

Name: _____



2018 CA-1 TUTORIAL TEXTBOOK 12th Edition

STANFORD UNIVERSITY MEDICAL CENTER
DEPARTMENT OF ANESTHESIOLOGY

Aileen Adriano, M.D.
Jeffrey Skanchy, M.D.



TABLE OF CONTENTS

| | |
|--|-----|
| Introduction..... | 3 |
| Acknowledgements..... | 4 |
| Contributors..... | 4 |
| Key Points and Expectations..... | 8 |
| Goals of the CA-1 Tutorial Month..... | 9 |
| Checklist for CA-1 Mentorship Intraoperative Didactics..... | 10 |
| CA-1 Tutorial Didactic Schedule..... | 11 |
| CA-1 Mentorship Intraoperative Didactic Lectures (with hyperlinks) | |
| Standard Monitors..... | 12 |
| Inhalational Agents..... | 29 |
| MAC and Awareness..... | 44 |
| IV Anesthetic Agents..... | 56 |
| Rational Opioid Use..... | 72 |
| Intraoperative Hypotension & Hypertension..... | 94 |
| Neuromuscular Blocking Agents..... | 106 |
| Difficult Airway Algorithm..... | 127 |
| Fluid Management..... | 147 |
| Transfusion Therapy..... | 163 |
| Hypoxemia..... | 183 |
| Electrolyte Abnormalities..... | 199 |
| Hypothermia & Shivering..... | 222 |
| PONV..... | 235 |
| Extubation Criteria & Delayed Emergence..... | 250 |
| Laryngospasm & Aspiration..... | 261 |
| Oxygen Failure in the OR..... | 275 |
| Anaphylaxis..... | 289 |
| Local Anesthetics..... | 301 |
| Malignant Hyperthermia..... | 314 |
| Perioperative Antibiotics..... | 327 |
| Topics for Discussion..... | 339 |
| CA-1 Exams, Dates & Preparation..... | 340 |

INTRODUCTION TO THE CA-1 TUTORIAL MONTH

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

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

There is so much material to cover in your first couple months of residency that independent study is a must. Teaching in the OR is lost without a foundation of knowledge. Afternoon lectures are more meaningful if you have already read or discussed the material. This booklet serves as a launching point for independent study. While you review the tutorial with your mentor, use each lecture as a starting point for conversations or questions.

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

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

CA-1 Introduction to Anesthesia Lecture Series:

The Introduction to Anesthesia Lecture series, given by attendings designed to introduce you to the basic concepts of anesthesia. Topics covered include basic pharmacology of anesthetics, basic physiology, and various clinical skills and topics. You will be relieved of all clinical duties to attend these lectures. The department has purchased Miller's *Basics of Anesthesia* for use as a reference for these lectures.

ACKNOWLEDGEMENTS

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

Thanks to Dr. Pearl for his support and assistance with this endeavor. His guidance is appreciated by all. If you ever feel like you're staying too late, know that Dr. Pearl is probably still working in his office when you leave the OR.

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

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

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

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

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

Aileen Adriano, MD
Jeffrey Skanchy, MD

CONTRIBUTORS

12th Edition (2018)

Editors:

Jeffrey Skanchy, MD
Aileen Adriano, MD

Section Editors:

Robert Arrigo, MD
Gregory Atkinson, MD
Michael Chen, MD
Angela Ji, MD
Richard Kim, MD
Theresa Lii, MD
Daniel Orlovich, MD
Elizabeth Ozery, MD
Gabriel Reyes, MD
Alexandra Ruan, MD
Jeffrey Skanchy, MD

11th Edition (2017)

Editors:

Anna Bettini, MD
Sean Paschall, MD
Aileen Adriano, MD

Section Editors:

Anna Bettini, MD
Natalie Bodmer, MD
Emmett Culligan, MD
Kaitlin Flannery, MD
Andrew Guistini, MD
Lynn Ngai, MD
Chris Rishel, MD
Jeffrey Skanchy, MD
Brian Tse, MD
Jessica Zvara, MD

10th Edition (2016)

Editors:

Sandra Sacks, MD
Kelly O'Hear, MD
Aileen Adriano, MD

Section Editors:

Francesca Betti, MD
Sean Paschall, MD
Tenille Bany, MD
Emmett Culligan, MD
Wendy Ma, MD
Erin Connor, MD
Andrew Guistini, MD
David Creighton, MD
Sara Smith, MD
Noelle Fabian, MD

Dan Moy, MD
Jocelyn Wong, MD

9th Edition (2015)

Editors:

Lindsay Borg, MD
Ann Ng, MD
Aileen Adriano, MD

Section Editors:

Anuj Aggarwal, MD
Shara Cohn, MD
Erin Crawford, MD
Amit Joseph, MD
Tyler King, MD
Luke McCage, MD
Quynh Nguyen, MD
Kelly O'hear, MD
Patty Olszynski, MD
Jordan Ruby, MD
Sandra Sacks, MD
Clair Secomb, MD
Lauren Steffel, MD
Anna Swenson, MD
Louise Wen, MD

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

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

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

5th Edition (2011)

Editors:

Becky Wong, MD

Natalya Hasan, M.D
Aileen Adriano, MD

4th Edition (2010)

Editors:

Becky Wong, MD
Kate Ellerbrock, M.D
Aileen Adriano, MD

3rd Edition (2009)

Editors:

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

Section Editors:

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

2nd Edition (2008)

Editors:

Jerry Ingrande, MD
Aileen Adriano, MD

1st Edition (2007)

Editors:

Ryan Green, MD, PhD
Aileen Adriano, MD

ACKNOWLEDGEMENT TO MENTORS

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

FACULTY & RESIDENT MENTORS

2018 MENTORS

Resident Mentors:

David Allain, MD
Nicole Arkin, MD
Robert Arrigo, MD
Ashley Black, MD
Tyler Ewing, MD
Kaitlin Flannery, MD
Mae Gillespie, MD
Patrick Minot, MD
Josianna Schwan, MD
Elizabeth Ozery, MD
Lindsey Stephens, MD
Brian Tse, MD
Sophia Tukmani-Bazzi, MD
Chelsea Zur, MD
Jessica Zvara, MD

2017 MENTORS

Resident Mentors:

Bob Arrigo, MD
Tenille Bany, MD
Francesca Betti, MD
Anna Bettini, MD
Cedar Fowler, MD
Eric Lee, MD
Patrycja Olszynski, MD
Jason Reminick, MD
Sara Smith, MD
Emily Stockert, MD
Aiden Tait, MD
Brian Tse, MD
Jessiva Zvara, MD

2016 MENTORS

Resident Mentors:

Sophie Turkmani-Bazzi, MD
Rett Quattlebaum, MD
Cynthia Khoo, MD
Anna Harter, MD
Melissa Vogelsong, MD
Sean Paschall, MD
Sarah Stone, MD
Amy Kloosterboer, MD
Jason Reminick, MD
Anna Bettini, MD

David Creighton, MD
Luke McCage, MD
Patty Olszynski, MD

Faculty Mentors

Timothy Angelotti, MD, PhD
Martin Angst, MD
Naola Austin, MD
Jennifer Basarab-Tung, MD
Marianne Chen, MD
Pamela Flood, MD
Natalya Hasan, MD
Boris Heifets, MD
Praveen Kalra, MD
Steven Lipman, MD
Javier Lorenzo, MD
Amy Lu, MD
Chris Painter, MD
Jessica Patterson, MD
Roya Saffary, MD
Sunita Sastry, MD
Amit Saxena, MD
Steven Shafer, MD
Eric Sun, MD
Pedro Tanaka, MD, PhD

2015 MENTORS

Mentor Coordinators:

Lindsay Borg, MD

Resident Mentors:

Lindsey Bergman, MD
Alvin Garcia, MD
Glorilee Harper, MD
Ken Ike, MD
Eric Lee, MD
Quynh Nguyen, MD
Lena Scotto, MD
Christina Stachur, MD
Lauren Steffel, MD
Anna Swenson, MD
Phil Wang, MD
Vicky Yin, MD
Meghana Yajnik, MD

Faculty Mentors

Aileen Adriano, MD

Timothy Angelotti, MD, PhD
Naola Austin, MD
Jennifer Basarab-Tung, MD
Jessica Brodt, MD
Mark Burbridge, MD
Marianne Chen, MD
Jeremy Collins, MD
Alimorad Djalali
David Drover, MD
Anthony Doufas, MD, PhD
Roy Esaki, MD
Ruth Fanning, MD
Eric Gross, MD, PhD
Natalya Hasan, MD
Boris Heifets, MD, PhD
Maeve Hennessy, MD
Gillian Hilton, MD
Bassam Kadry, MD
Meredith Kan, MD
Vivek Kulkarni, MD
Hendrikus Lemmens, MD, PhD
Steve Lipman, MD
Javier Lorenzo, MD
Vladimir Nekhendzy, MD
Jordan Newmark, MD
Rachel Outterson, MD
Christopher Painter, MD
Periklis Panousis, MD
Xiang Qian, MD, PhD
Suma Ramzan, MD
Myer Rosenthal, MD
Sunita Sastry, MD
Steven Shafer, MD
Pedro Tanaka, MD
Alex Tzabazis, MD
Sam Wald, MD
Ahmed Zaafran, MD
Karl Zheng, MD

2014 MENTORS

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
Gillian 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
Vladimir 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

2013 MENTORS

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 Hennessey, 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
Vladimir 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

2012 MENTORS

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

2011 MENTORS

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

2010 MENTORS

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

2009 MENTORS

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, M

KEY POINTS AND EXPECTATIONS

Key Points:

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

Expectations of CA-1 Residents:

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

Expectations of Senior Resident Mentors:

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

Expectations of Faculty Mentors:

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

GOALS OF THE CA-1 TUTORIAL MONTH

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

I. Preoperative Preparation:

- a. Perform a complete safety check of the anesthesia machine.
- b. Understand the basics of the anesthesia machine including the gas delivery systems, vaporizers, and CO₂ absorbers.
- c. Set up appropriate equipment and medications necessary for administration of anesthesia.
- d. Conduct a focused history with emphasis on co-existing diseases that are of importance to anesthesia.
- e. Perform a physical examination with special attention to the airway and cardiopulmonary systems.
- f. Understand the proper use of laboratory testing and how abnormalities could impact overall anesthetic management.
- g. Discuss appropriate anesthetic plan with patient and obtain an informed consent.
- h. Write a pre-operative History & Physical with Assessment & Plan in the chart.

II. Anesthetic Management

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

III. Post-operative Evaluation

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

**SUGGESTED CHECKLIST FOR CA-1 MENTORSHIP
INTRAOPERATIVE DIDACTICS**

Mentors *initial* completed lectures

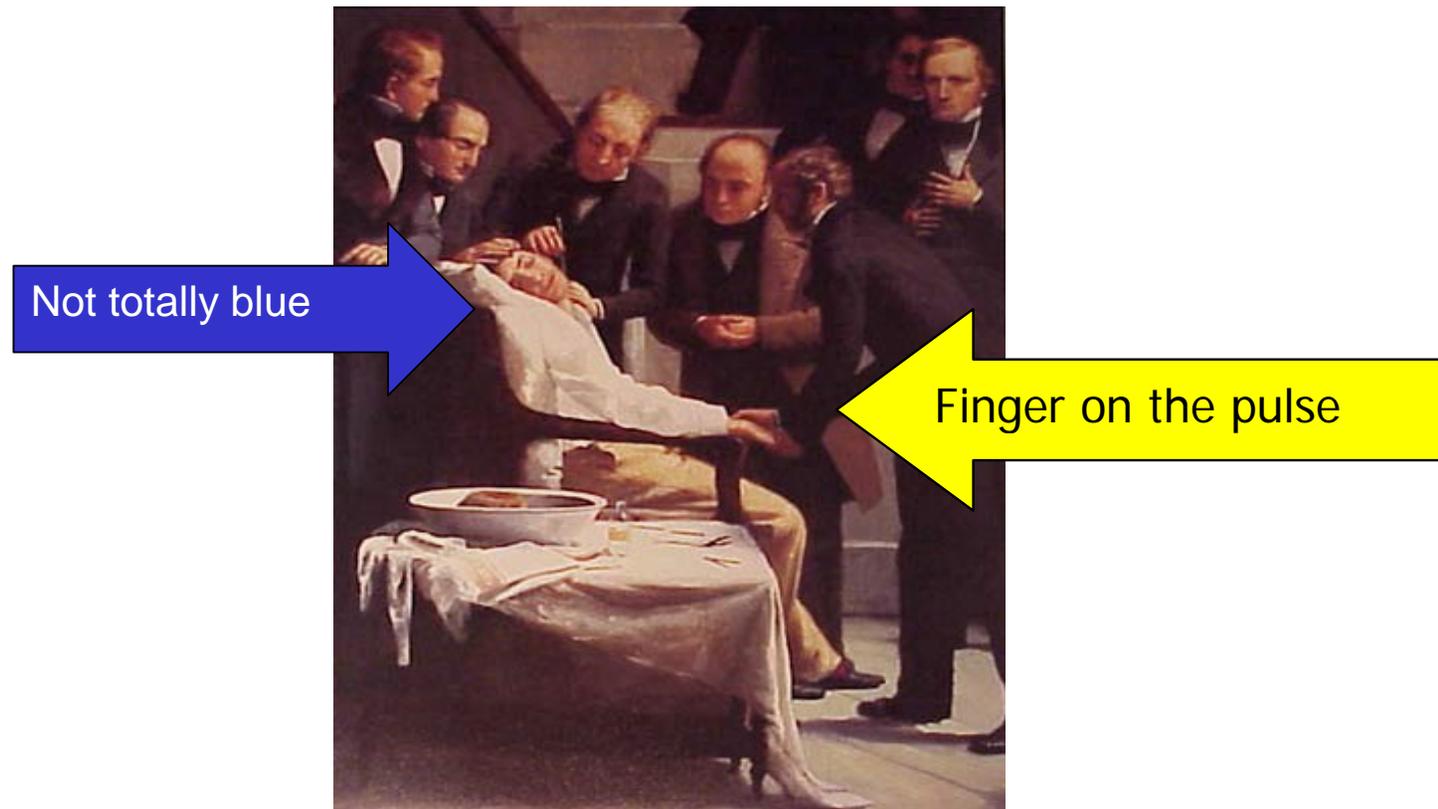
- | | |
|--------------------------|---|
| First Days July 5-7 | <input type="checkbox"/> Discuss GOR Goals and Objectives for CA-1 <input type="checkbox"/> Discuss etiquette in the OR <input type="checkbox"/> Discuss proper documentation <input type="checkbox"/> Discuss proper sign out <input type="checkbox"/> Discuss post-op orders <input type="checkbox"/> Machine check |
| Week One July 10-14 | <input type="checkbox"/> Standard Monitors <input type="checkbox"/> Inhalational Agents <input type="checkbox"/> MAC & Awareness <input type="checkbox"/> IV Anesthetic Agents <input type="checkbox"/> Rational Opioid Use <input type="checkbox"/> Intra-operative Hypotension & Hypertension <input type="checkbox"/> Neuromuscular Blocking Agents |
| Week Two July 17-21 | <input type="checkbox"/> Difficult Airway Algorithm <input type="checkbox"/> Fluid Management <input type="checkbox"/> Transfusion Therapy <input type="checkbox"/> Hypoxemia <input type="checkbox"/> Electrolyte Abnormalities <input type="checkbox"/> Hypothermia & Shivering <input type="checkbox"/> PONV <input type="checkbox"/> Extubation Criteria & Delayed Emergence |
| Week Three July 24-28 | <input type="checkbox"/> Laryngospasm & Aspiration <input type="checkbox"/> Oxygen Failure in the OR <input type="checkbox"/> Anaphylaxis <input type="checkbox"/> Local Anesthetics <input type="checkbox"/> ACLS <input type="checkbox"/> Malignant Hyperthermia <input type="checkbox"/> Perioperative Antibiotics |

CA-1 INTRODUCTORY LECTURES – JULY 2018

| Date | Time | Lecture | Chapter |
|---|----------------|--|---------|
| 7/5/2018 | 5:00 pm | Ethics and Professionalism Dr. Brock-Utne | |
| | 5:30 pm | Chief Resident Rounds 1 | |
| 7/9/2018 | 4:00 pm | ASA Monitoring Dr. Jaffe | |
| 7/10/2018 | 4:00 pm | Basic Anesthesia Machines Dr. Jaffe | |
| 7/11/2018 | 4:00 - 6:30 pm | Central Line Workshop Dr. Mihm (located at LKSC, LK005) | |
| 7/12/2018 | 4:00 - 4:15 pm | Wellness Retreat Dr. Hasan-Hill | |
| | 4:15 pm | The Drugs in the Drawer Dr. Heifets | |
| | 5:00 pm | Chief Resident Rounds 2 | |
| 7/16/2018 | 4:00 pm | Principles of Pharmacology Dr. Steve Shafer | 24 |
| | 5:00 pm | Chief Resident Rounds 3 | |
| 7/17/2018 | 4:00 pm | Airway Management Dr. Collins | 55 |
| | 5:00 pm | Chief Resident Rounds 4 | |
| 7/18/2018 | 4:00 pm | Devising an Anesthetic Plan Dr. Schmiesing | 38 |
| | 5:00 pm | Chief Resident Rounds 5 | |
| 7/19/2018 | 4:00 pm | Positioning and Associated Risks Dr. Drover | 41 |
| | 5:00 pm | Chief Resident Rounds 6 | |
| 7/23/2018 | 4:00 pm | Respiratory Physiology Dr. Lorenzo | 19 |
| | 5:00 pm | Chief Resident Rounds 7 | |
| 7/24/2018 | 4:00 - 4:30 pm | Introduction to Libero Lecture App Dr. Tanaka | |
| | 4:30 - 5:30 pm | iStat Training | |
| 7/25/2018 | 4:00 pm | Pharmacology of Inhalational Agents Dr. Painter | 25, 26 |
| | 5:00 pm | Chief Resident Rounds 8 | |
| 7/26/2018 | 4:00 pm | Pharmacology of Intravenous Agents Dr. Painter | 30 |
| | 5:00 pm | Chief Resident Rounds 9 | |
| 7/30/2018 | 4:00 pm | Pharmacology of Neuromuscular Blockade Dr. Joseph | 34 |
| | 5:00 pm | Chief Resident Rounds 10 | |
| 7/31/2018 | 4:00 pm | SAB/Epidural Regional Anesthesia Dr. Basarab-Tung | |
| | 5:00 pm | Chief Resident Rounds 11 | |
| *Miller's Anesthesia is the reference text for these lectures. | | | |
| **All lectures are held in the Anesthesia Conference Room unless otherwise noted. | | | |

Standard Monitors

Monitoring in the Past



Basic Anesthetic Monitoring

ASA Standards for Basic Anesthetic Monitoring

STANDARD I

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

STANDARD II

“During all anesthetics, the patient’s *oxygenation, ventilation, circulation, and temperature* shall be continually evaluated.”

OXYGENATION

- If using anesthesia machine: Inspired gas FiO₂ analyzer + low O₂ concentration alarm
- All anesthetics: Blood oxygenation/Pulse oximetry with variable pitch tone

VENTILATION

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

CIRCULATION

- EKG: Minimum 3 lead; consider 5 lead if any cardiac concerns
- Blood pressure: Minimum cycle q5 minutes
- At least one continuous circulatory assessment: Pulse ox tracing, a line tracing, palpable pulse, auscultation, doppler

TEMPERATURE

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

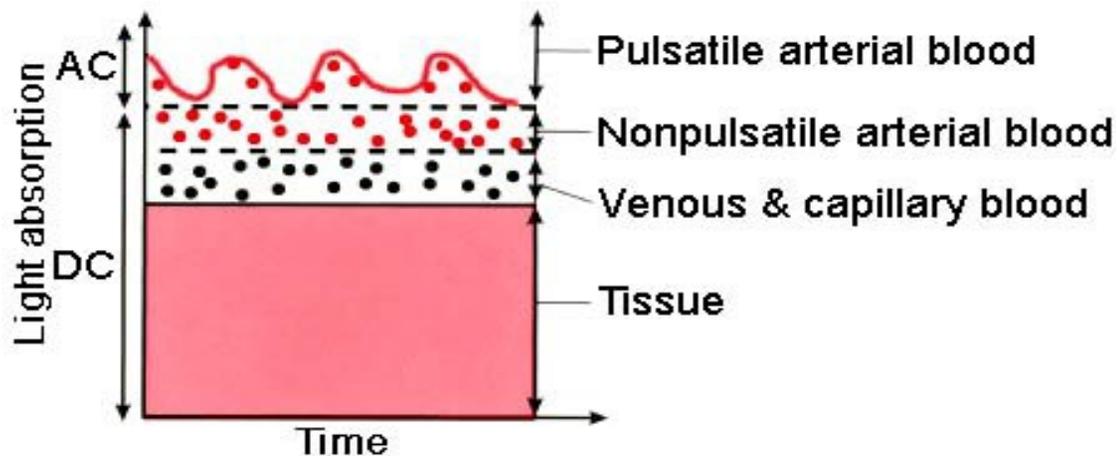
Pulse Oximetry

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% à why a pulse ox not connected to the patient reads usually 85%).



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

Pulse Oximetry Pearls

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

EKG

3-Electrode System

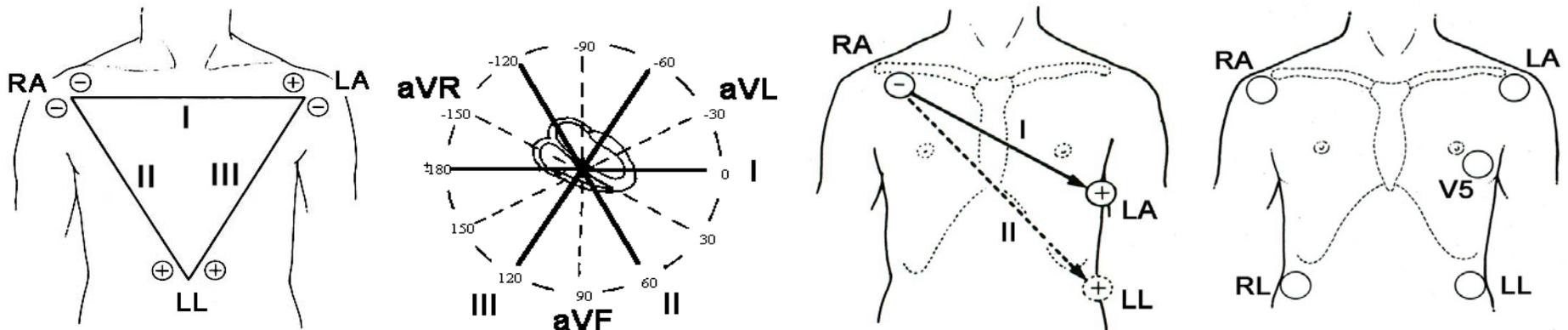
- Allows monitoring of Leads I, II, and III, but only one lead (i.e. electrode pair) can be examined at a time while the 3rd electrode serves as ground.
- Lead II is best for detecting P waves and sinus rhythm.

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.

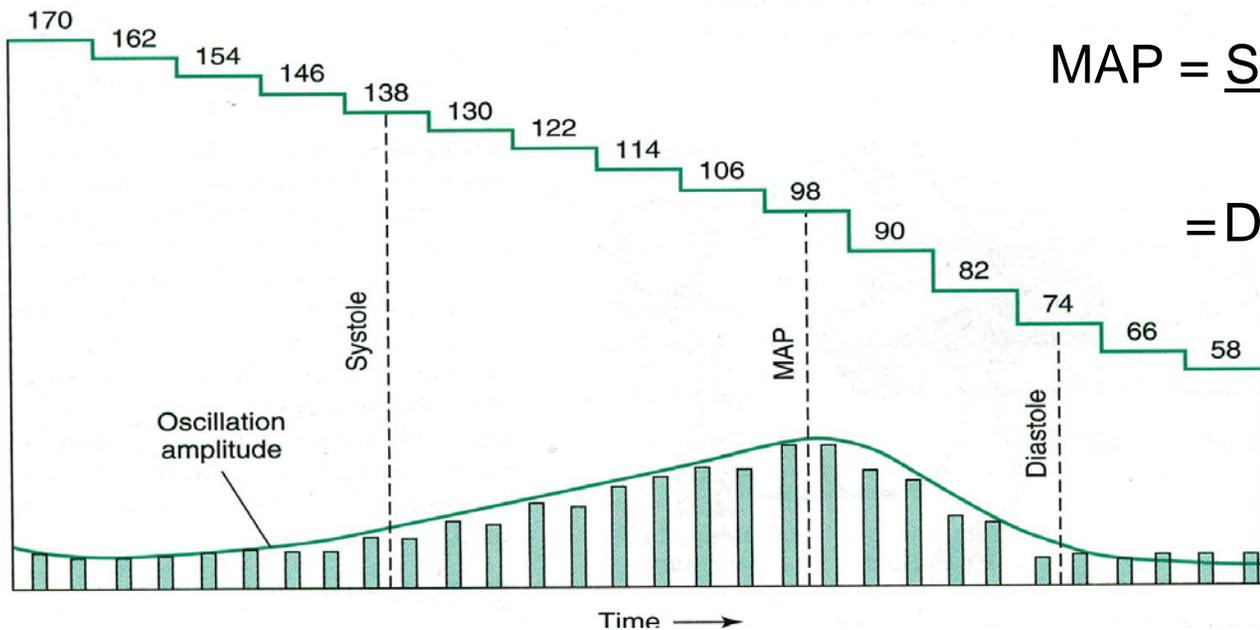
5-Electrode System

- 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 >80% of extremity
Bladder Width should be > 40% arm circumference
- Cuff too small = falsely HIGH BP. Cuff too big = falsely LOW BP.
**Small cuffs have a more detrimental effect than large cuffs on BP accuracy



$$\text{MAP} = \frac{\text{SBP} + 2\text{DBP}}{3}$$
$$= \text{DBP} + \frac{1}{3} * (\text{pulse pressure})$$

Invasive Blood Pressure

Indications

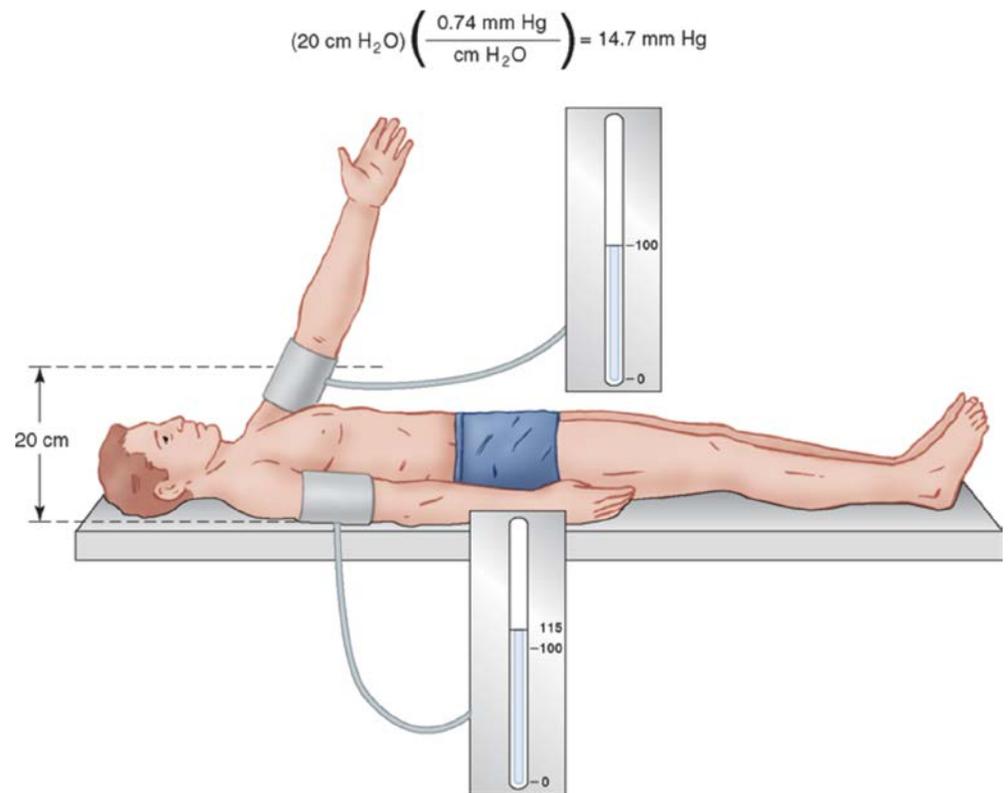
- Moment-to-moment BP changes anticipated and rapid detection is vital.
- Planned pharmacologic or mechanical manipulation.
- Repeated blood sampling.
- Failure of NIBP.
- Supplementary diagnostic information (e.g. pulse pressure variation to guide volume status).

Transducer Setup

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

Blood pressure, cont

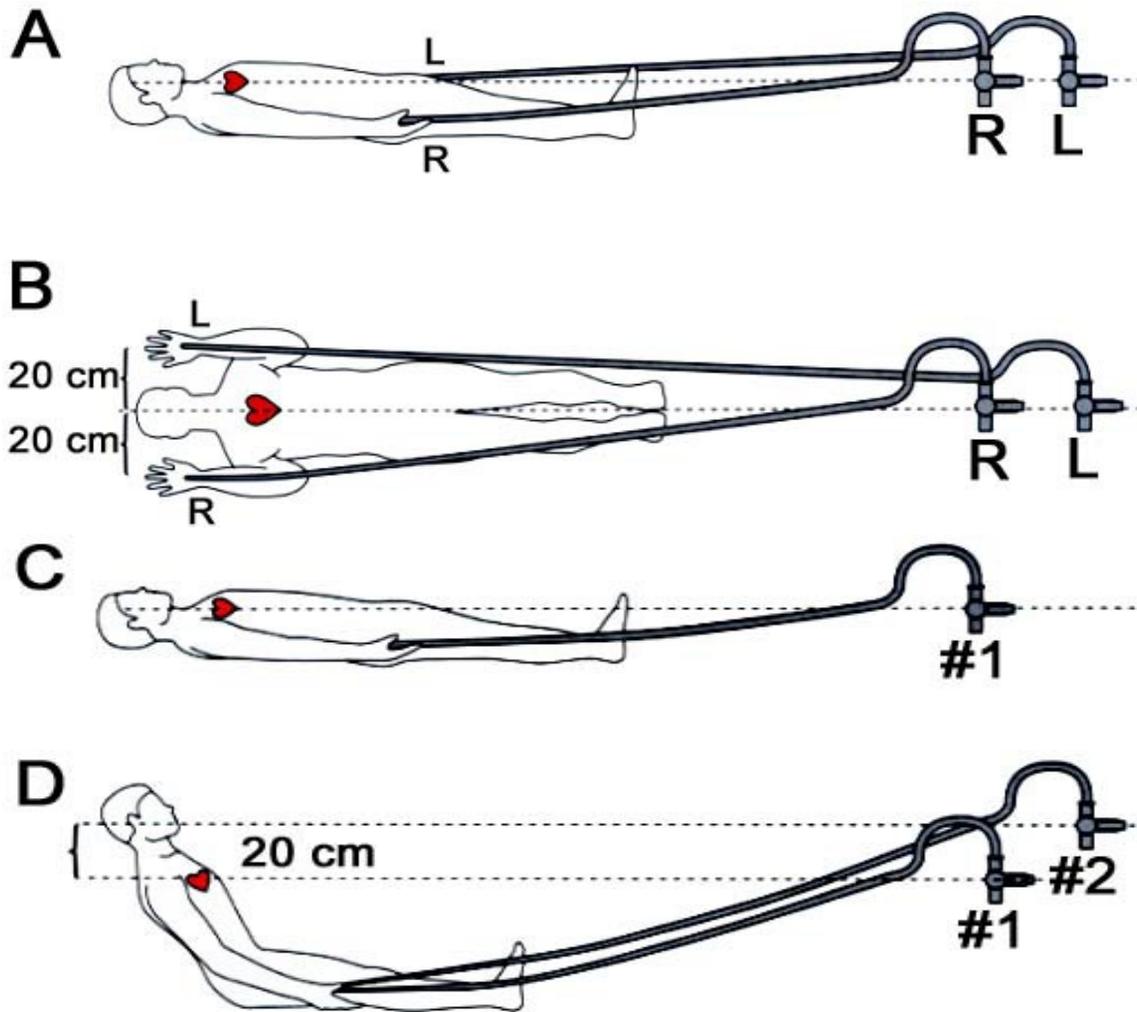
- Systolic amplification: increase in peak systolic pressure as you move away from proximal aorta (caused by reflected waves) is offset by the narrowing of the systolic pressure wave, so the mean arterial pressure remains unchanged.
- BP varies by position: The difference in blood pressure (mm Hg) at two different sites of measurement equals the height of an interposed column of water (cm H₂O) multiplied by a conversion factor (1 cm H₂O = 0.74 mm Hg, or 15 cm height = 10 mm Hg)
 - Mnemonic: pH 7.410 = a change in “p” pressure of 7.4 mm Hg coincides with a “H” height change of 10 cm
- Example: In the Beach chair position, the BP cuff on leg may read 120/80. But if the brain is 60cm vertically higher than the cuff, the BP in the brain would be closer to 75/35



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

Effect of Patient & Transducer Position on BP Measurement

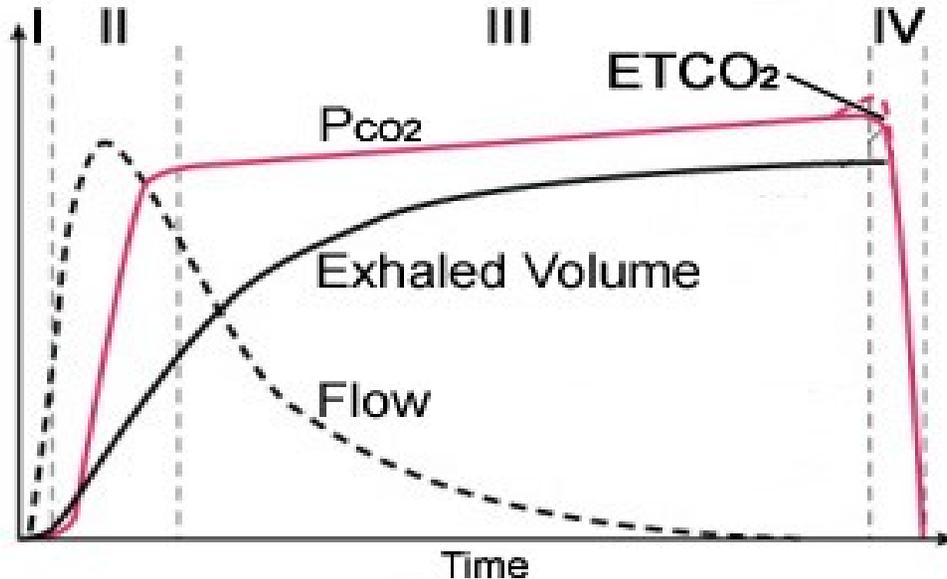


| | R | L |
|----------|--------|-----------|
| A | | |
| ABP | 120/80 | 120/80 |
| NIBP | 120/80 | 120/80 |
| B | | |
| ABP | 120/80 | 120/80 |
| NIBP | 135/95 | 105/65 |
| C | | |
| | #1(RA) | #2(Brain) |
| ABP | 120/80 | |
| D | | |
| ABP | 120/80 | 105/65 |

Remember “pH=7.410”:
 7.4 mm Hg = 10 cm H₂O

Capnography

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



Capnography Phases

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

Capnography

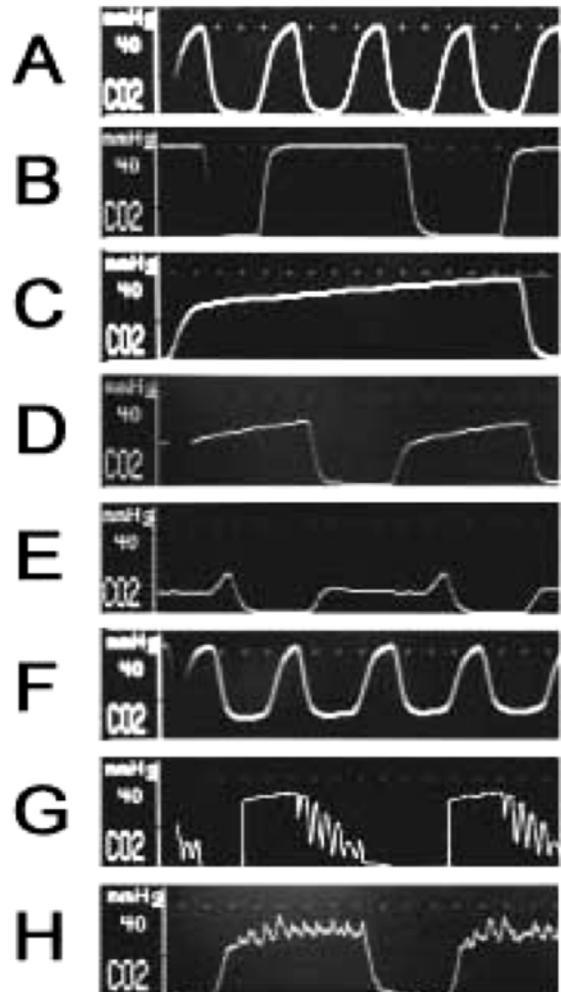
Both the number and tracing provide much physiologic information

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

Clinical pearl:

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

Capnography



Example Traces

- A. Spontaneous ventilation
- B. Mechanical ventilation
- C. Prolonged exhalation (spontaneous)
- D. Emphysema (notice upsloping plateau)
- E. Sample line leak
- F. Exhausted CO₂ absorbant
- G. Cardiogenic oscillations
- H. Electrical noise

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

Temperature

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

Sites

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

*Anticipate heat loss with GA as vasodilation causes blood redistribution from core to periphery. Main cause of heat loss is radiation (but other forms include conduction, convection, evaporation)

Other Monitors/Adjuncts to Consider

Depth of anesthesia:

- BIS monitor/Sedline

Circulation/Fluids:

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

I just intubated, now what?!

Remember your A's

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

References

- ASA. Standards for basic anesthetic monitoring (http://www.asahq.org/publications_and_services/standards/02.pdf). 2015.
- 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

Historical Facts

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



Pharmacokinetics

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

PK: F_I , F_A , and Uptake

- F_I (inspired concentration)
 - Determined by fresh gas flows, volume of breathing system, and absorption by machine/circuit
 - \uparrow fresh gas flow, \downarrow circuit, and \downarrow circuit absorption allow actual F_I to be close to delivered F_I
- F_A (alveolar concentration)
 - Determined by uptake, alveolar ventilation, and concentration/second gas effects
 - P_A (alveolar partial pressure) is determined by input (delivery) minus uptake (loss)
- » Uptake: gas taken up by the pulmonary circulation.
 - Affected by blood solubility, alveolar blood flow (i.e. cardiac output), alveolar-to-venous partial pressure difference
 - \downarrow blood solubility, \downarrow CO, \downarrow alveolar-venous partial pressure difference \rightarrow \downarrow uptake
 - \downarrow uptake \rightarrow $\uparrow F_A/F_I \rightarrow$ faster induction
 - Highly soluble gases = more gas required to saturate blood before it is taken up by CNS
 - High CO = equivalent to a larger tank; have to fill the tank before taken up by CNS

PK: More on Uptake

Alveolar Blood Flow:

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

** Shunt States **

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

- increases alveolar partial pressure, decreases arteriolar partial pressure; dilution from non-ventilated alveoli → slows onset of induction
- will have more significant delay in onset of poorly soluble agents
- IV anesthetics = faster onset (if bypassing lungs, quicker to CNS)

Left to Right Shunt

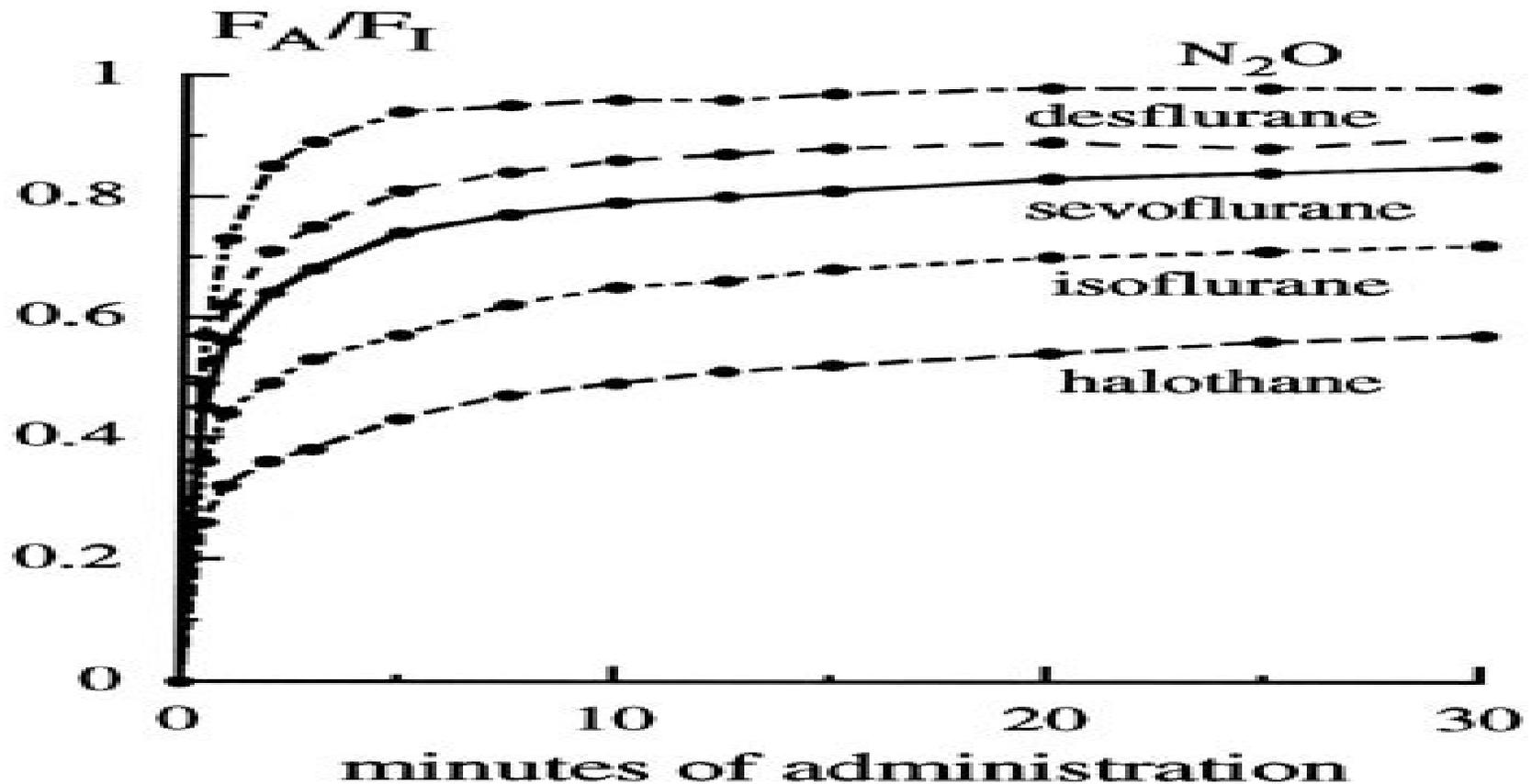
- little effect on speed of induction for IV or inhalation anesthetics

Concentration effect:

- ↑ F_i not only ↑ F_A , but also ↑ rate at which F_A approaches F_i (see following graph)

Second Gas Effect:

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



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

Anesthetic Gas Properties

| | Blood:Gas Partition Coefficient | Partial Pressure (mmHg) at 20°C | MAC |
|---------------|---------------------------------|---------------------------------|-------|
| Nitrous Oxide | 0.47 | ~39000 | 104% |
| Desflurane | 0.42 | 681 | 6% |
| Sevoflurane | 0.69 | 160 | 2.15% |
| Isoflurane | 1.40 | 240 | 1.2% |
| Halothane | 2.3 | 243 | 0.75% |
| Enflurane | 1.8 | 175 | 1.68% |

Example: Blood:gas partition coefficient of nitrous = 0.47 = at steady state 1ml of blood contains 0.47 as much nitrous oxide as does 1 ml of alveolar gas. In other words, at steady state if your fraction inspired gas is 50% N₂O then 1ml of blood will contain 0.47x0.5 ml's of N₂O or 0.235 ml (Jaffe)

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

Pharmacodynamics

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

PD: Shared Properties

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

Nitrous Oxide

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

Isoflurane

- Highly pungent
- Least expensive among clinically used volatile anesthetics
- Second most potent of the clinically used inhalational agents (MAC 1.2%)
- Has been implicated for causing “coronary steal”
 - Dilation of “normal” coronary arteries causing blood to be diverted away from maximally dilated, stenotic vessels to vessels with more adequate perfusion
- Causes vasodilation
 - Decreases BP
 - Increases CBF (usually seen at 1.6 MAC)
 - Minimal compared to halothane
 - Increases ICP (usually at above 1 MAC; short lived)
 - Minimal compared to halothane
- At 2 MAC produces electrically silent EEG

Sevoflurane

- Half as potent as isoflurane (MAC 2.15%)
- Rapid uptake and elimination
- Sweet smelling, non-pungent
 - Popular for inhalational induction
- Can form CO in desiccated CO₂ absorbent
 - Can cause fires
- Forms Compound A in CO₂ absorbent (nephrotoxic in rats)
 - Guidelines recommended to keep fresh gas flows >2 L/min to prevent rebreathing of Compound A (not formation of it)
 - Occurs in alkali such as barium hydroxide lime or soda lime but NOT calcium hydroxide

Desflurane

- Lowest blood:gas solubility coefficient (lower than N₂O)
- Low potency (MAC 6.6%)
- High vapor pressure (669 mmHg) is close to atmospheric pressure therefore boils at sea level
 - Must be stored in a heated, pressurized vaporizer so pressure stays constant (the vaporizer is set to 2 atm).
 - **Remember that the anesthetic effect correlates to the partial pressure, NOT the concentration.
- Very pungent
 - Can cause breath-holding, bronchospasm, laryngospasm, coughing, salivation when administered to an awake patient via face mask
- Can form CO in desiccated CO₂ absorbent (more so than other volatiles)
- 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 8th edition; Miller R.; Churchill Livingstone, 2014
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

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

Never drive on an empty tank.

MAC & Awareness

Minimum Alveolar Concentration

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

Important Points

- Remarkably consistent across species
- MAC mirrors brain partial pressure of agent
 - At equilibrium, brain anesthetic partial pressure = alveolar partial pressure
- MAC is population average, thus not true predictor of individual response (MAC = **ED**₅₀)
 - the **ED**₉₅ is $\pm 25\%$ - so at 1.3 MAC, 95% of patients will not respond to incision
- MAC values are **additive** (e.g. 0.5 MAC iso + 0.5 MAC N₂O = 1 MAC)
- MAC is inversely related to anesthetic potency (lipid solubility)
 - Potency (and lipid solubility) are determined by oil:gas partition coefficient (NOT blood:gas partition coefficient)

MAC of Inhaled Anesthetics

| Gas | Blood:Gas Partition Coefficient | Oil:Gas Partition Coefficient | MAC* |
|------------------|------------------------------------|----------------------------------|-------------|
| Halothane | 2.5 | 197 | 0.75% |
| Enflurane | 1.9 | 98.5 | 1.7% |
| Isoflurane | 1.4 | 90.8 | 1.2% |
| Sevoflurane | 0.65 | 50 | 2.0% |
| N ₂ O | 0.47 | 1.3 | 104% |
| Desflurane | 0.45 | 19 | 6.0% |

*MAC values for adults 36-49 years old

- MAC is indicator of anesthetic **potency**.
 - **Oil:gas partition coefficient** is indicator of anesthetic potency
- Blood:gas partition coefficient is indicator of **solubility**, which affects rate of induction and emergence. It is NOT related to MAC.

More MAC Definitions

MAC_{Awake} (a.k.a. MAC-Aware)

- MAC necessary to prevent response to verbal/tactile stimulation
- Volatiles: ~0.4 MAC; N₂O: ~0.6 MAC

MAC_{Movement}

- 1.0 MAC

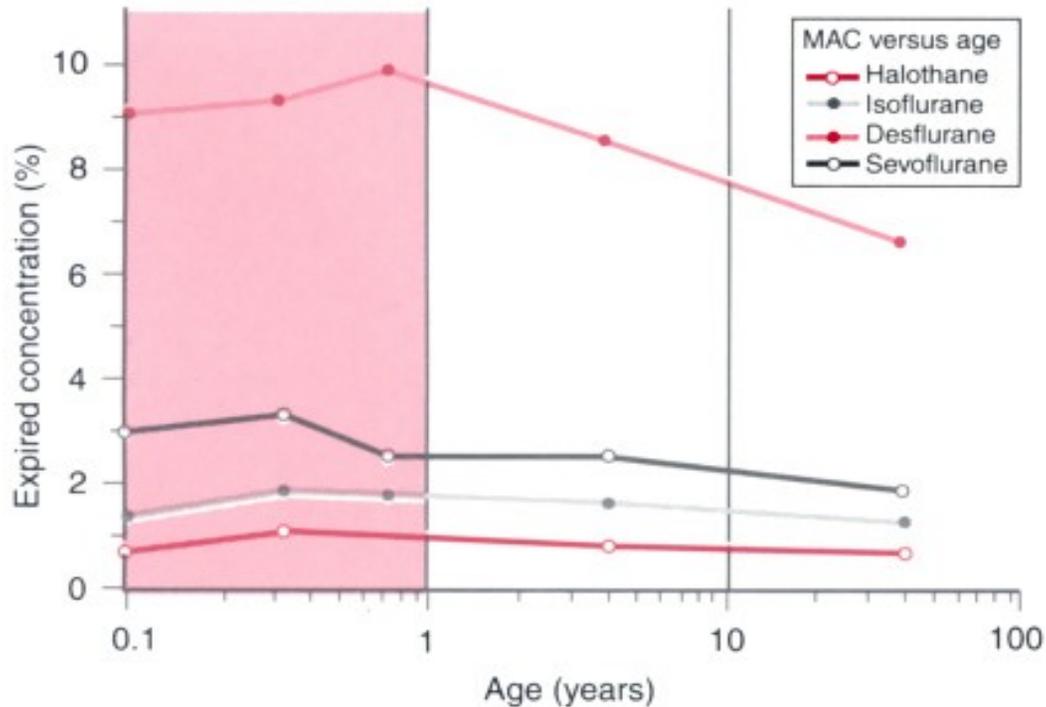
MAC_{EI} (a.k.a. LS, IT, or LMI = laryngoscopy, intubation, LMA insertion)

- MAC necessary to prevent laryngeal response to “endotracheal intubation”
- Prevents movement in 95% of patients (ED₉₅)
- ~1.3 MAC

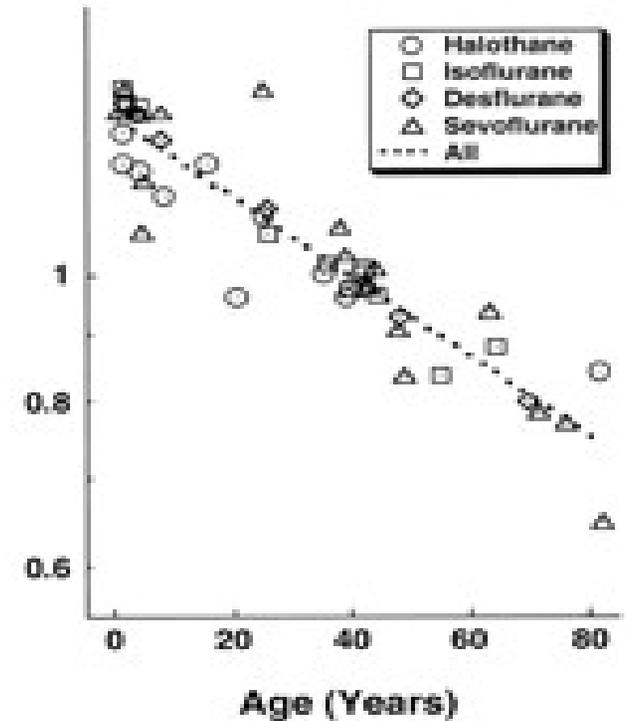
MAC_{BAR}

- MAC necessary to “blunt autonomic response” to noxious stimulus
- Opiates (even small amounts) and N₂O often added to achieve this level and thus spare requirement of high concentrations of halogenated anesthetics
- ~1.6 MAC

Effect of Age on MAC



Fraction of MAC at Age 40 Years



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

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

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

Awareness

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

Signs of Light Anesthesia

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

Preventing Awareness

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

BIS & Sedline

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

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.
- Miller RD, et al. 2014. *Miller's Anesthesia, 8th ed*.
- Murray, MJ, et al. 2015. *Faust's Anesthesiology Review, 4th ed*.

IV Anesthetic Agents

Mechanism of Action

- Most IV anesthetics exert sedative and hypnotic effects via interaction with GABA receptors
 - GABA is primary inhibitory neurotransmitter in CNS
 - Activation of receptor causes increased chloride conductance, and therefore hyperpolarization (promotion of inhibition)
 - Other IV anesthetics exert effect via NMDA receptors (*ketamine*) or alpha-2 receptors (*dexmedetomidine*)
- *Propofol* and *Barbiturates* decrease the rate of dissociation of GABA and its receptor
- *Benzodiazepines* increase the efficiency of GABA-receptor and chloride ion channel coupling

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

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

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

[‡]↓ = decrease; ↑ = increase.

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

Pharmacokinetic Values for the Currently Available Intravenous Sedative–Hypnotic Drugs

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

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

Pharmacodynamics

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

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

Propofol

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

Etomidate

- High incidence of pain on injection
- Induction dose 0.2-0.3 mg/kg
- Rapid onset due to high lipid solubility and large non-ionized fraction at physiologic pH
- Myoclonus, hiccups, thrombophlebitis
- Decreases CMRO₂, CBF, ICP; CPP maintained because less decrease in SBP
- Anticonvulsant properties; but minimal effect on duration of ECT-induced seizure activity
- Maintains hemodynamic stability (even in the presence of pre-existing disease)
 - Does not induce histamine release
- Inhibits adrenocortical synthetic function (11-beta-hydroxylase)
 - Inhibition for 4-8 hours even after a single induction dose; more prominent with infusions
- Increased incidence of PONV

Thiopental

- Highly alkaline (pH 9)
- Can precipitate in acidic solutions (DO NOT MIX with Rocuronium or LR)
- Intra-arterial injection can cause intense vasoconstriction, thrombosis and tissue necrosis; treat with papaverine and lidocaine or regional anesthesia-induced sympathectomy and heparinization
- Induction dose 3-5 mg/kg in adults, 5-6 mg/kg in children, 6-8 mg/kg in infants
- Rapidly redistributed into peripheral compartments
- Larger doses can saturate peripheral compartments -> prolonged duration of action
- Decreases CMRO₂, CBF, ICP
 - Causes EEG burst suppression in larger doses (previously commonly used for neurosurgical procedures)
- Anticonvulsant activity
 - Exception: Methohexital
- Decreases SVR, direct myocardial depressant
- Dose-dependent respiratory depression
- Unlikely to use at Stanford (no longer produced in US) but may use internationally

Ketamine

- Produces a dissociative anesthetic state
 - Profound analgesia and amnesia despite maintenance of consciousness
 - High incidence of psychomimetic reactions (attenuated by co-administration of midazolam)
- Induction dose 1-2 mg/kg
- NMDA antagonist (implications in prevention/treatment of chronic pain)
- Increases CMRO₂, CBF, ICP
 - Contraindicated in neurosurgical procedures
- Most likely to preserve airway reflexes among the IV anesthetics
- Minimal respiratory depression
- Cardio-stimulating effects secondary to direct sympathetic stimulation
 - Can be unmasked in patients with increased sympathetic outflow
 - Negatively effects myocardial oxygen supply-demand ratio
- Intrinsic myocardial depressant, may be significant in severely ill patients with depleted catecholamine reserves
- Increases PVR
- Causes bronchodilation
- Causes increased oral secretions (consider co-admin of glyco)
- Useful for chronic pain patients (common dose for intra-operative management is 0.5-1 mg/kg prior to incision (after intubation, unless using for induction) and then 0.25 mg/kg each hour (infusion or bolus))

Midazolam

- All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant properties (but not analgesia!)
- Premedication dose 0.04-0.08 mg/kg IV (typically 1-2 mg)
- Induction dose 0.1-0.2 mg/kg IV
- Decreases $CMRO_2$, CBF, ICP
 - Does not produce EEG burst suppression
- Decrease SVR and BP when used as induction dose
- Causes dose-dependent respiratory depression
 - Exaggerated when combined with opioids and in patients with chronic respiratory disease
- Flumazenil = specific antagonist
 - Very short acting
 - 45-90 minutes of action following 1-3 mg dose
 - May see re-sedation as benzodiazepine is eliminated more slowly compared to effects of flumazenil

Dexmedetomidine

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

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

Opioid Receptor Subtypes and Their Effects

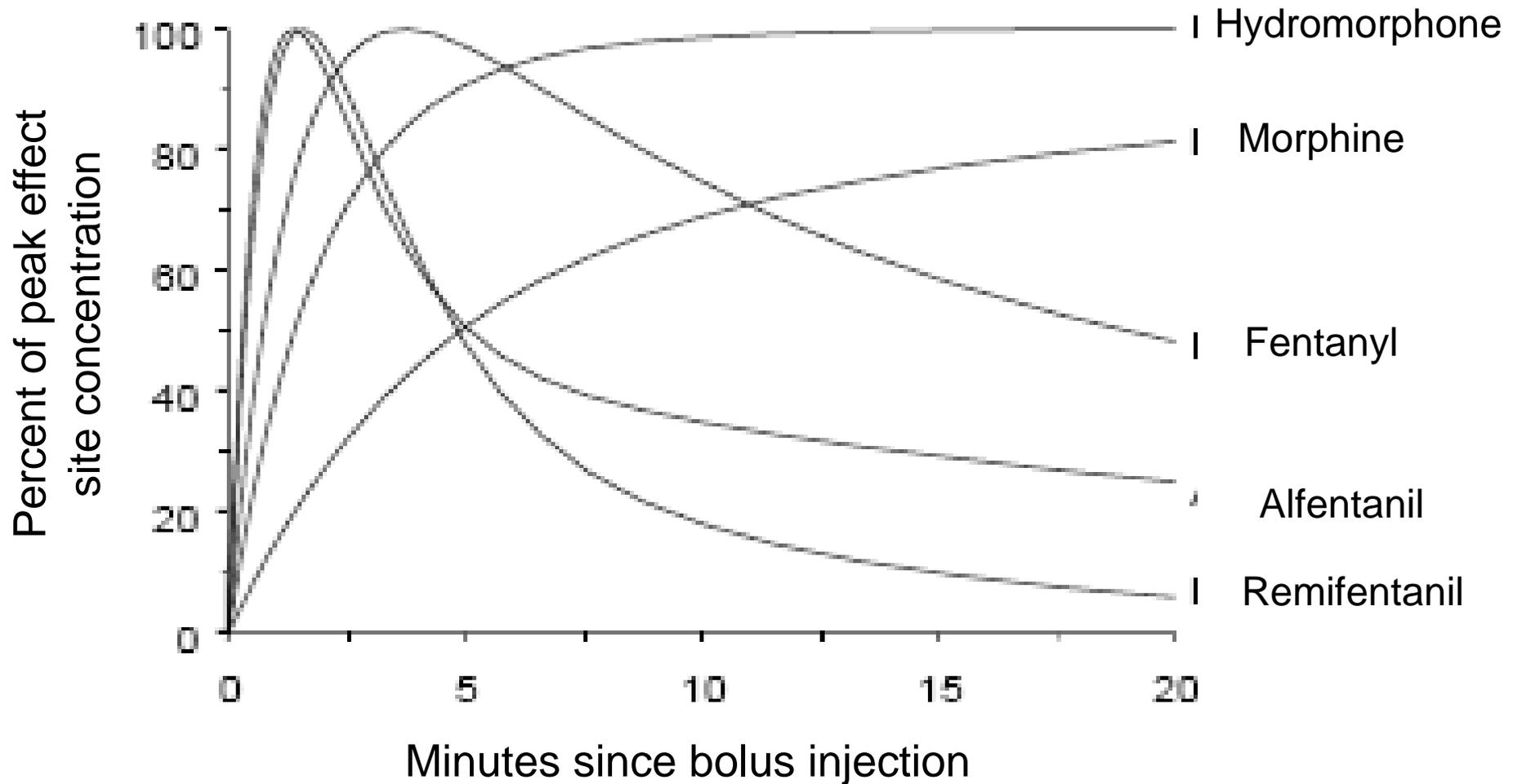
| Receptor | Clinical effect | Agonists |
|----------|---|---|
| μ | Supraspinal (μ 1) Respiratory depression (μ 2) Physical dependence Muscle rigidity | Morphine Met-enkephalin B-Endorphin Fentanyl |
| κ | Sedation Spinal analgesia | Morphine Nalbuphine Butorphanol Dynorphin Oxycodone |
| δ | Analgesia Behavioral Epileptogenic | Leu-enkephalin B-Endorphin |
| σ | Dysphoria Hallucinations | Pentazocine Nalorphine Ketamine |

Opioid comparison

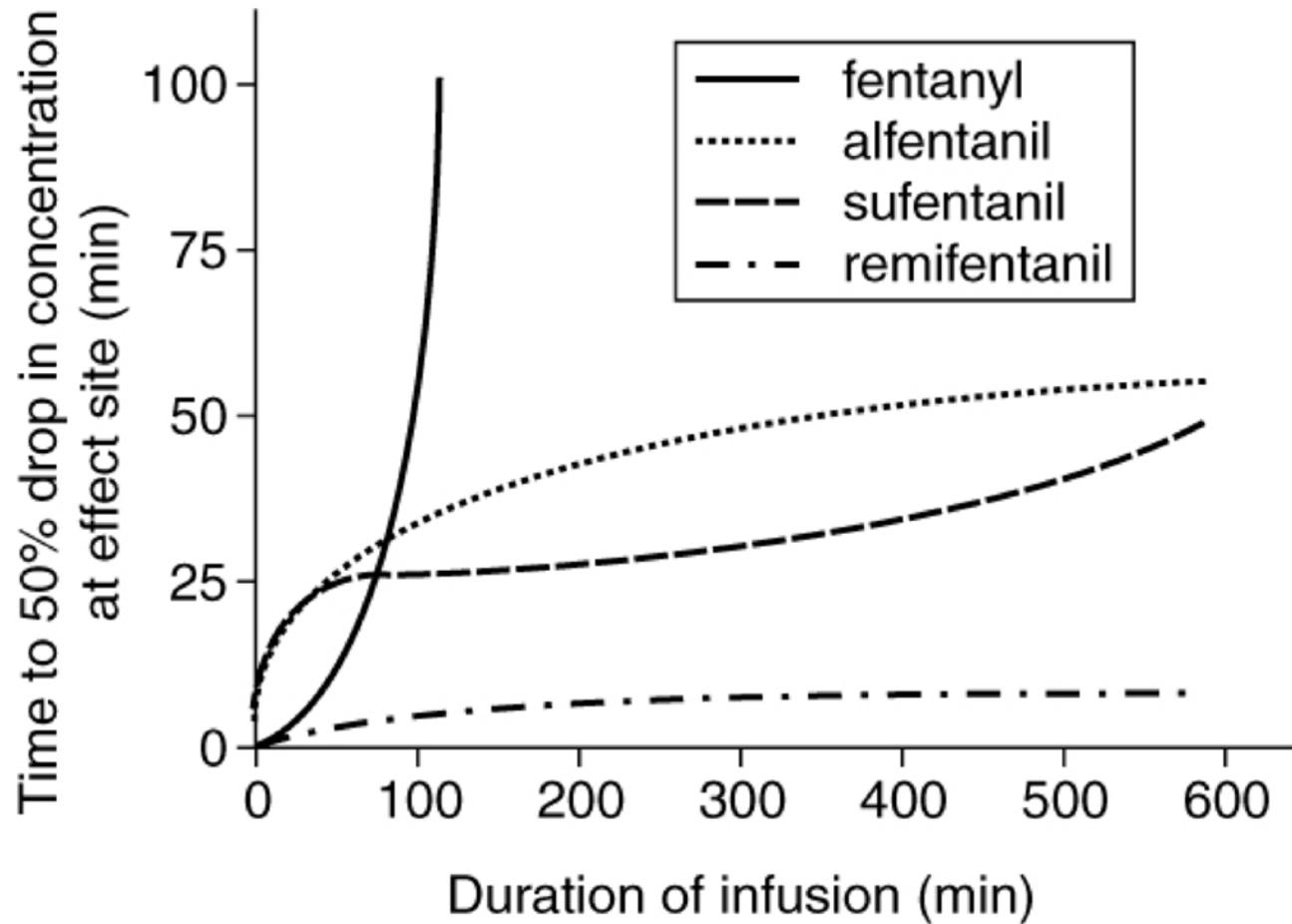
| Drug | Approximate analgesic equivalent | Peak onset | Duration of action (single bolus only!) | Used as infusion |
|---------------|----------------------------------|-------------|---|--------------------|
| Alfentanil | 150-250 mcg | 1 – 2 min | 5 – 10 min | Not common |
| Fentanyl | 50 mcg | 3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

*Infrequently used given long context-sensitive half-life

Single bolus pharmacokinetics



Infusion pharmacokinetics



Special considerations

Fentanyl

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

Special considerations

Hydromorphone

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

Special considerations

Remifentanyl

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

Special considerations

Remifentanil

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

Special considerations

Sufentanil

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

Opioids

Alfentanil

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

Opioids

Morphine

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

Opioids

Methadone

- Longest terminal half-life (about 1 day)
- May accumulate during titration to steady state
 - VERY BAD IDEA TO SEND PATIENTS HOME ON METHADONE
- Supplied as a racemic mixture
 - L methadone is an opioid agonist
 - D methadone is an NMDA antagonist
- Underutilized in anesthesia practice

Opioids

Meperidine (Demerol)

- Bad drug (no role in pain management unless of course you lack other options)
- Most commonly used to treat shivering upon emergence
- Originally discovered as a local anesthetic (“pethidine”)
- Toxic metabolite (**normeperidine**) lowers the seizure threshold; renally excreted
- Anticholinergic side effects: tachycardia
- Avoid using with **MAOIs**; can cause CNS excitation (agitation, hyperpyrexia, rigidity), CNS depression (hypotension, hypoventilation, coma)
 - Libby Zion Law: Demerol interacted with haldol
- Causes histamine release
- Has a euphoric effect with less respiratory depression than other opioids

Rational Opioid Use

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

With that disclaimer in mind, continue reading...

Strategies for Opioid Use

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

Strategies for Opioid Use

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

Strategies for Opioid Use

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

Strategies for Opioid Shortages

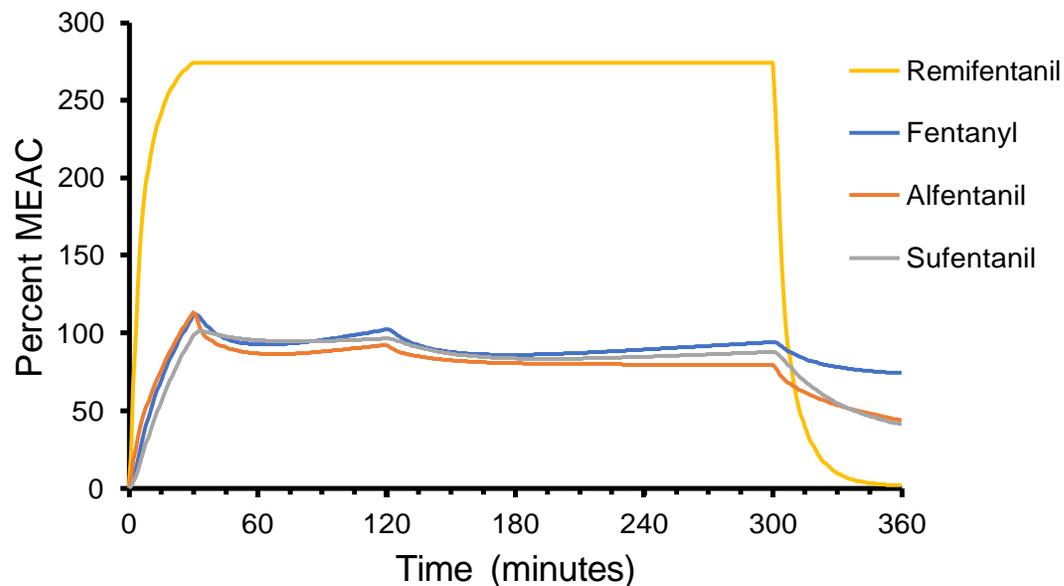
- Recommend **preop multimodal analgesics**:
 - Acetaminophen 1000mg PO (unless liver dz)
 - Gabapentin 600mg PO (reduce dose for impaired renal fxn)
 - One of:
 - Tramadol 100mg PO (unless codeine doesn't work for the patient, i.e. poor 2D6 metabolizer)
 - Oxycodone 10mg PO
- **Intraop opioid boluses**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

| | Induction | Hourly | |
|-----------------|-----------|--------|--|
| Alfentanil (µg) | 500 | 250* | *for fentanyl and alfentanil: first dose at 30 min |
| Meperidine (mg) | 100 | 25 | |
| Methadone (mg) | 5 | 2.5 | |

Strategies for Opioid Shortages

- Intraop opioid infusions

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



References

1. Barash P., Cullen B., Stoelting R. *Clinical Anesthesiology, 7th Ed.* Lippincott Williams and Wilkins, 2013.
2. Butterworth J., Mackey D, Wasnick, J., *Moran and Mikhail's Clinical Anesthesiology, 5th ed.* New York: McGraw Hill, 2013.
3. Fukuda K. Intravenous opioid anesthetics. In Miller RD (ed), *Miller's Anesthesia, 8th ed.* Philadelphia: Elsevier Churchill Livingstone, 2015.
4. 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.
5. 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.
6. Shafer S, 2018. "Perioperative Use of Alfentanil, Meperidine, and Methadone," presented at Stanford University Department of Anesthesia Grand Rounds, March 19, 2018.
7. 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 cardiac output and SVR:
 - **$(MAP - CVP) = CO \times SVR$**

Cardiac Output (CO) = HR x SV

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

Determinants of Blood Pressure

Stroke Volume (SV):

Dependent on 1) preload, 2) afterload, and 3) myocardial contractility.

Preload

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

Afterload

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

Contractility

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

Components of Blood Pressure

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

Blood Pressure Measurement

Non-Invasive Blood Pressure (NIBP)

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

Invasive Arterial Blood Pressure (IABP)

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

Intraoperative Hypertension: DDX

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

Treatment of Hypertension

- **Temporize** with fast-onset, short-acting drugs
- Diagnose and treat the **underlying cause**.
- Pharmacologic Interventions:
 - Deepen anesthesia:
 - Propofol or volatile anesthetics
 - Opioids (increase analgesia, histamine release causes hypotension)
 - Short-acting vasodilators
 - Clevidipine
 - Calcium-channel blocker.
 - In a lipid emulsion (looks like propofol)
 - Nitroglycerin (venous > arterial dilatation)
 - Nitroprusside (arterial > venous); very expensive; risk for cyanide toxicity
 - Avoid both NTG and NTP in setting of intracerebral hemorrhage (cerebral vasodilator)
 - Beta-blockers
 - Labetalol
 - Esmolol, affects HR >> BP
 - Long-acting vasodilators
 - Hydralazine – Less predictable pharmacokinetics & pharmacodynamics

Antihypertensive comparison

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

Intraoperative Hypotension Causes

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

Treatment of Hypotension

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

Antihypotensive comparison

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

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.
- Marino PL. Arterial Pressure Monitoring. In *The ICU Book, 4th ed.* Philadelphia: Lippincott Williams & Wilkins, 2014.
- Morris RW Watterson LM Westhorpe RN Webb RK. Crisis management during anaesthesia: hypotension. *Qual Saf Health Care* 2005;14:e11
- Stoelting RK and Miller RD. *Basics of Anesthesia, 4th ed.* Philadelphia: Churchill Livingstone, 2000.

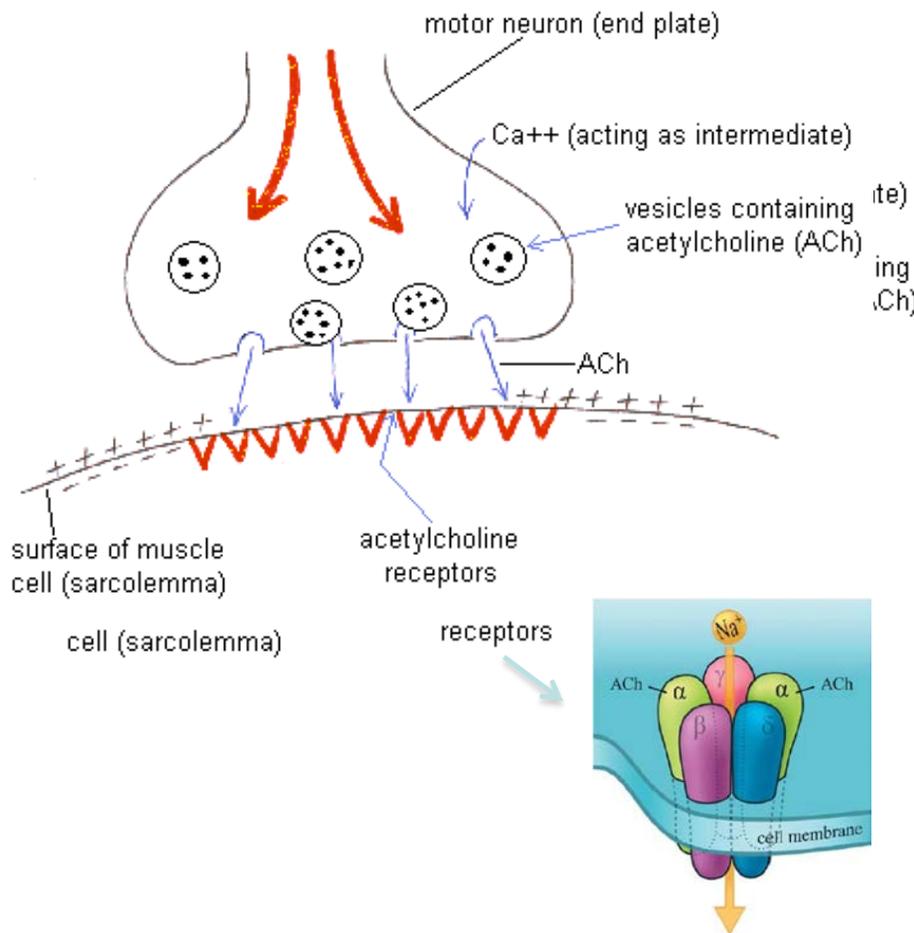
Neuromuscular Blocking Agents

Introduction

- Neuromuscular blocking agents (NMBA) are used to facilitate intubation, mechanical ventilation, and surgical relaxation
- There are two categories of NMBAs with distinct properties:
 - Depolarizing (succinylcholine)
 - Non-depolarizing (eg. rocuronium, vecuronium, cisatracurium).
- Postoperative residual paralysis occurs frequently. Monitoring of neuromuscular blockade and pharmacological reversal are standard of care.¹
- NMBAs should be used carefully; there are also many surgical and patient-specific contraindications. Neuromuscular blocking agents play a prominent role in the incidence of adverse reactions that occur during anesthesia. The Committee on Safety of Medicines in the United Kingdom reported that 10.8% (218 of 2014) of adverse drug reactions and 7.3% of deaths (21 of 286) were attributable to neuromuscular blocking drugs.
- Nondepolarizing agents account for >50% cases of intraoperative anaphylaxis (incidence <0.1%). Cross-reactivity has been reported between neuromuscular blocking drugs and food, cosmetics, disinfectants, and industrial materials (anaphylaxis can happen on a patient's first exposure to the drug).

Neuromuscular Transmission

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



Depolarizing NMBA: Succinylcholine

- **Structure:** two ACh molecules joined by methyl groups
- **Mechanism of action:** ACh receptor agonist and prolonged muscle depolarization
- **Intubating Dose:** 1 – 1.5 mg/kg (*1.5 – 2.0 if using a defasciculating dose of rocuronium)
- **Onset:** within 30-60 sec; duration ~10 min depending on dose
- Diffuses away to extracellular fluid → then rapidly metabolized by pseudocholinesterase (aka: plasma cholinesterase, butyrylcholinesterase)
- ~1:3000 individuals are homozygous for an abnormal plasma cholinesterase; paralysis can last 3-8 hours. Consider checking twitches before giving nondepolarizing NMBA after sux.
- **Dibucaine number:** percentage of pseudocholinesterase inhibited by dibucaine; dibucaine inhibits *normal* pseudocholinesterase
 - 80 for normal pseudocholinesterase; 20 for abnormal homozygous pseudocholinesterase deficiency (50 for heterozygote)

Contraindications to Sux

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

Additional Side Effects

- Fasciculations. (can be decreased with **defasciculating dose of rocuronium = 0.3 mg/kg** 3 minutes prior to sux)
- Myalgia: **Less frequent** in children, ages 50-60 years old, and those with good muscular training. **More frequent** in women and ambulatory patients.
- Bradycardia (especially in children -- often given with atropine).
- Tachycardia
- Anaphylaxis (approx. 1:5000 – 1:10,000)
- Trismus
- Increased ICP & IOP
- Increased intragastric pressure and lower esophageal sphincter pressure.

Nondepolarizing NMBA

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

Nondepolarizing NMBA (cont.)

- Intubating doses are **2 x ED₉₅** (ED₉₅ = average dose required to produce 95% suppression of the twitch height in 50% of population).
- A larger intubating dose speeds onset time but lengthens duration of block.
- **Priming dose:** to increase speed of onset, can give 10% of intubating dose 3-5 minutes prior to administering actual intubating dose (efficacy debatable).
- Wide interindividual response to nondepolarizing agents. Monitor twitches and adjust doses accordingly.
- **Rocuronium can be used for rapid sequence inductions** when sux cannot, although roc is still slower. However, the increased 1 – 1.2mg/kg rocuronium necessary for RSI causes prolonged relaxation.
- Cisatracurium is degraded via **Hoffman elimination**. It can be useful for patients with hepatic or renal dysfunction.

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

*Vecuronium's 3-OH metabolite (80% potency) accumulates in renal failure. Rocuronium however does not have any active metabolites

**Recovery of neuromuscular function takes place as plasma concentrations decline, and the greater part of this decrease initially occurs primarily because of distribution after initial drug administration. After a large or repeated dose, recovery relies more on elimination

**Rocuronium has lower molar potency (requires a larger mg/kg dose) and in effect has faster onset (i.e. it equilibrates faster from plasma to the neuromuscular junction)

NMBA Monitoring

- The **train-of-four (TOF) ratio** is the common modality of monitoring nondepolarizing NMBA. The number of twitches and the ratio between the 4th and 1st twitch are measured with the TOF.
- In the OR, we often monitor twitch # and twitch height with sight or feel – which is not nearly as accurate as mechanomyography or accelerometry.
 - A patient with “four strong twitches” can still misleadingly have significant weakness.
 - A **TOF of 0.9** (when comparing 4th to 1st twitch) is considered fully strong. Similarly, 5 seconds of **sustained tetanus** at 50-100 Hz with no fade indicates full recovery.
 - Human hand is incapable to reliably measure and differentiate TOF ratios greater than 0.6
- Surgical relaxation can be achieved when the patient has 2-3 twitches though this depends on the surgical site and the nerve being monitored. NMBA with the goal to achieve beyond zero twitching (i.e. “negative twitches”) is controversial.

NMBA Monitoring

- The **train-of-four (TOF) ratio** is the common modality of monitoring nondepolarizing NMBA. The number of twitches and the ratio between the 4th and 1st twitch are measured with the TOF.
- In the OR, we often monitor twitch # and twitch height with sight or feel – which is not nearly as accurate as mechanomyography or accelerometry.
 - A patient with “four strong twitches” can still misleadingly have significant weakness.
 - A **TOF of 0.9** (when comparing 4th to 1st twitch) is an endpoint of recovery. Similarly, 5 seconds of **sustained tetanus** at 50-100 Hz with no fade indicates full recovery.
 - The human hand is incapable to reliably measure and differentiate TOF ratios greater than 0.6!
- Surgical relaxation can be achieved when the patient has 2-3 twitches though this depends on the surgical site and the nerve being monitored. NMBA with the goal to achieve beyond zero twitching (i.e. “negative twitches”) is controversial.

Depolarizing vs Nondepolarizing NMBA Monitoring

| Normal Stimulus | Depolarizing Block | | Nondepolarizing Block |
|--------------------------|-------------------------|----------|-----------------------|
| | Phase I | Phase II | |
| Train-of-four | Constant but diminished | Fade | Fade |
| Tetany | Constant but diminished | Fade | Fade |
| Double-burst (DBS) | Constant but diminished | Fade | Fade |
| Posttetanic potentiation | Absent | Present | Present |

An aside about sux:

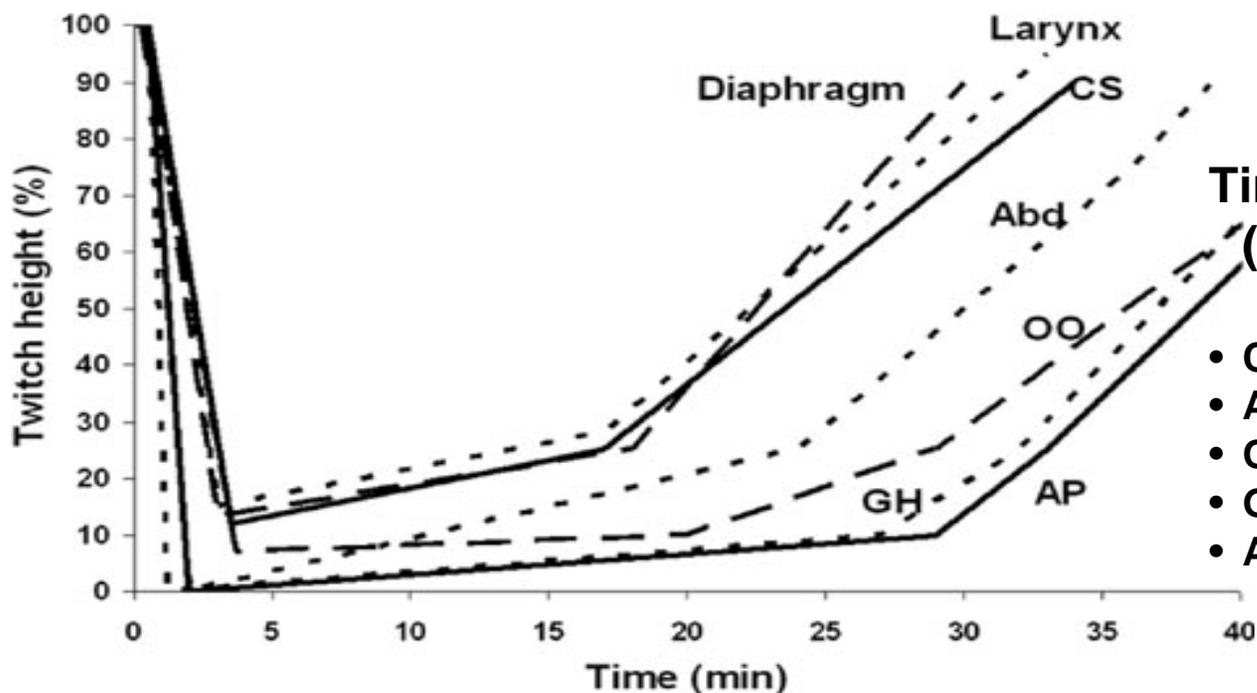
Phase I block is typical for a single bolus of sux.

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

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

Variability in NMBA Monitoring

- Variability in muscle blockade (most resistant è most sensitive): vocal cords > diaphragm > corrugator supercilii > abdominal muscles > adductor pollicis > pharyngeal muscles
- To assess deep blockade (ablate any breathing or diaphragmatic movement): monitor **corrugator supercilii**. However, to assess return of function of pharyngeal muscles and readiness for extubation: monitor **adductor pollicis**
- If placing electrodes on the face, you may stimulate facial muscles directly and may be fooled.



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

Nondepolarizing NMBA Reversal

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

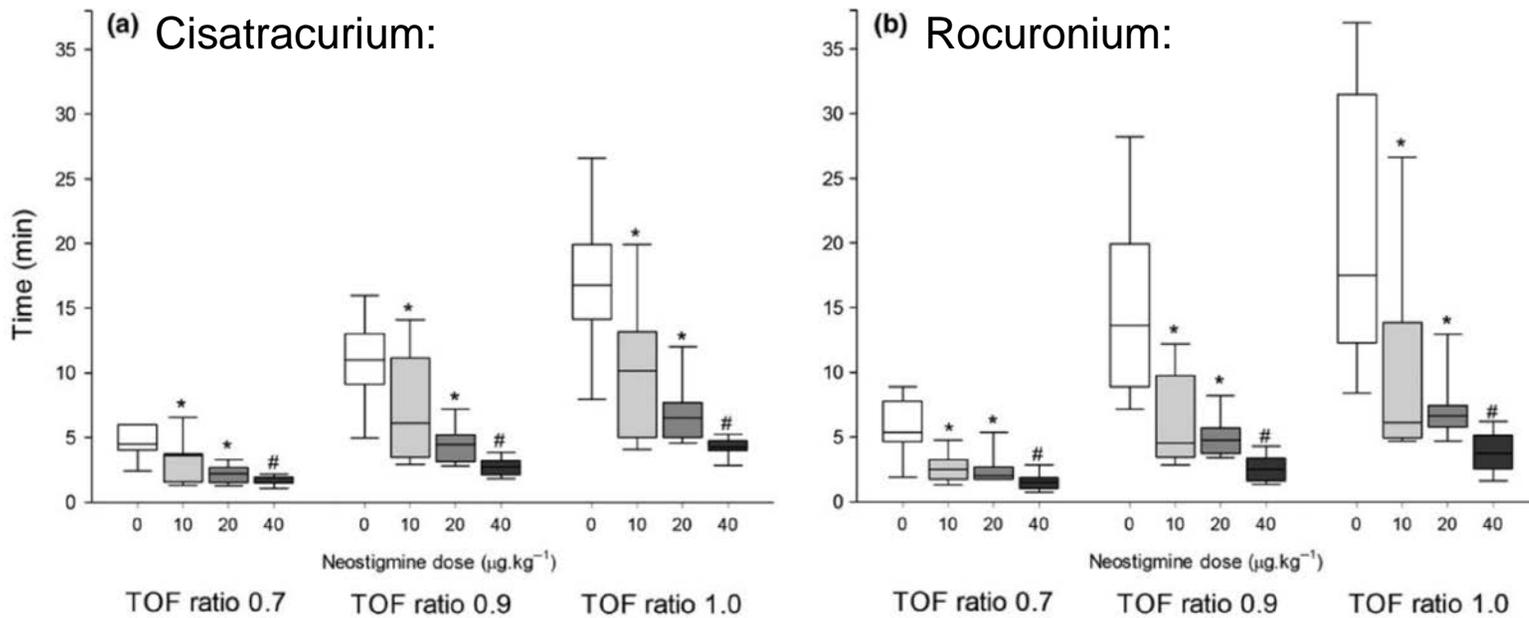


Figure 2 Times to reach the stated train-of-four (TOF) ratio of 0.7, 0.9 and 1.0 after receiving 0, 10, 20 or 40 $\mu\text{g.kg}^{-1}$ of neostigmine at a TOF ratio of 0.5 after the use of cisatracurium (a) or rocuronium (b). Horizontal line = median; box = IQR; whiskers = 5th–95th percentile. * $p 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

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

Nondepolarizing NMBA Reversal

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

Sugammadex

- A modified γ -cyclodextrin with a hollow truncated core that traps rocuronium & vecuronium for a more rapid and effective blockade reversal.
- Examples of indications to use sugammadex:
 - “Cannot intubate, cannot ventilate”: after receiving a 1.2mg/kg dose of rocuronium, a 16mg/kg dose of sugammadex decreases time to full recovery from 122 minutes to <2 minutes.
 - Neuromuscular blockade is too deep or inadequately reversed by neostigmine
 - For surgery during pregnancy it may be preferable to use sugammadex rather than neostigmine as sugammadex does not cross the placenta.
 - Gaining increased use as routine reversal agent given less side effects, faster onset, and cheaper cost than combined neostigmine & glycopyrrolate

Sugammadex (Cont.)

- Per the Committee on Quality, Efficiency and Patient Satisfaction (QEP) at Stanford Anesthesia Department:

Recommended Dosages

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

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

- Caution:*
 - Patients **using hormonal contraceptives** must use an additional, non-hormonal method of contraception for the next 7 days.
 - Not recommended in patients with **severe renal insufficiency or dialysis**, albeit the complex is removed with hemodialysis
 - PTT and PT** will be prolonged by ~ 25% for up to 60 minutes.
 - Do not mix in line with ondansetron, verapamil, and ranitidine.
 - Anaphylaxis reported as 0.3% (seen in 1 healthy volunteer with study N=375)
 - During post-marketing use, spontaneous reports of anaphylaxis occurred with approximately 0.01% of sugammadex doses.

Important Facts to Know

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

Intra-op Discussion Topics

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

References

- 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.
- Choi ES et al. Optimum dose of neostigmine to reverse shallow neuromuscular blockade with rocuronium and cisatracurium. *Anesthesia*, 2016, 71, 443–449.
- 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.
- Min KC et al. Incidence of hypersensitivity and anaphylaxis with sugammadex. *J Clin Anesth.* 2018 Jun; 47:67-73.
- Mohamed Naguib M, Lien CA. Chapter 29, Pharmacology of Muscle Relaxants and Their Antagonists in *Miller's Anesthesia* (8th edition), 2015. Elsevier inc.
- 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.
- Sokół-Kobielska, E. Sugammadex — indications and clinical use. *Anaesthesiol Intensive Ther.* 2013 Apr-Jun;45(2):106-10.
- 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.

Difficult Airway Algorithm

Difficult Airway Algorithm

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

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

Difficult Airway Algorithm

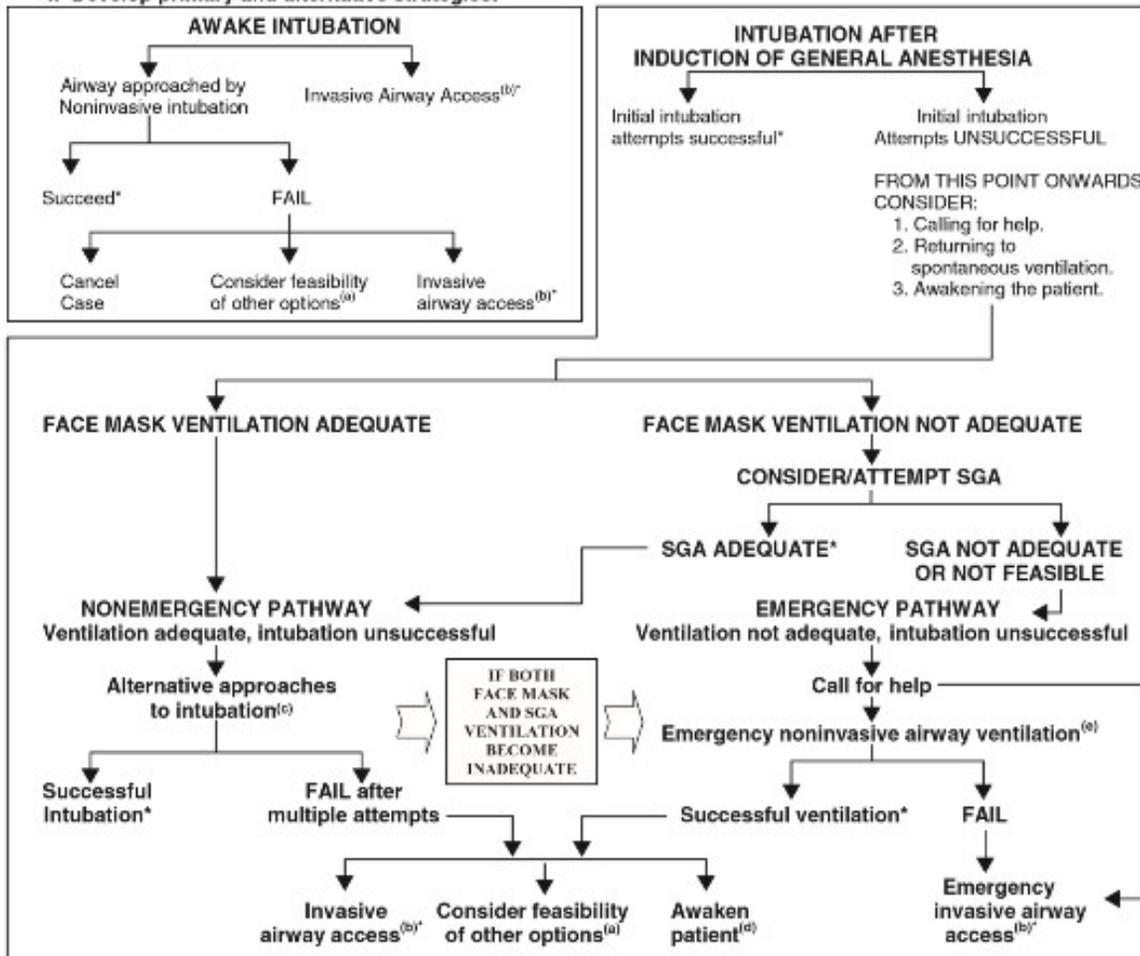
STEPS: *(verbatim from the 2013 ASA Practice Guidelines)*

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

Difficult Airway Algorithm

STEPS: (continued...)

4. Develop primary and alternative strategies:



Please note:

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

*Confirm ventilation, tracheal intubation, or SGA placement with exhaled CO₂.

Difficult Airway Algorithm

BE PREPARED!

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



VS



Difficult Airway Algorithm

STEP 1: Assess the Likelihood of Airway Management Problems:

Any possible difficulty with:

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

Difficult Airway Algorithm

STEP 1: Assess the Likelihood of Airway Management Problems

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

DIFFICULT Mask Ventilation

“MaMaBOATS”

- **M**allampati III or IV
- **M**andibular protrusion decreased
- **B**eard
- **O**besity (BMI > 30 kg/m²)
- **A**ge >57-58
- **T**eeth (Lack of)
- **S**norning

IMPOSSIBLE Mask Ventilation

“MaMaBORa”

- **M**allampati III-IV
- **M**ales
- **B**eard
- **O**SA or Upper Airway Surgery
- **R**adiation changes (neck)

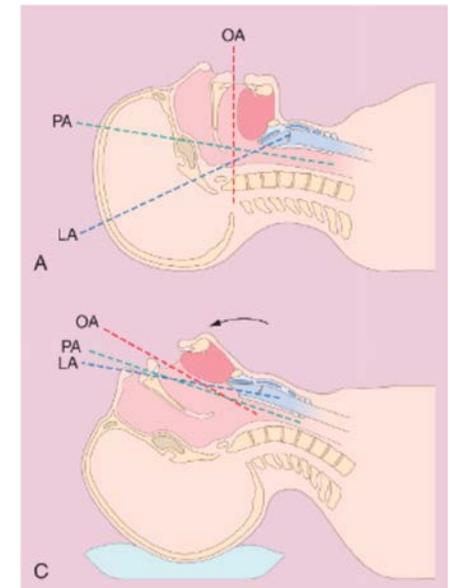
And of course... History of prior difficulty

Difficult Airway Algorithm

STEP 1: Assess the Likelihood of Airway Management Problems

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

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



And of course... History of prior difficulty

Difficult Airway Algorithm

STEP 1: Assess the Likelihood of Airway Management Problems

Difficulty with Patient Cooperation

- Age
- Mental capacity
- Level of consciousness
- Intoxication

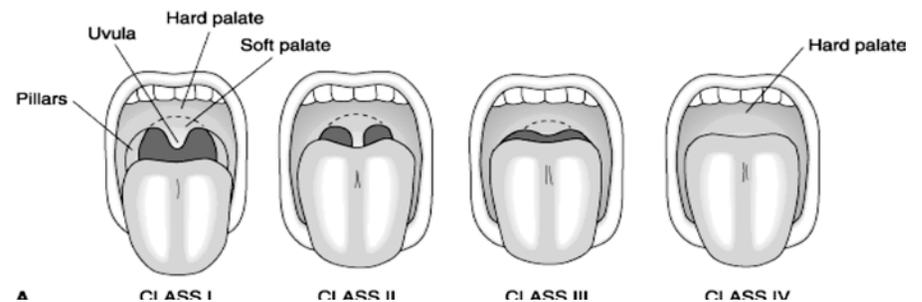
Predictors of Supraglottic Airway Failure

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

Difficult Surgical Airway Access

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

Mallampati Score Assessment



Difficult Airway Algorithm

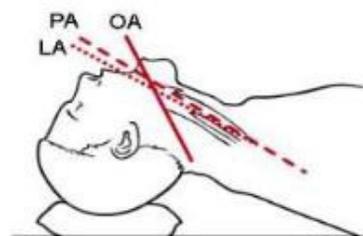
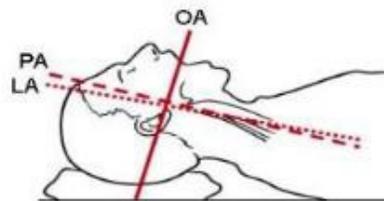
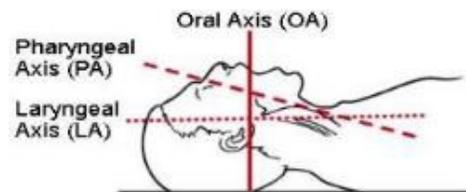
STEP 2: Attempt to Oxygenate the Patient throughout the Process

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

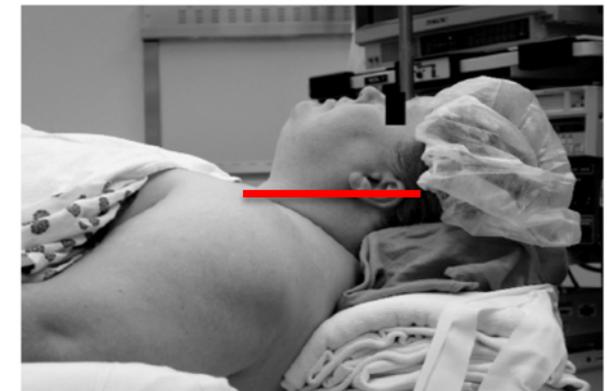
Difficult Airway Algorithm

Obtaining the Sniffing Position

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



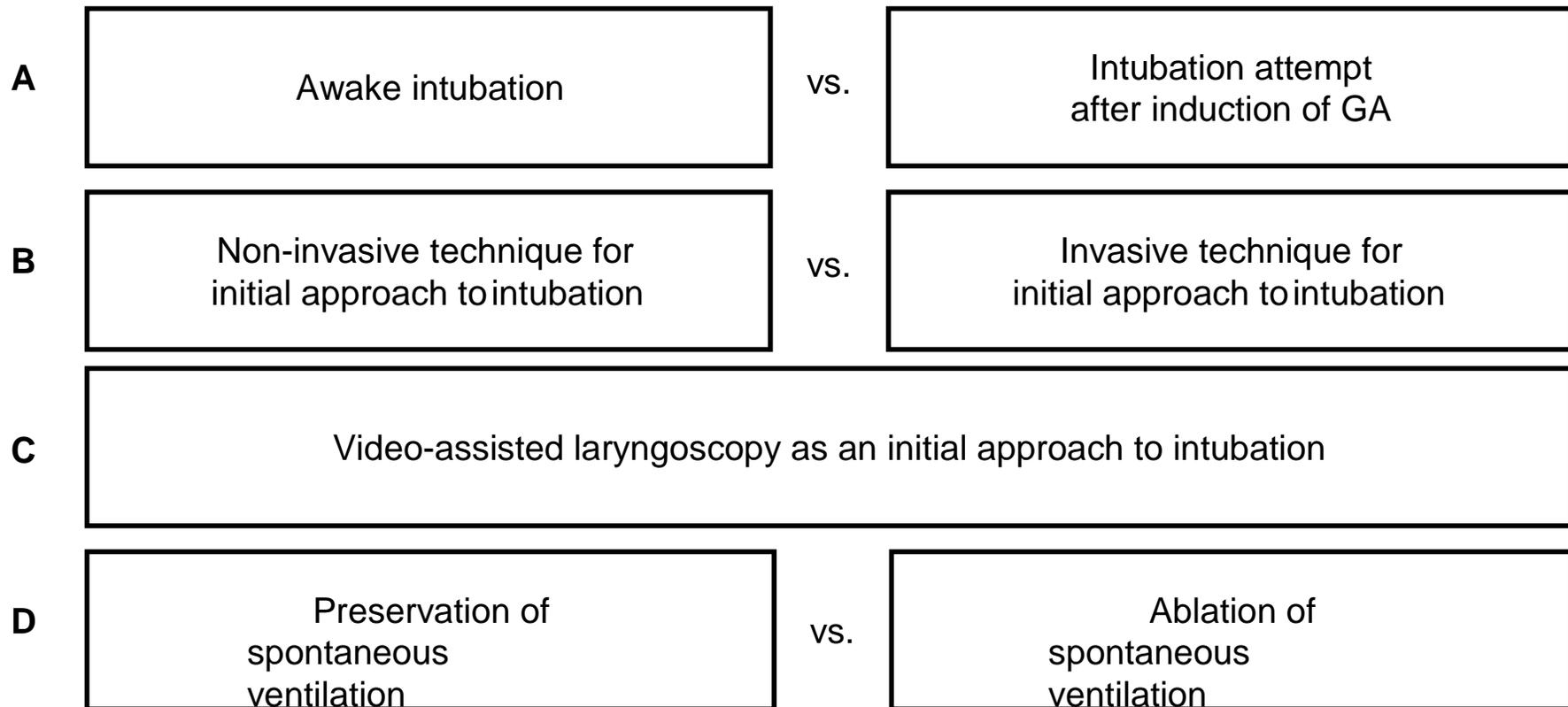
Head elevation helps to align PA & LA before DL



Ramp obese patients until tragus is aligned with sternum

Difficult Airway Algorithm

STEP 3: Think Broadly About Your Management Options

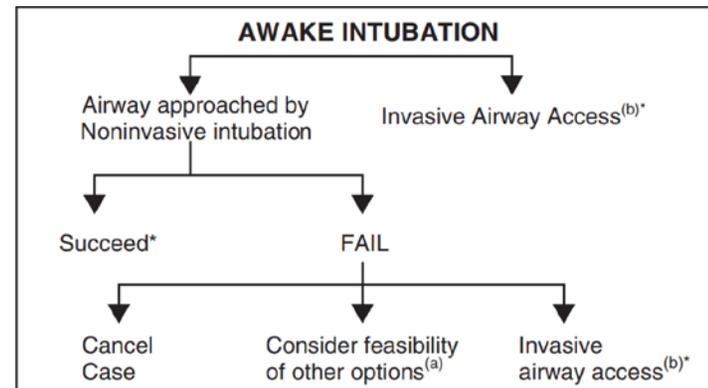


Difficult Airway Algorithm

STEP 4: Awake vs. Post-induction Algorithms

Awake Intubation

- Invasive options include tracheostomy or cricothyroidotomy with local anesthesia, and retrograde intubation
- Non-invasive options include fiberoptic intubation, but also Video and Direct laryngoscopy
 - The airway can be coated in local anesthetic (inhaled, directly sprayed, or swished around by the patient) or you can perform select nerve blocks
 - A fully-awake patient can tolerate a Glidescope if the airway is properly topicalized!



Difficult Airway Algorithm

STEP 4: Awake vs. Post-induction Algorithms

Post-Induction Intubation

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

Difficult Airway Algorithm

STEP 4: Awake vs. Post-induction Algorithms

Post-Induction Intubation – Non-emergency Pathway

- Your initial attempt at intubation failed. Ventilation is adequate, so you may wake the patient up, or try alternative airway management approaches
- Alternative approaches include:
 - Using an SGA throughout the case
 - Video-assisted laryngoscopy
 - Fiberoptic intubation
 - Light wand
 - Blind nasal intubation
 - Intubating SGA
- Limit direct laryngoscopy attempts. Don't repeat the same DL attempt – change blades or positioning
- Throughout all of this, be *very* careful to avoid causing airway trauma – the oropharynx and larynx are delicate, and bleeding and swelling may turn a maskable airway into a “Cannot Intubate, Cannot Oxygenate” emergency.

Difficult Airway Algorithm

STEP 4: Awake vs. Post-induction Algorithms

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

- Your initial attempt at intubation failed. So now *if at any time* ventilation becomes inadequate, you enter the Emergency Pathway:
 - You should already have called for help. If not, do so now.
 - Perform emergency noninvasive airway ventilation
 - Try a different SGA
 - Place a Combitube
 - Use apneic oxygenation (e.g. Optiflow)
 - Perform rigid bronchoscopy
 - Perform emergency invasive airway access *before* the SpO₂ drops
 - Cricothyrotomy
 - Surgical tracheostomy
 - Trans-tracheal jetventilation

Now review the ASA Difficult Airway Algorithm flow chart from earlier in this chapter. It should be much more comprehensible. If not, repeat these slides until it is.

Difficult Airway Algorithm

The Vortex Approach

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



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

Difficult Airway Algorithm

A Few Comments on Surgical Airways

- From an ENT Chief Resident:
 - Even in an emergency, *always* invest 20 seconds to do three things:
 - Identify someone to **assist**
 - Place a **shoulder roll** to expose the trachea
 - Point a **light source** at the exposed trachea
- Cannula-based aka percutaneous techniques have a far higher failure rate than **surgical techniques**, which are successful greater than 90% of the time
- Learn a simple, quick method and know how and where to get the tools you need.
- Emergency surgical airway access can be performed in under 60 seconds with just a #20 scalpel on a handle, a Trousseau dilator or clamp, and an ETT over a Bougie introducer
- You will get to practice the procedure on an animal model during your training!

Difficult Airway Algorithm

Clinical Pearls

- Call for help early!
- Anticipate difficulties
- Be prepared with the proper thoughtful mindset
- Be prepared with tested equipment
- Always pre-oxygenate the patient to buy yourself safe apneic time
- The first DL attempt is the best attempt
- If two DL attempts fail, move on to another approach
- Understand the pharmacokinetics of your induction and paralytic meds

References

- Difficult/Impossible Mask Ventilation Acronyms courtesy of Dr. Vladimir Nekhendzy
- ASA Task Force on Management of the Difficult Airway. 2013. Practice guidelines for management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on Management of Difficult Airway. *Anesthesiology*, **118**.
- 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.
- El-Orbany M, Woehlck H. 2009. Difficult mask Ventilation. International Anesthesia Research Society, 109: 1870-1880
- Gal TJ. Airway Management. In Miller RD (ed), *Miller's Anesthesia, 6th ed*. Philadelphia: Elsevier Churchill Livingstone, 2005.
- Holmes et al. 1998 paper "Comparison of 2 Cricothyrotomy techniques"
- Langeron O, Masso E, Huraux C, et al. 2000. Prediction of difficult mask ventilation. *Anesthesiology*, **92**: 1229-36.
- 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.
- Stackhouse RA, Infosino A. Airway Management. In Miller RD (ed), *Basics of Anesthesia, 6th ed*. Philadelphia: Elsevier Churchill Livingstone, 2011.

Fluid Management



Evaluation of Intravascular Volume

HPI

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

Physical Exam

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

Labs/Studies

- *Hypovolemia*: rising Hct, contraction alkalosis then metabolic acidosis, Ur specific gravity > 1.010, Urine Na < 10, Urine Osm > 450, hypernatremia, BUN:Cr > 10:1; bedside ultrasound (IVC <1.7cm OR 1.7cm with >50% IVCCI)
- *Hypervolemia*: increased pulmonary vascular markings on CXR

Intraoperative Intravascular Assessment

Monitor trends and compare multiple modalities to confirm clinical impressions

Vitals

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

Foley Catheter

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

Arterial Line

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

Intraoperative Intravascular Assessment

Monitor trends and compare multiple modalities to confirm clinical impressions

Central Venous Catheter

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

Pulmonary Artery Catheter

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

Transesophageal Echocardiogram

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

Body Fluid Compartments

Males: Total Body Water = weight x 60%

Females: Total Body Water = weight x 50%

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

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

┌──────────────────────────────────┐
Extracellular 20% of weight

*Values shown for a 70kg male

Remember the **5 – 15 – 40 Rule**:

5% weight is intravascular water, 15% is interstitial, 40% is intracellular

All other calculation can be extrapolated from this

Physiologic Regulation of Extracellular Fluid Volume

Aldosterone

- Enhances sodium reabsorption
- Increases intravascular volume

Antidiuretic Hormone/Vasopressin

- Enhances water reabsorption

Atrial Natriuretic Peptide

- Enhances sodium and water excretion

Crystalloids

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

Advantages

Disadvantages

- NS**
- Preferred in brain injury/swelling (hyperosmolar)
 - Preferred for diluting pRBCs
- LR**
- More physiologic ("balanced crystalloid")
 - Lactate is converted to HCO₃⁻ by liver

- In large volumes produces **hyperchloremic metabolic acidosis**
- Hyperchloremia → low GFR and risk AKI
- Watch K⁺ in renal patients
- Ca²⁺ may interfere with citrate's chelating properties of pRBCs (debated if this is clinically relevant)

Colloids

Use

- Initial intravascular volume resuscitation with crystalloid administration inadequate or when you expect to give over 3-4L of crystalloid for fluid resuscitation
 - $\frac{1}{2}$ life is 3-6 hrs vs 20-30 minutes for crystalloids
- Patients with large protein losses and decreased oncotic pressure (ie cirrhotic patients and burn patients)
- Fluid resuscitation in hemorrhagic shock when blood is not initially available - give 1cc colloid for every cc of blood lost
- Concern that continued crystalloid may cause volume overload in certain clinical situations (e.g. pulmonary edema, bowel edema)

Mechanism

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

Colloids

Albumin (5% and 25%)

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

Hetastarch (6% hydroxyethyl starch, HES)

* RARELY used; may encounter on OB rotation at LPCH

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

Crystalloid or Colloid?

| | Advantages | Disadvantages |
|--------------------|--|--|
| Crystalloid | <ul style="list-style-type: none">• Lower cost• Readily available | <ul style="list-style-type: none">• Requires more volume for the same hemodynamic effect• Short IV $t_{1/2}$ (20-30 min)• Dilutes plasma proteins \Rightarrow peripheral/pulmonary edema |
| Colloid | <ul style="list-style-type: none">• 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 | <ul style="list-style-type: none">• Expensive• Coagulopathy (dextran > HES)• Potential renal complications• May cause cerebral edema (in areas of injured brain where BBB not intact) |

"Classical" Fluid Management

Maintenance

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

Preexisting Fluid Deficits

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

Ongoing Losses

Evaporative and Interstitial Losses (capillary leak)

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

Blood Loss

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

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

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

Suggestions for Fluid Management

Tailor management to patient, surgery, and clinical scenario

Use a balanced approach

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

Liberal vs. Restrictive Management

Consequences of Volume Overload

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

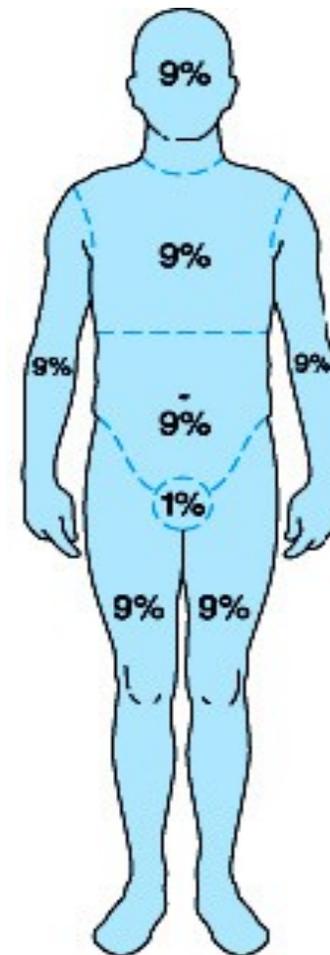
Suggestions for Rational Fluid Management

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

Burns

- Increased evaporative losses
- H₂O, electrolytes, and protein shift from normal to burned tissue causing intravascular hypovolemia
- Volume to infuse is calculated by the Parkland Formula:

$$\text{Volume} = \underline{\%BSA \times 4 \text{ ml/kg} \times \text{kg}}$$
- Give 1/2 over the 1st 8 hours
- Give 1/2 over the next 16 hours
- Replace with **Lactated Ringers**
- %BSA is determined by the "Rule of Nines"



Posterior surface of upper trunk = 9%.

Posterior surface of lower trunk = 9%.

*Hand = 1%.

Posterior surface of each leg = 9%.

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

Intraoperative Oliguria

Pre-renal (decreased renal perfusion)

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

Post-renal (post-renal obstruction)

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

Renal

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

Treatments

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

References

- Barash, Paul G., et. al. *Handbook of Clinical Anesthesia, 7th ed.* Philadelphia: Lippincott Williams & Wilkins, 2013.
- 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.
- 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.
- P. Panera, et al.. The RUSH exam: Rapid Ultrasound in SHock in the evaluation of the critically ill. *Emerg Med Clin North Am.* 2010 Feb;28(1):29-56

Transfusion Therapy

Type and Screen

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

- Type: test ABO-Rh antigens on RBC
 - Recipient RBCs tested with anti-A&B and anti-D (Rh) antibodies
- Screen: indirect Coomb's test to assess for antibodies in recipients serum
 - Recipient serum mixed with RBCs of known antigens
 - no agglutination = negative screen
 - If antibody screen is positive: the serum is tested further
- Use when there is a low likelihood of transfusion. If you give blood in an emergency situation (only a T&S and no crossmatch available), risk of a serious hemolytic reaction is <1%

Type and Crossmatch

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

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

Packed Red Blood Cells

Definition, Use, & Storage

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

Packed Red Blood Cells

Indications (ASA Guidelines)

1. Hg < 6 in *young, healthy patients*
2. Usually unnecessary when Hg >10
3. At Hgb 6-10 g/dl, the decision to transfuse is based on:
 - Ongoing indications of organ ischemia
 - Potential for ongoing blood loss
 - Volume status
 - Risk factors for complications of inadequate O₂
 - Example: myocardial ischemia

Platelets

Definition, Use, & Storage

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

Indications (ASA Guidelines)

1. Rarely when plt > 100,000
2. Usually when plt < 50,000 (spontaneous bleed at < 20K)
3. When plt 50-100,000, based on risk of bleeding
4. With platelet dysfunction (e.g. CPB, plt inhibitors, renal dysfunction)

Fresh Frozen Plasma

Definition, Use, & Storage

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

Indications (ASA Guidelines)

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

Cryoprecipitate

Definition, Use, & Storage

- Fraction of plasma that precipitates when FFP is thawed
- Contains Factors I (fibrinogen), VIII, XIII and vWF
- 1 unit contains ~5X more fibrinogen than 1 unit FFP
- Typically, **0.1 units/kg** would be expected to increase the fibrinogen concentration by **100 mg/dL**
- Use within 4-6 hours after thawed if you want to replace Factor VIII

Indications (ASA Guidelines)

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

Equations

Arterial O₂ Content

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

Allowable Blood Loss

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

Volume to Transfuse

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

Estimated Blood Volume (ml/kg)

| | |
|-----------|-----|
| Preemie | 100 |
| Term | 90 |
| < 1 year | 80 |
| 1-6 years | 75 |
| Male | 70 |
| Female | 65 |
| Obese | ≤60 |

Ordering Products

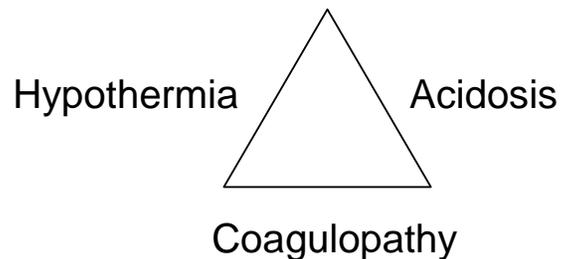
- Consider special needs of the patient:
 - Special populations to consider:
 - Cancer patients, BMT recipients, pregnant patients, solid organ transplant patients, those at risk of volume overload, patients with immunodeficiencies
- Examples of special requests of blood products with certain populations: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

Massive Transfusion

Definition and Use

- Administration of greater than 1 blood volume (~10 units) in 24 hours
- At Stanford, calling the blood bank for the Massive Transfusion Guideline (MTG) will get you **6 pRBCs, 4 FFP, and 1 unit of platelets**
- May take *up to 30 minutes* to have blood prepared and picked up for OR use. Plan ahead and use closed-loop communication with support staff.
- Also consider location, getting blood in the ASC or OB department takes much longer than the MOR
- Typically will utilize Belmont, Level 1 or both for rapid infusion

Lethal Triad of Trauma:



Massive Transfusion

Complications

1. Hypothermia

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

2. Coagulopathy

a. Dilutional thrombocytopenia

- Platelet count likely $<100,000$ after ~ 10 units pRBCs

b. Dilutional coagulopathies

- $\hat{=}$ Factors V & VIII (“labile factors”) in stored blood

3. Citrate Toxicity

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

Massive Transfusion

Complications, cont

4. Acid-Base Abnormalities

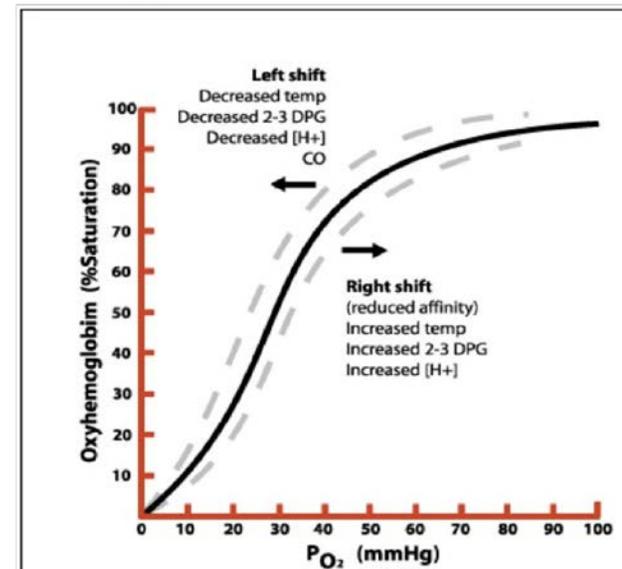
- At 21 days, stored blood has pH <7.0, due mostly to CO₂ production, which can be rapidly eliminated with respiration
- Acidosis more commonly occurs due to \hat{e} tissue perfusion

5. Hyperkalemia

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

6. Impaired O₂-Delivery Capacity

- 2,3-DPG decreases in stored blood, causing a left-shifted O₂-Hb dissociation curve rendering Hgb to hold on to & not release as much oxygen at target sites



Transfusion-Related Infections

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

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

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

Transfusion Reactions

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

Transfusion Reactions

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

Febrile Non-Hemolytic Reaction

- Due to recipient reaction to residual donor WBCs or platelets
- Benign; occurs with 0.5-1% of transfusions
- Treatment: Tylenol, Benadryl, slow transfusion, prevention by giving a patient leukoreduced blood

Anaphylactic Reaction

- Occurs within minutes; life-threatening
- Usually associated with **IgA deficiency**- they have IgA antibodies
- Signs/Symptoms: shock, angioedema, ARDS
- Treatment:
 - 1) Stop blood
 - 2) Give fluids, Epi, antihistamines, ACLS
- In a patient with known IgA deficiency, get washed blood (it reduces the amount of plasma proteins and immunoglobins)

Transfusion Reactions

- **Acute Hemolytic Reaction**

- Due to ABO incompatibility
- Symptoms: fever, chills, flank pain usually masked by GA; watch for unexplained tachycardia and hypotension, diffuse oozing and brown urine; monitor for ARF and DIC
- Treatment:
 - 1) Stop Blood products
 - 2) Maintain alkaline UOP (bicard, mannitol, Lasix/crystalloid), supportive care

- **Delayed Hemolytic Reaction**

- Due to antibodies (not anti-A or anti-B) to antigens on donor RBCs
- More insidious, develops on day 2-21

- **TACO (Transfusion Associated Circulatory Overload)**

- Can order volume reduced blood for those with severe CHF

Transfusion-Related Acute Lung Injury (TRALI)

- Occurs 4-6 hours after transfusion
- Due to plasma-containing products (platelets and FFP > pRBCs) - **usually donor antibodies reacting to recipient leukocytes**
- Incidence: 1:1100 (but likely under-reported)
- Mortality 5-10% - Leading cause of transfusion-related mortality
- Signs & symptoms
 - Dyspnea, hypoxemia, hypotension, fever, pulmonary edema
- Diagnosis of exclusion
 - First rule out sepsis, volume overload, and cardiogenic pulmonary edema
- Treatment
 - Supportive care, similar to ARDS (O₂, mechanical ventilation, tidal volume 6-8 cc/kg)
 - Diuretics are not indicated (etiology = microvascular leak, not fluid overload)

Alternative Strategies for Management of Blood Loss During Surgery

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

References

- <http://transfusionmedicine.stanford.edu/>
- ASA Task Force on Perioperative Blood Management. 2015. Practice guidelines for perioperative blood management. *Anesthesiology*, **122**:241-75.
- Goodnough LT. 2003. Risks of blood transfusion. *Crit Care Med*, **31**: S678-86.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 5th ed.* New York: McGraw-Hill Companies, Inc., 2013.

Hypoxemia

Causes of Hypoxemia

| | $P_a\text{CO}_2$ | A-a Gradient | DLCO | Corrects w/ supplemental O_2 ? |
|---------------------------|------------------|--------------|--------|---|
| Low inspired O_2 | Normal | Normal | Normal | Yes |
| Hypoventilation | ↑ | Normal | Normal | Yes |
| Diffusion Impairment | Normal | ↑ | ↓ | Yes |
| Shunt | Normal | ↑ | Normal | No |
| V/Q Mismatch | Normal / ↓ | ↑ | Normal | Yes |

Shunt: perfusion without ventilaton ($V/Q=0$); see ↓ $p\text{O}_2$. No increase in $p\text{CO}_2$ (2/2 chemoreceptor mediated hyperventilation) until shunt fraction → 50%

Dead Space: ventilation without perfusion ($V/Q=\infty$); see ↑ $p\text{CO}_2$

Equations

Alveolar-arterial (A-a) Gradient

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

Alveolar Gas Equation

$$\begin{aligned} P_AO_2 &= F_iO_2 (P_{atm} - P_{H_2O}) - (P_aCO_2 / 0.8) \\ &= 0.21 (760 - 47) - (40 / 0.8) \\ &\approx \underline{100 \text{ mm Hg}} \end{aligned}$$

Normal A-a Gradient:

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

Normal P_aO_2 :

- 103 - age/3

Causes of Hypoxemia

1. Low inspired O₂

- Altitude (normal F_iO₂, decreased barometric pressure)
- Hypoxic F_iO₂ gas mixture (crossed gas lines, loss of pipeline pressure)

2. Hypoventilation

- Drugs (opioids, benzodiazepines, barbiturates), chest wall damage (e.g. splinting from rib fx, neuromuscular diseases, obstruction (e.g. OSA, upper airway compression))
- Very responsive to supplemental O₂ - (PaCO₂/0.8) term of alveolar gas equation becomes insignificant at higher FiO₂ even with relatively high PaCO₂.
 - FiO₂ 21%
 - PaCO₂ 40 → PAO₂ = 0.21(760-47) - 40/0.8 ≈ **100mmHg** → **SpO₂ 100%**
 - PaCO₂ 80 → PAO₂ = 0.21(760-47) - 80/0.8 ≈ **50mmHg** → **SpO₂ 80%**
 - FiO₂ 30%
 - PaCO₂ 40 → PAO₂ = 0.3(760-47) - 40/0.8 ≈ **160mmHg** → **SpO₂ 100%**
 - PaCO₂ 80 → PAO₂ = 0.3(760-47) - 80/0.8 ≈ **115mmHg** → **SpO₂ 100%**

3. Diffusion Impairment

- Increased diffusion pathway (e.g. pulmonary edema, fibrosis)
- Decreased surface area (e.g. emphysema, pneumonectomy)
- Decreased rate of O₂-Hb association (e.g. high CO, anemia, PE)

Causes of Hypoxemia

4. R → L Shunt (i.e. perfusion w/o ventilation; $V/Q = 0$)

- Congenital (e.g. TOF, TA, ASD/VSD/PDA w/ Eisenmengers)
- AVM (AVF, congenital)
- Pulmonary fluid (pneumonia, CHF, ARDS, NPPE, TACO, TRALI)
- Atelectasis (mucus plugging, GA)
- Endobronchial intubation (ETT is “mainstemmed”)

5. V/Q Mismatch

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

6. Mixed Process

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

Hypoxemia in the OR

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

Suggestion: *Alveoli → Machine*

1. Listen to the lungs

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

2. Check ETT

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

Hypoxemia in the OR

3. Check circuit

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

4. Check machine

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

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

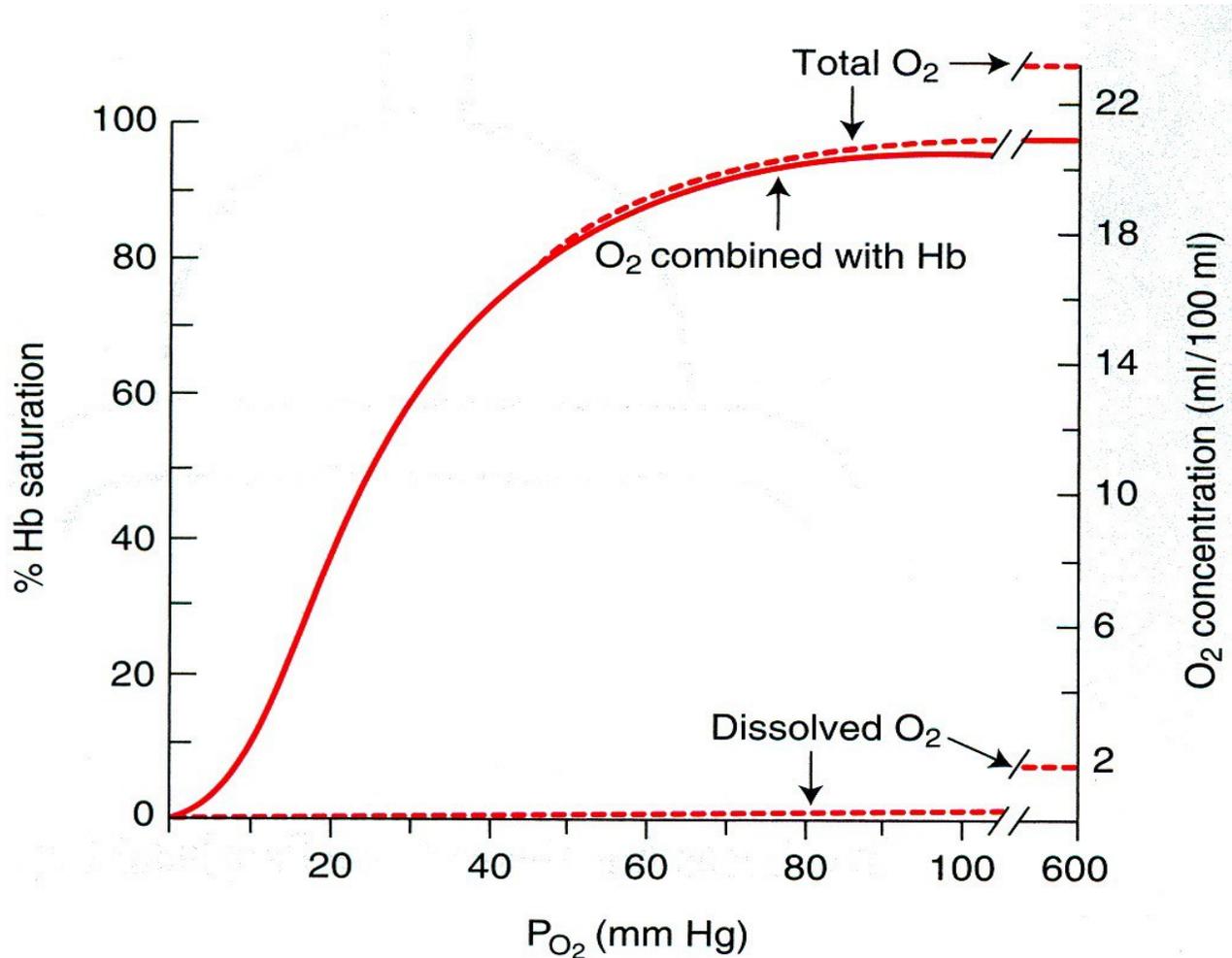
- Pulse oximeter waveform
- Look at the patient! - are they cyanotic? mottled?
- Gas analyzer

Management of Hypoxemia

Assuming proper oximeter function, placement, and waveform:

- Place patient on 100% O₂.
- Perform recruitment maneuver (30 sec at 30mmHg *if pt can tolerate hemodynamically*), then add or increase PEEP.
- Confirm ETT placement by auscultation, bilateral chest rise, and FOB if necessary.
- Suction airway and ETT
- Consider cardiovascular causes and restore volume, RBCs and/or cardiac output
- Send ABG/VBG

O₂-Hb Dissociation Curve



Useful "anchor" points:

| S _{O₂} | P _{O₂} (mm Hg) |
|----------------------------|------------------------------------|
| 50% | 27 |
| 75% | 40 |
| 97% | 100 |

Note:
P₅₀ ≈ 27 mm Hg

O₂-Hb Curve Shifts

Left Shift

(hemoglobin has higher affinity for O₂
= decreased unloading at tissues)

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

Right Shift

(hemoglobin has lower affinity for O₂
= 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
- O₂ Saturation
- Cardiac Output
- O₂ Consumption
- O₂-Hb Affinity (P₅₀)
- Dissolved O₂ in plasma (little effect)

See “Equations” for a mathematical explanation of these factors.

Equations

Arterial O₂ Content

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

Mixed Venous O₂ Content

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

Equations

O₂ Delivery

$$\begin{aligned} \text{DO}_2 &= \text{CO} \times \text{C}_a\text{O}_2 \\ &= 5 \text{ L/min} \times 20 \text{ cc O}_2/\text{dl} \\ &\approx \underline{1 \text{ L O}_2/\text{min}} \end{aligned}$$

O₂ Consumption (Fick Equation)

$$\begin{aligned} \text{VO}_2 &= \text{CO} \times (\text{C}_a\text{O}_2 - \text{C}_v\text{O}_2) \\ &= 5 \text{ L/min} \times 5 \text{ cc O}_2/\text{dl} \\ &\approx \underline{250 \text{ cc O}_2/\text{min}} \end{aligned}$$

O₂ Extraction Ratio

$$\begin{aligned} \text{ER}_{\text{O}_2} &= (\text{VO}_2 / \text{DO}_2) \times 100 \\ &= 250 / 1000 \\ &\approx \underline{25\% \text{ (normal 22-30\%)}} \end{aligned}$$

Other Concepts

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

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

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

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

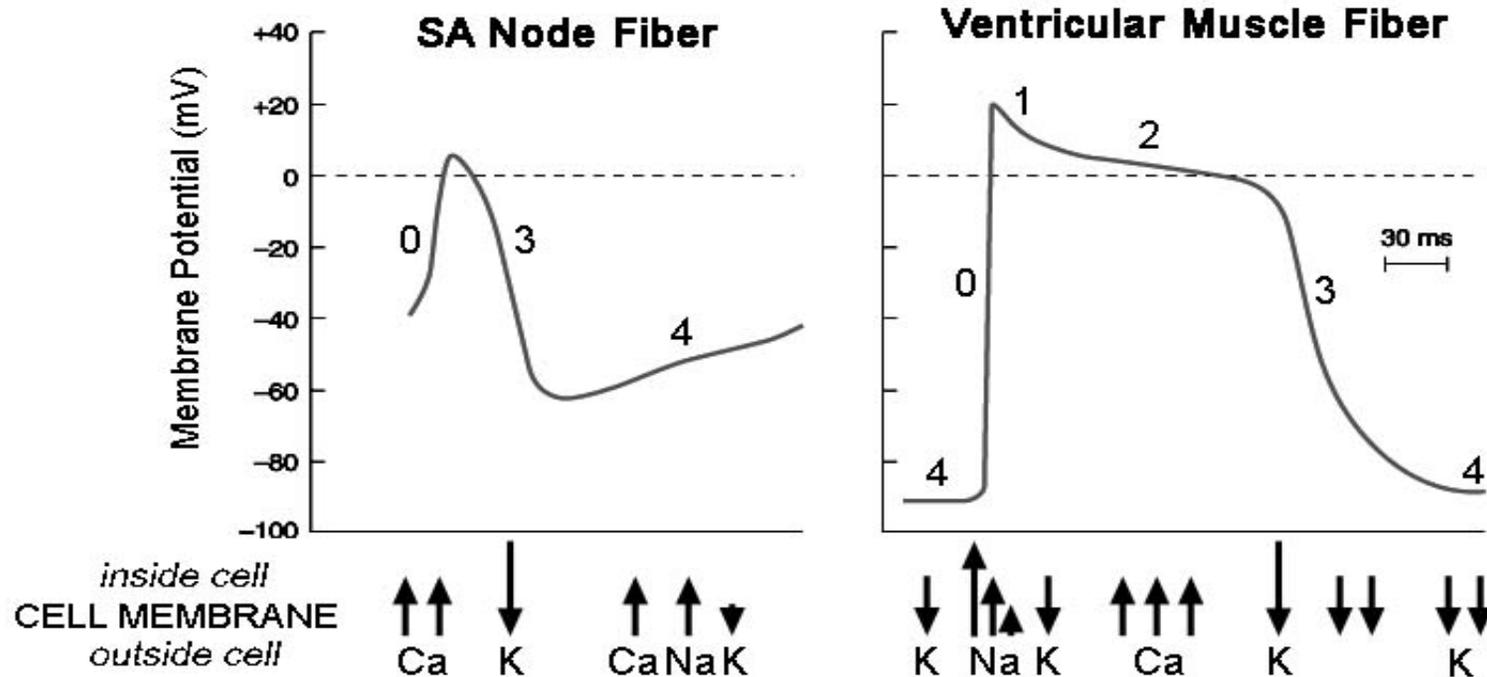
References

- 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 | — | Outward $I_K =$ Slow Inward I_{Ca} |
| 3 | Final Rapid Repolarization | Outward I_K | Outward $I_K >$ Inward I_{Ca} |
| 4 | Diastolic Depolarization/ Resting Potential | Slow inward I_{Ca} Slow inward I_{Na} Outward I_K (minimal) | Outward I_K |

Summary of EKG Changes

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

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

Hyperkalemia

Definition

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

Contributing Factors

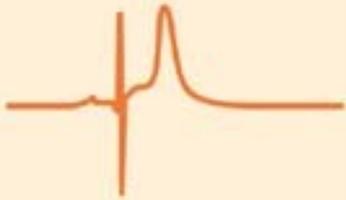
- Renal disease (esp GFR <15)
- Drugs (ACEI/ARBs, NSAIDs, K-sparing diuretics, digoxin, β -blockers)
- Acidosis
- Hyponatremia, hypocalcemia
- Hemolysis, transfusions (esp old PRBCs -- $[K^+]$ of 50 or greater!)
- Release from muscle
 - Succinylcholine: acute, transient $\approx 0.5-1$ mEq/L (*may be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

Hyperkalemia

Signs and Symptoms

- Cardiac: dysrhythmias, conduction abnormalities, cardiac arrest
 - Classically associated with giving succinylcholine to immobilized (ICU), spinal cord injury, neurological diseases (e.g. MS, ALS), burn patients – upregulated extrajunctional AChR (fetal AChR)
 - Usually with $[K^+] > 6.0$ mEq/L
 - Progression with increasing K concentration:
 1. Tall peaked T waves, esp precordial leads
 2. Long PR interval, low P wave amplitude
 3. Wide QRS complex → sine wave → VF arrest, asystole
- $[K^+] > 7.0$ mEq/L: ascending flaccid paralysis, inability to phonate, respiratory arrest

EKG Progression of Hyperkalemia

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

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

Hyperkalemia

Treatment

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

Hyperkalemia

Anesthetic Considerations

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

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

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

Hypokalemia

Definition

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

Contributing Factors

Preoperative

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

Intraoperative

- Alkalosis (metabolic or respiratory)
- Insulin
- Hypothermia

Hypokalemia

Signs & Symptoms

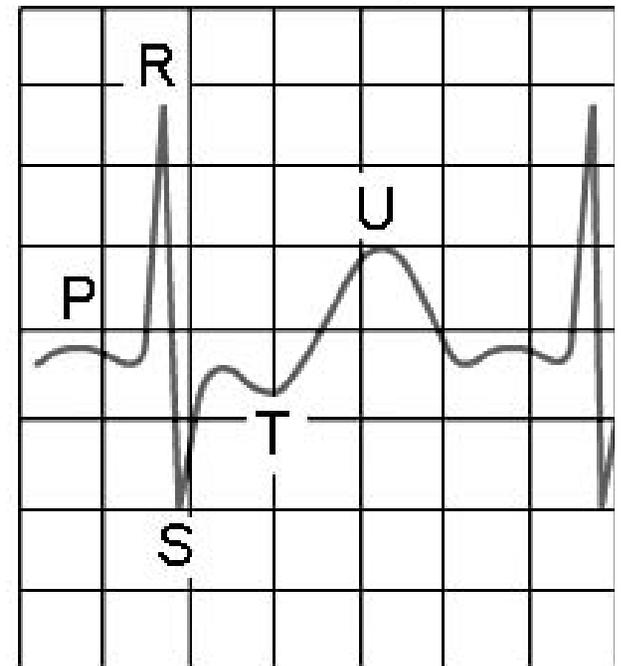
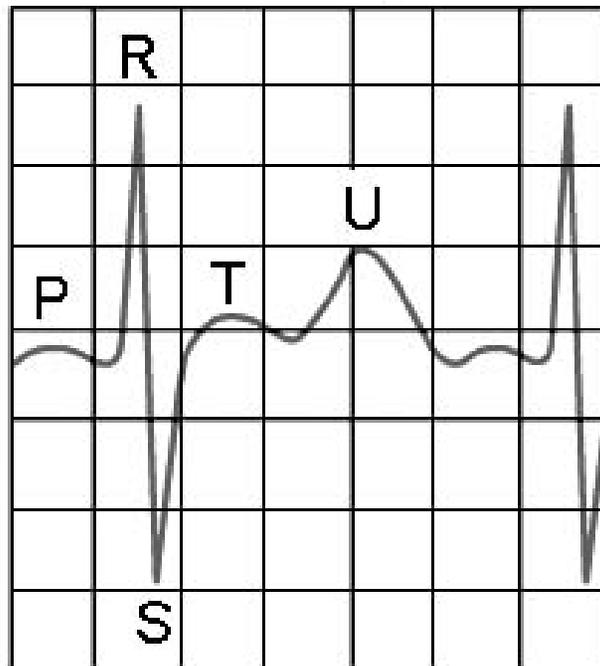
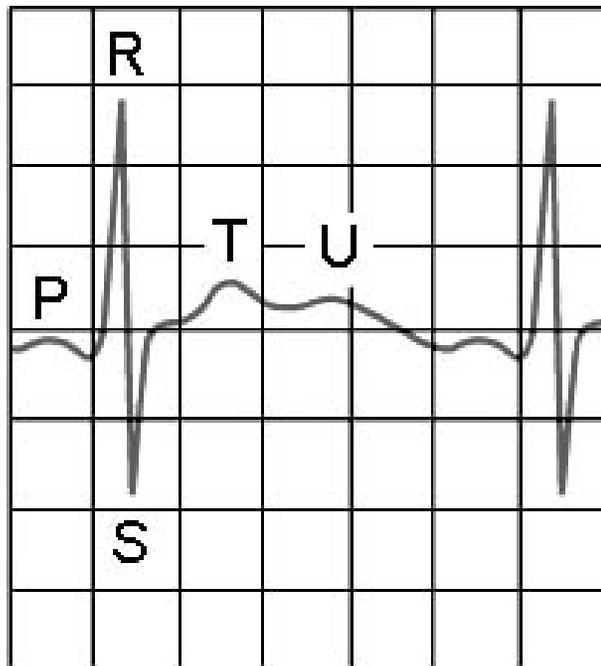
- Cardiac: hyperpolarization → ventricular escape, re-entrant phenomena, ectopic tachycardias, conduction delay
 - PACs, PVCs
 - SVTs (esp afib, aflutter)
- Metabolic alkalosis
- Autonomic lability
- Weakness, ↓DTRs
- Ileus
- Digoxin toxicity
- Increased sensitivity to neuromuscular blockers

EKG Progression of Hypokalemia

3.9 mEq/L

2.7 mEq/L

1.3 mEq/L



Flattened/inverted T wave → U waves, ST depression

Hypokalemia

Treatment

Acute hypokalemia = likely from cellular shifts

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

Chronic hypokalemia = total body K⁺ depletion

(1 mEq/L = 175-350 mEq total body deficit)

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

Hypokalemia

Anesthetic Considerations

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

Hypercalcemia

Contributing Factors

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

Signs & Symptoms

- EKG changes (short QT)
- Hypertension
- Polyuria

Treatment

- Hydration (bolus crystalloid) + Lasix diuresis
- Dialysis

Hypercalcemia

Anesthetic Considerations

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

Hypocalcemia

Contributing Factors

Preoperative

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

Intraoperative

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

Signs & Symptoms

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

Hypocalcemia

Treatment

- Calcium gluconate 1 g = 4.5 mEq Ca²⁺
(PIV or central line)
- Calcium chloride 1 g = 13.6 mEq Ca²⁺
(central line only)
- Do NOT give Ca²⁺ and NaHCO₃ together in the same IV - it will precipitate!
- Replace magnesium

Anesthetic Considerations

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

Hypermagnesemia

Contributing Factors

- Renal failure
- Hypothyroidism
- Iatrogenic (OB tocolysis)

Signs & Symptoms

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

Treatment

- Hydration (bolus crystalloid) + Lasix diuresis
- Ca²⁺ administration
- Diuresis

Anesthetic Considerations

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

Hypomagnesemia

Contributing Factors

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

Signs & Symptoms

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

Treatment

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

Anesthetic Considerations

- EKG monitoring
- Check for coexistent electrolyte deficiencies

References

- Barash PG et al. *Clinical Anesthesiology*, 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2009.
- Barash, Paul G., et. al. *Handbook of Clinical Anesthesia*, 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2013.
- Kaye AD and Kucera IJ. Intravascular fluid and electrolyte physiology. In Miller RD (ed), *Miller's Anesthesia*, 6th ed. Philadelphia: Elsevier Churchill Livingstone, 2005.
- Khajavi MR, et al. Effects of normal saline vs. lactated ringer's during renal transplantation. *Renal Failure*. 2008; 30(5):535-9.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology*, 4th ed. New York: McGraw-Hill Companies, Inc., 2006.
- Murray, Michael J., et. al. *Faust's Anesthesiology Review*, 4th ed. Philadelphia: Elsevier Saunders, 2015.
- 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.

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 themselves in the kitchen or have a paper cut. Odds are they stabbed themselves with a needle drawing up drugs in the morning. Hope it was clean!

Hypothermia & Shivering

Definition and Measurement

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

Pathways of Thermoregulation

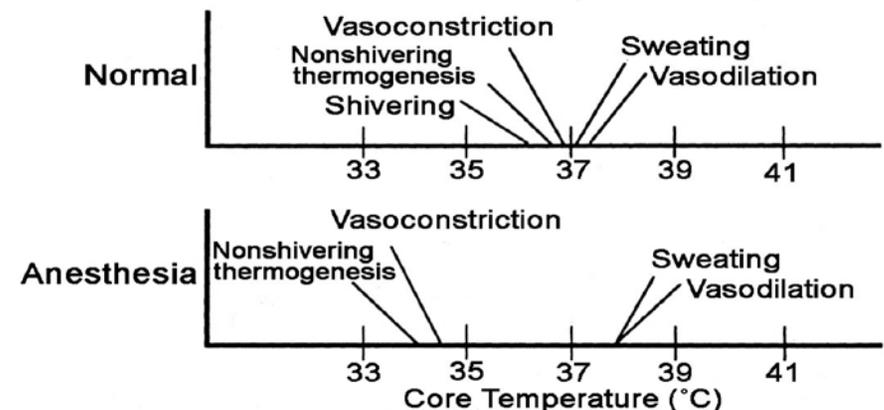
- **Afferent Sensing**
 - Nerve endings are found in the the skin, deep abdominal and thoracic tissues, spinal cord, brain matter, and the hypothalamus
 - These thermal inputs travel along A-delta fibers (cold sensation) and C fibers (warm sensation) to the brain via the spinothalamic tracts
- **Central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

Mechanisms to Control Body Temperature

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

Interthreshold Range

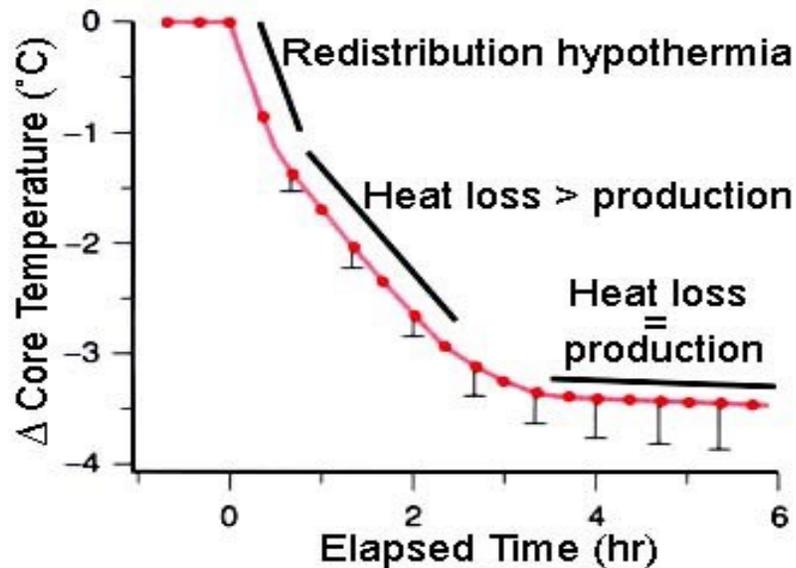
- **Interthreshold Range:** the core temperature range between cold-induced and warm-induced responses, usually as narrow as 0.2°C .
- **General anesthesia**
 - inhibits thermoregulation globally
 - increases the interthreshold range 20-fold to around 4°C .
- **Regional anesthesia**
 - inhibits thermoregulation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



Development of Hypothermia

Phases of Anesthetic-impaired thermoregulation

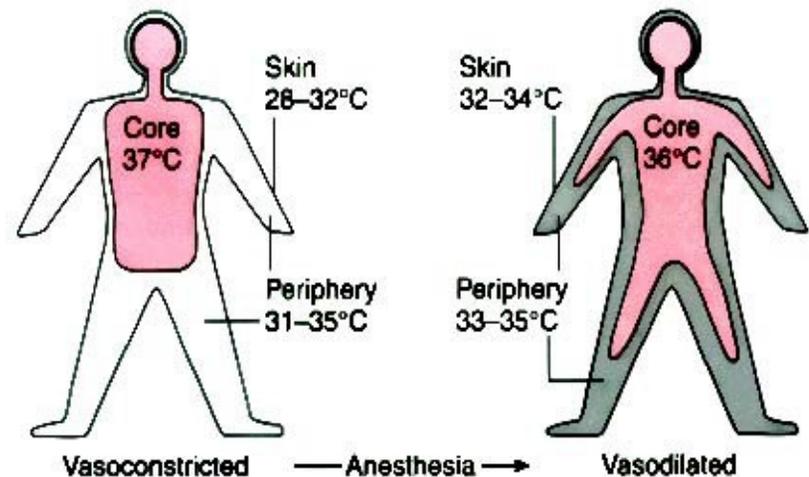
1. Redistribution hypothermia
2. Heat loss > heat production
3. Heat loss = heat production
 - heat balance is at steady state



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

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

Redistribution Hypothermia



Benefits of Hypothermia

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

Drawbacks of Hypothermia

- Increases infection rates up to 3-fold
- Delays wound healing and increases risk of surgical graft failure
- Induces a coagulopathy as platelet function fails and coagulation factor function slows (part of the trauma's "lethal triad")
 - Leads to increased surgical blood loss and greater transfusion rates
- Delays emergence from general anesthesia
 - Prolongs the activity of many anesthetic drugs
- Left-shifts the oxygen-hemoglobin dissociation curve, which impairs delivery of O₂ delivery
- While it decreases cardiac output requirements, hypothermia has a negative effect on inotropy and chronotropy, increases EKG intervals, leads to dysrhythmias, and increases systemic vascular resistance.
- Increases the systemic stress response
- Increases postoperative shivering rates
- Prolongs PACU stays

Warming Strategies

Prevention of hypothermia is much more effective than treatment!

Active Warming

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

Passive Insulation

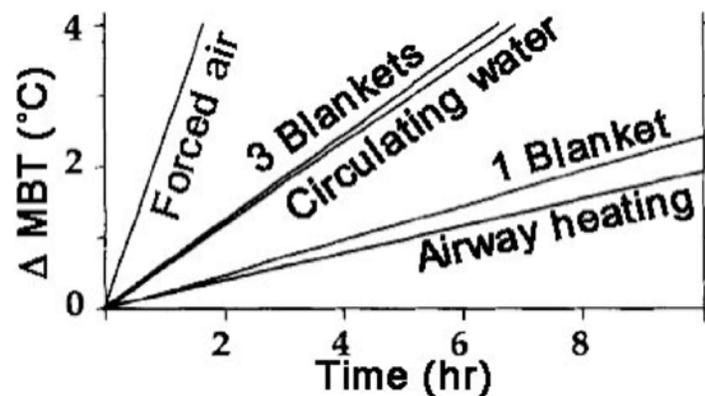
(not as effective)

- Cotton blankets
- Surgical drapes
- Heat-reflective “space” blanket

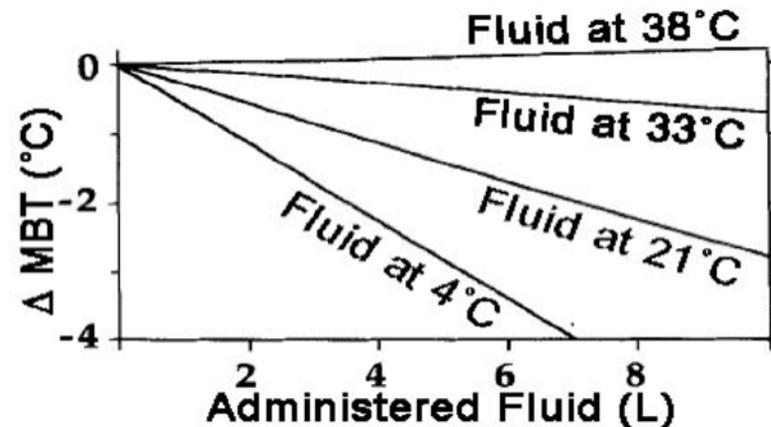
Also...

- Preoperative skin warming is excellent prophylaxis!

Efficacy of Warming Strategies



Efficacy of IV Fluid Warming



Rhythmic Muscular Activity

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

Consequences of Shivering

- Dramatic increase in O₂ consumption
 - Up to 500% in some studies
- Increased CO₂ production
 - Can greatly increase minute ventilation requirement
- Not all patients can tolerate the increased metabolic and respiratory demands!
- Also associated with shivering:
 - Trauma
 - Elevated intraocular pressure
 - Elevated intracranial pressures
- Distressing or even painful
- Disrupts monitoring, especially oscillometric blood pressure measurements and pulse oximetry

Treatment of Shivering

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

References

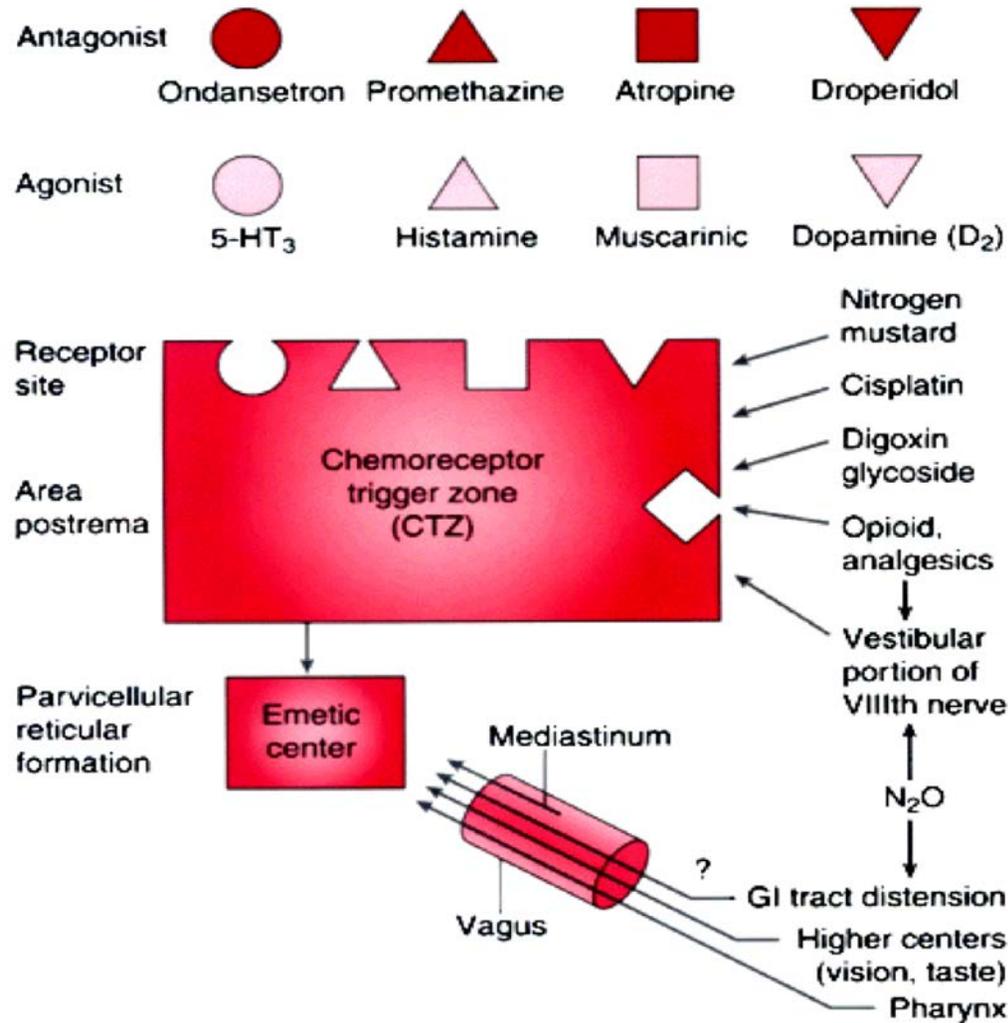
- De Witte J, and Sessler DI. 2002. Perioperative shivering: physiology and pharmacology. *Anesthesiology*, 96: 467-84.
- Sessler DI. Temperature monitoring. In Miller RD (ed), *Miller's Anesthesia, 6th ed*. Philadelphia: Elsevier Churchill Livingstone, 2005.
- Sessler DI. Mild perioperative hypothermia. *NEJM*, 336: 1730-7.
- Morgan, GE. *Clinical Anesthesiology*, 4th ed. New York: Lange Medical Books/McGraw-Hill
- Sessler, DI. Opioids and postoperative shivering. *J Clin Anesth*. 2016 Jun;31:42-3.
- Dr. Pearl's lectures.
- Bindu B, Bindra A, Rath G. Temperature management under general anesthesia: Compulsion or option. *J Anaesthesiol Clin Pharmacol*. 2017 Jul-Sep;33(3):306-316.

Postoperative Nausea & Vomiting (PONV)

Why do we care about PONV?

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

Chemoreceptor Trigger Zone



Major Risk Factors

Patient-Related

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

Anesthetic-Related

- Volatile anesthetics including N₂O
- Drugs (postoperative narcotics, neostigmine)
- Aggressive hydration (gut edema)

Surgery-Related

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

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

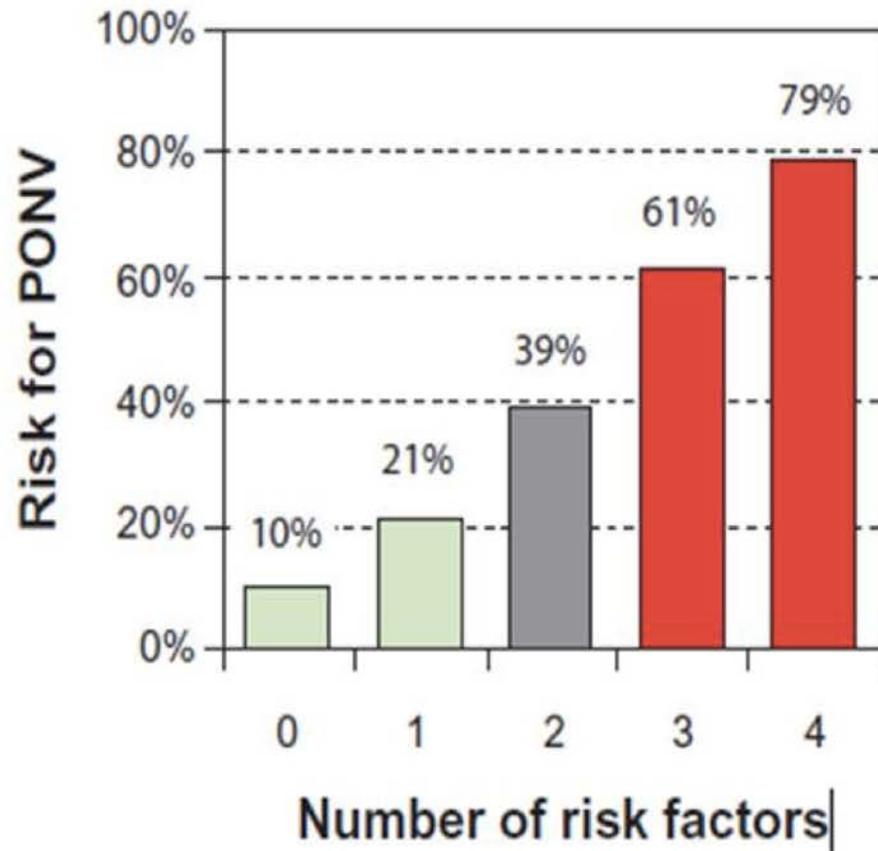
- Christian Apfel (UCSF PONV guru) meta-analysis of 22 PONV studies (>95,000 pts)
- Highest risk factors:

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

Simplified Apfel Score

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

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



PONV Prophylaxis Based on Apfel Score

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

- Combinations should be with drugs that have a different mechanism of action
- Try not to order agents for treatment in PACU that have already been used for ppx (e.g. Re-administration of Zofran in PACU not as effective as first dose used for ppx)

Antiemetic Classes

5-HT₃ Antagonists (e.g. Ondansetron, Granisetron)

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

Steroids

- Cheap and effective; for prolonged PONV relief
- Uncertain mechanism of action
- Weigh risks/benefits in diabetics and sepsis
- Decadron 4-10 mg IV anytime during case (give post-induction and not when awake: s/e at time of administration is severe perineal itching)

Induction agents

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

Antiemetic Classes

Anticholinergics (e.g. Scopolamine patch)

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

Phenothiazines (e.g. Promethazine, Prochlorperazine)

- Dopamine antagonist (promethazine also exhibits H₁ antagonism as well)
- Given IV or IM
- Can cause sedation and extrapyramidal side effects
- Phenergan 12.5-25 mg at end of case

Gastrokinetic (e.g. Metoclopramide)

- Dopamine antagonist; can cause extrapyramidal SEs
- Increases GI motility and LES tone, avoid in patients with bowel obstruction
- Reglan 10-20 mg IV before end of case
- Contraindicated in Parkinson’s patients

Antiemetic Classes

Butyrophenones (e.g. Droperidol, Haloperidol)

- Central dopamine antagonist
- Droperidol cheap and very effective, but a “black box” warning regarding QT prolongation has caused it to fall out of favor (based on data when given at doses 50-100x than standard dosing)
- Contraindicated in Parkinson’s patients
- Droperidol 0.625-1.25 mg IV at end of case.

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

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

Other Antiemetic Agents

Vasopressors

- Ephedrine 50 mg IM
 - Prevents intestinal hypoperfusion

Antihistamines (H₂-blockers)

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

IMPACT Trial: Results

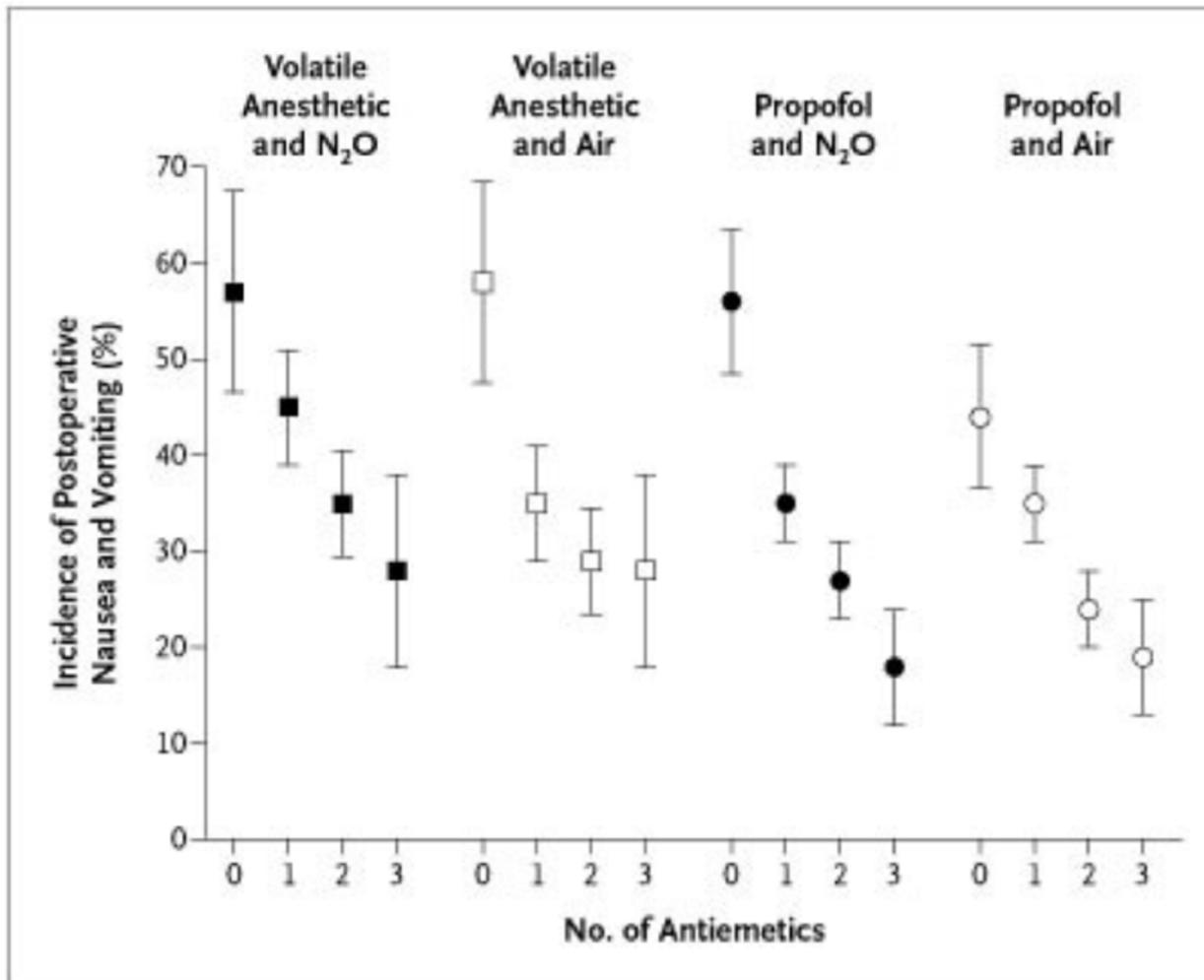
(Apfel et al., 2004)

| 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 ₂ O) | 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 + N₂O + remi + no antiemetics; 17% with propofol + N₂ + fentanyl + antiemetics x 3).
- Use the safest and cheapest antiemetic first; use combined therapy only in moderate or high-risk patients.

IMPACT Trial: Results

(Apfel et al., 2004)



Strategies to Reduce PONV

- Use regional anesthesia vs. GA
- Use propofol for induction and maintenance of anesthesia (TIVA)
- Avoid N₂O and/or volatile anesthetics
 - N₂O's role in PONV is controversial, possibly related to duration of exposure
- Minimize opioids (consider Tylenol, NSAIDs, etc.)
- 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 postoperative 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 Overview

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

Extubation Overview (cont)

- As a result, Difficult Airway Society (DAS) published 2012 guidelines with low & high risk algorithm
 - Low Risk: awake vs. deep extubation
 - *Awake: usual way of extubating*
 - *Deep: more advanced, ask your attending, usually has specific indications, others may use it to expedite transfer to PACU and turn over room*
 - High Risk: awake (with possible Airway Exchange Catheter (AEC), LMA, or remifentanyl technique) vs. postponing extubation vs. tracheostomy
 - *AEC: shaped like a bougie but hallowed so you can ventilate through it, left in place which doesn't bother patient, able to 'rail-road' ETT over if needed*

Extubation Risk Stratification:

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

“Routine Extubation Criteria”

1. **Vital signs stable**
 - BP/HR stable within acceptable ranges (on minimal pressors)
 - T > 35.5C
 - Spontaneous RR >6 and <30, SpO₂ > 90%
2. **ABG “reasonable” with FiO₂ ≤40%**
 - pH ≥7.30, PaO₂ ≥60 mmHg, PaCO₂ ≤50-60, normal lytes
3. **Adequate reversal or neuromuscular blockade**
 - TOF 4/4, TOF ratio >0.7-0.9, tetany >5 secs
 - The “direct palpation” method cannot determine if the TOF ratio is ≥0.9.
 - Sustained head lift or hand grasp >5 secs (sensitive but not specific)
 - Not adequate to rule out residual paralysis or incomplete reversal
4. **Respiratory mechanics adequate**
 - Spontaneous VT >5 mL/kg, Vital Capacity >15mL/kg
5. **Protective reflexes (gag, swallow, cough) returned**
6. **Awake, alert, able to follow commands**

Causes of Failed Extubation

| Causes | Checklist prior to extubation (to help avoid failure) |
|--|---|
| Failure to oxygenate | <ul style="list-style-type: none"> • TV >5cc/kg & VC > 15cc/kg • SpO₂ >90% with FiO₂ < 0.4 |
| Failure to ventilate | <ul style="list-style-type: none"> • Same TV parameters above • NM Blockade appropriately reversed • RR >6 & <30? • No excessive hypercapnea (EtCO₂ < 50s-60) |
| Inadequate clearance of pulmonary secretions | <ul style="list-style-type: none"> • Oropharynx suctioned? • Intact gag reflex? Able to cough? Alert/awake? • If aspiration risk, OG tube suction and consider emergence in lateral decubitus position |
| Loss of airway patency | <ul style="list-style-type: none"> • Soft bite block or oral airway placed? • Alert? Following commands? • If edema a concern, is cuff leak >10-15%** • Placed in optimal position (sniffing position, head up) • Reduced risk of laryngospasm? (not in stage 2, airway suctioned) • Airway exchange catheter for high risk patient? |

**to calculate cuff leak (advanced maneuver: ask attending): while on volume control, deflate cuff; measure before & after exhaled tidal volumes and calculate percent difference

Standard preparation any extubation

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

Stages of Anesthesia

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

Stage 1 – Amnesia

- Ranges from awake to loss of consciousness, amnestic throughout

Stage 2 – Delirium/Excitement *

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

Stage 3 – Surgical Anesthesia

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

Stage 4 – Overdose

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

* Avoid extubation in Stage 2 to reduce risk of laryngospasm

Causes of Delayed Emergence

| | |
|-------------------------------|--|
| <p>Anesthesia Related</p> | <p>Residual anesthetic</p> <ul style="list-style-type: none"> • Rapid shallow breaths? MAC still showing? • Time since propofol turned off? <p>Excessive narcotics</p> <ul style="list-style-type: none"> • Recent administration? Pinpoint pupils? <p>Residual muscle relaxant, pseudocholinesterase deficiency.</p> |
| <p>Metabolic</p> | <p>Hypothermia ($T < 34^{\circ}\text{C}$)</p> <p>Hypoxemia</p> <p>Hypercarbia/hyponatremia/hypocalcemia/hypoglycemia</p> <p>Renal/hepatic failure</p> |
| <p>Intracranial event</p> | <p>Stroke/CVA (2.5-5% in high risk patients)</p> <p>Seizure</p> <p>Intracranial HTN</p> |

Diagnosis and Treatment

Stanford Protocol for Delayed Emergence

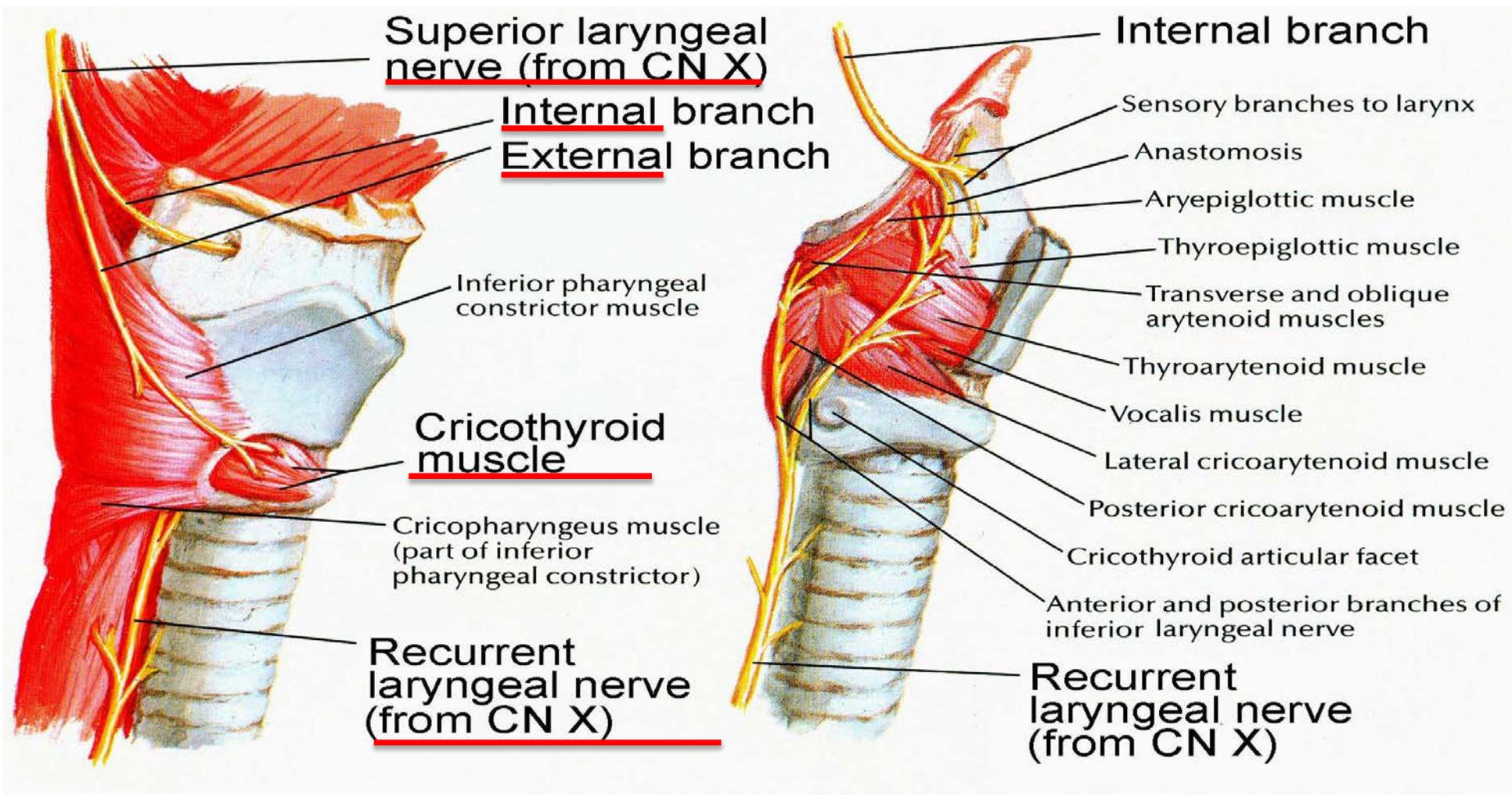
- Confirm that all anesthetic agents (inhalational/IV) are off
- Check for residual NMB paralysis, reverse as appropriate
- Consider opiate reversal (medications delivered, evaluate pupils & respiratory rate)
 - Start with 40mcg naloxone IV, repeat Q2 mins up to 200mcg total
- Consider inhalational anesthetic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

References

- Asai T, Koga K, Vaughan RS. Respiratory complications associated with tracheal intubation and extubation. *British Journal of Anaesthesia*. 1998 Jun 1;80(6):767-75.
- Bittner, E, et al. Postoperative Complications. In *Longnecker's Anesthesiology* (2nd edition), 2012. The McGraw Hill Companies.
- Knapp, R, et all. Emergence from Anesthesia. In *Essential Clinical Anesthesia* (1st edition), 2011. Cambridge University Press.
- Hagberg, CA & Artime CA. Airway Management in the Adult. In *Miller's Anesthesia* (8th edition), 2015. Elsevier inc.
- Popat, M, et al. Difficult Airway Society Guidelines for the management of tracheal extubation. *Anesthesia*, 2012; 67: 318-340
- Rajala, MM. The Evaluation and Management of Prolonged Emergence from Anesthesia. In *Faust's Anesthesia Review* (4th edition), 2015. Elsevier Inc.
- Roth, R, et al. Extubation: Making the Unpredictable Safer. *Anesthesiology News*, 2012.
- Stanford Medicine. Delayed Emergence from Anesthesia. Retrieved April 28, 2016, from http://ether.stanford.edu/delayed_emergence.html
- Urman, RD & Ehrenfeld, JM. *Pocket Anesthesia* (2nd edition), 2013. Lippincott Williams & Wilkins.
- Membership of the Difficult Airway Society Extubation Guidelines Group: M. Popat (Chairman), Mitchell V, Dravid R, Patel A, Swampillai C, Higgs A. Difficult Airway Society Guidelines for the management of tracheal extubation. *Anaesthesia*. 2012 Mar;67(3):318-40.

Laryngospasm & Aspiration

Larynx Anatomy

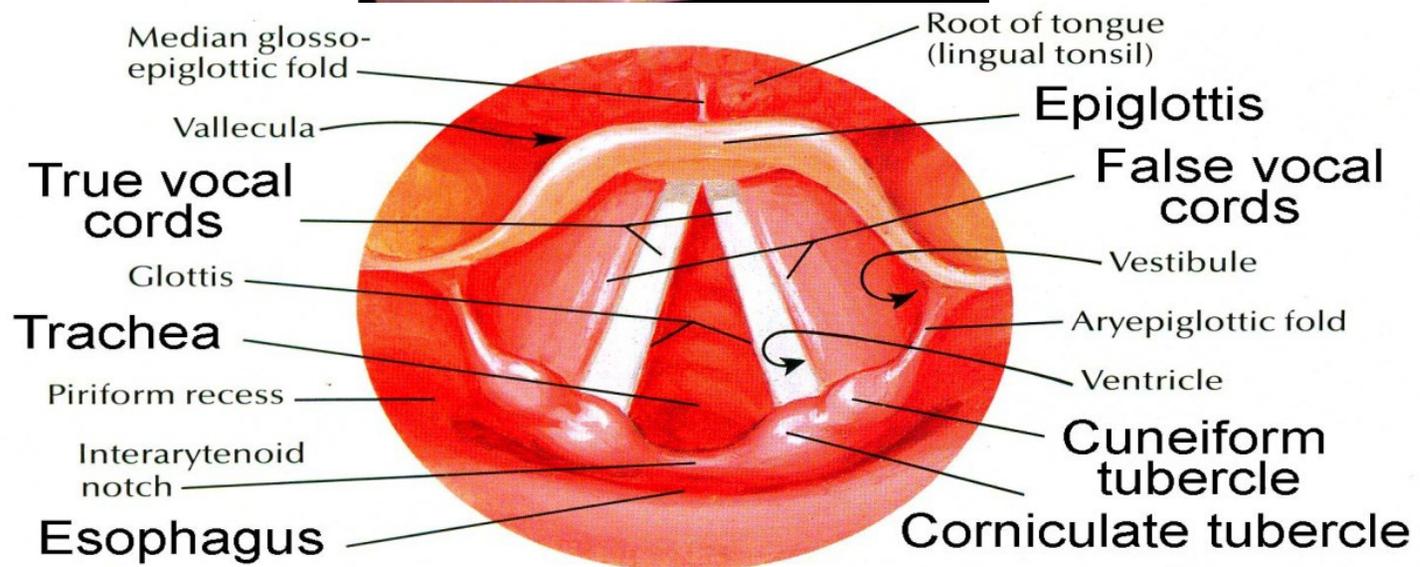
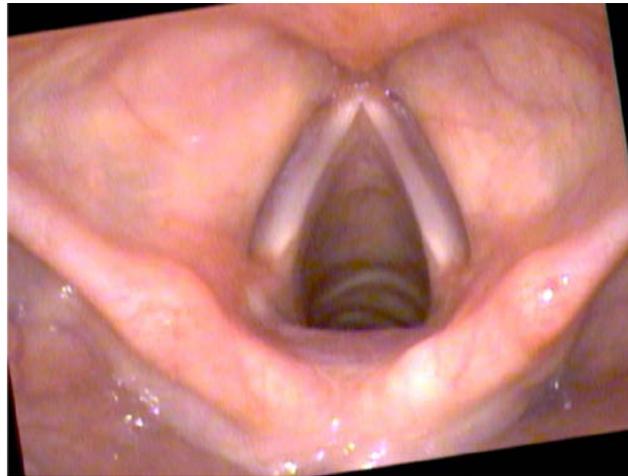


Larynx Anatomy: Innervation

| Nerve | Motor | Sensory |
|---|--|---|
| Recurrent Laryngeal (from CN X) | Thyroarytenoid (tensor) Lateral Cricothyroid (adductor) Transverse Arytenoid (adductor) Posterior Cricothyroid (abductor, tensor) | Subglottic mucosa |
| Superior Laryngeal (from CN X) | | |
| <ul style="list-style-type: none"> Internal branch | None | Epiglottis/Tongue Base Supraglottic mucosa |
| <ul style="list-style-type: none"> External branch | <u>Cricothyroid (adductor)</u> | Anterior subglottic mucosa |

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

Larynx Anatomy



Laryngospasm

What is laryngospasm?

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

Predisposing Factors

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

Laryngospasm

Prevention

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

Detecting

- Inspiratory stridor/ airway obstruction
- Increased inspiratory effort/tracheal tug
- Paradoxical chest/abdominal movements
- Auscultate with stethoscope over trachea to listen for degree of obstruction & airway patency
- Poor EtCO₂ tracing, desaturation, bradycardia, central cyanosis

Laryngospasm

Management - *CALL FOR HELP EARLY!*

1. Jaw thrust, head tilt, oral or nasal airway
 - Larson's Maneuver: a jaw thrust with bilateral pressure on the body of the mandible anterior to the mastoid process
2. Suction oropharynx
3. CPAP via bag-mask ventilation with 100% O₂
4. Deepen anesthesia with IV agent (e.g. Propofol)
 - Consider IV lidocaine, as well
5. Succinylcholine 10-20 mg IV, maintain airway with bag-mask or ETT until spontaneously breathing
 - May also give succinylcholine via IM route
6. Reintubation vs. prepare for surgical airway
7. Monitor for post-obstructive negative pressure pulmonary edema (NPPE)

Negative Pressure Pulmonary Edema

Causes

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

Risk Factors

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

Presentation

- Laryngospasm, chest wall retraction
- Frothy, serosanguinous or bloody airway secretions
- $\hat{e}S_pO_2$, $\acute{e}ET_{CO_2}$, hypotension, large $P_{(A-a)}$ gradient
- CXR with pulmonary edema

Negative Pressure Pulmonary Edema

Pathogenesis

- Negative intrathoracic pressure (up to -100 cmH₂O)
- ↓RV preload → ↓pulmonary hydrostatic pressure
- ↓RV preload → interventricular septum shift → LV diastolic dysfunction → ↑PCWP
- Hypoxia, hypercapnea, acidosis → Hypoxic Pulmonary Vasoconstriction (HPV) & ↑PVR
- Stress response → ↑SVR and ↑LV afterload
- Alveolar-capillary membrane leak → protein loss

Treatment

- Supportive care (O₂, IPPV, PEEP/CPAP)
- Conservative management until process reverses; consider volume and/or pressors PRN.
- Lasix is usually NOT helpful
- Does not typically require ETT

Pulmonary Aspiration

Predisposing Conditions

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

Pulmonary Aspiration

Prevention

- Follow NPO guidelines for routine elective cases
- Use metoclopramide, H₂-blockers, and antacids in high-risk patients
- Consider awake, regional anesthetic (e.g. spinal or epidural for c-sections)
- Consider awake, upright intubation and/or RSI
- If present, leave NGT to suction
- Apply cricoid pressure until ETT position confirmed
 - Although this practice is debated, one could contend it is considered the 'standard of care.'
- Minimize bag-mask PPV and/or keep pressure <20 cmH₂O
- Extubate after recovery of protective reflexes
- Remain vigilant: aspiration occurs during emergence and maintenance and not just during induction

NPO Guidelines

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

- There is no evidence for the routine use of metoclopramide, H₂-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% O₂, intubate (if needed), apply PEEP or CPAP
- Supportive care - monitor for chemical PNA/ARDS
- Possible bronchoscopy for removal of particulate matter, if suspected
- Antibiotics are not necessary unless subsequent infection develops (or, as happens more commonly in pediatrics, fecal matter is aspirated)
- Steroids are not indicated

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.
- Miller, RD et al. *Miller's Anesthesia*, 7th ed, Churchill Livingstone: p 2359-60. 2009
- Von Ungern-Sternberg BS, et al. Risk assessment for respiratory complications in paediatric anaesthesia: a prospective cohort study. (Sept 2010). *The Lancet*.
- Olsson GL, Hallen B. Laryngospasm during anaesthesia: a computer-aided incidence study in 136,929 patients. *Acta Anaesthesiol Scand* 1984;28:567-75.
- Mevorach DL. The management and treatment of recurrent postoperative laryngospasm. *Anesthesia & Analgesia*. 1996 Nov 1;83(5):1110-1.
- Visvanathan T, Kluger MT, Webb RK, Westhorpe RN. Crisis management during anaesthesia: laryngospasm. *BMJ Quality & Safety*. 2005 Jun 1;14(3):e3-.
- Kluger MT, Short TG. Aspiration during anaesthesia: a review of 133 cases from the Australian Anaesthetic Incident Monitoring Study (AIMS). *Anaesthesia*. 1999 Jan 1;54(1):19-26.

Oxygen Failure in the OR

Etiology

Loss of Pipeline Oxygen

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

Faulty Oxygen Supply

- Crossing of pipelines during construction/repairs.
- Incorrect connection of gas hoses.
- Non-O₂ cylinder at the O₂ yoke.
- Wrong gas in the O₂ cylinder.
- Broken flowmeter.

Prevention of O₂ Failure is KEY

Selected Daily Pre-anesthesia Machine Checks

- Verify Auxiliary Oxygen Cylinder (with regulator) and Self-Inflating Manual Ventilation Device (ie AMBU) are Available and Functioning
- Verify pipeline gas pressure ≥ 50 psi.
- Verify that pressure is adequate ($>50\%$) on the spare oxygen cylinder mounted on the anesthesia machine
- Verify calibration of O₂ analyzer and that the low O₂ alarm is audible
 - Self calibrating O₂ monitors should read 21% when sampling room air

Supply-Side Safety Features

- Color-coded gas tanks
- DISS, PISS, and Quick Connects

Anesthesia Machine Safety Features

- Flow-meter arrangement
- O₂:N₂O ratio controller
- Oxygen supply failure protection device (“fail-safe valve”)

Medical Gas Cylinders

- Designations A (smallest) through H (largest)
- E-cylinders most common in the OR (portable)
- H-cylinders most common in central pipeline
- O₂ E-cylinders are used as backup in case of pipeline supply failure (2200 psi)
 - Attached to anesthesia machine via **pin index safety system (PISS)** and must be checked prior to delivering anesthetics (maintain in closed position unless needed to avoid depletion)

Gas Cylinders

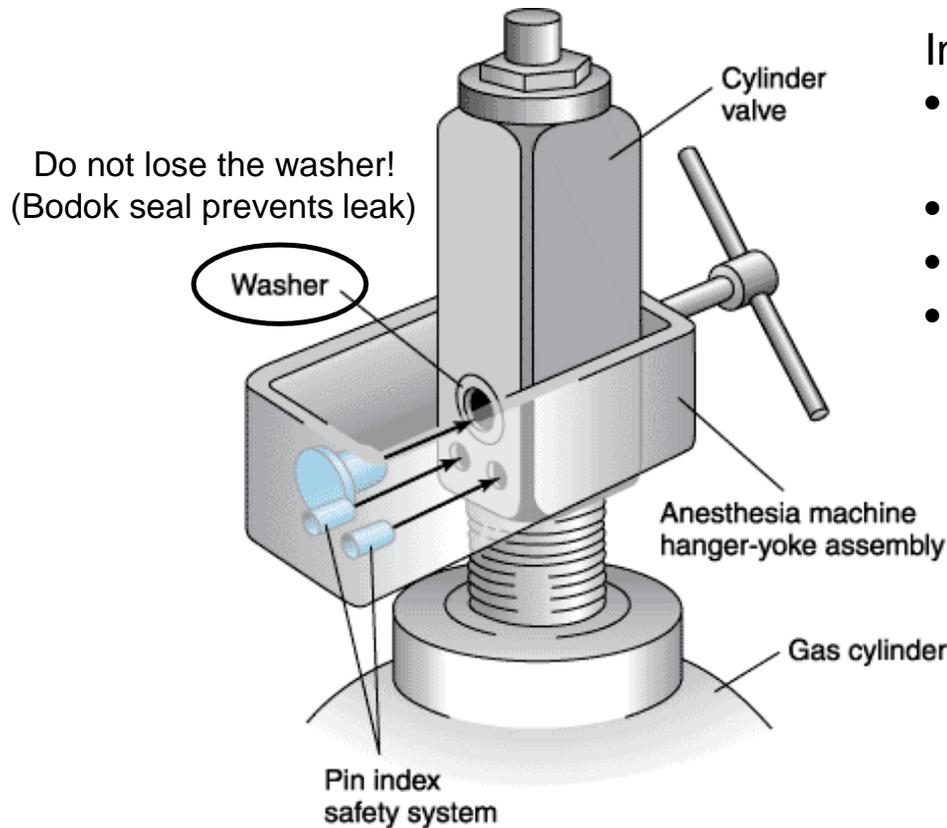
| Gas | E-Cylinder Capacity (L) | Pressure (psi) | Color (USA) | Color (Int'l) | Form |
|------------------|-------------------------|----------------|-------------|---------------|---------------|
| O ₂ | 660 | 1900 | Green | White | Gas |
| Air | 625 | 1900 | Yellow | White & Black | Gas |
| N ₂ O | 1590 | 745 | Blue | Blue | Liquid + Gas* |
| N ₂ | 650 | 1900 | Black | Black | Gas |

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

How long can you use an O₂ tank starting at 430 psi running at 5 L/min? (remember 3 psi = 1 Liter for oxygen)

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

Pin Index Safety System

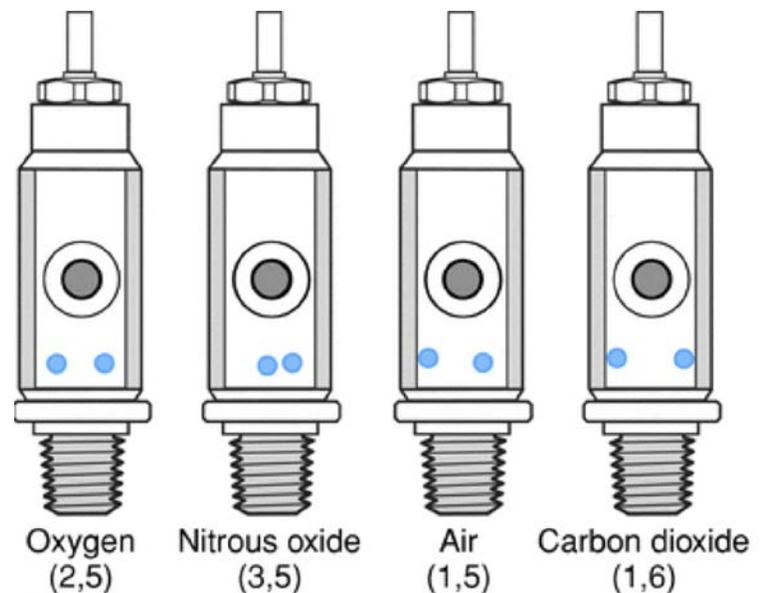


Copyright ©2006 by The McGraw-Hill Companies, Inc.
All rights reserved.

P.I.S.S. for Gas Cylinders

International Standard:

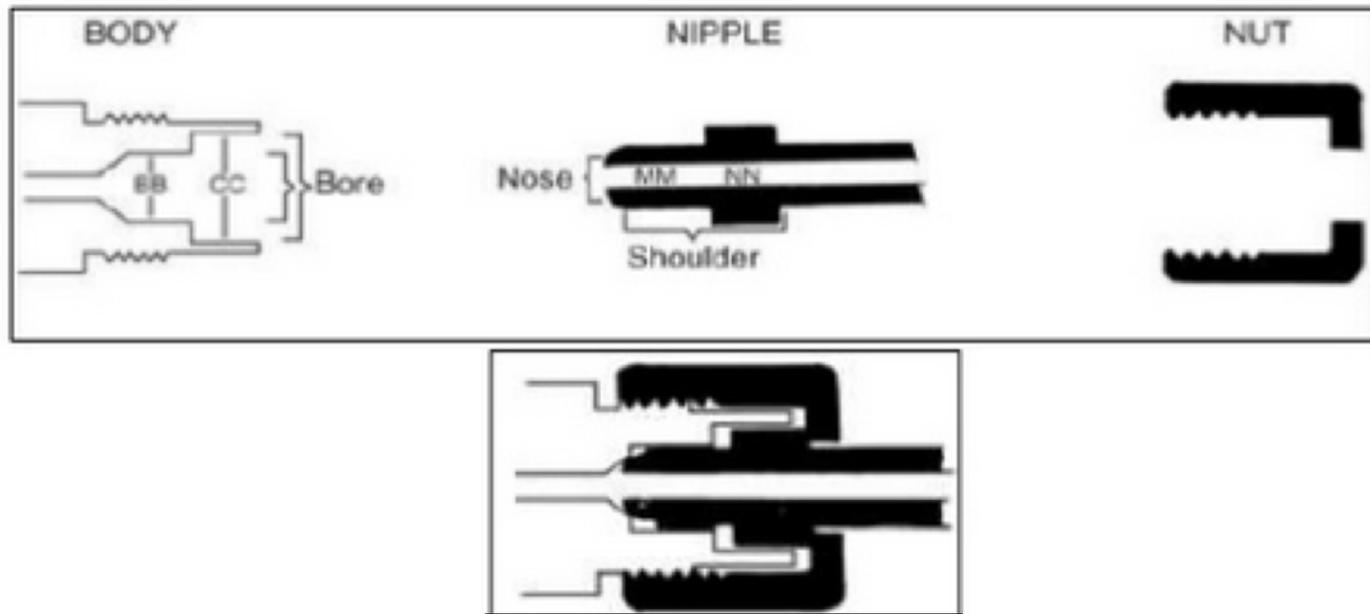
- Physical Barrier to ensures that the correct gas is connected to the correct cylinder type
- Pin positions for each gas is unique
- Do not break or force pins to connect
- Possible to bypass safety check if pins are eroded, damaged, or corroded



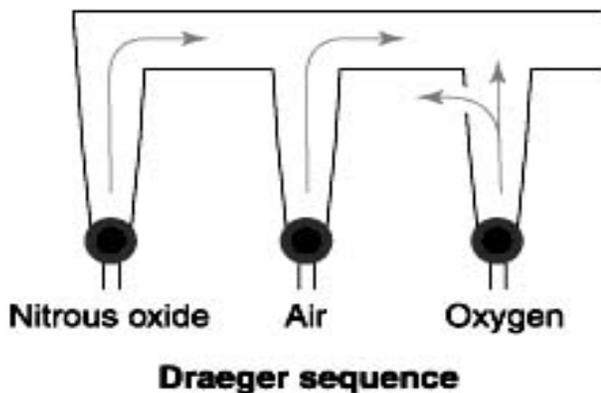
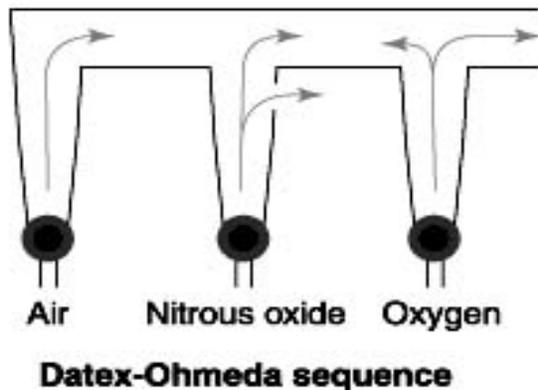
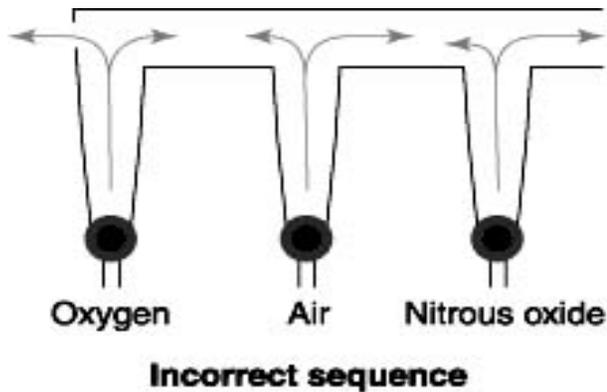
Diameter Index Safety System

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

3 Components: body, nipple, nut



Flowmeter Arrangement



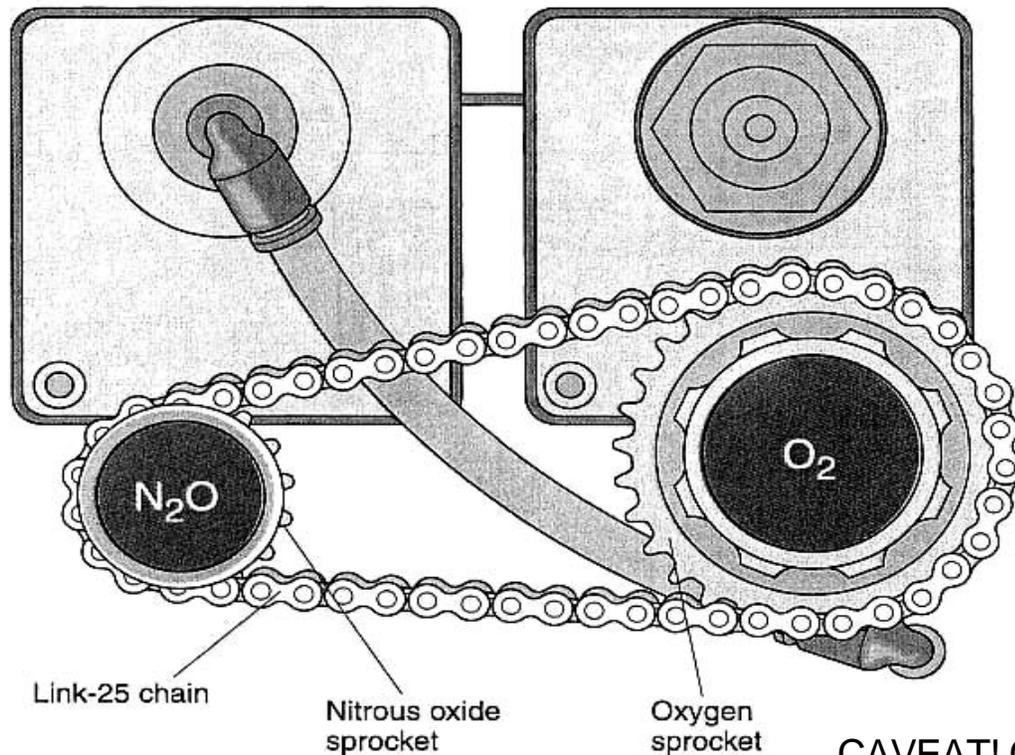
- A leak in the upstream O₂ flowmeter (“Incorrect sequence”) results in a hypoxic gas mixture.
- A leak in the Datex-Ohmeda or Draeger flowmeter arrangements may deliver less Air or N₂O than expected, but the mixture will NOT be hypoxic because O₂ is closest to the FGF outlet.

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

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

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

O₂:N₂O Proportioning System “hypoxic guard”

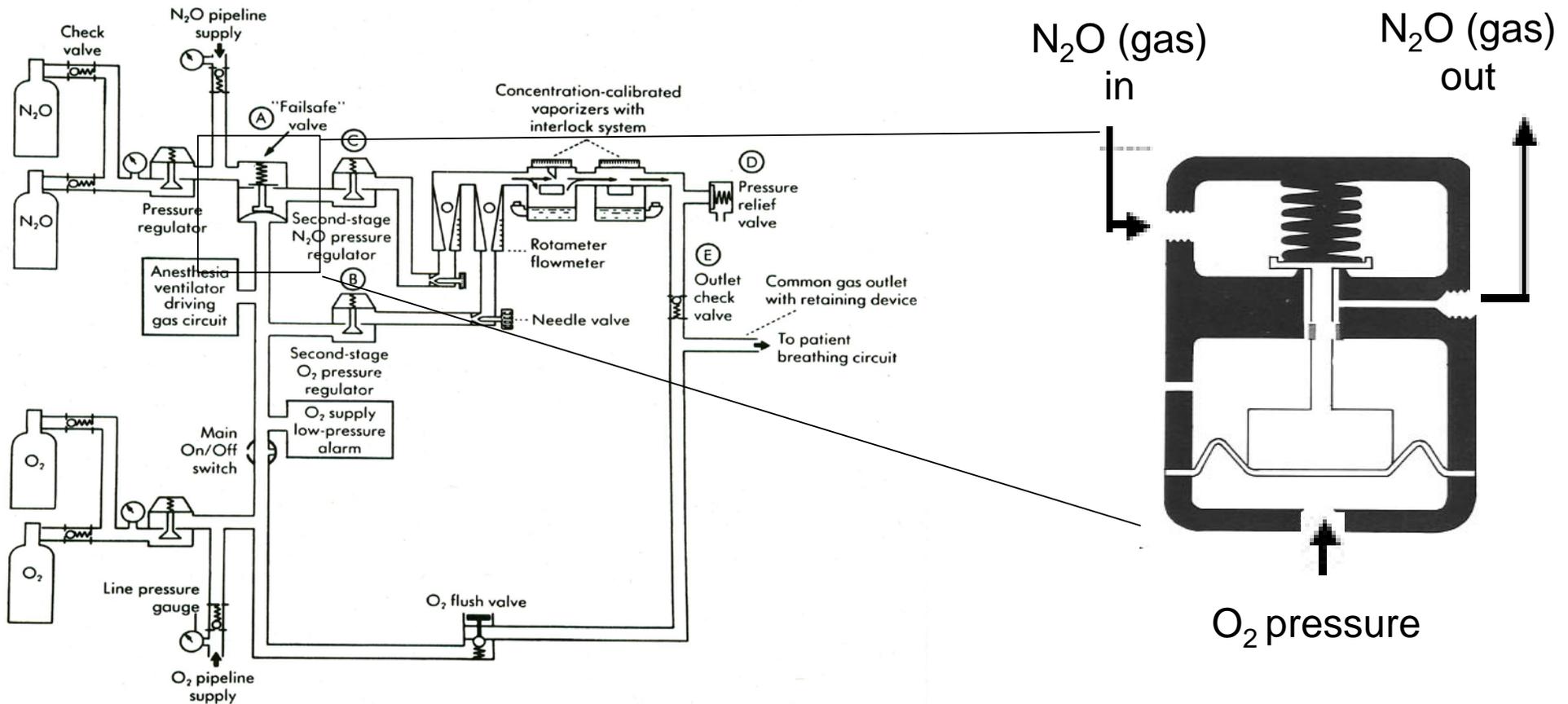


Linkage mechanisms between flow valves can be either mechanical (above), pneumatic, or electronic to prevent FiO₂ <25% when N₂O is used.

CAVEAT! Can still deliver hypoxic mixtures IF there are:

- Incorrect supply gas connections
- Errors in or defective components/links
- Downstream leaks
- Introduction of third inert gas like helium

Oxygen Failure Protection Device



Fail-safe Valve: If P_{O_2} falls <30 psi, N₂O cannot flow AND alarm sounds (Datex-Ohmeda)

Note: Does not prevent 100% N₂O delivery! (this is accomplished by the proportioning system)

Detection

- Pressure gauges fall (pipeline, tanks)
- Low O₂ alarms (O₂ supply failure, F_iO₂ analyzer)
- Flowmeters fall (O₂ and other gases)
- O₂ flush inoperative
- Bellows inoperative
- Apnea alarms (spirometer, capnograph)
- Increasing O₂ flow makes the problem worse
- Hypoxemia, hypercarbia
- Arrhythmias, bradycardia, cardiac arrest

Management

- Notify surgeon, call for help, use emergency manual.
- Verify problem
- Disconnect patient from machine and ventilate with Ambu bag. **Do not use auxiliary O₂ on machine as the source is the same.** If patient needs higher FiO₂ call for extra E-cylinders early.
- To keep patient connected to anesthesia machine, open O₂ cylinder on the back of the anesthesia machine and disconnect from pipeline O₂.
- Use manual ventilation to conserve O₂.
- D/C supply lines if crossed pipelines suspected.
- Check pipeline gas supply content prior to restarting
- Consider switching to TIVA/maintain low gas flows to avoid awareness until cause of failure is known.

Management of O₂ Pipeline Failure

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

Anaesthesia, 2007, 62, pages 122–126

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

Table 1 Anaesthetists' management of oxygen failure.

Commonly missed steps:

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

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.
- Weller, et al. Anaesthetists' management of oxygen pipeline failure: room for improvement. *Anesthesia*, 2007.

Anaphylaxis

Overview

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

Anaphylaxis vs. Anaphylactoid

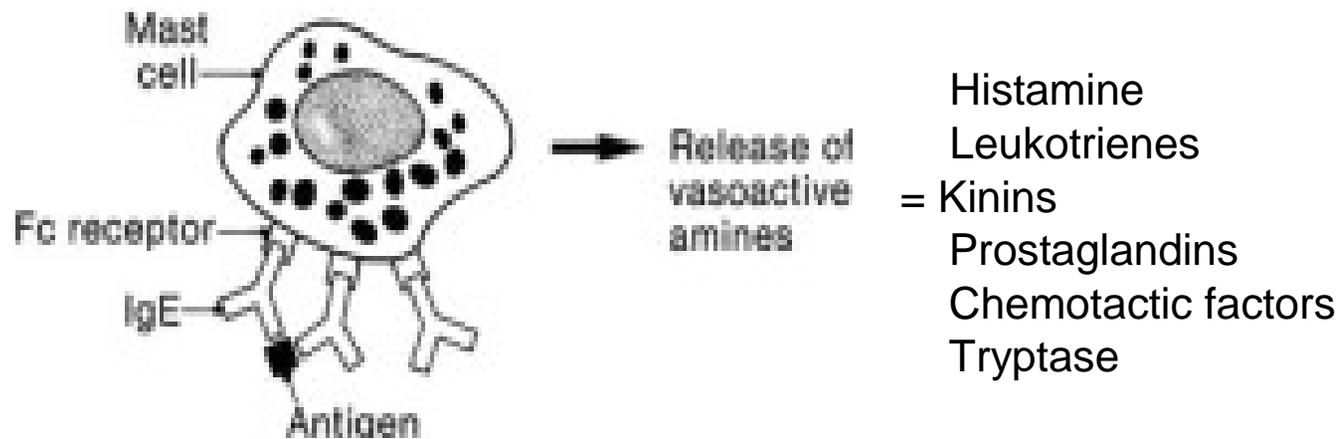
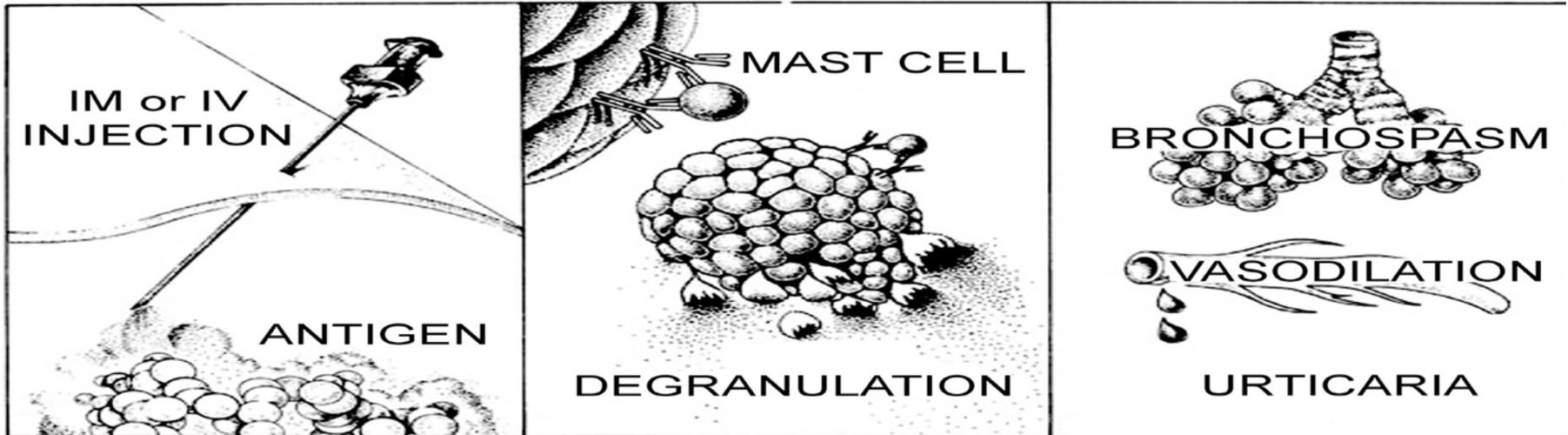
Anaphylaxis

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

Anaphylactoid

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

Sequence of Events



Signs and Symptoms

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

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

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

*There is a wide variation in the reported incidence of anaphylaxis amongst common precipitants.

- **Rocuronium's** incidence of anaphylaxis is quoted anywhere from 1/3,500 to 1/445,000
- **Sugammadex**: quoted around 1/35,000

Latex Allergy

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

Management

Acute Phase

1. Stop administration of offending antigen (muscle relaxants, latex, antibiotics, colloids, blood, contrast, etc.)
2. Notify surgeon **AND** call for help
3. Increase to 100% FiO₂
4. In hypotensive, consider discontinuation of agents that may augment hypotension. Give other amnestic agent (e.g. midazolam, ketamine)
 1. inhaled anesthetics causes vasodilation
 2. narcotic infusions suppress sympathetic response
5. Give **IV fluid** bolus.
 1. May require many liters, 2-4 L *or more!* (compensate for vasodilation, hypotension)
6. Give **Epinephrine** (α -1à supports BP; β -2à bronchial smooth muscle relaxation)
 1. Start **10-100 mcg IV boluses** for hypotension; escalate as needed
 2. Start early epinephrine infusion (0.02-0.3 mcg/kg/min)
 3. If no IV, give **0.3-0.5 mg IM** in anterolateral thigh, repeat q5-15 min
 4. ACLS doses (0.1-1 mg) for cardiovascular collapse
7. Consider vasopressin bolus or norepinephrine infusion
8. Treat bronchospasm with **albuterol** and epinephrine (if severe)

Management

Secondary Treatment

- **Intubation**, especially if signs of angioedema
- **Invasive lines**: large-bore IVs, arterial line, central venous catheter, Foley catheter
- Drugs to consider after stable
 - **H₁-blocker**: diphenhydramine 0.5-1 mg/kg IV
 - **H₂-blocker**: ranitidine; not a first-line agent, but not harmful either!
 - **Steroids**: decrease airway swelling, **prevent recurrent symptoms** in biphasic anaphylaxis
 - Hydrocortisone 0.25-1 g IV, or methylprednisolone 1-2 g IV

Post event

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

Prevention

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

Testing for an Allergy

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

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.
- Takazawa T, et al. Sugammadex and rocuronium-induced anaphylaxis. *J Anaesth*. 2016, Apr;30(2):290–7.
- 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.
- Miller, R. D. (2010). *Miller's anesthesia* (7th ed.). Philadelphia, PA: Churchill Livingstone/Elsevier. 35:1110-1111.

Local Anesthetics

Local Anesthetics (LA)

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

Physiochemical Properties

- Local anesthetics are weak bases in equilibrium:

Nonionized (lipid-soluble) \longleftrightarrow *Ionized (water-soluble)*

B (neutral) + H⁺

HB⁺

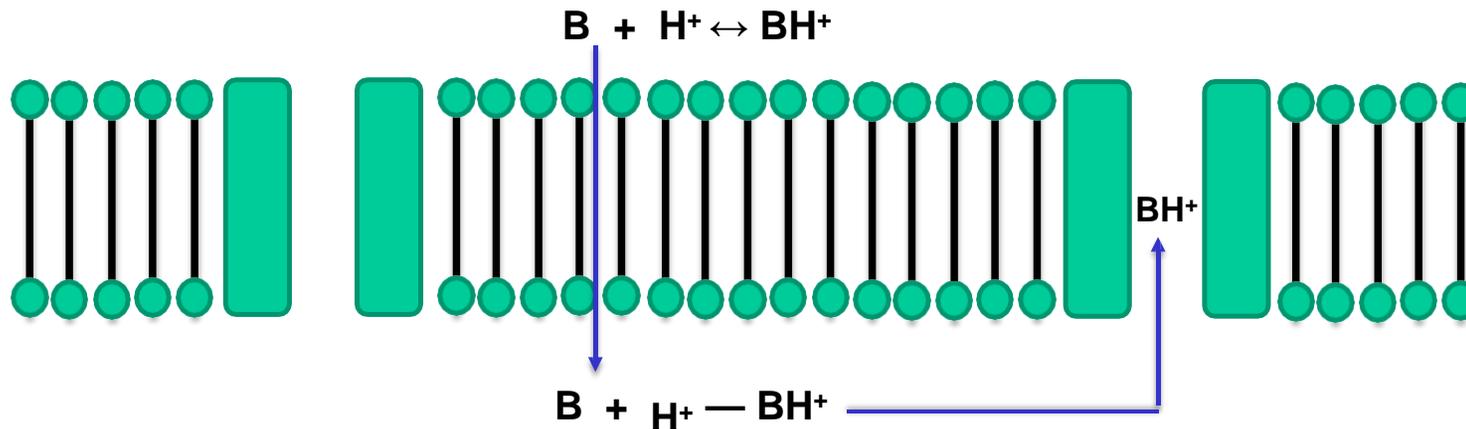
Lower pKa ←—————→ Higher pKa
Higher tissue pH Lower pH



$$pK_a = -\log \left(\frac{[B][H^+]}{[HB^+]}\right)$$

Mechanism of Action & Physiochemical Properties

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



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

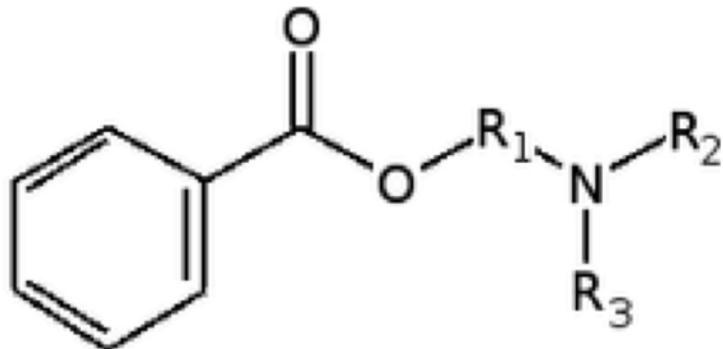
- Having a **pKa closer to physiologic pH** means a greater fraction of nonionized form (able to cross the neuronal membrane) for a **faster onset**
- Conversely, in an infected (acidic) environment, the pKa will be further from the environmental pH and have a slower onset

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

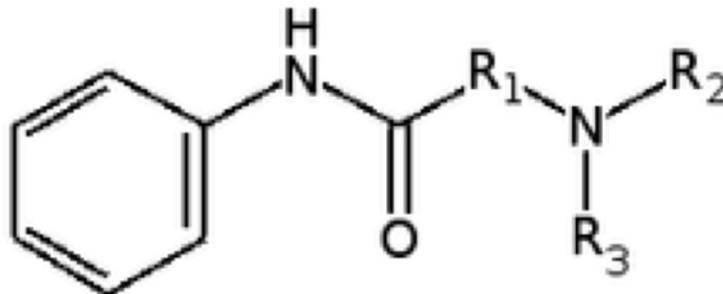
| Amides | pKa | Esters | pKa |
|-------------|-----|---------------|-----|
| Lidocaine | 7.9 | Procaine | 8.9 |
| Mepivacaine | 7.6 | Chlorprocaine | 8.7 |
| Prilocaine | 7.9 | Tetracaine | 8.5 |
| Bupivacaine | 8.1 | | |
| Ropivacaine | 8.1 | | |

Note: chlorprocaine is unique in that it has a fast onset NOT because of its pKa but because its low systemic toxicity allow us to use relatively high concentrations

Local Anesthetic Structure



Aminoester



Aminoamide

3 Major Chemical Moieties

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

Local anesthetics are weak bases

pKa > 7.4

Categories

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

Routes of Delivery

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

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

***Bupivacaine** (Marcaine) is commonly used by surgeons for infiltration at 0.25% (2.5mg/ml), with max dose 2.5mg/kg

****i.e. they can use a max volume of 1cc/kg** (70kg patient gets max 70cc).

LAST (Local Anesthetic Toxicity)

Systemic absorption by injection site (vascularity)

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

*mnemonic: ICEBALLS

Rate and extent of systemic absorption depends on:

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

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

CNS toxicity

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

Cardiovascular toxicity

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

Treatment of LAST

- Initial management:
 - Call for intralipid kit
 - ABCs if indicated: being CPR? Airway?
 - Stop local anesthetic
 - Give benzodiazepines for seizure, careful with propofol when there are signs of CV instability.
 - Reducing individual epinephrine doses to <1 mcg/kg. AVOID: vasopressin, Ca channel blockers, Beta blockers, and local anesthetics
- Initiate early intralipid (IL) therapy
 - Rapidly give **1.5 cc/kg bolus** of 20% intralipid IV (*max 3 doses)
 - Start infusion at 0.25 cc/kg/min (*max rate 0.5 cc/kg/min)
 - *if patient remains unstable, may repeat bolus and increase infusion rate

References

Liu SS, Lin Y. Local anesthetics. In Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MD eds. Clinical Anesthesia. 6th ed. Philadelphia, 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.

ASRA guidelines for management of local anesthetics toxicity. 2015.

Butterworth, John F., David C. Mackey, John D. Wasnick, G. Edward. Morgan, Maged S. Mikhail, and G. Edward. Morgan. Morgan & Mikhail's Clinical Anesthesiology. New York: McGraw-Hill, 2013.

Malignant Hyperthermia

Basics

Definition

- A **hypermetabolic** crisis that occurs when susceptible patients are exposed to a triggering anesthetic agent (halogenated anesthetics or succinylcholine)
 - Underlying defect is abnormally increased Ca^{2+} levels in skeletal muscle resulting in sustained muscle contraction
- Calcium pump attempts clearance à increased ATP usage
- Results of hypermetabolic rate
 - increase O_2 consumption, CO_2 production, severe lactic acidosis, hyperthermia, risk of rhabdomyolysis, hyperkalemia, and arrhythmia.

Genetics

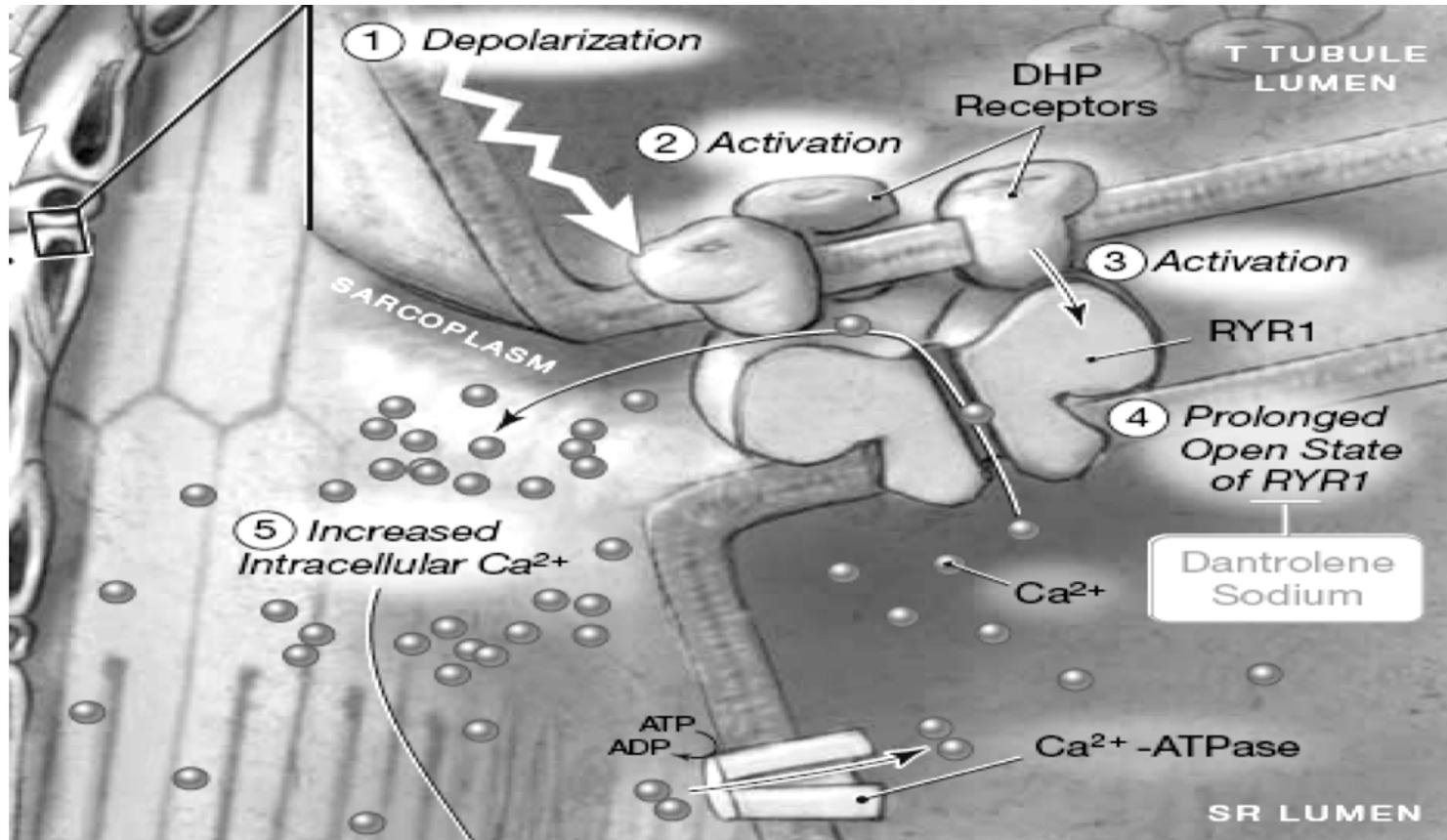
- Genetic hypermetabolic muscle disease
- 80% of cases: RYR-1 receptor mutation (affects calcium release channel in sarcoplasmic reticulum)
 - **Autosomal dominant** inheritance **with variable penetrance and expression**, but autosomal recessive forms also described (especially that associated with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

Basics (cont.)

Incidence

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

Excitation-Contraction Coupling



MH: Depolarization à **mutant RYR-1 receptor *remains open*** à unregulated calcium from SR into intracellular space à sustained contraction & increased activity of Ca^{2+} -ATPase to remove Ca^{2+} à heat generation, CO_2 production, metabolic acidosis, and rhabdomyolysis/hyperkalemia

Sequence of Events

1. Triggers

- All halogenated **inhalational agents** (not N₂O)
- **Succinylcholine**

2. Increased Cytoplasmic Free Ca²⁺

- Masseter muscle rigidity (**trismus**)*; more common if succinylcholine used
 - If there is rigidity of other muscles in addition to trismus, the association with MH is absolute
- Total body rigidity

3. Hypermetabolism

- Increased CO₂ production (most sensitive and specific sign of MH!) and metabolic acidosis
 - Note sympathetic surge of **increased HR and BP**
- Increased O₂ consumption (decreased ScvO₂)
 - Body will compensate with **tachypnea**
- Increased heat production
 - A late sign of MH; **temperature** can rise 1-2°C every 5 minutes
- Increased utilization of ATP to clear calcium: metabolic acidosis

4. Cell Damage & Rhabdomyolysis

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

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

Earliest recognized signs of MH= **muscle rigidity, tachycardia, and hypercarbia

Sequence of Events (2)

5. Secondary systemic manifestations

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

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

- Clinically, you may first see **trismus**, but often **hypercarbia** will be your first sign.
 - Without another reasonable explanation for this (hypoventilation, pneumoperitoneum), you should start looking for other signs.
 - Any increased oxygen consumption? (decreased SpO₂ or ScvO₂?)
 - Increased metabolic & sympathetic activity? (increased etCO₂, HR, temperature, lactate)
 - Signs of rhabdo or any electrolyte abnormalities? (Hyperkalemia/arrhythmias, CKMB, urine myoglobin/blood tinged urine)

Differential Diagnosis

| | |
|---|--|
| Neuroleptic Malignant Syndrome (NMS)** | More common in patients receiving antidopaminergic agents or in withdrawal from dopamine agents as in Parkinson's, usually develops over days rather than minutes to hours |
| Thyroid Storm** | Usually associated with hypokalemia |
| Sepsis | fever, tachypnea, tachycardia, metabolic acidosis |
| Pheochromocytoma | ↑HR, ↑BP, but <u>normal EtCO₂</u> and Temp |
| Drug-induced | e.g. ecstasy, cocaine, amphetamines, PCP, LSD |
| Serotonin Syndrome | associated drugs interactions MAOIs + merperidine or MAOIs+ SSRIs |
| Iatrogenic Hyperthermia | |
| Hypercarbia from CO2 insufflation for laparoscopy | see ↑EtCO ₂ with tachycardia |

**Dantrolene can also treat both of these conditions

Treatment - Acute Phase

| | |
|---|---|
| Immediate Actions | <ul style="list-style-type: none"> • Call for Help & obtain MH cart; inform team and start preparing dantrolene or ryanodex • D/C volatile agents and succinylcholine (no need to change machine or circuit) **Switch to 100% O₂ with high flows >10L/min; increase minute ventilation • Halt surgery vs. finish ASAP with TIVA; arrange for ICU bed • Call MH hotline (1-800-MH-HYPER) • Labs: ABG, lactate, K⁺/electrolytes, CK, Coags; place foley to monitor UOP |
| Dantrolene (interferes with RYR-1 Ca ²⁺ channel) | <ul style="list-style-type: none"> • 2.5 mg/kg IV push q5min; patient may need >10mg/kg; continue giving until stable. Give through large bore IV or central line (risk of phlebitis); assign several people to prepare this • 1 vial = 20mg Dantrolene (dissolve in 60 cc sterile water); solution has mannitol **New Ryanodex (250mg vial in 5cc sterile water) • Continue until stable (decrease in EtCO₂, rigidity, and tachycardia); continue dantrolene infusion 0.25mg/kg/hr for at least 24 hrs |
| Treat Acidosis | <ul style="list-style-type: none"> • Hyperventilate patient • Sodium Bicarbonate 1-2 mEq/kg |
| Treat hyperkalemia & ARF | <ul style="list-style-type: none"> • CaCl₂ (10mg/kg) or Calcium gluconate (30mg/kg); Bicarbonate, hyperventilate • Insulin and glucose (10 units in 50cc D50) • Sodium bicarbonate (1-2 mEq/kg) • Diuresis; urine output goal > 1-2cc/kg/hr to help prevent pigment induced nephropathy/ARF and reduce hyperkalemia; consider IV fluids, diuretics, and alkalinize urine |
| Treat dysrhythmias | <ul style="list-style-type: none"> • Avoid CCBs (may promote hyperkalemia and depress cardiac output) • Treat hyperkalemia and acidosis; if refractory, may need to add an antiarrhythmic |
| Treat temp | <ul style="list-style-type: none"> • Cool if temp >39 degrees C (cooling blankets, ice, cold NS, lavage stomach/bladder/rectum) |
| Labs | <ul style="list-style-type: none"> • ABG, lactate, K⁺/electrolytes, CK, urine myoglobin, Coagulation studies |

Treatment – Post Acute Phase

| | |
|-----------------------------------|---|
| Admit to ICU | <ul style="list-style-type: none">• ICU admission for at least 24 hrs (recrudescence rate 25%) |
| Continue monitoring | <ul style="list-style-type: none">• Labs: serial ABG, lactate, Electrolytes (K⁺, Ca²⁺), CK/serum myoglobin, Urine myoglobin, Coags• EtCO₂, temp, urine output/color• *Watch for DIC and renal failure* |
| Counsel patient and family | <ul style="list-style-type: none">• Future precautions• Refer to MHAUS• Refer patient and family to nearest Biopsy Center for follow-up |

Who is Susceptible to MH?

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

Susceptibility Testing

Caffeine-Halothane Contracture Test (CHCT)

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

Molecular Genetics

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

Prevention in Susceptible Patients

1. Machine

- Change circuit and CO₂ absorbent
- Remove or disable vaporizers
- Refer to anesthetic machine regarding time required to flush machine (FGF of 10 L/min for ≥20 minutes)
 - During case, keep flows > 10L/min to avoid “rebound phenomenon” (release of dissolved residual volatile anesthetic agent)

2. Monitors

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

3. Anesthetic

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

4. Emergency

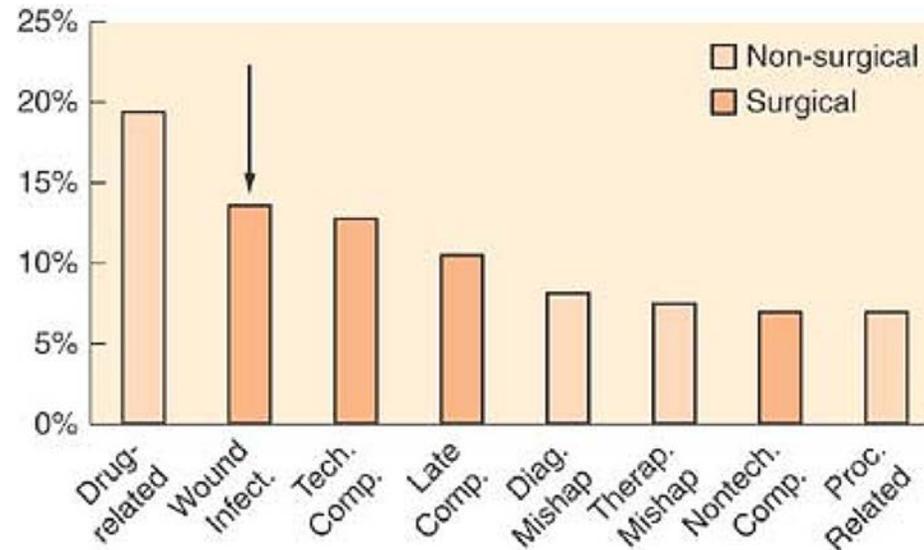
- Know where to find the MH cart
- Have dantrolene or ryanodex available

References

- 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.
- 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.
- Murray MJ, et al. *Faust’s Anesthesiology Review, 4th ed.* (2015)
- UCLA Department of Anesthesiology (<http://www.anes.ucla.edu/dept/mh.html>)

Perioperative Antibiotics

Why Antibiotics?



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

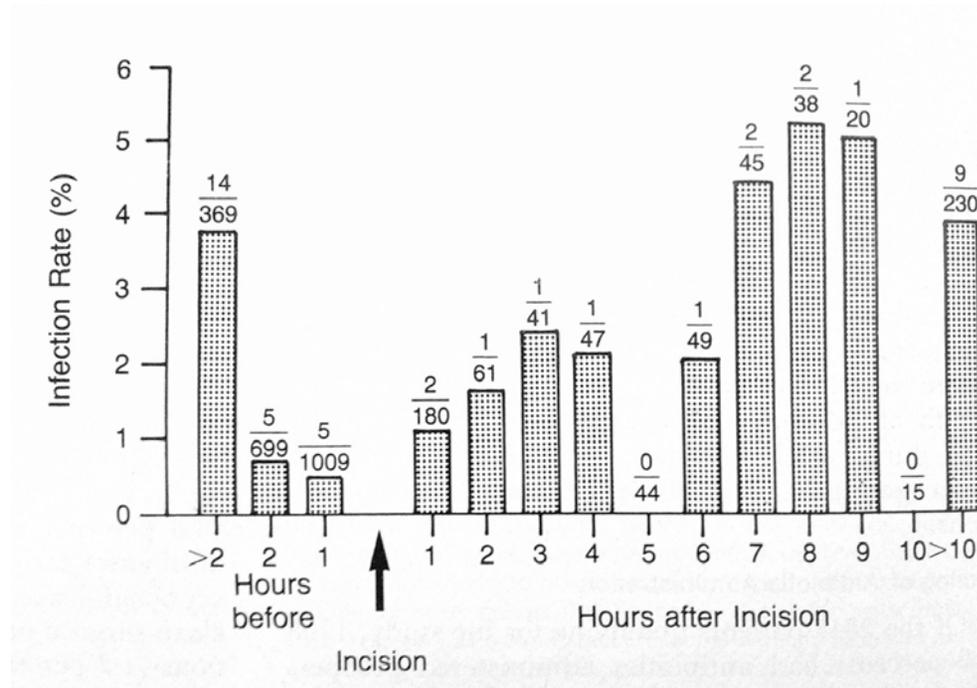
Perioperative antibiotic prophylaxis – administration of abx prior to surgery to prevent surgical site infections, **but best practice also includes sterility (surgeon and instruments), skin prep (clipping hair, allowing skin antiseptic to dry)**

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

Timing of prophylaxis

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

Timing of prophylaxis



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

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

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

Types of Wounds (per CDC/NHSN)

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

2017 SHC Surgical Antimicrobial Prophylaxis Guidelines*

| Surgery | Preferred Agent | Beta-lactam allergy |
|--|--|---|
| Cardiac Surgery/Vascular/Thoracic Cardiac device insertion (PM implant) Other General Surgery (hernia, breast) Neurosurgery Orthopedics Plastic Surgery | Cefazolin | Vancomycin (preferred) <i>Clindamycin can be used as an alternative. Based on 2015 SHC Antibiogram, 81% MSSA susc to clinda vs 100% MSSA susc to vanc</i> |
| Cardiac Surgery w/ prosthetic material | Cefazolin + Vancomycin | Vancomycin |
| Gastroduodenal | Cefazolin | Vancomycin + Gentamicin |
| Biliary Tract | Cefazolin | Metronidazole + Levofloxacin |
| Colorectal, Appendectomy | Cefazolin + Metronidazole | Metronidazole + Levofloxacin |
| Gynecological (hysterectomy/Cesarean) | Cefazolin | Clindamycin + Gentamicin |
| <i>Urology</i> <i>These are EMPIRIC abx recs when no preoperative urine cx available or culture negative. Ask urology team for recs.</i> | <i>If clean: Cefazolin</i> <i>If clean contaminated (eg open or lap with ileal conduit)- cefoxitin</i> <i>If prosthetic material involved, should add gentamicin x1 dose</i> | Gentamicin + Clindamycin ¹ <i>If clean: (skin incision only)- clinda¹</i> <i>If clean-contaminated: metronidazole + levofloxacin</i> ¹ sub vanc for clinda if MRSA due to clinda poor urinary penetration |
| Head & Neck | Clean or ear/sinonasal: Cefazolin <i>If contaminated (include oral mucosa breach)- Cefazolin+ Metronidazole</i> | Clindamycin |

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

Selected 2017 SHC Dosing and Re-dosing Guidelines

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

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

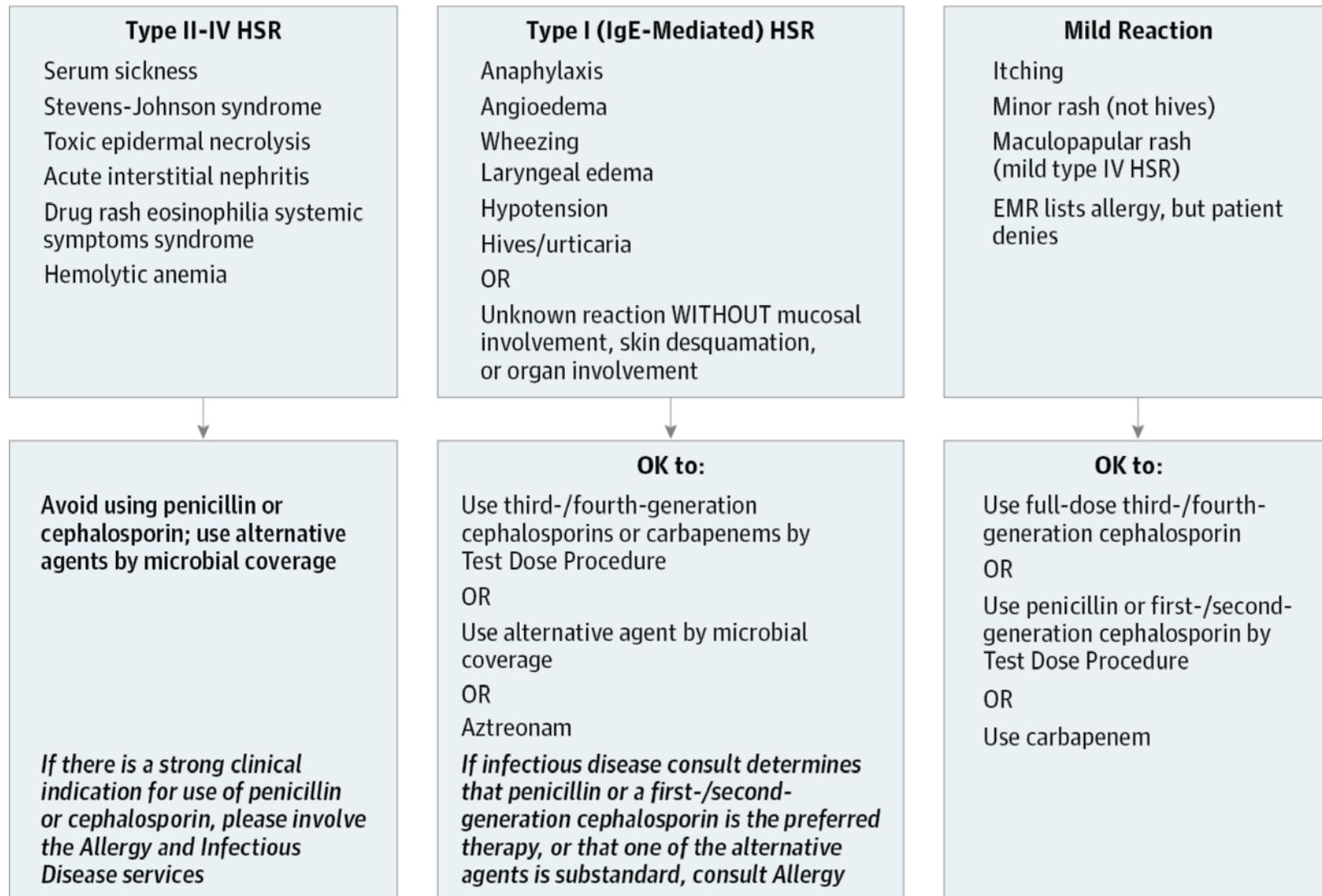
Allergies and Interactions

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

Allergies and Interactions

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

Penicillin Allergy Pathway for Antibiotic Prescriptions



Endocarditis Prophylaxis

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

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

Topics for Discussion

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

Anesthesia Exams & Dates

| | | |
|--|---|--|
| ABA In-Training Exam (ITE) | February every year | Percentile scoring; important for fellowship programs |
| ABA BASIC Exam | June of CA-1 year | Pass/Fail. No percentile reported |
| ABA ADVANCED Written | Post training (July & January) | You must pass the Advanced written exam to be eligible to take Applied |
| ABA Applied Exams (Oral Boards & OSCE)** | Post training (9 sessions offered per year) | |

**To help better prepare residents for the ABA Oral Boards & OSCE:

- Mock Orals are offered November & May of each year
- Mock OSCEs are offered in April of CA3 year

What to study?

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

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

What to study?

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

- Online question banks Truelearn
 - Truelearn: <https://truelearn.com/> (department group discount available)
- Online resources
 - Open Anesthesia: <http://openanesthesia.org>
 - Learnly: <https://learnly.org>
- Podcasts
 - ACCRaC: <http://accrac.com/>
- Online library
 - Stanford Anesthesia: <http://inkling.com/read> - (*ask others for the username and password)
 - Lane Library: <https://lane.stanford.edu/index.html>
- Textbooks
 - *Faust's Anesthesia Review* (concise short chapters to cover ITE topics)
Available through Lane Library: *Basics of Anesthesia* (Miller), *Clinical Anesthesiology* (Morgan & Mikhail), *Clinical Anesthesia* (Barash), *Anesthesiology* (Yao & Artusio)