Name:_____

2014 CA-1 TUTORIAL TEXTBOOK 8th Edition

STANFORD UNIVERSITY
MEDICAL CENTER
DEPARTMENT OF ANESTHESIOLOGY

Aileen Adriano, M.D.
Christopher Miller, M.D.

STANFORD
SCHOOL OF MEDICINE
Stanford University Medical Center

TABLE OF CONTENTS

Introduction…….2

Acknowledgements…….3

Contributors…….3

Key Points and Expectations……...6

Goals of the CA-1 Tutorial Month……..7

Checklist for CA-1 Mentorship Intraoperative Didactics……8

CA-1 Mentorship Intraoperative Didactic Lectures

Standard Monitors……..
Inhalational Agents…….....
MAC and Awareness……..
IV Anesthetic Agents…….
Rational Opioid Use……..
Intraoperative Hypotension & Hypertension……
Neuromuscular Blocking Agents……..
Difficult Airway Algorithm……..
Fluid Management ……...
Transfusion Therapy…….
Hypoxemia…….....
Electrolyte Abnormalities…….
Hypothermia & Shivering…….……
PONV……
Extubation Criteria & Delayed Emergence…….…..…
Laryngospasm & Aspiration…….
Oxygen Failure in the OR…….
Anaphylaxis……..
Local Anesthetics…..…….……
Malignant Hyperthermia……...
Perioperative Antibiotics……..
Topics for Discussion……

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, is designed to introduce you to the basic concepts of anesthesia. Topics covered include basic pharmacology of anesthetics, basic physiology, and various clinical skills and topics. This lecture series starts on July 7th at ***4pm in the Anesthesia Conference room***. You should receive a schedule of lectures separate from this book. The last lecture is July 30th. You will be relieved of all clinical duties to attend these lectures and it is best to attend them in person. 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, 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.

Aileen Adriano, MD
Christopher Miller, MD

CONTRIBUTORS

8th Edition (2014)

Editors:
Christopher Miller, MD
Aileen Adriano, MD

Section Editors:
Lindsay Borg, MD
Sarah Clark, MD
Stephen Kelleher, MD
Amanda Kumar, MD
Josh Melvin, MD
Christopher Miller, MD
Ann Ng, MD
Lena Scotto, MD
Clair Secomb, MD
Jan Sliwa, MD
Shaina Sonobe, MD

Mentor Coordinator:
Christopher Miller, MD

Resident Mentors:
Jessica Ansari, MD
James Li, MD
Josh Melvin, MD
Christopher Miller, MD
Brita Mittal, MD
Kristen Noon, MD
Shelly Pecorella, MD
Lena Scotto, MD
Jan Sliwa, MD
Shaina Sonobe, MD
Lauren Steffel, MD
Anna Swenson, MD

Faculty Mentors:
Martin Angst, MD
Jennifer Basarab-Tung, MD
Melissa Berhow, MD, PhD
Divya Chander, MD, PhD
Marianne Chen, MD
Jeremy Collins, FRCA, MB ChB
Anna Crawford, MD, MS
Larry Chu, MD, MS
Alimorad Djalali, MD
Anthony Doufas, MD, PhD
Ruth Fanning, MD
Sara Goldhaber-Fiebert, MD
Natalya Hasan, MD
Erin Hennessey, MD
Maeve Hennessy, MD
Gilliam Hilton, FRCA, MB ChB
Bassam Kadry, MD

Jennifer Lee, MD
Meredith Kan, MD
Vivek Kulkarni, MD, PhD
Kevin Malott, MD
Ethan McKenzie, MD
Sesh Mudumbai, MD
Vladamir Nekhendzy
Jordan Newmark, MD
Sara Nikravan, MD
Periklis Panousis, MD
Andrew Patterson, MD, PhD
Catherine Reid, MD
Steven Shafer, MD
Pedro Tanaka, MD
Vivianne Tawfik, MD, PhD
Alexander Tzabazis, MD
Lindsay Vokach, MD
Tara Weineger, MD
Ahmed Zaafran, MD
Karl Zheng, MD

7th Edition (2013)

Editors:
Tammy Wang, MD
Aileen Adriano, MD

Section Editors:
Kevin Blaine, MD, MPH
James Flaherty, MD
Robert Groff, MD
Jason Johns, MD
Joseph Kwok, MD
Barrett Larson, MD
Ken Lau, MD
Eric Mehlberg, MD
Christopher Miller, MD
Kristen Noon, MD
Justin Pollock, MD
Christopher Press, MD
Alex Quick, MD
Lindsay Raleigh, MD
Jan Sliwa, MD
Shaina Sonobe, MD
Vicky Yin, MD

Mentor Coordinator:
Lindsay Raleigh, MD

Resident Mentors:
Nick Anast, MD
Kevin Blaine, MD MPH
Sarah Clark, MD
Rob Groff, MD
Leslie Hale, MD
John Johns, MD
Barrett Larson, MD
Ken Lau, MD
Josh Melvin, MD
Rafee Obaidi, MD
Shelly Pecorella, MD
Anil Pranigrahi, MD PhD
Alex Quick, MD
Amit Saxena, MD
Jan Sliwa, MD
Shana Sonobe, MD
Tanya Travkina, MD

Faculty Mentors:
Martin Angst, MD
Jennifer Basarab-Tung, MD
Melissa Berhow, MD, PhD
Divya Chander, MD, PhD
Marianne Chen, MD
Jeremy Collins, FRCA, MB ChB
Anna Crawford, MD, MS
Larry Chu, MD, MS
Alimorad Djalali, MD
Anthony Doufas, MD, PhD
Ruth Fanning, MD
Sara Goldhaber-Fiebert, MD
Natalya Hasan, MD
Erin Hennessey, MD
Maeve Hennessy, MD
Gilliam Hilton, FRCA, MB ChB
Bassam Kadry, MD
Jennifer Lee, MD
Meredith Kan, MD
Vivek Kulkarni, MD, PhD
Kevin Malott, MD
Ethan McKenzie, MD
Sesh Mudumbai, MD
Vladamir Nekhendzy
Jordan Newmark, MD
Sara Nikravan, MD
Periklis Panousis, MD
Andrew Patterson, MD, PhD
Catherine Reid, MD
Steven Shafer, MD
Pedro Tanaka, MD
Vivianne Tawfik, MD, PhD
Alexander Tzabazis, MD
Lindsay Vokach, MD
Tara Weineger, MD
Ahmed Zaafran, MD
Karl Zheng, MD

6th Edition (2012)

Editors:
Natalya Hasan, MD
Aileen Adriano, MD

Section Editors:
Kevin Blaine, MD
Marie McHenry, MD
Shelly Pecorella, MD
Lindsay Raleigh, MD
Natacha Telusca, MD
Tammy Wang, MD

Mentor Coordinator:
Marie McHenry, MD

Resident Mentors:
Marianne Chen, MD
Marc Dobrow, MD, MBA
Morgan Dooley, MD, MPH
King Ganguly, MD
Estee Garazi, MD
Brice Gaudilliere, MD, PhD
Robert Groff, MD
Ashley Hawrylshyn, MD
Boris Heifets, MD, PhD
Michael Marques, MD, PhD
Vanessa Moll, MD
Marie McHenry, MD, MS
Jared Pearson, MD
Catherine Reid, MD, MS
Dora Rodriguez, MD
James Tan, MD
Vivianne Tawfik, MD, PhD
Tanya Travkina, MD
Luis Verduzco, MD

Faculty Mentors
Aileen Adriano, MD
Martin Angst, MD, PhD
Alex Butwick, MB, FRCA, MS
Divya Chander, MD, PhD
Fiona Clements, MD
Anna Crawford, MD, MS
Alimorad Djalali. MD
Anthony Doufas, MD, PhD
David Drover, MD
Ruth Fanning, MD
Rosario Garcia, MD
Sara Goldhaber-Fiebert, MD
Eric Gross, MD, MS, PhD
Maeve Hennessey, MD
Bassam Kadry, MD
Meredith Kan, MD
Vivek Kulkarni, MD
Neil Lawande, MD
Kevin Malott, MD
Diana McGregor, MB, BS, FRCA
Farheen Mirza, MD
Periklis Panousis, MD
Suma Ramzan, MD
Edward Riley, MD
Kimberly Valenta, MD
Karl Zheng, MD

5th Edition (2011)

Editors:
Becky Wong, MD
Natalya Hasan, M.D
Aileen Adriano, MD

Resident Mentors:
Catherine Reid, MD
Andrea Goodrich, MD
Roy Esaki, MD
Tatyana Travkina, MD
Calvin Lew, MD

Boris Heifets, MD, PhD
Ethan Mckenzie, MD
JJ Desai, MD
Laura Downey, MD
Christie Brown, MD
Josh Edwards, MD, MBA
Sam Chen, MD
Justin Workman, MD

Faculty Mentors
Tim Angelotti, MD, PhD
Martin Angst, MD, PhD
Aileen Adriano, MD
Divya Chander, MD, PhD
Fiona Clements, MD
Jeremy Collins, MD
Tara Conaby, MD
Ana Crawford, MD
Ali Djalali, MD
Anthony Doufas , MD, PhD
Ruth Fanning, MD
Sara Goldhaber-Fiebert, MD
Vivek Kulkarni, MD, PhD
Alex Macario, MD, MBA
Diana McGregor, MD
Periklis Panousis, MD
Andrew Patterson, MD, PhD
Lindsay Ralls, MD
Suma Ramzan, MD
Ed Riley, MD
Pedro Tanaka , MD, PhD
Karl Zheng, MD

4th Edition (2010)

Editors:
Becky Wong, MD
Kate Ellerbrock, M.D
Aileen Adriano, MD
Resident Mentors:
Sarah Bain, MD
Christie Brown, MD
Dora Castaneda, MD
Michael Charles, MD, PhD
Kate Ellerbrock, MD
Erin Hennessey, MD
Jody Leng, MD
Javier Lorenzo, MD
David Medina, MD
Brett Miller, MD
John Peterson, MD
Rohith Piyaratna, MD
Becky Wong, MD
Andrew Wall, MD
Romy Yun, MD

Faculty Mentors
Tim Angelotti, MD, PhD
Martin Angst, MD, PhD
Lindsay Atkinson, MD
Alex Butwick, MD
Divya Chander, MD, PhD
Larry Chu, MD, MS
Jeremy Collins, MD
Ana Crawford, MD
Ali Djalali, MD
Anthony Doufas , MD, PhD
Ruth Fanning, MD
Sara Goldhaber-Fiebert, MD
Lee Hanowell, MD
Gill Hilton, MD
Jerry Ingrande, MD, MS
Richard Jaffe, MD, PhD
Vivek Kulkarni, MD, PhD
Steve Lipman, MD
Alex Macario, MD, MBA
Kevin Malott, MD
Diana McGregor, MD
John Nguyen, MD
Periklis Panousis, MD
Suma Ramzan, MD
Ed Riley, MD
Vanila Singh, MD
Pedro Tanaka , MD, PhD
Ying Ting, MD
Kimberly Valenta, MD
Karl Zheng, MD

3rd Edition (2009)

Editors:
Jessica Kentish, MD
William Hightower, M.D
Tara Cornaby, MD

Resident Mentors and Contributing Authors:

Sarah Bain, MD
Marisa Brandt, MD
Erin Hennessey, MD
Billy Hightower, MD
Jesse Hill, MD
Meredith Kan, MD
Zoe Kaufenberg, MD
Jessica Kentish, MD
Zeest Khan, MD
Milo Lochbaum, MD
Nate Ponstein, MD
Tzevan Poon, MD

Faculty Mentors
Aileen Adriano, MD
Tim Angelotti, MD, PhD
Jeremy Collins, MD
Tara Conaby, MD
Anthony Doufas, MD, PhD
Ruth Fanning, MD
Sara Goldhaber-Fiebert, MD
Cosmin Guta, MD
Leland Hanowell, MD
Vivek Kulkarni, MD
Hendrikus Lemmens, MD, PhD.
Diana McGregor, MD
Alex Macario, MD, MBA
Kevin Malott, MD
Ed Riley, MD
Cliff Schmiesing, MD
Pedro Tanaka, MD
Alex Tzabazis, MD

2nd Edition (2008)

Editors:
Jerry Ingrande, MD
Aileen Adriano, MD

1st Edition (2007)

Editors:
Ryan Green, MD, PhD
Aileen Adriano, MD

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.
- All CA-1s (including those starting at Stanford, VAMC, and SCVMC) will receive the syllabus of intra-operative mini-lecture topics to be covered with their mentors. These mini-lectures provide goal-directed intra-operative teaching during the first month. CA-1s will document the completion of each mini-lecture by obtaining their mentors' initials on the "Checklist for CA-1 Mentorship Intra-operative Didactics."
- CA-1s will receive verbal feedback from their mentors throughout the week, as appropriate, as well as at the end of each week. Mentors will communicate from week to week to improve longitudinal growth and mentorship of the CA-1.

Expectations of CA-1 Residents:

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

Expectations of Senior Resident Mentors:

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

Expectations of Faculty Mentors:

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

GOALS OF THE CA-1 TUTORIAL MONTH

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

I. Preoperative Preparation:

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

II. Anesthetic Management

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

III. Post-operative Evaluation

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

SUGGESTED CHECKLIST FOR CA-1 MENTORSHIP
INTRAOPERATIVE DIDACTICS

Mentors ***initial*** completed lectures

First Day
July 7

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

Week One
July 7-11

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

Week Two
July 14-18

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

Week Three
July 21-25

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

Standard Monitors

Monitoring in the Past

Basic Anesthetic Monitoring

ASA Standards for Basic Anesthetic Monitoring

STANDARD I

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

STANDARD II

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

OXYGENATION
- F_iO_2 Analyzer
- Pulse Oximetery

VENTILATION
- Capnography
- Disconnect alarm

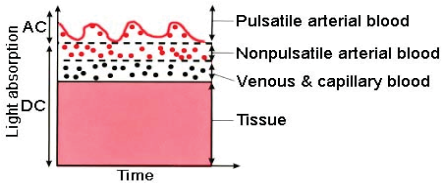
CIRCULATION
- EKG
- Blood Pressure
- Pulse Oximetery

TEMPERATURE
- Temperature Probe

Pulse Oximetry

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

Fundamentals
- The probe emits light at 660 nm (red, for Hb) and 940 nm (infrared, for O_2Hb); sensors detect the light absorbed at each wavelength.
- Photoplethysmography is used to identify arterial flow (alternating current = AC) and cancels out the absorption during non-pulsatile flow (direct current = DC); the patient is their own control!
- The S value is used to derive the S_pO_2 ($S = 1{:}1$ ratio = S_pO_2 85%).



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

Pulse Oximetry

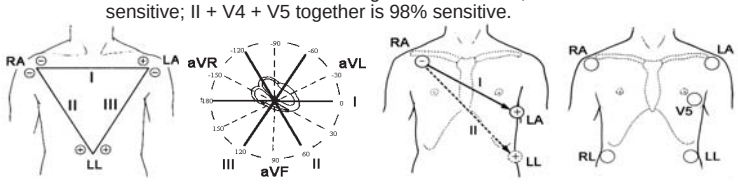
Pearls
- Methemoglobin (MetHb) - Similar light absorption at 660 nm and 940 nm (1:1 ratio); at high levels, S_pO_2 approaches 85%.
- Carboxyhemoglobin (COHb) - Similar absorbance to O_2Hb. At 50% COHb, S_aO_2 = 50% on ABG, but S_pO_2 may be 95%, thus producing a falsely HIGH S_pO_2.
- Other factors producing a falsely LOW S_pO_2 = dyes (methylene blue > indocyanine green > indigo carmine), blue nail polish, shivering, ambient light.
- Factors with NO EFFECT on S_pO_2 = bilirubin, HbF, HbS, SuHb, acrylic nails, flourescein dye.
- Cyanosis - clinically apparent with 3 g/dl desaturated Hb. At Hb = 15 g/dl, cyanosis occurs at S_aO_2 = 80%; at Hb = 9 g/dl (i.e. anemia), cyanosis occurs at S_aO_2 = 66%.

EKG

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

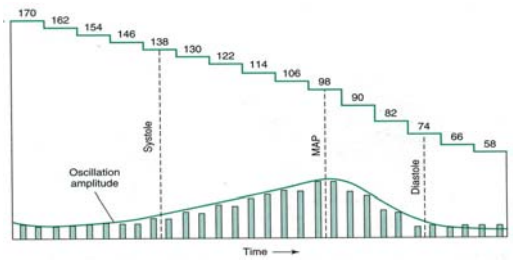
Modified 3-Electrode System
- If you have concerns for anterior wall ischemia, move L arm lead to V5 position, and monitor Lead I for ischemia.

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



Noninvasive Blood Pressure

- Automated, microprocessor-assisted interpretation of oscillations in the NIBP cuff.
- MAP is primary measurement; SBP and DBP are derived from algorithms.
- Bladder should encircle ≥50% of extremity; width should be 20-50% greater than diameter of extremity.
- Cuff too small = falsely HIGH BP. Cuff too big = falsely LOW BP.



FYI:

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

Arterial Blood Pressure

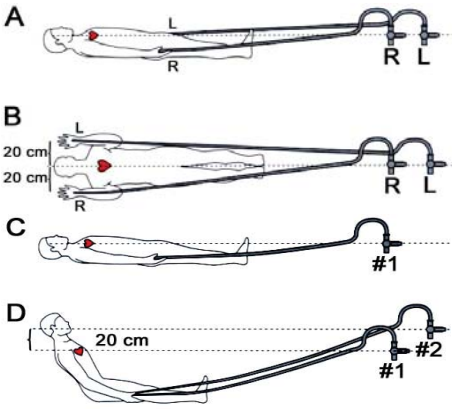
Indications

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

Transducer Setup

- Zeroing = exposes the transducer to air-fluid interface at any stopcock, thus establishing P_{atm} as the "zero" reference pressure.
- Leveling = assigns the zero reference point to a specific point on the patient; by convention, the transducer is "leveled" at the right atrium.

Effect of Patient & Transducer Position on BP Measurement



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

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

FYI:

10 cm H_2O = 7.5 mm Hg

Capnography

- Gives you tons of information (both number and 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)

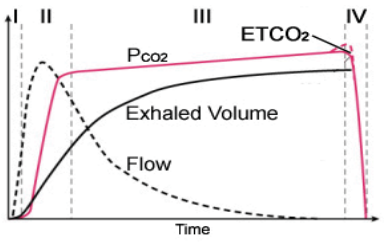
-pt breathing spontaneously (more rounded trace)

-esophageal intubation, circuit disconnect (no ETCO2 tracing)

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

Capnography

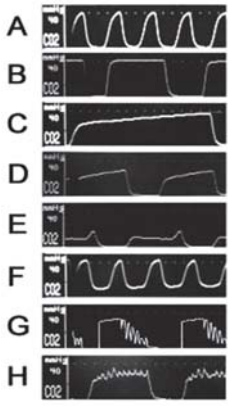
- Measures exhaled CO_2 (and other gases).
- Time delay exists due to length and volume of sample tube as well as sampling rate (50-500 ml/min).



Capnogram Phases

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

Capnography



Example Traces

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

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
- OG tube
- CVC
- Esophageal stethoscope
- ICP
- Pulmonary Artery catheter
- BIS monitor/Sedline

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

References

- ASA. Standards for basic anesthetic monitoring (http://www.asahq.org/publications AndServices/standards/02.pdf). 2005.
- Mark JB, and Slaughter TF. Cardiovascular monitoring. In Miller RD (ed), *Miller's Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Moon RE, and Camporesi EM. Respiratory monitoring. In Miller RD (ed), *Miller's Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.
- Narang J, and Thys D. Electrocardiographic monitoring. In Ehrenwerth J, and Eisenkraft JB (eds), *Anesthesia Equipment: Principles and Applications*. St. Louis: Mosby, 1993.
- Skeehan TM and Jopling M. Monitoring the cardiac surgical patient. In Hensley FA, Martin DE, and Gravlee GP (eds), *A Practical Approach to Cardiac Anesthesia, 3rd ed*. Philadelphia: Lippincott Williams & Wilkins, 2003.

Inhalational Agents

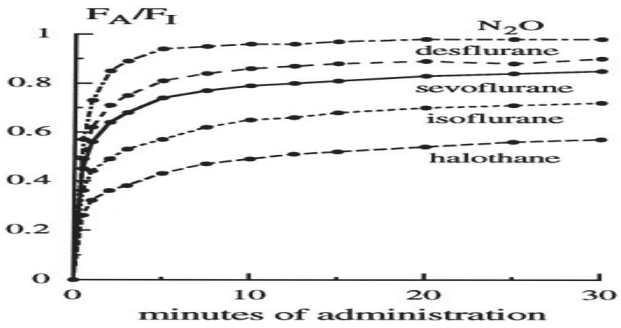
Pharmacokinetics

- 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

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

Uptake and Distribution

- P_A is determined by input (delivery) minus uptake (loss)
  - Input: inspired partial pressure, alveolar ventilation, breathing system
  - Uptake: solubility, cardiac output, alveolar-to-venous partial pressure difference
- Inhalational anesthetic uptake is commonly followed by the ratio of fractional concentration of alveolar anesthetic to inspired anesthetic (F_A/F_I)
- Uptake into the bloodstream is the primary determinant of F_A
- The greater the uptake (in blood), the slower the rate of rise of F_A/F_I
  - Uptake is proportional to tissue solubility
    - The gases with the lowest solubilities in blood (i.e. desflurane) will have the fastest rise in F_A/F_I
    - They also have the fastest elimination
  - Rate of rise of F_A/F_I is proportional to clinical effect (i.e. the faster the rate of rise, the faster the induction and also elimination/emergence)



The rise in alveolar (F_A) anesthetic concentration toward the inspired (F_I) concentration is most rapid with the least soluble anesthetics, nitrous oxide, desflurane, and sevoflurane. It rises most slowly with the more soluble anesthetics, for example, halothane. All data are from human studies. (Adapted from Yasuda N, Lockhart SH, Eger EI II *et al*: Comparison of kinetics of sevoflurane and isoflurane in humans. Anesth Analg 72:316, 1991; and Yasuda N, Lockhart SH, Eger EI II *et al*: Kinetics of desflurane, isoflurane, and halothane in humans. Anesthesiology 74:489, 1991.)

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

•INCREASE	•DECREASE	
Low λ_B	High λ_B	The lower the blood:gas solubility, the faster the rise in F_A/F_I
Low Q	High Q	The lower the cardiac output, the faster the rise in F_A/F_I
High $_A$	Low $_A$	The higher the minute ventilation, the faster the rise in F_A/F_I
High (P_A - P_v)	Low (P_A - P_v)	At the beginning of induction, P_v is zero but rises rapidly (thus [P_A-P_v] falls rapidly) and F_A/F_I increases rapidly. Later, during induction and maintenance, P_v rises more slowly so F_A/F_I rises more slowly.

Parameters as described in Equation 15-16: λ_B, blood solubility; Q, cardiac output; $\dot{V}$, minute ventilation; P_A, P_v, pulmonary arterial and venous blood partial pressure. (Clinical Anesthesia 5th Edition; Barash, P.; Lippincott Williams and Wilkins; 2006)

Pharmacodynamics

- All inhalational agents decrease CMO_2 and increase CBF (via direct vasodilatation)
  - Increases in CBF can increase ICP
- All agents cause a dose-related decrease in blood pressure
- All agents produce muscle relaxation
- The older inhalational agents (halothane, enflurane) cause decreases in myocardial contractility
  - The newer agents have little to no effect
- All inhalational agents produce a dose-dependent depression of the ventilatory response to hypercarbia and hypoxia
- Increase RR + decrease tidal volume = preserved minute ventilation

Nitrous Oxide

- Low potency (MAC 104% - can never reach 1 MAC!)
- Insoluble in blood
  - Facilitates rapid uptake and elimination
- Commonly administered as an anesthetic adjuvant
- Does not produce skeletal muscle relaxation
- 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

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 seen at 1.6 MAC)
    - Minimal compared to halothane
  - Increases ICP (usually at above 1 MAC; short lived)
    - Minimal compared to halothane
- At 2 MAC produces electrically silent EEG

Sevoflurane

- Half as potent as isoflurane (MAC 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 CO_2 absorbent
  - Can cause fires
- Forms Compound A in CO_2 absorbent (nephrotoxic)
  - Recommended to keep fresh gas flows >2 L/min

Desflurane

- Lowest blood:gas solubility coefficient (lower than N_2O)
- Very fast uptake and elimination
- Low potency (MAC 6.6%)
- High vapor pressure
  - Must be stored in a heated, pressurized vaporizer
- Very pungent
  - Can cause breath-holding, bronchospasm, laryngospasm, coughing, salivation when administered to an awake patient via face mask
- Can form CO in desiccated CO_2 absorbent
- Can cause an increased sympathetic response (tachycardia, hypertension) when inspired concentration is increased rapidly

References

1. Clinical Anesthesia 5th Edition; Barash P., Cullen B., Stoelting R.; Lippincott Williams and Wilkins, 2006
2. Miller's Anesthesia 6th edition; Miller R.; Churchill Livingstone, 2005
3. The Pharmacology of Inhalational Anesthetics 3rd edition; Eger E., Eisenkraft J., Weiskopf R.; Library of Congress, 2003
4. Yasuda N, Lockhart SH, Eger E *et al*: Comparison of kinetics of sevoflurane and isoflurane in humans. Anesth Analg 72:316, 1991
5. Yasuda N, Lockhart SH, Eger E *et al*: Kinetics of desflurane, isoflurane, and halothane in humans. Anesthesiology 74:489, 1991

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

MAC & Awareness

Minimum Alveolar Concentration

Alveolar concentration of a gas at 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 $\underline{ED_{50}}$ concentration. The $\underline{ED_{95}}$ is $\pm$25%, so at 1.3 MAC, 95% of patients will not respond to incision.
- MAC values are <u>additive</u> (e.g. 0.5 MAC isoflurane + 0.5 MAC N_2O = 1 MAC)

MAC of Inhaled Anesthetics

Gas	Blood:Gas Partition Coefficient	MAC*
Halothane	2.4	0.75%
Enflurane	1.9	1.7%
Isoflurane	1.4	1.2%
Sevoflurane	0.65	2.0%
N_2O	0.47	104%
Desflurane	0.42	6.0%

*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.

More MAC Definitions

MAC-Awake (a.k.a. MAC-Aware)

- The MAC necessary to prevent response to verbal/tactile stimulation.
- Volatiles: ~0.4 MAC; N_2O: ~0.6 MAC

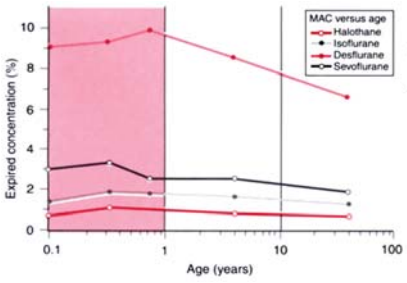
MAC-BAR

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

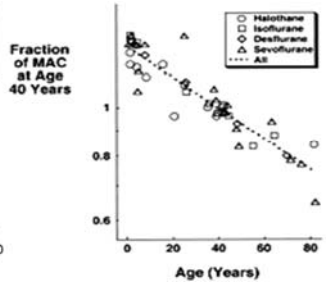
MAC-EI

- 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
- Hyperthermia (over 42C)
- Hypernatremia
- Chronic EtOH abuse
- Genetic factors
  - Redheaded females may have a 19% increased MAC requirement compared to brunettes.

Factors Decreasing MAC

- Drugs decreasing central catecholamines:
  - Reserpine, α-methyldopa
  - Chronic amphetamine abuse
- Other drugs:
  - Opioids, benzodiazepines, barbiturates, α_2-agonists (clonidine, dexmedetomidine), ketamine, lidocaine, lithium, verapamil, hydroxyzine.
- Acute EtOH intoxication
- Pregnancy (↓1/3 after 8-12 weeks, normal by 72h post-partum)
- Hypothermia (↓50% per 10˚C)
- Hypotension (MAP<40 in adult)
- Hypoxemia (P_aO_2 < 38 mm Hg)
- Hypercarbia (P_aCO_2 > 95 mm Hg)
- Hyponatremia
- Metabolic acidosis
- Anemia (Hct < 10%)

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

Signs of Light Anesthesia

- Increase in HR or BP by 20% above baseline
- Tearing
- Dilated pupils
- Coughing or bucking
- Patient movement
- Signs of consciouness 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

- ASA and AANA. *Patient awareness under general anesthesia - what is it?* (www.asahq.org/patientEducation/Awarenessbrochure.pdf), 2005.
- Chen X, Tang J, et al. 2002. A comparison of PSI and BIS values during the perioperative period. *Anesth Analg*, **95**: 1669-74.
- Ebert TJ. Inhalation anesthesia. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed.* Philadelphia: Lippincott Williams & Wilkins, 2006.
- Evers AS and Crowder CM. Cellular and molecular mechanisms of anesthesia. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.

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
  - Others work through NMDA receptors (Ketamine) or alpha-2 receptors (Dexmedetomidine)
- Propofol and the barbiturates decrease the rate of dissociation of GABA and its receptor
- Benzodiazepines increases the efficiency of GABA-receptor and chloride ion channel coupling

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

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

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

‡↓ = decrease; ↑ = increase.

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

Pharmacokinetic Values for the Currently Available Intravenous Sedative-Hypnotic Drugs

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

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

Pharmacodynamics

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

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

Propofol

- Produced in an egg lecithin emulsion because of its high lipid solubility
- Pain on injection occurs in 32-67% of subjects
- Can be attenuated with lidocaine or administering the drug in a larger vein
- Induction dose 1.5-2.5 mg/kg
  - Children require higher doses (larger Vd and higher clearance)
  - Elderly require lower doses (smaller Vd and decreased clearance)
- Infusion doses ~100-200 mcg/kg/min for hypnosis and ~25-75 mcg/kg/min for sedation (depends on desired level of consciousness and infusion duration)
- Decreases $CMRO_2$, CBF, and ICP; CPP may decrease depending on effect on SBP
- Anticonvulsant properties
- Decreases SVR (arterial and venous), direct myocardial depressant
- Dose-dependent respiratory depression
- Has anti-emetic properties – often used for TIVA cases and as a background infusion for patients with PONV
- Formulations support growth of bacteria, good sterile technique and labeling of expiration times (typically 12 hours) is critical
- *Propofol infusion syndrome:* Risk in critically ill patients receiving high dose propofol infusions (>4mg/kg/hr) for prolonged periods of time. Causes severe metabolic acidosis, rhabdomyolysis, cardiac failure, renal failure, and possibly death

Etomidate

- High incidence of pain on injection
- Induction dose 0.2-0.3 mg/kg
- Rapid onset due to high lipid solubility and large non-ionized fraction at physiologic pH
- Myoclonus common upon injection
- Decreases CMRO2, CBF, ICP; CPP maintained because less SBP decrease
- Anticonvulsant properties; but minimal effect on duration of ECT- induced seizure activity
- Maintains hemodynamic stability (even in the presence of pre-existing disease)
  - Does not induce histamine release
- Inhibits adrenocortical synthetic function
  - 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)
- Intra-arterial injection can cause intense vasoconstriction, thrombosis and tissue necrosis; treat with papaverine and lidocaine or regional anesthesia-induced sympathectomy and heparinization
- Induction dose 3-5 mg/kg in adults, 5-6 mg/kg in children, 6-8 mg/kg in infants
- Rapidly redistributed into peripheral compartments (accounts for short duration of action)
- Larger doses can saturate the peripheral compartments resulting in a prolonged duration of action
- Decreases CMRO2, CBF, ICP
  - Causes EEG burst suppression in larger doses (often used for neurosurgical procedures)
- Anticonvulsant activity
  - Exception: Methohexital
- Decreases SVR, direct myocardial depressant
- Dose-dependent respiratory depression
- Unlikely to use at Stanford but may use internationally

Ketamine

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

Midazolam

- All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant properties
- Premedication dose 0.04-0.08 mg/kg IV
- Induction dose 0.1-0.2 mg/kg IV
- Decreases CMRO2, CBF, ICP
  - Does not produce EEG burst suppression
- Decrease SVR and BP when used as induction dose
- Causes dose-dependent respiratory depression
  - Exaggerated when combined with opioids and in patients with chronic respiratory disease
- Flumazenil is a specific antagonist
  - Very short acting
  - 45-90 minutes of action following 1-3 mg dose
    - May see re-sedation as benzodiazepine is eliminated more slowly compared to effects of flumazenil

Dexmedetomidine

- Selective α_2 adrenergic agonist
- 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 10min
- Infusion rate 0.2-0.7 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
- May cause nausea
- Can be utilized for sedation during awake FOB intubations

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

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

** Names have been changed*

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

References

1. Clinical Anesthesia 6th Edition; Barash P., Cullen B., Stoelting R.; Lippincott Williams and Wilkins, 2011.
2. Clinical Anesthesiology 4th edition; Morgan G.E., Mikhail M.S., Murray M.J.; Lange Medical Books/McGraw-Hill, 2006.
3. Miller's Anesthesia 6th edition; Miller R.; Churchill Livingstone, 2005.
4. Avramov M. Anesth Analg 1995;81:596-602

Rational IV Opioid Use

Basic Opioid Pharmacology

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

Opioid Receptor Subtypes and Their Effects

- μ
  - Analgesia: Peripheral
  - GI: ↓GI secretion, ↓GI transit (supraspinal and peripheral), antidiarrheal
  - Other: Puritus, skeletal muscle rigidity, ?urinary retention, biliary spasm
- μ_1
  - Analgesia: Supraspinal
  - Endocrine: Prolactin release
  - Other: Acetylcholine, catalepsy
- μ_2
  - Analgesia: Spinal and supraspinal
  - Resp: Respiratory depression
  - GI: ↓GI transit (supraspinal and spinal)
  - Other: Most cardiovascular effects
- μ_3
  - Other: Anti-inflammatory

Opioid Receptor Subtypes and Their Effects

- κ
  - Analgesia: Peripheral
  - Endocrine: ↓ADH release
  - Other: Sedation
- κ_1
  - Analgesia: Spinal
  - Other: Antipruritic
- κ_2
  - Pharmacology unknown
- κ_3
  - Analgesia: Supraspinal

Opioid Receptor Subtypes and Their Effects

- δ
  - Analgesia: Peripheral
  - Resp: ?Respiratory depression
  - GI: ↓GI transit (spinal), antidiarrheal (spinal and supraspinal)
  - Endo: ?Growth hormone release
  - Other: ?Urinary retention
- δ_1
  - Analgesia: spinal
  - Other: Dopamine turnover
- δ_2
  - Analgesia: Supraspinal
- Unknown (receptor type not identified)
  - Analgesia: Supraspinal
  - Other: Pupillary constriction, nausea and vomiting

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.

Opioids

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.

Opioids

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.

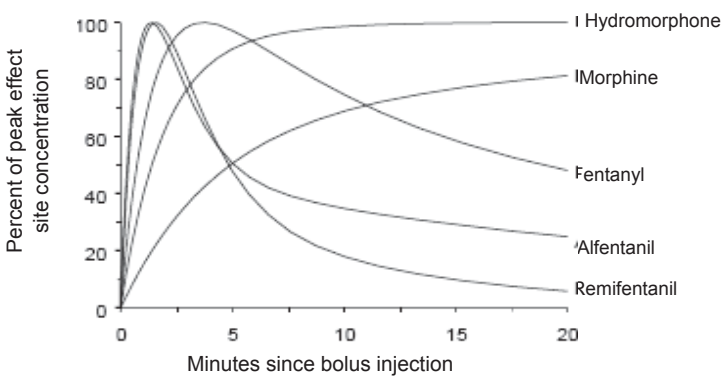
Opioids

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.
- Useful 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.

Comparison of Peak Effect Times

Onset and duration of action of each opioid depend on their lipid solubility and ionization



Rational Opioid Use

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

With that disclaimer in mind, continue reading…

Strategies for Opioid Use

- For a standard GETA induction, use fentanyl to blunt the stimulation caused by DL and intubation.
- For brief, intense stimulation (e.g. retrobulbar block, Mayfield head pins, rigid bronchoscopy), consider a bolus of short-acting opioid like 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).

Strategies for Opioid Use

- 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

1. Barash P., Cullen B., Stoelting R. *Clinical Anesthesiology, 6th Ed*. Lippincott Williams and Wilkins, 2011.
2. Fukuda K. Intravenous opioid anesthetics. In Miller RD (ed), *Miller's Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
3. Gustein HB and Akil H. Opioid analgesics. In Hardmann JG, Limbird LE, and Goodman Gilman A (eds), *Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th ed*. New York: McGraw-Hill, 2001.
4. Saidman L and Shafer S. 2005. "Rational Use of Opioids: Intraoperative and Postoperative," presented at Stanford University Department of Anesthesia Grand Rounds, July 18, 2005.
5. Shafer S, Varvel, J. Pharmacokinetics, Pharmacodynamics, and Rational Opioid Selection. Anesthesiology 75:53-63, 1991.

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.

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 EF is ~60%).

Components of Blood Pressure

Systolic Blood Pressure (SBP)

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

Diastolic Blood Pressure (DBP)

- Lowest arterial pressure in the cardiac cycle

Mean Arterial Pressure (MAP)

- **MAP = 2/3 DBP + 1/3 SBP, or (2xDBP + SBP) ÷ 3**

Components of Blood Pressure

Pulse Pressure

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

Blood Pressure Measurement

Non-Invasive Blood Pressure (NIBP)

- Oscillometric BP determination: oscillations in pressure are detected through the cuff as it deflates.
- MAP is measured as the largest oscillation; it is the most accurate number produced by NIBP.
- SBP and DBP are calculated by proprietary algorithms in the machine.

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 > T5 = severe; < T10 = mild)
- Endocrine disorders (e.g. pheochromocytoma, hyperaldosteronism)
- Hypervolemia
- Drug contamination - intentional (e.g. local anesthetic + Epi) or unintentional (e.g. "Roc-inephrine")

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. esmolol, labetalol)
  - Vasodilators (e.g. hydralazine (takes 20min for peak), NTG, SNP)

Intraoperative Hypotension

- **Hypovolemia**: Blood loss, dehydration, diuresis, sepsis
  - Ensure: Adequate IV access, fluid replacement, cross match if necessary
- **Drugs**: Induction and volatile agents, opioids, anticholinesterases, local anesthetic toxicity, vancomycin, protamine, vasopressor/vasodilator infusion problem, syringe swap or drugs given by surgeon
- **Regional/Neuraxial Anesthesia**: Vasodilation, bradycardia, respiratory failure, local anesthetic toxicity, high spinal
  - Ensure: Volume loading, vasopressors, airway support, left lateral displacement during pregnancy
- **Surgical Events**: Vagal reflexes, obstructed venous return, pneumoperitoneum, retractors and positioning
  - Ensure: Surgeon aware
- **Cardiopulmonary Problems**: Tension PTX, hemothorax, tamponade, embolism (gas, amniotic fluid, or thrombotic), sepsis, myocardial depression (from drugs, ischemia, electrolytes, trauma)

Treatment of Hypotension

- **Temporize** with fast-onset, short-acting drugs, but ultimately diagnose and treat the underlying cause.
  - Turn down (sometimes turn off) the anesthetic
  - Call for help. Inform surgeons
- **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) = α_1 agonist (start at 100mcg)
  - Direct vasoconstrictor
  - Use in vasodilated state with tachycardia
  - Will cause reflex bradycardia

•**Ephedrine** = α_1, β_1, and β_2 (less so) agonist (start at 5mg)
  - Direct and indirect adrenergic stimulation via NE release
  - Use in vasodilated, bradycardic, low CO states

•**Epinephrine** = β_1, α_1, α_2, and β_2 agonist (start at 5mcg)
  - Endogenous catecholamine
  - Causes vasoconstriction and increased CO

•**Inotropes** (in low CO states)
  - Epinephrine, Dopamine, Milrinone, Dobutamine (the last 2 vasodilate)

•**Stress-dose steroids** – consider 100mg hydrocortisone if steroids taken in past 6 months

References

- Costanzo LS. *Physiology, 1st ed*. Philadelphia: WB Saunders Company, 1998.
- Lawson NW and Johnson JO. Autonomic nervous system: physiology and pharmacology. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Stoelting RK and Miller RD. *Basics of Anesthesia, 4th ed*. Philadelphia: Churchill Livingstone, 2000.
- Morris RW Watterson LM Westhorpe RN Webb RK. Crisis management during anaesthesia: hypotension. Qual Saf Health Care 2005;14:e11

Neuromuscular Blocking Agents

Introduction

- Neuromuscular blocking agents (NMBA) are used to facilitate tracheal intubation and mechanical ventilation, assure immobility, 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.[1]
- 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 many times during residency!

The Depolarizer: Succinylcholine

- Structure = 2 adjoined ACh molecules
- Mechanism of action is by ACh receptor activation 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
- Rapidly metabolized by pseudocholinesterases
- ~1:2000 individuals is homozygous for an abnormal plasma cholinesterase and paralysis can last 3-6 hours in such individuals. Consider checking twitches before giving nondepolarizing NMBA after sux.
- The test for abnormal plasma cholinesterase is the dibucaine test. Be sure to understand how this test works for the ITE.

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 cells may result in hyperkalemic arrest. This includes burn injury (after 24-48hrs), muscular dystrophy, myotonias, prolonged 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
- Fasciculation + myalgia. Largely 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 ICP 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 is 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, Pipecuronium
     - No histamine release
     - Possible vagolytic effects (Pancuronium > Rocuronium > Vecuronium)
- There are many non-depolarizing agents and they are divided into classes based on duration of action.

Non-Depolarizing NMBA (cont.)

- The most used non-depolarizing agents are the intermediate duration agents cisatracurium, rocuronium and vecuronium.
- Intubating doses are 2 x ED_{95} ($ED_{95=}$ 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 with have 95% suppression of a monitored twitch.) A larger intubating dose speeds onset time but lengthens duration of block.
- In an effort to speed up onset, some anesthesiologist use a priming dose. 10% of the intubating dose is given 3 minutes prior to intubating dose (as with defasciculating doses prior to sux). Efficacy of a priming dose is debatable.
- Individuals can vary widely in their responses to non-depolarizing agents. Monitor twitches and adjust doses accordingly.
- Rocuronium can be used for rapid sequence inductions when sux cannot be used. However, the dose of roc necessary for RSI (1-1.2 mg/kg) causes prolonged relaxation.
- Cisatracurium is degraded by plasma esterases and Hoffman elimination. It is useful for patients with hepatic or renal dysfunction.

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

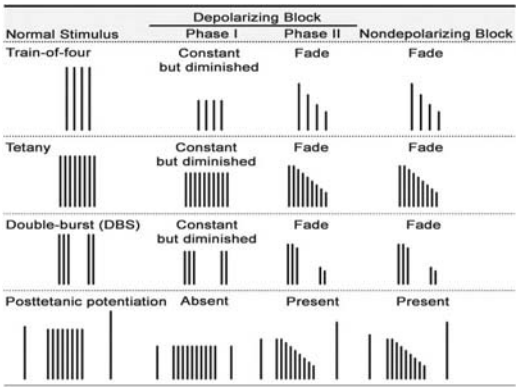
Adopted from Table 20-2, Ch 20, Barash Clincial Anesthesia 6th edition

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 as no pre-NMBA control is necessary (see next slide). 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 -- in studies, authors use mechanomyography or accelerometry.
- While number of twitches can be accurately assessed by feel/sight, the TOF ratio can NOT be accurately assessed. This means that 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 with prolonged infusions.

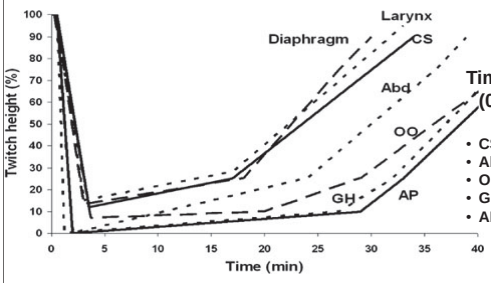
N.B. Neostigmine will potentiate a phase I block from sux but will reverse a phase II block.

Monitoring NMBA 3

- 5 seconds of sustained tetanus at 100hz indicates full recovery. 5 seconds of head lift does not.
- If placing electrodes on the face, do not deliver more than 20 – 30 mA or you will 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 as different muscle groups respond differently to NMBA. See next page.
- 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 (<u>most resistant ➔ most sensitive</u>): vocal cords > diaphragm > currogator supercilii (muscle controlling the eyebrow) > abdominal muscles > adductor pollicis > **pharyngeal muscles** > extraocular
- Pick one site to monitor (e.g. AP or eyebrow or posterior tibial nerve), but 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
- **OO** = orbicularis oculi (eyelid)
- **GH** = geniohyoid (upper airway)
- **AP** = adductor pollicis (thumb)

Reversal of NMBA 1

- Anticholinesterase "reversal agents" indirectly increase the amount of Ach in the NMJ by <u>inhibiting acetylcholinesterase</u>.
- Reversal should not be given until spontaneous recovery has started as anticholinesterases can paradoxically slow recovery if given too early. Many authors advocate waiting until 4 twitches are visible before giving reversal.
- Anticholinesterases cause <u>vagal side effects</u> (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 is seems complete (4 equal twitches), 15-20mcg/kg of neostigmine is probably OK
  - Dose of glycopyrrolate is 20% of the neostigmine does (e.g. 3mg neostigmine with 0.6mg glyco)

Reversal of NMBA 2

- There are other Anticholinesterases besides neostigmine.
  - <u>Neostigmine</u>, <u>Pyridostigmine</u>, and <u>Edrophonium</u> do not cross the BBB.
  - <u>Physostigmine</u> crosses the BBB and can be used to treat central anticholinergic syndrome/atropine toxicity
- It is important to pair anticholinesterases and anticholinergics based on speeds of onset:
  - Edrophonium (rapid) w/ Atropine
  - Neostigmine (intermediate) w/ Glycopyrrolate
  - Pyridostigmine (slow) w/ Glycopyrrolate
- Does reversal increase the risk of PONV? A metanalyses says no. Cheng CR, Sessler DI, Apfel CC. Does neostigmine administration produce a clinically important increase in postoperative nausea and vomiting? Anesth Analg 2005;101:1349-55.

Additional NMBA Facts

- Diseases RESISTANT to nondepolarizing NMBA:
  - Guillain-Barré, Burns, Spinal cord injury, CVA, Prolonged immobility, Multiple sclerosis
- Diseases SENSITIVE to nondepolarizing NMBA:
  - Myasthenia gravis (fewer AChR), Lambert-Eaton Syndrome (less ACh release), amyotrophic lateral sclerosis
- Factors ENHANCING block by NMBA:
  - Volatile anesthetics, aminoglycosides, Mg, IV local anesthetics, CCBs, Lasix, Dantrolene, Lithium, anticonvulsants, sux, hypokalemia, hypothermia
- Common surgeries where you avoid NMBA
  - Axillary node dissection, ENT cases involving dissection near nerves, cases with neuromonitoring

Intra-op Discussion Topics

- How do you induce a patient with full stomach and open globe?
- Can you use sux with increased ICP?
- What degree of immobility can cause hyperkalemia with sux?
- Can you use rocuronium for a renal transplant?
- Does reversal cause PONV?
- You just gave reversal and there is a lap in the abdomen. How do you paralyze the patient?

References

- Donati F and Bevan DR. Neuromuscular blocking agents. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.
- Schreiber J-U, Lysakowski C, Fuchs-Buder T, et al. 2005. Prevention of succinylcholine-induced fasciculation and myalgia: a meta-analysis of randomized trials. *Anesthesiology*, **103**: 877-84.
- Stoelting RK and Miller RD. *Basics of Anesthesia, 4th ed*. Philadelphia: Churchill Livingstone, 2000.

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

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.

Difficult Airway Algorithm

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

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

STEP 1a

Assess the likelihood of airway management problems:
Predictors of Difficult Face Mask Ventilation

- History of prior difficulty
- Facial hair
- Obesity (BMI > 26 kg/m^2)
- History of snoring
- OSA
- No teeth
- Age > 55 years
- Mallampati III or IV
- Limited mandibular protrusion
- Male gender
- Airway masses/tumors

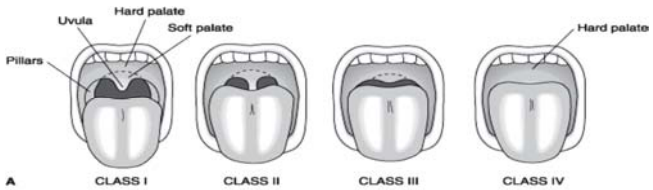
STEP 1b

Assess the likelihood of airway management problems:
Predictors of Difficult Intubation

- History of prior difficulty
- Underlying pathology (e.g. laryngeal/tracheal stenosis, epiglottitis, tumors)
- Neck range of motion (patient can't touch chin to chest or extend neck)
- Thyromental distance (less than 3 finger breadths)
- Short, thick neck
- Long incisors
- Interincisor distance less than 3 cm
- Prominent "overbite"
- Highly arched or very narrow palate
- Decreased submandibular compliance (stiff, indurated, occupied by mass)
- Mallampati score (see next slide)

STEP 1c

Mallampati Score Assessment



C. Difficulty with patient cooperation
- Age
- Mental capacity
- Level of consciousness

D. Difficulty with tracheostomy
- Obesity
- Facial hair
- Prior ENT surgery
- Prior radiation to neck

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

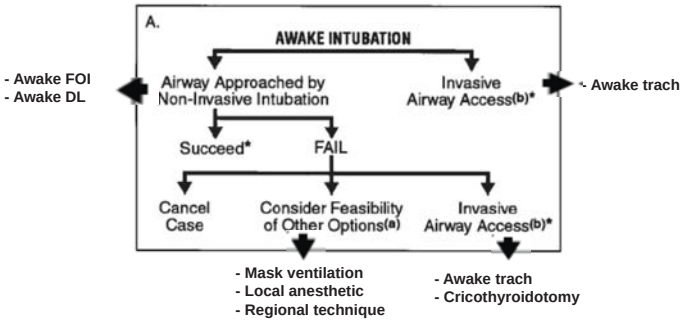
Consider the relative merits and feasibility of basic management choices

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	Preservation of spontaneous ventilation	vs.	Ablation of spontaneous ventilation

STEP 4

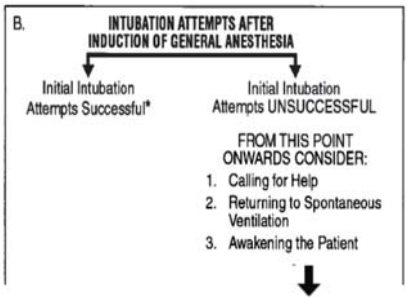
Develop primary and alternative strategies:

Algorithm A: Awake Techniques



STEP 4

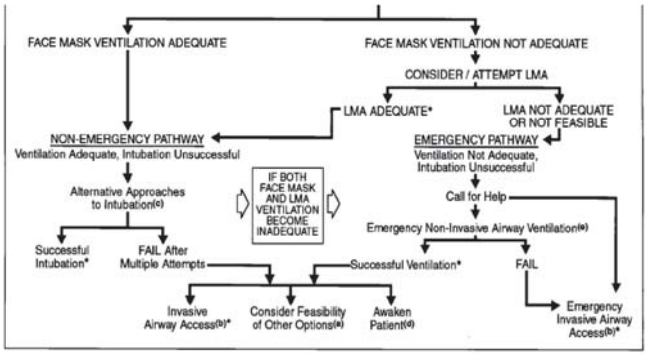
Algorithm B: Intubation After Induction of GA



Continue to next slide

STEP 4

Algorithm B: Intubation After Induction of GA



Algorithm B

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
  - LMA or intubating LMA
  - Video laryngoscope
  - Light wand
  - Fiberoptic intubation
  - Retrograde intubation

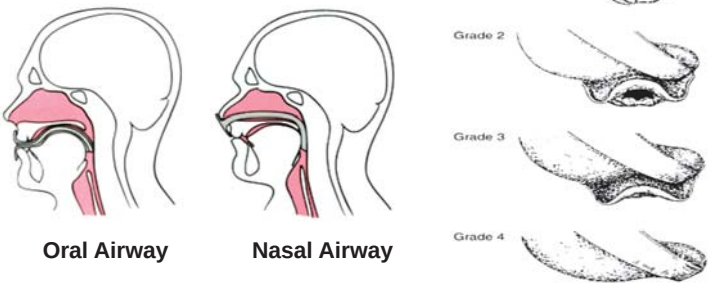
Algorithm B

Emergent Pathway

- "Can't intubate, can't ventilate"
- CALL FOR HELP
- <u>Emergency Non-Invasive Airway Ventilation</u>
  - Rigid bronchoscopy
  - Combitube
  - Transtracheal Jet Ventilation
- <u>Emergency Invasive Airway Ventilation</u>
  - Cricothyroidotomy
  - Surgical tracheostomy

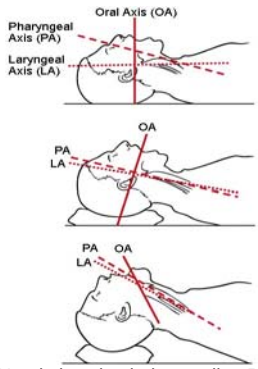
Basics of Airway Management

Direct Laryngoscopy Views

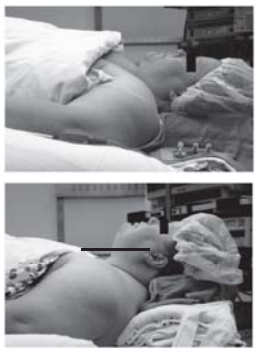


Oral Airway **Nasal Airway**

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
- Consider other airway options after 3 attempts at DL
  - Further attempts can cause airway edema and trauma
- Know airway anatomy
- Know pharmacology of anesthetic agents

References

- ASA Task Force on Management of the Difficult Airway. 2003. Practice guidelines for management of the difficult airway. *Anesthesiology*, **98**: 1269-77.
- Benumof JL. 1996. Laryngeal mask airway and the ASA difficult airway algorithm. *Anesthesiology*, **84**: 686-99.
- Collins JS, Lemmens HJM, Brodsky JB, et al. 2004. Laryngoscopy and morbid obesity: a comparison of the “sniff” and “ramped” positions. *Obesity Surgery*, **14**: 1171-5.
- Langeron O, Masso E, Huraux C, et al. 2000. Prediction of difficult mask ventilation. *Anesthesiology*, **92**: 1229-36.
- Gal TJ. Airway Management. In Miller RD (ed), *Miller´s Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Rosenblatt WH. Airway management. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Rosenblatt WH, Wagner PJ, Ovassapian A, et al. 1998. Practice patterns in managing the difficult airway by anesthesiologists in the United States. *Anesth Analg*, **87**: 153-7.
- El-Orbany M, Woehlck H. 2009. Difficult mask Ventilation. International Anesthesia 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 preop, I was relieved that he had really great veins, and I knew he would be really easy. However, I kept missing IV after IV. After the third failed attempt, I finally paged my attending to come over. When he put on the tourniquet, I suddenly realized that that's what I had neglected to do in my previous attempts!

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

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
  - PPV to assess for volume responsiveness, but has limitations
  - Commonly used when blood loss, fluid shifts, or prolonged OR time anticipated

Intraoperative Intravascular Assessment

- *Monitor trends and compare multiple modalities to confirm clinical impressions*
- Central Venous Catheter
  - CVP not reliable for volume assessment
  - Catheter serves as additional central IV access for medications (vasopressors, inotropes) and fluids
  - Consider risks/benefits of central line placement
- Pulmonary Artery Catheter
  - Most commonly used in RV dysfunction, PHTN, valvular pathology (AS, MR), LV dysfunction
  - Consider risks/benefits of PAC placement as improved outcomes have not been demonstrated
- Transesophageal Echocardiogram
  - Most commonly used in major cardiac surgeries and liver transplants
  - Valuable in narrowing differential of hemodynamic instability

Fluid Compartments

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

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

TBW = Total Body Water

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

Crystalloids

	Osm (mOsm/L)	Na^+ (mEq/L)	Cl^- (mEq/L)	K^+ (mEq/L)	Ca^{2+} (mEq/L)	Buffer (mEq/L)	pH
NS	308	154	154	0	0	0	5.0
LR	273	130	109	4	3	28 (lactate)	6.6
plasmalyte	294	148	98	5	0	27 (acetate)	7.4

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

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
- Intravascular volume expansion from increased oncotic pressure

Dextran 40, 70
- Not available in United States

Colloids

Hetastarch (6% hydroxyethyl starch, HES)

- Hespan (in NS) and Hextend (in LR) solutions
- Solution of highly branched glucose chains (average MW 450 kD)
- Degraded by amylase, eliminated by kidney
- Intravascular $t_{1/2}$ = 25.5 hrs; tissue $t_{1/2}$ = 10-15 days
- Maximum Dose: 15-20 ml/kg/day
- Side effects:
  - Can increase PTT (via factor VIII/vWF inhibition) and clotting times
  - Anaphylactoid reactions with wheezing and urticaria may occur
  - May interfere with platelet function
- Contraindications: coagulopathy, heart failure, renal failure

Albumin (5% and 25%)

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

Crystalloid or Colloid?

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

"Classical" Fluid Management

Maintenance

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

Preexisting Fluid Deficits

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

Ongoing Losses

Evaporative and Interstitial Losses (2/2 capillary leak)

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

Blood Loss

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

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

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

Suggestions for Fluid Management

- Tailor management to patient, surgery, and clinical scenario
- Use a balanced approach
  - Typically start with NS or LR
  - 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

Liberal vs. Restrictive Management

Consequences of Volume Overload

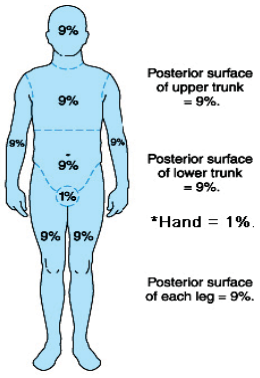
- Increased mortality and length of ICU/hospital stay
- Increased myocardial morbidity
- Increased pulmonary, periorbital, and gut edema
- Decreased hematocrit and albumin
- Worsened wound healing/ increased anastomosis dehiscense (2/2 edema)

Suggestions for Rational Fluid Management

- Use good clinical judgment.
- Tailor management to patient, surgery, and clinical picture.
- Maintain UOP > 0.5 ml/kg/hr, adequate CVP, and stable VS.
- Use balanced fluid therapy: use crystalloid for maintenance, consider use of colloid.
- Consider conservative replacement of interstitial losses or UOP unless VS unstable.

Burns

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



Parkland Formula

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

Intraoperative Oliguria

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 lasix

References

- Holte K, Sharrock NE, and Kehlet H. 2002. Pathophysiology and clinical implications of perioperative fluid excess. *Br J Anaesth*, **89**: 622-32.
- Joshi GP. 2005. Intraoperative fluid restriction improves outcome after major elective gastrointestinal surgery. *Anesth Analg*, **101**: 601-5.
- Kaye AD and Kucera IJ. Intravascular fluid and electrolyte physiology. In Miller RD (ed), *Miller's Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- McKinlay MB and Gan TJ. Intraoperative fluid management and choice of fluids. In Schwartz AJ, Matjasko MJ, and Otto CW (eds), *ASA Refresher Courses in Anesthesiology*, **31**: 127-37. Philadelphia: Lippincott Williams & Wilkins, 2003.
- Butterworth JF, Mackey DC, and Wasnick JD. Fluid Management and Blood Component Therapy. In *Morgan and Mikhail's Clinical Anesthesiology, 5th ed.* New York: McGraw-Hill Companies, Inc., 2013.
- http://openanesthesia.org/index.php?title=Intraoperative_oliguria:_hyperventilation

The first time I emptied urine, it sprayed all over my scrubs. Apparently it's better to aim the spout downwards into the empty bottle before you release the clamp, not up at yourself.

Transfusion Therapy

Type and Screen/Crossmatch

Type and Screen (takes 30-120 min, lasts 72 hr)
- ABO-Rh typing and 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
  - Recipient RBCs for presence of A or B antigens

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%
- Stored at 4˚C in CPD (lasts 21 days), CPDA (lasts 35 days), or Adsol (lasts 42 days).
- CPDA:
  - Citrate (anticoagulant) - also binds iCa
  - Phosphate (buffer)
  - Dextrose (energy source)
  - Adenosine (precursor to ATP synthesis)

Packed Red Blood Cells

Indications (ASA Guidelines)

1. Hg < 6 in *young, healthy patients*
2. Usually unnecessary when Hg >10
3. At Hgb 6-10 g/dl, the decision to transfuse is based on:
   1. ongoing indications of organ ischemia
   2. potential or ongoing blood loss
   3. volume status
   4. risk factors for complications of inadequate O_2.

Note: Solutions incompatible with pRBC:

LR (theoretical clot formation due to calcium)

D5W, hypotonic solutions (less than 0.9% saline → hemolysis)

- "Blood pumps" use Normal Saline for this reason

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. Urgent reversal of Coumadin
2. Correction of known factor deficiency
3. Correction of 1) microvascular bleeding with INR > 1.5, 2) INR > 2, or 3) PTT > 2x normal
4. During massive transfusion (before lab results available)
5. Heparin resistance (i.e. antithrombin III deficiency) in patients requiring heparinization.

Cryoprecipitate

Definition

- Fraction of plasma that precipitates when FFP is thawed.
- Contains Factors VIII, XIII, I (fibrinogen), and fibronectin
- 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 vWF disease
5. Congenital fibrinogen deficiency

Equations

Arterial O_2 Content

$C_aO_2 = O_2\text{-Hb} + \text{Dissolved } O_2$

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

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

$\approx$ 20 cc O_2/dl

Allowable Blood Loss

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

Volume to Transfuse

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

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

Transfusion-Related Infections

Viral

- CMV >1:100
- Hepatitis B 1 in 220,000
- Hepatitis C 1 in 1,600,000
- HIV 1 in 2,000,000

(Figures based on 2000-2001 estimated risk)

Bacterial

- Most common with platelets (1:2000) due to their storage in dextrose at *room temperature*.
- pRBCs not a major source (1:500,000) due to their storage at 4°C, but *Yersinia* is most likely organism.

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

Transfusion Reactions

Febrile Non-Hemolytic Reaction

- Benign; occurs with 0.5-1% of transfusions
- R/O acute hemolytic reaction
- Treatment: Tylenol, Benadryl, supportive care

Allergic/Anaphylactic Reaction

- Occurs within minutes; life-threatening
- 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 & brown urine; monitor for ARF and DIC.
- Treatment: D/C blood, maintain alkaline UOP ($NaHCO_3^-$, mannitol, Lasix), supportive care.

Transfusion-Related Acute Lung Injury (TRALI)

TRALI

- An acute RDS that occurs ~4 hours after transfusion.
- Incidence: 1 in 1120 (but likely under-reported)
- Mortality 5-10% - Leading cause of transfusion-related mortality
- Due to plasma-containing products (platelets and FFP > pRBCs) - usually donor origin antibodies to leukocytes
- 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

- Acute 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 a fluid warmer! Connect tubing through Ranger Warmer.
2. Coagulopathy
   a. Dilutional thrombocytopenia
      - Platelet count likely <100,000 after ~10 units pRBCs
   b. Dilutional coagulopathies
      - ↓ Factors V & VIII ("labile factors") in stored blood
      - Hypofibrinogenemia

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.
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

- ASA Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. 2006. Practice guidelines for perioperative blood transfusion and adjuvant therapies. *Anesthesiology*, **105**: 198-208.
- Goodnough LT. 2003. Risks of blood transfusion. *Crit Care Med*, **31**: S678-86.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.

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

	P_aCO_2	A-a Gradient	DLCO	Corrects w/ 100% F_iO_2?
Low F_iO_2	Normal	Normal	Normal	Yes
Hypoventilation	↑	Normal	Normal	Yes
Diffusion Impairment	Normal	↑	↓	Yes
Shunt	Normal	↑	Normal	No
V/Q Mismatch	Normal / ↑	↑	Normal	Yes

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

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

Equations

Alveolar-arterial (A-a) Gradient

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

Alveolar Gas Equation

$P_AO_2 = F_iO_2 (P_{atm} - P_{H2O}) - (P_aCO_2 / 0.8)$
$= 0.21 (760 - 47) - (40 / 0.8)$
$\approx$ <u>100 mm Hg</u>

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

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

Causes of Hypoxemia

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

2. Hypoventilation
- Drugs (opioids, benzodiazepines, barbiturates)
- Chest wall damage
- Neuromuscular diseases
- Obstruction (e.g. OSA, upper airway compression)

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

Causes of Hypoxemia

4. Shunt (i.e. perfusion w/o ventilation; V/Q = 0)
- Congenital (e.g. ASD, VSD, PDA)
- AVM (AVF, congenital)
- Pulmonary fluid (pneumonia, CHF, ARDS, NPPE, TACO, TRALI)
- Atelectasis (mucus plugging, bronchial intubation, GA)

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: *Alveoli ➔ Machine*

1. Listen to the lungs

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

2. Check ETT

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

Hypoxemia in the OR

3. Check circuit

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

4. Check machine

- Inspiratory & expiratory valves
- Bellows
- Minute ventilation
- F_iO_2
- Pipeline & cylinder pressures

5. Check monitors to confirm (you will probably do this 1st!)

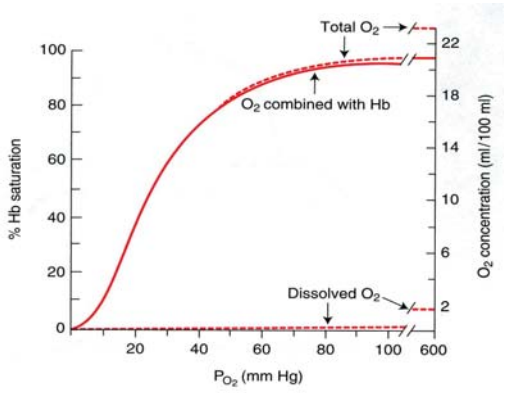
- Pulse oximeter waveform
- Gas analyzer

Management of Hypoxemia

Assuming proper oximeter function, placement, and waveform:

- Place patient on 100% O_2.
- Perform recruitment maneuver (30 sec at 30mmHg if tolerates), 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_2-Hb Dissociation Curve



Useful "anchor" points:

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

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

O_2-Hb Curve Shifts

Left Shift

(higher affinity for O_2 = decreased unloading at tissues)

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

Right Shift

(lower affinity for O_2 = increased unloading at tissues)

- Acidosis
- Hyperthermia
- Hypercarbia
- Increased 2,3-DPG
- Sickle Cell Hb
- Pregnancy
- Volatile anesthetics
- Chronic anemia

Factors Affecting Tissue Oxygenation

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

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

Equations

Arterial O_2 Content

$C_aO_2 = O_2$-Hb + Dissolved O_2

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

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

$\approx$ 20 cc O_2/dl

Mixed Venous O_2 Content

$C_vO_2 = O_2$-Hb + Dissolved O_2

$= (Hb \times 1.36 \times S_vO_2/100) + (P_vO_2 \times 0.003)$

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

$\approx$ 15 cc O_2/dl

Equations

O_2 Delivery

$DO_2 = CO \times C_aO_2$

$= 5$ L/min x 20 cc O_2/dl

$\approx$ 1 L O_2/min

O_2 Consumption (Fick Equation)

$VO_2 = CO \times (C_aO_2 - C_vO_2)$

$= 5$ L/min x 5 cc O_2/dl

$\approx$ 250 cc O_2/min

O_2 Extraction Ratio

$ER_{O2} = (VO_2 / DO_2) \times 100$

$= 250 / 1000$

$\approx$ 25% (normal 22-30%)

Other Concepts

Diffusion Hypoxia = low P_AO_2 as a result of breathing air, in combination with the washout of N_2O into the alveoli, upon termination of an anesthetic.

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

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

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

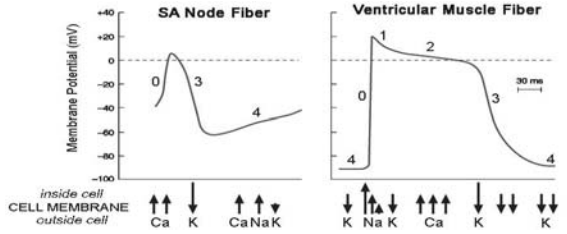
References

- Gaba DM, Fish KJ, and Howard SK. *Crisis Management in Anesthesiology*. Philadelphia: Churchill Livingstone, Inc., 1994.
- West JB. *Respiratory Physiology: The Essentials, 7th ed.* Philadelphia: Lippincott Williams & Wilkins, 2005.
- West JB. *Pulmonary Pathophysiology: The Essentials, 6th ed.* Philadelphia: Lippincott Williams & Wilkins, 2003.

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

Electrolyte Abnormalities

Cardiac Action Potentials



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

Hyperkalemia

Definition

- Mild K^+ = 5.5-6.5 mEq/L
- Moderate K^+ = 6.5-8 mEq/L
- Severe K^+ > 8 mEq/L

Contributing Factors

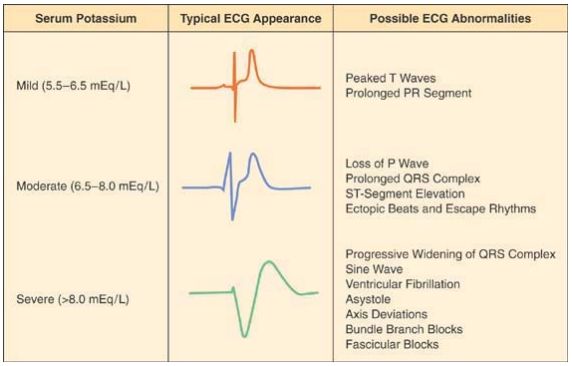
- Renal disease
- Drugs (ACEI, NSAIDs, K-sparing diuretics, Digoxin, ß-blockers)
- Succinylcholine: acute increase of 0.5-1 mEq/L
- Acidosis
- Transfusions
- Hemolysis
- Rhabdomyolysis (tourniquet), trauma
- Administration of Dantrolene to patients on Verapamil or concurrent administration of both drugs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

Hyperkalemia

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 $[K^+]$ is <6.0 mEq/L, cardiac effects are generally negligible.
  - As the concentration increases, may see tall, peaked T waves, especially in the precordial leads.
  - With further increases, the PR interval becomes prolonged, followed by a decrease in the amplitude of the P wave.
  - Finally, the QRS complex widens into a pattern resembling a sine wave and eventually culminates in VF arrest and asystole
- At plasma $[K^+]$ 7.0 mEq/L, may have ascending paralysis that progresses to flaccid paralysis, inability to phonate, and respiratory arrest.
- Hyperkalemia may also accompany Malignant Hyperthermia.

EKG Progression of Hyperkalemia



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

Hyperkalemia

Treatment

- **Reverse membrane effects**
  - Ca gluconate (peripheral IV)
  - Ca chloride (central line)
- **Transfer extracellular [K+] into cells**
  - Bicarbonate ($NaHCO_3$) - 50-100 mEq over 5-10 minutes
  - Insulin (10-15 units) w/ Glucose (25 g)
  - 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 $K^+ \leq 3$ mEq/L with PACs
- Severe $K^+ < 3$ mEq/L with PVCs

Contributing Factors

Preoperative

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

Intraoperative

- Alkalosis (both metabolic and respiratory)
- Insulin therapy
- Hypothermia

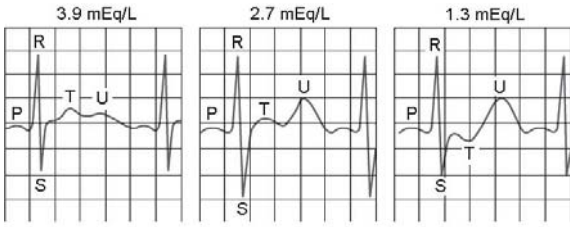
Hypokalemia

Signs & Symptoms

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

EKG Progression of Hypokalemia

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



Hypokalemia

Treatment

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

Hypokalemia

Anesthetic Considerations

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

Hypercalcemia

Contributing Factors

- Hyperparathyroidism
- Malignancy (especially lung, ENT, GU, GYN, and multiple myeloma)
- Immobilization
- ARF
- Drugs (thiazide Ca^{2+} sparing diuretics, lithium)

Signs & Symptoms

- EKG changes(short QT)
- Hypertension
- Polyuria

Treatment

- Hydration (bolus crystalloid) + Lasix diuresis
- Dialysis

Hypercalcemia

Anesthetic Considerations

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

Hypocalcemia

Contributing Factors

Preoperative

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

Intraoperative

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

Signs & Symptoms

- EKG (prolonged QT, bradycardia)
- Hemodynamics (vasodilation, hypotension, decreased myocardial contractility, LV failure)
- Respiratory (laryngospasm, stridor, bronchospasm, respiratory arrest)
- Neuro (cramps, tetany, ↑DTRs, perioral numbness, seizures, Chvostek's sign, Trousseau's sign)

Hypocalcemia

Treatment

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

Anesthetic Considerations

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

Hypermagnesemia

Contributing Factors

- Renal failure
- Hypothyroidism
- Iatrogenic (tocolysis)

Signs & Symptoms

- EKG (widened QRS, prolonged PRI, bradycardia)
- Hemodynamics (vasodilation, hypotension, myocardial depression)
- Neuro (↓DTRs, sedation, weakness, enhanced neuromuscular blockade)

Treatment

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

Anesthetic Considerations

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

Hypomagnesemia

Contributing Factors

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

Signs & Symptoms

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

Treatment

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

Anesthetic Considerations

- EKG monitoring
- Check for coexistent electrolyte deficiencies.

References

- Kaye AD and Kucera IJ. Intravascular fluid and electrolyte physiology. In Miller RD (ed), *Miller's Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.
- Prough DS, Wolf SW, Funston JS, and Svensén CH. Acid-base, fluids, and electrolytes. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Barash PG et al. *Clinical Anesthesiology, 6th ed.* Philadephila: Lippincott Williams & Wilkins, 2009.

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

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

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

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

Hypothermia & Shivering

Definition and Measurement

- Hypothermia is defined as a core body temperature less than 36 degrees C
- Temperature is measured from:
  - Nasopharynx (accurately reflects core temp, but can cause epistaxis)
  - Tympanic Membrane (reflects brain temp, but can cause perforation of ear drum)
  - Esophagus
  - Bladder (lags behind core temperature with low urine flow)
  - 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

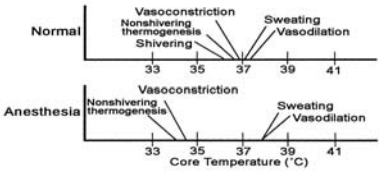
- Thermal inputs are “preprocessed” at numerous levels within the spinal cord and brainstem.
- Modulated by NE, DA, 5-HT, ACh, PGE, and neuropeptides.
- The preoptic-anterior hypothalamus is the central autonomic thermoregulatory center.

Efferent Responses

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

Interthreshold Range

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



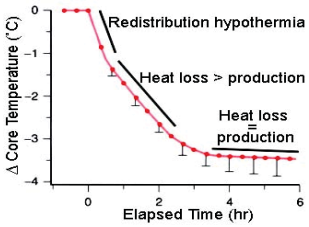
Development of Hypothermia

Anesthetic-impaired thermoregulation

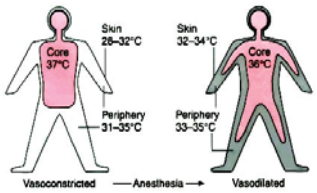
1. Redistribution hypothermia
2. Heat loss > heat production
3. Heat loss = heat production (steady-state heat balance)

Heat transfer to cold OR (in order of importance)

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



Redistribution Hypothermia



Benefits of Hypothermia

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

Consequences of Hypothermia

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

Warming Strategies

Prevention of hypothermia is more effective than treatment!

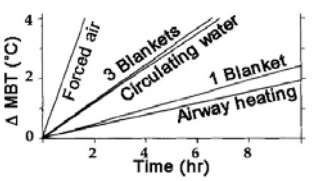
Active Warming

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

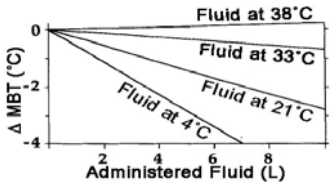
Passive Insulation (not as effective)

- Cotton blankets
- Surgical drapes
- Space blanket (silver plastic)

Effect of Warming Strategies



Effect of IVF Warming



Etiology of Postop Shivering

Intraoperative hypothermia (duh!)… *however*…

- Shivering does NOT always occur in hypothermic patients, and…
- Shivering DOES occur in normothermic patients

Other possible etiologies:

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

Consequences of Shivering

- Increased O_2 consumption
  - Can be up to a 400-500% increase
- Increased CO_2 production and V_E
- Increased incidental trauma
- Increased intraocular and intracranial pressures
- Uncomfortable and/or painful
- Stresses wound edges
- Disrupts monitoring (e.g. NIBP, EKG, S_pO_2)

Rates of MI do NOT correlate with shivering!

Treatment of Shivering

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

References

- De Witte J, and Sessler DI. 2002. Perioperative shivering: physiology and pharmacology. *Anesthesiology*, **96**: 467-84.
- Sessler DI. Temperature monitoring. In Miller RD (ed), *Miller´s Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Sessler DI. Mild perioperative hypothermia. *NEJM*, **336**: 1730-7.
- Morgan, GE. Clinical Anesthesiology, 4th ed. New York: Lange Medical Books/McGraw-Hill

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:

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

Major Risk Factors

Patient-Related

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

Anesthetic-Related

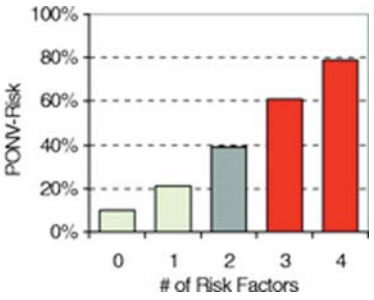
- Volatile anesthetics including N_2O
- Drugs (postoperative narcotics, neostigmine)
- Aggressive hydration (gut edema)

Surgery-Related

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

Simplified Apfel Score

Risk Factors	Points
Female Gender	1
Non-Smoker	1
History of PONV	1
Postoperative Opioids	1
Sum =	0 ... 4



PONV Prophylaxis Based on Apfel Score

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

- Combinations should be with drugs that have a different mechanism of action
- Try not to order agents for treatment in PACU that have already been used for ppx

Antiemetic Classes

5-HT_3 Antagonists (e.g. Ondansetron, Granisetron)

- Serotonin receptor antagonist
- More effective at preventing emesis than nausea
- All agents equally effective
- Zofran 4-8 mg IV or Kytril 0.1-1 mg IV before end of case (usually given ~30 minutes before emergence)

Steroids

- Cheap and effective
- Can be given anytime, for prolonged PONV relief
- Weigh risks/benefits in diabetics
- Decadron 4-10 mg IV anytime during case

Gastrokinetic (e.g. Metoclopramide)

- Dopamine antagonist; can cause extrapyramidal SEs
- Increases GI motility and LES tone, avoid in patients with bowel obstruction
- Reglan 20 mg IV before end of case
- Contraindicated in Parkinson's patients

Antiemetic Classes

Phenothiazines (e.g. Promethazine, Prochlorperazine)

- Dopamine antagonist
- Can cause sedation and extrapyramidal side effects
- Phenergan 12.5-25 mg at end of case.

Anticholinergics (e.g. Scopolamine)

- 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

Butyrophenones (e.g. Droperidol, Haloperidol)

- Central dopamine antagonist
- Cheap and 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 gut hypoperfusion

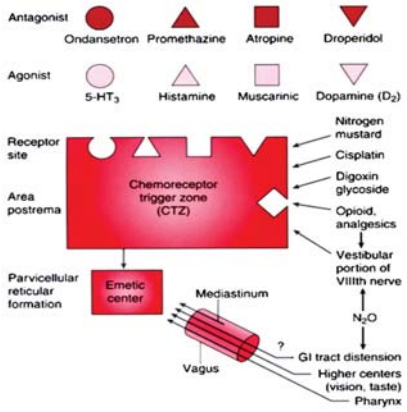
Induction agents

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

Antihistamines (H_2-blockers)

- Cimetidine 300 mg IV
- Ranitidine 50 mg IV

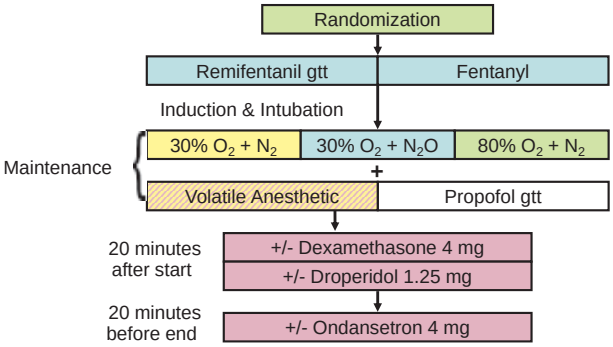
Chemoreceptor Trigger Zone



IMPACT Trial: Study Design

(Apfel et al., 2004)

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



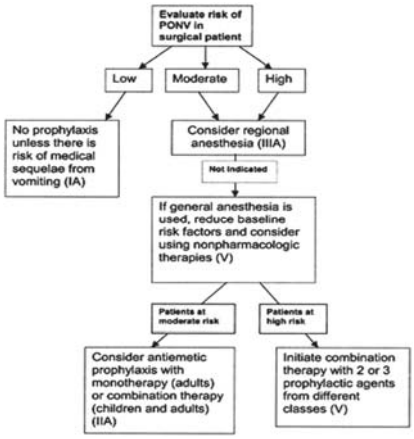
IMPACT Trial: Results

(Apfel et al., 2004)

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

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

Algorithm for PONV Treatment



Strategies to Reduce PONV

- Use regional anesthesia vs. GA
- Use propofol for induction and maintenance of anesthesia
- Avoid N_2O and/or volatile anesthetics
- Minimize opioids (consider tylenol, NSAIDs, etc.)
- Minimize (<2.5 mg) or eliminate neostigmine
- Maintain euvolemia; avoid hypervolemia (gut edema)
- Avoid hypotension and cerebral hypoxia
- Use a combination of antiemetics in different classes
- Consider acupuncture, acupressure, or transcutaneous electrical nerve stimulation (rarely used)

References

- Apfel CC, et al. 2012. Evidence-based analysis of risk factors for posteroperative nausea and vomiting. *BJA*, 109 (5): 742-53.
- Apfel CC, et al. 2004. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *NEJM*, 350: 2441-51.
- Feeley TW and Macario A. The postanesthesia care unit. In Miller RD (ed), *Miller´s Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- Gan TJ, et al. 2001. How much are patients willing to pay to avoid postoperative nausea and vomiting? *Anesth Analg*, **92**: 393-400.
- Gan TJ, et al. 2003. Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg*, **97**:62-71.
- Gan TJ. 2006. Risk factors for postoperative nausea and vomiting. *Anesth Analg*, **102**: 1884-98.
- Watcha MF and White PF. 1992. Postoperative nausea and vomiting: its etiology, treatment, and prevention. *Anesthesiology*, **77**: 162-84.

Extubation Criteria & Delayed Emergence

Extubation Criteria - OR

1. **Adequate Oxygenation**
   - S_pO_2 > 92%, P_aO_2 > 60 mm Hg
2. **Adequate Ventilation**
   - V_T > 5 ml/kg, spontaneous RR > 7 bpm, ET_{CO2} < 50 mm Hg, P_aCO_2 < 60 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

Extubation Criteria - OR

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_aO_2 > 90%, P_aO_2 > 60 mm Hg, P_aO_2/F_iO_2 > 150 on PEEP < 5-8 cm H_2O and F_iO_2 < 0.4-0.5
- P_aCO_2 < 60 mm Hg, pH > 7.25

Ventilator Criteria (during SBT)

- RSBI (RR/V_T) < 100, NIF > 20 cm H_2O
- 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).
- 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.

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

Delayed Emergence

Causes

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 0.40mg – 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 P_aO_2, P_aCO_2, 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

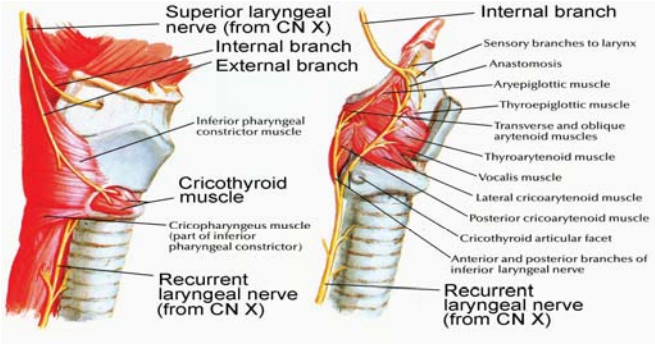
References

- Feeley TW and Macario A. The postanesthesia care unit. In Miller RD (ed), *Miller´s Anesthesia, 6th ed.* Philadelphia: Elsevier Churchill Livingstone, 2005.
- 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)
- Rosenblatt WH. Airway management. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.

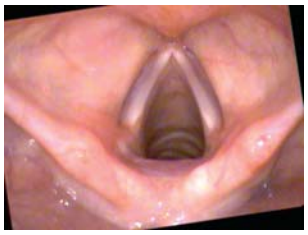
At the end of a general anesthesia case with a 60 yo male patient, I wheeled him into the PACU and he looked straight at me and very seriously said, "So, can I have your number?" His wife was in the waiting room, and I was 7 months pregnant. Classic VA.

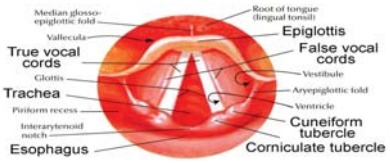
Laryngospasm & Aspiration

Larynx Anatomy



Larynx Anatomy





Larynx Anatomy: Innervation

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

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

Laryngospasm

What is laryngospasm?

- Closure of the true vocal cords (+/- the false vocal cords) from the action of laryngeal muscles → occlusion of the glottis/laryngeal inlet
- Consequences include hypoxia, hypercapnia, and negative pressure pulmonary edema

Predisposing Factors

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

Laryngospasm

Prevention

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

Management - *CALL FOR HELP EARLY!*

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

Negative Pressure Pulmonary Edema

Causes

- Laryngospasm
- Upper airway obstruction/ETT obstruction
- Incidence 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
- ↓S_pO_2, ↑ET_{CO2}, hypotension, large $P_{(A-a)}$ gradient
- CXR with pulmonary edema

Negative Pressure Pulmonary Edema

Pathogenesis

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

Treatment

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

Pulmonary Aspiration

Predisposing Conditions

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

Pulmonary Aspiration

Prevention

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

NPO Guidelines

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

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

Pulmonary Aspiration

Aspiration Pneumonitis

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

Management

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

References

- 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
- Deepika K, et al. 1997. Negative pressure pulmonary edema after acute upper airway obstruction. *J Clin Anesth*, **9**: 403-8.
- Gaba DM, Fish KJ, and Howard SK. *Crisis Management in Anesthesiology*. Philadelphia: Churchill Livingstone, Inc., 1994.
- Netter FH. *Atlas of Human Anatomy, 4th ed*. Philadelphia: WB Saunders, 2006.

Oxygen Failure in the OR

Etiology

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

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

Prevention

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

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

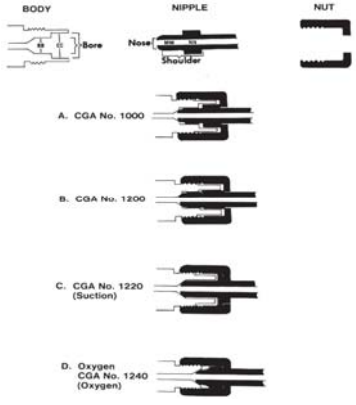
Anesthesia Machine Safety Features
- Flow-meter arrangement
- O_2:N_2O ratio controller
- Oxygen supply failure protection device (“fail-safe valve”)

Gas Cylinders

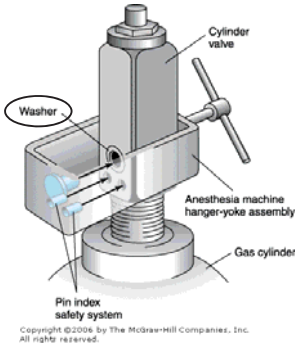
Gas	E-Cylinder Capacity (L)	Pressure (psi)	Color (USA)	Color (Int’l)	Form
O_2	660	1900	Green	White	Gas
Air	625	1900	Yellow	White & Black	Gas
N_2O	1590	745	Blue	Blue	Liquid + Gas
N_2	650	1900	Black	Black	Gas

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

Diameter Index Safety System



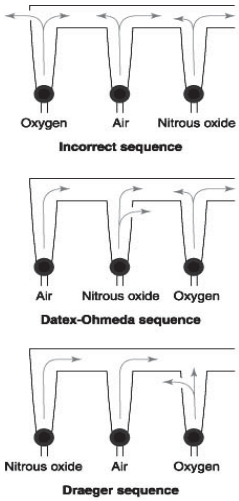
Pin Index Safety System



PISS for Gas Cylinders

N_2O

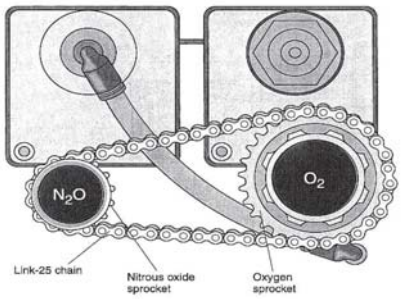
Quick Connects for Supply Lines



Flowmeter Arrangement

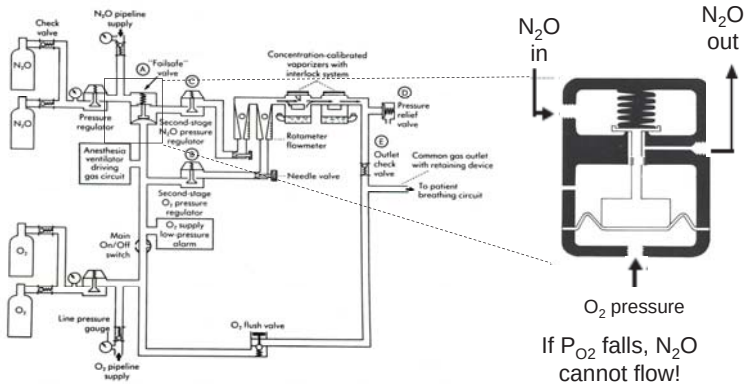
- A leak in the upstream O_2 flowmeter ("Incorrect sequence") results in a hypoxic gas mixture.
- A leak in the Datex-Ohmeda or Draeger flowmeter arrangements may deliver less Air or N_2O than expected, but the mixture will NOT by hypoxic because O_2 is closest to the FGF outlet.

O_2:N_2O Ratio Controller



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

Oxygen Failure Protection Device



If P_{O2} falls, N_2O cannot flow!

Detection

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

Management

- Notify surgeon, call for help.
- Verify problem (pressure gauges, flowmeters, O_2 flush, O_2 analyzer, capnograph).
- Switch to O_2 cylinder (calculate remaining time).
- Use manual ventilation to conserve O_2.
- Check valves, hoses, couplers.
- D/C supply lines if crossed pipelines suspected.
- Call for backup O_2 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

- Dorsch JA and Dorsch SE. *Understanding Anesthesia Equipment: Construction, Care, and Complications, 3rd ed.* Baltimore: Williams & Wilkins, 1994.
- Gaba DM, Fish KJ, and Howard SK. *Crisis Management in Anesthesiology*. Philadelphia: Churchill Livingstone, Inc., 1994.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.

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

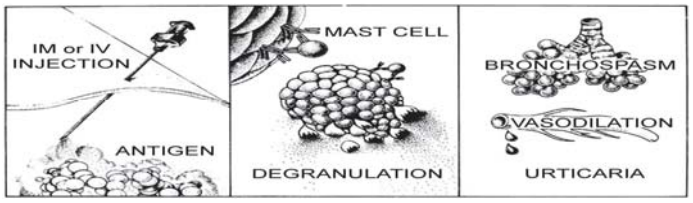
<u>Anaphylaxis</u>

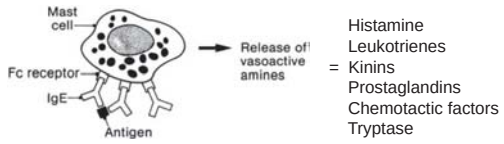
- IgE-mediated Type I hypersensitivity reaction
- Sensitization = prior exposure to an antigen which produces antigen-specific IgE antibodies that bind to Fc receptors on mast cells and basophils.
- Upon re-exposure to the antigen, IgE antibodies then cross-link Fc receptors causing degranulation and release of stored mediators (vasoactive)
- Reaction is <u>Dose *Independent*</u>!

<u>Anaphylactoid</u>

- Direct acitvation 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
Kinins
Prostaglandins
Chemotactic factors
Tryptase

Common Precipitants

Table 1. Drugs Involved in Perioperative Anaphylaxis

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

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

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

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).
   - Give other amnestic agents (e.g. scopolamine, midazolam)
5. Fluids 2-4 L *or more!* (compensate vasodilation, hypotension)
6. Epinephrine = 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

Management

Secondary Treatment

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

Prevention

- Obtain a careful history:
  - Previous allergic reactions?
  - Atopy or asthma?
  - Food allergies?
- 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

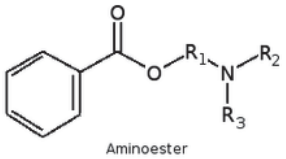
- Gaba DM, Fish KJ, and Howard SK. *Crisis Management in Anesthesiology*. Philadelphia: Churchill Livingstone, Inc., 1994.
- Krause RS. 2006. "Anaphylaxis." eMedicine, June 13, 2006. (http://www.emedicine.com/emerg/topic25.htm)
- Levy JH. The allergic response. In Barash PG, Cullen BF, and Stoelting RK (eds), *Clinical Anesthesia, 5th ed*. Philadelphia: Lippincott Williams & Wilkins, 2006.
- Matthey P, Wang P, Finegan BA, Donnelly M. Rocuronium anaphylaxis and multiple neuromuscular blocking drug sensitivities. Can J Anaesth. 2000 Sep;47(9):890-3.
- Romano, A, Gueant-Rodriguez, RM, Viola, M, et al. Cross-reactivity and tolerability of cephalosporins in patients with immediate hypersensitivity to penicillins. Ann Intern Med 2004; 141:16
- Hepner DL, Castells MC. Anaphylaxis during the perioperative period. *Anesth Analg* 2003; 97: 1381-95.

Local Anesthetics

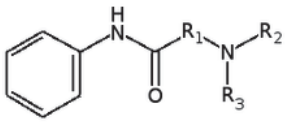
Local Anesthetics (LA)

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

Local Anesthetic Structure



Aminoester



Aminoamide

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

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, et al.

Structure

- The type of linkage divides the local anesthetics into 2 categories:

Esters

- Cocaine
- 2-Chloroprocaine
- Procaine
- Tetracaine

Amides (*i* before -caine)

- Lidocaine
- Bupivacaine
- Ropivacaine
- Mepivacaine
- Etidocaine
- Levobupivacaine

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

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

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).

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 dysrhythmias, 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

- Prevention is the 1st step
  - Avoid intravascular injection (aspirate prior to injection, small test doses), use appropriate monitoring
- Treatment if signs of toxicity
  - Stop local anesthetic
  - Begin supportive care – ACLS: CPR, meds (may need decreased dose of epi), airway management as appropriate
- Initiate early intralipid (IL) therapy
  - Bolus IL 20% 1.5 ml/kg over 1 minute
  - Follow by infusion of 0.25 ml/kg
  - May repeat boluses q3-5 min
  - Total dose 12 ml/kg
  - Consider early initiation of cardiopulmonary bypass

References

Liu SS, Lin Y. Local anesthetics. In Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MD eds. Clinical Anesthesia. 6th ed. Philedelphia, PA: Lippincott Williams & Wilkins; 2009:531-548

Covino BG, Wildsmith JAW. Clinical pharmacology of local anesthetic agents. In Cousins MJ, Bridenbaugh PO, eds. Neural Blockade in Clinical Anesthesia and Management of Pain. 3rd ed. Philadelphia: JB Lippincott, 1998:97-128.

Drasner K. Local anesthetics. In Stoelting RK, Miller RD, eds. Basics of anesthesia. 5th ed. Philadelphia: Churchill Livingstone Elsevier, 2007:123-134.

Malignant Hyperthermia

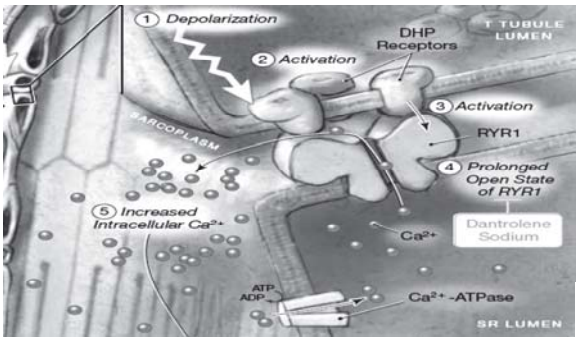
Basics

Definition
- A **hypermetabolic** crisis that occurs when susceptible patients are exposed to a triggering anesthetic agent; underlying defect is abnormally increased Ca^{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^{++} 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 → mutant RYR-1 receptor *remains* open → unregulated calcium entry into cell from sarcoplasmic reticulum → sustained contraction → heat generation, CO_2 production, and cell damage

Sequence of Events

(heralded by uncontrolled increase in intracellular calcium causing sustained muscle contraction, and thus hypermetabolism increasing O_2 consumption and CO_2 production)

1. Triggers

- All potent inhalational agents (except N_2O)
- Succinylcholine

2. Increased Cytoplasmic Free Ca^{2+}

- Masseter muscle rigidity (trismus*)
- Total body rigidity

3. Hypermetabolism

- Increased CO_2 production (most sensitive and specific sign of MH!)
- Increased O_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*
***Earliest recognized signs of MH= masseter muscle rigidity, tachycardia, and hypercarbia*

Sequence of Events

4. Cell Damage

– Leakage of K^+, myoglobin, CK *(may see dark-colored urine)*

5. Compensatory Mechanisms

– Increased catecholamines - tachycardia, hypertension, cutaneous vasoconstriction
– Increased cardiac output - decreased $S_{cv}O_2$, decreased P_aO_2, metabolic acidosis
– Increased ventilation - increased ET_{CO2}, increased V_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.

Sequence of Events

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

Differential Diagnosis

- Neuroleptic Malignant Syndrome (NMS) (in patients receiving antidopaminergic agents or in withdrawal from dopamine agents as in Parkinson's)
- Thyroid Storm *(would not see hyperkalemia or acidosis)*
- Sepsis *(b/c see fever, tachypnea, tachycardia, metabolic acidosis)*
- Pheochromocytoma (↑HR, ↑ BP, but normal $EtCO_2$ and Temp)
- Drug-induced (e.g. ecstasy, crack, amphetamines, PCP, LSD)
- Serotonin Syndrome (associated drugs interactions MAOIs + merperidine or MAOIs+ SSRIs)
- Iatrogenic Hyperthermia
- Hypercarbia from CO2 insufflation for laparoscopy (see ↑$EtCO_2$ with tachycardia)

Treatment (Acute Phase)

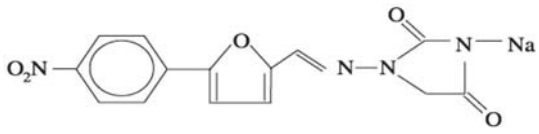
1. Immediate reactions

– Call for help; get MH cart (contains ALL the drugs you need)
– D/C volatile agents and succinylcholine, switch to 100% O_2 and increase fresh gas flows
– 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 H_2O
– Repeat until signs of MH are controlled – titrate to HR/CO_2
– Sometimes, more than 10 mg/kg is necessary (= 35 vials of dantrolene! – consider dedicating an assistant to this).

Dantrolene



- A hydrophobic, hydantoin derivative with 12 hour $t_{1/2}$
- Interferes with excitation-contraction coupling by binding the RYR-1 Ca^{2+} 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 (Acute Phase)

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 $CaCl_2$, or 10-50 mg/kg Ca gluconate)

Treatment (Acute Phase)

6. Treat dysrhythmias
- Standard therapies, but avoid CCBs in the presence of dantrolene (may promote hyperkalemia).
- May need antiarrhythmic 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
- $ETCO_2$, Temp, UOP & color, Electrolytes, ABG, CK, PT/PTT/INR

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
    - Definitively 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 muscle biopsy and exposes to triggers
- Sensitivity >97%, Specificity 80-93% (rule-out)
  - 10-20% false positive rate but zero false negative rate
- Available at 9 U.S. testing centers

Molecular Genetics
- *RYR1* mutation screening
- Low sensitivity, but high specificity (rule-in)
  - 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 CO_2 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" (see ↑ 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 N_2O)

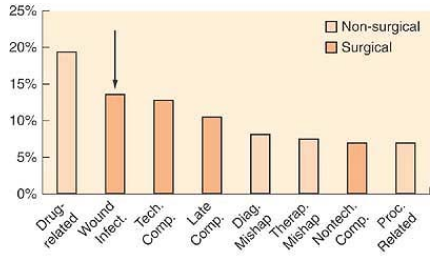
Emergency
- Know where to find the MH cart
- Have dantrolene available

References

- Malignant Hyperthermia Association of the United States (MHAUS, http://www.mhaus.org)
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 5th ed.* New York: McGraw-Hill Companies, Inc., 2013.
- Benca J and Hogan K. Malignant hyperthermia, Coexisting disorders, and Enzymopathies: Risk and Management Options. *Anesthesia and Analgesia* 2009, 109: 1049-1053.
- Brandom, BW. "Pro-Con: Anesthesia and the Patient with Neuromuscular Disease." Manuscript from 2004 Pediatric Anesthesia society annual meeting. http://www.pedsanesthesia.org/meetings/2004annual/man/manuscript6.pdf
- Litman RS, Rosenberg H. 2005. Malignant hyperthermia: update on susceptibility testing. *JAMA*, **293**: 2918-24.
- UCLA Department of Anesthesiology (http://www.anes.ucla.edu/dept/mh.html)

Perioperative Antibiotics

Why Antibiotics?



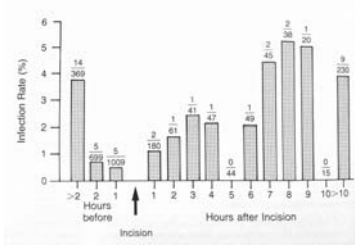
Because in 1984 a study including 51 acute care hospitals in New York State found that surgical site infection (SSI) was the most common adverse surgical event (and the second most common adverse event overall).

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

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 in-patients) or after a specimen is sent for culture.
- Epic tip: Click on "Patient Summary", then the "Micro" tab. It will show you which antibiotics the patient is on and when they need to be released

Timing of prophylaxis



- Rates of Surgical-Wound Infection Corresponding to the Temporal Relation between Antibiotic Administration and the Start of Surgery
- The number of infections and the number of patients for each hourly interval appear as the numerator and denominator, respectively, of the fraction for that interval. The trend toward higher rates of infection for each hour that antibiotic administration was delayed after the surgical incision was significant (z score = 2.00; P<0.05 by the Wilcoxon test).

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

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
  - Gentamicin* 1.5mg/kg
  - Metronidazole 500mg
  - Zosyn 3.375gm
  - Ceftriaxone 1gm
  - 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.)

Table 1.
Recommended Doses and Redosing Intervals for Commonly Used Antimicrobials for Surgical Prophylaxis

Antimicrobial	Recommended Dose		Half-life in Adults With Normal Renal Function, hr[a]	Recommended Redosing Interval (From Initiation of Preoperative Dose), hr[c]
	Adults[a]	Pediatrics[b]		
Ampicillin–sulbactam	3 g (ampicillin 2 g/sulbactam 1 g)	50 mg/kg of the ampicillin component	0.8–1.3	2
Ampicillin	2 g	50 mg/kg	1–1.9	2
Aztreonam	2 g	30 mg/kg	1.3–2.4	4
Cefazolin	2 g, 3 g for pts weighing ≥120 kg	30 mg/kg	1.2–2.2	4
Cefuroxime	1.5 g	50 mg/kg	1–2	4
Cefotaxime	1 g[d]	50 mg/kg	0.9–1.7	3
Cefoxitin	2 g	40 mg/kg	0.7–1.1	2
Cefotetan	2 g	40 mg/kg	2.8–4.6	6
Ceftriaxone	2 g[e]	50–75 mg/kg	5.4–10.9	NA
Ciprofloxacin[f]	400 mg	10 mg/kg	3–7	NA
Clindamycin	900 mg	10 mg/kg	2–4	6
Ertapenem	1 g	15 mg/kg	3–5	NA
Fluconazole	400 mg	6 mg/kg	30	NA
Gentamicin[g]	5 mg/kg based on dosing weight (single dose)	2.5 mg/kg based on dosing weight	2–3	NA
Levofloxacin[f]	500 mg	10 mg/kg	6–8	NA
Metronidazole	500 mg	15 mg/kg Neonates weighing <1200 g should receive a single 7.5-mg/kg dose	6–8	NA

Continued on next page

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.)

Table 1 (*continued*)

Antimicrobial	Recommended Dose		Half-life in Adults With Normal Renal Function, hr[a]	Recommended Redosing Interval (From Initiation of Preoperative Dose), hr[c]
	Adults[a]	Pediatrics[b]		
Moxifloxacin[f]	400 mg	10 mg/kg	8–15	NA
Piperacillin–tazobactam	3.375 g	Infants 2–9 mo: 80 mg/kg of the piperacillin component Children >9 mo and ≤40 kg: 100 mg/kg of the piperacillin component	0.7–1.2	2
Vancomycin	15 mg/kg	15 mg/kg	4–8	NA
Oral antibiotics for colorectal surgery prophylaxis (used in conjunction with a mechanical bowel preparation)				
Erythromycin base	1 g	20 mg/kg	0.8–3	NA
Metronidazole	1 g	15 mg/kg	6–10	NA
Neomycin	1 g	15 mg/kg	2–3 (3% absorbed under normal gastrointestinal conditions)	NA

Re-Dosing Guidelines

According to Stanford Pharmacy Guidelines

Antibiotic	Re-dosing Interval
Cefazolin	4 hours
Cefoxitin	3 hours
Clindamycin	6 hours
Ciprofloxacin	8 hours
Ertapenem	24 hours (n/a)
Gentamicin	n/a
Metronidazole	n/a
Vancomycin	n/a

See also previous slide.

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.
- Craniotomies
  - 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:

Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect 2013;14:73–156.

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)

Allergies and Interactions

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

Special considerations

- The American Heart Association guidelines recommend prophylaxis for those with conditions that place them at increased risk for infective endocarditis AND for those at highest risk for adverse outcomes when endocarditis does occur. These are patients with:
  - Prosthetic cardiac valve
  - Previous history of infective endocarditis
  - Congenital heart disease and completely repaired congenital heart defect if it' s within the first 6 months.
  - Cardiac transplant patients who develop cardiac valvulopathy
- Bacterial Endocarditis prophylaxis
  - Ampicillin 1-2gm IV, 30min prior to surgery and
  - Gentamicin 1.5mg/kg IV, 30min prior to surgery
  - IF PCN allergic, use Cefazolin or ceftriaxone 1gm IV, or Clindamycin 600mg IV
- For mitral valve prolapse, do not need prophylaxis because, while there is increased risk for IE, the most serious adverse outcomes of IE do not usually occur in patients with this condition.
- Do not need prophylaxis for bronchoscopy without biopsy, vaginal delivery, hysterectomy, or GI/GU procedures, including colonoscopy.

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

Hall Question

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

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

- See next slide for answer.

Hall Answer

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

References

- American Society of Anesthesiologists, ACE Program 2008. Pages 44-47.
- Ann S, Reisman RE. Risk of administering cephalosporin antibiotics to patients with histories of penicillin allergy. *Ann Allergy Asthma Immunol* 1995; 74:167-170
- Antimicrobial prophylaxis for surgery. *Treat Guidel Med Lett* 2009; 7:47
- Barash, Paul G. *Clinical Anesthesia*. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2009. Print.
- ***Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect 2013;14:73–156.
- Bratzler, DW, Hunt, DR. The surgical infection prevention and surgical care improvement projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis* 2006; 43:322
- Bratzler, DW, Houck, PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis* 2004; 38:1706
- Classen DC, et. Al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *The New England Journal of Medicine* 1992; 326:281-286.
- Nishimura RA, Carabello BA, Faxon DP, et al. ACC/AHA 2008 Guideline Update on Valvular Heart Disease: Focused Update on Infective Endocarditis: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol.* 2008;52(8):676-685. doi:10.1016/j.jacc.2008.05.008.
- Pinichero ME. Use of selected cephalosporins in penicillin-allergic patients: a paradigm shift. *Diagnostic Microbiology and Infectious Disease 2007;* 57:13-18.
- Urman, Richard D. and Jesse M. Ehrenfeld. "Pocket Anesthesia" Second Ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2013. Print

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

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

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

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

Topics for Discussion

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