed onset, can use a priming dose (efficacy debatable) 10% of the intubating dose is given 3-5 minutes prior to intubating dose (as with defasciculating doses prior to sux).
- Wide inter-individual response to non-depolarizing agents. Monitor twitches and adjust doses accordingly.
- Rocuronium can be used for rapid sequence inductions when sux cannot, although roc still slower. However, the 1-1.2mg/kg roc necessary for RSI causes prolonged relaxation.
- Cisatracurium is degraded by plasma esterases and Hoffman elimination. It is useful for patients with hepatic or renal dysfunction. There is less laudanosine (seizure-precipitating metabolite) produced and histamine released than with atracurium.

<table>
<thead>
<tr>
<th>Agent</th>
<th>ED_{95} (mg/kg)</th>
<th>Intubating Dose (mg/kg)</th>
<th>Onset (min)</th>
<th>Duration to 25% recovery (min)</th>
<th>Intra-op Maintenance</th>
<th>Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylcholine</td>
<td>0.3</td>
<td>1</td>
<td>1-1.5</td>
<td>6-8</td>
<td>Rarely done</td>
<td>plasma cholinesterase</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>0.3</td>
<td>0.6</td>
<td>1.5-2</td>
<td>30-40</td>
<td>0.1-0.2 mg/kg prn</td>
<td>Liver</td>
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<tr>
<td>Vecuronium</td>
<td>0.05</td>
<td>0.1-0.2</td>
<td>3-4</td>
<td>35-45</td>
<td>0.01-0.02 mg/kg prn</td>
<td>Liver</td>
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<tr>
<td>Cisatracurium</td>
<td>0.05</td>
<td>0.15-0.2</td>
<td>5-7</td>
<td>35-45</td>
<td>0.3 mg/kg q20min prn</td>
<td>Hoffman elimination</td>
</tr>
</tbody>
</table>

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

Monitoring NMBA 1

- It is recommended you read a detailed reference about NMBA monitoring.
- The train-of-four 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 monitor twitch # and twitch height with sight or feel – which is not nearly as accurate as mechanomyography or accelerometry.
- Again, the TOF ratio can NOT be accurately assessed by feel/sight. A patient with “four strong twitches” can have significant weakness.
- A mechanomyographic TOF of 0.9 is considered fully strong.
- Surgical relaxation can be achieved when the patient has 2-3 twitches though this depends on where you monitor and the location of surgery.

Monitoring NMBA 2

Peripheral Nerve Stimulation Patterns

An aside about sux:
- Phase I block is typical for a single bolus of sux.
- Sux can develop a Phase II block at high doses or 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.

Monitoring NMBA 3

- 5 seconds of sustained tetanus at 50hz indicates full recovery. However this is a painful test and not advised when anesthesia is being lightened. Patient will buck, and surgeon will be angry. Be ready with propofol.
- If placing electrodes on the face, you may stimulate facial muscles directly. You would not be the first to be fooled into thinking your patient has twitches when he/she actually has none!
- Where you place the twitch monitor matters—different muscle groups respond differently to NMBA.
- N.B. pharyngeal muscles are one of the last muscle groups to recover and thus inadequate or lack of reversal leads to airway obstruction and aspiration. It also causes atelectasis and decreased pulmonary reserve.

Monitoring NMBA 4

- Variability in muscle blockade (most resistant→most sensitive): vocal cords > diaphragm > corrugator supercilii > abdominal muscles > adductor pollicis > pharyngeal muscles
- Pick one site to monitor, and know how different muscles respond relative to that site.

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

- CS = corrugator supercilii (eyebrow)
- Abd = Abdomen
- LD = internal oblique (abdomen)
- DO = orbicularis oculi (eyelid)
- CH = geniohyoid (upper airway)
- AP = adductor pollicis (thumb)
Reversal of NMBA 1

- Anticholinesterase "reversal agents" inhibit acetylcholinesterase. Less acetylcholinesterase working = more Ach in NMJ = stronger muscle firing.
- 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.
- Anticholinesterases cause vagal side effects (e.g. bradycardia, GI stimulation, bronchospasm) by increasing Ach activity at parasympathetic muscarinic receptors. Always administer with anticholinergics.
- Neostigmine with glycopyrrolate is most commonly used.
- 40-50 mcg/kg of neostigmine is appropriate for most instances.
- There is a ceiling effect. Do not give >70mcg/kg of neostigmine.
- If recovery seems complete (4 equal twitches), 15-20mcg/kg of neostigmine is probably OK. Attendings will differ.
- Dose of glycopyrrolate is 20% of the neostigmine does (e.g. 3mg neostigmine with 0.6mg glyco).

Know this slide

- 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-Barré, muscular dystrophy (at least Duchenne), +/- myotonia
- Diseases Sensitive to Sux:
  - SLE, myositises
- 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 where you avoid NMBA:
  - Axillary node dissection, ENT cases near nerves, neuromonitoring

References

I was giving report in the PACU and mistakenly reported that the patient was an otherwise healthy 64 year-old woman. She was awake, and corrected me, noting that she was in fact 44. She was indeed healthy, though.
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.

### Difficult Airway Algorithm

**STEP 1**

Assess the likelihood of airway management problems:

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

<table>
<thead>
<tr>
<th>Difficult Mask Ventilation</th>
<th>Impossible Mask Ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>“MAMABOATS”</td>
<td>“MAMABORA”</td>
</tr>
<tr>
<td>- Mallampati III or IV</td>
<td>- Mallampati III or IV</td>
</tr>
<tr>
<td>- Mandibular protrusion decreased</td>
<td>- Males</td>
</tr>
<tr>
<td>- Beard</td>
<td>- Beard</td>
</tr>
<tr>
<td>- Obesity (BMI &gt; 30 kg/m²)</td>
<td>- OSA (mod-to-severe; on CPAP/ BIPAP or hs upper airway surgery)</td>
</tr>
<tr>
<td>- Age &gt; 57-58</td>
<td>- Radiation changes (Neck)</td>
</tr>
<tr>
<td>- (Lack of) Teeth</td>
<td></td>
</tr>
<tr>
<td>- Snoring</td>
<td></td>
</tr>
</tbody>
</table>

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
- Long incisors
- Intercusp distance (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
- 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**

C) **Difficulty with patient cooperation**

- Age
- Mental capacity
- Level of consciousness

**STEP 1**

D) **Difficulty with tracheostomy**

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

**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)
**STEP 3**

Consider the relative merits and feasibility of basic management choices:

- **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**

- Awake FOI
- Awake DL
- Awake video-laryngoscopy
- Awake trach
- Jet ventilation
- Retrograde intubation

**Algorithm B: Intubation After Induction of GA**

---

**Non-Emergent Pathway**

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

---

**Emergent Pathway**

- “Can’t intubate, can’t ventilate”
- CALL FOR HELP
- Emergency Non-Invasive Airway Ventilation
  - Supraglottic airway: LMA, ILMA
  - Rigid bronchoscopy
  - Combitube
- Emergency Invasive Airway Ventilation
  - Cricothyroidotomy
  - Surgical tracheostomy
  - Transtracheal Jet Ventilation

Continue to next slide
Basics of Airway Management

Direct Laryngoscopy Views

Oral Airway  Nasal Airway

Airway Axis: “Sniffing” Position

Head elevation helps to align PA & LA before DL
Ramp obese patients until tragus is aligned with sternum

Pearls

• CALL FOR HELP
• Always pre-oxygenate (de-nitrogenate)
  – A pre-oxygenated patient can be apneic for 8-10
    minutes until desaturation occurs
• The first attempt at DL is the best attempt
• Move to other airway options after 2-3 attempts
  at DL
  – Further attempts can cause airway edema and
    trauma
• Know airway anatomy
• Know pharmacology of anesthetic agents

References

• Difficult/Impossible Mask Ventilation Acronyms courtesy of Dr. Vladimir Nekhendzy
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  Anesthesiologists Task Force on Management of Difficult Airway. Anesthesiology, 118.
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  obesity: a comparison of the “sniff” and “ramped” positions. Obesity Surgery, 14:
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  Research Society, 109: 1870-1880

The first time I had a patient with HIV, I was really nervous about
putting in the IV. When I met him in prep, 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 came the 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.
Fluid Management

Evaluation of Intravascular Volume

- **HPI**
  - Hypovolemia: vomiting, diarrhea, fever, sepsis, trauma
  - Hypervolemia: weight gain, edema, acute renal failure, liver disease (ascites)
- **Physical Exam** (signs often unreliable)
  - Hypovolemia: skin turgor, thready pulse, mucous membranes, tachycardia, orthostasis, axillary perspiration, decreased UOP
  - Hypervolemia: (in setting of CHF) pitting edema, rales, wheezing, cyanosis, elevated JVP
- **Labs**
  - 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 (assess influence of positive pressure ventilation and anesthetics which may cause state of relative hypovolemia)
  - Pulse Oximetry: waveform wander from baseline (assuming patient normothermic and not in shock)
- **Foley Catheter**
  - UOP – consider that ADH levels may be increased 2/2 stress response to surgery (not reliable measure of volume status)
- **Arterial Line**
  - Serial ABGs to follow 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

Body Fluid Compartments

<table>
<thead>
<tr>
<th>Fluid as % of TBW (%)</th>
<th>Fluid as % of body weight (%)</th>
<th>Volume, in 70 kg male (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracellular</td>
<td>67</td>
<td>40</td>
</tr>
<tr>
<td>Extracellular</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Intestinal</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>- Intravascular</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>100%</strong></td>
<td><strong>60%</strong></td>
</tr>
</tbody>
</table>

TBW = Total Body Water

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

Evaluation of Intravascular Volume

- **TTE (The RUSH Exam)**
  - Can be used in any setting (ICU, Preop, Intraop, PACU, etc.)
  - Valuable in narrowing differential of hemodynamic instability
  - Hypovolemia: Hypercontractile heart, small chamber size, flat IVC, flat jugular veins
  - Hypervolemia: Distended IVC, distended jugular veins
    - Cardiogenic shock: hypocontractile, dilated heart

Physiologic Regulation of Extracellular Fluid Volume

- Aldosterone
  - Enhances sodium reabsorption

- Antidiuretic Hormone
  - Enhances water reabsorption

- Atrial Natriuretic Peptide
  - Enhances sodium and water excretion

Colloids

When to Consider Using Colloids
- 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 (burns), mostly benefit from albumin

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?

<table>
<thead>
<tr>
<th>Crystalloids</th>
<th>Colloids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advantages</td>
<td>Disadvantages</td>
</tr>
<tr>
<td>• Lower cost</td>
<td>• Requires more volume for the same hemodynamic effect</td>
</tr>
<tr>
<td>• Readily available</td>
<td>• Short IV t&lt;sub&gt;1/2&lt;/sub&gt; (20-30 min)</td>
</tr>
<tr>
<td>• Maintains plasma oncotic pressure</td>
<td>• Dilutes plasma proteins peripheral pulmonary edema</td>
</tr>
<tr>
<td>• Less cerebral edema (in healthy brain tissue)</td>
<td>• May cause coagulopathy</td>
</tr>
<tr>
<td>• Less intestinal edema</td>
<td></td>
</tr>
<tr>
<td>• Restores IV volume and HD with less volume, less time</td>
<td>• Expensive</td>
</tr>
<tr>
<td>• Longer IV t&lt;sub&gt;1/2&lt;/sub&gt;</td>
<td>• Coagulopathy (dextran &gt; HES)</td>
</tr>
<tr>
<td>• Maintains plasma oncotic pressure</td>
<td>• Limited by max dose</td>
</tr>
<tr>
<td>• Less cerebral edema (in healthy brain tissue)</td>
<td>• Potential renal complications</td>
</tr>
<tr>
<td>• Less intestinal edema</td>
<td>• May cause cerebral edema (in areas of injured brain)</td>
</tr>
</tbody>
</table>

“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 Intestinal Losses (2/2 capillary leak)
- Minimal tissue trauma (e.g. hemia repair) = 0.2 ml/kg/hr
- Moderate tissue trauma (e.g. cholecystectomy) = 2.4 ml/kg/hr
- Severe tissue trauma (e.g. bowel resection) = 4.5 ml/kg/hr

Blood Loss
- EBLL = Evacuated blood loss (intraperitoneal) + "taps" (100-150 ml each) + 4x4 sponges (10 ml each) + field estimate (very approximate estimation)
- Replace with pRBCs, colloids, 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. For most cases, you will use less than recommended by this strategy.
**Suggestions for Fluid Management**

- **Tailor management to patient, surgery, and clinical scenario**
- **Use a balanced approach**
  - Typically start with NS or LR
  - Switch to LR, except in neuro cases (because of decreased osmolality) or patients with hyperkalemia
  - 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); be aware that rapid volume resuscitation may worsen coagulopathy**
- **Consider colloid for persistent hypotension despite adequate crystalloid administration.**
- **Typically start with NS or LR**
- **Switch to LR, except in neuro cases (because of decreased osmolality) or patients with hyperkalemia**
- **Consider serum albumin and albumin**
- **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); be aware that rapid volume resuscitation may worsen coagulopathy**

---

**Intraoperative Oliguria**

1. **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 or abdominal compartment syndrome)

2. **Post-renal (post-renal obstruction)**
   - Foley kinked, clogged, displaced, or disconnected
   - Surgical manipulation of kidneys, ureters, bladder, or urethra

3. **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

---

**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**

**Parkland Formula**

<table>
<thead>
<tr>
<th>Volume</th>
<th>% BSA x 4 ml/kg x kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2</td>
<td>Over the 1st 8 hours.</td>
</tr>
<tr>
<td>1/2</td>
<td>Over the next 16 hours.</td>
</tr>
<tr>
<td></td>
<td>Replace with LR.</td>
</tr>
<tr>
<td></td>
<td>% BSA is determined by the “Rule of Nines”</td>
</tr>
</tbody>
</table>

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**References**

Transfusion Therapy

Type and Screen/Crossmatch
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

Type and Crossmatch (if T&S negative takes 30-60 min)
- Immediate phase: recipient serum + donor cells test for recipient Ab to donor (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

Packed Red Blood Cells
Definition, Use, & Storage
- Single donor; volume 250-300 ml with Hct ~70%
- 1 unit pRBCs ↑ adult Hgb ~1 g/dl or Hct ~3%
- 10 ml/kg PRBC ↑ Hct 10%
- 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)
- CPDA:
  - Citrate (anticoagulant) - also binds Ca
  - Phosphate (buffer)
  - Dextrose (energy source)
  - Adenosine (precursor to ATP synthesis)

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 or ongoing blood loss
   - Volume status
   - Risk factors for complications of inadequate O₂

Platelets
Definition, Use, & Storage
- Platelet Concentrate (PC)
  - Platelets from one donated unit, vol = 50-70 ml, ↑ plt ~5000-10,000
  - “6-pack” = 6 pooled PCs; rarely used anymore
- Apheresis Unit
  - Platelets from a single donor; vol = 200-400 ml, ↑ plt ~50,000
  - Can give ABO-incompatible platelets, Rh tested only
  - Stored at room temperature for ≤5 days.
  - Hang separately - not 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)

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

\[ C_aO_2 = O_2 - Hb + Dissolved O_2 \]
\[ = (Hb \times 1.36 \times S_aO_2/100) + (P_aO_2 \times 0.003) \]
\[ = (15 \times 1.36 \times 100%) + (100 \times 0.003) \]
\[ = 20 cc O_2/ml \]

Allowable Blood Loss

\[ ABL = [Hct (start) - Hct (allowed)] \times EBV \]

Volume to Transfuse

\[ Volume = [Hct (desired) - Hct (current)] \times EBV \]

Estimated Blood Volume (ml/kg)

<table>
<thead>
<tr>
<th></th>
<th>Premie</th>
<th>Term</th>
<th>1-6 years</th>
<th>Male</th>
<th>Female</th>
<th>Obese &lt;= 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preemie</td>
<td>100</td>
<td>90</td>
<td>80</td>
<td>70</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>1 year</td>
<td>80</td>
<td>1-6 years</td>
<td>75</td>
<td>70</td>
<td>Female</td>
<td>65</td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>75</td>
<td>Male</td>
<td>70</td>
<td></td>
<td>Female</td>
<td>65</td>
</tr>
</tbody>
</table>

Transfusion-Related Infections

Viral

- CMV
- Hepatitis B
- Hepatitis C
- HIV
- (Figures based on 2000-2001 estimated risk)

Bacterial

- Most common with platelets
- pRBCs not a major source due to storage at 4°C, but Yersinia is most likely organism

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

Transfusion Reactions

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: D/C blood, fluids, Epi, antihistamines, ACLS

Acute Hemolytic Reaction

- Due to ABO incompatibility
- Symptoms (fever, chills, flank pain) masked by GA; watch for hypotension, diffuse ooze & brown urine; monitor for ARF and DIC
- Treatment: D/C blood, maintain alkaline UOP (bicarb, mannitol, Lasix), supportive care

Transfusion-Related Acute Lung Injury (TRALI)

- An acute RDS that occurs ~4 hours after transfusion
- Due to plasma-containing products (platelets and FFP > pRBCs) - usually donor antibodies reacting to recipient leukocytes
- Incidence: 1 in 1120 (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 R/O 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)
- TRALI is usually self-limited and resolves within 48 hours with supportive care

Massive Transfusion

Definition, 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.
- Typically will utilize Belmont, Level 1 or both for rapid infusion

Consequences

1. Hypothermia
   - Blood products are stored cold!
   - Use fluid warmer for all products except platelets
2. Coagulopathy
   a. Dilutional thrombocytopenia
   b. Dilutional coagulopathies
   - Factors V & VIII ("labile factors") in stored blood
Massive Transfusion

Consequences (cont’d)

3. Citrate Toxicity
   • Citrate is in CPDA storage solution as a Ca\(^{2+}\) chelator
   • Massive transfusion can cause an acute hypocalcemia
   • Binds magnesium also causing hypomagnesemia

4. Acid-Base Abnormalities
   • At 21 days, stored blood has pH < 7.0, due mostly to CO\(_2\) production, which is rapidly blown off after transfusion
   • 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

References


Actual conversation in a case:

Nameless neurosurgeon (NN) “What’s the MAP”
Anesthesia Attending (AA) “65”
NN “Too high. Make it 55”
45 seconds later
AA “The MAP is now 55”
NN “That’s way too low. Make it 65 again”

Moral = sometimes you can just never win.

I was about to infiltrate a pt’s arm with lidocaine for an IV, when both the patient and I both realized that he had an anaphylactic allergy to lidocaine! He recoiled in fear. I then proceeded to blow his IV without lidocaine.
Hypoxemia

Causes of Hypoxemia

<table>
<thead>
<tr>
<th></th>
<th>$P_{CO_2}$</th>
<th>A-a Gradient</th>
<th>DLCO</th>
<th>Corrects w/supplemental $O_2$?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low inspired $O_2$</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Yes</td>
</tr>
<tr>
<td>Hypoventilation</td>
<td>↑</td>
<td>Normal</td>
<td>Normal</td>
<td>Yes</td>
</tr>
<tr>
<td>Diffusion Impairment</td>
<td>Normal</td>
<td>↑</td>
<td>↓</td>
<td>Yes</td>
</tr>
<tr>
<td>Shunt</td>
<td>Normal</td>
<td>↑</td>
<td>Normal</td>
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</tr>
<tr>
<td>V/Q Mismatch</td>
<td>Normal / ↑</td>
<td>Normal</td>
<td>Normal</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### 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 (opiates, benzodiazepines, barbiturates), chest wall damage (e.g. splinting from rib fx, neuromuscular diseases, obstruction (e.g. OSA, upper airway compression))
   - Very responsive to supplemental $O_2$: $(P_{aCO_2}/0.8)$ term of alveolar gas equation becomes insignificant at higher $F_iO_2$ even with relatively high $P_{aCO_2}$. E.g. —
     - $F_iO_2 21%$
     - $P_{aCO_2} 40 — P_{aO_2} = 0.21(760-47) - 40/0.8$
     - $≈ 100 mmHg$ —> $SpO_2 100%$
     - $P_{aCO_2} 80 — P_{aO_2} = 0.21(760-47) - 80/0.8$
     - $≈ 50 mmHg$ —> $SpO_2 80%$
   - $F_iO_2 30%$
     - $P_{aCO_2} 40 — P_{aO_2} = 0.3(760-47) - 40/0.8$
     - $≈ 160 mmHg$ —> $SpO_2 100%$
     - $P_{aCO_2} 80 — P_{aO_2} = 0.3(760-47) - 80/0.8$
     - $≈ 115 mmHg$ —> $SpO_2 100%$
3. Diffusion Impairment
   - Increased diffusion pathway (e.g. pulmonary edema, fibrosis)
   - Decreased surface area (e.g. emphysema, pneumonectomy)
   - Decreased rate of $O_2$-Hb association (e.g. high CO, anemia, PE)
4. $R → L$ Shunt (i.e. perfusion w/o ventilation; $V/Q<1$)
   - Congenital (e.g. TOF, TA, ASD/VSD/PDA w/ Eisenmengers)
   - AVM (AVF, congenital)
   - Pulmonary fluid (pneumonia, CHF, ARDS, NPPE, TACO, TRALI)
   - Atelectasis (mucus plugging, IA)
   - Endobronchial intubation (ETT is “mainstemmed”)
5. V/Q Mismatch
   - Often multifactorial
   - COPD, ILD
   - Dead space (i.e. ventilation w/o perfusion; PE, surgical clamping)
   - Decreased CO (e.g. 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!

**Suggestion:** Atelectasis $→$ Machine

1. Listen to the lungs
   - Atelectasis (rales)
   - Pulmonary edema (rales, decreased $RS$)
   - Bronchial constriction (rales, $P_{aCO_2}$, shark-fin end-tidal $CO_2$ tracing, TV)
   - Mucus plug or secretions ($P_{apAP}$, TV, mucus in ET, rhonchi)
   - Right mainstem ETT ($SpO_2 <90%$, $P_{apAP}$, TV, unilateral $BS$. Repositioning, inflation with (laryngoscopic procedures)
   - Pneumothorax (unilateral $BS$, $P_{apAP}$, TV, HD instability, tracheal deviation if tension physiology)
   - Esophageal intubation (no end-tidal $CO_2$ tracing, $BS$ in stomach & not lungs)
2. Check ETT
   - Cuff deflation
   - Kinked/bitten or detached ETT
   - Extubation (ENT/Neuro cases when bed turned 180, surgeons near head, leaning on end-tetino or circuit)

### Equations

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

$P_{(A-a)O_2} = P_{aO_2} - P_{aO_2} = P_{aO_2} - P_{aO_2} / 0.8$

**Alveolar Gas Equation**

$P_{aO_2} = F_{iO_2}(P_{atm} - P_{H2O}) - (P_{aCO_2} / 0.8) = 0.21(760 - 47) - (40 / 0.8) \approx 100 mmHg$

**Normal A-a Gradient**

- $< 10 mmHg (F_{iO_2} = 0.21)$
- $< 60 mmHg (F_{iO_2} = 1.00)$
- $< (age / 4) + 4$
- $a/A$ ratio $> 0.75$

**Normal $P_{aO_2}$**

- $103 - age/3$
**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	extsubscript{i}O	extsubscript{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	extsubscript{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
- Consider cardiovascular causes and restore volume, RBCs and/or cardiac output
- Send ABG/VBG

---

**O	extsubscript{2}-Hb Dissociation Curve**

![O2-Hb Dissociation Curve](image)

**Factors Affecting Tissue Oxygenation**

- Hb concentration
- O	extsubscript{2} Saturation
- Cardiac Output
- O	extsubscript{2} Consumption
- O	extsubscript{2}-Hb Affinity (P	extsubscript{50})
- Dissolved O	extsubscript{2} in plasma (little effect)

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

---

**O	extsubscript{2}-Hb Curve Shifts**

**Left Shift** (lower affinity for O	extsubscript{2} = decreased unloading at tissues)
- Alkalosis
- Hypothermia
- Hypocarbia
- Decreased 2,3-DPG
- CO-Hb
- Met-Hb
- Sulf-Hb
- Fetal Hb
- Myoglobin

**Right Shift** (higher affinity for O	extsubscript{2} = increased unloading at tissues)
- Acidosis
- Hyperthermia
- Hypercarbia
- Increased 2,3-DPG
- Sickle Cell Hb
- Pregnancy
- Volatile anesthetics
- Chronic anemia

---

**Equations**

**Arterial O	extsubscript{2} Content**

\[ C_{O_2} = O_2\text{-Hb} + \text{Dissolved O}_2 \]

\[ = (Hb \times 1.36 \times S_{O_2}/100) + (P_{O_2}/1000) \]

\[ = (15 \times 1.36 \times 100\%) + (100 \times 0.003) \]

\[ = 20 \text{ cc O}_2/\text{dl} \]

**Mixed Venous O	extsubscript{2} Content**

\[ C_{O_2} = O_2\text{-Hb} + \text{Dissolved O}_2 \]

\[ = (Hb \times 1.36 \times S_{O_2}/100) + (P_{O_2}/1000) \]

\[ = (15 \times 1.36 \times 75\%) + (40 \times 0.003) \]

\[ = 15 \text{ cc O}_2/\text{dl} \]
Equations

**O₂ Delivery**
\[ \text{DO}_2 = \text{CO} \times \text{C}_a \text{O}_2 \]
\[ = 5 \text{ L/min} \times 20 \text{ cc O}_2/\text{dl} \]
\[ = 100 \text{ cc O}_2/\text{min} \]

**O₂ Consumption (Fick Equation)**
\[ \text{VO}_2 = \text{CO} \times (\text{C}_a \text{O}_2 - \text{C}_v \text{O}_2) \]
\[ = 5 \text{ L/min} \times 5 \text{ cc O}_2/\text{dl} \]
\[ = 25 \text{ cc O}_2/\text{min} \]

**O₂ Extraction Ratio**
\[ \text{ER}_O2 = \left( \frac{\text{VO}_2}{\text{DO}_2} \right) \times 100 \]
\[ = \frac{25}{100} \times 100 \]
\[ = 25\% \] (normal 22-30%)

Other Concepts

**Diffusion Hypoxia** = when using N₂O — low PₐO₂ as a result of hypoventilation in combination with the washout of N₂O from blood into the alveoli (dilutes the O₂ molecules decreasing PₐO₂)

**Absorption Atelectasis** = the tendency for airways to collapse if proximally obstructed or poorly ventilated; poorly soluble N₂ normally stents alveoli open, but patients on 100% O₂ have greater tendency toward atelectasis.

**Bohr Effect** = a property of Hb in which increasing CO₂, temperature, and acidosis promote decreased O₂-Hb affinity (i.e. right-shift of O₂-Hb curve).

**Haldane Effect** = a property of Hb in which O₂ binding promotes dissociation of CO₂ from Hb to the plasma (e.g. as when venous blood enters the lungs).

References


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 obstructing 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

<table>
<thead>
<tr>
<th>Phase</th>
<th>Phase Name</th>
<th>SA Node Fiber</th>
<th>Ventricular Muscle Fiber</th>
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<tr>
<td>0</td>
<td>Rapid Upstroke</td>
<td>Slow inward I&lt;sub&gt;ca&lt;/sub&gt;</td>
<td>Fast inward I&lt;sub&gt;na&lt;/sub&gt;</td>
</tr>
<tr>
<td>1</td>
<td>Early Rapid Repolarization</td>
<td>–</td>
<td>Inactivation of I&lt;sub&gt;ca&lt;/sub&gt;</td>
</tr>
<tr>
<td>2</td>
<td>Plateau</td>
<td>–</td>
<td>Start outward I&lt;sub&gt;k&lt;/sub&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Final Rapid Repolarization</td>
<td>Outward I&lt;sub&gt;k&lt;/sub&gt;</td>
<td>Slow inward I&lt;sub&gt;ca&lt;/sub&gt; + Outward I&lt;sub&gt;k&lt;/sub&gt;</td>
</tr>
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<td>4</td>
<td>Diastolic Depolarization/Resting Potential</td>
<td>Slow inward I&lt;sub&gt;ca&lt;/sub&gt;</td>
<td>Inward I&lt;sub&gt;ca&lt;/sub&gt; &lt; Outward I&lt;sub&gt;k&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

### Hyperkalemia

**Definition**
- Mild: K<sup>+</sup> = 5.5-6.5 mEq/L
- Moderate: K<sup>+</sup> = 6.5-8 mEq/L
- Severe: K<sup>+</sup> > 8 mEq/L

**Contributing Factors**
- Renal disease
- Drugs (ACEI, NSAIDs, K-sparing diuretics, Digoxin, β-blockers)
- Succinylcholine: acute 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

**Signs and Symptoms**
- Cardiac conducting system abnormalities including dysrhythmias, conduction abnormalities, and cardiac arrest.
  - Classically associated with administration of succinylcholine to paralyzed or burn patients.
  - If plasma [K<sup>+</sup>] 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<sup>+</sup>] > 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.

**Treatment**
- Reverse membrane effects
  - Ca gluconate (peripheral IV)
  - Ca chloride (central line)
- Transfer extracellular [K<sup>+</sup>] into cells
  - Bicarbonate (NaHCO<sub>3</sub>): 50-100 mEq over 5-10 minutes
  - Insulin (10-15 units) w/ Glucose (25 g)
  - 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
- Use NS instead of LR
- Monitor for increased sensitivity to muscle relaxants

Hypokalemia

Definition
- Mild K⁺ = 3.1-3.5 mEq/L
- Moderate K⁺ ≤ 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
3. 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 Ca²⁺ sparing diuretics, lithium)

**Signs & Symptoms**
- EKG changes (short QT)
- Hypertension
- Polyuria

**Treatment**
- Hydration (bolus crystalloid) + Lasix diuresis
- Dialysis

---

Hypocalcemia

**Contributing Factors**
- Preoperative
  - Hypoparathyroidism
  - Renal failure (decreased Vitamin D)
  - Sepsis
  - Magnesium deficiency (decreased end-organ response to PTH)
- Intraoperative
  - Alkalosis (increased Ca²⁺-albumin binding)
  - Massive pRBC transfusion (due to citrate binding)
  - Drugs (heparin, protamine, glucagon)

**Signs & Symptoms**
- EKG (prolonged QT, bradycardia)
- Hemodynamics (vasodilation, hypotension, myocardial depression)
- Respiratory (laryngospasm, stridor, bronchospasm, respiratory arrest)
- Neuro (cramps, tetany, DTRs, perioral numbness, seizures, Chvostek’s sign, Trousseau’s sign)

**Treatment**
- Calcium gluconate - 1 g = 4.5 mEq elemental Ca²⁺ (give via peripheral or central IV)
- Calcium chloride - 1 g = 13.6 mEq elemental Ca²⁺ (give via central IV)
- Do NOT give Ca²⁺ and NaHCO₃ 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 PRI, 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)

**Treatment**
- Hydration (bolus crystalloid) + Lasix diuresis
- Calcium administration
- Diuresis

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

---

Hypomagnesemia

**Contributing Factors**
- GI/Renal losses
- β-agonists (cause intracellular shift)
- Drugs (diuretics, theophylline, aminoglycosides, amphotericin 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 MgSO₄ to [Mg²⁺] > 2 mg/dl
- Watch for hypotension & arrhythmias with rapid administration!

**Anesthetic Considerations**
- EKG monitoring
- Check for coexistent electrolyte deficiencies.
### Summary of EKG Changes

<table>
<thead>
<tr>
<th></th>
<th>PR interval</th>
<th>QRS complex</th>
<th>QT interval</th>
<th>T waves</th>
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<td>Hypocalcemia</td>
<td>short</td>
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<td>Inversion</td>
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<td>--</td>
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<td>short, narrow</td>
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<td>short</td>
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<td>Flat, u-waves</td>
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<tr>
<td>Hyperkalemia</td>
<td>prolonged</td>
<td>wide</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

### References

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 tips: 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 tips: 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

**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 vasoconstrictor 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

**Development 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 O₂-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
- 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)

Consequences of Shivering

- Increased \( O_2 \) consumption
  - Can be up to a 400-500% increase
- Increased \( CO_2 \) 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!

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.

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)

References

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)
• Prolonged PACU stay
• A leading cause of 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:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (versus not having risk factor)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Gender</td>
<td>2.57 (2.32-2.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of PONV/Motion Sickness</td>
<td>2.09 (1.90-2.29)</td>
<td>&lt;0.001</td>
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<tr>
<td>Non-smoking Status</td>
<td>1.82 (1.68-1.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Younger Age</td>
<td>0.88 per decade</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use of Volatile Anaesthetics</td>
<td>1.62 (1.56-2.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-op Opioids</td>
<td>1.39 (1.20-1.60)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Major Risk Factors
Patient-Related
– Female > male
– History of PONV or motion sickness
– Young > old
– Non-smoker > Smoker

Anesthetic-Related
– Volatile anaesthetics including N₂O
– 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

PONV Prophylaxis Based on Apfel Score

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Prevalence PONV</th>
<th>Prophylaxis No of Anti-emetics</th>
<th>Examples*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9%</td>
<td>0-1 Deramaxin 4 mg</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>20%</td>
<td>1 Deramaxin 4 mg + Dexamethasone 4mg</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>39%</td>
<td>2 Deramaxin 4 mg + Dexamethasone 4mg + Propofol infusion</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>60%</td>
<td>3 Deramaxin 4 mg + Dexamethasone 4 mg + Propofol infusion + Scopolamine patch</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>78%</td>
<td>4 Deramaxin 4 mg + Dexamethasone 4 mg + Propofol infusion + Scopolamine patch</td>
<td></td>
</tr>
</tbody>
</table>

* 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-HT3 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

**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.

**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 (H2-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)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>RR Reduction</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone (vs. none)</td>
<td>26.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ondansetron (vs. none)</td>
<td>26.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Droperidol (vs. none)</td>
<td>24.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nitrogen carrier (vs. N2O)</td>
<td>12.1%</td>
<td>0.003</td>
</tr>
<tr>
<td>Propofol gtt (vs. volatiles)</td>
<td>18.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Remifentanil gtt (vs. fentanyl)</td>
<td>-5.2%</td>
<td>0.21</td>
</tr>
</tbody>
</table>

- Interventions acted independently of each other; relative risk reduction (RRR) of combined therapy can be estimated by multiplying individual RRrs.
- Average PONV = 34% (50% with volatile + N2O + remi + no antiemetics; 17% with propofol + N2O + 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 N₂O and/or volatile anesthetics
- Minimize opioids (consider tylenol, NSAIDs, etc.)
- Minimize (<2.5 mg) or eliminate neostigmine
- Maintain euovolemia; 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)

References

**Extubation Criteria - OR**

1. Adequate Oxygenation
   - $S_\text{O}_2 > 92\%$, $P_\text{a}O_2 > 60$ mm Hg
2. Adequate Ventilation
   - $V_t > 5$ ml/kg, spontaneous RR > 7 bpm, $ET_{CO_2} < 50$ mm Hg
3. Hemodynamically Stable
4. Full Reversal of Muscle Relaxation
   - Sustained tetany, TOF ratio >0.9 (cannot be accurately assessed visually)
   - Sustained 5-second head lift or hand grasp
5. Neurologically Intact
   - Follows verbal commands
   - Intact cough/gag reflex
6. Appropriate Acid-Base Status
   - $pH > 7.25$
7. Normal Metabolic Status
   - Normal electrolytes
   - Normovolemic
8. Normothermic
   - Temp > 35.5°
9. Other Considerations
   - Aspiration risk
   - Airway edema
   - Awake vs. Deep (i.e. NOT in Stage II)

**Extubation Criteria - ICU**

**Subjective Criteria**
- Underlying disease process improving.

**Objective Criteria**
- Adequate mentation (GCS > 13, minimal sedation)
- Hemodynamically stable, on minimal pressors (e.g. dopamine < 5 mcg/kg/min)
- $S_\text{O}_2 >90\%$, $P_\text{a}O_2 > 60$ mm Hg, $P_\text{a}O_2/\text{FiO}_2 > 150$ on $PEEP < 5-8$ cm H$_2$O and $F\text{O}_2 < 0.4-0.5$
- $P_\text{a}CO_2 < 60$ mm Hg, $pH > 7.25$

**Ventilator Criteria (during Spontaneous Breathing Trial) - at least 20-30mins**
- RSBI ($RR/V_t$) < 100, $NIF > 20$ cm H$_2$O
- $V_t > 5$ ml/kg, $VC > 10$ ml/kg
- RR < 30 bpm

**Potential Difficult Extubation**
- History of difficult intubation
- OSA
- Maxillofacial trauma
- Generalized edema (e.g. prolonged surgery with significant fluid/blood resuscitation)
- Paradoxical vocal cord motion (preexisting)
- Post-procedural complications:
  - Thyroid surgery (~4% risk of RLN injury, late hypocalcemia)
  - Diagnostic laryngoscopy +/- biopsy (laryngospasm, edema)
  - Uvulopalatoplasty (edema)
  - Carotid endarterectomy (hematoma, nerve palsies)
  - ENT surgeries (hematoma, jaw wires)
  - Cervical decompression (edema)

**Approach to Difficult Extubation**
- If intubation was technically difficult (e.g. multiple DLs, FOI), consider maintaining a “pathway” to the trachea (e.g. bougie, FOB, Airway Exchange Catheter).
- Make sure patient is fully awake/protecting airway prior to extubation
- If airway edema is suspected due to fluids or traumatic intubation, consider performing a “Cuff-Leak Test”
  - Deflate cuff, occlude ETT, observe whether patient can breath around the tube.
  - A failed leak test does NOT always lead to failed extubation, but may warrant further patient observation; likewise, passing a leak test does NOT guarantee successful extubation.
Stages of Anesthesia

Historical terminology to describe depth of anesthesia upon gas induction. Today, more important for emergence.

Stage 1
- Sedated, intact lid reflex, follows commands

Stage 2
- Excited/disinhibited, unconscious, unable to follow commands or exhibit purposeful movement
- Irregular breathing & breath-holding, dilated & disconjugate pupils, conjunctival injection
- Increased incidence of laryngospasm, arrhythmias, and vomiting - don’t extubate during stage 2

Stage 3
- Surgical anesthesia

Stage 4
- Medullary depression, cardiovascular/respiratory collapse

Delayed Emergence

Definition
Failure to regain consciousness as expected within 20-30 minutes of the end of a surgical procedure – with all anesthetic off.

Causes
1. Residual drug effects
   - Absolute or relative overdose
   - Potentiation of agents by prior intoxication (e.g. EtOH, illicit drugs) or medications (e.g. clonidine, antihistamines)
   - Organ dysfunction (e.g. renal, liver) interfering with metabolism/excretion.
2. Hypercapnia and/or Hypoxemia
3. Hypothermia (<34˚C)
4. Hypo-/Hyperglycemia
5. Metabolic Disturbances
   - Acid-base, hyponatremia, hypo-/hypercalcemia, hypomagnesemia
6. Organ Dysfunction
   - Renal failure, liver failure (e.g. hepatic encephalopathy)
7. Neurologic Insults
   - Seizure/post-ictal state
   - Increased ICP
8. Perioperative Stroke
   - Risk factors: AFib, hypercoagulable state, intracardiac shunt
   - Incidence: 0.1-0.4% in low-risk procedures; 2.5-5% in high-risk procedures

Diagnosis and Treatment

Ensure adequate oxygenation, ventilation, and hemodynamic stability first, then proceed with:

1. Administer “reversal agents”
   - Naloxone 0.4mg – 2mg IV Q 2-3 minutes. (Can dilute to give in 0.04mg increments)
   - If no response after 10 mg, reconsider narcotic overdose as cause of delayed emergence
   - Flumazenil 0.2 mg IV bolus Q 45-60 seconds over 15 seconds
   - May repeat doses. Maximum of 1 mg IV bolus. No more than 3 mg total in one hour.
   - Physostigmine 1-2 mg IV (for central cholinergic syndrome)
   - Neostigmine – maximum of 5 mg IV. Give with glycopyrrolate.
2. Ensure patient is normothermic
   - Use Bair Hugger, warm the room
3. Check ABG for PaO2, PaCO2, glucose, and electrolytes
4. Consider neurological insults – discuss with primary surgeon
   - Perform pertinent neurologic exam
   - Consider further workup (e.g. CT, MRI, EEG)
   - Consider Neuro consult

References

- MacIntyre NR et al. 2001. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the ACCP, AARC, and the ACCCM. Chest, 120: 375S-95S.
- Rashad Net University (www.rashaduniversity.com/delem.html)

At the end of a general anesthesia case with a 60 yo male patient, I wheeled him into the PACU and he looked straight at me and very seriously said, “So, can I have your number?” His wife was in the waiting room, and I was 7 months pregnant. Classic VA.
Laryngospasm & Aspiration

Larynx Anatomy

Larynx Anatomy: Innervation

<table>
<thead>
<tr>
<th>Nerve</th>
<th>Motor</th>
<th>Sensory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent Laryngeal nerve (from CN X)</td>
<td>Thyroarytenoid (tensor)</td>
<td>Subglottic mucosa</td>
</tr>
<tr>
<td></td>
<td>Lateral Cricoarytenoid (adductor)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transverse Arytenoid (adductor)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Posterior Cricoarytenoid (abductor, tensor)</td>
<td></td>
</tr>
<tr>
<td>Superior Laryngeal (from CN X)</td>
<td>Internal branch</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>External branch</td>
<td>Epiglottis/Tongue Base</td>
</tr>
<tr>
<td></td>
<td>Cricothyroid (adductor)</td>
<td>Supraglottic mucosa</td>
</tr>
<tr>
<td></td>
<td>Anterior subglottic mucosa</td>
<td></td>
</tr>
</tbody>
</table>

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% O₂
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 of 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
- \text{S}_\text{O}_2, \text{ETCO}_2, hypotension, large \text{P}_{\text{Aa}}\text{O}_2\text{ gradient}
- CXR with pulmonary edema

**Pathogenesis**
- Negative intrathoracic pressure (up to 100 cmH\text{2}O)
- RV preload $\rightarrow$ pulmonary hydrostatic pressure
- RV preload $\rightarrow$ interventricular septum shift $\rightarrow$ LV diastolic dysfunction $\rightarrow$ PCWP
- Hypoxia, hypercapnea, acidosis $\rightarrow$ HPV & $\uparrow$PVR
- Stress response $\rightarrow$ $\uparrow$SVR and $\uparrow$LV afterload
- Alveolar-capillary membrane leak $\rightarrow$ protein loss

**Treatment**
- Supportive care (O\text{2}, IPPV, PEEP/CPAP)
- Conservative management until process reverses; consider volume and/or pressors PRN.
- Lasix is usually NOT helpful.

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

**Prevention**
- Follow NPO guidelines for routine elective cases
- Use metoclopramide, H\text{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\text{2}O
- Extubate after recovery of protective reflexes

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\text{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 (if aspiration more commonly infection present)
- Steroids are not indicated

NPO Guidelines

<table>
<thead>
<tr>
<th>Ingested Material</th>
<th>Minimum Fasting Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>2 hours</td>
</tr>
<tr>
<td>Breast Milk</td>
<td>4 hours</td>
</tr>
<tr>
<td>Formula</td>
<td>6 hours</td>
</tr>
<tr>
<td>Non-human Milk</td>
<td>6 hours</td>
</tr>
<tr>
<td>Light Meal</td>
<td>6 hours</td>
</tr>
<tr>
<td>Fatty Meal</td>
<td>6-8 hours</td>
</tr>
</tbody>
</table>

• There is no evidence for the routine use of metoclopramide, H\text{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.
References

• Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedure: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2011. Mar;114(3):495-511
**Oxygen Failure in the OR**

**Etiology**

**Loss of Pipeline Oxygen**
- Exhaustion of central O₂ supply
- Obstruction of central O₂ supply line to OR
- O₂ shutoff valve in OR is off
- Obstruction or disconnection of O₂ hose in the OR
- Failure of O₂ regulator in the anesthesia machine

**Faulty Oxygen Supply**
- Crossing of pipelines during construction/repairs.
- Incorrect connection of gas hoses
- Non-O₂ cylinder at the O₂ yoke – *This can happen!!*
- Wrong gas in the O₂ cylinder
- Broken flowmeter

**Prevention**

**Pre-anesthesia Machine Check**
- Check pipeline pressure ~50 psi
- Check O₂ tanks >50% full
- Calibrate O₂ analyzer

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

**Anesthesia Machine Safety Features**
- Flow-meter arrangement
- O₂ N₂O ratio controller
- Oxygen supply failure protection device (*“fail-safe valve”*)

**Gas Cylinders**

<table>
<thead>
<tr>
<th>Gas</th>
<th>E-Cylinder Capacity (L)</th>
<th>Pressure (psi)</th>
<th>Color (USA)</th>
<th>Color (In'l)</th>
<th>Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>O₂</td>
<td>660</td>
<td>1900</td>
<td>Green</td>
<td>White</td>
<td>Gas</td>
</tr>
<tr>
<td>Ar</td>
<td>625</td>
<td>1900</td>
<td>Yellow</td>
<td>White &amp; Black</td>
<td>Gas</td>
</tr>
<tr>
<td>N₂O</td>
<td>1590</td>
<td>745</td>
<td>Blue</td>
<td>Blue</td>
<td>Liquid + Gas</td>
</tr>
<tr>
<td>N₂</td>
<td>650</td>
<td>1900</td>
<td>Black</td>
<td>Black</td>
<td>Gas</td>
</tr>
</tbody>
</table>

How long can you use an O₂ E-cylinder tank starting at 430 psi running at 5 L/min?

- Full tank has ~1900 psi
- Cross multiply: (430psi/1900psi) * (x L remaining/625L)
  - X = 141L remaining
  - 141L / 5L/min = 28 minutes!
- This calculation does not work for N₂O tanks because N₂O tanks pressure will not change until 25% of the gas is remaining in the E-cylinder. Why? N₂O exists as a liquid/gas in the E-cylinder!

**Common Board Question**

**Diameter Index Safety System**

- A. pressure gauge
- B. flowmeter
- C. shutoff valve
- D. pressure gauge
- E. flowmeter
- F. shutoff valve
**Pin Index Safety System**

- Used to prevent accidental connection of wrong gas cylinder.
- Yoke assembly includes index pins, a washer, a gas filter, and a check valve that prevents retrograde gas flow.
- Cylinders are color coded:
  - Oxygen – green
  - N\textsubscript{2}O – blue
  - Air – yellow
  - CO\textsubscript{2} – gray
  - Helium – brown

**Flowmeter Arrangement**

- A leak in the upstream O\textsubscript{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\textsubscript{2}O than expected, but the mixture will NOT be hypoxic because O\textsubscript{2} is closest to the FGF outlet.

**O\textsubscript{2}-N\textsubscript{2}O Ratio Controller**

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

**Oxygen Failure Protection Device**

- Pressure gauges fall (pipeline, tanks)
- Low O\textsubscript{2} alarms (O\textsubscript{2} supply failure, F\textsubscript{O}2 analyzer)
- Flowmeters fall (O\textsubscript{2} and other gases)
- O\textsubscript{2} flush inoperative
- Bellows inoperative
- Apnea alarms (spirometer, capnograph)
- Increasing O\textsubscript{2} flow makes the problem worse
- Hypoxemia, hypercarbia
- Arrhythmias, bradycardia, cardiac arrest
Management

- Notify surgeon, call for help
- Verify problem (pressure gauges, flowmeters, O₂ flush, O₂ analyzer, capnograph)
- Switch to O₂ cylinder (calculate remaining time)
- Use manual ventilation to conserve O₂
- Check valves, hoses, couplers
- D/C supply lines if crossed pipelines suspected
- Call for backup O₂ tanks
- Close breathing circuit, manually ventilate,
- Switch to self-inflating bag (Ambu-Bag), Jackson-Reese with external tank, or mouth-to-ETT if necessary
- Consider switching to TIVA until cause of failure is known

References

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 = 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 complement system
- May occur on 1st exposure to an antigen

Sequence of Events

Histamine
Leukotrienes
Prostaglandins
Chemotactic factors
Tryptase

Common Precipitants

<table>
<thead>
<tr>
<th>Substance</th>
<th>Incidence of perioperative anaphylaxis (%)</th>
<th>Most commonly associated with perioperative anaphylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle relaxants</td>
<td>46.2</td>
<td>Succinylcholine, vecuronium, atracurium [Roc &gt; Vec &gt; Ca &gt; Sai]</td>
</tr>
<tr>
<td>Natural rubber latex</td>
<td>12.1</td>
<td>Latex gloves, urinary Foley catheters</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>10.1</td>
<td>Propofol, midazolam</td>
</tr>
<tr>
<td>Opioids</td>
<td>5.7</td>
<td>Dextrose, gelatin</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.4</td>
<td>HES 6%</td>
</tr>
<tr>
<td>Opioids</td>
<td>2.7</td>
<td>Morphine, remifentanil</td>
</tr>
<tr>
<td>Other substances</td>
<td>2.4</td>
<td>Propacetamol, aprotinin, chymopapain,protamine, heparin</td>
</tr>
</tbody>
</table>

Latex Allergy

- Obtain a careful history:
  - Healthcare workers
  - Children with spina bifida
  - Urogenital abnormalities (h/o multiple urogenital catheters)
  - Food allergies (mango, kiwi, avocado, passion fruit, bananas)
- 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
Sign and Symptoms

<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms (e.g. MAC/Regional)</th>
<th>Signs (e.g. General or Regional)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Dyspnea</td>
<td>Hypoxia, Pulmonary edema</td>
</tr>
<tr>
<td></td>
<td>Chest tightness</td>
<td>Wheezing, Compliance/PPIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laryngeal edema</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Dizziness</td>
<td>Hypotension, Tachycardia</td>
</tr>
<tr>
<td></td>
<td>L/DIC</td>
<td>Dysrhythmia, Cardiac arrest</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pulmonary HTN</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>Itching</td>
<td>Peripheral edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flushing, Periorbital edema</td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td>Decreased urine output</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting, diarrhea</td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td>DIC</td>
</tr>
</tbody>
</table>

Anaphylactic reactions may have variable presentations with some or all of these signs & symptoms.

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).
5. Give other amnestic agents (e.g. scopolamine, midazolam)
6. Fluids 2-4 L or more (compensate vasodilation, hypotension)
7. Epinephrine is drug of choice due to 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 access, give 0.3-0.5 mg IM in anterolateral thigh, repeat q5-15 min
   3. ACLS doses (0.1-1 mg) for cardiovascular collapse

### Secondary Treatment
- Intubation: large-bore IVs, arterial line, central venous catheter, Foley catheter
- Drugs
  - H1-blocker: diphendydramine 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?
- Test dose drugs followed by slow administration
  - reduces anaphylactoid, but not anaphylactic reactions
- Judicious use of blood products
- 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.
- Follow up with an allergist may be useful for establishing a diagnosis (e.g. skin testing)

References

Local Anesthetic Structure

- Three Major Chemical Moieties:
  - Lipophilic aromatic benzene ring
  - Ester or amide linkage
  - Hydrophilic tertiary amine

- Local anesthetics are weak bases
  pKa > 7.4

Physiochemical Properties

- At physiologic pH, local anesthetics are in equilibrium:
  Ionized (water-soluble) <-> nonionized (lipid-soluble)

- The ratio of the 2 forms depends on the pKa of the drug and the tissue pH

Physiochemical Properties

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

Physiochemical Properties

- Potency is related to lipid solubility
- Duration of action is related to protein binding
- Speed of onset is related to pKa (degree of ionization)
- Other factors involved: dosage, rate of systemic absorption, rate of elimination, etc.
Structure
- The type of linkage divides the local anesthetics into 2 categories:

<table>
<thead>
<tr>
<th>Esters</th>
<th>Amides (i.e. before -caine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>Cocaine</td>
</tr>
<tr>
<td>2-Chloroprocaine</td>
<td>Bupivacaine</td>
</tr>
<tr>
<td>Procaine</td>
<td>Ropivacaine</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>Mepivacaine</td>
</tr>
</tbody>
</table>

Amides vs. Esters
- Amides:
  - Metabolized by the liver
  - Aromatic hydroxylation, N-dealkylation, Amide hydrolysis
- Esters:
  - Relatively unstable in solution
  - Metabolized by plasma cholinesterases
  - Hydrolysis occurs at ester linkage
  - p-Aminobenzoic acid (PABA) metabolite can induce allergic-type reactions in a small percentage of patients

Clinical Usage
- Provide anesthesia and analgesia through several routes of delivery
- Topical
- Intravenous
- Epidural
- Intrathecal

Toxicity
- Systemic absorption varies by site of injection (and is related to the vascularity of the tissue)
  - IV > tracheal > intercostal > caudal > epidural > brachial plexus > sciatic/femoral > subcutaneous
- Rate and extent of systemic absorption also depends on dose, the drug’s intrinsic pharmacokinetic properties, and the addition of a vasoactive agent (i.e. epinephrine).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset</th>
<th>Max dose (mg/kg)</th>
<th>Max dose with Epi (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>Rapid</td>
<td>4.5</td>
<td>7</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>Medium</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Slow</td>
<td>2.5</td>
<td>3</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>Slow</td>
<td>4</td>
<td>N/A</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>Slow</td>
<td>1.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Chlorprocaíne</td>
<td>Rapid</td>
<td>10</td>
<td>15</td>
</tr>
</tbody>
</table>

Toxicity
- CNS toxicity
  - Local anesthetics readily cross the blood brain barrier
  - Clinical manifestations: Lightheadedness, tinnitus, tongue numbness → CNS depression, seizure → coma
- Cardiovascular toxicity
  - Dose dependent blockade of Na channels → disruptions of cardiac conduction system → bradycardia, ventricular dysrythmias, decreased contractility, cardiovascular collapse/ circulatory arrest
  - In general, much greater doses of local anesthetics are required to produce cardiovascular toxicity than CNS toxicity
Treatment of LA toxicity

• Initial management:
  – Stop local anesthetic
  – Give benzodiazepines for seizure, avoid 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, follow by infusion of 0.25 ml/kg/min
  – 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

References


ASRA guidelines for management of local anesthetics toxicity. 2015.
Malignant Hyperthermia

Definition
- A hypermetabolic crisis that occurs when susceptible patients are exposed to a triggering anesthetic agent; underlying defect is abnormally increased Ca\textsuperscript{2+} levels in skeletal muscle causing acceleration of muscle metabolism.

Genetics
- Genetic hypermetabolic muscle disease; autosomal dominant inheritance with variable penetrance and expression.
- At least 6 chromosomal loci identified, but >80 genetic defects associated with MH.
- Ryanodine receptor-1 (RYR-1), the skeletal muscle Ca\textsuperscript{2+} channel regulator, is best characterized.

Incidence
- Rare, see in 1:15,000 pediatric vs. 1:40,000 adult patients.
- May occur on a patient’s 2nd exposure to triggers (nearly 50% of MH episodes had at least one uneventful exposure to an anesthetic prior).
- May occur late in the anesthetic, possibly even in PACU!
- Risk factors include personal/family history of MH, pediatric age, comorbid myopathies, caffeine intolerance, history of unexplained fevers/cramps/weakness, trismus on induction (precedes 15-30% of MH).

Excitation-Contraction Coupling

MH: Depolarization \rightarrow\text{mutant RYR-1 receptor remains open} \rightarrow \text{unregulated calcium entry into cell from sarcoplasmic reticulum} \rightarrow \text{sustained contraction} \rightarrow \text{heat generation, CO}_2 \text{production, and cell damage.}

Sequence of Events

1. Triggers
   - All potent inhalational agents (except N\textsubscript{2}O).
   - Succinylcholine.

2. Increased Cytoplasmic Free Ca\textsuperscript{2+}
   - Masseter muscle rigidity (trismus\textsuperscript{*}).
   - Total body rigidity.

3. Hypermetabolism
   - Increased CO\textsubscript{2} production (most sensitive and specific sign of MH!).
   - Increased O\textsubscript{2} consumption.
   - Increased heat production.

*Not all patients with trismus will go on to have MH, and not all MH cases will be heralded by trismus.

4. Cell Damage (Rhabdomyolysis)
   - Leakage of K\textsuperscript{+}, myoglobin, CK (may see dark-colored urine).

5. Compensatory Mechanisms
   - Increased catecholamines - tachycardia, hypertension, cutaneous vasoconstriction.
   - Increased cardiac output - decreased S\textsubscript{v}O\textsubscript{2}, decreased P\textsubscript{a}O\textsubscript{2}, metabolic acidosis.
   - Increased ventilation - increased ET\textsubscript{CO}_2, increased V\textsubscript{E}.
   - Heat loss - sweating, cutaneous vasodilation.

6. Temperature Rise
   - A late and inconsistent sign of MH.
   - Temperature can rise 1-2°C every 5 minutes.

7. Secondary systemic manifestations
   - Arrhythmias.
   - DIC.
   - Hemorrhage.
   - Cerebral Edema.
   - Acute Renal Failure.
   - Compartment Syndrome.
   - Death (due to DIC and organ failure as result of delayed administration of dantrolene).

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

It’s important to be thinking of MH as missing it will have devastating consequences. Clinically, you may first see trismus, but often hypercarbia will be your first sign. Without another reasonable explanation for this (hyperventilation, 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).

Sequence of Events

- DIC
- Hemorrhage
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- Acute Renal Failure
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**Differential Diagnosis**

- Neuroleptic Malignant Syndrome (NMS) (in patients receiving antidopaminergic agents or in withdrawal from dopamine agents as in Parkinson’s)
- Thyroid Storm (if see fever, tachypnea, tachycardia, metabolic acidosis)
- Pheochromocytoma (HR, BP, but normal EtCO₂ and Temp)
- Drug-induced (e.g., ecstasy, crack, amphetamines, PCP, LSD)
- Serotonin Syndrome (associated drug interactions MAOIs + meperidine or MAOIs + SSRIs)
- Iatrogenic Hyperthermia
- Hypercarbia from CO₂ insufflation for laparoscopy (see EtCO₂ with tachycardia)

**Treatment (Acute Phase)**

1. Immediate reactions
   - Call for help: get MH cart (contains ALL the drugs you need)
   - D/C volatile agents and succinylcholine, switch to 100% O₂ and increase fresh gas flows (to > 10 L to flush circuit)
   - Notify surgeon; halt surgery ASAP, or continue with non-triggering agents (TIVA) if necessary.
   - Call the MH Hotline 1-800-MH-HYPER.
   - Check an ABG and place a foley catheter

2. Give Dantrolene, give more dantrolene
   - 2.5 mg/kg IV push.
   - Dissolve 20 mg in 60 ml sterile, preservative-free H₂O
   - Repeat until signs of MH are controlled – titrate to HR/CO₂
   - Sometimes, more than 10 mg/kg is necessary (= 35 vials of dantrolene! – consider dedicating an assistant to this).

3. Treat acidosis
   - Hyperventilate patient.
   - Bicarbonate 1-2 mEq/kg until ABG available.

4. Treat hyperthermia
   - Cool if T > 39˚C, but D/C if T < 38˚C.
   - Apply ice to body surfaces; Cold NS via IV; Lavage stomach, bladder, or rectum PRN.

5. Treat hyperkalemia
   - Hyperventilate
   - Bicarbonate
   - Insulin & glucose (10 units in 50 ml D50)
   - Calcium (10 mg/kg CaCl₂ or 10-50 mg/kg Ca gluconate)

6. Treat dysrhythmias
   - Standard therapies, but avoid CCBs in the presence of dantrolene (may promote hyperkalemia).
   - May need antarrhythmic if persists despite correction of hyperkalemia and acidosis

7. Maintain UOP/place foley
   - Lasix (1 mg/kg) to establish diuresis and prevent ARF, and/or
   - Mannitol (0.25 g/kg) (dantrolene also contains mannitol)

8. Continue to monitor
   - ETCO₂, Temp, UOP & color, Electrolytes, ABG, CK, PT/PTT/INR

**Dantrolene**

- A hydrophobic, hydantoin derivative with 12 hour t₁/₂
- Interferes with excitation-contraction coupling by binding the RYR-1 Ca²⁺ channel
- Relatively safe drug: causes generalized muscle weakness (including respiratory muscles).
- Formulation contains mannitol (hope you placed a foley!)
- Can also be used to treat NMS or thyroid storm.

**Treatment (Post Acute Phase)**

1. Observe in ICU for at least 24 hours.
   - Recrudescence rate is 25%.

2. Continue Dantrolene
   - 1 mg/kg IV q4-6hrs for at least 24 hours.

3. Follow labs (watch for DIC, renal failure)
   - ABGs, CK, myoglobinuria, coags, electrolytes, UOP and color

4. Counsel patient and family
   - Future precautions.
   - Refer to MHAUS.

5. Refer patient and family to nearest Biopsy Center for follow-up.
Who is Susceptible to MH?

- Since autosomal dominant inheritance pattern, all closely related family members considered susceptible in absence of testing
  - This is even if have had previous 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)
    - Should monitor capnography, minute ventilation, and core temperature; experts suggest that there be means to check serum electrolytes and urine screen for myoglobin if patient is signs of neuromuscular disorder so can document that individual has not suffered complication from anesthetic
    - History of exertional heat stroke—some suggestion that these people may harbor genetic changes found in MH susceptible individuals

Susceptibility Testing

Caffeine-Halothane Contracture Test (CHCT)

- Gold Standard
- Takes fresh skeletal muscle biopsy and exposes to ryanodine receptor agonists (eg caffeine, halothane)
- Sensitivity >97%, Specificity 80-93% (rule-out)
  - 10-30% 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)
  - 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

Machine

- Change circuit and CO₂ absorbent
- Remove or disable vaporizers
- Flush machine at FGF of 10 L/min for ≥20 minutes and during case keep flows > 10L/min to avoid “rebound phenomenon” (release of residual volatile anesthetic; agent when FGF is reduced after a set period of flushing)

Monitors

- ASA monitors, especially temperature and ET CO₂

Anesthetic

- Avoid succinylcholine and volatiles
- All other non-triggering agents are OK (including N₂O)

Emergency

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

References

- Malignant Hyperthermia Association of the United States (MHAUS, http://www.mhaus.org)
- UCLA Department of Anesthesiology (http://www.anes.ucla.edu/dept/mh.html)
Perioperative Antibiotics

Why Antibiotics?

Because 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).


Timing of prophylaxis

- Antibiotic therapy should be given within 60 min 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 inpatients) 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).


Administration and Common Dosages

- To be given via slow infusion (reconstitute in 100ml NS and give with microdripper)
  - Vancomycin (Red Man Syndrome) – over 30-60 mins
  - Gentamicin (ototoxicity/nephrotoxicity) - over 30-60 mins
  - Metronidazole (low pH) – over 60 mins
  - Cipro – over 30 mins
  - Clindamycin (QT prolongation) – over 10-15 mins
  - Ertapenem – over 30 mins
- Typical dosages for antibiotics commonly used in the OR: (these are frequently requested dosages here at Stanford – however this may change given new published guidelines)
  - Ampicillin 1gm
  - Cefazolin 1-2gm (2gm for patients > 80kg)
  - Cefoxitin 1-2gm
  - Clindamycin* 600-900mg
  - Metronidazole 500mg
  - Zosyn 3.375gm
  - Ceftriaxone 1g
  - Vancomycin 1gm
  - Cipro 400mg
- * can potentiate neuromuscular blockers
- Adjust for renal insufficiency (except for Clindamycin and Ceftriaxone)
- Note: Ertapenem 1gm is favored by Drs. Shelton and Rhoades for their colorectal cases

These are the most up to date guidelines from the 2013 IDSA, ASHP, and SIS (Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect 2013;14:73–156.)
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Re-Dosing Guidelines
According to Stanford Pharmacy Guidelines

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Re-dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>4 hours</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>3 hours</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>6 hours</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8 hours</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>24 hours (n/a)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>n/a</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>n/a</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Types of Procedures

• Clean procedures (i.e. ortho, breast)
  – 1st generation cephalosporin (Cefazolin/Ancef) covers staphylococci and streptococci
• Procedures involving bowel anaerobes, Gram neg- bacilli, enterococci
  – 2nd generation cephalosporin (Cefoxitin or Cefotetan)
  – Bowel aerobic gram-neg bacilli (i.e. E. coli) can be resistant, so consider adding metronidazole.
• Cranietomies
  – 3rd generation cephalosporin for good CSF penetration (i.e. Ceftriaxone)
  – Procedures involving groin incisions (i.e. vascular surgery, hysterectomy, colorectal surgery)
    – Consider adding gentamicin, ciprofloxacin, levofloxacin, or aztreonam to cover gram-neg bacteria.
• For more specific guidelines you can refer to:

Allergies and Interactions

• Penicillins and cephalosporins have similar β-lactam ring
• True incidence of allergy in patients with a 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%
• For PCN-allergic patients, consider vancomycin or Clindamycin ± one of the following for Gram neg coverage (ciprofloxacin, levofloxacin, gentamicin, or aztreonam)

Special considerations

• The American Heart Association guidelines recommend prophylaxis for those with conditions that place them at increased risk for infective endocarditis AND those at highest risk for adverse outcomes when endocarditis does occur. These are patients with:
  – Prosthetic cardiac valve
  – 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
  – 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.
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 lidocaine. 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).

References

- Weigelt JD. Microbiologic Aspects of Surgical Wound Infections. JAMA 1958; 168:1187-1191

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."
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?