

# CRASH 2019

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## CRASH 2019 Program

### Sunday, February 24

- 4:00-5:00 pm What's New in Obstetric Anesthesia? – Joy L. Hawkins, MD
- 5:00-6:00 pm Anesthesia for Patients on Mechanical Circulatory Support for NCS – Breandan Sullivan, MD
- 6:00-6:30 pm Q&A
- 6:30-7:30 pm Opening Night Reception

### Monday, February 25

#### Morning

- 7:00-8:00 am Anesthesia for the Critically Ill Patient – Jeffrey Kirsch, MD
- 8:00-9:00 am Trauma – Bethany Benish, MD
- 9:00-9:30 am Q&A

#### Afternoon

- 4:00-6:00 pm Questions and Controversies in Obstetric Anesthesia Practice– Joy Hawkins, MD; Rachel Kacmar, MD; Brenda Bucklin, MD
- 4:00-6:00 pm Cardiac Panel – Breandan Sullivan, MD; Maung Hlaing, , MD; Richard Ing, MD
- 4:00-7:00 pm Airway Workshop: Bethany Benish, MD; Marina Shindell, DO; Brian Somerset, DO; David Abts, MD; Nicole Arboleda, MD

### Tuesday, February 26

#### Morning

- 7:00-8:00 am Regional Anesthesia for Vascular Surgery –Kyle Marshall
- 8:00-9:00 am Anesthesia for Spine Surgery & Neuromonitoring – Jeffrey Kirsch
- 9:00-9:30 am Q&A

#### Afternoon

- 4:00-6:00 pm Healthcare Management Panel – Randall Clark, MD; Brian Davidson, MD; Steven Zeichner, MD
- 4:00-6:00 pm Trauma Panel – Bethany Benish, MD; Mark Chandler, MD; Nicole Arboleda, MD
- 4:00-6:00 pm Basic Regional Ultrasound Workshop: Christopher Ciarallo, MD; Seth Eisdorfer, MD; Roland Flores, MD; Kyle Marshall, MD; Olivia Romano, MD; Marina Shindell, DO; Inge Tamm-Daniels, MD; Jillian Vitter, MD

### Wednesday, February 27

#### Morning

- 7:00-8:00 am High risk ambulatory patients – Bobbie Jean Sweitzer
- 8:00-9:00 am Anesthesia for Neurovascular Surgery – Jeffrey Kirsch
- 9:00-9:30 am Q&A

#### Afternoon

- 4:00-6:00 pm Pain Panel – Alan Bielskij, MD; Narayana Varhabhatla, MD; Rachael Rsaza-Lynn, MD
- 4:00-6:00 pm Ethics Panel – Lawrence Schwartz, MD; Mark Twite, MD; Nathaniel Brown, MD
- 4:00-7:00 pm Advanced Regional Ultrasound Workshop: Christopher Ciarallo, MD; Seth Eisdorfer, MD; Roland Flores, MD; Kyle Marshall, MD; Olivia Romano, MD; Marina Shindell, DO; Inge Tamm-Daniels, MD; Jillian Vitter, MD

### Thursday, February 28

#### Morning

- 7:00-8:00 am Update on Pediatric Anesthesia – Patrick Fernandez
- 8:00-9:00 am Seeing Ketamine in a new light – Bobbie Jean Sweitzer
- 9:00-9:30 am Q&A

Afternoon

- 9am - 5pm Full Day Wilderness Survival Medicine Workshop–Jay Lemery, MD; Todd Miner, Ed.D, FAWM  
4:00-6:00 pm Pediatric Anesthesia Panel – Lawrence Schwartz, MD; Debnath Chatterjee, MD;  
Patrick Fernandez, MD  
4:00-6:00 pm Wellness Panel – Norah Janosy, MD; Alison Brainard, MD; Melanie Donnelly, MD

**Friday, March 1**

Morning

- 7:00-8:00 am Perioperative Evaluation and Anesthetic Management of Patients with Cardiac Disease for Non-  
Cardiac Surgery – Bobbie Jean Sweitzer, MD  
8:00-9:00 am Environmental impact of Anesthesia - David Abts, MD  
9:00-9:30 am Q&A  
10:00 am Adjourn



University of Colorado  
Anschutz Medical Campus  
School of Medicine

# Disclosure of Relevant Financial Relationships

## **CRASH** Colorado Review of Anesthesia for Surgicenters and Hospitals

**Feb 24 – Mar 1, 2019**  
**Vail, CO**

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**Racheal Rzasa-Lynn and Olivia Romano** have reported intentions to discuss unapproved uses for drug products and/or devices.

All other contributors have reported no commercial affiliation associated with this conference or intentions to discuss unapproved uses for drug products and/or devices.

# Sunday

## WHAT'S NEW IN OBSTETRIC ANESTHESIA FROM 2018?

Joy L. Hawkins, M.D.  
University of Colorado SOM  
(\* I have no conflicts to disclose. \*)

1

## GOALS & OBJECTIVES

Discuss how literature from the past year may:

1. Change clinical practice in obstetric anesthesia via new guidelines and policies.
2. Produce best practices for analgesic and anesthetic techniques during labor and delivery.
3. Optimize and expedite management of anesthetic and obstetric complications.
4. Alter practices affecting the fetus and newborn.

2

## NEW GUIDELINES AND POLICIES

3

## INDUCTION OF LABOR

At 38 weeks, low-risk nulliparous women were randomized to IOL at 39 weeks or expectant management.

- Multi-center U.S. study with 3000+ in each group.
- Neonatal death or complications were less in IOL group (4.3% vs. 5.4%, RR 0.80).
- Cesarean delivery rate was lower in the IOL group (18.6% vs. 22.2%, RR 0.84).
- Result: we will see more elective inductions at 39 weeks.  
N Engl J Med 2018; 379: 513

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## REDUCING PRIMARY CESAREANS

Consensus bundle from the National Partnership for Maternal Safety includes best practice recommendations for care of women with neuraxial in labor:

- Encourage position changes for fetal rotation
- Allow a longer second stage for pushing
- Allow passive descent if no urge to push
- Preserve motor function as much as possible
- Maintain the epidural infusion during 2<sup>nd</sup> stage
- Allow the woman control by using PCEA + infusion.

Obstet Gynecol 2018; 131: 503

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## CLINICAL TRIALS & PREGNANCY

Women with chronic conditions requiring medication –e.g. asthma, depression, epilepsy, bipolar disorder – get conflicting advice about their medications due to lack of data.

- Pregnant women are drug orphans, excluded by trials.
- Not doing research with pregnant women is unethical because 73% will *need* to take medications during pregnancy.
- They are not a *vulnerable population*. Being pregnant does not change your ability to make decisions for yourself.

JAMA 2018; 320: 742

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## NONOBSTETRIC SURGERY

Joint statement with ACOG updated October 2018. Edits:

- There is no evidence that in utero anesthetic or sedative drugs have any effect on the developing fetal brain.
- A pregnant woman should never be denied medically necessary treatment or have it delayed.
- Steroids for fetal benefit should be considered preoperatively.
- Screen for VTE risk and use appropriate prophylaxis.
- Fetal monitoring may be appropriate....the woman should have provided informed consent for emergency C/S.

ASAHQ.ORG and ACOG.ORG

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## MH ON L&D

The Malignant Hyperthermia Association of the U.S. recommends that dantrolene be available within 10 minutes; often an MH cart.

- Maintaining an MH cart and full dantrolene dose on L&D is expensive, rarely used, and the drugs often expire.
- A cost-benefit analysis found that costs for a full dantrolene supply on L&D exceeded benefits.
- Modeling found a more cost-effective approach was to keep an initial dose of dantrolene (250 mg) on L&D with a central (OR?) supply source available within 30 minutes.

Anesthesiology 2018; 129: 249

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## ANALGESIA FOR LABOR

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## PLATELETS IN PREGNANCY

What is the normal trend in platelet count over the course of an uncomplicated pregnancy?

- First trimester mean platelet count = 251,000. Count declines 17% during pregnancy to 217K at delivery.
- Lower than the mean for nonpregnant women = 273K.
- At delivery, 10% of women with an *uncomplicated* pregnancy had a platelet count < 150,000.

N Engl J Med 2018; 379: 32

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An example of a mobile N2O delivery system with oxygen and scavenging connections.



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## NITROUS OXIDE FOR LABOR

- Commonly used worldwide for labor analgesia.
- Minor side effects for the mother; no known fetal effects (neurotoxicity?), and rapidly reversible vs opioids.
- Can be used if an alternative to neuraxial is needed (e.g., external cephalic version for breech, perineal repair).
- No relevant occupational exposure for L&D nurses.
- Satisfaction scores are similar for neuraxial analgesia, N2O, or when women transition from N2O to an epidural.
- Meets CMS guidelines for conscious sedation.

OBG Management 2018; 30: 29

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## NITROUS OXIDE FOR LABOR

	UCSF	UColorado
% using N <sub>2</sub> O	14%	20%
N <sub>2</sub> O→epidural	42%	65%
Epidural only	76%	75%
Adverse events	0	0

UCSF found N<sub>2</sub>O use did not affect admission to NICU, 5-minute Apgars, maternal bleeding.

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## NITROUS OXIDE

A survey of women who used N<sub>2</sub>O for labor analgesia found the determinants of satisfaction were quite variable:

- Appreciated relaxation, the distraction, focus on breathing.
- Analgesia was *sufficient* for their expectations.
- Equated with “natural childbirth”, so it fit their birth plans.
- Felt it was a vital component of their birth experience.
- Used nitrous when epidural was not possible.

Birth 2018; Richardson et al.

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## AIR vs. SALINE

For labor epidural catheters, does LOR to saline facilitate better analgesia at 30 minutes than LOR air?

- 376 randomized parturients
- Pain score reduction, efficacy of the block, and motor block were no different between groups.
- LOR to air versus saline is not clinically important to initial pain relief during labor.

Anesth Analg 2018; 126: 532

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## PROGRAMMED INTERMITTENT BOLUSES

Cochrane review of automated bolus (PIEB) vs. continuous infusion for epidural labor analgesia:

- Included 12 RCT and 1121 women.
- The use of automated boluses ↓ breakthrough pain, ↓ hourly consumption of local anesthetic, and ↑ maternal satisfaction in comparison to continuous infusion.
- No difference in duration of labor, risk of cesarean or instrumental delivery, or neonatal outcome.

Cochrane Database 2018: 011344

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## BUPRENORPHINE THERAPY

Buprenorphine has high mu-receptor affinity making it difficult to displace by other opioids. Would substituting clonidine for fentanyl in the epidural solution improve adequacy of analgesia?

- 2 µg/ml clonidine + usual bupivacaine infusion.
- Good / excellent analgesia during labor & postop.
- Hypotension occurred, but no sedation or ↓ HR.

Int J Obstet Anesth 2018; 34: 67

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## IMMEDIATE VS DELAYED PUSHING

A randomized trial of 2404 nulliparous women with neuraxial analgesia studied whether immediate or delayed pushing affects spontaneous vaginal delivery.

- No different in spontaneous vaginal delivery (~ 86%)
- Immediate pushing → more 3<sup>rd</sup> and 4<sup>th</sup> degree lacerations
- Delayed pushing → more chorioamnionitis, hemorrhage
- Delay lengthens labor without benefit to mother, infant

JAMA 2018; 320: 1444

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## PP TUBAL LIGATION

Procedure completion rates for PPTL are only 31% to 52%.  
Reasons for failure to do the procedure:

- Too sick: e.g. severe anemia from sickle cell disease
- Too busy: team can't fit her into the busy day on L&D
- Too soon: signed her Medicaid consent < 30 days prior
- Too late: she ate after delivery and NPO time puts the procedure in the middle of the night
- Competing risks: L&D too busy to perform immediately after delivery, but she needs her anti-coagulation restarted ASAP

Anesth Analg 2018; 126: 1225

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## ANESTHESIA FOR CESAREAN DELIVERY

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## UTERINE DISPLACEMENT

100 healthy women having spinal anesthesia for their cesarean received a crystalloid co-load and a phenylephrine infusion, then were placed in 15 degrees left tilt or supine.

- There was no difference in fetal pH or base deficit.
- Maternal tilt did not improve neonatal acid-base status.
- But, phenylephrine requirements were *higher* when supine.
- And mean maternal cardiac output was *lower* if supine.

Anesthesiology 2017; 127: 241

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## UTERINE DISPLACEMENT

Counter-arguments (letter): What about the mother?!

- Maternal BP and cardiac output were both lower without tilt, despite receiving 29% more phenylephrine.
- A few women had classic *supine hypotensive syndrome* (study was not powered to find the expected 8% incidence).
- We don't know ahead of time who will benefit from tilt after spinal anesthesia and who will not, so better to be safe.

Anesthesiology 2018; 128: 858

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## ISOBARIC BUPIVACAINE

Systematic review of isobaric vs. hyperbaric spinal bupivacaine for cesarean delivery:

- 10 studies with 614 subjects using 12-13 mg (2.5 ml 0.5% isobaric bupivacaine) + fentanyl
- No difference in risk of conversion to general anesthesia or in need for supplemental analgesia.
- No difference in nausea, vomiting, use of ephedrine or dose of ephedrine used.

Anaesthesia 2018; 73: 499

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## ISOBARIC BUPIVACAINE

Meta-analysis of bupivacaine spinal anesthesia – isobaric vs. hyperbaric - in adult, *non-obstetric* surgeries:

- 16 RCT, 724 participants
- No difference in failure rates or onset times.
- No difference in hypotension or nausea and vomiting.
- The duration of sensory and motor block was longer with isobaric bupivacaine (by 29 and 45 minutes).

Anesth Analg 2017; 125: 1627

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## ERAS FOR CESAREAN

Does an ERAS protocol for *open gynecologic surgery* have benefits in the immediate and extended postoperative period? Yes!

- Median length of stay was decreased by 25%.
- 72% reduction in opioid consumption, yet no differences in pain scores. 16% were opioid-free during admission.
- Patients on the ERAS protocol reported less fatigue and less “interference” with their activities.

Obstet Gynecol 2018; 132: 281

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## ERAS FOR CESAREAN

One institution reported on patients undergoing elective cesarean delivery; 195 women Pre-ERAS and 162 with ERAS.

- Morphine-equivalent consumption ↓ (from 37 to 22 mg)
- The highest reported pain score was less using ERAS.
- Hospital length of stay ↓ (3 days to 2 days)
- Length of stay in hours ↓ (69 hours to 58 hours)

SOAP Newsletter Winter 2018; page 6

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## ERAS: ELECTIVE CESAREAN

### Preoperative education:

- Schedule a 1:1 meeting with RN at 32-34 weeks.
- Provide a comprehensive education booklet that includes SSI prevention and breastfeeding education.
- Discuss NPO guidelines and encourage fluid intake (e.g. Gatorade™) up to 2 hours before surgery.
- Encourage continued exercise.
- Call her the day before surgery to review checklist.

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## ERAS: ELECTIVE CESAREAN

### Intraoperative management:

- At admission, review checklist compliance and place IV.
- Administer appropriate antibiotic prophylaxis.
- Spinal anesthesia includes fentanyl and morphine.
- Fluid co-load, phenylephrine infusion at spinal injection.
- After delivery, do delayed cord-clamping for at least 60 s.
- Administer oxytocin and PONV prophylaxis.
- In OR skin-to-skin ± breastfeeding; room temp > 72 degrees.

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## ERAS: ELECTIVE CESAREAN

### Postoperative Care:

- Ice chips in PACU → food when on postpartum unit.
- Begin scheduled multi-modal non-opioid analgesia.
- Oxycodone 5 mg is available for breakthrough pain.
- Urinary catheter removed at 12 hours postop.
- Encourage early mobilization after block wears off.
- Remove IV 24 hours post-surgery.
- VTE prophylaxis. Lactation consult. Peds visit.

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## OTHER ERAS GUIDELINES

The ERAS Society is a multi-disciplinary group (OB/Gyn, Anesthesiology, Pediatrics, Medicine) that has published guidelines for scheduled and unscheduled cesarean deliveries using evidence-based knowledge, and rating recommendations by quality of evidence and strength of recommendation. Relative to anesthetic care:

- Preop meds (aspiration prophylaxis) and NPO guidelines
- Intraoperative SSI elements, regional anesthesia, normothermia, fluid management, delayed cord clamping.

Am J Obstet Gynecol, December 2018

30

### ACOG: PP PAIN MANAGEMENT

- Pain can interfere with a woman's ability to care for herself and her baby BUT 1:300 opioid-naïve women become persistent users of opioids after cesarean.
- Emphasize multi-modal non-opioid agents, with opioids reserved only for treating breakthrough pain.
- Median opioid tablets used after cesarean discharge = 20.
- Use shared decision-making approach to discharge opioid prescriptions using the shortest reasonable duration of use.

Obstet Gynecol 2018; 132: e1-e9

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### PREDICTING POST-C/S PAIN

What are the best predictors of severe post-Cesarean pain to plan for more intense interventions?

- This is a systematic review and infographic.
- Postop pain has a strong correlation with the patient's pain score during skin infiltration with local anesthetic.
- Use 3 preop questions: How anxious are you about your surgery? How much pain do you expect? How much pain medication do you anticipate needing?

Anesth Analg 2018; 126: 1606

32

### QL vs. TAP BLOCKS

A randomized trial compared quadratus lumborum (QL) to transversus abdominus plane (TAP) blocks after cesarean.

- QL block was more effective than TAP blocks in ↓ morphine requests and consumption after cesarean.
- This effect was observed up to 48 hours postoperatively.
- The QL block may facilitate spread of LA into the paravertebral space, achieving visceral pain relief.

Reg Anesth Pain Med 2016; 41: 757

Anesth Analg 2018; 126: 559

33

### DEXAMETHASONE

A meta-analysis to assess the prophylactic anti-emetic effect of dexamethasone in patients receiving long-acting neuraxial opioids (i.e. morphine).

- Dexamethasone reduced the need for rescue anti-emetics (RR 0.44) in the first 24 postoperative hours.
- There was no difference between doses (2.5-10 mg)
- No patient developed infection or restlessness.

Anaesthesia 2018; 73: 480

34

### RESPIRATORY DEPRESSION

Systematic review of respiratory depression in women receiving neuraxial morphine for cesarean delivery.

- Prevalence of respiratory depression is unknown.
- Highest and lowest prevalence using clinically relevant doses was 1.08 – 1.63 per 10,000.
- There were no cases in the ASA Closed Claims database.
- Conclusion: the prevalence of clinically significant respiratory depression in the obstetric population is low.

Anesth Analg 2018; 127: 1385

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### FAILED INTUBATION

Large QI database from community hospitals was used to determine difficult and failed intubation rates over 14 years from 2002-2015. 421,581 procedures were evaluated.

- There was a fourfold reduction in both event rates: **difficult** fell from 6.6 per 1000 to 1.6 and **failed** fell from 0.2 per 1000 to 0.06 per 1000.
- No results specific to obstetric cases.
- Is improvement due to airway devices, algorithms, other?

Anesthesiology 2018; 128: 502

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## ANESTHETIC COMPLICATIONS

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## CLOSED CLAIMS REVIEW

A closed claims review of the Harvard Medical Institutions' insurer from 2005-15 found 106 closed claims related to obstetric anesthesia.

- Largest number of claims (55%) were maternal nerve injury, but 78% of these did not result in payment.
- Maternal death / brain damage occurred in only 15% of cases but resulted in more and higher payments made.

(continued)

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## CLOSED CLAIMS REVIEW

- Causes of maternal death or brain injury → high neuraxial blocks, failed intubation and embolic events.
- Claims that were settled with payments made (versus claims that were dropped/denied/dismissed) more often involved general anesthesia (p=.03) and were associated with delays in care (p=.005).
- Failure of the anesthesiologist to address pain in a timely and compassionate fashion was a common issue.

Anesth Analg 2018; PAP

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## PAIN DURING CESAREAN

92% of cesareans in the UK are done using neuraxial. Intraop pain is *the most common* successful negligence claim.

- 360 cases of pain during C/S from NHS Litigation Authority
- Sub-standard consent in 50%; inadequate or undocumented.
- Surgery allowed to start despite inadequate block in 42%.
- Despite lack of adequate intra-operative anesthesia, there was a reluctance to convert to general anesthesia.
- Failed to document the events and their thought processes.

Anaesthesia 2018; 73: 223

40

## POC ULTRASOUND

Review of POC ultrasound uses on L&D:

1. Gastric ultrasound to determine risk of aspiration.
2. Crico-thyroid membrane identification for emergency airway access when you can't intubate, can't ventilate.
3. Evidence of pulmonary edema to guide fluid therapy.
4. Leg veins + cardiac ECHO if DVT or pulmonary embolus is suspected.
5. Determine causes of circulatory failure or cardiac arrest.

Anaesthesia 2018; 73: 1265

41

## POST-DURAL PUNCTURE HA

Meta-analysis: What is the association between spinal needle characteristics and incidence of PDPH?

- 57 RCT included
- Pencil-point design reduced PDPH (RR 0.41) in both obstetric and non-obstetric patients
- There is a correlation between ↑ needle gauge and PDPH for cutting-needle design, but not for pencil-point needles.

Reg Anesth Pain Med 2018; 43: 502

42

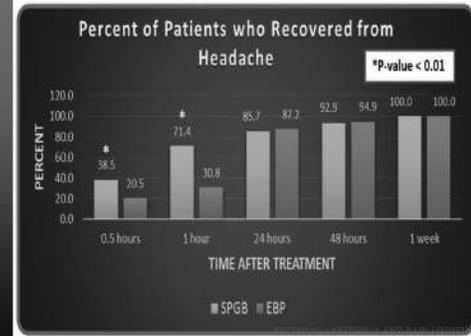
### SPHENOPALATINE BLOCK

Retrospective chart review compared 42 postpartum patients with PDPH who received SPG block with 39 having EBP.

- More women had relief after 30 and 60 minutes with SPG.
- Only EBP patients had post-treatment complications, all of which resolved in 48 hours.
- Only EBP patients returned to the ER due to return of HA (23% vs. 0%).
- All patients were headache-free 1 week after treatment.

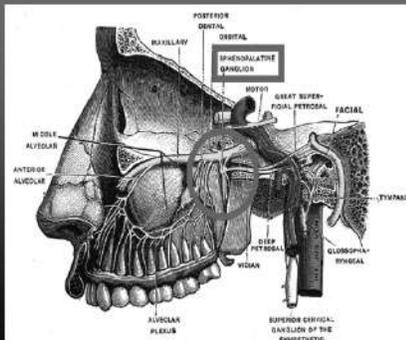
Reg Anesth Pain Med 2018; 43: 880

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1. Position supine in the sniffing position.
  2. Place a 2% or 4% lidocaine-soaked cotton-tipped applicator in the posterior naso-pharynx bilaterally.
  3. Leave for 10 minutes.
  4. Repeat for an additional 20 minutes.
- SOAP Newsletter, Winter 2019, page 10



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### OTHER PDPH TREATMENT

Can neostigmine and atropine improve PDPH symptoms?

- Neostigmine and atropine have effects on CSF secretion and cerebral vascular tone.
- Double-blinded RCT of 85 patients used saline as a placebo
- No patients in NA group needed blood patch vs. 16% in the placebo group (all received other conservative therapy).
- Complications included abdominal cramps, muscle twitches and bladder hyperactivity in the NA group.

Anesth Analg 2018; 127: 1434

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### ASRA GUIDELINES: HEPARIN

“The anticoagulant effect of heparin...increases disproportionately with increasing doses.” *Reg Anesth Pain Med 2018; 43: 269*

#### Intravenous heparin:

- D/C infusion 4-6 hours and verify normal PTT.

#### Preoperative SC low-dose heparin (5000 U BID or TID)

- Wait 4-6 hours after last dose or assess their PTT.

#### Preoperative SC “higher dose” UFH (daily dose ≤ 20,000 U)

- Wait 12 hours and assess PTT.

#### Preoperative SC therapeutic UFH (daily dose > 20,000 U)

- Wait 24 hours and assess PTT.

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### SOAP GUIDELINES: HEPARIN

Differ from ASRA guidelines in that they take into account:

- Different pharmacokinetics in pregnancy (↑ GFR and volume of distribution) → plasma heparin AUC was only 55% that of nonpregnant women.
- Potential risks of general anesthesia to mother and fetus.
- Notes the lack of cases of spinal hematoma in obstetric patients receiving thromboprophylaxis.

Anesth Analg 2018; 126: 928 (continued)

48

## SOAP GUIDELINES: HEPARIN

- For *low- intermediate dosing* (as defined by ASRA), optimal intervals to wait (4-6 hours and 12 hours respectively) are the same, but if PTT is normal or anti factor Xa level is undetectable, management may be different:
- “For urgent or emergent obstetric procedures, assess the competing risks of general anesthesia compared to the risk of spinal-epidural hematoma. With greater competing risk of GETA, the placement of neuraxial anesthesia without delay may be appropriate.”
- For *high-dose* > 20K U daily, there are insufficient data to recommend proceeding < 24 hours since the last dose.

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## TREATMENT OF LAST - 2018

Changes to the LAST checklist include the following:

- Lipid emulsion dosing is simplified; precise volumes and rate of administration are not important if  $\geq 70$  kg.
- Prolonged resuscitation may require volumes of lipid  $\geq 1$  liter.
- Emphasizes differences in resuscitation: reduce epinephrine doses to < 1 mcg/kg and avoid vasopressin, calcium channel blockers, beta blockers or other local anesthetics (e.g. lidocaine).
- Alert the CPB team earlier when calling for help.

Reg Anes Pain Med 2018; 43: 150

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## TREATMENT OF LAST - 2018

1. Secure the airway immediately to prevent hypoxia and respiratory acidosis.
2. Call for lipid emulsion 20% and administer ASAP: bolus 1.5 ml/kg (~100 ml), then 0.25 ml/kg/minute (~20 ml/min) up to 10-12 ml/kg of lipid delivered over 30 minutes.
3. If cardiac arrest occurs, deliver high-quality CPR using lower-doses of epinephrine (< 1 mcg/kg) to prevent the acidosis and arrhythmias seen with higher doses + amiodarone as an anti-arrhythmic agent.
4. Avoid vasopressin, lidocaine, Ca-channel blockers and  $\beta$ -blockers.

Anesth Analg 2018; 126: 736 (infographic) and 889

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## TREATMENT OF LAST - 2018

Detection of LAST requires attention to the following:

- CNS signs can present as agitation, twitching, confusion, seizures, or depression up to obtundation. There can be non-specific signs such as sensing abnormal sounds, tastes, or dizziness.
- CV signs may initially be hyperdynamic with HTN and  $\uparrow$  HR, followed by progressive hypotension and / or bradycardia leading to ventricular arrhythmias including Torsades or asystole.
- Monitor during and after the injection; toxicity can be delayed for 30 minutes or longer. Use standard ASA monitors.

Reg Anesth Pain Med 2018; 43: 150

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## MECHANISMS OF LIPID THERAPY

There are multi-modal mechanisms of lipid resuscitation therapy:

1. Scavenging effect: formerly “lipid sink” but “shuttle” better reflects the benefit of redistribution that moves drugs (e.g. bupivacaine) away from the heart and brain to muscle and liver where it can be stored, detoxified and excreted.
2. Improves myocardial contractility, cardiac output, blood flow and blood pressure through vasoconstriction and inotropic / lusitropic (rate of relaxation) effects on the heart.
3. Protects against ischemia-reperfusion injury in the heart and provides a post-conditioning benefit.

Reg Anesth Pain Med 2018; 43: 138

53

## PREGNANCY TESTING

Is universal pregnancy testing an effective process to identify otherwise unsuspected pregnancies?

- Mayo Arizona database  $\rightarrow$  8245 women > age 18 who had day of surgery pregnancy testing over 5 years.
- Found 11 positive tests of which 6 were false positives.
- 0.06% true positive rate  $\rightarrow$  cost of \$49K for each + test.
- Low yield + high false positive + expense  $\rightarrow$  utility?

Anesth Analg 2018; 127: August e4-7

54

## PREGNANCY TESTING

An alternative to testing: the *Pregnancy Reasonably Excluded Guide* is a 12-statement checklist endorsed by WHO and supported by CDC has > 99% negative predictive value.

- Women who were unable to read, understand or freely respond to the checklist received testing.
- Only 21% received testing and no tests were positive.
- No surgical delays were associated with assessment.

Obstet Gynecol 2018; 132: 1222

55

## NONOBSTETRIC SURGERY DATA

Pregnant women are often denied surgical treatment for conditions when surgery would clearly be indicated for an identical, nonpregnant patient. This reluctance to perform surgery (and anesthesia) is a major risk to pregnant women and based on poor quality data.

- Data comes from studies done decades ago when care was different.
- Studies often combined data from vastly different types of surgery in a single report, presented as outcome data of *all* nonobstetric surgery.
- Studies focus on maternal outcome, not pregnancy/neonatal outcome.
- Control groups *should* be pregnant women with the same condition who don't have surgery to obtain a valid comparison.

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## NONOBSTETRIC SURGERY DATA

With few exceptions, the indications for surgery in pregnant women are similar to those for the non-obstetric population.

Withholding indicated surgery from a pregnant woman as a result of fears of teratogenesis, pregnancy loss, or preterm birth would appear to be unfounded and may significantly contribute to both maternal and neonatal morbidity.

Such fears may themselves be a significant contributor to maternal and fetal morbidity associated with surgical disease in pregnancy, because pregnant women don't get optimal treatment.

Obstet Gynecol 2018; 132: 395

57

## NON-OBSTETRIC SURGERY

What is the risk of adverse birth outcomes for women who have surgery during pregnancy?

- Surgery occurred in 47,628 pregnancies from 2002-12; compared with 6.5 million pregnancies without surgery.
- Every 287 surgeries were associated with 1 additional stillbirth.
- Every 31 surgeries associated with 1 additional preterm delivery and every 39 with 1 low birth weight baby.
- Risk was low. Undetermined: Surgery vs underlying condition?

Ann Surg 2017; 266: 260

58

## SUGAMMADEX

Is sugammadex safe to administer to pregnant women?

- Does it cross the placenta? Unknown.
- What are its fetal effects? Unknown.
- What are its effects on maintaining the pregnancy? Unknown but its interaction with progesterone is concerning and there is no human data on safety.
- Amounts in breast milk should be very low and infant enteral absorption is unlikely, but unknown.

SOAP Newsletter (soap.org), Winter 2019

59

## ANESTHETIC EXPOSURE

Using comprehensive neuropsychological assessments, are there adverse outcomes of childhood exposure to general anesthesia?

- Mayo database, 997 children with anesthetic exposure at age < 3, followed by testing at ages 8-12 or 15-20.
- No association with deficits in general intelligence.
- Single exposure cases did not test differently than unexposed.
- Multiple exposures → modest ↓ in processing speed and fine motor coordination, ? difficulties with behavior and reading.

Anesthesiology 2018; 129: 89

60

## ANESTHETIC EXPOSURE

Clinical Opinion: The fetus can be exposed to IV and inhalation anesthetics during nonobstetric and fetal surgery in the 2<sup>nd</sup> or 3<sup>rd</sup> trimester. Strategies to mitigate neurologic effects:

- Use non-implicated agents when appropriate, i.e. opioids or dexmedetomidine.
- Minimize duration of exposure when possible; e.g. limit the interval between induction of anesthesia and surgery start.
- IV tocolytics can be used instead of high-dose volatile agents.

Am J Obstet Gynecol 2018; 218: 98

61

## SLEEP APNEA

Are sleep apnea screening tools useful in pregnancy? No.

- BMI  $\geq$  40 between 24 and 35 weeks gestation had screening + airway exam + overnight sleep apnea test.
- 24% had OSA on home sleep apnea testing.
- OSA screening tools performed very poorly.
- Strongest predictors: age, BMI, neck circumference, witnessed apneas, and falling asleep while driving.

Am J Obstet Gynecol 2018; 219: 613

62

## SLEEP APNEA

What are the adverse events associated with OSA in pregnancy?

- Hypertension: chronic, gestational, and preeclampsia
- Gestational diabetes
- Cardiovascular disease: cardiomyopathy (OR 3.6), congestive heart failure (OR 3.6) and pulmonary edema (OR 5)
- Fetal growth restriction and low birth weight
- Women with OSA are 5 times more likely to die during a pregnancy-related admission.

Anesth Analg 2018; 127: 1167

63

## CARDIAC ARREST

We must be prepared to respond to maternal cardiac arrest:

- Do high quality chest compressions + oxygenation + manual left uterine displacement after 20 weeks gestation.
- In the differential, consider diagnoses unique to pregnancy.
- Deliver the fetus *at the site of arrest* if ROSC does not occur in 4 minutes. Do not transport to an OR!
- Consider CPB or ECMO if ROSC is still not achieved.
- Participate in simulation and team training to be prepared.

Am J Obstet Gynecol 2018; 219: 52

64

## CARDIAC ARREST

This is a good review of the topic.

- The most common causes in developed countries: venous thromboembolism and pulmonary embolus, preeclampsia or eclampsia, hemorrhage, heart failure, acute MI, amniotic fluid embolism and sepsis.
- Therapeutic hypothermia post-arrest should be considered in pregnant women. Use fetal monitoring.

Sem Perinatol 2018; 42: 33

65

## OBSTETRIC & MEDICAL COMPLICATIONS

66

## ANTI-HYPERTENSIVE USE

Since the HTN bundle and ACOG guidelines were published, are hypertensive pregnant women more likely to get treated with anti-hypertensive medications? Yes!

- Cohort of 239,454 parturients with a diagnosis of pre-eclampsia were linked with prescribed anti-hypertensives.
- The proportion of women receiving any anti-hypertensive medication *rose* from 38% in 2006 to 49% in 2015.
- The risk of stroke also *decreased* from 14 per 10,000 in 2006 to 6 per 10,000 in 2014.

Obstet Gynecol 2018; 131: 441

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## PREVENTION OF PREECLAMPSIA

*Low-dose aspirin use during pregnancy*

ACOG Committee Opinion #743

- Low-dose aspirin (81 mg/day) should be initiated between 12 and 28 weeks gestation and continued until delivery in women at high risk of preeclampsia.
- It is not recommended for prior unexplained stillbirth, prevention of IUGR, prevention of preterm birth, or for prevention of early pregnancy loss.

Obstet Gynecol 2018; 132: e44

68

## PRESSORS & PREECLAMPSIA

Is it preferable to use phenylephrine to treat hypotension for parturients with preeclampsia? Maybe not.

- Double-blind RCT of 108 preeclamptic women having spinal anesthesia for cesarean delivery.
- They risk-stratified for gestational age, infant gender, magnesium therapy, and severity of preeclampsia.
- There was no difference in umbilical cord pH between the phenylephrine and ephedrine treatment groups.

Anesth Analg 2018; 126: 1999

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## PRESSORS & PREECLAMPSIA

A British RCT compared phenylephrine and ephedrine for treatment of hypotension after spinal anesthesia during cesarean delivery in preeclamptic women:

- Double-blind RCT of 80 women.
- P & E were equally effective in treating hypotension.
- There was no difference in umbilical artery pH or neonatal acidosis between groups.

Anaesthesia 2018; 73: 839

70

## NSAIDs & PREECLAMPSIA

ACOG suggests avoiding NSAIDs in women with postpartum hypertension. Do they adversely affect BP control?

- 100 women with preeclampsia were randomized to scheduled ibuprofen or acetaminophen after delivery.
- No difference in duration of severe-range hypertension.
- No difference in other outcomes or care in the first 6 weeks.

Am J Obstet Gynecol 2018; 218: 616

71

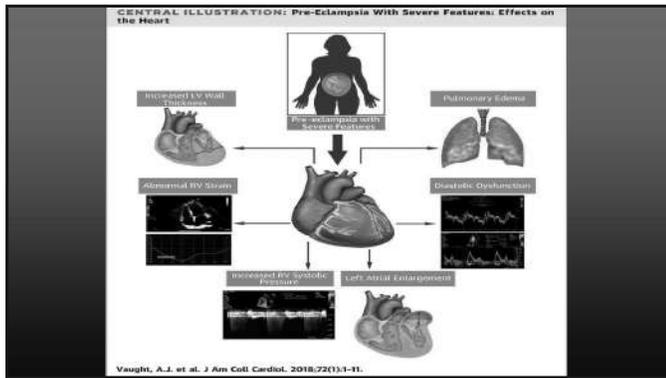
## SHORT-TERM CV CHANGES

Prospective observational comparison of echo and lab findings in severe preeclampsia and normal pregnancy.

- PEC: 13% had diastolic dysfunction, 39% had RV strain and ↑ RVSP (31 vs. 22.5 mmHg).
- They had ↑ LA size, ↑ LV wall thickness, ↑ LV filling pressures.
- 10% developed pulmonary edema.

J Am Coll Cardiol 2018; 72: 1 and 12

72



73

### FUTURE IMPLICATIONS

What is the association between hypertension during pregnancy and development of CV risk factors?

- 58,671 participants in the Nurse’s Health Study II program had hypertension during pregnancy but no CVD risk factors. They were followed for 25-32 years after delivery.
- Chronic HTN ↑: hazard ratio 1.8, especially within 5 years
- Type 2 diabetes ↑: HR 1.8
- Hypercholesteremia ↑: HR 1.4

Ann Intern Med 2018; 169: 224

74

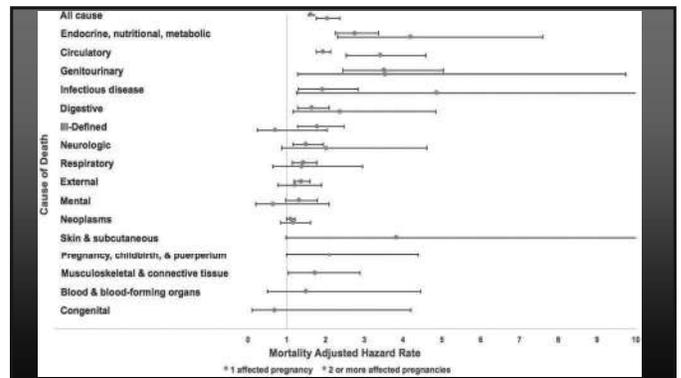
### FUTURE IMPLICATIONS

Is recurrent hypertensive disease of pregnancy associated with increased mortality? Yes.

- Women in Utah, 1939-2012 with 0, 1 or ≥ 2 pregnancies affected by HTN per birth certificate data were followed.
- Women with >2 affected pregnancies had ↑ all-cause mortality (aHR 2) and ↑ mortality from diabetes (aHR 4.3), ischemic heart disease (aHR 3.3) and stroke (aHR 5.1).

Am J Obstet Gynecol 2018; 219: 107

75



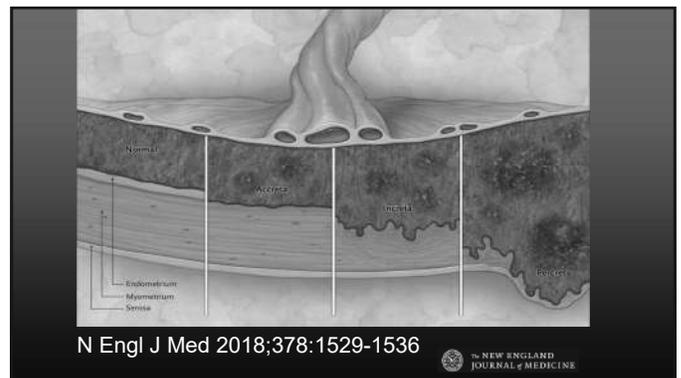
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### PLACENTA ACCRETA SPECTRUM

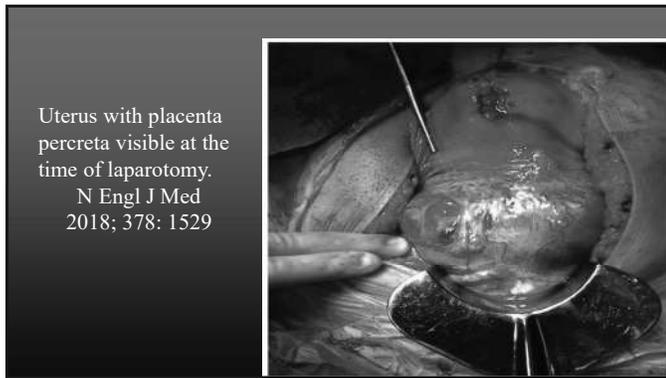
These are 3 excellent reviews published in 2018:

1. Clinical Practice: Placenta Accreta Spectrum  
N Engl J Med 2018; 378: 1529-36
2. Obstetric Care Consensus: Placenta Accreta Spectrum  
Obstet Gynecol 2018; 132: e259
3. Diagnosis and Management of Morbidly Adherent Placenta  
Sem Perinatol 2018; 42: 49-58

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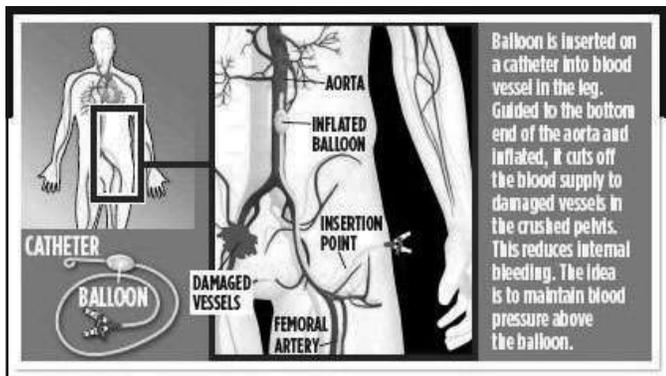
79

### REBOA IN PPH

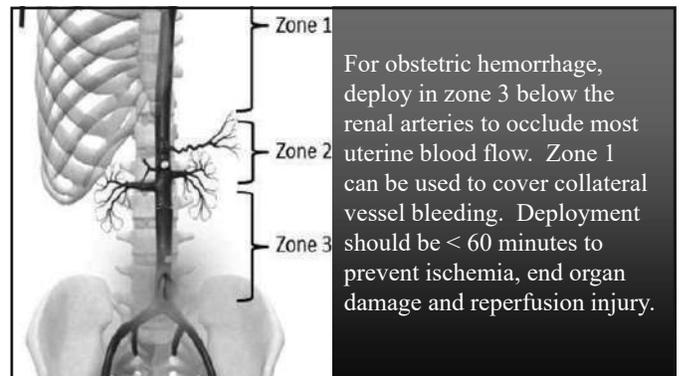
- The Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) device has been used in traumatic hemorrhagic shock. It provides the equivalent of an aortic cross-clamp.
- Recently it has been described for patients with morbidly adherent placenta, severe refractory uterine atony, during cesarean hysterectomy, and when there is bleeding from coagulopathy.

SOAP Newsletter, Winter 2019, p. 12

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### DAMAGE-CONTROL SURGERY

Consider abdomino-pelvic packing followed by medical stabilization in the ICU when:

- Arterial bleeding has been controlled.
- Persistent bleeding is deemed due to coagulopathy refractory to blood product replacement.
- Allows time to correct hypothermia, acidosis, need for vasopressors, ↓ calcium, and ↑ K.
- Maintain mechanical ventilation and monitor for abdominal compartment syndrome.

Obstet Gynecol 2018; 132: 423

83

### ANESTHESIA FOR ACCRETA

Single-center retrospective study of non-emergent cesarean for suspected accreta: neuraxial vs. general anesthesia.

- 95% received neuraxial even with BMI ≥ 40, history of ≥ 3 prior cesareans, suspected increta or percreta or Mallampati ≥ 3. 79% completed the case using neuraxial.
- 21% who required hysterectomy converted to general.
- Predictors for conversion were duration and prior C/S ≥ 3.
- GETA → more PRBC, more postop acuity/ICU admission.

Anesth Analg 2018; 127: 930

84

### IS TXA ABLE TO PREVENT PPH?

Does prophylactic TXA in addition to usual oxytocin treatment decrease the incidence of PPH after vaginal delivery? No.

- 4079 women at 15 French maternity units were randomized to 1 gram TXA or placebo at the time of delivery and after cord clamp.
- No difference in PPH > 500 ml (8.1% TXA, 9.8% placebo) or EBL.
- TXA group did have lower use of additional uterotonic agents.
- Nausea and vomiting were more common with TXA, but not severe.
- No difference in thromboembolic events 3 months after delivery.

N Engl J Med 2018; 379: 731

85

### POC TESTING ON L&D

A single-center study compared their outcomes pre- and post routine viscoelastic (ROTEM) testing during PPH.

- No difference in crystalloid, colloid, cryo use.
- Testing group did receive fewer PRBCs and platelets.
- The incidence of hysterectomy and ICU admission was ↓ in the testing group as was length of stay.
- Thus, cost of hospitalization was less in the ROTEM group.

J Clin Anesth 2018; 44: 50

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### POC TESTING

Case: 45-year old G5P2 had elective cesarean at 37 weeks for previa. After delivery she had PEA cardiac arrest. ACLS protocol was followed. TEE demonstrated dilated RV with ↓ function and an underfilled LV, and a mass in the right PA was identified consistent with saddle embolism. Severe coagulopathy ensued post-arrest and hysterectomy was required to control bleeding. ROTEM was used throughout the case, and diagnosed severe hypo-fibrinogenemia requiring 6 gram fibrinogen concentrate to correct. She survived without neuro-psychological deficits.

A&A Practice 2018; 10: 139

87

### SCREENING FOR SEPSIS

3 screening tools were tested in pregnant patients at 7 academic medical centers; 82 sepsis patients and 328 controls.

- SIRS had the best sensitivity, qSOFA had the best specificity and MEW was in between. None were ideal.
- Overall mortality was 12.2%, but fell to 8.3% if antibiotics were received in < 1 hour and rose to 20% if > 1 hour.
- Group A Strep and GNR were the most common organisms.
- 59% caused by chorio, endometritis or pneumonia.

Anesth Analg 2018; PAP (Bauer)

88

### HIV MANAGEMENT ON L&D

ACOG Committee Opinion #751:

- With anti-retroviral therapy and maternal viral loads < 1000 copies/mL, maternal-child transmission is 1-2%.
- Duration of ROM is not a factor in transmission if virally suppressed, and is not relevant to route of delivery.
- If viral load > 1000 or unknown, elective C/S is offered and mothers receive IV zidovudine for 3 hours preoperatively.
- Some HIV medications may interact with uterotonics.

Obstet Gynecol 2018; 132: 131

89

### ACUTE MI DURING PREGNANCY

NIS data from 2002-14 → 4471 cases of acute MI in > 55 million pregnancy-related hospitalizations (1 per 12,400).

- The rate of acute MI increased over the years.
- 24% occurred during L&D, 21% antepartum, 54% postpartum
- 42% were STEMI, 58% were non-ST elevation MI.
- In-hospital mortality was higher in women with AMI: aOR 40

Mayo Clinic Proceedings 2018; 93: 1404

90

### CARDIAC SURGERY IN PREGNANCY

Meta-analysis of 10 studies published since 1990 involving 154 women who had cardio-pulmonary bypass.

- Most common causes: mitral stenosis (29%), prosthetic valve dysfunction (26%), aortic stenosis (13%).
- 89% of cases were urgent or emergent.
- Maternal mortality was 11% and complications were 9%.
- Pregnancy loss was 33% and neonatal morbidity was 11%.
- Worse outcomes than reported previously.

Ann Thorac Surg 2018; 106: 618

91

### MARIJUANA USE IN PREGNANCY

	Alcohol	Cigarettes	Marijuana
2002	9.6%	17.5%	2.9%
2016	8.4%	10.3%	5.0%

- Data from the National Survey of Drug Use and Health data in women 18-44 years of age.
- 30% reported use in their first trimester of pregnancy. JAMA Pediatrics 2018; online 11/5

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### MARIJUANA USE IN PREGNANCY

Is prenatal marijuana use more common in women with a diagnosis of nausea & vomiting in pregnancy?

- Health system data with standard universal screening by both self-report and urine toxicology.
- Using no N&V as reference, mild N&V → OR 2.37 for use, and severe N&V (hyperemesis) → OR 3.8.
- Women use marijuana to self-medicate for N&V of pregnancy, even though it may contribute to N&V.

JAMA Int Med 2018; online 8/20

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### MARIJUANA USE IN PREGNANCY

What do cannabis dispensaries tell pregnant women regarding use of products for nausea during the 1<sup>st</sup> trimester?

- Used a mystery caller approach in Colorado; the caller stated she was 8 weeks pregnant and having morning sickness.
- 69% recommended treatment with cannabis products.
- 65% based their recommendation on personal opinion.
- 36% stated cannabis use is safe in pregnancy.
- Only 32% recommended discussion with a health care provider before prompting – then 82% did.

Obstet Gynecol 2018; 131: 1031

94

### THE FETUS AND NEONATE



### ONDANSETRON

Nausea and vomiting during pregnancy typically occurs during the first trimester, the most sensitive time for exposure to teratogens because of organogenesis. The available evidence on the fetal safety of ondansetron is limited and conflicting.

- 1.8 million pregnancies, 5% exposed in 1<sup>st</sup> trimester.
- No association between exposure and increased risk of cardiac malformations or congenital malformations overall.
- Small increase in the risk of oral clefts (relative risk at 1.48) corresponding to 5 additional cases per 10,000.

JAMA 2018; 320: 2429

95

96

## INTRAUTERINE RESUSCITATION

Oxygen is routinely administered to the mother as part of intrauterine resuscitation in the presence of category II (non-reassuring) FHR tracings. Is oxygen preferable to room air for improving fetal metabolic status?

- Randomized single center clinical trial of 99 women
- There was no difference in umbilical cord lactate or other elements of the arterial blood gas.
- There was no difference in mode of delivery.

JAMA Pediatr 2018; 172: 818

97

## DELAYED CORD CLAMPING

Can delayed cord clamping improve morbidity and mortality in preterm (< 37 weeks) infants?

- This is a systematic review and meta analysis.
- Delayed clamping ↓ hospital mortality (RR 0.68), ↑ hematocrit 2.73% and ↓ transfusion by 10%.
- No ↓ in other measures of morbidity.
- Delayed clamping reduces all-cause hospital mortality and is safe for mother and newborn.

Am J Obstet Gynecol 2018; 218: 1

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And we'll see what's new in 2019!



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# Left Ventricular Assist Devices for Non Cardiac surgery

By Breandan Sullivan MD  
Medical Director Cardiothoracic Surgery Intensive Care Unit  
University of Colorado  
Medical Director SICU Denver VA Hospital

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## Financial Disclosures

- I have no relevant financial disclosures

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## Outline

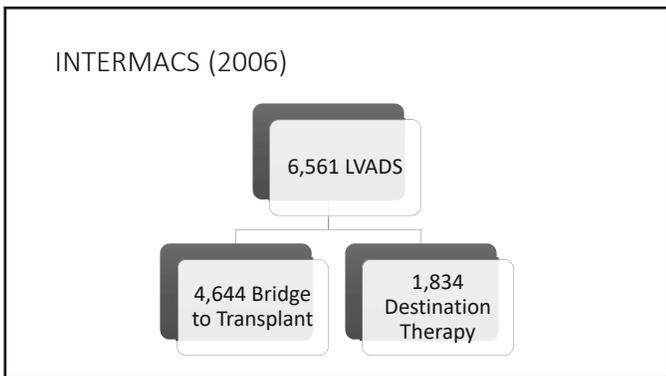
- Case Presentation
  - Heart Failure
  - Overview of LVAD's
  - Monitoring
  - Taking care of patients with LVADs

3

## Case Presentation

- 63 y/o
- HPI: Acute GI bleed
- PMHx:
  - ischemic cardiomyopathy
  - chronic renal insufficiency
  - prolonged respiratory failure
  - sudden cardiac arrest
  - s/p Heart Mate II 7 months ago

4



5

### INTERMACS (2012)

- 44% LVADs destination therapy
- Since 2010 all devices are continuous flow
- Survival:
  - 1 year 80%
  - 2 year 70%
  - 3 year 59% (3 year survival for a Whipple around 30%)
  - 4 year 47%

6

### Typical Patient?

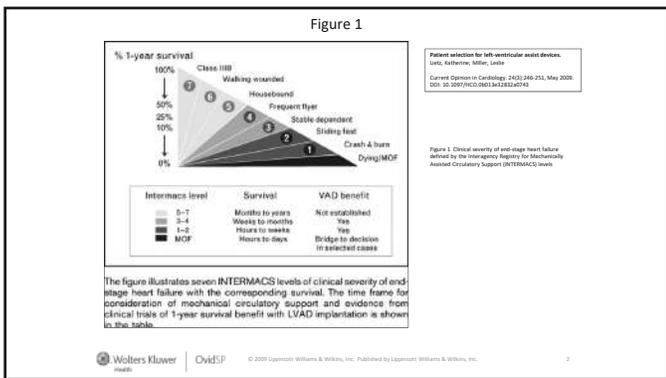
- Heart Failure
- One in five Americans over age of 40
  - (Circulation 2012; 125:e2-e220)
- Nearly 50% are dead in 5 years
  - (JAMA 2004; 292:344-350)

7

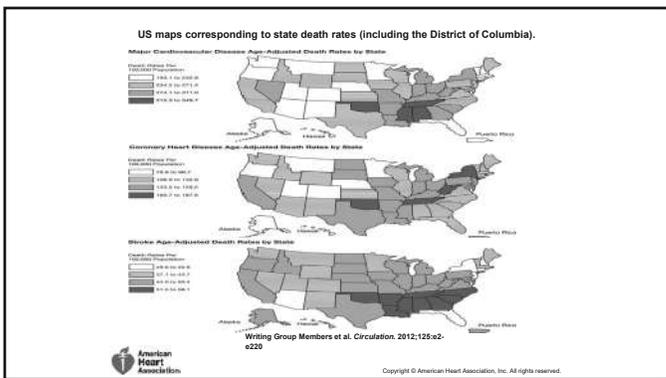
### Not run of the mill heart failure

- In its 2001 guidelines the American College of Cardiology/American Heart Association working group introduced four stages of heart failure:<sup>[30]</sup>
- Stage A: Patients at high risk for developing HF in the future but no functional or structural heart disorder.
- Stage B: a structural heart disorder but no symptoms at any stage.
- Stage C: previous or current symptoms of heart failure in the context of an underlying structural heart problem, but managed with medical treatment.
- Stage D: advanced disease requiring hospital-based support, a heart transplant or palliative care.

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9



10

### INTERMACS

- Interagency Registry for Mechanically Assisted Circulatory Support
- North American Registry
- Established in 2005
- Data points
- 1 week, 1 month, 3 months, 6 months and every 6 months after

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### Patients with VAD's get better

- Complete renal recovery occurs in 30% of patients (Ann Thorac Surg 2009;87:1072-8)
- 6 minute walk test improved by 200 meters
  - Average 42 meters pre-implant
  - Average 292 meters post-implant
- Liver function/injury improves
- Quality of life improves (n engl j med 357:9)
- They live so you can care for them...

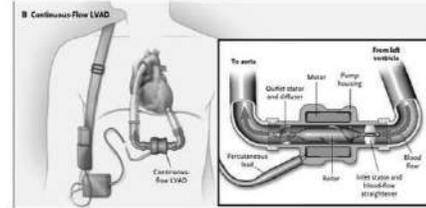
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### Two Major indications

- Bridge to heart transplant
  - Two major devices on market
    - Heart Mate 3
    - Heart Ware

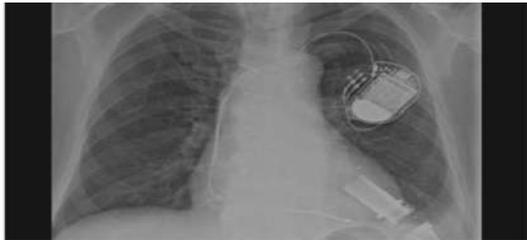
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### Heart Mate II



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### Chest x-ray heart mate II



15

### Heart Ware



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### Physical exam

- Monitors
  - EKG
  - Defibrillator hands free pads
    - Most have AICD
  - Pulse ox usually worthless
  - But you have something really nice...
- Blood pressure (recommendation)
  - Can be monitored non-invasively with a doppler
  - I would always put an arterial line in
    - You will need an ultrasound
    - Blood pressure
    - ABG monitoring, remember pulse ox doesn't work

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### Pulsatility index

- Magnitude of PI
  - Inversely related to assistance provided by pump
- PI increases
  - Increase in LV contractility
  - Increase in volume status (?)
- PI decreased
  - Pump support is increasing
  - Hypovolemic (?)
- Some people rely on it to tell them about volume status
- Measurement by the pump averaged over 15 sec's

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### Pump Flow

- Flow and power at a given speed are closely related
- Power is directly measured
- Under normal conditions reflect cardiac output of the pump
  - Divide by BSA you have CI
- Reported flow
  - An estimated value determined from power and pump speed
  - Not accurate if under 3L/min

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### Pump speed

- Usually 8,600 to 9,800
- Can be adjusted on the display
- Ideal speed
  - Determined by a ramped study
  - LV Size within normal range
  - No rightward or leftward shift of septum

20

### How to monitor?

- Arterial line
  - Always...
- Full plug in monitor
  - Continuous battery source
  - Large screen monitor
- CVP?
- PA catheter?
- TEE?
- Someone there that can adjust the pump
  - VAD coordinator

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### Trans esophageal Echo

- TEE
- Looking for RV function
- Will help you interpret the PI
  - Is the low PI from Volume?
  - Is the low PI from right heart failure?

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### Summary

- Heart failure is extremely common
- Surgical Treatment for heart failure works
- Patients with LVADs have a high risk of GI bleeding
- Best treatment of right heart dysfunction
- Always place an arterial line
- Make sure you have adequate back-up
  - CT Surgery
  - VAD coordinator
- Avoid right heart dysfunction
- First rule of fight club...
  - You don't talk about fight club

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# Monday

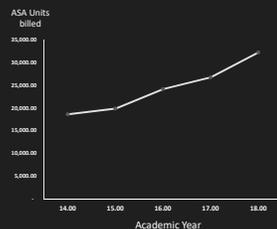
# Anesthesia for the Critically Ill Patient

Jeffrey R. Kirsch, MD FASA  
Chair, Emeritus OHSU

Evidence-based (when available) and personal approach to managing critically ill patients in the OR

## Disclosures

- Professor, but very busy clinical anesthesiologist
- I do not accept honoraria for lectures
- Consulting fees (case review, industry FDA activity) are paid directly to charity (e.g. Oregon Food Bank, FAER etc)



## Anesthesiology Stages of Care

- Preoperative evaluation and optimization
- Intraoperative management and optimization
- Postoperative management and optimization

Presentation will focus on care of patients with significant CV impairment, Sepsis and Morbid Obesity

## Outline/Objectives

- Defining high risk patients
- Infection control
- Management of patients with CV instability
  - Fluid management
  - Troponin measurement utility
  - Appropriate BP goals
  - Avoiding hypotension during anesthesia induction
  - Vasopressor choices
  - ICD/PM management
- Obesity

## Definitions of Critical Illness

- ASA Physical Status
- Frailty index: decrease in physiological reserve that exceeds what might be expected from advanced age alone
- Preoperative cognitive function
- Metabolic Syndrome
- Emergency Surgery Score
- ACS Universal Risk Calculator
- Gupta Perioperative Cardiac Risk Calculator
- 2014 ACC/AHA Perioperative Cardiac Stratification

## Who is a high-risk surgical patient?

Curr Opin Crit Care 2018, 24:000-000

Somnath Bose and Daniel Talmor

### KEY POINTS

- Timely identification of high-risk surgical candidates is a key step in mitigating perioperative morbidity and mortality.
- Commonly used indices (ASA PS, RCRI, ACS NSGIP, sAs, and P-POSSUM) complement each other to provide comprehensive perioperative risk assessment.
- Biomarkers (natriuretic peptide and troponin) measured both preoperatively and postoperatively can further enhance estimation of adverse cardiovascular events.
- Subjective assessment of functional capacity has poor sensitivity; instead practitioners should rely on objective measurements (e.g. DASI and CPET) to quantify functional status.
- Identification of effective strategies which reduce adverse outcomes and their successful integration within the perioperative risk estimation framework remains a greater challenge.

Duke Activity Status Index [DASI]  
Cardiopulmonary exercise testing [CPET]

## Most effective tools to predict post-op outcomes

- Duke Activity Status Index (DASI)
- Cardiopulmonary exercise testing (CPET)
- Serum N-terminal pro-B-type natriuretic peptide (NT pro-BNP)
- Both DASI and NT pro-BNP most accurately predict 30 day outcomes (Wijeyesundera DN et al., Lancet 391:2631, 2018)

BNP-guided therapy has been shown to be a safe and cost-effective treatment in heart failure though controversies still exist regarding its application in elderly with age more than 75 and in patients with severe renal impairment.

Shang C B-type natriuretic peptide-guided therapy for perioperative medicine?  
*Open Heart* 2014;1:e000105. doi: 10.1136/openhrt-2014-000105

## Perioperative B-type Natriuretic Peptide/N-terminal pro-B-type Natriuretic Peptide Next Steps to Clinical Practice

Amanda A. Fox, M.D., M.P.H. *Anesthesiology* 2015; 123:246-8

In summary, to move BNP and NT-proBNP assessment into perioperative clinical practice, useful cut-points or risk thresholds must be identified. These cut-points need to demonstrate reasonable sensitivity as well as specificity for adverse postoperative cardiac outcomes.



## Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study.

Wijeyesundera DN et al., *Lancet* 391, 2631, 2018

- Study to compare preop subjective assessment with alternative markers of fitness (cardiopulmonary exercise testing [CPET], scores on the Duke Activity Status Index [DASI] questionnaire, and serum N-terminal pro-B-type natriuretic peptide [NT pro-BNP] concentrations) for predicting death or complications after major elective non-cardiac
- Only DASI scores were associated with predicting the primary outcome (adjusted odds ratio 0.96, 95% CI 0.83–0.99; p=0.03).

Item	Activity	Yes	No
1	Can you take care of yourself (eating, dressing, bathing or using the toilet)?	2.75	0
2	Can you walk indoors such as around your house?	1.75	0
3	Can you walk a block or two on level ground?	2.75	0
4	Can you climb a flight of stairs or walk up a hill?	5.50	0
5	Can you run a short distance?	8.00	0
6	Can you do light work around the house like dusting or washing dishes?	2.75	0
7	Can you do moderate work around the house like vacuuming, sweeping floors, or anything in general?	3.50	0
8	Can you do heavy work around the house like scrubbing floors or lifting and moving heavy furniture?	8.00	0
9	Can you do yard work like raking leaves, weeding, or pushing a power mower?	4.50	0
10	Can you have sexual relations?	5.25	0
11	Can you participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	8.00	0
12	Can you participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	7.50	0
<b>Total Score *</b>			
Estimate peak O2 = 43 * (DAS) + 9.6 *			
<b>METS = ( / 3.3 ) Duke Activity Status Index (DASI)</b>			

## Appropriate consultation and treatment before surgery (Required vs. Ideal vs. Practical)

- When there is time:
  - Optimization of CV status (BP control, HR control, Lipid profile etc)
  - Physical therapy
  - Nutrition, weight loss
  - Pain management consultation
  - Smoking cessation
  - ID to decolonize pts from hypervirulent strains of bacteria (Loftus RW, Curr Opin Anaesth 29: 192, 2016)

Compulsive infection control to prevent a critically ill patient from further compromise

Are we part of the problem?  
Is there a solution?

## YES

- Desiccation tolerance is associated with *Staphylococcus aureus* hypertransmissibility, resistance and infection development in the OR. Loftus et al., J. Hosp Infect 100:299, 2018
- Frequency of Hand Decontamination of Intraoperative Providers and Reduction of Postoperative Healthcare-Associated Infections: A Randomized Clinical Trial of a Novel Hand Hygiene System. Koff MD et al., Infect Control Hosp Epidemiol 37:888, 2016
- Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a passive catheter care system. Loftus RW Anesth Anal, 115:1315, 2012

Table 1: Summary of Hand Hygiene Recommendations.

### Summary of Current Hand Hygiene Recommendations

Why practice Hand Hygiene?	Reduces spread of germs to patients
How to do hands hygiene?	<ul style="list-style-type: none"> <li>• Reduces risk of healthcare provider infection with infection from the patient.</li> </ul>
When to perform hand hygiene?	<ul style="list-style-type: none"> <li>• Before eating</li> <li>• Before and after direct contact with patient.</li> <li>• After contact with body fluids</li> <li>• After contact with inanimate objects surrounding the patient</li> <li>• When making contact from contaminated to non-contaminated areas in the patient</li> <li>• After gloves removal</li> <li>• After using the restroom</li> </ul>

Table 2: Summary of recommendations to decrease pathogen transmission.

Pre/Post Operative	Technique
Equipment	<ul style="list-style-type: none"> <li>• Disinfect anesthesia machine surfaces and handle with disinfectant between cases and at the end of each day</li> </ul>
Anesthesia Machine Surfaces	<ul style="list-style-type: none"> <li>• Wipe small surfaces with 70 percent isopropyl alcohol</li> <li>• Follow manufacturer's guidelines of equipment</li> <li>• Mechanism of function</li> <li>• Remove any material from dippers, check and clean if necessary regularly</li> <li>• Place a clean cover on top of the anesthesia cart prior to use</li> <li>• Cover of monitors (O<sub>2</sub>, SpO<sub>2</sub>, EtCO<sub>2</sub>)</li> <li>• Disinfect scales with 70% isopropyl alcohol</li> </ul>
Anesthesia Machine Carts	<ul style="list-style-type: none"> <li>• Remove paper covering of monitoring devices (O<sub>2</sub>, Pressure cuffs, pulse oximetry)</li> </ul>
Monitoring Equipment	<ul style="list-style-type: none"> <li>• Proper opening and closing of keyboard</li> <li>• Exclusion/covering of source</li> </ul>
Computer	
Intraoperative	<ul style="list-style-type: none"> <li>• Proper education on adequate technique</li> <li>• Advise anesthesiologist that gloves when to contact with the anesthesia machine</li> <li>• Available hand sanitizer on machine</li> <li>• Awareness of patient risk factors for contamination (e.g. central procedures, HOLA, etc)</li> <li>• Consider effect of antibiotic-resistant bacteria on patient and small culture</li> <li>• Antisepsis of general contamination (O<sub>2</sub>, EtCO<sub>2</sub>, and other devices)</li> <li>• Daily be used against the contaminated product</li> </ul>
Hand Hygiene	
Assessments	

**Perioperative Hyperglycemia and Risk of Adverse Events Among Patients With and Without Diabetes**  
*Ann Surg.* 2015 January ; 261(1): 97-103.  
 Meera Kotagal, MD<sup>1</sup>, Rebecca G. Symons, MPH<sup>1</sup>, Iq B. Hirsch, MD<sup>1</sup>, Guillermo E.

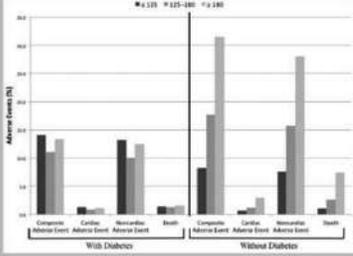
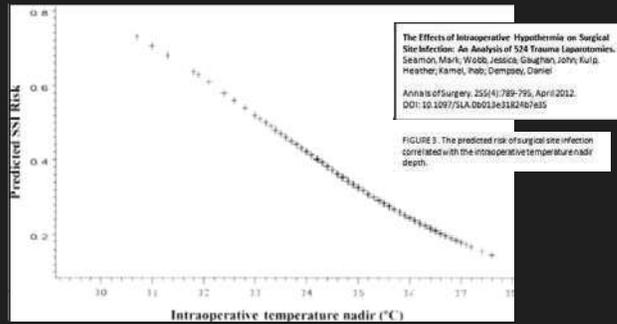


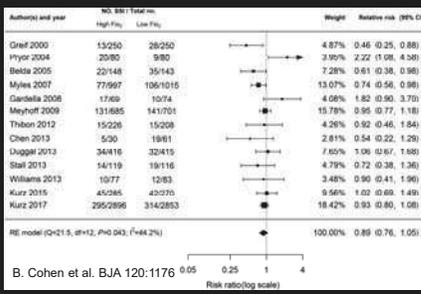
FIGURE 3. Adverse events, by diabetes status and postoperative glucose level.



The Effects of Intraoperative Hypothermia on Surgical Site Infection: An Analysis of 524 Trauma Laparotomies. Seamon, Mark; Wood, Jessica; Gagliardi, John; Kulp, Heather; Kamei, Peter; Dempsey, Daniel. *Annals of Surgery.* 255(4):789-795, April 2012. DOI: 10.1097/SLA.0b013e3182424635

FIGURE 3. The predicted risk of surgical site infection correlated with the intraoperative temperature nadir depth.

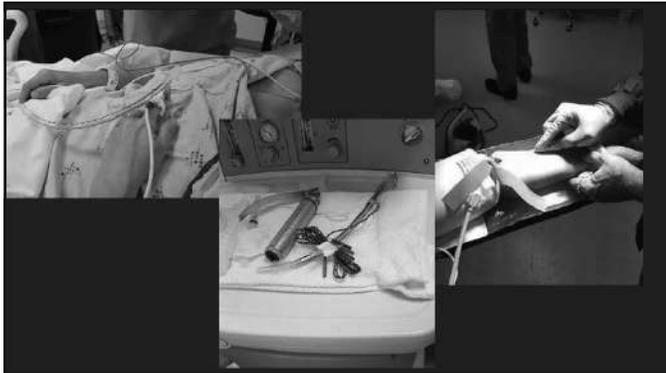
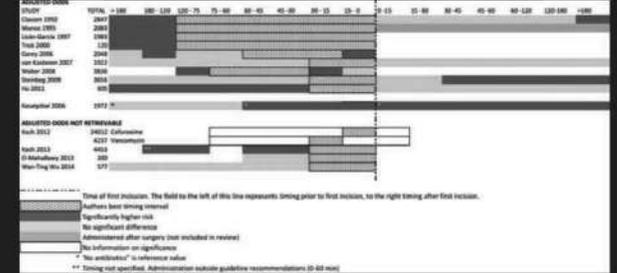
**Increased inspired oxygen does not consistently decrease infection rates**



B. Cohen et al. *BJA* 120:1176

**Timing of preoperative antibiotic prophylaxis in 54,552 patients and the risk of surgical site infection**

Medicine (2017) 96:29  
 A systematic review and meta-analysis  
 Stijn Willem de Jonge, MD<sup>1</sup>, Sarah L. Gans, MD, PhD<sup>1</sup>, Jasper J. Aterna, MD, PhD<sup>1</sup>, Joseph S. Solomkin, MD<sup>2</sup>, Patschen E. DeRinger, MD<sup>3</sup>, Marja A. Boermeester, MD, PhD<sup>3</sup>



**Barrier protection capacity of flip-top pharmaceutical vials**  
*Journal of Clinical Anesthesia* 25 (2013) 177-180

James G. Hilliard CRNA, MS (Instructor)<sup>a,\*</sup>, Eric D. Cambronne PhD (Assistant Professor)<sup>a</sup>, Jeffrey R. Kirsch MD (Professor)<sup>a</sup>, Michael F. Aziz MD (Associate Professor)<sup>a</sup>

Survey responses to Question 1: "Prior to removing the plastic flip-top cover, is the rubber stopper on a propofol vial sterile under routine clinical conditions?"

Responses n=878	Yes	No	Unsure
Anesthesiologist (%)	247 (48)	171 (33)	96 (19)
CRNA (%)	73 (48)	70 (46)	10 (6)
Resident (%)	140 (66)	41 (20)	30 (14)
Total (%)	460 (52)	282 (32)	136 (16)

Model	Exposure time	Results
Routine handling (n = 12)	n/a	2 vials: positive growth on brain heart infusion agar and Sabouraud-dextrose agar
Aerosol (pilot) (n = 5)	30 min	No growth
Submersion (pilot) (n = 5)	-30 min	No growth
Aerosol (n = 5)	(variable exposure model)	-24 hours: No growth
Submersion (n = 5)	(variable exposure model)	-30 min: 2 vials: positive growth on brain heart infusion agar, Sabouraud-dextrose agar.
		-24 hours: Tryptic soy 5% sheep blood agar 5 vials: positive growth on Luria-Bertani agar

Survey responses to Question 2: "Does the flip-top cover on a propofol vial create a sterile barrier which prevents contamination of the rubber stopper if the vial is exposed to an external contaminant?"

Responses n=876	Yes	No	Unsure
Anesthesiologist (%)	113 (22)	286 (56)	114 (22)
CRNA (%)	33 (22)	98 (64)	21 (14)
Resident (%)	54 (26)	118 (56)	39 (18)
Total	200 (23)	502 (57)	174 (20)

We could do better  
minimizing the ID risks for our  
patients in the OR

### Intraoperative Management of the patient with CV instability

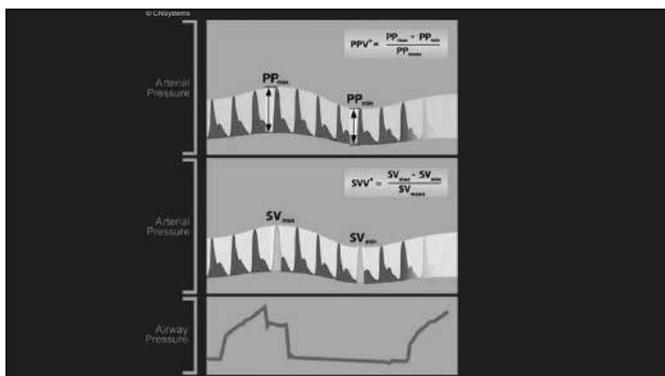
- Primarily cardiac in origin
- Sepsis
- Goal directed therapy
- Management of patients with implanted cardiac devices
- Postoperative troponin monitoring

Since there are very few things in medicine that are absolutes, I believe that it is best to discuss goals with surgical colleague at the beginning of the case

- Is the plan to achieve BP goals with fluids or pressors?
- If fluids, is the preference for albumin (avoid starch) or crystalloid?
- Normal or hypo intravascular volume state?
- Goal Hb/Hct?

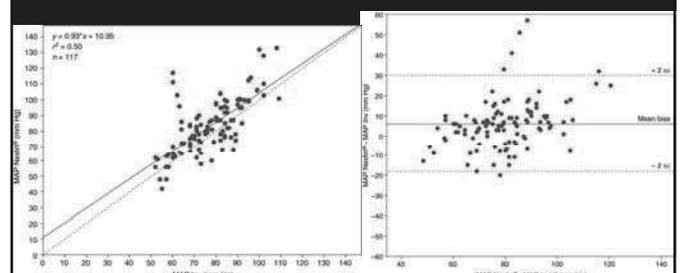
### What is Goal Directed Therapy?

- Tool that attempts to "optimize" fluid/pressor treatment
- Typical Variables: Pulse pressure variation (13 mmHg or less via arterial line) or stroke volume variation and/or mixed venous oxygen saturation (goal of 60% or greater)
- PICCO: Pulse Contour Cardiac Output; requires placement of CVP and thermodilution arterial line
- Optimization (probably best to individualize goals, within patient capacity) is associated with decrease PONV, ileus, morbidity, stress related organ dysfunction, hospital LOS



Non-invasive continuous arterial pressure monitoring with Nexfin® does not sufficiently replace invasive measurements in critically ill patients

A Hohn, J.M. et. Al. British Journal of Anaesthesia 111:178-184 2013





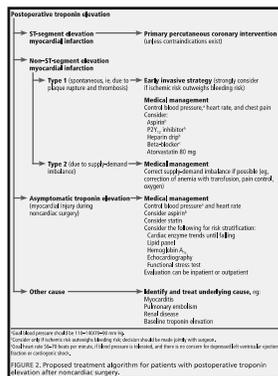
## Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery

JAMA. 2017;317(16):1642-1651.

Writing Committee for the VISION Study Investigators

Table 2. Peak Postoperative hsTnT Thresholds Associated With 30-Day Mortality\*

	hsTnT Thresholds, ng/L					
	<5	5 to <14	14 to <20	20 to <65	65 to <1000	≥1000
Patients, No. (%)	5318 (24.4)	8750 (40.1)	2530 (11.6)	4049 (18.6)	1118 (5.1)	54 (0.2)
Deaths, No. (%)	6 (0.1)	40 (0.5)	29 (1.1)	123 (3.0)	102 (9.1)	16 (29.6)
Adjusted hazard ratio (95% CI)	1 [Reference]	3.73 (1.58-8.82)	9.11 (3.76-22.09)	23.63 (10.32-54.09)	70.34 (30.60-161.71)	227.01 (87.35-589.92)
P Value		.003	<.001	<.001	<.001	<.001



## Troponin elevation after noncardiac surgery: Significance and management

S. Horr et al., Clev Clin JOURNAL 82:595, 2015

Elevated postoperative troponin is associated with increased morbidity and mortality but it is unknown if treatment to lower troponin mitigates this risk

Is there an ideal intraoperative blood pressure goal in critically ill patients?

Controversy: Specific MABP number (65 vs 80 mmHg) vs. individualized (10%, 20% or 30% of baseline)

## Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review

E. M. Wesselink<sup>1,4</sup>, T. H. Kappen<sup>1</sup>, H. M. Torn<sup>1</sup>, A. J. C. Slooter<sup>2</sup> and W. A. van Klei<sup>1</sup>

British Journal of Anaesthesia, 121 (4): 706–721 (2018)

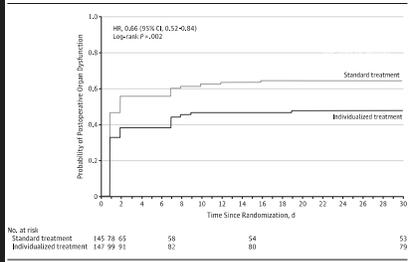
### Editor's key points

- In a systematic review of the association between intraoperative hypotension and adverse postoperative outcomes in noncardiac surgery, 42 relevant studies were identified and analysed.
- Elevated risks of end-organ injury were reported for exposures to mean arterial pressures <80 mm Hg for >10 min, and for shorter durations <70 mm Hg.
- Elevated risks were reported for increased durations for mean arterial pressures <65–60 mm Hg or for any exposure <55–50 mm Hg.

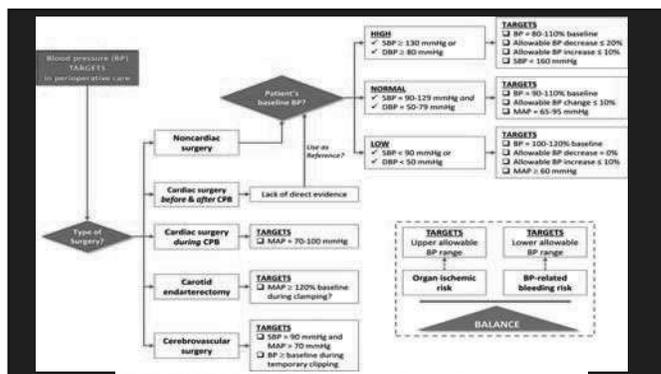
Effect of individualized vs standard blood pressure management strategies on postoperative organ dysfunction among high-risk patients undergoing major surgery. A randomized clinical trial.

Futier et al., JAMA 318:1346, 2017

Figure 3. Kaplan-Meier Estimates of the Probability of Postoperative Organ Dysfunction by Day 30 After Surgery

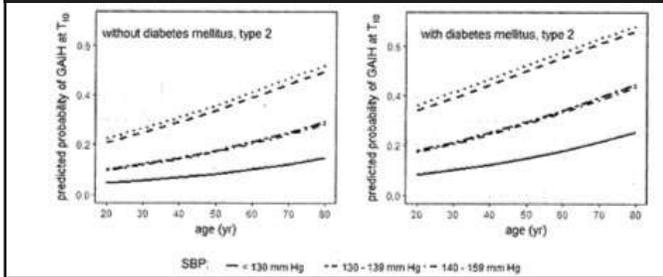


Organ dysfunction was assessed for renal, injury, failure, loss, and end-stage kidney injury (RIFLE) stage of risk or higher, respiratory (need for invasive or noninvasive ventilation), cardiovascular (acute cardiac failure or myocardial ischemia or infarction), neurologic (stroke or altered consciousness), and coagulation (Sequential Organ Failure Assessment subscore ≥ 2 points in the coagulation component) systems. Data for patients who did not develop organ dysfunction were censored at 30 days after surgery. The adjusted hazard ratio (HR) for postoperative organ dysfunction in the individualized treatment group, as compared with the standard treatment group, was 0.66 (95% CI, 0.52-0.84; P = .001). The median follow-up duration was 30 days (interquartile range, 30-30 days) in the 2 treatment groups.





## Patients with type 2 diabetes more commonly experienced hypotension during induction



## A Comparison of the Effects of Etomidate and Midazolam on Hospital Length of Stay in Patients With Suspected Sepsis: A Prospective, Randomized Study

Karis L, Tekwani, MD, Hannah F. Watts, MD, Rola T. Sweis, PharmD, Kathleen H. Rzechuda, RN, Erik B. Kulstad, MS, MD  
From the Department of Emergency Medicine, Advocate Christ Medical Center, Oak Lawn, IL.

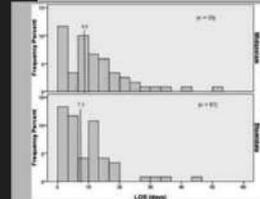


Figure 2. Histogram of hospital length of stay (LOS) for all patients, excluding surviving patients and patients who died. Vertical indicator lines show medians for each group: Etomidate 9.0 days for the etomidate group and 12.0 days for the midazolam group.

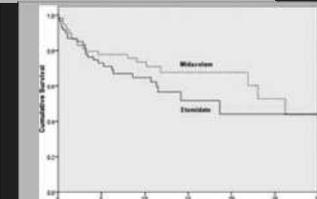


Figure 3. Kaplan-Meier survival curve.

## Single-Dose Etomidate Does Not Increase Mortality in Patients With Sepsis

CRIST 2015; 14(7):339-346

A Systematic Review and Meta-analysis of Randomized Controlled Trials and Observational Studies

Shivak G, MD; Per Wang, MD, Li Wang, MD, and Jing Chen Liu, MD

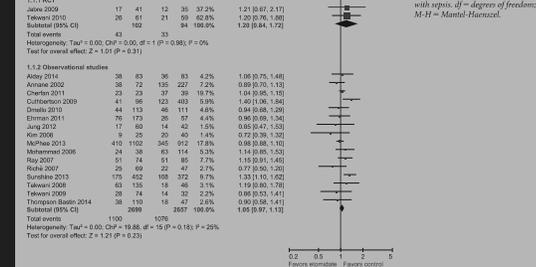


Figure 2 - Effect of single-dose etomidate on mortality in patients with sepsis. *I*<sup>2</sup> = degree of freedom; M-H = Mantel-Haenszel.

## A randomized trial of anesthetic induction agents in patients with coronary artery disease and left ventricular dysfunction

(Singh et al., Ann Card Anesth 13:3, 2010)

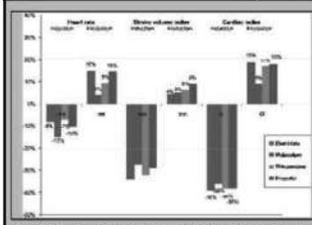


Figure 1: The maximum percentage change from baseline in heart rate, stroke volume index and cardiac index after induction and after intubation.

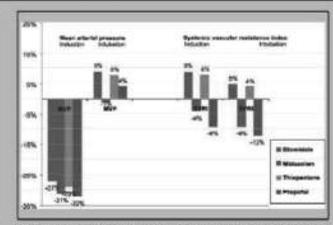
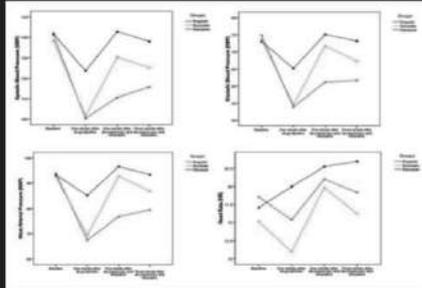


Figure 2: The maximum percentage change from baseline in mean systemic arterial pressure and systemic vascular resistance index after induction and after intubation.

Also no differences in values at individual time points after induction or intubation

## Comparing hemodynamic responses to diazepam, propofol and etomidate during anesthesia induction in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery: a double-blind, randomized clinical trial Soleimani et al., Med Arch 7:198, 2017



All pts: 0.03 mg/kg midazolam + 2 ug/kg fentanyl  
Prop: 1.5 mg/kg  
Etomid: 0.2 mg/kg  
Diaz: 0.3 mg/kg

## Etomidate Use and Postoperative Outcomes among Cardiac Surgery Patients

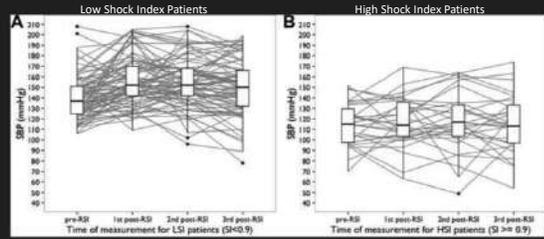
[ANESTHESIOLOGY 2014; 120:579-85]

Chad E. Wagner, M.D., Julian S. Bick, M.D., Daniel Johnson, Pharm.D., Rashid Ahmad, M.D.,

Characteristic	Retrospective study		P Value	
	N	Etomidate N = 1,928		No Etomidate N = 1,199
Severe hypotension	3,127	9.6%	10.8%	0.26
total time on mechanical ventilation (h)	2,978	8.5 (3.0-51.6)	7.4 (2.9-17.2)	0.005
hospital length of stay (days)	3,120	6.0 (3.0-13.0)	6.0 (3.0-18.0)	0.96
Mortality	3,127	3.0%	4.2%	0.07

Continuous variables were summarized with median (10th, 90th percentile) and tested with Wilcoxon rank sum test. Categorical variables were summarized with percentages and tested with chi-square test.

### Ketamine induction for patients in shock presenting to the ED



Patients without apparent shock generally exhibited the expected increases in BP from ketamine induction. These effects were blunted in patients with a high shock index, with 8 of these 31 experiencing hypotension. Miller M et al., Ann Emerg Med. 2016;68:181-188

### Effects of avoidance or use of neuromuscular blocking agents on outcomes in tracheal intubation: a Cochrane systematic review

British Journal of Anaesthesia, 120 (6): 1381-1391  
L. H. Lundström<sup>1,\*</sup>, C. H. V. Duez<sup>2</sup>, A. K. Nørskov<sup>1</sup>, C. V. Rosenstock<sup>1</sup>,



Fig. 5. Forest plot of secondary outcome: difficult intubation. Low risk of bias as high on overall risk of bias. NMBs, neuromuscular blocking agents.

### Perioperative acute kidney injury

British Journal of Anaesthesia, 115 (S2): ii3-ii14 (2015)  
O. Goren\* and I. Matot

- Identify patients at risk:**
- Patient related factors-** co-morbidities (obesity, CKD, DM, cardiovascular and hepatobiliary diseases, male sex, obesity, pulmonary disease, steroid use, cancer, ASA score, ICU patients, increased intraabdominal pressure, sepsis, older age and neonates)
  - Procedure related factors-**
    - a. Major surgery (extensive laparotomy lung resections, transplantations)
    - b. Emergency surgery
    - c. Cardiac surgery
    - d. Use of contrast dye
  - Anaemia-** Correct anaemia before to surgery when possible according to the patient management protocol.<sup>† 139 140 141 142 143 145</sup>

- Choice of fluid solution-** a. Avoid HES solutions when possible.<sup>† 22 91 108 112 113 117 118 119</sup>  
b. Balanced crystalloid solutions may prove superior to chloride rich solutions in preventing AKI.<sup>† 103 104 105</sup>

- Fluid management-** a. The use of intraoperative urinary output as a guide to fluid administration may not be beneficial.<sup>† 127 128 129 130</sup>  
b. Avoid the use of diuretics unless a need to treat volume overload arises.<sup>22 98 135 136 137</sup>  
c. Use measures during surgery to avoid blood loss and unnecessary PRBC transfusion.<sup>† 139 140 141 142 143 145</sup>

- Haemodynamic goals-** a. Avoid a low MAP even for relatively short periods of time.<sup>† 55 56</sup>  
b. Evidence so far do not recommend the use of one vasopressor over the other.<sup>22</sup>  
c. Low dose dopamine is no longer considered "renoprotective" and is not recommended.<sup>22 98 148</sup>

- General considerations-** a. Avoid the use of aminoglycosides unless no suitable less nephrotoxic alternative exists.<sup>22</sup>

### What are the pressor options to treat hypotension from:

- Sepsis?
- Anesthetic induction?
- Intolerance of general anesthetic?
- Poor cardiac function?

### Safety of the Peripheral Administration of Vasopressor Agents

J. Intensive Care Medicine  
Tyler Lewis, PharmD<sup>1</sup>, Cristian Merchan, PharmD, BCCCP<sup>1</sup>,  
Diana Alshaker, PharmD, BCCP, BCCP<sup>1</sup>  
and John Papadopoulos, PharmD, FCCM, BCCCP, BCNSP<sup>1</sup>

Vasopressor	Concentration	Indication	Starting Dose	Max Peripheral Dose*
Norepinephrine	4 mg/250 mL (16 µg/mL) NS	Septic shock	0.05-0.1 µg/kg/min	25 µg/min
Epinephrine	4 mg/250 mL (16 µg/mL) NS	Anaphylaxis	0.05-0.1 µg/kg/min	25 µg/min
Dopamine	200 mg/250 mL (800 µg/mL) D5W	Symptomatic bradycardia	2 µg/kg/min	10 µg/kg/min
Phenylephrine	100 mg/250 mL (400 µg/mL) NS	Second-line agent for septic shock	50 µg/min	250 µg/min

\*Consider placing a central line if vasopressor dose exceeds 25 µg/min of norepinephrine equivalents.

Yes, it is safe to administer all pressors via a peripheral IV. It is best if the IV site can be checked on a regular basis during the case

## Vasopressors and their mechanisms of action

- Phenylephrine: Alpha-1 vasoconstriction
- Norepinephrine: Acts at alpha-1 and beta-1 receptors to vasoconstrict and stimulate the cardiac chronotropy and inotropy
- Epinephrine: Beta-1 inotropy/chronotropy, alpha-1 constriction, beta-2 vasodilation
- Ephedrine: Like Epi, but less potent and indirect
- Vasopressin: Activation of V1; usually as a supplement to NE
- Dopamine: 1-2 mcg/kg/min dopamine vasodilation; 2-10 Beta 1 effects; >10 alpha-1 effects
- Angiotensin II: Increases intracellular calcium leading to vasoconstriction
- Dobutamine: Increases cardiac contractility and rate by Beta-1 and vasodilation by Beta-2

## Septic shock and the use of norepinephrine in an intermediate care unit: Mortality and adverse events

Mikael Häggren<sup>1</sup>\*, Per Astrand<sup>2</sup>, Staffan Eksborg<sup>3</sup>, Hans Barle<sup>1</sup>, Claes Frostell<sup>4</sup>

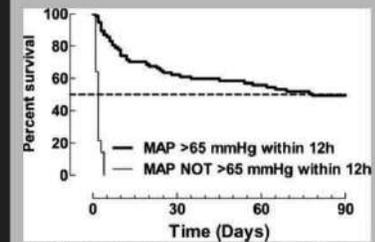


Fig 3. Mortality (%) for patients achieving versus not achieving MAP >65 mmHg within 12 hours. Kaplan-Meier curve with mortality (%) as outcome for patients achieving versus not achieving MAP >65 mmHg within 12 hours. (p=0.002) (Garcia-Cardena/Walsh.com Text).

## Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock

James A. Russell, M.D., Keith R. Walley, M.D., Joel Singer, Ph.D., Anthony C. Gordon, M.B., B.S., M.D.

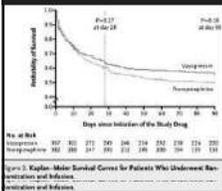


Table 4. Rates and Risks of Death from Any Cause According to the Severity of Shock.\*

Stratum	Norepinephrine Group n/N (n/N, %)	Vasopressin Group n/N (n/N, %)	P Value†	Absolute Risk Reduction (95% CI)‡	Relative Risk (95% CI)‡
<b>More severe septic shock</b>					
28-day mortality	85/200 (42.5)	88/200 (44.0)	0.76	-1.5 (-3.2 to 0.2)	1.04 (0.83 to 1.3)
90-day mortality	105/199 (52.8)	103/199 (51.8)	0.84	1.0 (-0.8 to 1.8)	0.98 (0.81 to 1.18)
<b>Less severe septic shock</b>					
28-day mortality	55/182 (30.2)	52/186 (28.5)	0.05	3.0 (-0.1 to 6.1)	0.74 (0.55 to 1.01)
90-day mortality	83/180 (46.1)	69/183 (37.8)	0.04	10.4 (6.4 to 14.4)	0.78 (0.61 to 0.99)

\*Patients with more severe septic shock were defined as those who required at least 15 µg of norepinephrine per minute or the equivalent at the time of randomization. Those with less severe septic shock were defined as those who required 5 to 14 µg of norepinephrine per minute or the equivalent at the time of randomization.

In patients with "less severe septic shock" vasopressin reduced mortality rate as compared to patients treated with norepinephrine

## FDA Approval of Angiotensin II for the Treatment of Hypotension in Adults with Distributive Shock

Fortunato Senatore<sup>1</sup>, Gowraganahalli Jagadeesh<sup>1</sup>, Martin Rose<sup>1</sup>, Venkateswaran C. Pillai<sup>2</sup>

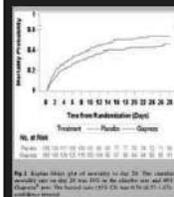


Fig 3. Effect of Angiotensin II on MAP. The mean MAP (mmHg) is shown over 24 hours for patients receiving Angiotensin II (n=10) and placebo (n=10). The Angiotensin II group shows a significantly higher MAP compared to the placebo group.

### Key Points

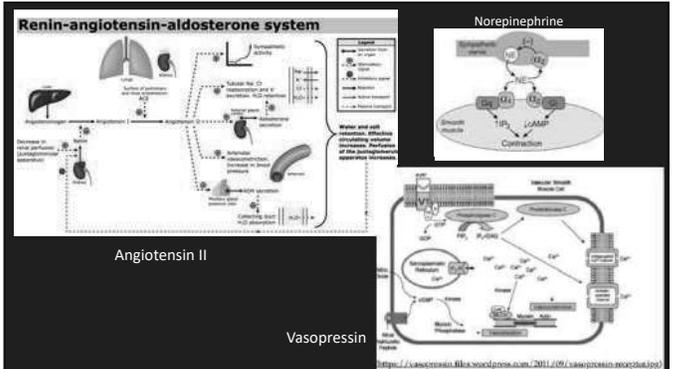
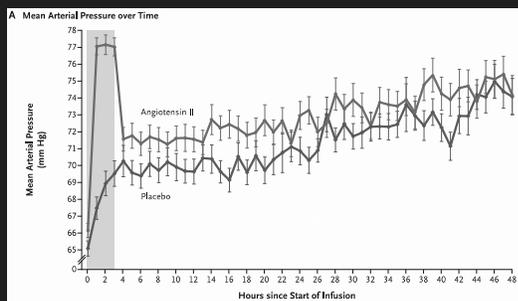
Angiotensin II (Giapreza<sup>®</sup>) was shown to be efficacious in raising the mean arterial pressure (MAP) to target levels >75 mmHg or 10 mmHg from baseline in patients at high risk of death.

The regulatory thinking behind approving a drug in distributive shock is to raise the MAP to provide time to treat the underlying condition.

The data from this trial did not conclusively demonstrate a clinical benefit other than raising the blood pressure.

## Angiotensin II for the Treatment of Vasodilatory Shock

Ashish Khanna, M.D., Shane W. English, M.D., Xueyan S. Wang, M.D., Kealy Ham, M.D., James Tumlin, M.D.

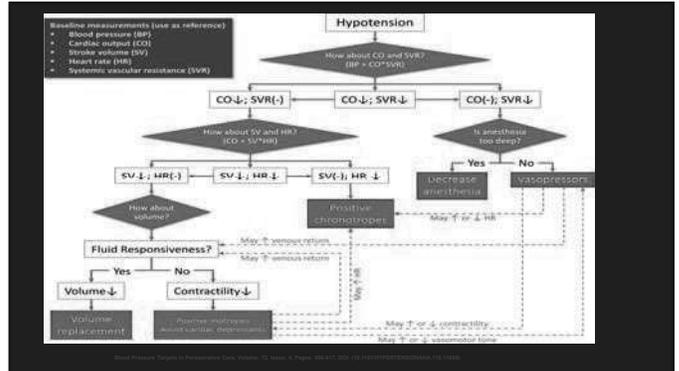


### Perioperative Vasopressors Are Associated with an Increased Risk of Gastrointestinal Anastomotic Leakage

World J Surg (2007) 31:1627–1634  
 Tanya Zakrisson · Bartolomeu A. Nascimento Jr ·  
 Lorraine N. Tremblay · Alex Kiss · Sandro B. Rizoli

**Table 3** Multivariable logistic regression analysis and odds ratio estimates for risk of leak

Risk factor	Chi-squared <i>p</i> value	Odds ratio (confidence interval)
Vasopressor	0.029	3.255 (1.128–9.390)
Cancer	0.227	0.466 (0.135–1.607)
Emergent surgery	0.980	0.984 (0.285–3.403)
Blood transfusion	0.615	1.269 (0.501–3.218)



### Impact of Focused Intraoperative Transthoracic Echocardiography by Anesthesiologists on Management in Hemodynamically Unstable High-Risk Noncardiac Surgery Patients

Journal of Cardiothoracic and Vascular Anesthesia 31 (2017) 602–609  
 Thomas Kratz, MD<sup>1</sup>, Thorsten Steinfeldt, MD<sup>2</sup>, Maik Exner, MD<sup>3</sup>

In summary, this study indicated that focused TTE altered therapy in 52% to 77% of patients with existing instability in the perioperative period, although extended hemodynamic monitoring already was implemented. TTE should be considered as an alternative to more invasive monitoring, such as TEE or PAC, in high-risk patients in the operating room. TTE may supply additional information to hemodynamic monitoring, especially in situations with inconclusive data.

### The Perioperative Management of Implantable Pacemakers and Cardioverter-Defibrillators

PM Schulman, MA Rozner Adv Anesth 34:117, 2016

- All modern ICDs can also perform all PM functions (ie, all ICDs also have anti-bradycardia capability).
- Before elective surgery, ensure that the patient's device is functioning
- With emergency surgery, practitioners must be prepared for perioperative device malfunction or outright failure: placement of transcutaneous pacing/defibrillation pads.

- Monopolar electrosurgery can create EM interference and adversely affect the function of a CIED.
- Strategic placement of the "Bovie Pad" decreases risks of interference.
- If intraoperative EM interference is anticipated, ICD anti-tachycardia pacing and shock should be disabled and external defibrillation pads applied.
- Reprogramming to an asynchronous pacing mode should also be considered for any pacing-dependent patient.
- Magnet behavior should be confirmed whenever magnet use is planned. A magnet never alters the pacing mode of an ICD.

### Use Caution When Applying Magnets to Pacemakers or Defibrillators for Surgery

Peter M. Schulman, MD\* and Marc A. Rozner, PhD, MD† Anesth Analg 2013;117:422

**Table 1. Caveats for Magnet Placement on CIEDs**

Improper magnet positioning	Only ICDs from BOS* (tones/beeping with magnet switch activation) and Sorin (rate change to 90 bpm) have a reliable means to ensure antitachycardia therapy has been suspended by magnet placement. A magnet might not alter CIED function in patients who are obese or have abdominal or submuscular implants.
Magnet switch off	All transvenous ICDs from BOS and SJM, and all PMs from Biot, BOS, and SJM have programmable magnet modes that include "OFF". All CIEDs from BOS are unresponsive to magnet placement after a reset until the magnet function is reactivated by programming.
Low battery voltage	Battery voltage can affect magnet function, and magnet behavior becomes unpredictable when the battery voltage falls below EOL† values even if the CIED appears to be working correctly.
Magnet reapplication	Magnet removal and reapplication is required for some Biot ICDs at 8 h to obtain an additional 8 h of antitachycardia suspension.

CIED = cardiac implantable electronic device; ICD = implantable cardioverter defibrillator; Biot = Biotronik (Berlin, Germany); US-Lake Oswego, OR); BOS = Boston Scientific (Natick, MA, and includes Guidant and CPI brands); SJM = St Jude Medical (Syl Mar, CA); Sorin (Milano, Italy); US—Arvado, CO); PM = pacemaker.

## Optimizing care of the morbidly obese

- Pre-operative assessment
  - What is the actual increase risk to patient?
  - Sleep apnea/CPAP-BIPAP?
  - Consequences of lying flat
  - IV access; accuracy of Non-invasive BP measurement
  - Is the OR bed going to be wide enough for the patient and able to handle the weight?
  - Is Lift of Hover-mat available?
- Intraoperative care
  - Plan for movement to OR table
  - PSV Pro to increase time to desaturation, High-flow NC?
  - Ramp?
  - Glidescope
  - Positioning to minimize risk of atelectasis
- Immediate post-operative care
  - Nasal trumpet
  - Positioning to maximize chance for success
  - Availability of CPAP

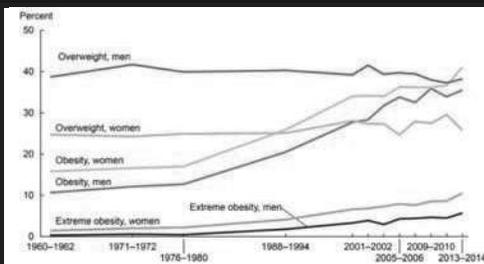
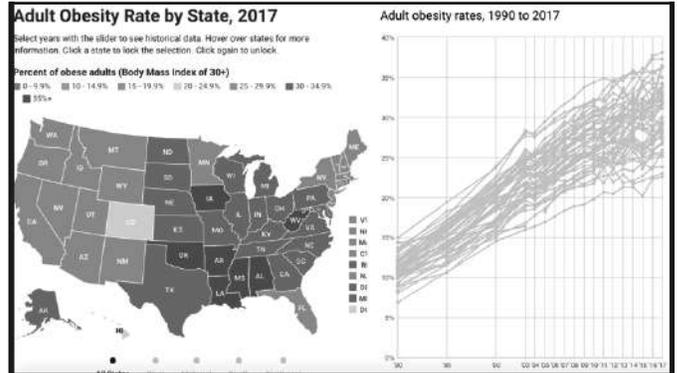


Figure 2  
Trends in adult overweight, obesity, and extreme obesity among men and women aged 20-74: United States, 1960-1962 through 2013-2014. Overweight is body mass index.

Table 5 The STOP-BANG screening questionnaire for obstructive sleep apnoea (adapted with permission [46, 47]). One point is scored for each positive feature; a score  $\geq 5$  is a significant risk.

Snoring	Do you snore loudly (louder than talking or heard through a closed door)?
Tired	Do you often feel tired, fatigued or sleepy during the daytime? Do you fall asleep in the daytime?
Observed	Has anyone observed you stop breathing or choking or gasping during your sleep?
Blood Pressure	Do you have, or are you being treated for, high blood pressure?
BMI	Age > 50 years
Age	Circumference (measured around Adam's apple) > 43 cm (17 in) for males, > 41 cm (16 in) for females.
Neck	Gender
Gender	Male

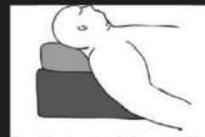


Figure 3 Ramping protocol for obese patients. Note the apex of the air bed with the rimmer.

Table 3 Suggested initial dosing scalars for commonly used anaesthetic drugs for healthy obese adults (notwithstanding the fact that titration to a suitable endpoint may be necessary).

Lean body weight*	Adjusted body weight*
Propofol (induction)	Propofol (infusion; see text)
Etomidate	Antibiotics
Fentanyl	Low molecular weight heparin
Rocuronium	Alfentanil
Atracurium	Neostigmine (maximum 5 mg)
Vecuronium	Sugammadex <sup>†</sup>
Morphine	
Paracetamol	
Bupivacaine	
Lidocaine	

\*See Table 1 for definitions/calculations.  
†See product literature.

Peri-operative management of the obese surgical patient 2015  
Association of Anaesthetists of Great Britain and Ireland  
Society for Obesity and Bariatric Anaesthesia

Nightingale CE et al. Anaesthesia 70:859, 2015

## Preoxygenation

- Standard anesthesia circuit (goal end-tidal oxygen > 80%?)
- PSV Pro (pressure support of 10 cm H2O) if patient tolerates
- Nasal canula during preoxygenation (along with standard mask) and during intubation
- High flow nasal canula during preoxygenation and during intubation

## Positioning of critically ill patients

- Frail patients are susceptible to nerve injury and tissue necrosis due to poor peripheral circulation and friable skin
- Obese patients higher risk of stretch injury to brachial plexus and increased muscle necrosis from not moving during the period of surgery
- In the supine position patients may have orthopnea and/or airway obstruction
- Prevention of skin breakdown with sacral dressings (e.g. Allevyn; hydrocellular adhesive sacral dressing)

## Take home points

- Establish common goals of management with your surgical colleague
- Optimize medical conditions, as much as possible, prior to going to OR
- Anticipate and aggressively treat induction hypotension
- Intraoperative blood pressure should be either at MABP of 80 mmHg or within 10% of baseline
- Minimize risk of infection; it matters

Thank you

1

- I have no conflicts of interest to disclose

2

### Objectives:

- Review the challenges and complexities of Acute Trauma Coagulopathy
- Discuss hemodynamic stabilization and hemostatic resuscitation including hypotensive resuscitation, MTP/Ratio and TEG driven transfusion
- Discuss the role of whole blood in Trauma
- Review the controversies surrounding TXA and other hemostatic concentrates

3

### Trauma Epidemiology

- Major cause of mortality worldwide, more than 5 million deaths annually
- Disease of the young, leading cause of "years of life lost"

4

### Challenges in Trauma

- Prehospital care
- Prompt Recognition of need for surgery
- Airway Management
- Safe Induction
- Hypoxia/lung injury
- Cardiac injury (tamponade, contusions, failure)
- Neurologic injury—TBI, SCI
- Postop complications....MOF, long term M&M, pain

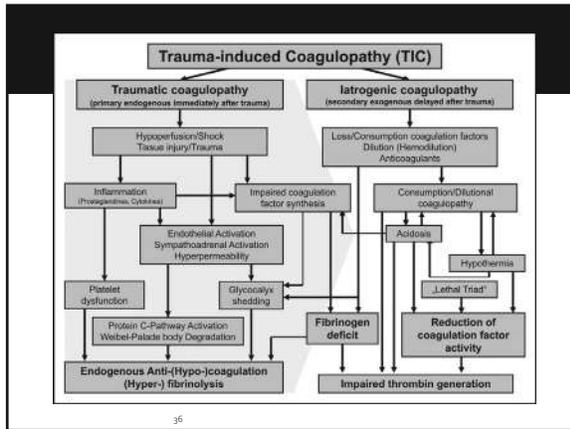
Exsanguination due to uncontrolled bleeding is the leading cause of potentially preventable deaths among trauma patients

5

### Acute Coagulopathy of Trauma

- 1/3 of trauma patients are coagulopathic on arrival to Emergency Department
- Develops very rapidly following tissue trauma and hemorrhagic shock → hypocoagulation and hyperfibrinolysis
- Independent predictor of transfusion, multi-organ failure and mortality
  - In patients with the same Injury Severity Score, the presence of coagulopathy nearly doubles mortality

6



7

### Management of Bleeding Trauma Patients

**Damage Control Resuscitation:**

- Permissive hypotension
- Correction of both endogenous & iatrogenic causes of coagulopathy
  - Minimizing crystalloid
  - Early & high ratio FFP, Platelets
  - TEG/ROTEM goal directed management of traumatic coagulopathy

8

### Damage Control Resuscitation

- Focuses on the hemostatic dysfunction of the severely injured patient
- Consists of:
  - Balanced resuscitation
  - Hemostatic resuscitation
  - Prevention of acidosis, hypothermia & hypocalcemia

9

### Hypotensive Resuscitation & Minimizing Crystalloid

- Risks of large volume crystalloid infusion
  - Dilutional coagulopathy
  - Hypothermia
  - Abdominal Compartment Syndrome
- Risks of high BP (SBP>100)
  - displace clots, worsen hemorrhage

10

### Hypotensive Resuscitation & Minimizing Crystalloid

- MAP 80-90 before surgical hemostasis + adverse effects of excessive crystalloid infusion → increased bleeding and higher mortality
- German Trauma Registry (17,200 Pts):
  - Coagulopathy increased with increasing pre-hospital IV fluids:
    - >2L = >40% had evidence of coagulopathy
    - >3L = >50%
    - >4L = >70%

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### Goal BP?

- **Trauma Hemostasis and Oxygenation Research Network (THOR):**
  - Target SBP 90-100 until surgical bleeding controlled
  - Goal to limit or reverse acidosis, hypothermia and blood dilution from crystalloid
- **ATLS-** eliminated the term "aggressive resuscitation" instead emphasizes "balanced resuscitation"
  - Recommend initiation of 1L crystalloid (instead of immediate 2L) and earlier blood products
- **Exception to hypotensive resuscitation is known or suspected TBI. Goal SBP>110**

12

## Hemostatic Resuscitation & MTP

### Massive Transfusion Protocols

- Predefined ratios delivered by blood bank
- Reproducible
- Reduces provider variability, facilitates staff communication and compliance

13

## MTP scoring systems

- Trauma-Associated Severe Hemorrhage Score
- Vandromme Score
- Prince of Wales Hospital/Rainer score
- Larsen Score
- Schreiber Score
- Assessment of Blood Consumption/Nunez (ABC) score
- PROMMTT showed using a scoring system to activate MTP was superior to "physician gestalt" in predicting which patients would require MTP

14

## ABC score

- 4 non-weighted parameters
  - Penetrating mechanism
  - Positive FAST (focused assessment sonography for trauma)
  - Arrival SBP < 90
  - Arrival HR > 120

Score > 2 = 75% sensitive, 86% specific for predicting need for MTP

15

## Let's talk ratios...



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## Transfusion Ratios

### Borgman & Holcomb et al '07: Retrospective Review

- High Plasma to RBC ratio (1:1.4) → independently associated with survival, decreased death from hemorrhage

### Holcomb et al. '13

- The PRospective, Observational, Multicenter, Major Trauma Transfusion Study (PROMMTT)
- First 6 hours, patients receiving ratios of less than 1:2 (FFP:RBC) were 3-4 times more likely to die than those receiving 1:1 or higher.

### J-OCTET '16 (Japanese Observation Study for Coagulation and Thrombolysis in Early Trauma)

- 189 with severe, blunt hemorrhagic trauma
- Transfusion of FFP/RBC ratio 1:1 or higher within first 6 hours reduces death by 60%

37, 38, 39

17

## Ratios

### Holcomb et al '15: PROPPR Trial

- RCT, 480 Pts. 1:1:1 vs 1:1:2 (Plasma:Platelet: pRBC)

### Conclusions:

- No significant mortality difference at 24 hour or 30 days (significantly underpowered for mortality differences)

### But:

- In 1:1:1, faster hemostasis and decreased death due to exsanguination in first 24hrs, similar complications rates to lower ratio protocol

40

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### Conclusions on Ratios...

- Sufficient evidence to support **high ratios of plasma and platelet** transfusion to improve survival and decreased hemorrhagic death.

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### What about whole blood?



20

### What does "whole blood," reconstituted in a 1:1:1 ratio of pRBC, PLT, FFP, actually contain?

- 680 mL, HCT=28%, PLT= 80K, Coag Factors=65% (of original)
- 800 mL, HCT=32%, PLT= 100K, Coag=75%
- 600 mL, HCT=37%, PLT=140K, Coag=85%
- 500 ml, HCT=43%, PLTs=150-400K Coag Factors=100%

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### History of Whole blood

- Whole Blood (WB) was the traditional transfusion product in military trauma since WWII.
- Component therapy was introduced in 1960s
- By 1990—only component therapy in civilian hospitals
- WB resurfaced in global war on terror in the form of "walking blood bank"
- Source of platelets in a field expedient fashion

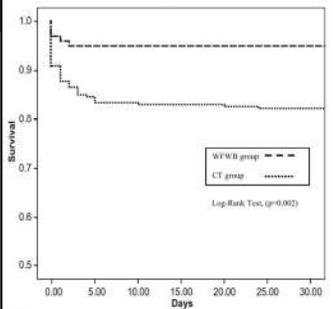
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### WB studies:

- Spinella et al '09. Retrospective Study, 354 pts
  - Warm Fresh Whole Blood (WFWB) group: (100 pts; 28%)
  - Component Therapy (CT) group: RBC, plasma, aPLT no WFWB (254 patients; 72%)
- Primary outcomes: 24 hr. and 30 day mortality

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### Spinella, et. al. WFWB: Results



**Fig. 1.** Kaplan-Meier curve of 30-day survival according to study group.

24

### Spinella et. al: Conclusions:

- "It is our belief that WFWB is more efficient than stored CT at correcting coagulopathy and shock in [trauma patients]..."
- WFWB is more concentrated product than CT to prevent/correct shock and O2 debt in critically ill patient.
- Minimizes adverse effects of transfusion of "storage lesion" of older RBCs.
  - WFWB group received less anticoagulants and additives than CT group.

25

### Myths/challenges of WB in Civilian trauma

**WB (both cellular and AB components) needs to be ABO matched to its recipient**

- **Solutions:**
  - Type specific WB (OK for military)
  - Low titer O WB (LTOWB) for civilians

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### Myths/challenges of WB in trauma

**WB must be leuko-reduced, which destroys platelets**

- New platelet-sparing leuko-reduction filters preserve platelets

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### Myths/challenges of WB in trauma

**Cold Storage of WB destroys platelets**

- "Cold activated platelets"
- Cold storage decreases lifespan but may actually be a better pro-thrombotic product than room temperature storage

28

### Initial safety and feasibility of cold-stored uncrossmatched whole blood transfusion in civilian trauma patients

Mark H. Yazer, MD, Byron Jackson, MD, Jason L. Sperry, MD, Louis Alarcon, MD, Darrell J. Triulzi, MD, and Alan D. Murdock, MD, Pittsburgh, Pennsylvania

**BACKGROUND:** The transfusion of cold-stored uncrossmatched whole blood (WB) has not been extensively used in civilian trauma resuscitation. This report details the initial experience with the safety and feasibility of using WB in this setting after a change of practice at a Level I trauma center was instituted.

**METHODS:** Up to two units of uncrossmatched group O positive WB that was leukoreduced using a platelet-sparing filter from male donors were transfused to male trauma patients with hypotensive secondary to bleeding. Hemolytic marker hemoglobin and signs of transfusion reactions in these patients were followed. Additionally, transfusion volumes and outcomes were compared to a historical cohort of male trauma patients who received at least one red blood cell (RBC) unit, but not WB, during the first 24 hours of admission.

**RESULTS:** There were 47 WB patients who were transfused with a mean (SD) of 1.74 (0.61) WB units. The median hemoglobin concentration on post-WB transfusion Day 1 was 25.1 (9.7) mg/dL, in 7 of 30 non-group O recipients. No adverse reactions in temporal relation to the WB transfusions were reported. There were 145 male historical control patients identified who were resuscitated with component therapy; the median volume of incompatible plasma transfused to the WB versus component therapy group was not significantly different (1,000 vs. 800 mL, respectively;  $p = 0.38$ ), the mean plasma:RBC (0.99[0.47] vs. 0.77[0.73], respectively;  $p = 0.006$ ) and platelet:RBC (0.72[0.40] vs. 0.51[0.734], respectively;  $p < 0.0001$ ) ratios were significantly higher in the WB group.

**CONCLUSION:** Transfusion of two units of cold-stored uncrossmatched WB is feasible and seems to be safe in civilian trauma resuscitation. Determining the efficacy of WB with regard to reducing the number of blood products transfused in the first 24 hours or improving recipient survival will require a larger randomized trial. (*J Trauma Acute Care Surg.* 2016;81: 21-26. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

**LEVEL OF EVIDENCE:** Therapeutic study, level IV.

**KEY WORDS:** Whole blood; transfusion; trauma; resuscitation; hemorrhage.

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### Yazer MH, Uncrossmatched WB in Civilian Trauma: Methods

- Feasibility Trial at a Level 1 civilian academic trauma center
- 2 units low titer type O whole blood cold stored in ED
- Male trauma, SBP < 90 due to hemorrhage, ABC  $\geq 2$ , could receive up to 2 units WB
- No type or screen necessary
- Historical cohort from 2 yrs. prior to WB program: 145 male trauma patients who received  $\geq 1$  unit RBC in ED

30

### Yazer MH, Uncrossmatched WB in Civilian Trauma: Results

- 1<sup>st</sup> ten months: 47 pts received avg 1.74 units
  - 30 recipients non-group O
  - 5 patients unknown blood type
- No transfusion reactions
- Plasma haptoglobin levels tested on day one 25.1 mg/dL (nml 30-300 mg/dL)
- Conclusion:
  - Small volumes of low-titer O WB can be safely transfused to non-O recipients.
  - Now using up to 4 low-titer group O uncrossmatched WB units for trauma patients

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### Shock, Whole Blood, and Assessment of TBI (SWAT) trial

- 4 year prospective, observational study
- N=895; 6 sites: 3 WB, 3 CT (DHMC)
- General Hypotheses
  - WB in poly-trauma will be associated with improved mortality & resuscitation/long-term neurologic outcomes compared to CT
  - Differences in prehospital/acute phase resuscitation/SBP will be associated with differential outcomes in TBI PTs @ discharge & 6 mo

44

32

### Pragmatic, Prehospital group O Whole blood Early Resuscitation Trial (PPOWER) Study

- Prospective, interventional, randomized, pilot clinical trial
- University of Pittsburgh
- 2 u LTLR-WB during transport + up to 6 u WB thru early in-hospital care vs. control (1:1:1)
- Injured air medical transport patients, SBP < 70 mmHg, or < 90 mmHg & HR>108.
- Outcomes
  - 1: 28 day mortality
  - MOF & 24 hr. mortality

45

33

### Conclusion on WB:

- Promising studies using cold stored LTOWB
- Could resolve the Ratio debate entirely
- Role in Prehospital care
  - minimizes product/factor delays in critical first hour of trauma

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### Role of Goal-directed management of Traumatic Coagulopathy

Laboratory diagnosis of Coagulopathy:

- Traditional Coagulation studies
  - PT/INR
  - aPTT
  - Platelet count
  - Fibrinogen levels
- Viscoelastic Hemostatic Assays (VHA)
  - TEG/ROTEM

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### Diagnosing ATC: Traditional tests

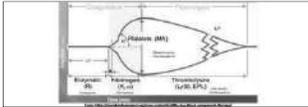
- PT/INR is more sensitive for ATC while aPTT is more specific
- PT/PTT/INR are inadequate for monitoring and guiding therapy in bleeding trauma patients
  - Too slow
  - Performed on plasma (platelet poor); excluding the cellular part of coagulation
  - Terminated once first fibrin strands are formed = 5% total amount of thrombin generated
  - No evaluation of clot lysis
- Platelet count does not assess thrombocytopeny

6

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## Viscoelastic hemostatic assays (VHA)

- TEG/ROTEM provide rapid, comprehensive in-vivo clot formation, strength, and breakdown of whole blood
- Used by most major trauma centers
- Key part of 2016 European Trauma Hemorrhage Guidelines



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## VHA in Trauma

- **Holcomb '12** found TEG superior to conventional coagulation in ATC: faster, cheaper, and more strongly associated with clinical outcomes
- **Cochrane Review '16** concluded that use of VHA guided transfusion improves morbidity in bleeding patients
- **Denver Health '16** first RCT, VHA vs conventional coagulation tests
  - TEG-guided MTP improved survival (at 6 hrs and 28 days) & utilized significantly less plasma and platelets during early phase of resuscitation compared to conventional coagulation tests

7, 8, 9

38

## Fixed Ratios vs VHA guided

- Heterogeneous nature of trauma probably makes ratio driven massive transfusion too simplistic to be applied to all trauma patients
- ATC changes over course of resuscitation, possible making fixed ratios inadequate after initial stages
- **Hybrid Protocol-**
  - Initial resuscitation with 1:1:1 as hemorrhage control is achieved, then transitioning to VHA-guided product replacement protocol

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## Let's talk TXA...

40

## Tranexamic Acid (TXA)

- ▶ Synthetic derivative of Lysine, irreversibly inhibits the proteolytic action of plasmin on fibrin clot and platelet receptors
- ▶ Inhibits fibrinolysis



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## What's Hyperfibrinolysis?

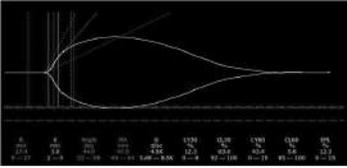
- Incidence varies widely in trauma literature
  - 2-15% of trauma patients on arrival
  - 34% of trauma patients requiring massive transfusion (DHMC study)
- Hyperfibrinolysis independently and significantly predicts mortality in trauma patients
- Associated with very high mortality (70-100%)
- Even low levels of hyperfibrinolysis predicts poor outcome in trauma

10, 11

42

## Diagnosing Hyperfibrinolysis

- Most studies use TEG/ROTEM for diagnosis
  - On rapid TEG defined as LY30>7.5% or EPL >15%
  - LY30>3% is associated with initial significant increase in mortality



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## The CRASH 2 Trial

- Largest randomized placebo-controlled trial reporting effect of early TXA (20,211 Pts)
  - Significant reduction in all-cause mortality with TXA
    - 14.5% vs 16% (p=0.035)
  - Significant reduction in risk of death due to bleeding with TXA
    - 4.9% vs 5.7% (p=0.0077)
  - No increase in fatal or non-fatal vascular occlusive effects
  - Early treatment (<1hr from injury) had the greatest reduction in mortality
  - Treatment after 3hrs from injury had increased mortality

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## MATTERS

Military combat injuries (UK & US), 896 consecutive trauma admissions from combat treatment facility in Southern Afghanistan

- ▶ TXA cohort had lower unadjusted mortality (17.4 vs 23.9%) despite higher injury severity scores (25.2 vs 22.5)
- ▶ Those requiring massive transfusion benefitted the most, with improved survival and less coagulopathy

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## Civilian TXA Trial

- First civilian study to evaluate prehospital TXA in trauma patients
- German Trauma Society registry 2012-2014 (propensity score based matched cohorts, n=258 each group)

Early mortality (up to 24hrs) was significantly lower in TXA group (5.8% vs 12.4%) especially in those severely injured (highest propensity score)



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## So...TXA for everyone???

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## Problems with CRASH 2

- Only 5% patients had bleeding as cause of death
- Only 50% patients received a transfusion, and TXA did not reduce blood transfusions
- Majority of patients enrolled were in low-income or developing countries where massive transfusion protocols and hemostatic resuscitation are not routinely used
- No data on lab values, injury severity & subtypes of transfused products (pRBC, FFP) were reported
- In civilian trauma, TBI is more common. TXA in TBI is still being evaluated

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## TXA trials in developed countries

- **Miami Ryder Trauma Center-**
  - Trauma patients arrived sooner after injury (<1hr vs 2.8hrs), earlier operative intervention and earlier use of fluid & blood products
  - RESULTS: In highest injury acuity patients, TXA was associated with **increased** mortality, regardless of time it was administered.
- Compared to CRASH2, Miami patients were more hypotensive, had more penetrating injuries, 97% transfused, 78% required surgery

**Authors Concluded:** Lack of benefit from TXA, may be attributable to rapid availability of fluid/blood and emergency OR.

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## More TXA trials in Developed countries:

- **Swendsen et al. '13-** Retrospective multiple cohort, 126 trauma patients US Level 1 trauma center
  - Confirmed early TXA survival benefit
- BUT:
  - Increased DVT/PE
  - Increased Acute kidney injury
  - No difference in transfusion

17, 29

50

## J-OCTET ( Japanese Observation Study for Coagulation and Thrombolysis in Early Trauma

### J-OCTET '17:

ISS>16 at 15 Japanese academic institutions  
Propensity-score matched analysis  
TXA vs no-TXA within 3hrs of injury (n=250 each)

#### Results:

- TXA decreased all cause mortality (10 vs 18.4%)
- TXA decreased death related to TBI (6 vs 13%)
- No difference in transfusion

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## Current TXA trials in trauma

- **PATCH:** Prehospital Antifibrinolytics for Traumatic Coagulopathy and Hemorrhage Trial
  - Multicenter study in Australia/New Zealand looking at risk reduction and mortality of TXA in advanced medical system. Currently recruiting with target 1184 Patients
- **CRASH-3:** International multicenter, randomized, double blind, placebo controlled trial
  - Goal: quantify the effects of early TXA vs. placebo on death and disability in TBI (n>10,000 expected)

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## Why TXA only works in first 3 hrs?

- Early fibrinolysis is common after major trauma, is associated with high mortality
- Tissue plasminogen activator (TPA) is release by endothelium after trauma
- TPA is an enzyme that converts plasminogen to fibrinolytic plasmin → Fibrinolysis & diffuse bleeding
- TPA levels peak 30 min, Plasmin levels peak at 60min
- TXA inhibits this early fibrinolysis, prevents early exsanguination



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## But!

- 2hrs after injury, plasminogen activator inhibitor-1 (PAI-1) levels increase, peaking at 3hrs
- PAI-1 inhibits fibrinolysis causing "fibrinolytic shutdown"
- May explain why antifibrinolytics only benefit within first 3hrs
- Adverse effect of late TXA may be due to fibrinolytic suppression and onset of thrombotic DIC (manifesting as bleeding)

32

54

## Fibrinolysis in Trauma is complex

- Trauma patients have both promoters and inhibitors of fibrinolysis
  - Shock promotes tPA-mediated fibrinolysis
  - Tissue injury inhibits fibrinolysis
- Spectrum of fibrinolysis in severe trauma has been described with hyperfibrinolysis at one end to “fibrinolytic shut down” at the other end

11

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## 'Fibrinolytic shutdown'

HB Moore et al. J Trauma Acute Care Surg Found 3 phenotypes

1. Hyperfibrinolysis
2. Physiologic fibrinolysis
3. Fibrinolytic shutdown.

▶ t-PA TEG assay may differentiate between these phenotypes and determine which patients will benefit from antifibrinolytic treatment

32

56

## Conclusions on TXA:

- In populations represented by CRASH-2, and in remote areas of developing countries where access to definitive care might be delayed, routine, early use of TXA is recommended.
- Other patients, consider more judicious & selective TXA administration
  - Consider use of TEG to rapidly detect fibrinolysis (If Ly30 >3%)
- If no TEG, consider TXA in those who are likely to have the highest mortality reduction (SBP <75, severe hemorrhagic shock, less than 3hrs from injury)
- More studies needed to predict which patients benefit from TXA

18, 15

57

## How about other Hemostatic agents?

58

## Prothrombin Complex Concentrate

- Reconstitutable powder of purified donor pooled human plasma
- Contains Factors **II, VII, IX and X** and antithrombotic Proteins C & S
- Allows rapid reversal of Vitamin K antagonists
- When given with Vitamin K, INR reversal is maintained >48hrs.



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## Advantages of PCC over FFP

- Faster (no thawing)
- Smaller volume (1 mL of reconstituted PCC=10mL FFP)
- More rapid reversal of INR
  - INR <1.4 within 30 min (in 93% Pts) compared to <10% in FFP group
  - On average INR reversal with FFP took >8hrs to achieve
- Minimal risk of TRALI (lacks antigens)
- Fewer adverse events (death, MI, stroke, heart failure, VTE, peripheral arterial thromboembolism) compared to FFP (9.7% vs 19.5%)

19, 20, 21

60

## PCC in Trauma

- **Joseph et al.** 2 year retrospective analysis of 5146 Pts major ortho trauma (femurs/tibia/pelvic fx): 43% had INR > 1.5 on admission, PCC was given for INR > 1.5
  - Results: decreased time to reversal, lower blood transfusion, and earlier fixation of fracture
  - No increase in DVT/PE. No change mortality
- **Dickneite et al.** - porcine model of femur and spleen trauma-PCC faster time to hemostasis than FFP
- **Demeyere et al** -cardiac surgery, faster INR correction in PCC
- **Joesph et al** - Combo tx—FFP + PCC vs FFP alone? Earlier correction and better outcome

22, 23, 24, 25

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## FFP + PCC vs FFP alone in Trauma

### Faizal et al. JTACS 2018.

- 120 trauma patients (40 FFP+PCC and 80 FFP), Median ISS 29, INR > 1.5
- **Combination FFP +PCC group:**
  - Time to INR correction: 373 min vs 955 min.
  - Less RBC: 7 vs 9 units.
  - No difference in thromboembolic complications
  - Lower Mortality: 25 vs 33%
  - Lower Hospital Length of Stay: 5 vs 7 days.

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## Conclusions on PCC in trauma

- First line in urgent Vitamin K anticoagulant reversal in patient with active bleeding or urgent procedures
- Consider PCC for reversal of direct oral anticoagulants/factor Xa inhibitor if bleeding is life-threatening
- May have a role in coagulopathic patients with extremely tight brain, ESRD, decompensated CHF in whom high volume of plasma will be risky, maybe in combination with FFP.
- More human studies needed to evaluate safety & optimal dose
- Use in trauma in U.S is still off label

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## Recombinant Factor VIIa



- Binds exposed tissue factor, acts locally at site of injury, accelerates thrombin generation
- Off-label use in trauma
- May reduce transfusion PRBCs
- No clinical decrease in mortality
- Evidence of harm-increased thromboembolic events, particularly coronary arterial thromboembolic events, especially Patients >65
- Increased thromboembolic events after TBI

Can not be recommended as standard adjuvant in massive transfusion protocol

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## Hypofibrinogenemia in Trauma

- Normal plasma fibrinogen 200-400mg/dL (2-4 g/L)
- During hemorrhage, fibrinogen plays a key role in effective clot formation
- 1<sup>st</sup> factor to reach critically low levels
- Diagnosed by fibrinogen levels or VHA
- Associated with increased transfusion and mortality
- FFP (even at high ratios) fails to normalize fibrinogen levels
- Cryoprecipitate or fibrinogen concentrate are needed to correct hypofibrinogenemia and improve outcome

65

## Fibrinogen Concentrate



- ▶ Derived from Human donor plasma
- Contains 20mg/mL Fibrinogen (10xFFP)
- Smaller volume
- ▶ Standard Fibrinogen dose per vial = 20g/L (Cryo varies 8-16g/L)
- ▶ Stored at room temperature, role for administration outside the hospital
- ▶ Avoids infection, TRALI and ABO incompatibility

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## Fibrinogen Concentrate in Trauma

- **FiiRST** Trial—early FC in trauma was feasible and increased plasma fibrinogen for 12hrs
- **PRooF-iTH** (RCT Denmark) FC vs Placebo in trauma patients, endpoints VHA clot strength, transfusion and survival Placebo (concluded but no results yet published)
- **FlinTIC** (RCT) Prehospital trauma patients received FC vs Placebo (concluded but no results yet published)
- Based on studies of FC use in OB (FIB-PPH) & Cardiac (REPLACE, ZEPLAST)
  - No benefit to fibrinogen supplementation in patients with normal fibrinogen
- **FEISTY**- multicenter RCT Australia (ongoing)
  - FC vs Cryo using VHA triggers (ROTEM)
  - Optimal timing, method and dosing of FC

7, 18, 27, 32

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## Take-home points on FC

- Seems to be safe, multiple studies showing no increase in thromboembolic events
- Unanswered questions:
  - Lab triggers? Fibrinogen concentration vs functional Fibrinogen (TEG/FIBTEM on ROTEM)
  - Goal fibrinogen level in bleeding trauma patient?
    - Several studies support treatment trigger of Fibrinogen <150 mg/dL
  - FC optimal dose? Weight based dosing?
- Larger quality trials are justified
- Use is trauma in the U.S. remains off label

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## Role in Remote Damage Control Resuscitation (RDCR)

Early prehospital use of high ratio plasma and platelet to RBC

+

Coagulation Factor concentrate-based treatment

1. Stop hyperfibrinolysis, TXA
2. Support clot formation, FC
3. Increase thrombin generation, PCC

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## Objectives Covered:

- We discussed challenges and complexities of Acute Trauma Coagulopathy
- Discussed hemodynamic stabilization and hemostatic resuscitation including hypotensive resuscitation, MTP/Ratio and TEG driven transfusion
- Discussed the role of whole blood in Trauma
- Reviewed the controversies surrounding TXA and other hemostatic concentrates

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## The End, Thanks!



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# Why are you Coughing?

Richard Ing Singhal R  
Children's Hospital Colorado

1

You are on call at the hospital when you are informed by the CICU of a 10 year old 23 kg boy who needs a bronchoscopy for worsening respiratory distress. His history is significant for hypoplastic left heart syndrome which was successfully palliated with a modified extra-cardiac total cavo-pulmonary anastomosis at 2 years of age.

2

## Past Medical History

- At age 6, had a closure of the fenestration
- At age 8, had development of intermittent cough and recurrent respiratory tract infections
- At age 9 (1 year ago), had an episode of tracheobronchitis
- Doing well until now

3

## Past Medical History

- Normal Cardiac Function
- Fontan circulation within normal limits – no increase in pulmonary pressures or obstruction in flow
- No other significant past medical history – Neuro, GI, Renal, Hepatic, Musculoskeletal systems all within normal limits

4

## Physical

- HR – 87    RR – 24    SpO2 – 92%    BP – 101/51
- Afebrile
- Decreased breath sounds bilaterally
- Distant heart sounds
- Nasal cannula, agitated, anxious

5

## Labs

WBC – 11.4	Sodium – 137
Hemoglobin – 13.2	Potassium – 3.9
Hematocrit – 38.9	Chloride – 104
Platelets – 143	HCO3 – 25
	BUN – 15
	Creatinine – 0.34
	Glucose - 94

6



7

You are now at the patient's bedside in the ICU, and everything is going well – except for one thing. He is screaming, pulling at his lines, refusing to put on his nasal cannula, and his saturations are dropping. What are you going to do now?

8

### Sedatives

Midazolam injection, USP  
2 mg/2 mL (1 mg/mL)

KETAMINE  
JUST SAY NEIN

Precedax

9

You administer a combination of ketamine and midazolam, and the patient's respirations become normal, he allows you to place nasal cannula upon him, and his oxygen saturations improve to 95%. You proceed to the operating room. What is your plan for induction?

10

### Fontan Circulation

- Dependent on several factors
- Pulmonary vascular resistance, cardiac output

Figure 3. Fontan circulation

11

### Techniques for Induction

- Maintain Spontaneous Ventilation
- Maintain Cardiac Output
- Maintain normal oxygenation and ventilation
- Prevent acidosis

12

You proceed with an inhalational induction, supplemented with ketamine boluses, along with propofol infusion to maintain an adequate depth of anesthesia. What monitors and lines would you like to have available?

13

## Monitors



14

After induction, you place 2 large bore IV's as well as a right radial arterial line. At this point, you place an LMA in preparation for flexible bronchoscopy by the pulmonologist. While the right lung looks clear, the left main bronchus seems to be obstructed. What could this be?

15

## Respiratory Plugging

- Plugging could be caused for several reasons
- Mucus plugs
- Pneumonia
- Casts
- Inflammation



16

The pulmonologists are unsuccessful in removing the obstruction. The patient is prepared for rigid bronchoscopy, however, upon insertion of the rigid scope, he begins to cough violently. What is your next step?

17

## Deepen the Anesthetic

- Keep in mind that negative intrathoracic pressure helps Fontan circulation
- Increase the volatile agent
- Give boluses of Ketamine



18

You are able to proceed, and you intermittently assist the patients ventilation when the oxygen saturations begin to drop below 80%. The next attempt results in the plug obstructing the carina. Saturations are once again falling. What do you do now?

19

## Plastic Bronchitis

- Multiple casts extracted from the patients left bronchus
- Throughout rigid bronchoscopy, saturations maintained, pressures ranged from 85-95/50-60
- Pulse oximetry dropped to 70's requiring assisted ventilation



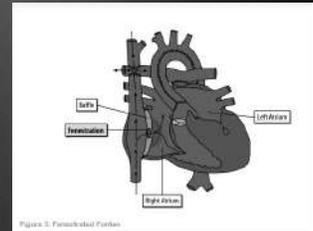
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Ventilation and oxygenation seems to be improving at this point, however, the capnogram is showing that the End Tidal Carbon Dioxide is 60-65, and the blood pressures are starting to drop. What could be going on?

21

## Fontan Circulation

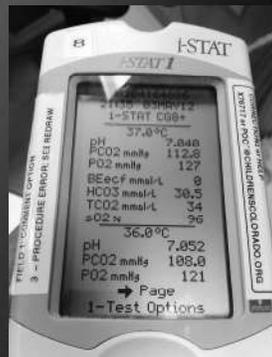
- Passive flow
- Dependent on preload, pulmonary vascular resistance
- If preload drops or PVR increases, flow through the circuit will decrease, causing a vicious cycle



22

## Arterial Blood Gas

- Capnogram showed CO<sub>2</sub> in the 60's, so an ABG was obtained
- With PaCO<sub>2</sub> of 112.8, aggressive ventilation started



23

Following this blood gas, you decide to aggressively ventilate the patient, keep him intubated, and stop the anesthetics (propofol, sevoflurane). The patient stabilizes, and you decide to transport to the Intensive Care Unit. After moving him over to the bed, the first pressure reads 35/17 mmHg. What's your next step?

24

## Treat the Problem

- Ensure the BP is actually real
- Check your EKG and Pulse Oximeter
- Vasodilation?
- Bradycardia?
- Both?



25

You administer 5 mcg of Epinephrine IV and have a good response – normal heart rate and blood pressure return. At the same time, you administer a 10 cc/kg bolus of Plasmalyte, and with the epinephrine in hand, you transport to the CICU. While in the elevator, you notice that the pressure is now 45/30. Now what?

26

## Treat the Problem

- Re-administer epinephrine
- Give fluids
- Minimize positive pressure
- Alert the CICU to have transducers available



27

You finally arrive in the CICU in critical condition. An ABG shows pH of 7.28, pCO<sub>2</sub> of 53, pO<sub>2</sub> of 166, and a bicarbonate of 27, and a base deficit of -2.9. He remains persistently hypotensive. What further information would be helpful at this time?

28

## Bedside Transthoracic Echo

- Showed decreased function in the RV
- Mild to moderate tricuspid regurgitation
- Normal, low velocity flow through the Fontan Circuit



29

After the TTE is performed, you place a central femoral venous line for resuscitation and vasoactive infusions. You start him on epinephrine, vasopressin, and norepinephrine for vasoplegia. A rectal temperature is noted to be 40.5 Celsius. What could be causing this response?

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### Complex Pathophysiology

- Sepsis
- Overwhelming inflammatory response
- Positive pressure ventilation
- Hyperventilation, down regulation of sympathetic nervous system
- Adrenal down regulation



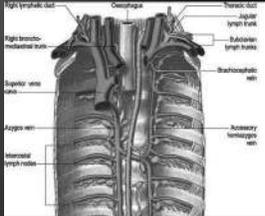
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Over the next several hours, the patient rapidly stabilized. A flexible bronchoscopy the next morning showed no residual casts, and he was extubated later the next afternoon. Within a few hours of normal ventilation, his vasoactive drips were weaned and he was sent to the floor. What intervention could possibly prevent a recurrence of this scenario?

33

### Thoracic Duct Ligation

- Increased lymphatic pressures can result in the deposit of these casts
- Fenestration of the Fontan Circuit can also be helpful



34

Our patient did very well on the floor, going to the catheterization laboratory on post-operative day 4. He had re-fenestration of his Fontan Circuit to reduce the pressures and potentially prevent the recurrence of the plastic bronchitis. He is now at home and doing very well.

35

### Fontan Pulmonary Circulation

Creates Systemic Venous Hypertension

Hepatic Congestion and Non-pulsatile Pulmonary Blood Flow

Begins the day the operation is performed Venous pressure rises abruptly 2-6 X baseline.

36

### Fontan Paradox

No pulsatile hydraulic force (RV) to drive pulmonary perfusion.

**Paradox:**  
**Systemic Venous Hypertension:**  
 >10 mmHg

**Pulmonary Artery Hypotension:**  
 MAP < 15 mmHg

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### Systemic Venous Hypertension

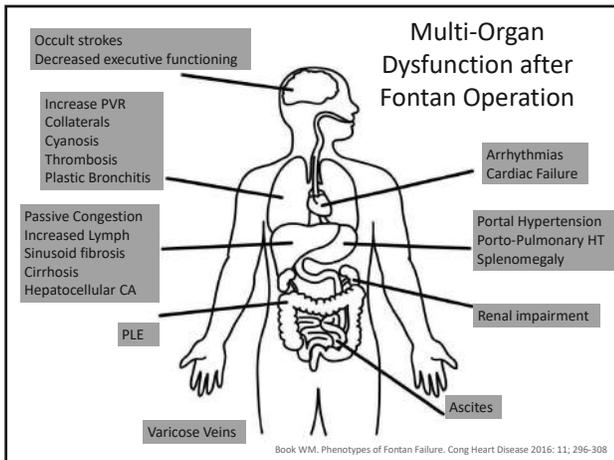
Loss of the Hepatic Venous Pressure Gradient  
 Passive Distention Hepatic Veins  
 Portal Venous Hypertension

**Contributes to Protein-losing Enteropathy (PLE)**

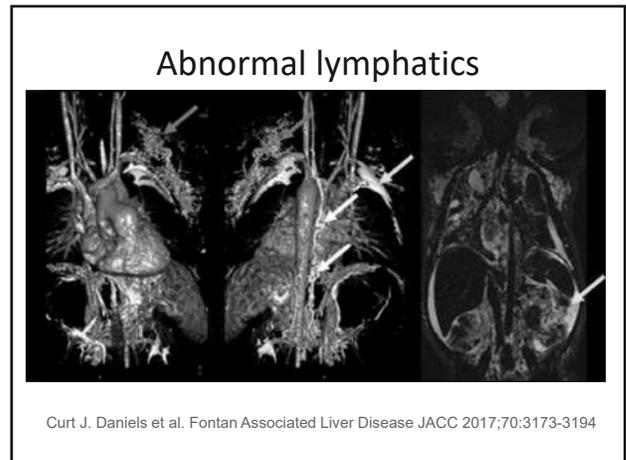
Altered Gut Blood Flow  
 Low Cardiac Output  
 Persistent Hypoxia  
 Inflammation

Khambadkone S. The Fontan Pathway: What's down the road? Ann Ped Cardiol 2008 1(2) 83-92

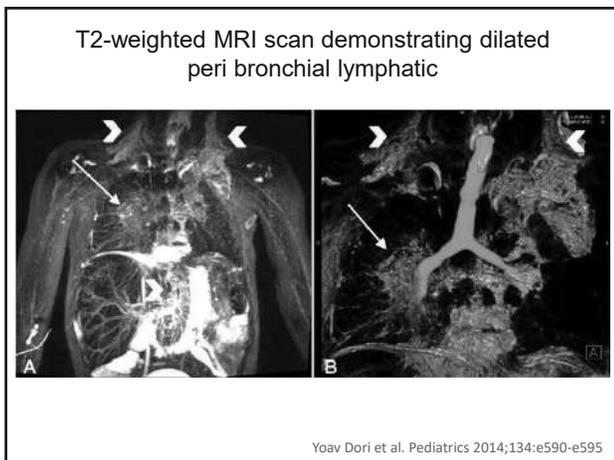
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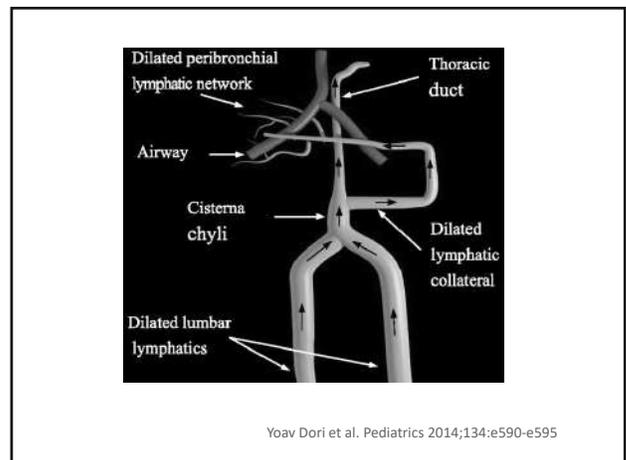
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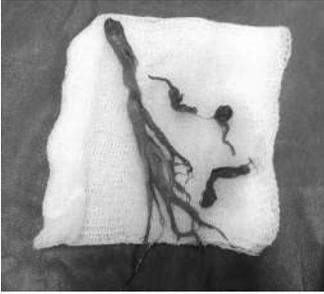


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Plastic Bronchitis in a child with Fontan physiology for urgent Rigid bronchoscopy



Vergheze S, et al. *Anesth Analg.* 2008 Oct;107(4):1446-7.

Singhal N et al. *Semin Cardiothorac Vasc Anesth.* 2013 Mar;17(1):55-60



Breandan Sullivan MD  
Assistant Professor  
Co-Director Cardiothoracic and Vascular Surgery ICU  
Department of Anesthesiology and Critical Care Medicine  
University of Colorado

## Perioperative Management of Cardiac Implantable Devices

1

### Financial Disclosures

- None

2

### Let's Talk Pacemakers!

**Practice Advisory for the Perioperative Management of Patients with Cardiac Implantable Electronic Devices: Pacemakers and Implantable Cardioverter-Defibrillators**

*An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Implantable Electronic Devices*

3

### Where did the rec's come from?

- Heart Rhythm Society
- ASA
- Tried to find evidence and then gain consensus

4

### Perioperative Experts!

- 3 million people worldwide with pacemakers
- 600,000 pacemakers implanted every year
- Most patients >60 years old
- They often need surgery
- We should know what's going on!

5

### Main Points of the talk

- Get help
- Interrogate the device
- Don't fly blindly
- Device Product reps get paid a lot of money
- Device companies make a lot of money
- They work to help you
- They are always on call
- Figure out what your hospital has
  - EP nurse, cardiologist, product rep

6

There is no level 1 A evidence

- You will not find level 1 A evidence for the perioperative management of pacemakers
- You will not find level 1 A evidence for the use of pulse oximetry either

7

Preoperative Evaluation  
(Anesthesiology 2011; 114:247-61)

- Establish if patient has a CIED
- Determine whether patient is CIED-dependent for antibradycardia pacing function
- Define the type of device
- Determine Device function
- **LEVEL B Evidence**
  - Suggestive literature

8

Preoperative Evaluation  
(Anesthesiology 2011; 114:247-61)

- Focused history
- Medicals records review
- Review of Chest x-ray
- EKG
- Check for scars palpate device

9

Peroperative Evaluation  
(Anesthesiology 2011; 114:247-61)

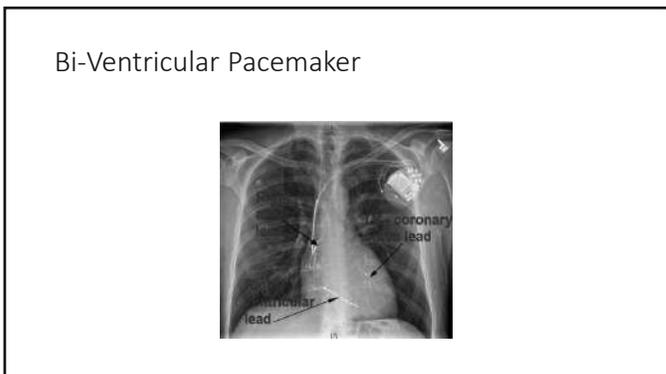
- Obtaining the manufacturer's ID card
- Order Chest x-ray
  - I found fluro works best because you can magnify
- Refer to supplemental resources
  - Manufacturer's database
  - Pacemaker clinic record
  - **Consultation with a cardiologist**
    - Rarely necessary if you know dangers of asynchronous pacing

10

Results  
(NEJM 1996; 335:1933-40)

- 196 patients enrolled
- 27 month follow up
- 15 deaths in defibrillator group
- 39 deaths in conventional therapy group
- Mortality reduction of 56%
  - $P < 0.009$

11



12

### Preoperative Evaluation

(Anesthesiology 2011; 114:247-61)

- CIED dependence
  - Verbal history or indication patient has experienced a bradyarrhythmia that has caused syncope or other symptoms requiring CIED implantation

13

### Painful Nomenclature

Position I Pacing Chamber(s)	Position II Sensing Chamber(s)	Position III Response(s) to Sensing
O = None A = Atrium V = Ventricle D = Dual (A+V)	O = None A = Atrium V = Ventricle D = Dual (A+V)	O = None I = Inhibited T = Triggered D = Dual (T+I)

14

### Preoperative Evaluation

(Anesthesiology 2011; 114:247-61)

- CIED dependence (cont' d)
  - History of successful AV node ablation
  - No evidence of spontaneous ventricular activity when the pacemaking function of the CIED is programmed to VVI pacing mode at lowest programmable rate

15

### Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Determine if electromagnetic interference is likely to occur during the procedure
  - Electrocautery
  - Radiofrequency ablation
  - MRI
  - Lithotripsy

16

### Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Determine:
  - **Preoperative programming to an asynchronous mode or disabling special algorithms is needed**

17

### Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Suspend:
  - **Antitachyarrhythmia function if present**
  - **Rate Adaptive Therapy**

18

## Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Advise:
  - **The individual performing the procedure to consider bipolar or ultrasonic (harmonic) scalpel to minimize adverse effects on the pulse generator or leads**

19

## Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Additional Programming
  - Pace maker **dependent** patients should be programmed to an asynchronous mode before surgery

20

## Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Assure:
  - **The availability of temporary pacing and defibrillation equipment**

21

## Preoperative Preparation

(Anesthesiology 2011; 114:247-61)

- Numerous descriptive studies and case reports suggest the following are associated with EMI
  - Electrocautery
  - Radiofrequency ablation
  - MRI
  - $\pm$  Radiation therapy
  - No STUDIES were found that reported EMI during ECT

22

## Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Monitor the operation of the device
- Prevent potential CIED dysfunction
- Perform emergency defibrillation, cardioversion, or heart rate support

23

## Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Continuous EKG
- Peripheral pulse monitoring
  - Pulse ox, A-line, ultrasound peripheral pulse(?)
- Category B3 Evidence

24

### Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Electrocautery
- Assuring cautery tool, current return pad positioning
- Current pathway does not pass through or near CIED pulse generator and leads
- **B2-B3 evidence**
  - Two case reports
  - One Observational study

25

### Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Encourage Short Bursts at lowest feasible energy level
- **B2-B3**
  - One case report
    - Total pacemaker failure when short burst of cautery used
- Multiple Case reports
  - Uneventful surgery with bipolar cautery or harmonic scalpels (**B 3 Evidence**)
  - One case report pacemaker failure with bipolar cautery

26

### Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- **Experts opinion/Summary**
- Position the cautery tool and current return pad away from device
- Avoid proximity of the cautery electrical field to the pulse generator and leads
- Use short intermittent and irregular bursts at the lowest feasible energy level
- Use bipolar or ultrasonic (harmonic) scalpel if possible

27

### Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Radiofrequency Ablation
  - High frequency alternating current
  - We will see it in OR and IR
  - Treatment of solid organ tumors/metastatic disease
- Keep RF current path as far away from the pulse generator and lead system as possible

28

### Intraoperative Management

(Anesthesiology 2011; 114:247-61)

- Lithotripsy
- Avoid focus of the lithotripsy beam near the pulse generator
- Disable atrial pacing if the lithotripsy system triggers on the R wave

29

### Hemodynamics of Pacing

- Hierarchy of rhythm
  - Normal sinus rhythm
    - If rate is fast enough
- Atrial Pacing
- AV pacing
- V pacing
- Switching Modes of pacing
  - Can have serious hemodynamic consequences

30

**Intraoperative Management**  
(Anesthesiology 2011; 114:247-61)

- Magnetic Resonance Imaging
- Observational studies and case reports suggest MRI can be done safely
- Expert Opinion
  - MRI is contraindicated
- If absolutely necessary
  - Consult
    - Manufacturer
    - Cardiologist
    - Ordering Physician
    - Radiologist

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**Intraoperative Management**  
(Anesthesiology 2011; 114:247-61)

- Electroconvulsive Therapy
  - No studies exist
  - Two case reports
  - ICD' s turned off for procedure
    - No mention of effect on device
- Radiation
  - The device should be out side of the field of radiation

32

**Intraoperative Management**  
(Anesthesiology 2011; 114:247-61)

- Electroconvulsive Therapy
- Expert Opinion
  - If patient has a defibrillator
  - Disable defibrillator
  - Interrogate device before procedure
  - Be prepared to treat ventricular arrhythmias
  - Pacer dependent patients may need to be placed in a asynchronous mode to preserve cardiac function

33

**Intraoperative Management**  
(Anesthesiology 2011; 114:247-61)

- Emergency Defibrillation or cardioversion
- Minimize the current through the pulse generator
- Expert Opinion
  - Anterior-Posterior Position should be used

34

**Intraoperative Management**  
(Anesthesiology 2011; 114:247-61)

- If life-threatening arrhythmia occurs
- Don' t screw around
- ACLS protocol
- Remember the MADIT, MADIT II, MADIT-CRT, CARE-HF
- These patients are sick!

35

**WHAT ABOUT A MAGNET?**

- Asynchronous ?
- Turns off AICD ?
- No industry standard
- Usually does...
- Would not depend on it if you have time
  - Interrogate
  - Interrogate
  - Interrogate

36

## Postoperative Management

(Anesthesiology 2011; 114:247-61)

- Interrogate and restore defibrillation function
- Observational study + case report
- Postoperative pacemaker check revealed the need to alter pacing mode or other parameters which include increasing ventricular thresholds
- **B2-B3 evidence**
- **My opinion**
  - **Don't take the pads off until the device is interrogated and activated!**

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## Conclusion

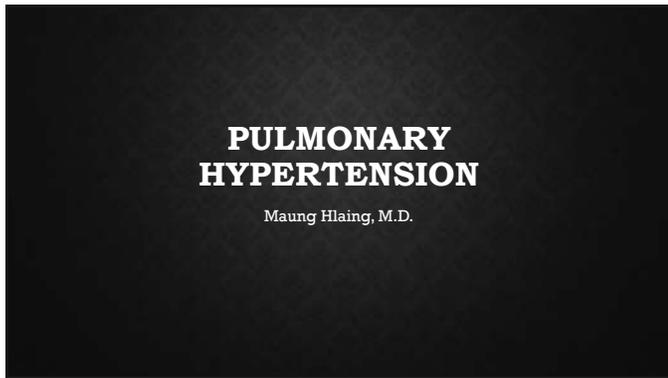
- Find out all the information you can
- Interrogate, interrogate, interrogate
- Prepare for the worst
  - These patients are sick
- Have a back up plan
- **GO RAIDERS!**

38

## Questions?



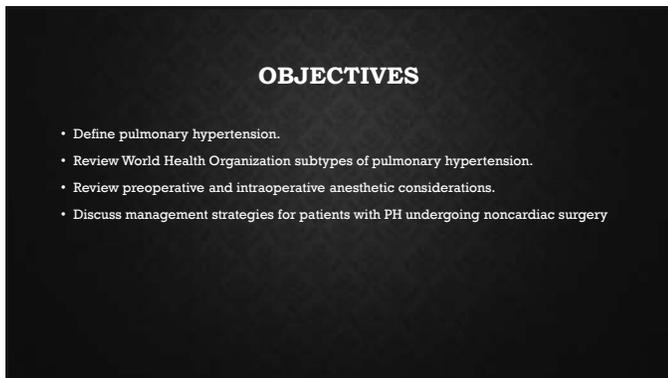
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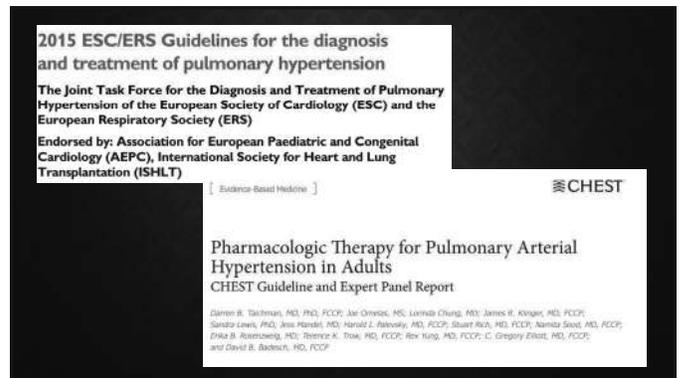
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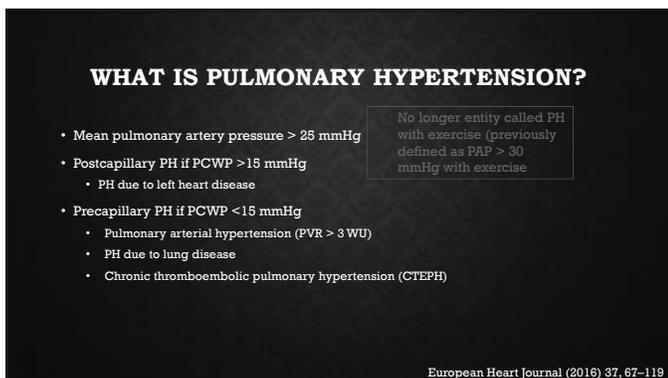
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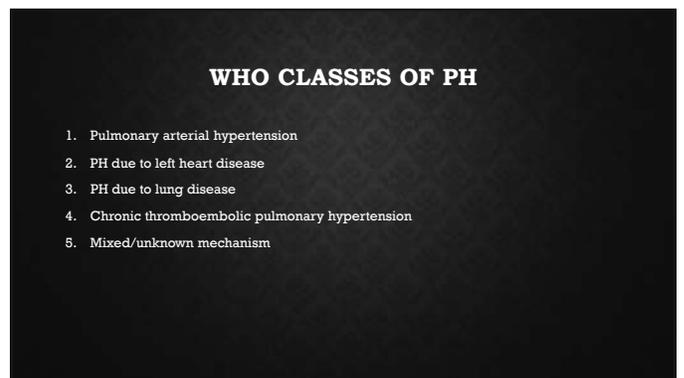
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5



6

<p><b>3. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis</b></p> <p>3.1 Hypoxia</p> <p>3.2 Inflammation</p> <p>3.3 Other causes</p> <p>3.4 Associated with:</p> <p>3.4.1 Connective tissue disease</p> <p>3.4.2 Human immunodeficiency virus (HIV) infection</p> <p>3.4.3 Drug hypersensitivity</p> <p>3.4.4 Congenital heart disease (Table 1)</p> <p>3.4.5 Miscellaneous</p>	<p><b>4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions</b></p> <p>4.1 Chronic thromboembolic pulmonary hypertension</p> <p>4.2 Other pulmonary artery obstructions</p> <p>4.2.1 Angiosarcoma</p> <p>4.2.2 Other intravascular tumors</p> <p>4.2.3 Arteritis</p> <p>4.2.4 Congenital pulmonary artery stenosis</p> <p>4.2.5 Parasites (hydatidosis)</p>
<p><b>5. Pulmonary hypertension with unclear and/or multifactorial pathogenesis</b></p> <p>5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy</p> <p>5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis, neurofibromatosis</p> <p>5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders</p> <p>5.4 Other pulmonary arterial thrombotic/microangiopathic (including mediastitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension)</p>	

7

### WHY SHOULD ANESTHESIOLOGISTS CARE ABOUT PH

- PH increases perioperative mortality (2% - 18%!!!)
- Increased risk for complications:
  - Heart failure exacerbation
  - Prolonged intubation
  - Prolonged hospital stay
- Risk increased by:
  - Emergency surgery
  - Increased right atrial pressure (RAP > 7 mmHg)
  - Decreased 6 minute walk test

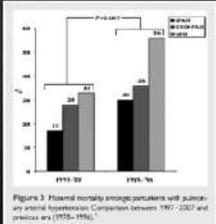


Prinos et al., Eur Respir J 2010; 35: 1294-1302  
Meyer et al., Eur Respir J 2010; 35: 1303-1307

8

### BUT I DO MOSTLY OB, MOST OF MY PATIENTS ARE HEALTHY

- Obstetric patients with PH are at significantly higher risk for mortality/morbidity.
- Risk higher with GA vs neuraxial.
- Outcomes seem to be improving over time.
- Recent review showed 5% mortality from 28% in pregnant pts with PH due to congenital heart disease.



Bedard et al., European Heart Journal (2009) 30, 256-265  
Endovician M, et al. Heart 2011; 110:251-252

9

### WHY DO PEOPLE DIE FROM PH?



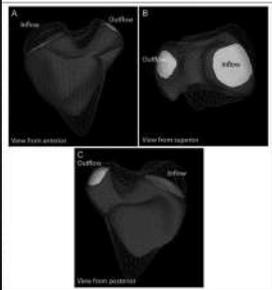
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### THE RIGHT VENTRICLE

- The RV is thin-walled.
- The RV is used to working with a low pressure system.
- The RV is dependent on the LV to function.
- The RV has a funky shape.
- The RV is sensitive to volume.



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SCVA, 2014, Vol. 18(4) 341-351

12

### WHO'S AT HIGHEST RISK?

Determinants of prognosis* (estimated 1-year mortality)	High risk >10%
Clinical signs of right heart failure	Present
Progression of symptoms	Rapid
Syncope	Repeated syncope†
WHO functional class	IV
6MWD	<165 m
Cardiopulmonary exercise testing	Peak VO <sub>2</sub> <1 l/min/kg (<35% pred) VE/VCO <sub>2</sub> slope ≥45
NT-proBNP plasma levels	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area >25 cm <sup>2</sup> Pericardial effusion
Haemodynamics	RAP ≥14 mmHg CI <2.0 l/min/m <sup>2</sup> SpO <sub>2</sub> <92%

European Heart Journal (2014) 35, 67–119

13

### WHAT I LOOK OUT FOR...

- Low functional capacity
- Rapidly progressive symptoms
- Mod-severe RV dysfunction
- Mod-severe tricuspid regurgitation
- Decompensated and volume overloaded



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### SHOULD I CANCEL THE CASE?

- Definitely if the patient is decompensated.
- Consider discussing with their PH specialist.
- Make sure all the equipment is there for you and for surgeons.



15

### PERIOPERATIVE MANAGEMENT

- Depends on WHO Class of PH.
- Will focus on Class I (pulmonary arterial hypertension).
- But first the other classes...

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### CLASS II – PH DUE TO LEFT HEART DISEASE

- Left heart is the problem. Fix the problem!
- Pulmonary arterial vasodilation may actually exacerbate the problem.



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### CLASS III – PH DUE TO LUNG DISEASE

- Severe PH is rare in this situation.
- Classic medicine consult advice:

“avoid hypotension, hypoxia & hypercarbia”



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### OTHER TREATMENTS FOR CLASS III

- Treat OSA
- Minimize hypoventilation
- Consider dexmedetomidine or ketamine to minimize respiratory depression



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### CLASS IV – CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

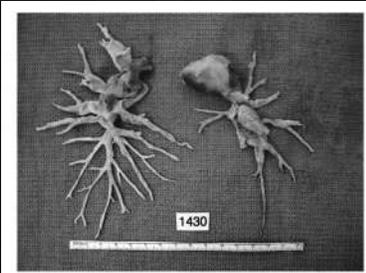
- Only class of PH with a surgical solution
- Lowest mortality in patients amenable to surgery.
- Surgical repair offered only in certain tertiary care centers.
- Potentially a cure, but...
  - Smooth muscle remodeling occurs as a result of chronic inflammation from PE's
  - Original hypercoagulable state isn't fixed



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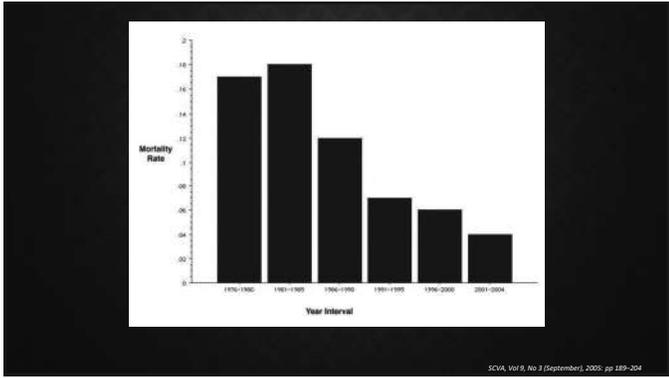
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**Figure 8.** A typical pulmonary thromboendarterectomy specimen. Dissection into the subsegmental regions is essential for a good hemodynamic result.

SCVA, Vol 9, No 3 (September), 2005; pp 189-204

22



23

### CLASS I – PULMONARY ARTERIAL HYPERTENSION

- Arterial vasoconstriction in pulmonary vasculature
- Causes:
  - Idiopathic
  - Connective tissue disease
  - HIV
  - Congenital heart disease
- Smooth muscle proliferation
- Two-hit hypothesis

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## TWO HIT HYPOTHESIS

- Genetic predisposition
  - Altered nitric oxide synthesis
  - Altered prostaglandin pathway
- Sentinal event
  - Hypoxia
  - Viral infection (HIV, etc)
  - Increased shear stress

25

## A WORD ON CHRONIC PH TREATMENT

- Calcium channel blockers – in patients with vasoreactivity on right heart cath
- Endothelin receptor antagonists (ETRA) – elevated LFT's & peripheral edema
- Phosphodiesterase Inhibitors (PDE5) – peripheral vasodilation
- IV & inhaled prostanoids – peripheral vasodilation, flushed skin

CRIST 2014; 146 (2): 449-475

26

## PERIOPERATIVE MANAGEMENT OF CHRONIC PH MEDS

- CCB – continue
- ETRA – continue; minimal side effects perioperatively
- IV & inhaled prostanoids – DEFINITELY continue;
  - very short half life; rebound effect
  - May cause hypotension in IV form
  - Potential to inhibit platelet aggregation
- Oral PDE5 – continue but be cautious of hypotension

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## INTRAOPERATIVE MANAGEMENT

- Fluid management
- Inotropes and vasopressors
- Pulmonary vasodilators
- Anesthetic agents

28

## FLUID MANAGEMENT

- In general, minimize fluids.
- However, because most of us are so cautious with fluids, there's a tendency to miss hypovolemia in these patients.

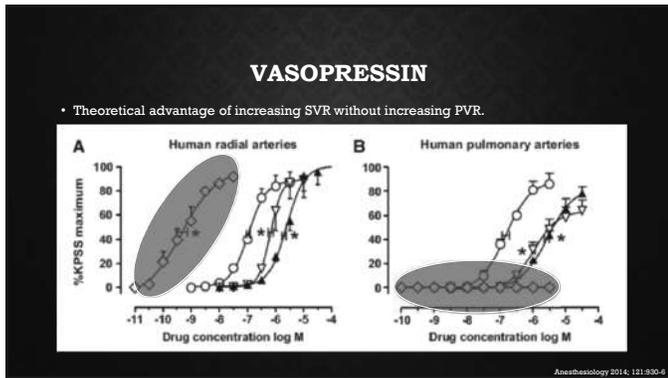


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## INOTROPES / VASOPRESSORS

- No RCT's or strong evidence favoring one inotrope over another.
- Dobutamine
- Milrinone
- SVR agents (Norepinephrine, Vasopressin, Phenylephrine)

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### PULMONARY VASODILATORS

- Nitric oxide
- Prostaglandins

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### NITRIC OXIDE

- Inhaled nitric oxide activates guanylate cyclase in vascular smooth muscle.
- After diffusing into blood stream, NO binds to oxy-Hb and is rapidly deactivated.
- Usual dose 1-20 PPM
- May have biologic effect at 10 **PPB**

Circulation. 2004;109:3106-3111

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### CONTRAINDICATIONS / TOXICITY

- Elevated wedge pressure
- Nitrogen dioxide & met-Hb
  - Effects usually not seen <80 PPM
- will **NOT** work in:
  - PH due to left heart disease
  - Chronic thromboembolic PH
  - Other mechanical obstructions

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### NASAL NITRIC OXIDE

- Anecdotal use reported
- Case reports of lowered PAP with NC-iNO use
- Provides ability to use iNO in non-intubated patients

Hlaing, et al. Chest, Volume 140, Issue 4, 63A  
 Costabile et al., Pediatrics Jan 2018, 141 (1 MeetingAbstract) 735

35

### PROSTAGLANDINS

- Prostacyclin
  - Epoprostenol (Veletri, Flolan)
    - Available IV or inhaled
    - Usual dose: 50 ng/kg/min of IBW
  - Iloprost (Ventavis)
    - Intermittent dosing as a nebulizer
    - Dosed 6-9 times per day
    - Not widely available

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### ANESTHETIC AGENTS

- Benzodiazepines Respiratory depression
- Opiates
- Propofol Systemic hypotension
- Etomidate Adrenal suppression but generally well tolerated
- Ketamine Generally unfounded concerns about increased PVR
- Inhaled anesthetics Generally well tolerated at 0.5-1 MAC

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### QUESTION #1

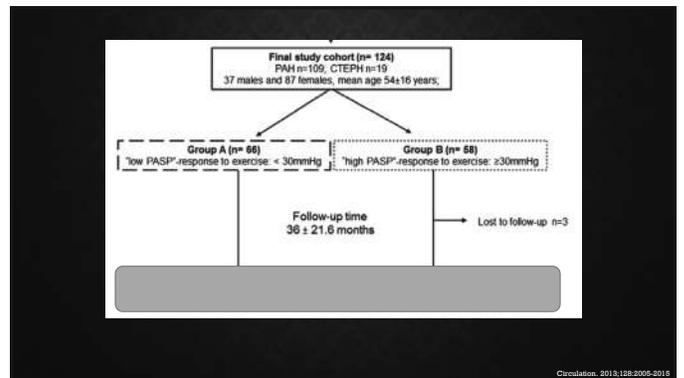
- An increase in PAP > 30 mmHg with exercise is indicative of poor prognosis in patients with PAH.

- True
- False

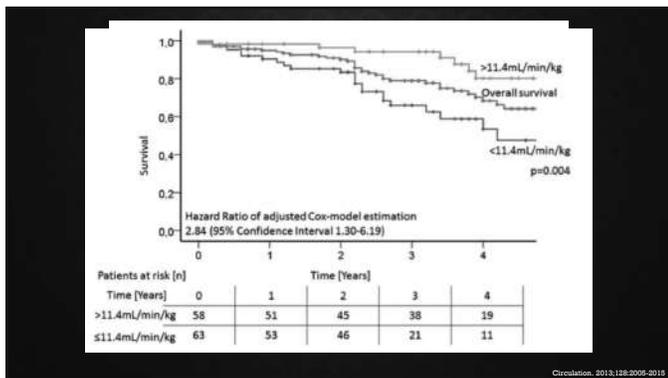
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### TIP #1: ALWAYS LOOK AT PA PRESSURES IN RELATION TO SYSTEMIC PRESSURES

39



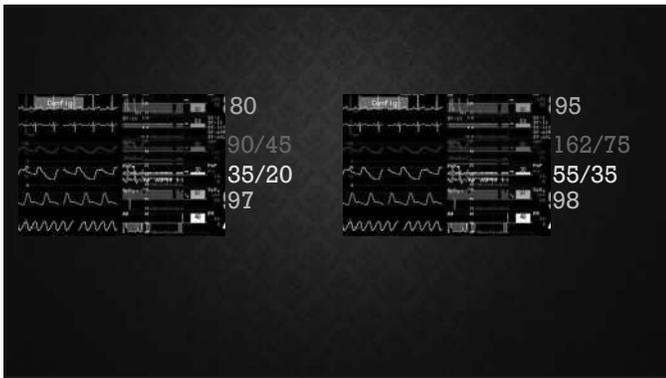
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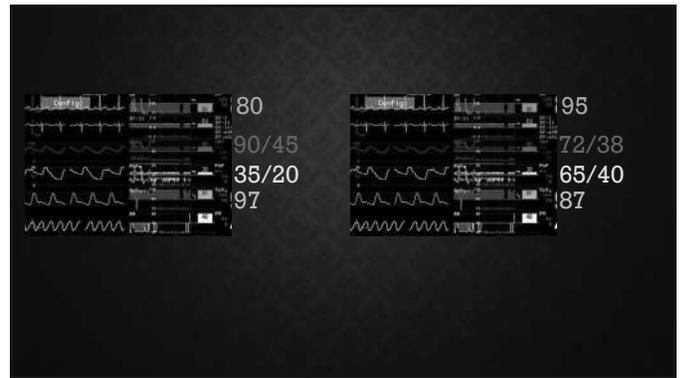
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**QUESTION 2:**

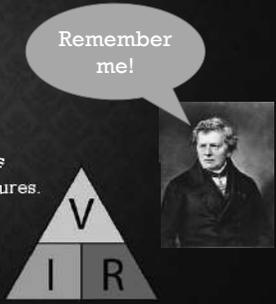
- An intraoperative decrease in PA pressure is always a good sign.
- True
- False

45

**TIP #2: REMEMBER OHM'S LAW**

46

- $V = I * R$
- Blood pressure = CO \* SVR
- Impending RV failure is sometimes preceded by decrease in PA pressures.
- TEE and CVP will help identify RV failure.



47

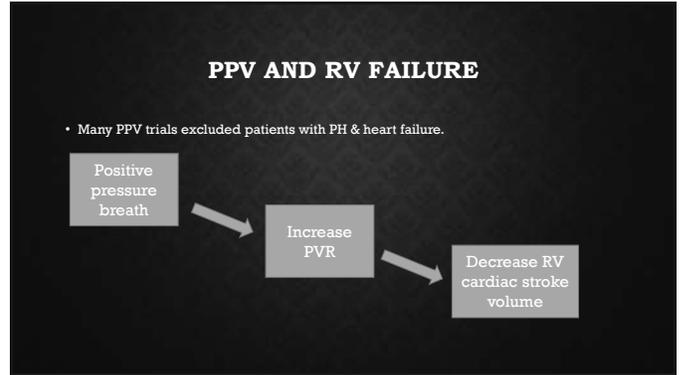
**QUESTION #3**

- Pulse pressure variation is not reliable in patients with pulmonary hypertension and RV failure.
- True
- False

48

**TIP #3: FALSE POSITIVE PULSE PRESSURE VARIATION CAN BE SEEN IN RV FAILURE**

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**CONCLUSION**

- Treating pulmonary hypertension requires a global view of the patient and their physiology.
- Don't get blinded by the pulmonary artery pressures. High doesn't always mean bad and low doesn't always mean bad.
- Evaluating right ventricle function is critical in patients with pulmonary hypertension.
- Always ensure that your patient has a stable and optimal PH regimen during the perioperative period.
- Inhaled pulmonary vasodilators are your friend.

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Tuesday

# Regional Anesthesia for Vascular Surgery

IN NEEDLES & LOCAL WE TRUST?

KYLE MARSHALL, MD  
ASSISTANT PROFESSOR  
ANESTHESIOLOGY  
UNIVERSITY OF COLORADO

1

## Disclosures

- ▶ I have no financial relationships or conflicts of interest.

2

## Objectives

- ▶ 1. Identify surgical cases which may be facilitated by the addition of regional anesthesia.
- ▶ 2. Decipher whether your patient is best suited for a regional, general or a combined anesthetic and choose the best choice to minimize adverse outcomes.
- ▶ 3. Assess patients whom may benefit from avoiding general anesthesia; with the intent of differentiating whom is a candidate from those with contraindications.
- ▶ 4. Implement evidence-based regional approaches that can lead to improved surgical and post-operative anesthetic outcomes.

3

## Overview

- ▶ The role of Regional Anesthesia in:
  - ▶ Carotid Endarterectomy
  - ▶ Abdominal Aortic Aneurysm Repair
  - ▶ Arterio-venous fistula creation

4

## First off, Thank you Vascular Surgeons!

- ▶ You don't judge...
- ▶ You bail us out from our vices... or try to!
  - ▶ Smoking?
  - ▶ Sugar?
  - ▶ And my favorite food...

5

## BACON!



Halloween, 2011  
NYC

6

Vascular Surgery



WORLD'S  
CRAYEST  
VASCULAR  
SURGEON

7

A Vascular surgeon



8

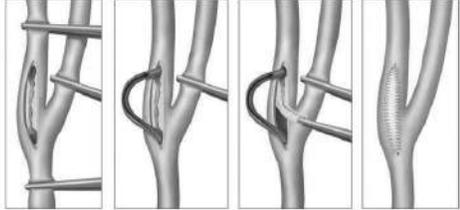
A Vascular surgeon



"COUNT VASCULA"

9

Carotid Endarterectomy



10

To Shunt or not?

- ▶ 2 Vertebral Arteries
- ▶ 2 Internal Carotids

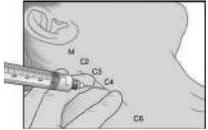


CIRCLE OF  
WILLIS

11

General Vs Local Anesthesia

- ▶ Superficial Cervical Plexus +/- Deep Cervical Plexus
- ▶ Surgeon Infiltration
- ▶ The good-old ET Tube



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### AWAKE CAROTID?

- ▶ Who would ever want that?
  - ▶ Surgeons – who trained with the technique
- ▶ Disadvantages – Many
- ▶ Advantages – ONE BIG ONE



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### Carotid Endarterectomy

- ▶ The gospel
- ▶ GA = LA from a safety standpoint
- ▶ Where did it come from?

14

### Carotid Endarterectomy

- ▶ The GALA Trial – Lancet, 2008
  - ▶ Multi-center, Randomized, Controlled
  - ▶ >3,500 patients


**General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial**

GALA Trial Collaborative Group

Summary

Background The effect of carotid endarterectomy in lowering the risk of stroke ipsilateral to severe atherosclerotic

15

### GALA

- ▶ Randomized to GA (1,753) vs LA (1,773)
- ▶ June 1999 to October 2007
- ▶ 95 Centers in 24 Countries
- ▶ Primary Outcome:
  - ▶ Stroke, Myocardial Infarction, Death
  - ▶ GA – 84 (4.8%) LA – 80 (4.5%)

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### GALA Further...

- ▶ 80% Smoking history
- ▶ 70% Male
- ▶ 70% Hypertension
- ▶ 35% Coronary Artery Disease
- ▶ 25% Diabetes
- ▶ 10% COPD
- ▶ 9% Contralateral Carotid Occlusion
- ▶ **65% were ASA II**

17

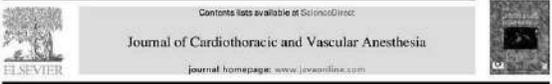
### GALA Further:

- ▶ Baseline Surgical Risk
  - ▶ 50% were low risk
  - ▶ 41% were medium risk
  - ▶ 9% were high risk

18

## I like to do Regional

▶ I am not alone!



Contents lists available at ScienceDirect  
Journal of Cardiothoracic and Vascular Anesthesia  
ELSEVIER  
Journal homepage: www.elsevier.com

Editorial  
**Regional Versus General Anesthesia for Carotid Endarterectomy: Do We Need Another Randomized Trial?**  
Lamivatorov, et al. 2018

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## Retrospective NSQIP data trials

- ▶ **Reduced rate of peri-operative Myocardial infarction**
- ▶ Reduced rate of pneumonia
- ▶ Reduced rate of aspiration
- ▶ Reduced rate of peri-op blood transfusion
- ▶ No difference in 30 day mortality or Stroke

Malik, et al. 2016  
Liu et al. 2014

20

## Retrospective Vascular Quality Initiative Data

Cx	GA	LA/RA	p-test	OR	95% CI
Myocardial Infarction	0.5%	0.2%	p=0.01	1.95	1.06-3.95
Acute CHF	0.5%	0.2%	P<0.001	3.92	1.84-8.34
Hemodyn. Instability	27%	20%	P<0.001	1.8	1.44-1.66

Dakour Aridi, et al. 2018.

21

## I TOLD YOU REGIONAL WAS BEST!!



- ▶ I wish I could say that...
- ▶ No difference in Mortality or Peri-op Stroke
- ▶ VQI/JVS Conclusion:
- ▶ The incidence of cardiac complications is so low, they deemed it "clinically irrelevant."

22

## So... What should I do for my patients?

- ▶ It's not a mind blowing conclusion
- ▶ **Do what fits the case/patient and your skills**
  - ▶ Differences are mostly non-significant
  - ▶ The significant differences are not necessarily clinically relevant
  - ▶ While GALA remains imperfect, there's nothing better... yet.

23

## A Vas

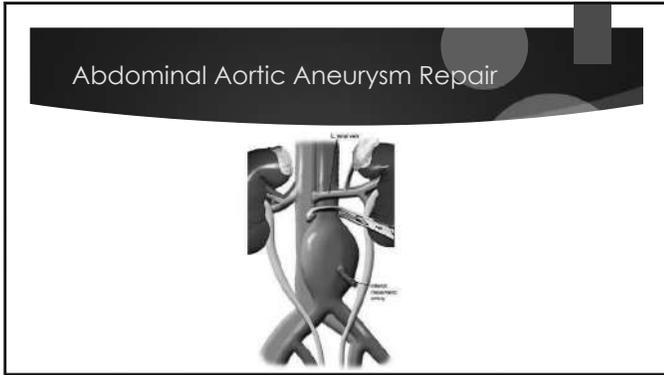


- ▶ Was hea
- ▶ Wouldn't
- ▶ Mumbled
- ▶ Said not

ogist."

VectorStock  
VectorStock.com/144304

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25

### Open AAA

- ▶ High Risk Surgery
- ▶ High Morbidity and Mortality
  - ▶ 30 day Morbidity – 12-26%
  - ▶ 30 day Mortality – 4-6%
    - ▶ Post-op bowel ischemia – 50% mortality

26

### Thoracic Epidural for Open AAA

- ▶ Commonly performed for elective cases
- ▶ When epidural used intra-operatively
  - ▶ Reduced stress response
  - ▶ Blunts sympathetic outflow
    - ▶ Reduced Afterload
    - ▶ Increased visceral/splanchnic perfusion

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### Open AAA Repair

- ▶ Again, ELECTIVE Open AAA Repair
- ▶ There are two primary reasons some anesthesiologists will forego Epidural:
  - ▶ "I'm concerned about surgical bleeding."
  - ▶ "They will anti-coagulate."

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### Open AAA Repair/Anti-coagulation

- ▶ ASRA Guideline, 2018
- ▶ Heparin IV

**Restart Medication After Procedure?**

**1 hour**

Although the occurrence of a **bloody or difficult neuraxial needle** placement may increase risk, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case are warranted.

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### Epidural and Mortality

#### Impact of Epidural Analgesia on Mortality and Morbidity After Surgery

*Systematic Review and Meta-analysis of Randomized Controlled Trials*

*Daniel M. Pöpping, MD,\* Nadia Elia, MD, MSc,† Hugo K. Van Aken, MD,\* Emmanuel Marret, MD,‡ Stephan A. Schug, MD,§ Peter Kranke, MD, MBA,¶ Manuel Wenk, MD,\* and Martin R. Tramèr, MD, DPhil||*

Annals of Surgery, 2014

30

### Epidural in Abdominal Surgery

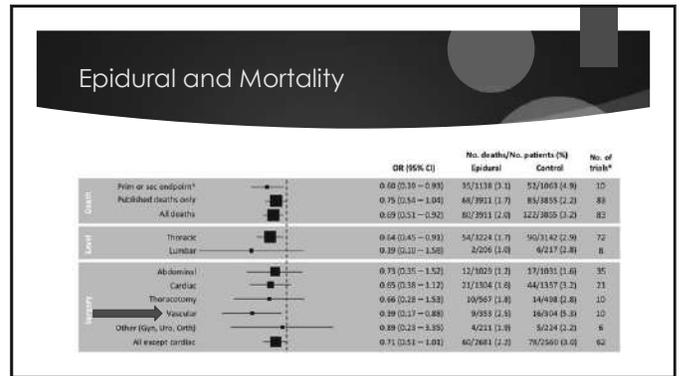
**Advantages (less of this)**

- ▶ **Mortality**
  - ▶ 3.1% vs 4.9% - OR 0.6
- ▶ Afib, SVT
- ▶ DVT
- ▶ Respiratory depression, pneumonia
- ▶ ileus

**Disadvantages (more of this)**

- ▶ Arterial hypotension
- ▶ Pruritus
- ▶ Urinary Retention

31



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### Thoracic Epidural After Open AAA

**Cochrane Library**  
Cochrane Database of Systematic Reviews

**Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery (Review)**

Guay J, Koop S

33

### Thoracic epidural vs IV Opioids

- ▶ Meta-analysis of 1498 patients from 1987-2009
- ▶ Looking at pain management.
  - ▶ Post-op only, no intra-op information...
- ▶ Primary endpoint – 30d mortality
  - ▶ No long term mortality endpoint
- ▶ Several Secondary endpoints

34

### Results

Significant Difference

- ▶ Improved:
  - ▶ Pain management
- ▶ Reduced:
  - ▶ Myocardial infarction
  - ▶ Time to Extubation
  - ▶ Respiratory Failure
  - ▶ GI Bleed
  - ▶ ICU Length of stay

No Difference

- ▶ 30 Day Mortality

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### Elective Open AAA Repair

JAMA Surgery | Original Investigation

**Combined Epidural-General Anesthesia vs General Anesthesia Alone for Elective Abdominal Aortic Aneurysm Repair**

Ami Borda, MBBS, Ashley Soori, MD, Feruze Mdarmoo, MD, Yousef Othman, MD, MPH, Ariel Mueller, MA, Mateo Montenegro-Gallegos, MD, Marc R. Strasser, MD, Ilan H. J. Utens, Marc L. Schermerhorn, MD, Robina Matyal, MD

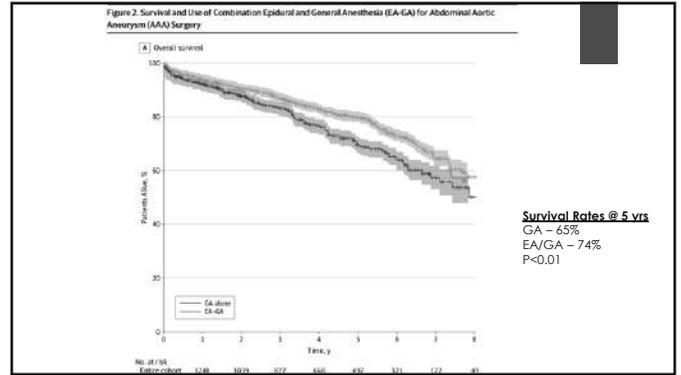
- ▶ 1540 patients from 2003-2011 – 560 (GA only) vs 980 (EA-GA)
- ▶ Retrospective analysis of prospectively collected data
- ▶ Vascular Society Group of New England (VSGNE)
- ▶ Primary outcome: All-cause Mortality

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## Results

<p>Significant Difference</p> <ul style="list-style-type: none"> <li>▶ Re-operation rate, &lt;30d</li> <li>▶ <b>Bowel Ischemia</b></li> <li>▶ Pulmonary Complications</li> <li>▶ Dialysis Requirement</li> </ul>	<p>No difference</p> <ul style="list-style-type: none"> <li>▶ 30d Mortality</li> <li>▶ Cardiac Complications</li> <li>▶ Wound Complications</li> </ul>
--	--

37



38

## Conclusions

- ▶ There is a significant long-term survival benefit when adding Epidural analgesia to General anesthesia for elective open AAA.
- ▶ This survival benefit is possibly due to significantly reduced rates of immediate major post-operative complications.
- ▶ **"Epidural Analgesia in addition to GA should be strongly considered in suitable patients undergoing elective AAA Repair."**

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## A Surgeon in Boston

- ▶ "He didn't do bypasses"
- ▶ "He didn't do endarterectomies"
- ▶ "I don't remember him doing anything else."

### THE CHOP-SHOP

40

## Arterio-Venous Fistula Creation

- ▶ Vs. Tunneled Caths
  - ▶ Reduced Mortality
  - ▶ Reduced Sepsis
  - ▶ Reduced Failures
- ▶ Still, Fail often...

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## AVF Creation

- ▶ Anesthesiologist's view:
  - ▶ Sick patients with multiple co-morbidities
  - ▶ Can be sensitive to fluids
  - ▶ Don't clear medications/alter plan
  - ▶ "Their Potassium is WHAAAT!?"

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### At University of Colorado Hospital

- ▶ We block nearly all:
  - ▶ Primary Arterio-venous fistula creations
  - ▶ Secondary Arterio-venous fistula creations
  - ▶ Arterio-venous fistula exploration/revisions
- ▶ MAC + Block

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### WHY DO WE BLOCK AVFistula CASES?

- ▶ 1. "Post-operative Pain."
- ▶ 2. "Reducing opioids."
- ▶ 3. "Patient co-morbidities."
- ▶ 4. "Avoiding General Anesthesia."

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### What do surgeons care LEAST about?

- ▶ 1. "Post-operative Pain."
- ▶ 2. "Reducing opioids."
- ▶ 3. "Patient co-morbidities."
- ▶ 4. "Avoiding General Anesthesia."

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### What do surgeons care MOST about?

- ▶ **\*\*\* IMPROVED SURGICAL CONDITIONS\*\*\***
  - ▶ Vaso-dilation
  - ▶ Reduced pulsatility index (PI)
  - ▶ Great success



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### Improved Surgical Conditions

#### Comparison between local and regional anesthesia in arteriovenous fistula creation

Attilio Ignazio La Monte<sup>1</sup>, Giuseppe Damiano<sup>1</sup>, Antonino Mularo<sup>1</sup>, Vincenzo Davide Palumbo<sup>1</sup>, Rosi Alessi<sup>2</sup>, Maria Concetta Gioviale<sup>1</sup>, Gabriele Spinelli<sup>3</sup>, Giuseppe Buscemi<sup>1</sup>

Pulsatility Index (PI)	Prior to meds	5mins after meds	10mins after meds	PI Ratio – PI-10/PI-0
Regional – Axillary BPB	6.53	4.38	<u>3.35</u>	<b>0.51</b>
Local infiltration	5.68	5.0	<u>5.23</u>	<b>0.91</b>

La Monte, et al. J. Vasc Access 2011

47

### Improved Surgical Conditions, cont.

- ▶ Veno-dilation

Anesthesia Type	Cephalic Vein Diameter T=0 (mm)	CV Diameter @ 5min post meds (mm)	CV Diameter @10min (mm)
Regional – Axillary BPB	6.4	7.8	8.7
Local Infiltration	6.3	6.4	6.6

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## Post-op Fistula Blood Flow

### Ultrasound-guided infraclavicular brachial plexus block enhances postoperative blood flow in arteriovenous fistulas

Levent Sahin, MD,<sup>a</sup> Rauf Gul, MD,<sup>a</sup> Ayse Mizrak, MD,<sup>a</sup> Hayati Deniz, MD,<sup>b</sup> Mehrican Sahin, MD,<sup>c</sup> Senem Koruk, MD,<sup>a</sup> Mehmet Cesur, MD,<sup>a</sup> and Sirke Goksu, MD,<sup>a</sup> *Gaziantep, Turkey*

J. Vascular Surgery, 2011

49

## Post-op Fistula Blood Flow, cont.

Fistula Flow Rate (mL/min)	3Hrs	7days	8wks
Infraclavicular	69.6 +/- 7.9	210.6 +/- 30.9	680.6 +/- 96.7
Local Infiltration	44.8 +/- 13.8	129 +/- 36.1	405.3 +/- 76.2
	P < 0.001	P < 0.001	P < 0.001

- ▶ No statistical difference in Primary Patency or Primary Failure
  - ▶ 2 failed in ICV group
  - ▶ 5 failed in Local infiltration group

50

## Well, let's take a closer look...

### Effect of regional versus local anaesthesia on outcome after arteriovenous fistula creation: a randomised controlled trial

Emmet Arlson, Andrew Johnson, Rachel Kierms, Mark Stearn, John Kerslake, Marc Clancy, Alan Macfarlane

**Summary**  
Background Arteriovenous fistulae are the optimum form of vascular access in end-stage renal failure. However, they have a high early failure rate. Regional compared with local anaesthesia results in greater vasodilatation and increases short-term blood flow. This study investigated whether regional compared with local anaesthesia improved medium-

Copyright 2016, BMJ, 2012-08  
Published Online  
August 1, 2016

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## Study design

- ▶ Observer-blinded, Randomized controlled trial – 126 pts (63LA vs. 63RA)
- ▶ Glasgow, UK – 3 University Hospitals
- ▶ Primary Radiocephalic or Brachiocephalic fistulas
- ▶ Supraclav - Experienced regionalists +/- directly supervised senior resident
- ▶ **Primary Endpoint:** fistula patency at 3 months.
- ▶ **Secondary:** immediate patency at D/C, functional patency at 3mos

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## Results

ALL AVF Patency	Immediate	Primary @ 3 months	Functional @ 3 months
Regional Anesthesia	<b>92%</b>	<b>84%</b>	41%
Local Infiltration	<b>73%</b>	<b>62%</b>	29%
	P 0.005	P 0.005	P 0.15

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## From ASRA 2018...

- ▶ The same research group presented their data from 1 year follow up.

ALL AVF Patency	Functional @ 1 year
Regional Anesthesia	<b>81%</b>
Local Infiltration	<b>56%</b>
	P < 0.001

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### Meta-analyses of RA for AVF Creation

- ▶ "The use of regional anaesthesia is associated with lower AVF failure rates when compared with local anaesthesia in patients undergoing primary forearm AVF formation for haemodialysis."
- ▶ Cerniviciute, et al. (2017) Eur. J of Vascular/Endovasc Surgery

55

### Meta-Analyses of RA for AVF Creation

- ▶ "RA is now the anesthetic technique of choice for fistula construction after solid proof by a randomized controlled trial has unequivocally demonstrated that the beneficial effects of BPB are translated into improved outcomes in the clinical setting."
- ▶ Shemesh, et al. (2017) - J. of Vascular Access
  - ▶ A surgeon

56

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Breaking News: Surgery accepts blame

Gomertblog.com

58

### Thank You!

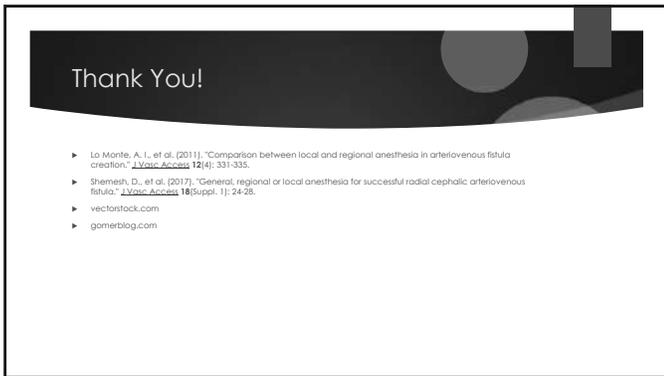
- ▶ Lewis, S. C., et al. (2008). "General anaesthesia versus local anaesthesia for carotid surgery (GALA): a multicentre, randomised controlled trial." *Lancet* **372**(9654): 2132-2142.
- ▶ Kloury, E., et al. (2015). "Carotid endarterectomy under local and/or regional anesthesia has less risk of myocardial infarction compared to general anesthesia: An analysis of national surgical quality improvement program database." *Vascular* **23**(3): 113-119.
- ▶ Dakour Aridi, H., et al. (2018). "Anesthetic type and hospital outcomes after carotid endarterectomy from the Vascular Quality Initiative database." *J Vasc Surg* **67**(5): 1419-1428.
- ▶ Lomivorotov, V. V., et al. (2018). "Regional Versus General Anesthesia for Carotid Endarterectomy: Do We Need Another Randomized Trial?" *J Cardiothorac Vasc Anesth*.
- ▶ Malik, O. S., et al. (2018). "The Use of Regional or Local Anesthesia for Carotid Endarterectomies May Reduce Blood Loss and Pulmonary Complications." *J Cardiothorac Vasc Anesth*.
- ▶ Stoneham, M. D., et al. (2015). "Regional anaesthesia for carotid endarterectomy." *Br J Anaesth* **114**(3): 372-383.

59

### Thank You!

- ▶ Horlocker, T. T., et al. (2018). "Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition)." *Reg Anesth Pain Med* **43**(3): 263-309.
- ▶ Bardia, A., et al. (2014). "Combined Epidural-General Anesthesia vs General Anesthesia Alone for Elective Abdominal Aortic Aneurysm Repair." *JAMA Surg* **151**(12): 1116-1123.
- ▶ Popping, D. M., et al. (2014). "Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials." *Ann Surg* **259**(6): 1056-1067.
- ▶ Guay, J. and S. Kopp (2016). "Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery." *Cochrane Database Syst Rev* (1): CD005059.
- ▶ Aitken, E., et al. (2016). "Effect of regional versus local anaesthesia on outcome after arteriovenous fistula creation: a randomised controlled trial." *Lancet* **388**(10049): 1067-1074.
- ▶ Cerniviciute, R., et al. (2017). "Regional Versus Local Anesthesia for Haemodialysis Arteriovenous Fistula Formation: A Systematic Review and Meta-Analysis." *Eur J Vasc Endovasc Surg* **53**(5): 734-742.
- ▶ Sahin, L., et al. (2011). "Ultrasound-guided infraclavicular brachial plexus block enhances postoperative blood flow in arteriovenous fistulas." *J Vasc Surg* **54**(3): 749-753.

60



Thank You!

- ▶ Lo Monte, A. L., et al. (2011). "Comparison between local and regional anesthesia in arteriovenous fistula creation." *Vascular Access* **12**(4): 331-335.
- ▶ Shemesh, D., et al. (2017). "General, regional or local anesthesia for successful radial cephalic arteriovenous fistula." *Vascular Access* **18**(Suppl. 1): 24-26.
- ▶ vectorstock.com
- ▶ gomerblog.com

## Anesthesia for Spine Surgery & Neuromonitoring

Jeffrey R. Kirsch, MD  
Professor, Chair Emeritus  
OHSU

1

## Conflict of interest and disclosures

- Professor, but very busy clinical anesthesiologist
- I do not accept honoraria for lectures
- Consulting fees (case review, industry FDA activity) are paid directly to charity (e.g. Oregon Food Bank, FAER etc)

2

## Presentation objectives

- Gain the knowledge to provide state-of-art perioperative anesthetic management for patients requiring spine surgery
- Gain the knowledge to create conditions to optimize neuromonitoring efficacy during spine surgery

3

## Spine Surgery

- Pre-operative preparation
- Risks of positioning
- Potential Clinical Scenarios
  - Acute spine trauma
  - Spine deformity
- Preventing injury during intubation
- Control of perfusion
- Neuromonitoring
- Timely emergence tricks to improve care for the patient and make your surgeon happier.



4

## Pre-operative

- Develop an anesthetic plan that recognizes:
  - Patient comorbidities
  - Surgeon needs: positioning, neuromonitoring, extent of the surgery
- Physical Therapy
- Pain Management
- Nutrition

5

## Multimodal analgesia prior to surgery

Kurd MF et al., J Am Acad Orthop Surg 2017;25: 260

- NSAIDs: Parecoxib (40 mg preop and q12 for 48 hrs) associated with sign less MS need and better pain control, but some increased risk of bone non-union with ketorolac.
- Neuromodulatory agents (pregabalin (75 or 150 mg) or gabapentin (1200 mg) preop dose associated with better pain control and less MS use.
- Acetaminophen (1000 mg): Not studied as a solo agent
- Intrathecal fentanyl (15 mcg) or MS (0.4 mg) associated with less IV MS, better pain relief and no complications
- Multi-modal: Consider Celecoxib+gabapentin+acetaminophen

6

## Many back surgery patients have Chronic Pain

- Pre-operative multi-modal medications
- Ketamine: Lower use of intraoperative and post-operative opioids and lower pain scores
- No increased risk of complications
- Ketamine dose
  - 0.5 mg/kg bolus, when hemodynamically appropriate at the beginning of surgery
  - 10 mcg/kg/min infusion
  - Consider post-operative at 0.12 mg/kg/hr for 24 hours

7

## Low dose ketamine is not associated with significant risks

Table 5. Adverse Events

	Placebo	Ketamine	P Value	RR (95% CI)
48 hr				
Nausea	22.5	26.9	0.603	1.20 (0.60, 2.38)
Vomiting	12.2	15.4	0.648	1.26 (0.47, 3.36)
Hallucinations	2.0	1.9	0.737	0.94 (0.06, 14.65)
Urinary Retention	2.0	7.7	0.200	3.77 (0.44, 32.56)
6 wk				
Nausea	17.0	11.8	0.458	0.69 (0.26, 1.84)
Vomiting	8.5	9.8	0.552	1.15 (0.33, 4.04)
Hallucinations	23.4	11.8	0.128	0.50 (0.20, 1.25)
Constipation	57.5	45.1	0.222	0.79 (0.53, 1.16)

CI = confidence interval; RR = risk ratio. Lofus RW et al, *Anesthesiology* 2010; 113:639 – 46

Table 3 Central nervous system side effects

	Naïve placebo, n=34	Naïve ketamine, n=24	Tolerant placebo, n=28	Tolerant ketamine, n=25	P
Headache	0	0	0	1	0.431
Confusion	1	0	1	0	1.000
Anxiety	0	1	0	0	0.431
Excessive sedation	0	0	0	1	0.431
Blurred vision	0	1	0	1	0.245

Values are numbers.

Boenigk, K et al., *Eur J Anaesthesiol* 2019; 36:8–15

8

## Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From RAPM, AAPM and ASA

Eric S. Schwenk, MD,\* et al. *Reg Anesth Pain Med* 2018;43

TABLE 6. Summary of ASRA/AAPM Recommendations for Subanesthetic Ketamine in Acute Pain

Recommendation Category	Recommendation	Level of Evidence*
Indications for use	(1) Perioperative use in surgery with moderate to severe postoperative pain (2) Perioperative use in patients with opioid tolerance (3) As analgesic adjunct in opioid-tolerant patients with sickle cell crisis (4) As analgesic adjunct in patients with OSA	(1) Grade B, moderate certainty (2) Grade B, low certainty (3) Grade C, low certainty (4) Grade C, low certainty
Dosing range	Bolus: up to 0.35 mg/kg Infusion: up to 1 mg/kg per hour	Grade C, moderate certainty
Relative contraindications	(1) Poorly controlled cardiovascular disease (2) Pregnancy, psychosis (3) Severe hepatic disease, ie, cirrhosis (avoid), moderate hepatic disease (caution) (4) Elevated intracranial pressure, elevated intraocular pressure	(1) Grade C, moderate certainty (2) Grade B, moderate (3) Grade C, low certainty (4) Grade C, low certainty
Personnel	Supervising clinician: a physician experienced with ketamine (anesthesiologist, critical care physician, pain physician, emergency medicine physician) who is ACLS certified and trained in administering moderate sedation Administering clinician: registered nurse or physician assistant who has completed formal training in safe administration of moderate sedation and is ACLS certified	Grade A, low certainty (see Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain from ASRA, AAPM, and ASA) <sup>3</sup>

\*Evidence was evaluated according to the USPSTF grading of evidence, which defined levels of evidence based on magnitude and certainty of benefit.<sup>2</sup>

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## Positioning for spine surgery

- Supine (Anterior approach)
- Prone (superman, arms up; arms tucked)
  - Jackson Table
  - Chest rolls
  - Wilson Frame
- Sitting (Cervical)

10

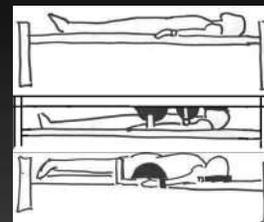
## Prone Head Support



Prone View



GentleTouch OSI



Rozet I, Vavilala MS: *Anesthesiol Clin*. 25(3): 631, 2007

11

12

## Prone Position Risks

- Ophth: Ischemic optic neuropathy (obesity, Wilson frame, long case duration, excessive blood loss, hypotension)
- Neuro: Cervical myelopathy (neck extension); Brachial plexopathy; Ulnar
- Compartment syndrome: padding over compartment, obesity
- Pressure ulcers: Procedure duration, advanced age, obesity, steroids

13

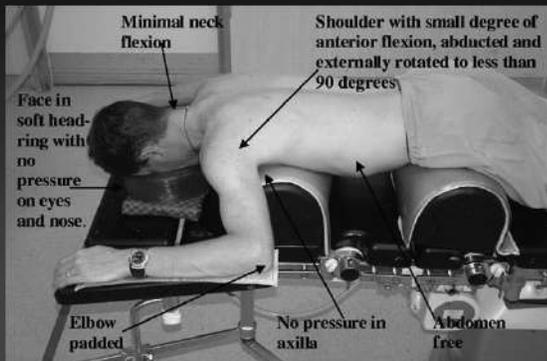
Table 2 Complications and level of evidence

Complication	Number of manuscripts included	Highest CEBM Level of evidence
Increased abdominal pressure and increased bleeding	3	2
Abdominal compartment syndrome	1	4
Limb compartment syndrome	2	2
Shoulder dislocation	1	4
Nerve palsies	2	4
Pressure sores	3	2
Cardiovascular compromise	13	1
Thrombosis and stroke	3	3
Hepatic dysfunction	1	4
Postoperative vision loss	23	1
Oropharyngeal swelling	2	4
Venous air embolism	2	1
Endotracheal tube dislodgement	3	3

Kwee MM et al., Int Surg 100:292, 2015

14

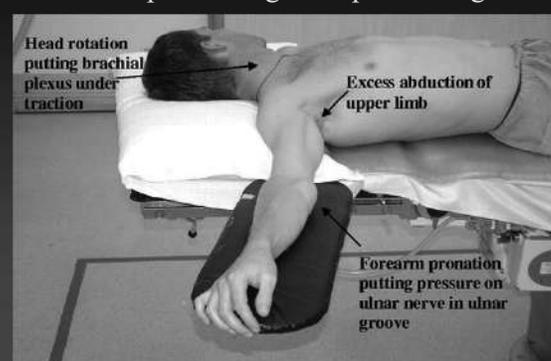
## Example of Careful Positioning



From: Patient positioning in anaesthesia Contin Educ Anaesth Crit Care Pain. 2004;4(5):160-163.

15

## Example of dangerous positioning



From: Patient positioning in anaesthesia Contin Educ Anaesth Crit Care Pain. 2004;4(5):160-163. doi:10.1093/ajaceccp/mkh044

16

## The Effect of the Prone Position on Pulmonary Mechanics Is Frame-Dependent

Anesth Analg 1998;87:1175-80

Sally C. Falmon, MD, Jeffrey R. Kirsch, MD, Jane A. Uppper, MD, and Thomas J. K. Young, MD

Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland

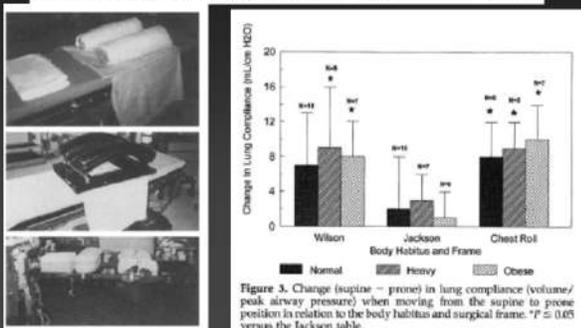


Figure 3. Change (supine - prone) in lung compliance (volume/peak airway pressure) when moving from the supine to prone position in relation to the body habitus and surgical frame. \*P ≤ 0.05 versus the Jackson table.

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## Brachial Plexus Injury in Supine and Prone positions

- Mechanism most commonly is from stretch or compression
- Role of obesity
- Trendelenburg position with patient prone
- Chest Pad positioning in prone position
- "Axillary roll" in the lateral position

18

## Postoperative Visual Loss/Injury (0.05% to 1%)

- Corneal abrasion
- Ischemic optic neuropathy: Inc IOP causing optic nerve damage
- Central retinal artery occlusion: vasospasm, emboli, compression or hypotension
- Cortical blindness: ischemia

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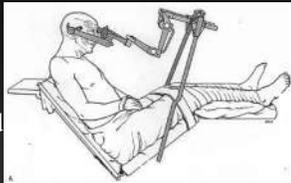
## Eye Injury Prevention

- Frame with a mirror to monitor for compression, open lid etc.
- Slight 10% reverse Trendelenburg
- “Tight control” of blood pressure (MABP>70), Hct>30%

20

## Sitting Position

- Advantages:
  - Surgical exposure; Decreased blood in surgical field
  - “Airway accessibility”
- Risks/disadvantages
  - VAE
  - Hemodynamics: Hypotension
  - Contraindicated in patients with open ventriculo-atrial shunt, cerebral ischemia when upright and awake, right to left cardiac shunts and cardiac instability



21

21 year old football player suffers incomplete cervical spine injury during a game



22

## Patient Care/Treatment Issues

- Steroids: AANS, Congress of NS, EM all indicate glucocorticoids is a treatment option, not treatment standard
- Surgery: Goal neural element decompression and stabilization, but no guidelines. Generally agreed that early surgery (before 24 hours) is associated with improved outcomes following incomplete injury
- Experimental treatments: None are recommended (e.g. cooling, electrical stimulation, GM-1 etc)

23

## Anesthesiology Issues

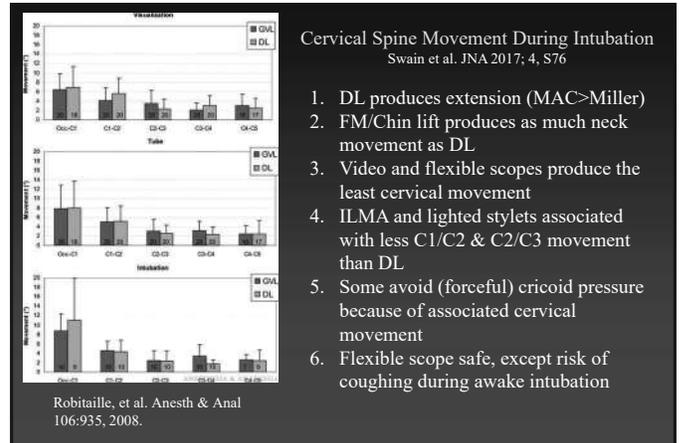
- Airway management;
- CV: Spinal shock; Autonomic hyper-reflexia, impact on myocardial function
- Impact on temperature control
- CV and Neuro Monitoring suggestions
- Positioning on frame
  - Lungs; CV; Eyes
- Preventing delayed emergence



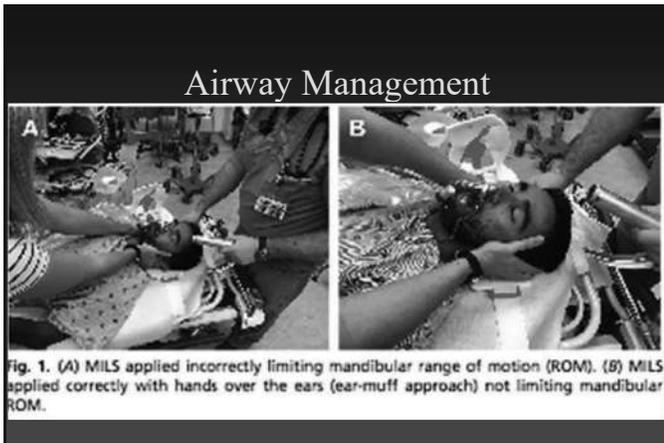
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27

Best approach to minimize neck movement during intubation

- Direct laryngoscopy has been shown to produce the most extension at the atlanto-occipital joint with the Mac blade producing more extension than the Miller blade
- Face mask, chin lift and jaw thrust have been found to produce equal to greater cervical movement than the actual process of direct laryngoscopy itself

Swain A, Sahu S, Swain BP. Cervical spine movement during intubation. J Neuroanaesthesiol Crit Care 2017;4, Suppl S1:76-80

28

- Video laryngoscopy (VL) is associated with reduced movement of the cervical spine during intubation due to obliteration of the need of a direct line of sight and lesser amount of force required for sighting of glottic structures.
- Movement from VL is similar to movement with fiberoptic intubation
- The ILMA, lighted stylets as well as optical laryngoscopes have been found to cause less extension at C1-C2 and C2-C3 than intubation by DL

Swain A, Sahu S, Swain BP. Cervical spine movement during intubation. J Neuroanaesthesiol Crit Care 2017;4, Suppl S1:76-80

29

Choices

- Awake vs RSI (surg airway backup) vs Awake trach?
- DL vs Video laryngoscopy vs flexible (Emergent vs. Elective)
- If awake: airway blocks or not?
- If RSI: In-line stabilization or leave collar in place?
- Cricoid pressure or not?
- Sux before 48 hrs or not? Roc with suggamadex?
- Pretreatment with glycopyrolate or not?
- Etomidate, Ketamine or Propofol?
- Early initiation of vasopressor infusion?

30

Airway management device	Pros	Cons
Awake fiberoptic intubation	Excellent for cooperative patients Allows for documentation of neurologic exam before and after intubation	Relatively expensive Longer time to perform (not ideal for urgent situation) Not appropriate for Anxious/uncooperative patient Excess blood/secretions in the airway Provider with little experience with this technique
Video laryngoscopy	Often excellent laryngeal visualization Less for laryngoscopic view required Less mouth opening required	Not always available (i.e., in the field) Blood/secretions may obscure camera view Relatively new technology, with lack of definitive outcome studies in this area
Direct laryngoscopy	Most studied technique Usually available, even in remote locations Allows rapid ability to secure airway	High percentage of Grade III and Grade IV views May require adjunctive equipment (i.e., gum elastic bougie)
Laryngeal mask airway	Essential tool in the difficult airway algorithm	May not be appropriate for routine intubation in cervical spine injury

Austin N, et al., Int J Crit Illn Inj Sci. 4: 50, 2014

31

## Ankylosing Spondylitis (AS)

- Chronic inflammatory ds causing back pain, SI joint pain, reduced chest expansion, IBD, uveitis, depression
- Rx goal to prevent contractures with anti-inflammatory agents (inc TNF inhibitor) and PT
- Surgery indicated for severe hip involvement, atlantoaxial subluxation with neuro impairment, severe flexion deformities or fracture
- CV risk: Aortic valve/root ds, MI, stroke, DVT, conduction abnormalities

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### Which approach is best for airway management in patients with acute cervical cord injury or AS?

- DL with in-line stabilization (airway blood may impair use of video-laryngoscopy)
- Video-laryngoscopy (minimizes neck movement)
- Flexible fiberoptic with airway blocks and cooperative patient
- Awake tracheostomy

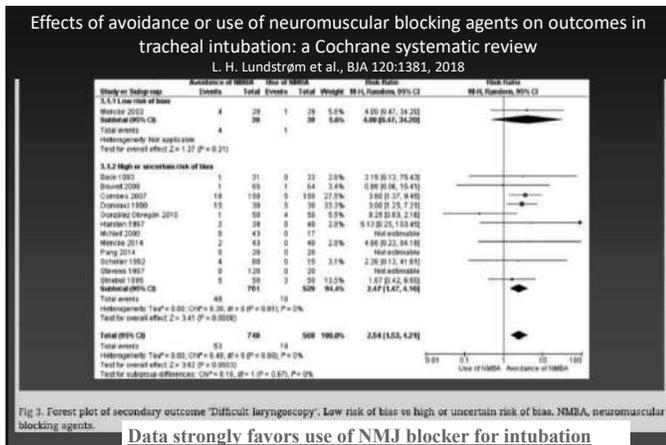
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### My Approach

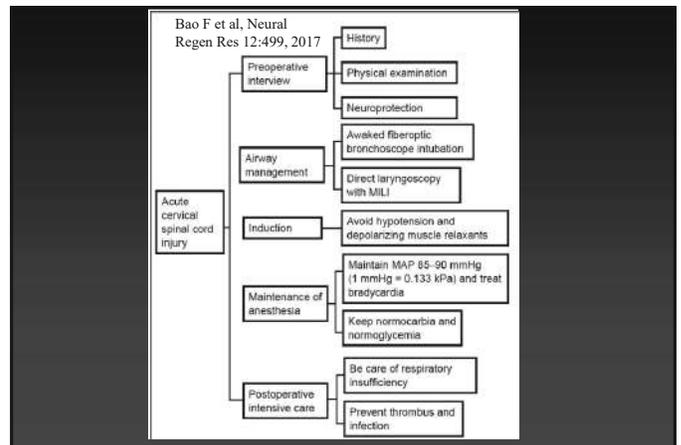
- After appropriate pre-oxygenation and confirming presence and functionality of:
  - Equipment: DL, VL, Emerg trach equip, suction, styletted ETT
  - Drugs: Induction, NMJ blocking, pressor in syringe, (sugammadex?)
  - personnel: Cricoid pressure, In-line stabilization, assistant for drug admin, expertise for surgical airway

**Induction agent plus non-depol NMJ blocker**

34



35



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## Cardiovascular Monitoring

- Standard monitors
- Invasive BP (arterial line) with PPV (placed prior to induction of anesthesia if possible)
- Two large bore (16 ga or larger) IVs
- Urine output
- +/- central access often require vasoactive infusion
- Monitoring for spinal shock, Autonomic hyper-reflexia, prone position

43

## Which Drugs for Induction of Anesthesia?

- No specific randomized controlled trials to inform decision
- I always give NMJ blocker prior to laryngoscopy (usually Roc; suggamadex for rescue; 16 mg/kg vs. emergency surgical airway)
- Remi (4-5 mcg/kg) or Alfentanil (50 mcg/kg) plus 2 mg/kg Propofol if NMJ contraindicated
- NE in line for infusion (or syringe of phenylephrine, ephedrine, vasopressin)
- Etomidate (0.3 mg/kg or local tradition), ketamine (1-2 mg/kg), Midaz, Propofol (It's all about the dose)

44

### A randomized trial of anesthetic induction agents in patients with coronary artery disease and left ventricular dysfunction (Singh et al., Ann Card Anesth 13:3, 2010)

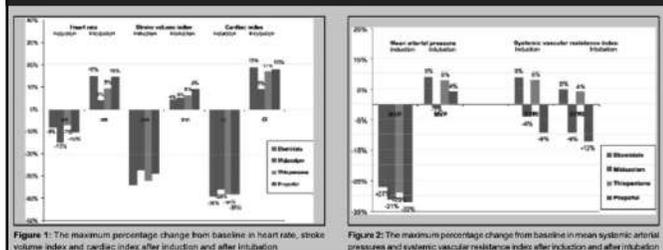


Figure 1: The maximum percentage change from baseline in heart rate, stroke volume index and cardiac index after induction and after intubation.

Figure 2: The maximum percentage change from baseline in mean systemic arterial pressures and systemic vascular resistance index after induction and after intubation.

Also no differences in values at individual time points after induction or intubation

45

### Comparing hemodynamic responses to diazepam, propofol and etomidate during anesthesia induction in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery: a double-blind, randomized clinical trial Soleimani et al., Med Arch 7:198, 2017

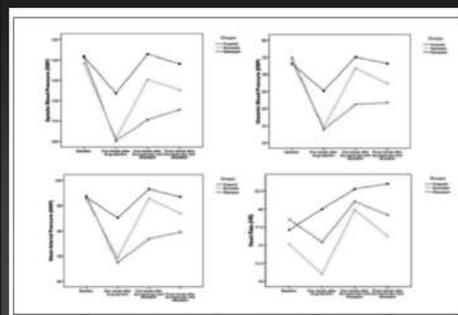


Figure 2. Change trends of hemodynamic parameters in the two groups during follow-up period.

All pts: 0.03 mg/kg midaz+2 ug/kg fentanyl

Prop: 1.5 mg/kg  
Etom: 0.2 mg/kg  
Diaz: 0.3 mg/kg

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### Single-Dose Etomidate Does Not Increase Mortality in Patients With Sepsis A Systematic Review and Meta-analysis of Randomized, Controlled Trials and Observational Studies

Wan-Jie Gu, MSc; Fei Wang, MD; Lu Tang, MD; and Jing-Chen Liu, MD

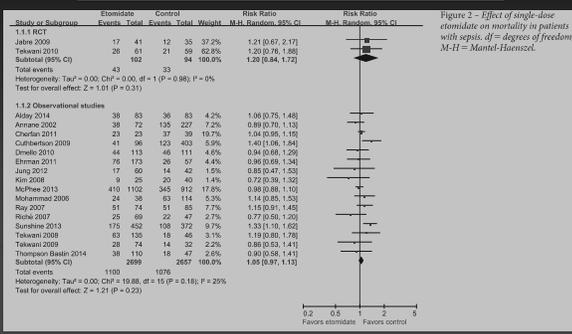
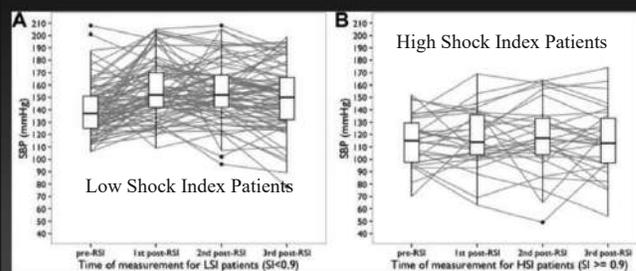


Figure 2 - Effect of single-dose etomidate on mortality in patients with sepsis. df = degrees of freedom; M-H = Mantel-Haenszel.

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### Ketamine induction for patients in shock presenting to the ED



Patients without apparent shock generally exhibited the expected increases in BP from ketamine induction. These effects were blunted in patients with a high shock index, with 8 of these 31 experiencing hypotension Miller M et al., Ann Emerg Med. 2016;68:181-188

48

## Vasopressors and their mechanisms of action

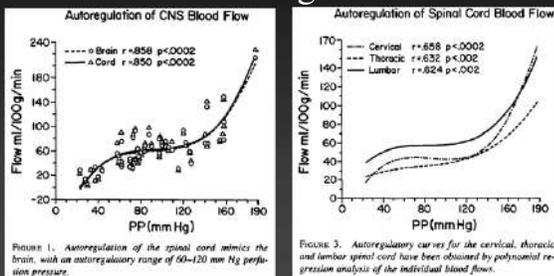
- Phenylephrine Alpha-1 vasoconstriction
- Norepinephrine Acts at alpha-1 and beta-1 receptors to vasoconstrict and stimulate the cardiac chronotropy and inotropy
- Epinephrine Beta-1 inotropy/chronotropy, alpha-1 constriction, beta-2 vasodilation
- Ephedrine Like Epi, but less potent and indirect
- Vasopressin Activation of V1; usually as a supplement to NE
- Dopamine 1-2 mcg/kg/min dopamine vasodilation; 2-10 Beta 1 effects; >10 alpha-1 effects
- Angiotensin II: Increases intracellular calcium leading to vasoconstriction
- Dobutamine Increases cardiac contractility and rate by Beta-1 and vasodilation by Beta-2

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## Is there an ideal BP goal and strategy?

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### SC Autoregulation



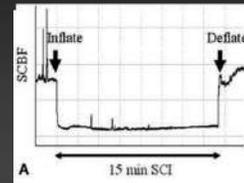
Hickey R et al Stroke. 1986;17:1183-9

51

### Blood Pressure Augmentation

Augmentation of systemic blood pressure during spinal cord ischemia to prevent postoperative paraplegia after aortic surgery in a rabbit model

- Rabbit late paraplegia model involving infrarenal aortic occlusion for 15 minutes



HBP group, n=8  
MAP 120 mm Hg - IV phenylephrine

LBP group, n=8  
MAP 50 mm Hg - IV nitroprusside

Control, n=8  
MAP 80 mm Hg

- At 48 hours 100% HBP group did not have paraplegia

Izumi S et al J Thorac Cardiovasc Surg. 2010;139(5):1261-8

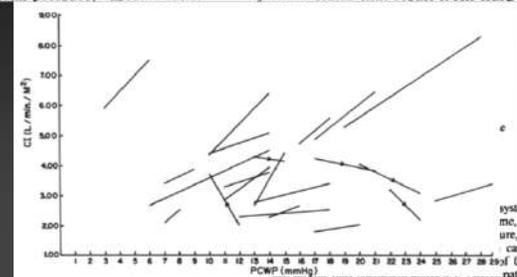
52

### BP Management

- American Association of Neurologic Surgeons recommends (based on retrospective studies)
  - MABP 85 to 90
  - SBP no lower than 90
  - Minimize duration of hypotension
- BP treated with IV fluid/blood for PPV greater than 11 to 13 (Be cognizant of myocardial dysfunction following spinal cord injury)
- Preference for norepinephrine as compared to phenylephrine
- No data exists to guide intraoperative use

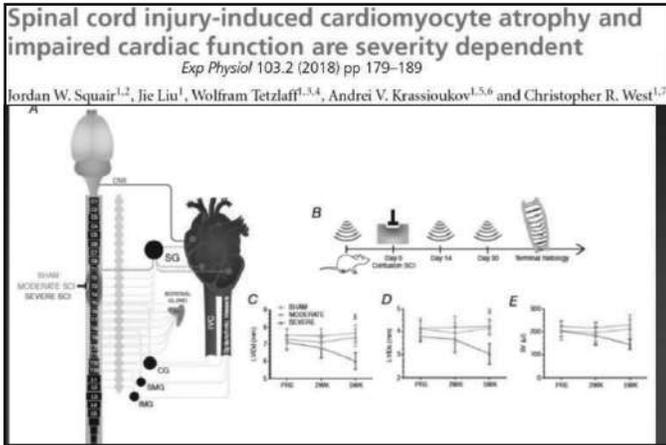
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Cervical spinal cord injury there is dysfunction. Cervical cord transection is an imbalance between parasympathetic control of the cardiovascular system with acute cervical spinal ontractility. As a result, these quadruplegic patient is less able than paraplegic patients to adapt to the changing dynamic states that result from fluid loss and



showed a fall in pulse rate with elevation of right filling pressures and 10 showed a rise. Pulse was

54



55

### Study Design

- Multi-centric Randomized Controlled Trial funded by Department of Defense (PI Miriam Treggiari MD, PHD)
- 152 participants with high spinal cord injury
- 2 concurrent groups with different MAP targets
  - Augmentation group: induced blood pressure with a MAP goal of 85-90 mm Hg
  - Conventional group: conventional blood pressure with a MAP goal of 65-70 mm Hg

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### Available Neuromonitoring Modalities

- Electroencephalography (EEG): regional continuous brain activity
- Electromyography (EMG): May be spontaneous (surgeon accidentally touches a nerve) or evoked (stimulator to avoid cutting a nerve)
- Somatosensory evoked potentials (SSEP): Electrical stimulus applied to a nerve (eg. Median, posterior tibial) and recorded centrally (e.g. sensory cortex)
- Motor evoked potentials (MEP): Transcranial electrical stimulation, with response in peripheral muscle groups
- Brainstem auditory evoked potential (BAEP): BS response to auditory stimuli

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### Neuromonitoring

(Hadley et al., Neurosurgery 81:713,2017)

- SSEPs and MEPs, are reliable and valid diagnostic adjuncts to assess spinal cord integrity.
- MEP recordings are superior to SSEP recordings during spinal cord/spinal column surgery as diagnostic adjuncts for assessment of spinal cord integrity.

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### General Principle of IONM

**Communication!**

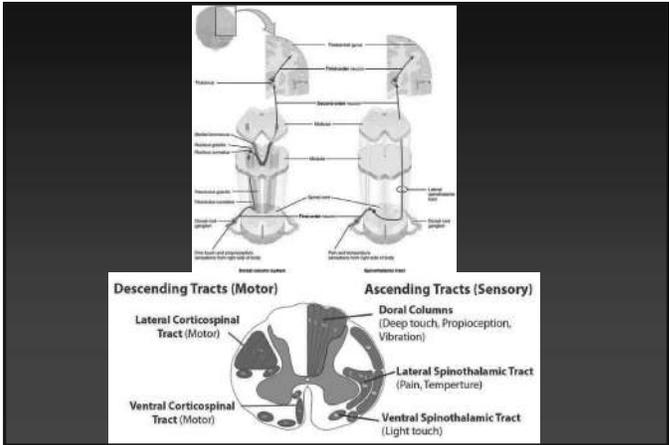
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  graph TD
    NP[neurophysiologist] <--> AN[Anesthesiologist]
    NP <--> S[Surgeon]
    AN <--> S
  
```

**Documentation**

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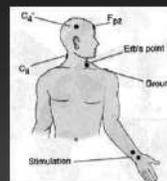
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## Somatosensory Evoked Potentials

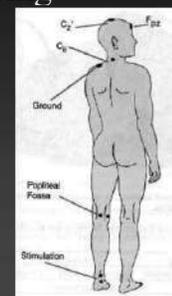
- SEP recording has become a standard method in intraoperative monitoring during spine surgery.
- It is based on a close relationship between spinal blood flow and SEP changes.
- SEPs are sensitive to local factors such as
  - Pressure,
  - Heat,
  - Systemic parameters like blood pressure, body temperature, and metabolic changes.

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## Recording



Upper Extremity



Lower Extremity

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## Anesthesia

Summary of neurophysiological effects of hypnotics

		EEG	SEP	AEP	MEP
Specific GABA agonist	Propofol	Spindles, vertex-wave, B-S	↓	↓↓	↓
	Etomidate	Spindles, vertex-wave, B-S	↑	↓↓	↓
GABA and others	Halothane	B-S variable	↓↓	↓↓	↓↓
	Isflurane	B-S	↓↓	↓↓	↓↓
	Enflurane	B-S, seizures	↓↓	↓↓	↓↓
	Sevoflurane	B-S, seizures	↓↓	↓↓	↓↓
	Desflurane	B-S	↓↓	↓↓	↓↓
	Barbiturates	B-S, epileptiform patterns	↓↓	↓↓	↓↓
	Alpha 2 agonist	Clonidine	Slow	↓	?
	Dexmedetomidine	Slow	↓	?	↓
NMDA antagonist	Nitrous oxide	Frontal beta	↓↓	-	↓↓
	Ketamine	Theta	↑	-	↓↓
Slow wave sleep	Xenon	Central slow	↓	↓	↓
		Spindles, vertex-wave	↓	↓	↓

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## Recommended Anesthetic Regimen for SSEP

- Continuous infusion of opioid (or dexmedetomidine) + Infusion of propofol with or without low dose isoflurane (0.5 – 1.0%) or sevoflurane (0.8-1.7%) in O<sub>2</sub>/air
- Muscle relaxants as required (omit if EMG or MEPs monitored). If no EMG or MEP NMJ blockade is preferred for SSEP

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## Recommended Anesthetic Regimen for MEP

- Continuous infusion of opioid (or dexmedetomidine) + infusion of propofol
- Avoid inhaled anesthetics, as appropriate
- Avoid all muscle relaxants \* during period of monitoring
- (lidocaine (1.5 mg/kg/hr; max 30 mg/hr) infusion may be a useful adjunct)

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## Most Important

- Once surgery has started, do not vary the concentration of inhaled agent, unless done so in collaboration with the NM technician/physician.
- The lower concentration of inhaled agent, the better will be the NM
- Consider using EEG (NM Technician) or BIS to guide IV anesthetic administration

66

### Strategies for rapid emergence from a propofol based anesthetic

- BIS/EEG Monitoring (don't forget extra propofol syringe in-line)
- Balanced with other short-acting agent (e.g. Dex, Remi, Sufenta)
- Esmolol bolus (500 mcg/kg 10 min prior to induction) plus infusion (200 mcg/kg/min) using BIS (Asouhidou I et al BMC Anesthesiol 2015;15:172)

67

If you were having multi-level spine surgery, would you want intraoperative neuro-monitoring?

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### Guidelines for the Use of Electrophysiological Monitoring for Surgery of the Human Spinal Column and Spinal Cord

Hadley et al., Neurosurgery 81:713, 2017

- Level 1: Multimodality intraoperative monitoring (MIOM), including somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) recording, during spinal cord/spinal column surgery is a reliable and valid diagnostic adjunct to assess spinal cord integrity and is recommended if utilized for this purpose.

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- Level 1: MEP recordings are superior to SSEP recordings during spinal cord/spinal column surgery as diagnostic adjuncts for assessment of spinal cord integrity and are recommended if utilized for this purpose.

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- SSEP recordings during spinal cord/spinal column surgery are reliable and valid diagnostic adjuncts to describe spinal cord integrity and are recommended if utilized for this purpose.

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- There is insufficient evidence to suggest a therapeutic relationship between electrophysiological monitoring, including SSEP and MEP recordings, during spinal cord/spinal column surgery, and neurological outcome; its use is not recommended for this purpose. While IOM may detect a neurological injury during spinal surgery, its use does not result in improved neurological outcome, even when IOM alerts occur.

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## My "standard" neuromonitoring anesthetic

- Induction with Propofol and Rocuronium
  - Although rocuronium prevents measurement of MEPs at the beginning of the case, most surgeons prefer NMJ blockade during the time of exposure.
  - Some will want baseline MEPs, which can be achieved with Sux and then followed by Rocuronium after baselines recorded

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## Anesthetic Maintenance

- 0.3-0.5 MAC Iso (or agent of choice other than N2O) (Consider BIS/EEG for TIVA)
- Propofol: usually started at 150 mcg/kg/min and titrate down to 30-50 mcg/kg/min per BP and EEG/BIS.
- Ketamine (0.5 mg/kg ± 10 mcg/kg/min infusion) in patients with chronic pain
- Dexmedetomidine: 0.2 - 0.7 mcg/kg/hr
- **Or**, Opioid Infusion
  - Sufenta 0.3 mg/kg/hour
  - Remifentanyl 0.1 - 0.4 mcg/kg/min

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THANK YOU!  
LET'S SKI!

75

Criteria for selection of patients undergoing microdiscectomy under spinal anaesthesia in the sitting position (group B)

Neurosurgical criteria	Anaesthetic criteria
Single lumbar space involvement	No allergy to anaesthetic medications
Soft disc prolapsed	No skin infection at injection site
No previous surgical procedure on lumbar spine	No hypovolaemia or fixed cardiac output states (additive risks with sympathetic block)

**Common criteria for anaesthesiology and neurosurgery**  
 Age younger than 50  
 Patient consent and cooperation  
 No coagulopathy or therapeutic anticoagulation  
 No anatomical abnormalities of vertebral column

*N. Nicassio et al./Journal of Clinical Neuroscience 17 (2010) 1537-1540*

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Satisfaction of patients who underwent microdiscectomy under spinal anaesthesia in the sitting position (Group B)

	Satisfaction for analgesia	Satisfaction for sitting position
Excellent	15	18
Fair	5	5
Poor	3	0

*N. Nicassio et al./Journal of Clinical Neuroscience 17 (2010) 1537-1540*

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## RA associated with lower incidence of PONV, blood loss & length of stay following spine surgery

TABLE 4. Summary of Subgroup Analyses for Anesthetic Technique

Subtype RA vs. GA	No. RCTs	Sample Size	Effect Size (95% CI)	P	I <sup>2</sup> (P for Heterogeneity)
Spinal anesthesia vs. GA					
PONV	10	RA: 377; GA: 379	RR = 0.49; 95% CI = 0.24-0.98	0.04	51% (P = 0.03)
Urinary retention	7	RA: 277; GA: 277	RR = 1.16; 95% CI = 0.67-2.02	0.59	38% (P = 0.14)
Analgesic requirement	6	RA: 246; GA: 248	RR = 0.87; 95% CI = 0.64-1.18	0.37	73% (P = 0.002)
Intraoperative hypotension	6	RA: 254; GA: 254	RR = 1.57; 95% CI = 0.81-3.01	0.18	67% (P = 0.01)
LOS	7	RA: 259; GA: 257	SMD = -0.79; 95% CI = -1.28 to -0.30	0.002	83% (P < 0.001)
Surgical time	9	RA: 314; GA: 316	SMD = -0.48; 95% CI = -1.44 to 0.48	0.32	97% (P < 0.001)
PACU time	4	RA: 181; GA: 181	SMD = 0.12; 95% CI = -0.77 to 1.02	0.79	94% (P < 0.001)
Blood loss	7	RA: 256; GA: 256	SMD = -1.25; 95% CI = -2.45 to -0.06	0.04	97% (P < 0.001)
Pain score at 24h	6	RA: 188; GA: 188	SMD = -0.06; 95% CI = -2.00 to 1.87	0.95	98% (P < 0.001)
Epidural anesthesia vs. GA					
PONV	2	RA: 40; GA: 37	RR = 0.20; 95% CI = 0.07-0.62	0.005	0% (P = 0.36)
Pain score at 24h	2	RA: 40; GA: 37	SMD = -1.72; 95% CI = -5.06 to 1.63	0.31	96% (P < 0.001)

CI indicates confidence interval; GA, general anesthesia; LOS, length of stay; NA, not applicable; PONV, postoperative nausea and vomiting; RA, regional anesthesia; RCTs, randomized controlled trials; RR, risk ratio; SMD, standardized mean difference.

*Zorrilla-Vaca et al*

*J Neurosurg Anesthesiol • Volume 29, Number 4, October 2017*

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## Anesthesia Demographics Past, Present and Future?

Steven J Zeichner, MD  
Assistant professor of Anesthesiology  
University of Colorado School of Medicine

1

**Objectives:**

- Participants will learn about the changing demographic of anesthesia practice in the US
- Participants will learn to anticipate positioning your practice for the future
- Participants will gain understanding of the cultural history of anesthesia practices and planning for the necessary changes the future will bring
- Participants will learn strategic planning for anesthesia group practice future
- Participants will engage in predictions of what the future might look like, and strategies for confronting



2

**Conflicts of interest:**

- I have no disclaimers



3

**Data Sources**

- ASA
  - From surveys of graduating residents
- MGMA
  - Surveys of members
- CU Resident Graduates
  - Recently obtained
  - Preliminary study
  - unpublished



4

**Background:**

- I spent the first 27 years of my professional career in private practice in South Florida
- I am presently (for the past four and one half years) endeavoring to be an academic anesthesiologist at the University of Colorado School of medicine in Denver Colorado



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**Traditionally anesthesia groups:**

- Owned by MD providers
- Niche Market, i.e. local
  - One or more hospitals
  - Ambulatory centers
  - Physician offices
- Lean overhead
  - Billing expenses
  - Malpractice insurance
- Primary objective
  - Job security
  - Preservation of income and lifestyle
  - Maintenance of status quo



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**Slide 6**

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**ZS1**

Zeichner, Steven, 2/10/2018



**• Evolution**

- One person (man) individual practices that coordinated to cover facility sites and call.
- Encouraged (read coerced) by hospitals to form group practices
  - Facilitates negotiations on behalf of hospitals

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**Evolution**

- Culturally the tradition of individuality persists
- Tension:
- Individuals make *clinical* decisions
- Group makes *practice* decisions

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**Currently-**

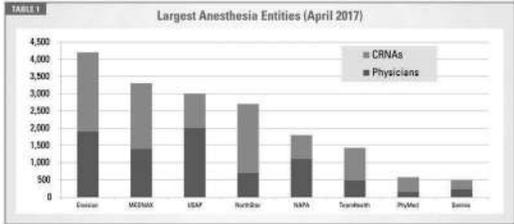
- As of April of 2017 eight entities employed more than 22 percent of all anesthesia providers in the US

• Greenfield, MD and Locke, MA; ABA Communique, Volume 22, Issue 3

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**TABLE 1 Largest Anesthesia Entities (April 2017)**



Entity	Physicians	CRNAs
Envision	~1,800	~2,200
MEDNAX	~1,200	~2,000
USAP	~1,000	~1,800
Northstar	~800	~1,200
NARA	~600	~1,000
TenetHealth	~400	~800
PhyMed	~200	~400
Sonnet	~100	~200

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**Large National Anesthesia Entities**

**Envision**



**MEDNAX**



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**Large National Anesthesia Entities**

**USAP**

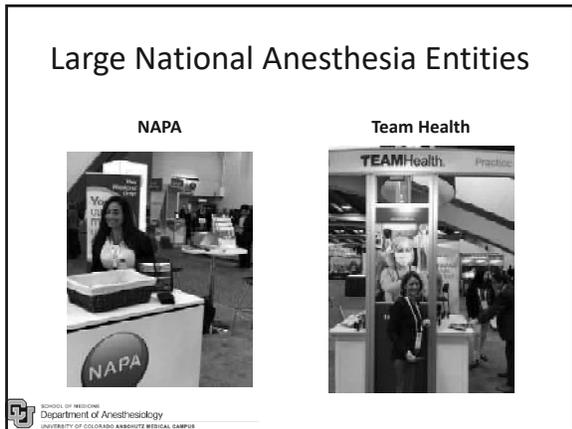


**Northstar**



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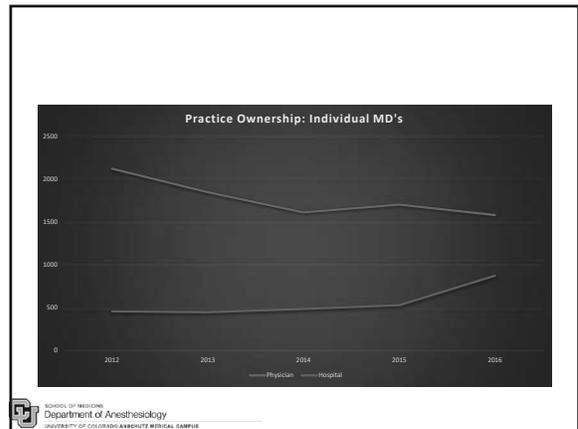
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### Group Ownership: Physician vs. Hospital

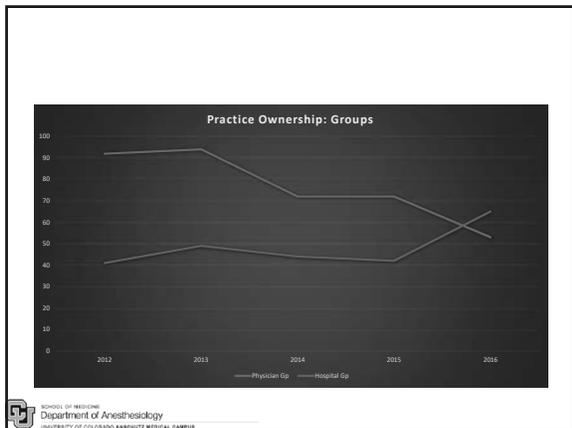
	Physician Gp	Physician #	Hospital Gp	Hospital #	
2012	92	2119	41	455	
2013	94	1845	49	445	
2014	72	1609	44	482	
2015	72	1699	42	528	
2016	53	1578	65	870	

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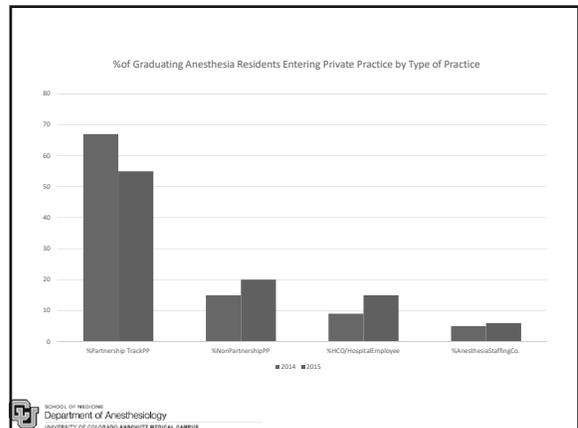
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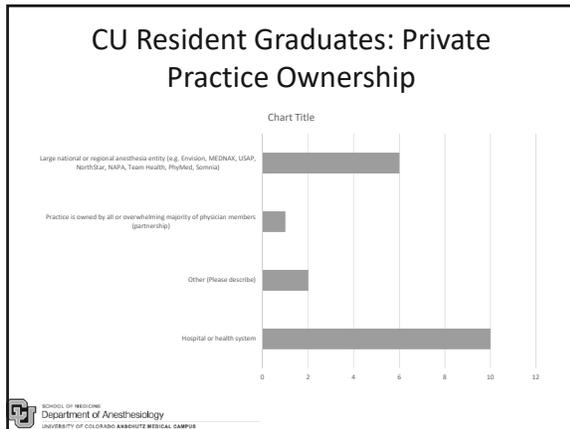
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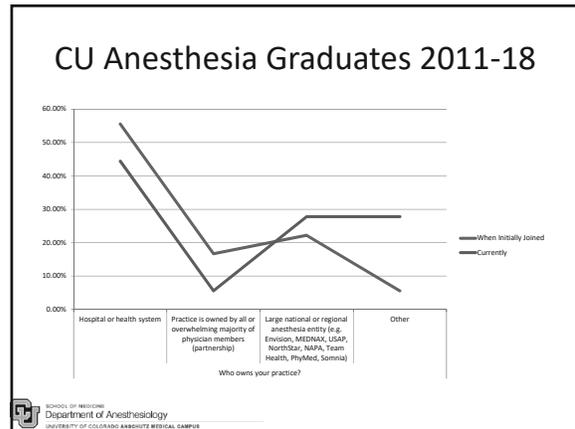
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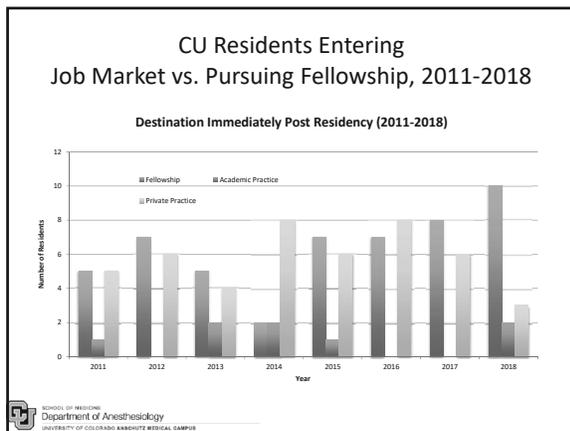
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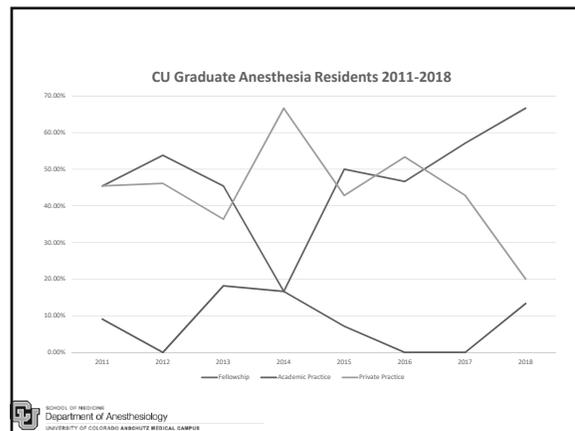
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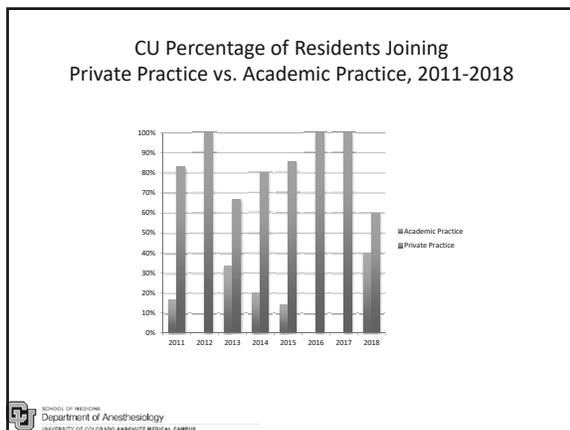
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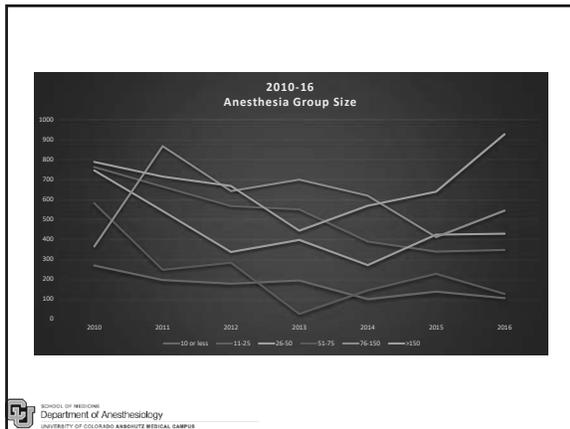


23

### MGMA: Anesthesia groups by size 2010-2016

Group Size	2010	2011	2012	2013	2014	2015	2016
10 or less							
Group Count	35	37	38	35	21	29	31
Individual Count	266	193	175	191	97	135	102
11-25							
Group Count	52	45	38	38	26	21	22
Individual Count	761	663	565	548	387	326	344
26-50							
Group Count	25	23	15	18	11	14	15
Individual Count	744	540	334	395	268	421	426
51-75							
Group Count	15	10	11	4	8	8	6
Individual Count	579	244	280	23	141	224	124
76-150							
Group Count	14	25	17	18	17	13	13
Individual Count	362	866	640	698	617	409	542
>150							
Group Count	23	28	22	28	20	27	26
Individual Count	787	713	666	441	567	637	926

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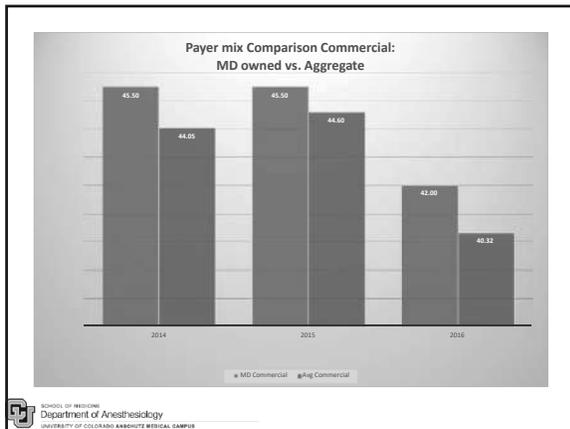


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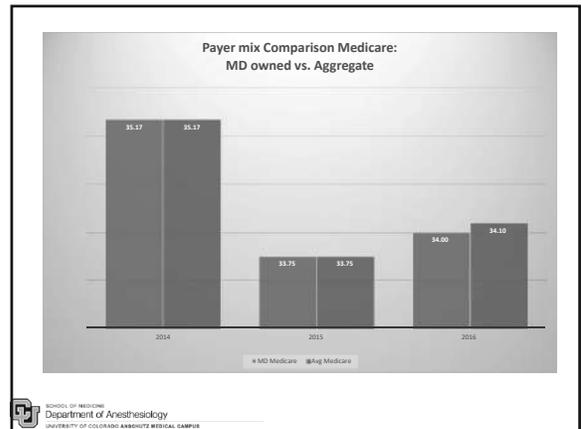
### Why Size Matters

- Better contracts with insurance provider
- More leverage in negotiations with facilities
- Cost of billing and compliance
- More health care facilities are part of large networks
- Greater security due to size and scope

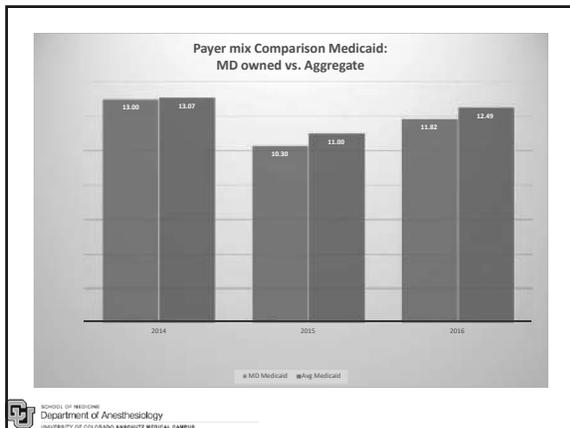
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28



29

### Strategy

30

The market for anesthesia services in the US has been traditionally bound by regional "cultural" differences

- The anesthesia care team model were more common in the South and East, much less so in the West.
- Anesthesia groups in the Mid-Atlantic region actively pursued opportunities to provide services endoscopic for endoscopy and endoscopic centers. Practices in the west, particularly California, avoided.



31

## Growth

- Challenges the fundamental nature of anesthesia groups-
- Anesthesia practices traditionally were professional associations with limited business and professional management
- Managing a practice of 100+ providers is drastically different from 10-20 (old mom & pop shop)



32

## Professional Management

Size does not guarantee success  
 Goal no longer income and lifestyle  
 Security and Predictability (long term goals) prioritized



33

## Strategic Planning

- Anesthesia could, in the past, be synopsized as the service of safely managing patients during surgery
- Quality was defined as safely and comfortably getting the patient through surgery



34

## Strategic Planning

- Moving into the future we should be engaging ourselves as strategic partners with our hospitals and health systems
- Leveraging our greatest attributes:
- The ability to keep the patient comfortable and secure throughout the surgical experience
- Anesthesiology has the greatest potential to positively influence the patients experience

35

## Strategic Partnership

- Hospitals: "We will provide you with work"
- Anesthesiologists: "We can provide optimized quality experience for your patients and facilitate your opportunities to attract more patients-increase your market share"



36

## What hospitals think of us-

- Over-paid
  - Make a lot of \$\$
- “Carpetbaggers”
  - We don’t have to go out and solicit business, just comes to us (through them)
- Lazy
  - All we do is sit there, surgeon does all the work

37

## Strategic Partnership

- We must seek to offer Value in our relationships with hospitals and health care institutions
- We must make sure these same hospitals and health care institutions are aware of our contributions

38

## Leverage Anesthesia group brings to hospital:

- Data
  - Manage Data Base
  - Run OR’s and off OR sites efficiently
  - Work 1:1 with surgeons
  - Improve efficiency
- Customer Satisfaction
- Quality
  - No longer anecdotal
  - Must be empirical and measurable

39

- Historically we have focused on what we do in the OR
- We must shift our focus to include what is happening outside the OR as well
- What happens outside the OR increasingly has more to do with the success of our practices

40

## Strategic Partners

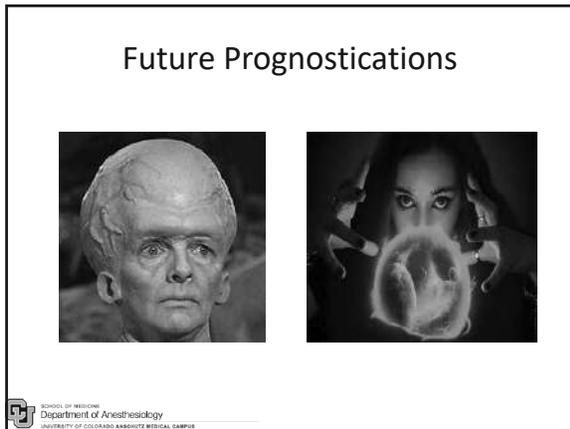
- Anesthesia groups should have a thorough understanding and command of data relative to our sites of service
  - Including, but not limited to OR’s, L&D suites, endoscopy, CVCU, Radiology suites and any other non traditional places we provide service
- Anesthesia must share this data with the hospitals and health care systems we partner with to optimally prove our value .

41

## The second law of thermodynamics=US Health Care



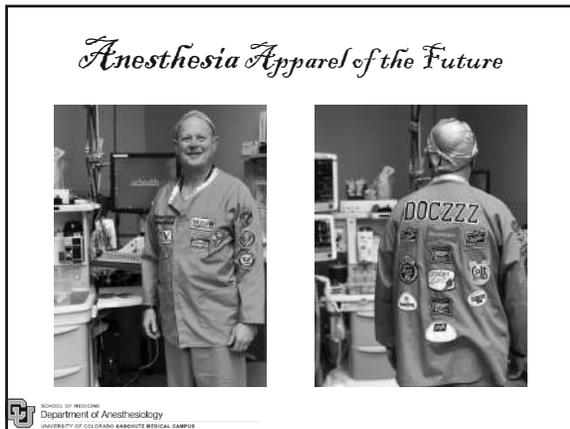
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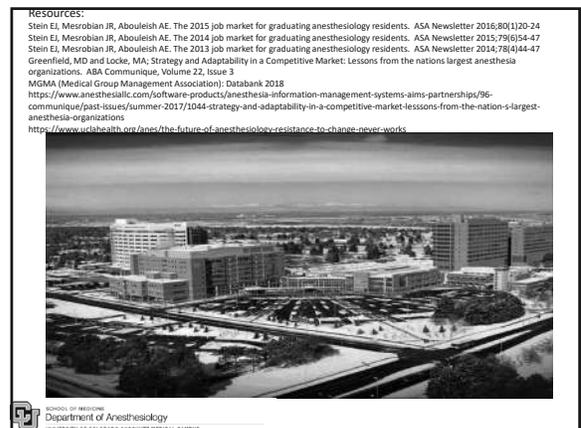
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47



48

**THE FUTURE OF ANESTHESIOLOGIST – HOSPITAL RELATIONSHIPS**

CRASH - HEALTHCARE MANAGEMENT  
FEBRUARY 2019  
VAIL, CO

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**Brian M. Davidson, MD, MBA, CPE**  
President  
SCL Health | St. Mary's Medical Center  
Grand Junction, Colorado

1

**Learning Objectives**

1. Understand the operational and financial drivers in the perioperative and hospital arenas that are important to hospital executives
2. Provide and review problem-based examples of opportunity
3. Review common pitfalls and successful techniques related to contract negotiations with hospitals
4. Demonstrate the changing landscape of physician/provider leadership in the healthcare marketplace

2

**Disclosures**

**Employed by SCL Health System  
Broomfield, CO**

3

**St. Mary's Medical Center**

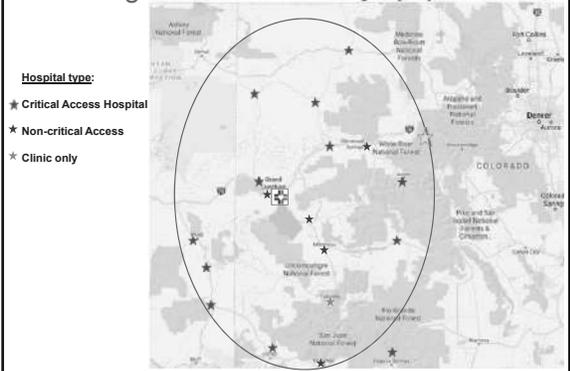


- 346-Bed, \$460M
- 12 OR, 4 ASC
- Level II Trauma
- Cardiac Surgery
- NICU Level III
- Blood Bank
- 44k ED visits
- 100+ mile area
- Aeromedical

- 2,500+ Associates
- 380+ Medical Staff (120+ employed)
- 500+ Volunteers

4

**The Regional Referral Geography**



**Hospital type:**

- ★ Critical Access Hospital
- ★ Non-critical Access
- ★ Clinic only

5

**My Own Path**

**St. Mary's Medical Center**

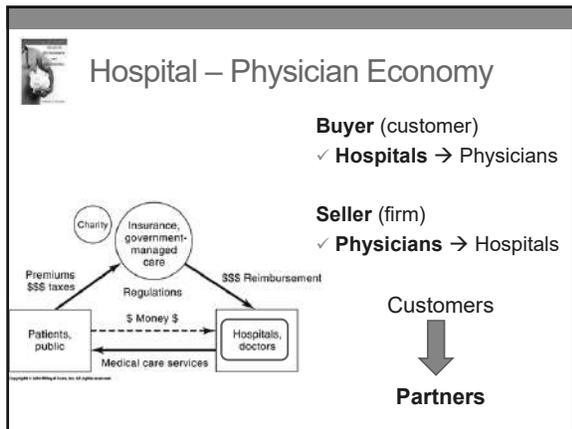
- Chief Medical Officer, July 2014
- Interim President, October 2015
- President, May 2016
- Regional Market Executive, Western CO, January 2017

**University of Colorado Anschutz Medical Campus**

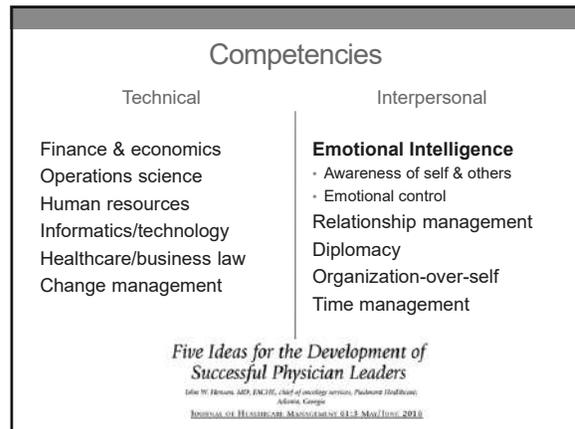
- Faculty anesthesiologist 2007-2014
- Vice Chair, quality/safety/performance improvement
- Associate medical director, perioperative svcs.
- Medical board, credentials, practice plan board
- Colorado State Dental Board, 9 years
- Administrative fellow, MBA - Healthcare



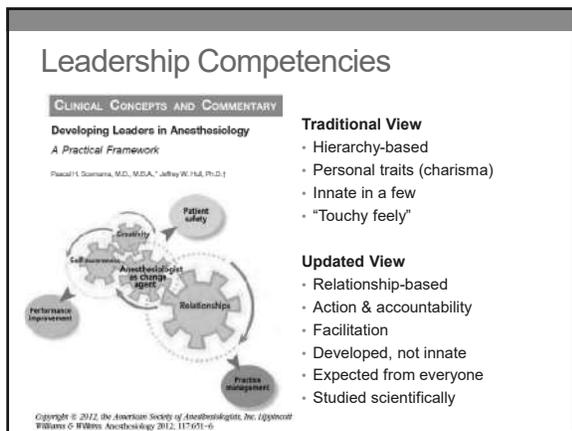
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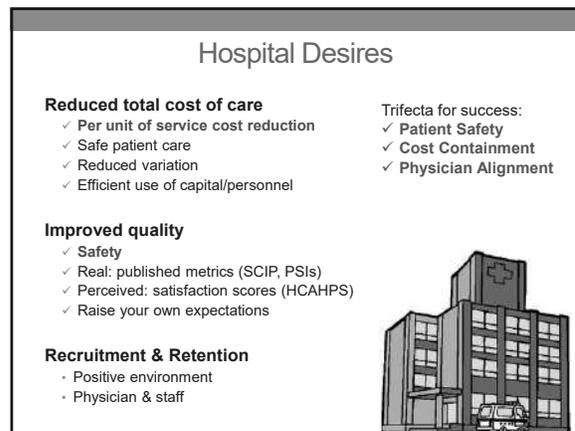
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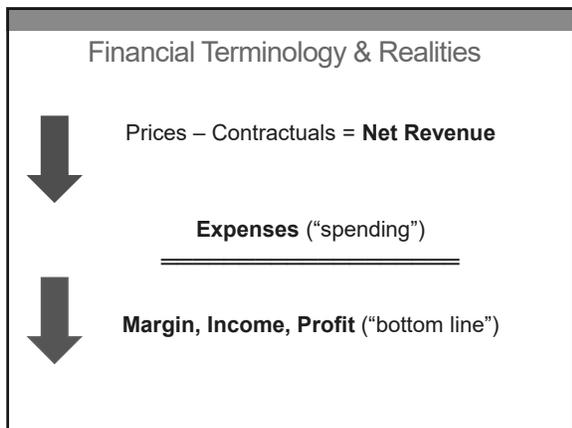
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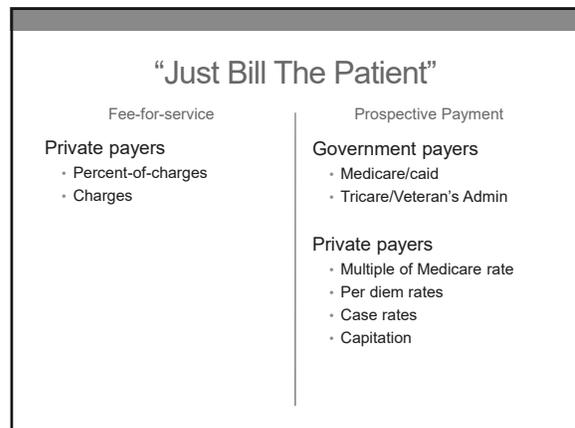
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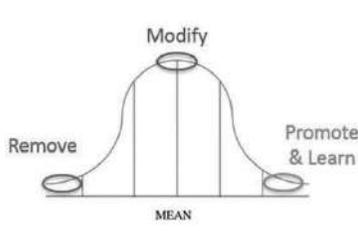
12

### Opportunities

<p>Growth/Revenue Generation</p> <ul style="list-style-type: none"> <li>✓ <b>OR = economic engine</b></li> <li>✓ <b>Case Volume</b></li> <li>✓ <b>Documentation &amp; Coding</b></li> <li>✓ <b>Payer mix optimization</b></li> </ul>	<p>Expense/Resources Control</p> <ul style="list-style-type: none"> <li>✓ <b>Time/processes</b></li> <li>✓ <b>Labor</b></li> <li>✓ <b>Length-of-stay (ERAS)</b></li> <li>✓ <b>Supplies</b></li> <li>✓ <b>Drugs</b></li> </ul>
--	---

13

### Where Is The Opportunity?



**Tail ends:**

- High impact
- Low frequency

**Curve height:**

- High frequency
- High impact (n)

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### Examples: Expense Control

↓ Disposable pain pump usage decrease = \$650,000

- Educate providers on drug/supply cost
- ERAS / PONV / Acute pain care pathways
- Pre-op screening: reduce cancellations
- Co-lead OR case management/block time

15

### Successful Provider Leadership?

✓ Lead by example	✓ Know the job
✓ Foster relationships	✓ Benchmark yourself
✓ Know your resources	✓ Constantly Improve
✓ Flatten Hierarchies	✓ Leadership Development

\*Roy Wilson, MD  
Chief of Anesthesiology  
Kaweah Delta Medical Center  
Visalia, CA

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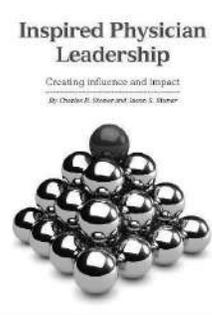


### Group & Leader Success

- Know the issues & understand the metrics**
- Be the solution, not the problem**
- Non-revenue producing valued added service (NRVAS)**
- Relationships, relationships, relationships**
- Know what keeps the CEO up at night**

17

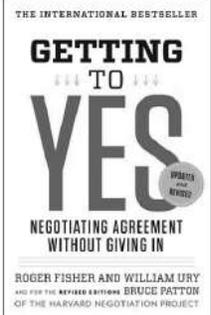
### Professional Development



1. Today: The Case for Physician Leadership
2. Transitions: The Nature & Challenge of Clinical/Leader Interplay
3. Tone: The Significance of the Interpersonal Factor
4. Dialogue: Communicating for Understanding and Influence
5. Teamwork: The Foundations of Collective Synergy
6. Conflict: The Power of Respectful Conflict Encounters
7. Negotiations: Influence and Principled Outcomes
8. Motivation: Building Performance through People
9. Change: A Future of Opportunity
10. Tomorrow: A Case for Possibility

18

### Learn to Negotiate



**GETTING TO YES**  
NEGOTIATING AGREEMENT WITHOUT GIVING IN

**Separate people from problem**

- ✓ Good people assumption
- ✓ Two rational interests
- ✓ Techniques (disassociation)

**Focus on interests, not positions**

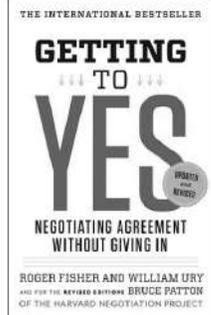
- ✓ Positioning = One interest
- ✓ Identify / empathize
- ✓ Befriend opposed positions

**The negotiation problem**

- ✓ Positions = *bargaining*
- ✓ Principled = *negotiation*

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### Learn to Negotiate



**GETTING TO YES**  
NEGOTIATING AGREEMENT WITHOUT GIVING IN

**Invent options for mutual gain**

- ✓ Understand counterparty needs
- ✓ Realize own capabilities

**Use objective criteria**

- ✓ Fair standards & metrics
- ✓ Reason → be open to reason
- ✓ Yield to principle, not pressure

**Yes, BUT they...**

- ✓ Have more power → BATNA
- ✓ Won't play
- ✓ Use dirty tricks

20

### Pitfalls In Negotiations

**Failure to actually negotiate**

- ✓ Make a list of desires first – needs vs. wants
- ✓ Refrain from bargaining - commodity



**Money is not the main goal**

- ✓ Optimize vs. maximize
- ✓ Lowest cost is not necessary the goal...just lower

**Relationship is an economic rent**

- No relationship = commodity pricing
- True throughout the local hospital economy (CEO, COO, etc.)
- Know the landscape (substitutes)
- Assess your political capital
- **Trust is golden for both sides!**

21

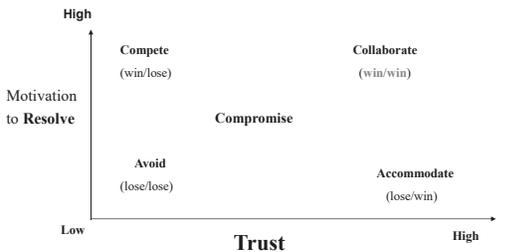
### Trust or trust?

<p><b>T</b></p> <p>Capital</p> <p><b>Character</b></p> <p><b>Integrity</b></p> <p><b>Honesty</b></p>		<p>Lowercase <b>t</b></p> <p><b>Competence</b></p> <p><b>Ability</b></p> <p><b>Experience</b></p> <p><b>Consistency</b></p> <p><b>Communication</b></p>
--	--	---

22

### What does "Win/Win" Look Like?

23



TK Associates

23

### Our Success: My Own

Optimize >> Maximize

Be the solution, not the problem

Read about *Clinical Integration* concepts

If people like you, they will help you

If you don't want to be treated like a commodity, don't represent yourself as one

24

References

**Harvard Business Review**

Engaging Doctors in the Health Care Revolution

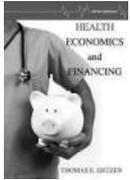
American Association for **PHYSICIAN LEADERSHIP**  
Inspiring Change. Together.

**PHYSICIAN LEADERSHIP LIBRARY**

*Five Ideas for the Development of Successful Physician Leaders*  
John W. Henson, MD, FRCPC, Chief of Cardiology Services, Piedmont Healthcare, Atlanta, Georgia  
*JOURNAL OF HEALTHCARE MANAGEMENT 61.3.60/June 2018*

**Grooming M.D. Leaders**  
GDAs need to target and develop physicians to play leading roles in health care transformation  
Carson F. Dye, FACHE  
American College of Healthcare Executives  
*for leaders who care™*

**HEALTH ECONOMICS and FINANCING**



THOMAS E. BREZLER

25

Thank You!



Winner: 2016 Associate Photo Contest, Lucas Cahalan

26



Kyle Marshall, MD  
University of Colorado  
CRASH 2019

## Ultrasound Guided Regional Anesthesia Workshop

SCHOOL OF MEDICINE  
Department of Anesthesiology  
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

1

## Disclosures

- There are NO disclosures for any of the faculty participating.



UNIVERSITY OF COLORADO  
LET YOUR LIGHT SHINE  
1876

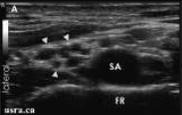
Children's Hospital Colorado

DENVER HEALTH  
Level One Care for ALL

uchealth

2

## Basic Physics



- Ultrasound machines produce sound waves
- They listen for what returns and create image
- Denser tissues reflect more waves
  - tissues are more "hyperechoic" or white
- Less Dense tissues allow them to pass through
  - Tissues which are "hypoechoic" reflect waves poorly or not at all

3

## Basic Physics, cont.

- High frequency waves (short wavelength)
  - Penetrates minimally into tissues
  - Excellent resolution
  - Great for shallow structures (up to about 6cm)
  - Linear probe
- 99% of use



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## Basic Physics, cont.

- Low frequency waves
  - Penetrate deep into tissues
  - Resolution not as good
  - Great for deep structures
  - Curvilinear probe
- Appropriate for deep (>5cm) U/S blocks



5

## Preferred Ultrasound Machine

- High Frequency: 10MHz –15MHz
- Depth 1-6 cm (for linear probe)
- Needle finding technology
- Color capability for vascular structures
- Time Gain Compensation
- Wireless capability for Medical Record upload
- As few buttons as possible/necessary

6

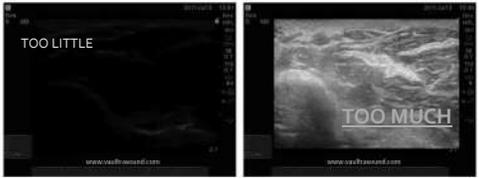
## Ultrasound Basics

- Depth
  - Find ideal depth!
    - Use as little depth as needed for a block, it will improve the picture of the structures you want
  - Increased depth, means decreased frequency will be needed to have a good picture
    - Due to low frequency, resolution will suffer!
    - Better penetration, worse resolution

7

## Ultrasound basics

- Gain:
  - Amplifies returning sound waves, to make signal brighter or darker... Need to get it JUUST right.
  - Newer machines are optimized



8

## How to use a Probe

- Gel: Allows for transmission of sound waves
- Always support your hand against the patient



- **Anisotropy:**
  - small changes in tilt of probe can vastly improve image

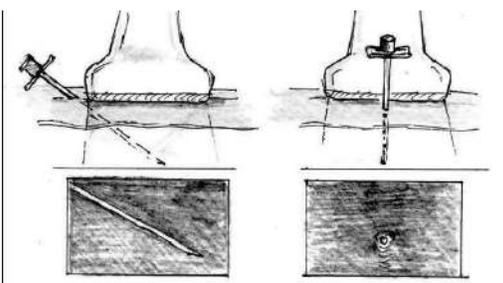
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## How to use a Probe & Needle

- Find your favorite view, and stick with it!
- Only small changes in anisotropy
- Don't chase your needle!
  - Finding it in "no man's land" does not help
  - Improve needle placement
    - So that changes in anisotropy will make it visible
  - Look at your hands, before the screen
  - Practice!

10

## Ultrasound and Needle



IN PLANE                      OUT OF PLANE

11

## Principles of UGRA

- Before the Block:
  - Know how to manage Local Anesthetic Toxicity!
  - Practice hand/eye coordination
  - Know your anatomy
  - Be patient and optimize picture (depth/gain)
  - Position your patient to optimize view and ergonomics
- Block Time!
  - Use in-plane view when possible
  - Don't advance needle if unsure of position
  - Do not penetrate nerve
    - Paresthesia, painful or difficult injection? Pull back, re-direct
  - Ensure good local anesthetic spread
  - Use less local anesthetic if block looks good

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### New Format for CRASH 2018

- Two Nights!
- Basic
  - Upper Extremity, TAP, Lower Extremity
- Advanced
  - Upper Extremity, Serr Anterior, PECs, PVB, Erector Spinae, Hip Fx
- 8 stations with models
- Blue Phantom/needle station for practice!
  - If you are beginner, this is a great place to start!

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### CRASH 2019 Faculty

- Kyle Marshall, MD UCH
- Chris Ciarallo, MD DH/CHC
- Seth Eisdorfer, MD CHC
- Roland Flores, MD UCH
- Olivia Romano, MD UCH
- Marina Shindell, DO UCH
- Inge Tamm-Daniels, MD UCH
- Jillian Vitter, MD UCH
  - Fellow: Ross Mirman, MD



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### Thank you to our Vendors!

- Mindray: Rob Kimbrough
- Philips: Aaron Rhoades, David Tamberlin
- Sonosite: Kristi Howe
- Pajunk: Brian Biggers

15

### Beer and Wine – end at 430!

- Don't get caught thirsty and empty handed



16

Wednesday

# High Risk Ambulatory Patients

*BobbieJean Sweitzer, M.D., FACP*  
 Director, Perioperative Medicine  
 Professor of Anesthesiology  
 Northwestern University  
 Bobbie.Sweitzer@northwestern.edu

I have no disclosures

1

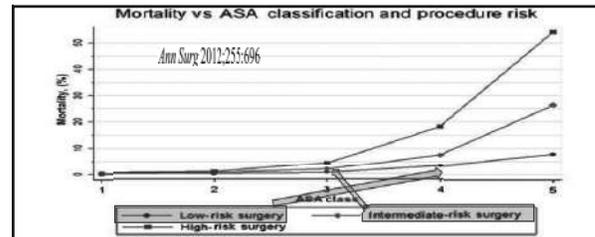


FIGURE 1. The observed mortality rate as a function of American Society of Anesthesiologists' physical status and surgery-specific risk.

TABLE 3. Observed Mortality Percent/Number at Risk as a Function of ASA PS and Surgery Risk Category

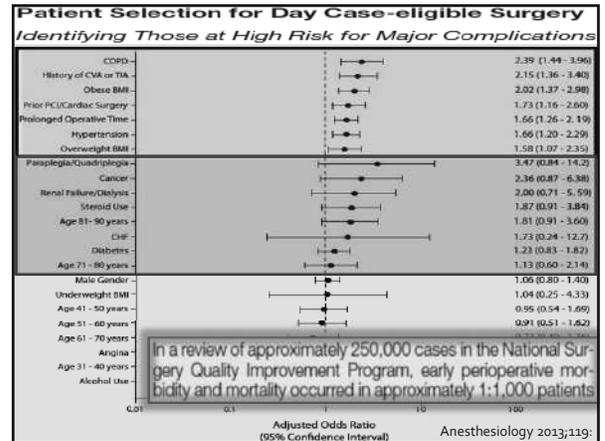
Surgery Risk Category	ASA PS				
	I	II	III	IV	V
Low risk	0.03	0.08	0.49	3.31	7.69
	14,352	42,050	33,300	24,500	13
Intermediate risk	0.65	0.52	2.21	7.15	32.7
	459	6673	12,338	2,319	49
High risk	0.00	0.75	4.81	19.2	54.2
	427	6306	10,267	3251	144

2

ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARDS or ESRD not undergoing regularly scheduled dialysis

ASAhq.org

3



4

## Predictors of unanticipated admission following ambulatory surgery: a retrospective case-control study

Unanticipated admission: 2.67%

Most common reasons:  
 Surgical 40%; anesthetic 20%; medical 19%

Predictors:

- > LOS 1-3 hrs: OR 16.70
- > LOS > 3 hrs: OR 4.26
- > ASA class 3: OR 4.60
- > ASA class 4: OR 6.51
- > Age > 80 yr: OR 5.41
- > BMI 30-35: OR 2.81

LOS= length of surgery  
 Can J Anesth 2013;60:675-

5

Table 3. Risk Factors for Inpatient Hospitalization Within 7 Days of Outpatient Surgery for Medicare Beneficiaries Undergoing 16 Procedures From 1995 Through 1999\*

Risk Factor	Odds Ratio (95% Confidence Intervals)
African American	1.66 (1.55-1.78)
Hispanic	3.03 (2.67-3.42)
Female	0.92 (0.88-0.96)
Age, Y	
70-74	1.12 (1.05-1.18)
75-79	1.30 (1.23-1.38)
80-84	1.51 (1.42-1.61)
≥85	1.89 (1.76-2.02)
Surgery at physician's office	1.80 (1.40-1.81)
Surgery at outpatient hospital	2.65 (2.45-2.84)
Prior inpatient hospital admission (per admission)	1.36 (1.32-1.39)
Type of outpatient surgery	
Transurethral resection of prostate	13.21 (12.12-14.39)
Inguinal hernia	4.44 (4.14-4.74)
Laparoscopic cholecystectomy	12.30 (11.59-13.05)
Dilation and curettage	3.87 (3.43-4.36)
Simple mastectomy	9.99 (7.16-14.20)
Radical mastectomy	16.70 (14.66-19.03)
Carpal tunnel	1.18 (1.03-1.35)
Knee arthroscopy	2.57 (2.35-2.81)
Femoral hernia	6.05 (4.69-7.84)
Hysteroscopy	2.73 (2.35-3.18)
Rotator cuff repair	7.87 (6.94-8.93)
Umbilical hernia repair	8.75 (8.01-9.53)
Arteriovenous graft placement	12.48 (11.30-13.75)
Hemorrhoidectomy	2.35 (2.03-2.72)

\*Compared with a white man aged 65 to 69 years undergoing cataract surgery at an ambulatory surgery center. C statistic = 0.80.

Arch Surg 2004;139

6

**2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery**

**≥60 days should elapse after a MI before noncardiac surgery**

**Postoperative myocardial infarction rates**

- 0-30 days from MI to OR: 33%
- 31-60 days from MI to OR: 19%
- 61-90 days from MI to OR: 8.5%



J Am Coll Card 2014;64:e77

7

**Medical Management After Coronary Stent Implantation: A Review**

Moreover, the highest-risk period for stent thrombosis is immediately after surgery, not before.<sup>61</sup> Given these risks, noncardiac surgery should be performed at centers with primary PCI capacity to enable rapid treatment if stent thrombosis occurs

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**Stents**

Time of Anticipated Surgery

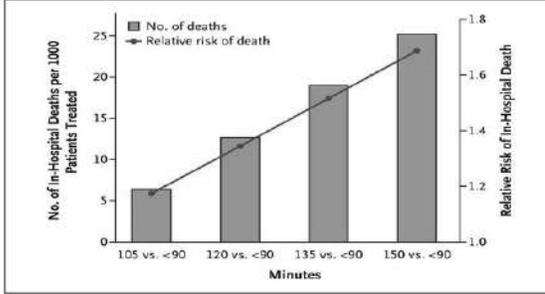
- <6 weeks after BMS implantation
  - elective: postpone surgery until BMS has been implanted 6 weeks\*
  - urgent: can clopidogrel and aspirin be continued in the perioperative period?
    - yes: Perform surgery where 24 hour interventional cardiology coverage is available
    - no: consider bridging therapy
- >6 weeks after BMS implantation: continue aspirin throughout surgery, if at all possible

**Coronary Artery Stents: II. Perioperative Considerations and Management**  
Newsome LT. Anesth Analg 2008;107:570

\* Perform surgery where 24 hour interventional cardiology coverage is available  
\* Restart clopidogrel/aspirin as soon as possible after surgery

9

**Relative Risk of In-Hospital Death with Each Additional 15-Minute Interval Associated with Increases in Door-to-Balloon Time as Compared with Treatment within 90 Minutes**



N Engl J Med 2007;357:1631

10

**High risk surgery** (A)  $\chi^2$ ; p=0.085

**Low risk surgery** (B)  $\chi^2$ ; p=0.119

**Conclusions** Patients with coronary stents undergoing an invasive procedure are at high risk of perioperative myocardial infarction including stent thrombosis irrespective of the stent type and major bleeding. Interruption of OAT more than 5 days prior to an invasive procedure is a key player for MACCE.

Heart 2011;97:1566

11

**2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery**

- 30 day mortality:
  - 9.3% with non-ischemic heart failure (HF)
  - 9.2% with ischemic HF
  - 6.4% with atrial fibrillation
  - 2.9% with coronary artery disease (CAD)
- Decompensated HF or NYHA class IV (symptoms at rest) is a contraindication for surgery
- Surgical survival worse w/EF <30% compared ≥ 30%

*"Although perioperative risk-prediction models place greater emphasis on CAD than on HF, active HF has a significantly higher risk of periop death than CAD."*

JACC 2014;64:e77-137

12

## Aortic Stenosis

- 2% of persons > 65 yr have significant aortic stenosis
- 9% of nursing home residents
- 1 out of 5 of patients w/systolic murmurs
- Risk factors for aortic stenosis:
  - Same as for CAD
- MOST COMMON** symptom of aortic stenosis: Decrease in exercise tolerance & dyspnea (insidious onset)



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2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

## 2.4. Valvular Heart Disease: Recommendations

Risk of surgery can be minimized by:

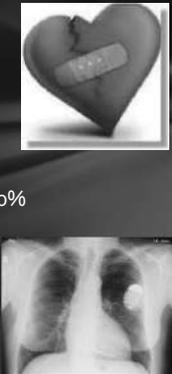
- Accurate diagnosis of type & severity of valvular disease
- Choosing the appropriate anesthetic
- Considering a higher level of monitoring
  - A-line, TEE (transesophageal echo) or PAC
- Managing postoperatively in an ICU**

evaluation of the patient undergoing noncardiac surgery can be performed for multiple purposes, including location and timing of surgery (e.g., ambulatory surgery center versus outpatient hospital, or inpatient admission)

14

## Healthy Hearts Don't Get ICDs

- Ventricular tachycardia/fibrillation
- Cardiomyopathy from any cause
  - EF  $\leq$  35%
  - Hypertrophy cardiomyopathy (HCM)
- Post-myocardial infarction with EF  $\leq$  30%
- Heart transplant wait-list patients
- Long Q-T syndrome



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### Table 1 General principles of CIED management

- The perioperative management of CIEDs must be individualized to the patient, the type of CIED and the procedure being performed. A single recommendation for all CIED patients is not appropriate
- The CIED team should communicate with the procedure team to deliver a prescription for the perioperative management of patients with CIEDs
- For most patients, the prescription can be made from a review of the records of the CIED clinic. A small percentage of patients may require consultation from CIED specialists if the information is not available
- It is inappropriate to have industry-employed allied health professionals independently develop this prescription

Heart Rhythm 2011;8:e1-18.

16

Rendering PMs asynchronous in pacemaker dependent patients is *not* a universal requirement of all procedures.

Rendering a PM asynchronous in a PM dependent patient is preferable for most procedures above the umbilicus.

But, only if electrocautery is planned

It is important to realize that in some cases an unnecessary and inappropriate use of a magnet can be associated with significant untoward hemodynamic effects;

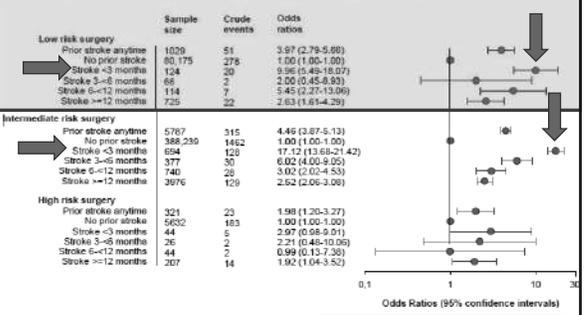
Heart Rhythm 2011;8:e1-18.

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### Time Elapsed After Ischemic Stroke and Risk of Adverse Cardiovascular Events and Mortality Following Elective Noncardiac Surgery

Figure 2. Risk of 30-day MACE Stratified by Surgery Risk\* for the Full Study Population

Surgery Risk	Stroke Timing	Sample size	Crude events	Odds ratios
Low risk surgery	Prior stroke anytime	1020	51	3.97 (2.79-5.68)
	No prior stroke	80,175	278	1.00 (1.00-1.00)
	Stroke <3 months	124	20	5.95 (0.45-78.07)
	Stroke 3-6 months	68	2	2.00 (0.45-8.93)
	Stroke 6-12 months	114	7	5.45 (2.21-13.09)
Stroke >=12 months	725	22	2.63 (1.61-4.29)	
Intermediate risk surgery	Prior stroke anytime	5767	315	4.46 (3.67-5.13)
	No prior stroke	388,230	1462	1.00 (1.00-1.00)
	Stroke <3 months	604	123	17.12 (11.63-21.42)
	Stroke 3-6 months	377	30	6.02 (4.00-9.05)
	Stroke 6-12 months	740	26	3.02 (2.02-4.53)
Stroke >=12 months	2976	129	2.62 (2.06-3.30)	
High risk surgery	Prior stroke anytime	321	23	1.98 (1.20-3.27)
	No prior stroke	5652	163	1.00 (1.00-1.00)
	Stroke <3 months	44	5	2.97 (0.68-9.01)
	Stroke 3-6 months	26	2	2.21 (0.48-10.05)
	Stroke 6-12 months	44	2	0.99 (0.13-7.30)
Stroke >=12 months	207	14	1.92 (1.04-3.52)	



MACE, major adverse cardiovascular events (acute myocardial infarction, stroke, or death due to cardiovascular causes); JAMA 2014;312(3):269-277 doi:10.1001/jama.2014.8165

\*Surgery risk according to the Rozena index.

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**Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery**

**Is There a Preoperative Blood Glucose Level Above Which One Should Postpone Elective Surgery?**  
 There are insufficient data to specifically recommend the level of preoperative fasting blood glucose or HbA1c levels above which elective ambulatory surgery should be postponed.

Surgery should be postponed in patients with significant complications of hyperglycemia such as severe dehydration, ketoacidosis, and hyperosmolar nonketotic states (LoE category 2A).<sup>1</sup>

Anesth Analg 2010;111:1378

19

**Should you at least check a potassium level?**

Absence of adverse outcomes in hyperkalemic patients undergoing vascular access surgery  
*[Absence de complications chez des patients hyperkaliémiques devant subir une intervention chirurgicale d'accès vasculaire]*

Ronald P. Olson MD, Adam J. Schow MD, Richard McCann MD, David A. Lubarsky MD MBA, Tong J. Gan MD

**3.3%: K >6 mEq/l. Mean K 7.0 mEq/l (range 6.1-8)**

- 8456 surgeries in patients with renal failure
- 4389 (52%) had preoperative K level
- 13 (2%) ≥ 6 mEq/dL
- 17 with K > 6.5 mEq/dL
- Adverse events no different among those with K level checked and those without preoperative K level
- Adverse effects did not correlate with K level

Can J Anesth 2003;50:553  
 Anesthesiology 2011;A1652

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**Ex- Premies**

- Risk of apnea inversely related to post-conceptual age (PCA)
- < 5% risk of apnea at 60 weeks PCA
- Preemie (32-36 weeks at birth) → should be ≥52 weeks PCA (4-5 months old)
- Micro preemie (<32 weeks) → should be ≥60 weeks PCA (at least 7 months old)
- Anemia (Hct < 30) increases risk further



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**3. FETAL MONITORING**

When non-obstetric surgery is planned, the primary obstetric care provider should be notified. If that provider is not at the institution where surgery is to be performed, another obstetric care provider with privileges at that institution should be involved. If fetal monitoring is to be used:

- 3.1 Surgery should be done at an institution with neonatal and pediatric services.
- 3.2 An obstetric provider with cesarean delivery privileges should be readily available.
- 3.3 A qualified individual should be readily available to interpret the fetal heart rate.
- 3.4 General guidelines for fetal monitoring include -
  - 3.4.1 If the fetus is considered pre-viable, it is generally sufficient to ascertain the fetal heart rate by Doppler before and after the procedure.
  - 3.4.2 At a minimum, if the fetus is considered to be viable, simultaneous electronic fetal heart rate and contraction monitoring should be performed before and after the procedure to assess fetal well-being and the absence of contractions.

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**Those likely to need blood transfusions**

- Severe anemia
- Sickle cell disease
- Procedures with significant blood loss
- Thrombocytopenia
- Hemophilia
- Coagulopathies



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**High-risk patients with liver disease for any type of surgery**

Child's C  
 MELD score greater than 15  
 Acute liver failure  
 Acute alcoholic hepatitis  
 High serum bilirubin (>11 mg/dL)

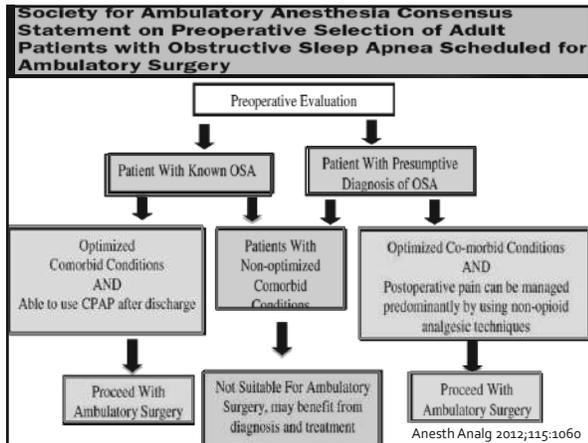
**High-risk surgery in patients with liver disease**

Abdominal surgery  
 Cholecystectomy

MELD Score = 0.957 x Log<sub>e</sub>(creatinine mg/dL) + 0.378 x Log<sub>e</sub>(bilirubin mg/dL) + 1.120 x Log<sub>e</sub>(INR) + 0.643.

Med Clin N Am 2009;93

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**STOP-Bang Scoring Model**

1. snoring (Loud enough to be heard through closed doors?)
2. tired (Often tired, or sleepy during daytime?)
3. observed (Observed to stop breathing during sleep?)
4. Blood pressure (Have or require treatment for high BP?)
5. BMI (More than 35 kg/m<sup>2</sup>?)
6. age (Over 50 yr old?)
7. neck circumference (Greater than 40 cm?)
8. gender (Male?)

≥ 3 = high risk of OSA  
5-8 = high risk for mod to severe OSA

Anesthesiology 2008;108:812-

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**Society for Ambulatory Anesthesia Consensus Statement on Preoperative Selection of Adult Patients with Obstructive Sleep Apnea Scheduled for Ambulatory Surgery**

**Management of Sedation with OSA**

- Avoid deep sedation
- Monitor ETCO<sub>2</sub> during sedation
- Avoid or minimize opioids
- Be prepared for difficulty with intubation
- Semi-upright or lateral position for recovery
- General anesthesia preferable to deep sedation

Anesth Analg 2012;115:1060

27

**Selection of Patients With Obesity Undergoing Ambulatory Surgery: A Systematic Review of the Literature**

**DISCUSSION:** The literature lacks adequate information to make strong recommendations regarding appropriate selection of the obese patients scheduled for ambulatory surgery. The literature does indicate that the super obese (BMI >50 kg/ m<sup>2</sup>) do present an increased risk for perioperative complications, while patient with lower BMIs do not seem to present any increased risk as long as any comorbidities are minimal or optimized before surgery. This review also iden-

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**Identifying Patients at High Risk for Venous Thromboembolism Requiring Treatment After Outpatient Surgery**

Two Point Factors	Three Point Factors	Five Point Factors	Overall outpatient VTE rate: 0.15%
<input type="checkbox"/> Age 40-59 yrs <input type="checkbox"/> OR time >120 min <input type="checkbox"/> BMI >40 kg/m <sup>2</sup>	<input type="checkbox"/> Age ≥60	<input type="checkbox"/> Active cancer	
Six Point Factors	Eight Point Factors	Ten Point Factors	Overall inpatient VTE rate: 1.44%
<input type="checkbox"/> Arthroscopic surgery	<input type="checkbox"/> Current pregnancy	<input type="checkbox"/> Sapheno-femoral junction surgery	
Eleven Point Factors	<b>TOTAL SCORE</b> _____		30-day VTE rates of highest risk outpatients: 1.18%
<input type="checkbox"/> Non-GSV venous surgery			
Total Score	30-d VTE Rate	Risk Level	Low risk inpatients: 0.61%-0.70%
0-2	<0.1%	Low	
3-5	0.1-0.3%	Moderate	
6-10	0.3-0.5%	High	
≥11	Up to 1.2%	Highest	

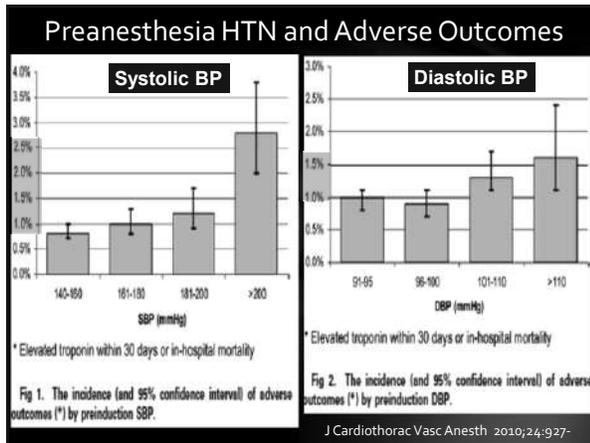
Ann Surg 2012;255:1093

29

**Hypertension, hypertensive heart disease and perioperative cardiac risk** Howell Br J Anesth 2004;92:570

- Association of HTN & perioperative cardiac risk: **OR 1.31**
- Little evidence of preop BP <180/110 mgHg & periop risk
- Recommend: No cancellation of surgery
- Equivocal evidence for BP >180/110 mgHg
- Recommend: May proceed, ensure CV stability
- Maintain intraoperative BP within 20% of preoperative BP
- **DOS: Continue ALL anti-hypertensive agents!!**

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### Guidelines

The measurement of adult blood pressure and management of hypertension before elective surgery

- Secondary care should accept referrals that document blood pressures below 160 mmHg systolic and below 100 mmHg diastolic in the past 12 months.
- Pre-operative assessment clinics need not measure the blood pressure of patients being prepared for elective surgery whose systolic and diastolic blood pressures are documented below 160/100 mmHg in the referral letter from primary care.
- Elective surgery should proceed for patients who attend the pre-operative assessment clinic without documentation of normotension in primary care if their blood pressure is less than 180 mmHg systolic and 110 mmHg diastolic when measured in clinic.

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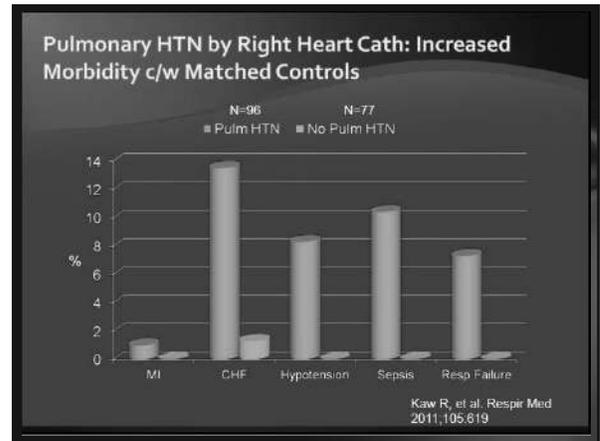
### The Risk of Hypertension after Preoperative Discontinuation of Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Antagonists in Ambulatory and Same-Day Admission Patients

Rebecca S. Twersky, MD, MPH,\* Vasudha Gool, MD,\* Preeti Narayan, MD,\* and Jeremy Weedon, PhD, MA, BS†

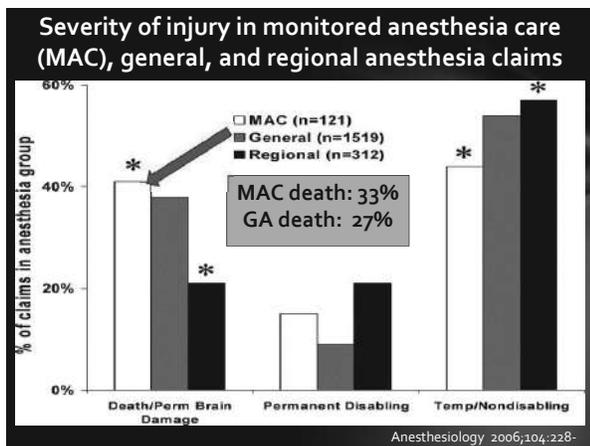
- Randomized 644 patients (ambulatory and same day surgery)
- Either continued or discontinued ACEIs and ARBs
- Primary outcome: HTN immediately preoperatively
- Secondary outcomes: cancellations 2<sup>nd</sup> HTN, prolonged hospitalization, adverse events, postop HTN

**CONCLUSIONS:** Discontinuing ACEIs and ARBs in patients on the day of surgery did not result in a substantively increased incidence of pre- or postoperative HTN compared with patients who continued these medications on the day of surgery. The results provide an evidentiary basis for the safety of discontinuing ACEIs and ARBs on the day of surgery without increasing adverse hemodynamic outcomes. (*Anesth Analg 2014;118:938-44*)

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<http://www.riskcalculator.facs.org/>

### ACS NSQIP Surgical Risk Calculator

Are there other potential appropriate treatment options?  Other Surgical Options  Other Non-operative options  None

Please enter as much of the following information as you can to receive the best risk estimates. A rough estimate will still be generated if you cannot provide all of the information below.

Age Group: 65-74 years | Diabetes:  Oral

Sex: Female | Hypertension requiring medication:  Yes

Functional status:  Independent | Previous cardiac event:  Yes

Emergency case:  No | Congestive heart failure in 30 days prior to surgery:  No

ASA class:  III - Severe systemic disease

Wound class:  Clean | Dyspnea:  With Moderate exertion

Steroid use for chronic condition:  No | Current smoker within 1 year:  No

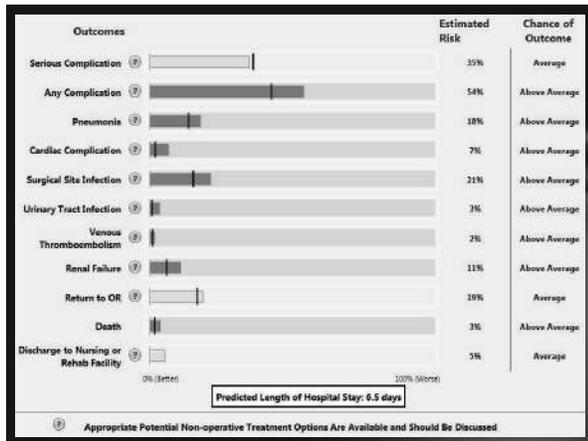
Asclies within 30 days prior to surgery:  No | History of severe COPD:  Yes

Systemic sepsis within 48 hours prior to surgery:  None | Dialysis:  No

Ventilator dependent:  No | Acute Renal Failure:  No

Disseminated cancer:  No | BMI Calculation: Height (in) 65, Weight (lbs) 200

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## Cataract Surgery is LOW risk!!

**Mortality: 1:10,000 (0.01%); Morbidity (major): 0.04%**  
 Cochrane Review (21,531 patients)  
 707 adverse events (3.3%); 61 hospitalizations (0.28%)  
 3 deaths (0.014%)

Limited (NO?) stress response (no major organ disruption;  
 no fluid shifts; no blood loss; minimal postoperative pain)

???Avoidance of General Anesthesia???

EVERYONE agrees: NO Preop TESTING!!

**Can patient get to the facility  
 and lie flat for 30-45 min?**

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## SUMMARY

- ❖ Which patients are too high risk depends on your type of facility
- ❖ Depends on the resources you have
- ❖ Depends on your willingness to accept risk

*If you don't like to gamble medicine isn't the job for you*

Bobbie.sweitzer@northwestern.org

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# ANESTHESIA FOR NEUROVASCULAR SURGERY

Jeffrey R. Kirsch, MD FASA  
Professor, Emeritus Chair  
Oregon Health and Science University

1

## CONFLICT OF INTEREST AND DISCLOSURES

- Professor, but very busy clinical anesthesiologist
- I do not accept honoraria for lectures
- Consulting fees (case review, industry FDA activity) are paid directly to charity (e.g. Oregon Food Bank, FAER, etc)

2

## PRESENTATION OBJECTIVES

- Gain the knowledge to provide state-of-art perioperative anesthetic management for patients requiring neurovascular surgery
- Gain the knowledge to optimize conditions to optimize outcomes following neurovascular surgery

3

## TOPICS COVERED:

- Anesthesia for carotid endarterectomy
- Anesthesia for cerebral endovascular clot retrieval
- Anesthesia for cerebral aneurysm surgery
- Anesthesia for cerebral AVM resection

4

## CEREBRAL ISCHEMIA:

CAROTID ENDARTECTOMY  
POST-STROKE CLOT RETRIEVAL

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79 Y.O. MAN WITH 85% LEFT CAROTID  
STENOSIS. HISTORY OF TIAS.

- Will you do the case awake or under GA?
- How will you monitor the patient?
- Will you recommend that the surgeons use a shunt or not?
- What anesthetic agents will you use?

6

## PREOPERATIVE

Optimize CV System  
to minimize risk of  
perioperative MI

7

## CESSATION OF BLOOD FLOW TO BRAIN (CEREBRAL ISCHEMIA)

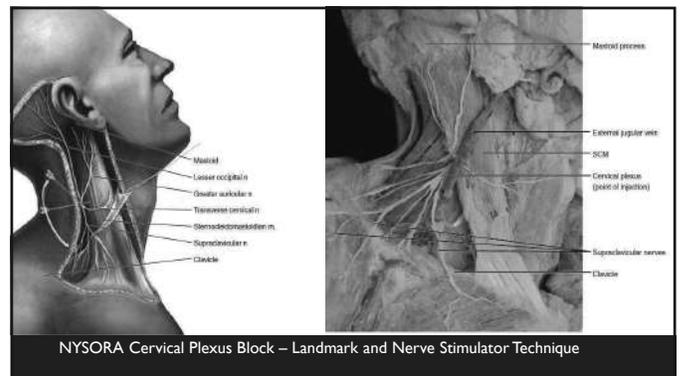
- Poor reserve of high energy phosphates
- Poor reserve of metabolic substrates
- High metabolic requirement
- Poor functional redundancy (functional deficit, even with relatively little damage in “eloquent” areas of brain)

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## RA VS GA

- Few prospective randomized studies but probably no difference in outcome (Liu J et al, *Trasl Perioper Pain Med* 1:14, 2014; Forssell et al., *Eur J Vasc Surg* 3:503, 1989)
- Biggest advantage of RA is neurologic exam during clamp/shunt. There may be some reduced CV risk.
- Decision should be collaborative between surgeon, anesthesiologist and patient

9



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## PREVENTING INJURY FROM ISCHEMIA

- Monitoring for ischemia
- Shunt: plastic bypass catheter can maintain perfusion during removal of plaque but may also cause plaque emboli during placement
- Precise BP and PaCO<sub>2</sub> management
- Temperature control
- Glucose management
- Pharmacologic treatment

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## CESSATION OF BLOOD FLOW TO BRAIN (CEREBRAL ISCHEMIA)

### Appropriate monitoring for ischemia

- Neuro-monitoring (EEG, SSEP, MEP)
- CBF: Xe, TCD (MCA flow and emboli detection), laser Doppler
- Stump Pressure
- Neurologic exam during awake surgery (RA)
- Near-infrared reflected spectroscopy (NIRS)
- Combined stump pressure and NIRS

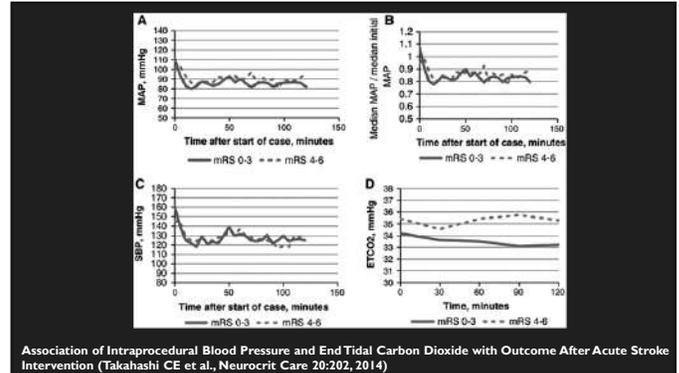
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## PREVENTING ISCHEMIA (2)

### To shunt or not to shunt?

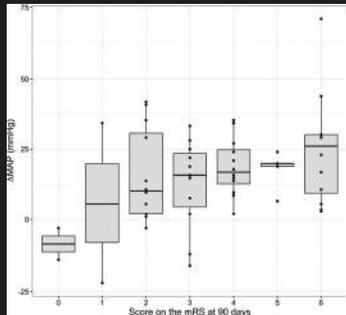
- During GA: Selective shunting with EEG monitoring is associated with better outcome than shunting all patients or no patients (Salvian AJ et al., Cardiovasc Surg 5:481, 1997; Plestis KA, J. Vasc Surg 25: 620, 1997)
- During GA: Selective shunting with stump pressure plus NIRS (Findlay JM et al., Can J NS 44: 692, 2017)
- During RA: Selective shunting based on the Neurologic Examination is best.
- Critical to engage surgical strategies to minimize plaque emboli during shunt placement

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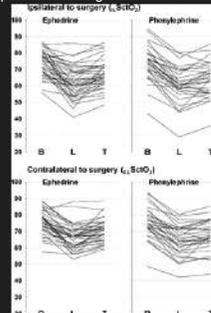
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The association of the difference between baseline mean arterial pressure (MAP) and average MAP during GA ( $\Delta$ MAP) with the score on the modified Rankin Scale (mRS) at 90 days.



15

Compared effects on cerebral oxygenation of ephedrine vs phenylephrine to treat hypotension during carotid endarterectomy



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## PREVENTING ISCHEMIA (3)

- Maintain MABP no less than normal baseline (ephedrine may be better than PE (from NIRS studies))
- Maintain adequate oxygen carrying capacity (Hb and PaO<sub>2</sub>)
  - Hb 11-12 g/dl is associated with less vasospasm & better outcomes after aSAH (Sun J et al., NeuroRpt 26:263, 2015; Stein M et al., J Clin Neurosci 22:530, 2015)
- Avoid hyperventilation

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## INTRAOPERATIVE ANESTHETIC MANAGEMENT

- Standard ASA monitors; Timing of a-line dependent on pt's CV situation
- CV Stable induction (e.g. Etomidate, Roc/Sux, PE/Ephedrine, Esmolol)
- Neuromonitoring needs (TIVA, no prolonged NMJ blockade for MEPs?)
- Plan for increased BP during carotid clamp; reduced BP during reperfusion (suture line pressure, excessive brain perfusion)
- Anesthetic allowing rapid emergence for Neuro-Exam; Deep extubation may prevent coughing and suture line stress
- Prepare for acute BP manipulation during surgical dissection of carotid bifurcation secondary carotid baroreceptor manipulation (Rx with lidocaine by surgeon in bifurcation)

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### HANDY TO HAVE IMMEDIATELY AVAILABLE

- Blood pressure raising:
  - Bolus: Phenylephrine (50-100 mcg), Ephedrine (5-10 mg), Vaso (1-2 units)
  - Infusions: PE (0.2 mcg/kg/min), NE (0.02 mcg/kg/min), Vaso (1-6 U/hr)
- Blood pressure lowering:
  - Bolus: Labetalol (5 to 10 mg every 5 minutes), Nicardipine (100 to 500 mcg), or esmolol (10 to 20 mg).
  - Infusions: labetalol (0.5 to 2 mg/minute), nitroprusside (0.1 to 4.0 mcg/kg/min), nitroglycerin (0.1 to 4 mcg/kg/min), nicardipine (initial 3 to 6 mg/h titrated to a max of 15 mg/h), or esmolol (50 to 300 mcg/kg/min)

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### 79 Y.O. MAN WITH 85% LEFT CAROTID STENOSIS. HISTORY OF TIAS.

- Should this be done as a CEA or Stent? Carotid stenting is associated with a higher incidence of procedural stroke/death (Muller MD et al., 49:2715, 2018). If stent, deploying stent may be painful, as typically performed with sedation.
- Will you do the case awake or under GA? Primarily up to the surgeon: ETT for CEA; LMA for stenting
- How will you monitor the patient? ASA routine monitors plus A-line; Neuromonitoring up to surgeon
- Will you recommend that the surgeons use a shunt or not? I prefer shunt guided by EEG change during clamping.
- What anesthetic agents will you use? Tight control of BP, PaCO<sub>2</sub>, glucose, HR (high incidence of post-op MI) and tailored to optimize neuromonitoring

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### MECHANISTIC TREATMENT TO PREVENT BRAIN INJURY FROM CEREBRAL ISCHEMIA (TEMPORARY CLIP PLACEMENT)

- Reduce brain metabolism
- Calcium: blocking of VDCC, AOCC (EAA inhibitors) or release from ER
- Sigma receptor agonist (decrease release of EAA or impair their ability to act at receptor)
- Oxygen radical scavengers
- Inhibitors of nNOS and iNOS
- Stimulators of eNOS
- Protease inhibitors
- Anti-inflammatory/adhesion agents

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### MECHANISTIC TREATMENT TO PREVENT BRAIN INJURY FROM CEREBRAL ISCHEMIA

Mechanistic treatment only effective in rodents

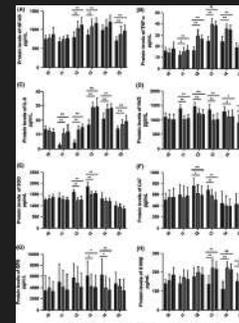
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### EXPERIMENTAL PHARMACOLOGIC TREATMENT TO PREVENT INJURY FROM CEREBRAL ISCHEMIA DURING CEA

- If anesthetics were neuroprotective during CEA, we would expect better outcomes following GA vs RA
- Melatonin: (Zhao Z et al., J Pineal Res 65:e12521, 2018)
  - Decreased brain injury and increased brain anti-inflammatory capacity in rats subjected to transient focal ischemia
  - Double blind RCT in patients treated with oral Melatonin (6 mg/day) for 3 days prior to and 3 days following CEA decreased evidence of brain injury (S100-Beta) and increased systemic anti-inflammatory capacity

23

The protective effect of melatonin on brain ischemia and reperfusion in rats and humans: In vivo assessment and a randomized controlled trial J Pineal Res. 2018; DOI: (10.1111/jpi.12521)



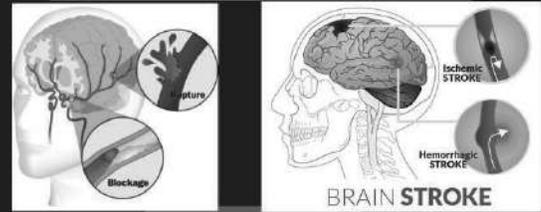
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## POSTOPERATIVE COMPLICATIONS

- Cerebral micro-emboli from plaque disruption
- BP Control: Instability due to baroreceptor injury and pain; SBP goal 100-150
  - HTN could lead to "cerebral hyperperfusion syndrome (cerebral edema, ICH) and suture line rupture
  - Hypotension: Stroke
- Slow emergence (anesthesia, hypothermia, residual NMJ blockade vs. Stroke)
- Neck Hematoma: residual anticoagulant +/- HTN; acute airway emergency
  - Associated with increased incidence of post-op MI and Stroke
- Vocal Cord Paralysis: Surgery associated recurrent laryngeal nerve injury or compression. Results in VC adduction, hoarseness and airway obstruction (if previous injury on contralateral side)

25

## ANESTHESIA FOR CLOT RETRIEVAL



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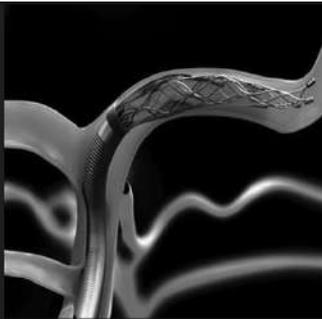
## 65 YEAR OLD MAN WITH RIGHT MCA OCCLUSION

- History of atrial fibrillation on aspirin treatment
- PMH: Hypertension, Type 2 diabetes, high cholesterol, inactive
- PE: BMI 32, MP 3 airway, NPO for 6 hours after a light meal
- Interventional radiologist wants to proceed with clot retrieval

27

- Additional preoperative assessment?
- GA vs Sedation?
- Specific plans for neuroprotection?

28



From: Interventional therapies in stroke management: anaesthetic and critical care implications  
BJA Educ. 2016;17(2):43-47. doi:10.1093/bjaed/mkw039

29

## Conscious Sedation Versus General Anesthesia During Endovascular Therapy for Acute Anterior Circulation Stroke

Preliminary Results From a Retrospective, Multicenter Study  
Stroke 2010 41:1175-1179

Alex Abou-Chebl, MD; Ridwan Lin, MD; Muhammad Shazam Hussain, MD; Tudor G. Jovin, MD;

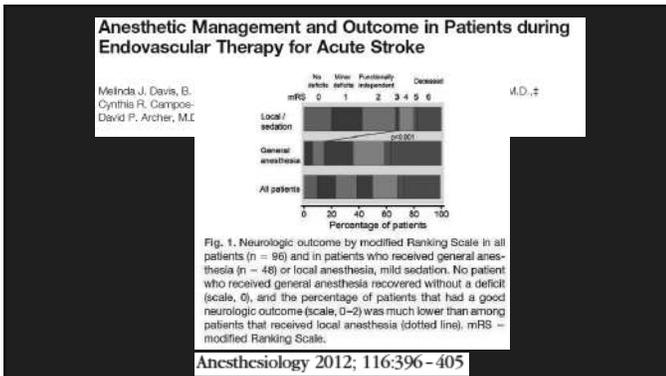
Saboor Qureshi, MD; Qing Hao, MD; Ravi N. Srinivasan, MD

Table 4. Independent Predictors of Mortality After Endovascular Therapy for AIS

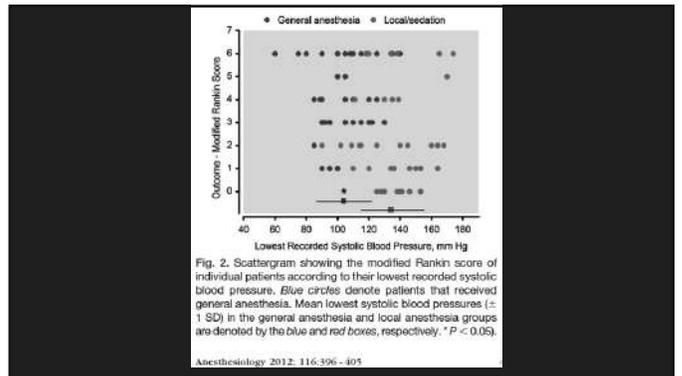
Variable	Odds Ratio (95% CI)	P Value
Age	1.05 (1.04-1.07)	0.0001
GA	1.68 (1.23-2.30)	0.0001
TIMI 0/1 recanalization	1.80 (1.29-2.50)	0.0005
Symptomatic ICH	4.09 (2.49-6.72)	0.0001
Carotid terminus occlusion	1.60 (1.09-2.33)	0.015
NIHSS score > 15	2.12 (1.47-3.05)	0.0001

TIMI Indicates Thrombolysis In Myocardial Infarction, and ICH, Intracranial hemorrhage.

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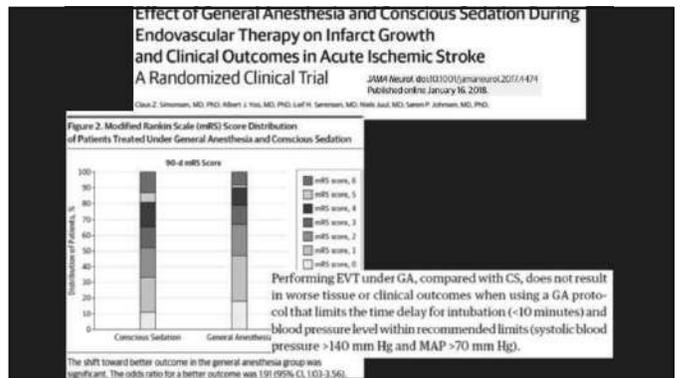
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RETROSPECTIVE STUDIES CANNOT EXCLUDE THE LIKELIHOOD THAT SICKER PATIENTS WERE CHOSEN FOR GA AND NO STUDY WAS CONTROLLED TO ADDRESS DIFFERENCES IN BLOOD PRESSURE OR PACO<sub>2</sub>.

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### ANESTHESIA FOR CLOT RETRIEVAL

- Consider sedation rather than GA
- Avoid hyperventilation
- Avoid hypotension
- Consider low dose (0.5 mg/kg; single dose) ketamine
- If GA: Desflurane for anesthetic maintenance

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### Intravenous Thrombolysis Plus Hypothermia for Acute Treatment of Ischemic Stroke (ICTuS-L)

Final Results (Stroke. 2010;41:2265-2270.)

Thomas M. Hemmen, MD, PhD; Rema Raman, PhD; Kama Z. Guluma, MD; Brett C. Meyer, MD; Joao A. Gomes, MD; Salvador Cruz-Flores, MD; Christine A. Wijman, MD, PhD; Karen S. Rapp, RN; James C. Grotta, MD; Patrick D. Lyden, MD; for the ICTuS-L Investigators

Table 3. Outcome Measures Between HY and NT Patients

	HY (Groups 2, 5, 6; n=28)	NT (Groups 1, 3, 4; n=30)	Fisher Exact Test P
mRS 0-1 at 90 days	5	7	0.747
NIHSS at 90 day (mean±SD)	6.3 (±6.6)	3.8 (±3.0)	0.355
At least one SAE (%)	75	43.3	0.018
Pneumonia (%)	50	10	0.001
All ICH (%)	28.6	20	0.752
Symptomatic ICH (%)	3.6	10	0.609
Mortality by 90 days (%)	21.4%	16.7	0.744

SAE indicates serious adverse event; ICH, intracerebral hemorrhage.

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# CEREBRAL ANEURYSM SURGERY

## ACUTE SUBARACHNOID HEMORRHAGE

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### SACULAR CEREBRAL ANEURYSMS (THE ISSUES)

- Different types; presenting signs and symptoms
- Natural course
- Rupture
- Cerebral vasospasm; pathophysiology and treatment
- Surgical treatment; anesthesia issues, suggested approach
- Endovascular treatment; anesthesia issues, suggested approach
- Common associated problems; hyponatremia, hydrocephalus
- Neuromonitoring optimization, neuroprotection



Joe Niekro Foundation

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### TYPICAL PATIENT PROFILE FOR CEREBRAL (SACULAR) ANEURYSM

- 3% of general population; 30% of these have multiple aneurysms
- Present at age 40 to 60
- No gender preference at 50 or younger but much more common in women, older than 50
- Most (particularly small) aneurysms do not rupture: rupture rate approximately 10 per 100,000
- Only 1/3 of patients with aneurysmal SAH (A-SAH) have a good outcome.
- 85% occur at vascular branch point in anterior circulation.
- Inc incidence of A-SAH with HTN, ETOH, Smoke, advanced age in women (dec estrogen)
- Dec incidence of A-SAH with high choles and exercise (statins may increase risk of SAH)
- Variety of genetic diseases predispose to presence of cerebral aneurysm and increased risk of rupture.

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### ANEURYSM RUPTURE

- Risk of rupture is higher as the aneurysm gets bigger, particularly more than 7 mm in diameter
- Posterior circulation aneurysms rupture with a higher frequency than anterior circulation aneurysms
- No clear association with activity or stress
- Surgeon decision regarding intervention vs. observation relates to size, location and patient age/co-morbidities



LaPlace's Law  
 $T = \frac{P \times R}{2 \times d}$   
 Wall Tension (T) = Transmural Pressure (P) x Radius (R) / 2 x Wall Thickness (d)

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### SAH CONSEQUENCES

- Increased ICP and immediate death (most severe), severe headache/altered LOC or minimal symptoms
- Delayed hydrocephalus from adhesions or reduced CSF resorption in arachnoid granulations; often require permanent LP/VP shunt
- Delayed cerebral ischemia (AKA vasospasm)
- Stress cardiomyopathy (myocardial ischemia in distribution of sympathetic nerves, rather than vascular territory)
- Hyponatremia

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### Etiologies of thunderclap headache

<b>Most common causes of thunderclap headache:</b>
Subarachnoid hemorrhage
Reversible cerebral vasoconstriction syndromes (RCVS)
<b>Conditions that less commonly cause thunderclap headache:</b>
Cerebral infection (eg, meningitis, acute complicated sinusitis)
Cerebral venous thrombosis
Cervical artery dissection
Spontaneous intracranial hypotension
Acute hypertensive crisis
Posterior reversible leukoencephalopathy syndrome (PRES)
Intracerebral hemorrhage
Ischemic stroke

Clinical manifestations and diagnosis of aneurysmal subarachnoid hemorrhage - UpToDate

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**Hunt and Hess grading system for patients with subarachnoid hemorrhage**

Grade	Neurologic status
1	Asymptomatic or mild headache and slight nuchal rigidity
2	Severe headache, stiff neck, no neurologic deficit except cranial nerve palsy
3	Drowsy or confused, mild focal neurologic deficit
4	Stuporous, moderate or severe hemiparesis
5	Coma, decerebrate posturing

Based upon initial neurologic examination.

Adapted from: Hunt W, Hess R. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. *J Neurosurg* 1968; 28:14.

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**Fisher grade of cerebral vasospasm risk in subarachnoid hemorrhage**

Group	Appearance of blood on head CT scan
1	No blood detected
2	Diffuse deposition or thin layer with all vertical layers (in interhemispheric fissure, insular cistern, ambient cistern) less than 1 mm thick
3	Localized clot and/or vertical layers 1 mm or more in thickness
4	Intracerebral or intraventricular clot with diffuse or no subarachnoid blood

Fisher, CM, Kistler, JP, Davis, JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by CT scanning. *Neurosurgery* 1980; 6:1.

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**World Federation of Neurological Surgeons subarachnoid hemorrhage grading scale**

Grade	GCS score	Motor deficit
1	15	Absent
2	13 to 14	Absent
3	13 to 14	Present
4	7 to 12	Present or absent
5	3 to 6	Present or absent

GCS: Glasgow Coma Scale.

Based upon data from: Report of World Federation of Neurological Surgeons Committee on a Universal Subarachnoid Hemorrhage Grading Scale. *J Neurosurg* 1988; 68:985.

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**Glasgow Coma Scale (GCS)**

Clinical manifestations and diagnosis of aneurysmal subarachnoid hemorrhage - UpToDate

	Score
<b>Eye opening</b>	
Spontaneous	4
Response to verbal command	3
Response to pain	2
No eye opening	1
<b>Best verbal response</b>	
Oriented	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1
<b>Best motor response</b>	
Obeys commands	6
Localizing response to pain	5
Withdrawal response to pain	4
Flexion to pain	3
Extension to pain	2
No motor response	1
<b>Total</b>	

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- CAUSES OF SAH**
- Ruptured cerebral aneurysm
  - Trauma
  - AVM/fistulae
  - Vasculitides
  - Arterial dissection
  - Amyloid angiopathy
  - Bleeding diatheses
  - Illicit drugs (Cocaine/Amphetamines)

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- REBLEEDING**
- Approximately 20% chance of rebleeding within first 24 (particularly first 6) hours
  - Acute rebleeding increases risk of death 12 fold
  - Only effective treatment to prevent rebleeding is surgery/endovascular treatment
  - Rebleeding during anesthesia induction is usually fatal
  - Antifibrinolytic therapy (e.g.TXA) decreases risk of rebleeding but increases risk of vasospasm
  - Higher rates in patients after endovascular treatment compared to surgery

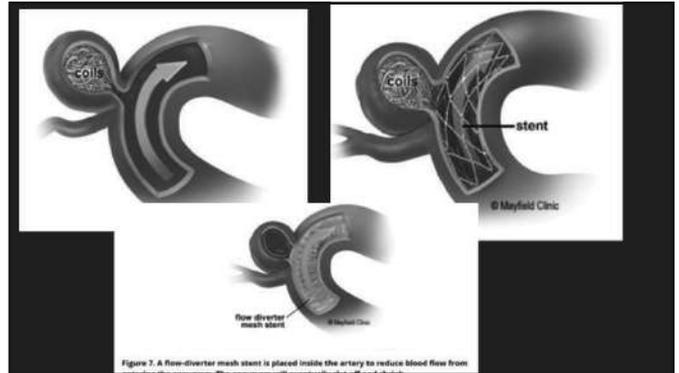
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## SURGERY VS. ENDOVASCULAR

- For patients who fit the specific criteria (based on previous randomized studies) for endovascular treatment, outcomes are better than with surgery
- Endovascular more often associated with rebleeding (early and late)
- Endovascular associated with lower rate of post event seizures
- There is no long-term benefit of endovascular vs. surgery for patients with high grade SAH



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TABLE 1: Intraoperative factors contributing to intraoperative aneurysm rupture. Chowdhury et al., Anesh Res/Pract 2014

Factors	Controversies
Hypertension	Upper limit of blood pressure Poorly controlled BP/controlled BP Chronic/acute hypertension
Anesthetic factors	Sympathetic responses (intubation/extubation) Coughing/gagging
ICP	Sudden decrease in ICP during hyperventilation, use of large dose mannitol, and CSF drain
Maneuvers	Valsalva, application of PEEP (upper limit)
Comorbidities	COPD, CAD, and hyperlipidemia

### **SURGICAL DISSECTION!!!!**

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TABLE 2: Diagnosis of IAR.

Method	Findings
(1) Clinical	Hypertension, bradycardia, and arrhythmias Blown pupil
(2) Surgical	Increase ooze from surgical incision Brain bulge, Hematoma
(3) Monitoring	
ICP	Sudden rise in ICP, presence of pathological waves
TCD	No diastolic flow to reversal of diastolic flow
Cerebral oximetry	Sudden decrease in values
Neurophysiological monitoring	

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TABLE 3: Controversies in the management of IAR.

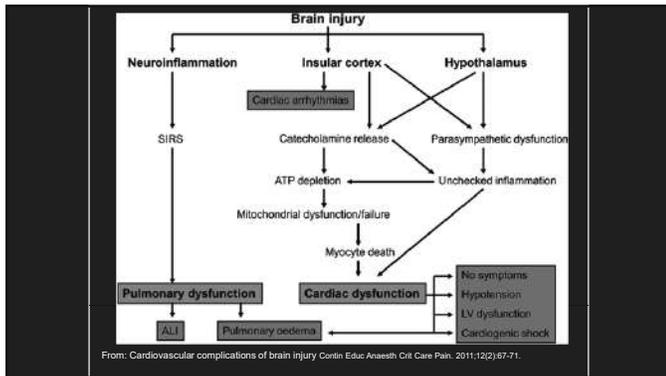
Management strategy	Controversies
IAR at anesthesia induction	Role of rescue clipping versus cancellation of surgery
Preoperative variables	Effect on IAR, role of optimization, and smoking cessation (minimal time)
Neurophysiological monitoring	Role of EEG during burst suppression during IAR Role of SSEP to detect ischemia outside the somatosensory pathway
Clip placement (temporarily)	Effect on outcome of induced hypertension with or without burst suppression Effect of normotension Hypotension or normotension
	Hemodynamic
	Goal of MAP during IAR
	Role of adenosine and ventricular pacing Mild to moderate hypothermia (time and duration)
	Hypothermia
	In good-grade patients/poor-grade patients In cooling patients With or without neuroprotective agents
	Neuroprotection
	Role of different agents on outcome With or without hypothermia Thiopental and requirement of burst suppression Values at the time of IAR
	Hyperventilation
	Time and duration Role of measuring cerebral oxygenation

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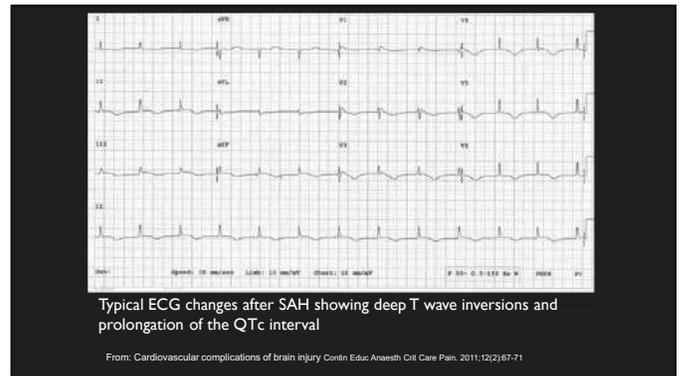
## ANESTHETIC MANAGEMENT FOR **SURGICAL** ANEURYSM TREATMENT

- If surgeons place lumbar drain for brain relaxation, will that increase transmural pressure and result in aneurysm re-rupture?
- Re-rupture is less likely but also may occur with early, aggressive brain relaxation with mannitol or hypertonic saline
- Will hyperventilation result in cerebral ischemia?
- Define BP goals with surgeon for period of dissection, during clip (temporary) placement and following placement of permanent clip
- Will neuromonitoring be used and if so which modalities? Will TIVA be required?
- Risks associated with surgical position; assess for VAE risk and aggressive head turning
- Effects of acute increase ICP on cardiac function
- Hyponatremia common: SIADH vs. Cerebral Salt Wasting ; dehydration associated with more frequent vasospasm-associated cerebral ischemia

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- Cardiovascular complications are common after brain injury and are associated with increased mortality and morbidity.
- Neurogenic cardiac injury is related to brain injury-induced catecholamine and inflammatory responses.
- The neurogenic stunned myocardium (NSM) syndrome is caused by local release of norepinephrine from myocardial sympathetic nerve terminals.
- The NSM syndrome is characterized by ECG changes, cardiac arrhythmias, release of biomarkers of cardiac injury, and left ventricular dysfunction
- Neurogenic cardiac abnormalities are often transient and management should focus on general supportive care and treatment of the injured brain.

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- ### NEUROGENIC CARDIAC DYSFUNCTION
- No history of cardiac problems
  - Temporal relationship between brain injury and cardiovascular abnormalities
  - ECG changes in isolation
  - Modest elevations in cardiac troponin (cTnI)
  - New onset LV dysfunction,
  - Cardiac wall motion abnormalities that do not correspond with coronary vascular territories,
  - Inconsistency between echocardiographic and ECG findings,
  - Inconsistency between cTnI and LV ejection fraction (cTnI <2.8 µg litre<sup>-1</sup> in association with LV ejection fraction <40%),

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- ### BP GOALS DURING SURGERY IN PATIENTS WITH CEREBRAL ANEURYSM
- Include surgeon in discussion
  - Is elevated BP secondary to elevated ICP; BP treatment results in cerebral ischemia?
  - Pts with unruptured aneurysm: SBP less than patient's normal BP
  - CPP of 60 or greater if monitoring ICP; treatment should focus on avoiding acute BP spikes from patient's preoperative values.

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- ### PATIENTS WITH CEREBRAL VASOSPASM
- Occurs in 20-30% of patients following Aneurysm SAH
  - Symptoms start around day 3 following SAH and peak at day 7/8; usually gone by 14 days
  - Structural thickening of arterial wall (media); not true spasm
  - Diagnosis made by TCD and signs/symptoms (vs. Hydrocephalus)
  - Treatment is oral nimodipine (only agent known to improve outcomes in patients); should be continued intraoperatively
  - Normovolemia, avoiding hypotension, removal of SAH blood (surgery); intraluminal treatment (balloon or vasodilators)
  - No benefit of HHH treatment (Gathier C et al., Stroke 49:76, 2018)

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## INTRAOPERATIVE ANESTHETIC MANAGEMENT

- Continue nimodipine via OG tube
- Hb 8 to 11.5 (higher Hb associated with less vasospasm)
- Be prepared for administration of vasoactive medications, including adenosine for cardiac pause during clip placement
- External pads if adenosine anticipated
- Standard monitors plus arterial line (placement prior to or following induction of anesthesia?)
- Two large bore (16 ga or larger) IVs
- Minimize inhaled anesthetics if neuromonitoring.
- BIS/EEG if plan TIVA and/or burst suppression

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## CRITICAL INTRAOPERATIVE EVENTS

- Anesthesia induction: Lower BP is better
- Skull pinning and incision: Avoid HTN; Scalp block (0.5% ropivacaine), Esmolol, Short-acting Opioid (500 mcg Alfentanyl), Propofol
- Dissection: Avoid movement (NMJ blockade or GA/norepi)
- Temporary clipping: Increase BP per surgeon with pressor; discuss "neuroprotection" Propofol neither helps or hurts
- Adenosine for flow reduction during clip placement: 0.4 mg/kg for 20-40 seconds of flow cessation (can be repeated if necessary). TC pacing pads should be placed prior to adenosine administration
- Intraoperative rupture: call for help, massive transfusion, lower BP, Adenosine?, brain protection?
- Confirmation of correct placement: Angio, micro Doppler, indocyanine green (artifactual desat)
- End of case: plan for emergence for neuro-exam regardless of plans for extubation

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### Venous air embolism during craniotomy: Rapid overview

Risk factors
<ul style="list-style-type: none"> <li>• Craniotomy in the sitting position</li> <li>• Surgery involving major intracranial venous sinuses; air entry possible from any venous opening above the level of the heart</li> </ul>
Clinical signs
<ul style="list-style-type: none"> <li>• Air visible on TEE</li> <li>• Change in preaxial Doppler tone</li> <li>• Decrease in ET<sub>CO<sub>2</sub></sub>*</li> <li>• Decrease in SPO<sub>2</sub>*</li> <li>• Hypotension*</li> <li>• Increase in CVP*</li> </ul>
Treatment
<ul style="list-style-type: none"> <li>• Notify surgeon                             <ul style="list-style-type: none"> <li>• Flood field with saline</li> <li>• Repair site of air entry</li> </ul> </li> <li>• Lower the head                             <ul style="list-style-type: none"> <li>• May result in bleeding from air entry site</li> <li>• May limit surgical access to operative site</li> </ul> </li> <li>• Discontinue N<sub>2</sub>O and administer 100 percent O<sub>2</sub></li> <li>• Aspirate air from central venous catheter</li> <li>• Discontinue PEEP</li> <li>• Cardiovascular support                             <ul style="list-style-type: none"> <li>• IV fluids</li> <li>• Vasopressors as needed</li> </ul> </li> </ul>

TEE: transesophageal echocardiography; ET<sub>CO<sub>2</sub></sub>: end-tidal carbon dioxide; SPO<sub>2</sub>: oxygen saturation; CVP: central venous pressure; N<sub>2</sub>O: nitrous oxide; O<sub>2</sub>: oxygen; PEEP: positive end-expiratory pressure; VAE: venous air embolism.  
\* Clinical signs depend on severity of VAE.

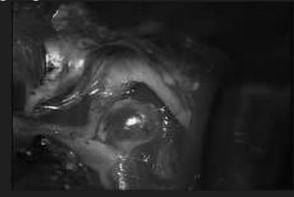
Paisansathan & Ozcan Up to date 2018

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## 43 Y.O. MOTHER OF THREE WITH MULTIPLE CEREBRAL ANEURYSMS

• As the surgeons approach the aneurysm they indicate that they are going to use a temporary clip and ask you to institute "brain protection". What are going to do?

- Propofol?
  - To what end-point?
- Desflurane?
- Hypothermia?
- Hypertension?
- Ketamine?



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## PREVENTING INJURY FROM CEREBRAL ISCHEMIA

- Monitoring for ischemia: Neurologic exam, EEG, SEPs, Near Infrared spectroscopy Jugular bulb oxygen saturation, paratrend, micro-dialysis
- Facilitating perfusion: BP control (particularly in a non-autoregulating vascular bed)
- Avoiding unnecessary hyperventilation
- Avoiding hyperthermia
- Avoiding hyperglycemia and hypoglycemia

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## MECHANISTIC TREATMENT TO PREVENT BRAIN INJURY FROM CEREBRAL ISCHEMIA (TEMPORARY CLIP PLACEMENT)

- Reduce brain metabolism
- Calcium: blocking of VDCC, AOCC (EAA inhibitors) or release from ER
- Sigma receptor agonist (decrease release of EAA or impair their ability to act at receptor)
- Oxygen radical scavengers
- Inhibitors of nNOS and iNOS
- Stimulators of eNOS
- Protease inhibitors
- Anti-inflammatory/adhesion agents

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MECHANISTIC TREATMENT TO PREVENT BRAIN INJURY FROM CEREBRAL ISCHEMIA

Mechanistic treatment only effective in rodents

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HYPOTHERMIA?

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Table 3. Outcomes.<sup>a</sup> IHAST 2 Todd MM, NEJM 352:135, 2005

Outcome	Hypothermia Group		Normothermia Group		P Value <sup>f</sup>	Odds Ratio (95% CI) <sup>g</sup>
	No. Analyzed	No. with Score (%)	No. Analyzed	No. with Score (%)		
Score for Glasgow Outcome Scale	499		501			
1 (Minor or no disability) <sup>h</sup>		329 (66)		314 (63)	0.32	1.14 (0.88–1.48)
2 (Moderate disability)		105 (21)		108 (22)		
3 (Severe disability)		35 (7)		47 (9)		
4 (Vegetative state)		1 (<1)		0		
5 (Death) <sup>i</sup>		29 (6)		32 (6)		
Rankin score	499		501			
Score 0 or 1 (mild or no neurologic disability)		333 (67)		318 (63)	0.32	1.14 (0.88–1.49)
Score for Barthel's index <sup>j</sup>	469		468			
95–100		416 (89)		403 (86)	0.23	1.27 (0.86–1.87)
60–90		29 (6)		35 (7)		
0–55		24 (5)		30 (6)		
Score for NIH Stroke Scale <sup>k,m</sup>	461		452			
0 (No deficit)		306 (66)		291 (64)	0.60	1.08 (0.82–1.42)
1–7 (Mild deficit)		139 (30)		138 (31)		
8–14 (Moderate deficit)		7 (2)		17 (4)		
15–42 (Severe deficit)		9 (2)		6 (1)		

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RISKS OF HYPOTHERMIA

- Increased incidence of morbid cardiac events (Frank et al., JAMA 277:1127, 1997)
- Coagulopathy (Staab et al., J Trauma 36: 634, 1994), not due to hypothermia induced platelet dysfunction (Faraday, Anesthesiology 88, 1579, 1998)
- WBC dysfunction and decreased number (Akriotis J Leukocy Biol 37:51, 1985)
- RBC sludging
- Poor release of oxygen from RBC.

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HYPOTHERMIA IS NO LONGER INDICATED AS AN TREATMENT TO PREVENT POST-ISCHEMIC NEUROLOGIC INJURY (EXCEPT IF YOU ARE TAKING THE 2015 ACLS RECERTIFICATION EXAMINATION). EFFICACY OF REGIONAL CEREBRAL HYPOTHERMIA (MICROCATHETERS) IS CURRENTLY UNDER INVESTIGATION

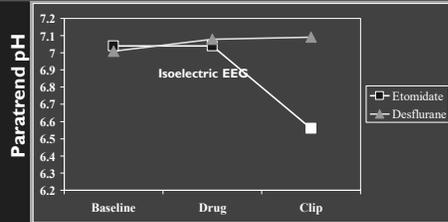
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INHALED ANESTHETICS?

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## DESFLURANE PREVENTS ISCHEMIA-INDUCED ACIDOSIS IN HUMANS (IMPROVED COLLATERAL FLOW?)

HOFFMAN WE ANESTHESIOLOGY 88:1188, 1998



Should desflurane or etomidate/propofol be used for burst suppression during aneurysm or CEA surgery?

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## PROBLEMS WITH HIGH DOSE DESFLURANE

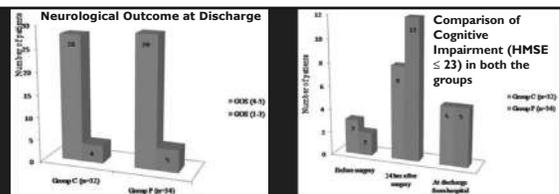
Cost Prevents neuromonitoring

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## PROPOFOL?

- Antioxidant (free rad scavenger) (Aarts et al., FEBS Lett 357:83, 1995)
- Decrease in CMRO<sub>2</sub> and CBF/ICP
- Prevents neuronal injury in an *In Vitro* model of anoxia-reoxygenation (DeLa Cruz et al., Brain Res 800:136, 1998)
- Prevents neuronal injury (as compared to isoflurane) in a model of transient MCAO in rats (Tsai et al., Acta Anaesthesiol Sin 32:99, 1994)
- Does not improve neurologic outcome in cats exposed to incomplete global ischemia (Weir JNA 1:284, 1989)
- **At burst suppression doses, does not improve neurologic outcome following valve surgery** (Roach, Anesth 90:1255)

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Variables	Group C (n=32)	Group P (n=34)	P value
Hematoma	3 (9.4%)	3 (8.8%)	1.0
Vasospasm	8 (25.1%)	9 (26.5%)	0.66
Cerebral infarct	5 (15.6%)	5 (14.7%)	1.0
Tracheostomy	2 (6.1%)	2 (5.9%)	1.0
ICU stay (days)	4±2.7	5.2±4.9	0.23
Total hospital stay (days)	12.0±11.2	11.5±6.8	0.81

C - Control, P - Propofol

Mahajan C, Chouhan RS, Rath GP, Dash HH, Suri A, Chandra P S, Mahajan A. Effect of intraoperative brain protection with propofol on postoperative cognition in patients undergoing temporary clipping during intracranial aneurysm surgery. Neuro India 2014;62:262-8

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## NITROUS OXIDE

- Decreases efficacy of Barbiturates as a neuroprotectant (Warner et al., Anesthesiology 73:686, 1990)
- Decreases efficacy of isoflurane as a neuroprotectant (Baughman et al., Anesthesiology 70:767, 1989)
- May worsen outcome because of an increase in CMRO<sub>2</sub>
- Alone provides inadequate anesthesia - high catecholamine concentration may contribute to worse outcome
- **Increases transient neurologic deficits in humans exposed to temporary clipping for aneurysm surgery** (Pasternak JJ et al., Anesthesiology 110:563, 2009)

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Metric	Univariate Analysis		Multivariate Analysis			
	Nitrous Oxide Group	No Nitrous Oxide Group	P Value	Odds Ratio	95% CI	P Value
ENID, yes or no	199	242	0.108	1.78	1.08-2.95	0.025
DIND - yes	55 (28)	51 (21)				

In summary, use of nitrous oxide in a group of patients at high risk for cerebral ischemia had no detrimental effect on long-term gross neurologic or neuropsychological function. Nitrous oxide use was associated with an increased risk of developing DIND, but this did not correlate with long-term outcome. ....There is no evidence to support the unconditional avoidance of nitrous oxide in patients at risk for cerebral ischemia.

Metric	Univariate Analysis		Multivariate Analysis			
	Nitrous Oxide Group	No Nitrous Oxide Group	P Value	Odds Ratio	95% CI	P Value
Impairment on at least 1 neuropsychological tests, yes or no	187	221	0.008	0.56	0.36-0.89	0.013
Impairment - yes	187 (54)	148 (67)				

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Alpha 2 agonists do not protect human brain from ischemia induced injury. May prevent post-op delirium following deep GA

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**No Association between Intraoperative Hypothermia or Supplemental Protective Drug and Neurologic Outcomes in Patients Undergoing Temporary Clipping during Cerebral Aneurysm Surgery**

Archives of Neurology 2010; 67:1280-1285  
 Findings from the Intraoperative Hypothermia for Aneurysm Surgery Trial  
 Brackley J, Hindman M.D., Emilio C, Boyman, Ph.D., Wolfgang K, Pfisterer, M.D., J. Kerven, G. Torres, Ph.D., S. Mikovics, M. Tocco, M.D. on behalf of the ISACT Investigators

Table 5. Multivariate Models with Variables of Interaction Terms (Odds Ratio)

Outcome	Variable	P Value (95% CI)
Good outcome (no neurologic deterioration) at 3 mo after surgery	Temperature (hypothermia vs. normothermia) at induction	0.584 (0.18-1.86)
	Supplemental protective drug (propofol, fentanyl, rocuronium) vs. none	0.582 (0.18-1.86)
	Normothermia vs. hypothermia (1-2°C)	0.916 (0.31-2.64)
	Normothermia vs. hypothermia (3-4°C)	0.280 (0.10-0.78)
	Normothermia vs. hypothermia (5-6°C)	0.188 (0.07-0.48)
	Normothermia vs. hypothermia (7-8°C)	0.181 (0.07-0.48)
	Normothermia vs. hypothermia (9-10°C)	0.088
	Normothermia vs. hypothermia (11-12°C)	0.170 (0.06-0.47)
	Normothermia vs. hypothermia (13-14°C)	0.084 (0.03-0.23)
	Normothermia vs. hypothermia (15-16°C)	0.202 (0.08-0.51)
Good outcome (no neurologic deterioration) at 3 mo after surgery	Temperature (hypothermia vs. normothermia) at induction	0.244 (0.08-0.68)
	Supplemental protective drug (propofol, fentanyl, rocuronium) vs. none	0.142 (0.05-0.38)
	Normothermia vs. hypothermia (1-2°C)	0.916 (0.31-2.64)
	Normothermia vs. hypothermia (3-4°C)	0.280 (0.10-0.78)
	Normothermia vs. hypothermia (5-6°C)	0.188 (0.07-0.48)
	Normothermia vs. hypothermia (7-8°C)	0.181 (0.07-0.48)
	Normothermia vs. hypothermia (9-10°C)	0.088
	Normothermia vs. hypothermia (11-12°C)	0.170 (0.06-0.47)
	Normothermia vs. hypothermia (13-14°C)	0.084 (0.03-0.23)
	Normothermia vs. hypothermia (15-16°C)	0.202 (0.08-0.51)

80

**Importance of Metabolic Substrate**

- Severe hypo- or hyper-glycemia is detrimental to neurologic outcome following ischemia (Sieber et al)
- Alteration in glucose value effects metabolic supply and intracellular pH (Hurn et al)
- Tight control of blood glucose has never been shown conclusively to prevent ischemic brain injury in humans
- My practice: maintain glucose >80 and <180 mg/dl.

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**MY APPROACH FOR INTRAOPERATIVE CARE FOLLOWING A-SAH**

- Pre-oxygenate
- "Modified" Rapid Sequence Induction
- Dose induction drugs (Propofol, fentanyl, rocuronium) to avoid hypertension
- DL with deep GA (+/- LTA) to avoid BP spike
- 2 Large Bore (16 ga or larger) IV and arterial line (placed after induction)
- If CVP required for access (large bore not available), consider femoral or axillary/subclavian
- +/- Scalp block
- Cardiac pacing pads applied if plan intraoperative adenosine
- Maintenance with Neuromonitoring friendly agents (TIVA+); Propofol or Alfentanil for pin placement; BIS or EEG to facilitate timely emergence
- OG tube for nimodipine; push syringes to increase or decrease BP
- Plan for emergence for neurologic examination and extubation as indicated

82

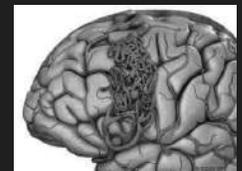
**INTRAOPERATIVE ADMINISTRATION OF ANTICONVULSANTS**

- Lack of consistent efficacy to reduce post-operative seizures
- CV depressant effects of anticonvulsants are worse during GA
- Change effective half life of NMJ blocker
  - Acute administration inhibit Ach release at the nerve terminal resulting in **acute increased sensitivity** to NDMR
  - After 2 weeks of therapy they cause increased Ach receptor number
  - Induce liver metabolism of NDMR
  - Increase release of acute phase reactant proteins that bind to many drugs (changing the volume of distribution of the NDMR drugs)

83

**CEREBRAL ARTERIO-VENOUS MALFORMATION (AVM)**

- Presenting signs and symptoms (HA, Seizures, Hemorrhage)
- Natural Course (Bleeding)
- Associated cerebral aneurysms
- Embolization, Gamma knife and/or open surgery
- Anesthesia issues
- Normal Pressure Breakthrough



84

Spetzler-Martin Intracranial AVM grading scale	
	Score
<b>Size</b>	
0 to 3 cm	1
3.1 to 6.0 cm	2
>6 cm	3
<b>Location</b>	
Noneloquent brain area	0
Eloquent brain area*	1
<b>Deep venous drainage</b>	
Absent	0
Present	1

Score = sum of all categories, with lesions graded I to V based upon total sum (eg, grade I = 1 point).  
 \* Associated with significant neurologic impairment (eg, language area, motor cortex, others).  
 From: Spetzler RF, Martin NA, J Neurosurg 1986; 65:476.

85

**AVM TREATMENT**

- Surgery is standard for most
- Radiosurgery (Gamma Knife) should be considered for deep, small AVM without bleeding; cure can occur in 1 to 3 years
- Embolization is not a treatment for cure. It is often implemented prior to surgery to decrease surgical risks

86

**ANESTHETIC MANAGEMENT OF SURGICAL REMOVAL OF CEREBRAL AVM**

- Same as for cerebral aneurysm PLUS very large bore access if incompletely embolized preoperatively
- Not usually associated with vasospasm or hyponatremia

87

**NORMAL PRESSURE BREAK THROUGH (COMPULSIVE AND COLLABORATIVE MANAGEMENT OF BP)**

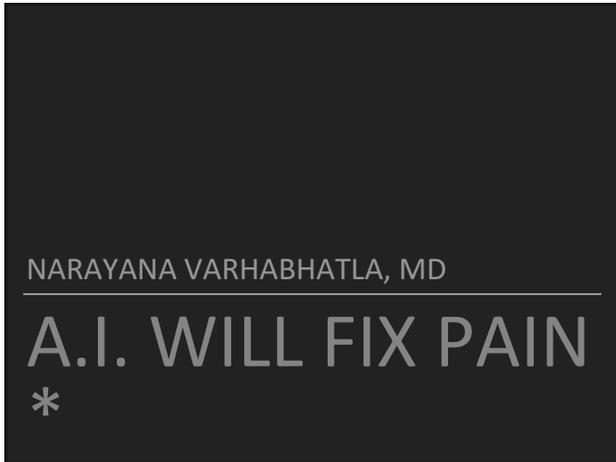
- “The occurrence of multifocal areas of hemorrhage associated with cerebral edema in the postoperative of totally-resected high-flow arteriovenous malformations (AVMs)” Mattei TA BJNS 26:786, 2012
  - Impaired autoregulation
  - Abnormal capillaries
  - Impaired venous drainage

88

**TAKE HOME POINTS**

- Anesthesia for carotid endarterectomy
  - Avoid poor perfusion during clamping; anesthetic tailored for optimal neuro-monitoring; compulsive management of CV variables to avoid perioperative MI and post-op bleed; post-op recognize and treat neck hematoma
- Anesthesia for cerebral endovascular clot retrieval
  - Timely implementation of anesthetic; avoid hyperventilation; adhere to anesthetic request (MAC vs GA) of proceduralist
- Anesthesia for cerebral aneurysm surgery
  - Avoid HTN prior to clip placement; CV control in compliance with surgeon goal during temporary clipping; anesthetic tailored for neuro-monitoring; vascular access to support rupture; close control of serum electrolytes; vigilance regarding VAE
- Anesthesia for cerebral AVM resection
  - Similar consideration as aneurysm care plus BP control to avoid normal pressure break through

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1



2



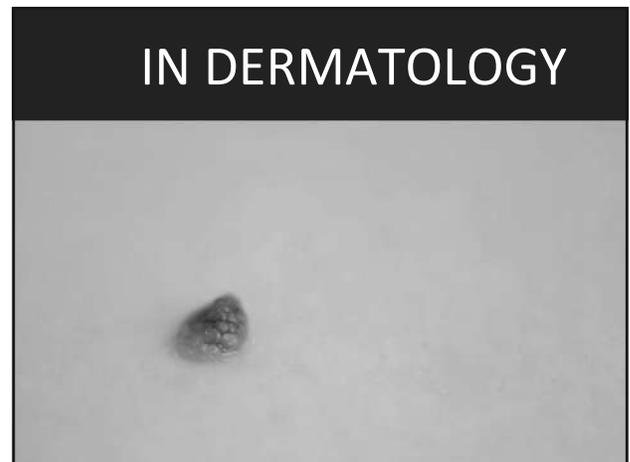
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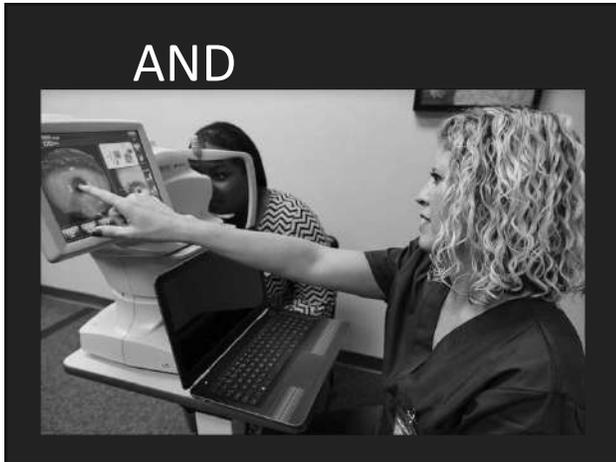
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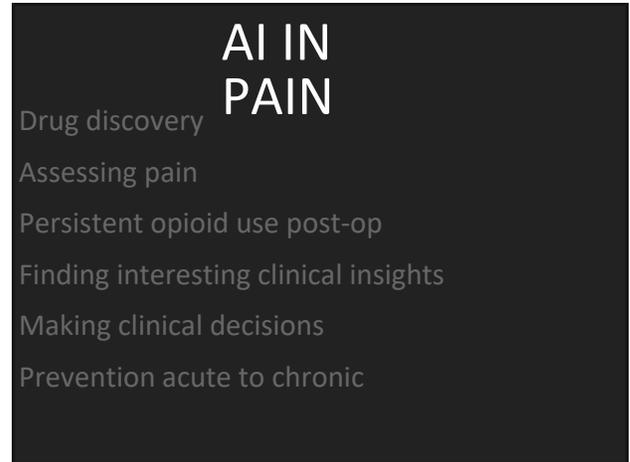
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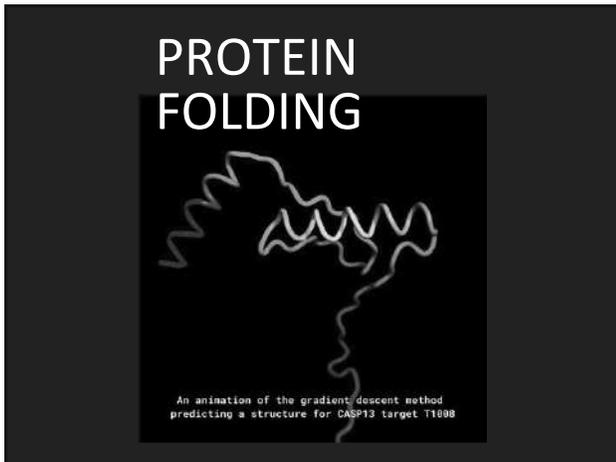
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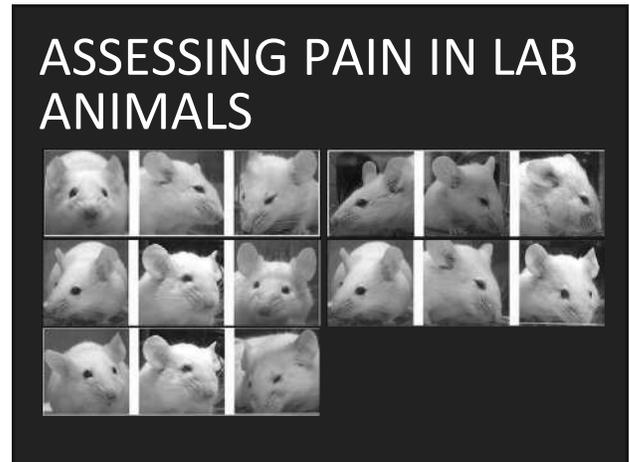
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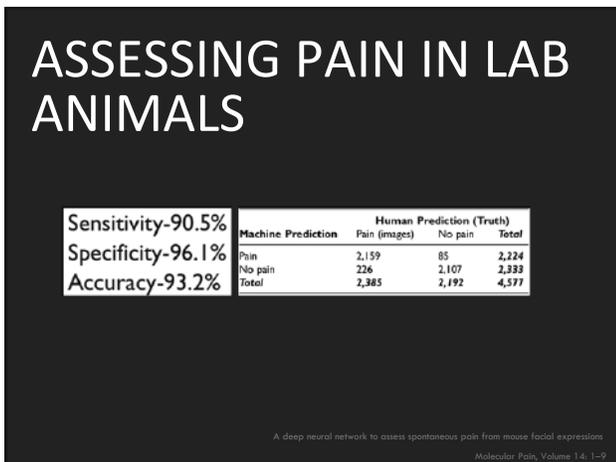
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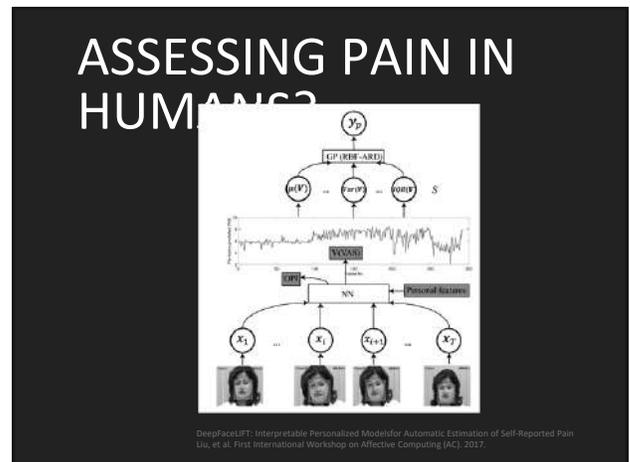
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10



11



12

# POST OP PAIN IN CHILDREN

Source	Condition	Study Visit Number		
		1	2	3
Child	Ongoing	4.2 ± 0.33	2.7 ± 0.31	0
	Transient	4.06 ± 0.28	3.61 ± 0.22	0.08 ± 0.03
Machine	Ongoing	4.3 ± 0.05	2.5 ± 0.06	0.25 ± 0.06
	Transient	4.90 ± 0.10	3.0 ± 0.09	0.80 ± 0.15
Nurse	Ongoing	1.72 ± 0.26	0.99 ± 0.18	—
	Transient	3.04 ± 0.24	2.59 ± 0.22	—
Parent	Ongoing	3.02 ± 0.33	2.04 ± 0.25	0.12 ± 0.05
	Transient	5.56 ± 0.28	3.49 ± 0.22	0.37 ± 0.07

Automated Assessment of Children's Postoperative Pain Using Computer Vision. PEDIATRICS Volume 136, number 1, July 2015.

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# INSIGHTS FROM HUGE DATA SETS

## Machine Learning for Prediction of Sustained Opioid Prescription After Anterior Cervical Discectomy and Fusion

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# INSIGHTS FROM HUGE DATA SETS

## Predicting inadequate postoperative pain management in depressed patients: A machine learning approach

Wenyan Peng, PhD, Steven D. Smith, PhD, Christopher A. Harte, PhD, Robert W. Harty, MD, PhD, David A. Clark, MD, Andrew P. Grossman, MD, PhD, and Roger B. Fillingim, PhD

Time Period	Total Cohort	SHAP		SHAP		P-Value
		Preop	Postop	Preop	Postop	
Discharge Pain, mean (SD), (min, max)	0.434	0.230 (0.155, 0.377, 0.159)	0.101 (0.20, 0.10, 0)	0.0822	0.492 (0.16, 0.16, 0.22)	0.9960
F-score Postoperative, mean (SD), (min, max)	2.680	2.774 (2.22, 4.14, 10)	1.658 (0.30, 9.10)	< .0001	2.139 (2.19, 1.8, 1)	0.9430
F-score Postoperative, mean (SD), (min, max)	0.489	0.484 (0.89, 1.4, 1)	0.210 (0.89, 1.15, 1)	0.0132	0.798 (0.15, 0.74, 0.44)	0.7939

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# MAKING CLINICAL DECISIONS

## Evaluation of three machine learning models for self-referral decision support on low back pain in primary care

Wendy Oude Nijeme-d'Onofry, Lex van Velsen, Manos Poul, Catharina G.M. Groothuis-Oudshoorn, Ronko Smeets, Harrie Vriens

16

# MAKING CLINICAL PREDICTIONS

## Teaching a Machine to Feel Postoperative Pain: Combining High-Dimensional Clinical Data with Machine Learning Algorithms to Forecast Acute Postoperative Pain

Patrick A. Tighe, MD, MS, Christopher A. Harte, PhD, Robert W. Harty, MD, PhD, David A. Clark, MD, Andrew P. Grossman, MD, PhD, and Roger B. Fillingim, PhD

POD1*	Yes/No	Outcome: Moderate to Severe Pain	
		Yes	No
Prediction: moderate to severe pain	Yes	880	443
	No	401	699

Sensitivity = 0.68696331  
Specificity = 0.612084063

POD3†	Yes/No	Outcome: Moderate to Severe Pain	
		Yes	No
Prediction: moderate to severe pain	Yes	399	204
	No	279	629

Sensitivity = 0.588495575  
Specificity = 0.755102041

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# The pain of pain or: Patience for Patients

Alan Bielsky

1

- ### Objectives
- Discuss mechanisms of acute on chronic pain
  - Explain the practical use of multimodal analgesia
  - Detail different regimens that may benefit the chronic pain patient

2

- ### The Problem
- 35 yo male with chronic lower back pain s/p spinal chord stimulator
  - Obesity and OSA
  - Fibromyalgia
  - Major depressive disorder
  - Presents for Lap Chole

3

### The surgeon

- No regional for Lap Chole!
- My Lap Chole's don't hurt
- This patient is going to do fine

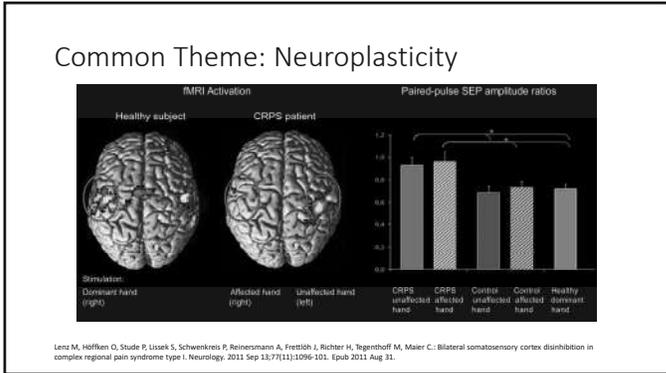


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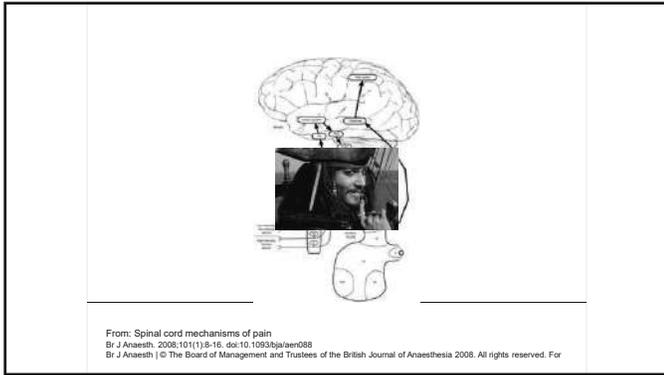
### The anesthesiologist



5



6



7

### Risk factors for severe postoperative pain

- Preexisting pain
- Anxiety
- Age
- Type of surgery

*Ijp et al. Predictors of Postoperative Pain and Analgesic Consumption: A Qualitative Systematic Review. Anesthesiology December 2009.*

8

### Risk factors for opioid abuse

- Preoperative opioid use
- Preoperative benzodiazapene use
- Depression
- Male
- Age greater than 50 years
- Substance abuse history

9

### The bad outcome

- Patient stays past due
- Patient complains about lack of pain control
- Patient goes home on unreasonable analgesic regimen

10

### Let's pivot then

A black and white photograph showing a patient lying in a hospital bed. A nurse is standing at the foot of the bed, and another person is partially visible on the right side of the frame. The room appears to be a standard hospital ward.

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### Chronic pain....

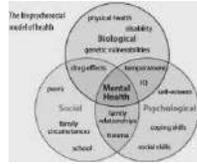
“pain intensity is not the best measure of the success of chronic-pain treatment. When pain is chronic, its intensity isn't a simple measure of something that can be easily fixed. Multiple measures of the complex causes and consequences of pain are needed to elucidate a person's pain and inform multimodal treatment”

*Balantyne JC, Sullivan MD . NEJM 2015*

12

Think about it

- Neuroplastic changes to somatosensory system
- Upregulation of opioids and GABA receptors
- Psychosocial change
- Intraoperative nerve injury and tissue damage



13

So what do you do?

- Patience
- Multimodal analgesia
- Aggressive regional
- Patience
- Patience
- Avoid worsening the hijacking of the somatosensory system

14

Multimodal Therapy

- Using multiple methods to achieve highest satisfaction
- Hit multiple targets
- Minimize side effects and toxicity
- Maximize function
- Opioid reduction to rescue role only

15

Step 1: therapeutic relationship

- Establish that you are advocating for the patient
- Set and explain boundaries
- Continue pain meds
- Expect for plans to change
- Be patient
- Set realistic goals of analgesia

16

Most importantly

- Forget pain scores. They are of no use to you now!!!!
- Focus on functional pain relief
- Don't let volume control the amplitude of your reaction

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Tools!

- Regional
- Ketamine
- Lidocaine
- Esmolol
- Other stuff

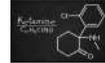
18

### Aggressive Regional

- Benefit of regional usually outweighs risks
- Takes some convincing of surgeons
- May seem like overkill
- It isn't

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### Ketamine



20

### What is ketamine

- Phencyclidine anesthetic
- Dissociative anesthetic

21

### How does ketamine work?

- Reversible antagonism of the N-methyl-D-aspartate receptor 2-4
- $\mu$ -opioid receptors
- Muscarinic receptors
- Monoaminergic receptors
- $\gamma$ -aminobutyric acid receptors

22

### Where do we use it?

- First given to soldiers in Vietnam
- Extensive use as an anesthetic agent
- First line drug in battlefields, underdeveloped countries
- Typically given IV, but can be given IM/SC and orally.

23

### Dose and Effect and effects



24

Side effects

- Sedation
- Somnolence
- Dizziness
- Sensory illusions
- Hallucinations
- Nightmares
- Blurred Vision



25

REGIONAL ANESTHESIA AND ACUTE PAIN  
SPECIAL ARTICLE

**Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists**

*Eric S. Savarese, MD,\* Eugene R. Fricton, MD,\* Ashkaner Benzonononon, MD,† Robert W. Tharpe, MD, PhD,‡  
Ajay D. Hirani, MD, MSc,§ Nancy Narasim, MD, PhD,|| Amy Blum, MD, MIBS,\*\* Fred N. Datta, MD,††  
William H. Bennett, MD,‡‡ and Steven P. Cohen, MD,§§*

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In whom should we consider subanesthetic ketamine?

- **Patients undergoing painful surgery** (grade B recommendation, moderate level of certainty).
- **Opioid-dependent or opioid tolerant patients undergoing surgery** (grade B recommendation, low level of certainty).
- **Opioid dependent or opioid-tolerant patients with acute or chronic sickle cell pain** (grade C recommendation, low level of certainty).
- For **patients with sleep apnea**, ketamine may be considered as an adjunct to limit opioids (grade C recommendation, low level of certainty).

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How do you run it

- Bolus dosing should not exceed 0.35 mg/kg, and infusions for acute pain generally.
- Infusions generally should not exceed 1 mg/kg/hr, though adverse effects will generally limit infusion rates below 0.5 mg/kg/hr

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Does the evidence support it?

“Overall, we conclude that moderate evidence supports use of subanesthetic IV ketamine bolus doses (up to 0.35 mg/kg) and infusions (up to 1 mg/kg per hour) as adjuncts to opioids for perioperative analgesia (grade B recommendation, moderate level of certainty)”.

29

Are there contraindications?

- poorly controlled cardiovascular disease
- pregnancy
- active psychosis
- Severe liver disease
- Caution with moderate liver disease hepatic dysfunction, evidence supports

30

### What about ICP

- Should be avoided in uncontrolled ICP and IOP
- Evidence is only C level here
- Historic usage in polytrauma

31

### Practicalities

- Prone to errors
- Run in a secure box
- You don't have to wear it

32

### Lidocaine



33

### Lidocaine infusions: What is it?

- Effects come with infusion rates that mimic levels seen with epidural administration
- Clinical effect (8 hrs) exceeds half life of 1.5 hrs.

34

### Huh?? Lidocaine: Why?

- Interferes with pro-inflammatory signaling
- Blocks excitatory responses in wide dynamic range neurons
- Seems to block the priming of polymorphonuclear granulocytes

35

- Unstable coronary disease
- Recent MI
- Heart failure
- Heart block
- Electrolyte disturbances
- Liver disease
- Cardiac arrhythmia disorders
- Seizure disorders

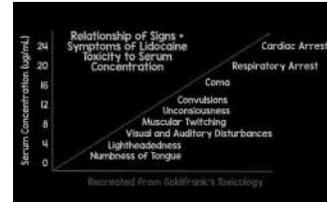
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So what do you do?

- Bolus 1 mg/kg
- Infusion of 2 mg/kg/hr
- Steady state reached at 8 hours
- No evidence for use beyond 24 hours
- At these lower infusion rates, no need to check levels

37

Toxicity- Peripheral to Central



38

On the floor?

- Same monitoring as an opioid PCA
- Nurse education vital
- Ongoing observation needed
- Select your own place

39

Esmolol



40

Esmolol? Why

- Mechanism unclear
- Thought to be related to voltage gated calcium channels being regulated by beta adrenergic antagonists
- Might also block hippocampal activation by glutamate receptors

41

Esmolol How

- Loading dose of 0.5 mg/kg
- Run from 200-400 mcg/kg/min
- Titrate for BP and HR
- Contraindicated in reactive type lung disease

42

### Does it work?

- Evidence seems to be in big bowel cases and chest cases
- Limited data in acute on chronic pain
- Spine surgery has benefit
- Hysterectomy and breast surgery have not shown benefit

43

### What about what not to do?

44

### Things to avoid

- Remifentanyl: Hyperalgesia
- Discontinuing home meds: Withdrawal
- Minimizing pain: Why
- Silver Bullet Theory

45

### Thinking outside the box

- TENS units!
- Lidoderm patches
- Massage/acupuncture/healing touch
- Whatever gets you through the night

46

### Back to our patient

- 35 yo male with chronic lower back pain s/p spinal chord stimulator
- Obesity and OSA
- Fibromyalgia
- Major depressive disorder
- Presents for Lap Chole

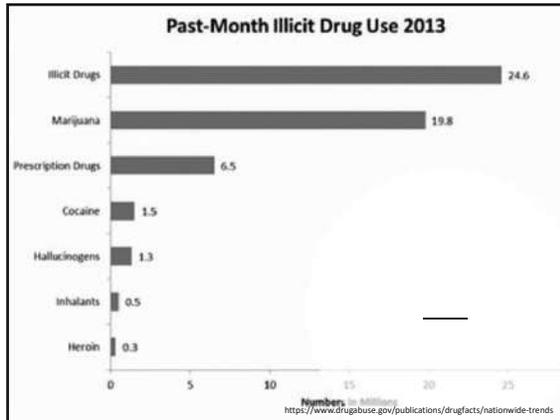
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### Reasonable Things

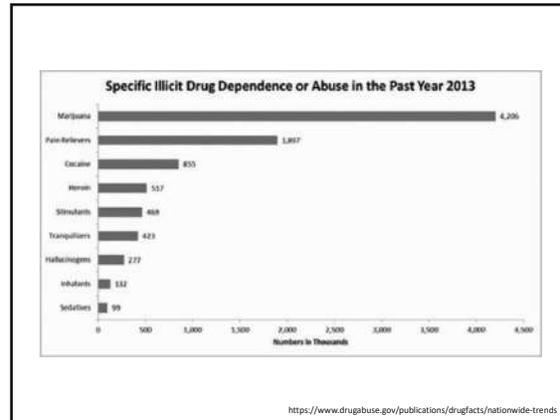
- General anesthetic
- Continue home meds
- Ketamine infusion x 24 hrs
- Quadratus Lumborum block
- PO celecoxib and acetaminophen
- Postop metaxolone, low dose oxycodone
- Acupuncture session at POD 3

48





7



8

### Cannabis Basics

- Marijuana = *Cannabis sativa* (also *indica*, *ruderalis*, *afghanica*)
  - Cultivation can be traced back to 10,000 BC
    - First evidence of medicinal use (analgesic) in 4,000 BC
  - High degree of inbreeding or hybridization
- Synthetic cannabinoids (eg, spice): highly potent, up to 85x more than THC

Piomelli D and Russo EB (2016) Cannabis Cannabinoid Res 1(1): 44-46.  
Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

9

### Cannabis Basics

- Multiple active components
  - Psychoactive:
    - Δ<sup>9</sup>-tetrahydrocannabinol (THC)
      - Δ<sup>9</sup>-tetrahydrocannabinol
        - is psychoactive, found in trace amounts if at all
      - Cannabinol
        - Nonsynthetic oxidative breakdown product of THC found in old Cannabis
        - 25% the potency of THC
      - Tetrahydrocannabinarin (THCV)
        - Neutral antagonist of CB<sub>1</sub> at low doses but agonist at high doses
        - Not found in high levels in most Cannabis strains
      - Cannabidiol
        - Non-intoxicating BUT
        - Anti-anxiety, anti-psychotic, anti-depressant?
    - Anti-inflammatory and other
      - CBD
        - Numerous other minor cannabinoids
          - Cannabichromene, cannabigerol, cannabidivarin
        - Flavonoids
          - May be anti-arthritic
          - Apigenin
          - quercetin
        - Numerous terpenoids
          - Marijuana smell
          - In addition to anti-inflammatory, also modulate THC effects
          - Myrcene: sedating terpene of "indica"
          - High limonene can reduce or eliminate the short-term memory impairment caused by THC.
  - "Herbal Synergy" between these components

Piomelli D and Russo EB (2016) Cannabis Cannabinoid Res 1(1): 44-46.  
Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

10

### Cannabis Basics

- CANNOT predict the biochemical content based upon physical appearance
  - As high-CBD is rather new to the market, differences users perceive between high-THC strains can be attributed to terpenoid content (not CBD)
    - Sedation of "*indica*" is falsely attributed to CBD, which is stimulating at low-moderate doses, and rather due to myrcene, a monoterpene that resembles a narcotic
    - Terpenoids are rarely assayed and never reported to the consumer, so your patient will have no idea what they take!

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### Endocannabinoid System

- Endocannabinoids
  - Chemically similar to arachidonic acid
    - Arachidonylethanolamide (AEA) aka anandamide
    - 2-arachidonoylglycerol (2-AG)
    - Also N-oleoylethanolamine and N-palmitoylethanolamine
- Act primarily through 2 G-protein-coupled receptors
  - CB1
    - Expressed on nerve axons and presynaptic terminals
      - Retrograde signaling: depolarization of the postsynaptic cell results in production and release of eCBs that then activate the presynaptic CB1 receptors. → overall inhibitory effect on the presynaptic cell
    - Also in thyroid, adrenals, liver, adipose tissue, GI tract, reproductive organs and immune cells
  - CB2
    - Activation causes increased intracellular Ca<sup>2+</sup> via phospholipase C
    - Expressed on immune cells
      - (but also chondrocytes, osteocytes, fibroblasts, FLSs and DRG as well as microglia)

Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498

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### Endocannabinoid System

- CB1
  - Expressed in CNS
    - Throughout the brain, especially in frontal cortex, basal ganglia and cerebellum
      - Low expression in brainstem → low toxicity?
    - Also spinal cord
    - Modulates multiple brain functions
      - Executive
      - Reward
      - Emotional
      - Memory processing
    - Direct interactions with endocannabinoids
    - Indirect effects on glutamatergic, GABAergic and dopaminergic systems

Wu, J. (2019) Acta Pharmacol Sin.

13

### Endocannabinoid System

- CB2
  - “Peripheral” cannabinoid receptor
    - But identified throughout the CNS
      - Lower expression levels so maybe not normally involved in cannabis effects
      - Inducible: upregulated under certain conditions like addiction, inflammation, anxiety, epilepsy
      - Mainly expressed in post-synaptic (somatodendritic) areas vs CB1s in presynaptic terminals
        - » May have opposite role from CB1
    - Thought to be important for neuroprotection

Wu, J. (2019) Acta Pharmacol Sin.

14

### Endocannabinoid System

- Other receptors for endocannabinoids
  - TrpV1: ligand-gated cation channel
    - Pain receptor: responds to capsaicin, high temp and low pH/high H+
    - Mostly on C-fibers and Aδ
    - Activated by AEA, CBD and cannabigerol
  - “CB3” aka G protein-coupled receptor 55 (GPR55)
    - Expressed in CNS, immune and GI systems
  - Peroxisome proliferator-activated receptor-α (PPARα)
    - Fatty-acid-activated transcription factor
    - Expressed on skeletal muscle and in liver
      - Site of action of fibrates (for hypercholesterolemia)
    - Stimulated by several cannabinoids, such as AEA, THC and a synthetic cannabinoid
- System also includes enzymes and proteins responsible for synthesis, degradation and re-uptake
  - AEA synthesis involves different enzymes that 2-AG synthesis
  - Both AEA and 2-AG degraded by either oxygenation or hydrolysis
    - Fatty-acid amide hydrolase (FAAH) degrades AEA
    - Monoacylglycerol lipase degrades 2-AG
    - Oxygenation of both by either COX-2, lipoxygenases or CYP450 enzymes

Katz-Talimor D (2018) Nat Rev Rheumatol 14(8): 488-498

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### Anti-inflammatory effects of endocannabinoids

- Endogenous cannabinoids are produced and released by activated immune cells
  - Activation of MΦs, PBMCs and dendritic cells with LPS results in increased production of eCBs
    - Activated PBMCs also show reduced expression of AEA-degrading enzyme Fatty-Acid Amid Hydrolase (FAAH)
    - Activation of immune cells affects the expression of CB<sub>1</sub>R and CB<sub>2</sub>R on these cells
      - Varying studies show increase or decrease, likely related to cell-type studied and stimulatory agent used
  - May be chemotactic for several types of immune cells in *in vitro* studies
    - Morphine is similarly chemotactic and shares this neuroimmune function w/ eCBs
  - May also bias T<sub>H</sub>-cells, suppressing T<sub>H</sub>-1 activity and increasing T<sub>H</sub>-2 activity

Klein TW (2005) Nat Rev Immunol 5(5): 400-411.

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### Endocannabinoid System

- For the most part, cannabinoids, including THC, suppress the production of immune-response cytokines (TNF, GCSF, IL-6, etc.)
  - May induce regulatory cytokines such as IL-10
  - In animal models of TBI, reduces brain edema after closed head injury
    - Results in humans not robust
  - May suppress GI motility and ulceration in animal models of colitis
  - In animal models of MI, this may result in reduced tissue injury
    - Other Cardiovascular effects:
      - Cannabinoids mediate vasodilation: eCB levels increased in patients with endotoxic shock and antagonists can prevent hypotension in animals
        - » Levels of AEA and 2-AG increased in patients with endotoxic shock
        - » CB1R antagonists prevented LPS-induced hypotension in animals
      - cannabinoids are hypotensive via CB1R and anti-inflammatory via CB2R or non-CBR pathways

Klein TW (2005) Nat Rev Immunol 5(5): 400-411.

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### Endocannabinoid System

Cannabinoid receptor dependent			Cannabinoid receptor independent		
Neurodegeneration	Inflammatory bowel disease	Brain injury	Vascular inflammation	Arthritis	
<ul style="list-style-type: none"> <li>• ↑ Cannabinoids</li> <li>• ↓ TNF responses</li> <li>• ↓ Neuroinflammation</li> </ul>	<ul style="list-style-type: none"> <li>• ↓ Sub-ventricular lesions</li> <li>• ↑ Prostaglandins</li> <li>• ↑ Nitric oxide</li> <li>• ↓ COX-2/IL-6/IL-1</li> </ul>	<ul style="list-style-type: none"> <li>• ↓ Cell death</li> <li>• ↓ Neuroinflammation</li> <li>• ↓ CB1R binding</li> <li>• ↑ Neuroinflammation</li> <li>• ↓ CB2R</li> </ul>	<ul style="list-style-type: none"> <li>• ↑ Vascular lesions</li> <li>• ↓ Prostaglandins</li> <li>• ↓ COX-2</li> <li>• ↓ IL-1β</li> <li>• ↓ TNF</li> </ul>	<ul style="list-style-type: none"> <li>• ↑ Prostaglandins</li> <li>• ↑ Cell mediated immunity</li> <li>• ↑ IL-1β</li> <li>• ↑ TNF</li> </ul>	

Klein TW (2005) Nat Rev Immunol 5(5): 400-411.

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## Adverse effects of cannabinoids

- Nervous system
  - Acute effects on learning, attention and memory
  - Limited evidence of long-term effects on the above, but may be reduced even after abstinence
  - Chronic cannabis use does induce anatomical changes in the brain on imaging
    - Cerebellum, medial temporal cortex and frontal cortex as well as reduction in size of hippocampus
  - Effects may vary with the age of the user
    - More hazardous in adolescence

Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

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## Adverse effects of cannabinoids

- Mental health
  - Strong association between cannabis and development of psychosis
  - May slightly increase risk of depressive disorder
    - Increased incidence of SI, suicide attempts and completions
- Addiction
  - 9% of adult users develop cannabis dependence
    - Greater risk among male smokers, young users
    - May have large genetic component

Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

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## Adverse effects of cannabinoids

- Cardiovascular
  - Tachycardia and hypertension with acute low-dose use
    - Ectopic activity and T-wave abnormalities
  - Bradycardia and hypotension with chronic or high dose use
  - Acute MI: risk increased 5x in first hour after smoking
    - Increased cardiac output, myocardial VO<sub>2</sub>, catecholamines, carboxyHb and hypotension
  - Ischemic stroke
- Respiratory
  - Smoking effects: wheezing, phlegm, chronic bronchitis
    - Improved with cannabis cessation
    - Light-to-moderate smoking over 20 years likely does not adversely affect lung function, but heavier use may
    - Accidental overdose in children can lead to respiratory distress
- Mortality
  - Deaths in phase I study of a reversible inhibitor of FAAH

Nugent S (2017). Ann Intern Med 167(5): 319-331.  
Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.  
Beaulieu (2017) Can J Anaesth 64(12): 1236-1264.

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## Adverse effects of cannabinoids

- In clinical trials, the most common AEs include
 

– Fatigue	– Drowsiness
– balance problems	– dry mouth
– Confusion	– Hallucination
– Dizziness	– Nausea
– Disorientation	– Somnolence
– Diarrhea	– vomiting.
– Euphoria	

Whiting PF (2008) JAMA 313(24): 2456-2473

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## Adverse effects of cannabinoids

- 2008 systematic review of RCTs found more non-serious adverse events in cannabinoids than controls (RR 1.86) but no difference in serious adverse events
  - Common side effects: dizziness (#1), nausea, dry mouth, tachycardia and agitation
  - Rare: cardiovascular events, AKI, seizures, psychosis

Wang T, 2008. CMAJ. 178(13): 1669-1678

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## Adverse effects of cannabinoids

- More recent systematic reviews have found adverse events to be more common:
  - Whiting, 2015:
    - Any AE: 3.03 OR (95% CI, 2.42-3.80)
    - Serious AE: 1.41 (95% CI, 1.04-1.92)
    - W/drawal due to AE: 2.94 (95% CI, 2.19-3.96)
  - Stockings, 2018:
    - All AE: 2.33 (1.88-2.89)
      - Pooled event rate: 81.2% vs 66.2%
    - Serious AE: 1.82 (0.93-3.59)
    - W/drawal due to AE: 3.47 (2.64-4.56)

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### Cannabinoid Drug-Drug Interactions

- Cytochrome P450
  - Induces CYP1A2
  - Substrate for:
    - CYP3A4
    - CYP2C9
    - CYP2C19
- Combination of cannabis and EtOH increases plasma THC
- Case report of MI in 41 yo male who consumed cannabis and sildenafil
- Case report of GI bleed in patient on warfarin
  - INR 10.4-11.5 in 2 separate incidents
  - INR remained 1.1-4.4 after cannabis cessation

Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

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### Cannabinoid Drug-Drug Interactions

Potential drug interactions

Drug	Potential impact of interaction with cannabinoids	Ref.
Diazepam	Epileptogenesis	14
Diclofenac	Mixed old receptor can form a hexamer with CB1	15
Cocaine	Might cause tachycardia and angiotonia	16
Diazepam	Hypotension	17
Ethanol	THC in serum	18
Warfarin	THC in serum	19
Sildenafil	Myocardial infarction case report	20
Sildenafil	Transient cognitive changes, delirium and tachycardia case report	21
SSRIs	Myocardial infarction	22
Urticaria	Tachycardia	23
Barbiturates	CNS depression	24
Anti-cholinergic agents	Sedation	25
Opioids	Delirium	26

Katz-Talmor D (2018) Nat Rev Rheumatol 14(8): 488-498.

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### CBD

- Major non-psychoactive phytocannabinoid
- Anti-inflammatory analgesic
  - In mouse model of collagen-induced arthritis, CBD reduced severity, inflammatory cell infiltration, bone destruction, production of anti-collagen type II IgG1, IFN $\gamma$  production and TNF release
- Relatively low affinity for CBR
  - Partial agonist at CB1
  - Weak inverse agonist at CB2
    - May activate both indirectly by increasing AEA and 2-AG
  - Combo w/ THC synergistic
    - Entourage effect: better to use cannabis than synthetic cannabinoids

Piomelli D and Russo EB (2016) Cannabis Cannabinoid Res 1(1): 44-46.

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### PAIN

#### Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies

Emily Stockings<sup>1,2</sup>, Gabriele Campese<sup>1,2</sup>, Wayne D. Hall<sup>1,2</sup>, Suzanne Nisamen<sup>1,2</sup>, Dino Zagac<sup>1,2</sup>, Rahn Rahmani<sup>1,2</sup>, Bebin Mamon<sup>1,2</sup>, Michael Farnell<sup>1,2</sup>, Megan Viner<sup>1,2</sup>, Louisa Degenhardt<sup>1,2</sup>

- 2018 meta-analysis
- 104 studies identified
  - 47 RCTs (24 parallel, 23 cross-over)
  - 57 observational
  - Total 9,958 participants
- Nabiximols (Sativex)
  - In the UK, approved for MS spasticity
  - In Canada, also approved for MS neuropathic pain
- Nabilone
  - oral synthetic cannabinoid, mimics THC
- Oral THC
  - Extract
  - Synthetic: dronabinol (Marinol [cap] or Syndros [liquid])
    - Anorexia and weight gain in AIDS
    - Chemo n/v
  - Whole flower, inhaled (smoked or vaporized)

<https://www.bayer.ca/omr/online/sativex-dhcg-laps-04-01-2005-en.pdf>  
<https://www.bayer.ca/omr/online/sativex-gm-en.pdf>  
[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2006/018677r011lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677r011lbl.pdf)  
[https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2016/205252Orig1s000Appr.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2016/205252Orig1s000Appr.pdf)

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### Cannabis for CNCP: 2018 Meta-analysis

- Overall, cannabinoids were more likely than placebo to produce a 30% reduction in pain or significant reduction in pain intensity
- BUT
- These effects were **SMALL**
  - For 30% reduction in pain, OR 1.46 (95% CI 1.16-1.84)
    - 29.0% achieved this with cannabinoids vs 25.9% with placebo
    - However in observational studies, the pooled prevalence of 30% pain reduction was 72%
  - Change in pain intensity standardized mean difference was only -0.14 vs placebo (95% CI -0.20 to -0.08)
    - = reduction of **2.9mm on 100mm VAS!**
  - The longer the intervention, the smaller the effect
    - Single-administration and very short term (<4 weeks) studies remained significant, but longer studies >13 weeks, did not

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### Cannabis for CNCP: 2018 Meta-analysis

- No significant effect on physical functioning
- No difference in emotional functioning, nor depression or anxiety symptoms specifically
- 2x greater risk of study withdrawal, for any reason, if receiving cannabinoid
  - 3.47x odds of withdrawing due to AE
  - Those receiving placebo were more likely to withdraw due to lack of effects
- 2.33x greater risk of adverse events vs placebo
  - Dizziness (OR 5.52), cognitive or attention disturbance (OR 5.67), confusion and disorientation (OR 5.35)

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### Cannabis for CNCP: 2018 Meta-analysis

- Number Needed to Benefit: 24
  - 24 patients have to be exposed for 1 to achieve 30% reduction in pain
  - WAY higher than other analgesics
    - For neuropathic pain, previous studies show NNTB
      - Strong opioids: 4.3
      - Pregabalin: 7.7
      - TCAs: 3.6
- Number Needed to Harm: 6
  - 1 out of every 6 patients will experience an AE
    - Similar to opioids

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### More Meta-analyses Cannabis for Chronic Pain

- Whiting, 2015
  - Pooled studies of cancer pain and non-cancer pain

**Figure 2. Improvement in Pain**

Improvement in Pain NNTB	Controlled vs. Placebo (95% CI)	Weight (%)
Alvares et al., 2007	3.43 (1.03-5.81)	6.51
Subtotal		19.02
GW Pharmaceuticals, 2005	0.86 (0.54-1.37)	10.87
Langford et al., 2013	2.81 (1.22-4.50)	20.18
Nurmikko et al., 2007	1.35 (0.83-1.93)	9.84
Subtotal		14.04
Wang et al., 2010	0.90 (0.40-1.70)	4.61
Singh et al., 2014	1.97 (1.05-2.70)	14.91
Subtotal		15.41
<b>Overall</b>	<b>1.41 (0.99-1.70)</b>	<b>100.00</b>

- For NRS, nabiximols was associated with a greater average reduction in the NRS (WMD -0.46 [-0.8 to -0.11])

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### More Meta-analyses Cannabis for Chronic Pain

- Aviram, 2017: Pooled studies of cancer pain and CNCP

**Aviram 2017**

Study	Mean	SD	Total	Weight	Mean Difference (IV, Random, 95% CI)
Berman 2004 (Ref #12)	4.1	2.4	40	14.3%	-0.50 (-0.96, 0.06)
Frank 2009 (Ref #23)	6	2.4	96	12.6%	0.10 (-0.58, 0.78)
Langford 2013 (Ref #13)	4.5	2.2	167	17.2%	-0.20 (-0.86, 0.08)
Larivi 2014 (Ref #14)	6	1.2	64	11.3%	-0.40 (-0.78, -0.08)
Nurmikko 2007 (Ref #15)	5.8	1.4	63	6.2%	-0.50 (-1.41, 0.39)
Rog 2005 (Ref #16)	3.8	2.1	34	5.2%	0.00 (-1.30, 1.34)
Schrago 2010 (Ref #17)	4	2.9	15	3.3%	1.50 (0.58, 2.58)
Smeets 2004 (Ref #18)	4	2.7	24	6.0%	-1.00 (-2.30, 0.30)
Todd 2012 (Ref #19)	3.5	3.2	13	7.0%	-1.00 (-2.06, 0.06)
Turcotte 2015 (Ref #21)	3.5	1.4	8	5.0%	-2.10 (-3.52, -0.68)
<b>Total (95% CI)</b>			<b>488</b>	<b>100.0%</b>	<b>-0.65 (-0.84, -0.46)</b>

Heterogeneity:  $I^2 = 0.23$ ;  $Chi^2 = 22.55$ ,  $df = 9$  ( $P = 0.007$ );  $I^2 = 60\%$   
Test for overall effect:  $Z = 3.07$  ( $P = 0.002$ )

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### More Meta-analyses Cannabis for Chronic Pain

- Meng, 2017: Chronic Neuropathic Pain
  - Minimum study duration of 2 weeks

**Meng 2017**

Study or Subgroup	Experimental	Control	Total	Weight	Mean Difference (IV, Random, 95% CI)
Berman 2004 (Ref #12)	4.1	2.4	40	14.3%	-0.50 (-0.96, 0.06)
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### More Meta-analyses Cannabis for Chronic Pain

- Mücke, 2018: Neuropathic Pain Cochrane Review
  - Treatment duration  $\geq 2$  weeks,  $\geq 10$  patients per arm
  - For 50% reduction in pain, NNTB = 20
  - For 30% reduction in pain, NNTB = 11
  - Nervous system adverse events NNTH = 3;
  - Psychiatric disorder adverse events NNTH = 10
  - Study withdrawal due to AE NNTH = 25

**Mücke 2018**

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## More Meta-analyses Cannabis for Chronic Pain

- Nugent, 2017
  - Only plant-based or extracts (available in dispensaries)
    - Low strength evidence that defined THC:CBD ratio cannabis products may reduce neuropathic pain
      - Depends upon whether outcome reported was dichotomous (ie, 30% reduction in pain; cannabis more likely to show benefit) or continuous

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## A little perspective....

- EtOH is also an analgesic!
  - Most studies show that alcohol can reduce pain
  - Mean BAC of 0.08% (3-4 cocktails) slightly increases pain threshold (level at which pain first detected) but reduces pain intensity ratings by the equivalent of 1.25 points on 0-10 NRS
    - In one study, the equivalent of 2 cocktails produced an analgesic effect comparable to that of ~10mg SQ morphine

Horn-Hoffman, 2015; Thompson, 2017; Woodrow, 1988

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## Cannabinoids and Anesthesia

- Chronic users:
  - Cardiac: tachycardia or bradycardia, hypotension, risk of MI
  - Pulmonary: like Tob users with cough, bronchitis, bronchospasm, obstruction
  - Drug-drug: CYP3A4 (most opioids, among others) and CYP2C9 (warfarin, clopidogrel, NSAIDs/COXIBs)
    - Cannabis use may increase or decrease so effect unpredictable
      - Combined with sedatives may increase sedation
      - With stimulants like cocaine or amphetamine, may increase stimulant effect (Vadivelu from Beaulieu; can't find)

Beaulieu (2017) Can J Anaesth 64(12): 1236-1264.

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## Cannabinoids and Anesthesia

- Chronic users:
  - Neurological: acute intoxication may prolong sedative effects of anesthesia
  - Chronic use may blunt response to anesthetics
    - Case reports of cannabis users requiring increased Propofol to maintain sedation
    - 30 cannabis users ( $\geq 1$ /wk for  $\geq 6$  months) vs 30 cannabis non-users
      - Randomized to 5 induction doses of Propofol, ranging from 1.5-3.5mg/kg
      - BIS and eyelid reflexes assessed 30 seconds after induction, if  $>60$ , induction "failed"
        - » BIS  $<60$  achieved in 57% of cannabis users, 73% of nonusers ( $p=0.18$ )
        - Significantly more additional Propofol required for LMA insertion for cannabis users ( $314 \pm 109.3$ mg) than non-users ( $263.2 \pm 69.5$ mg)

Flisberg, P. (2009). Eur J Anaesthesiol 26(3): 192-195. Symons (2002)

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## Cannabinoids and Anesthesia

- Chronic users:
  - Experience increased post-operative pain
    - Retrospective propensity-matched cohort study of orthopedic surgery patients found that cannabis users experienced significantly more pain at rest (5.0 vs 3.0), with movement (8.0 vs 7.0) and sleep interruption due to pain (72% vs 58%)
  - Another retrospective multi-institutional pilot study from 3 trauma centers in CO and 1 in TX
    - 21% (54/261) of patients reported marijuana use and 30% of those reported chronic use (daily or almost daily use or  $>1$ oz over past month)
      - Opioid use was greater in marijuana users, both chronic and episodic, vs non-users (7.1 and 7.8, respectively vs 5.7,  $p<0.05$ )
        - » This association was not true for marijuana users who also used other drugs
      - Pain scores were significantly greater throughout the duration of hospitalization for marijuana users
        - » Higher for episodic users than chronic users or non-users

Liu (2018) Anesth Analg. Salottolo (2018) Patient Safety in Surgery 12:16

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## Case

- 83 year old woman with chronic low back pain
  - Multiple degenerative changes
  - Few comorbidities (HTN, HLD, insomnia)
  - Has been taking oxycodone/APAP 5/325mg QID and this is no longer working
    - Gabapentin made her drowsy, pregabalin caused weight gain and duloxetine resulted in n/v
  - She asks you about marijuana for her pain....

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## CONFLICTS OF CONSCIENCE IN HEALTHCARE

Nathaniel J Brown, MD, PhD  
CRASH 2019

## LEARNING POINTS

1. Grapple with the idea that medicine is a practice deeply steeped in values.
2. Explore options for moving forward when the deeply held values of different parties in medicine are incompatible.
3. Reflect on the different ways ethically difficult terrain can be experienced.

## INTRODUCTION

- No universally accepted ethical interpretive framework
- Reflects lack of consensus on what the good life is and how to live it
- We sometimes think of medicine as a unitary endeavor (and, in a sense it might be)
- But... there is a lot of moral divergence
- Conscientious objectors in medicine are reminders of how strong and deep this division can be

## “CONSCIENTIOUS OBJECTION”

- Defining the term:
  - A conscientious objector in medicine is usually taken to be a medical practitioner who refuses to perform or participate in certain procedures or offer certain therapeutic modalities citing reasons of deep moral conflict.

## CONDITIONS

- Respect for moral pluralism
- Respect for moral convictions

## RESPECT FOR MORAL PLURALISM

- We live in a morally pluralistic society
- The project of pluralism, to paraphrase John Gray, is the attempt of different cultures to live together peacefully without rejecting their differences.

## MORAL PLURALISM AND CONFLICT

- Moral diversity or pluralism (particularly if it is deep) is essentially synonymous with a certain level of disunity
- Diversity can be maintained only if some people value their own systems more than competing systems
- Respect for this means “live and let live” (tolerance, essentially)

## MORAL PLURALISM IN CLINICAL PRACTICE

- Disunity means that, absent conversion, some medical encounters will reach an impasse when they are between members of moral communities that have little common ground

## RESPECT FOR MORAL CONVICTIONS

- We should give people as wide a latitude as possible to live out their lives according to their moral convictions
  - Conscience
- Bound up in the liberal commitment to avoid the establishment of religion
  - “Religion” here is (rightly) very broadly understood

## RELIGION?

- Conscience, for our purposes, is a distillation of how you view your potential actions in the light of your own understanding of morality.
- No doubt conscience is informed by religious commitments for many, but is by no means a concept to be equated with any particular set of beliefs.

## THE SIMPLE SOLUTIONS

- Doctors determine how they want to practice
  - Patients can agree or shop around
- \*Or\*
- Society determines scope of medical practice, which can change at any time
  - Doctors can agree or quit medicine

## CRITIQUE OF THE SIMPLE

- The main thrust of the “simple solutions” are untenably over simplistic.
- The most popular one in the bioethics literature essentially denies that physicians have moral agency.
- The other solution is currently impractical due to a lack of transparency.

## AGREE OR QUIT MEDICINE?

- Selection for willingness to participate in anything that is or becomes legal over the course of a career selects for people *without* an independently principled view of medical morality.
- Their view is, at best, technocratic

## A BETTER DEFINITION

- Conscientious objection occurs when a physician refuses to participate in a requested procedure, therapy, prescription, etc. on the grounds that the **request is outside the legitimate scope of the practice of medicine** (ideally, as defined by an explicitly articulated philosophy of medicine).

## PHILOSOPHY OF MEDICINE

- One does not need an explicitly articulated philosophy of medicine to appreciate:
  - You have a sense of what medicine is and how it evolves over time
  - You have a sense of what your own moral positions are and also how they evolve over time
  - You are able to make value judgements based on evidence (this is the essence of clinical practice)

## THE SECOND DEFINITION

- Tethering conscientious objections to reflections about what medicine properly is can prevent someone from hiding behind the concept of CO when perhaps they ought not to.

## WHAT CO IS NOT

- Conscientious objections are not objections based on moral discomfort, but rather ought to be deeper (in my opinion).
- CO is a distinct category.
- Need a way to curb the potential for abuse.

## SOME EXAMPLES

- Growth hormone for enhancement
- Surgery for enhancement/aesthetics
- Pediatric surgery: conflict b/t parents and the child
- Executions
- Assisted suicide / medical aid in dying

## DISTINGUISHING

- Important to distinguish between different levels of moral discomfort.
- Medicine is witness to a continuum of difficulties in the moral landscape of medicine.
- Degrees of acceptable cooperation.

## POSITIVE CLAIMS OF CONSCIENCE

- Conscience claims not just negative
  - Positive claims of conscience are gaining some more recognition in the field
    - “I am called to provide this service.”
- Value matching and a sense of duty.

## WRAPPING UP

- Living harmoniously in a morally pluralistic context requires respecting others and their considered moral judgments.
- Differences can be deep and painful, especially if competing moral communities are forced into tight spots.
- The good news is that there is already a diversity of views within medicine.

## CONCLUSION

- There are so many constraints to medical practice already and the concept of CO is a relatively narrow slice.
- It properly only applies when there are disagreements about what constitutes the core of medicine.

## QUESTIONS?

“Two things awe me most, the starry sky above me  
and the moral law within me.”

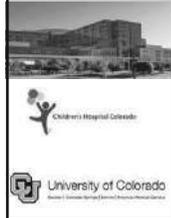
—Immanuel Kant



# CRASH

## Death at 50 & Organ Donation

Dr. Mark Twite MA MB BChF FRCP  
 Director of Congenital Cardiac Anesthesiology  
 Associate Professor  
 Department of Anesthesiology  
 University of Colorado, Anschutz Medical Campus &  
 Children's Hospital Colorado



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# CRASH



No Relevant Financial Disclosures



1

## Defining Death

Dying → Death → Dead  
 (obvious) (not so obvious) (obvious)



2

## Defining Death

- Severe neurological injury even when biological functions remain intact?
- Biological failure of the organism to maintain integrated functioning?
- Loss of higher brain function?
- Social and cultural construct that can be defined in different ways?



3




4

## Defining Death

Until the 1950s death defined in terms of failure of 3 critical organ systems:

1. Circulatory
2. Respiratory ← Mechanical Ventilation
3. Neurological



### ORGAN TRANSPLANTATION



5

### 1950 First Kidney Transplant, Chicago USA



6

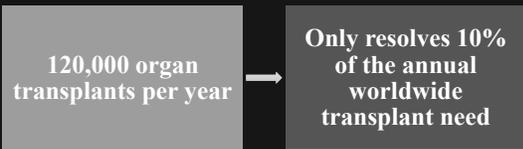
### Organ Transplantation

1. Supply of Organs  $\neq$  Demand
2. Optimize the organ(s) for the recipient  
AND Protect the donor and their family, to facilitate the gift of organ donation



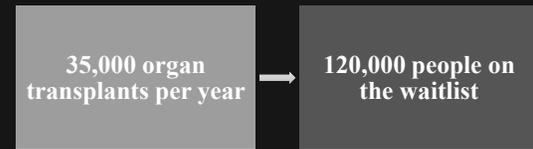
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### Supply $\neq$ Demand: Global Organ Transplants



8

### Supply $\neq$ Demand: USA Organ Transplants

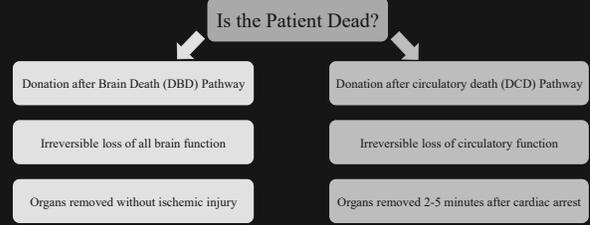


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### Two Pathways to Organ Donation



11

## Diagnosis of Brain Death

1. Confirm unconsciousness
2. Loss of vital brainstem functions
3. Rule out any reversible causes

'Permanent apneic unconsciousness'

Exclude Reversible Causes

- Low Body Temperature
- Metabolic disturbances
- Drugs

Brain Death Exam

- Motor
- Reflex
- Apnea

Confirm

- Lack of brain activity
- Lack of brain blood flow

Wait

- 6hrs in adults
- 12hrs in children
- 24hrs in neonates

Repeat

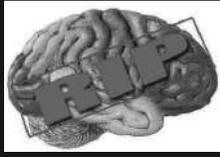
- Second physician

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12

## Does Brain Death = Dead?

- Patients look alive, warm & pink
- Digest & metabolize food
- Excrete waste
- Undergo sexual maturation



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## The Jahi McMath case

**Jahi McMath**  
Born October 24, 2000  
Declared dead by neurologic criteria December 12, 2013  
Declared dead by cardiac criteria June 22, 2018



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14

## Two Pathways to Organ Donation

Is the Patient Dead?

Donation after Brain Death (DBD) Pathway

Irreversible loss of all brain function

Organs removed without ischemic injury

Donation after circulatory death (DCD) Pathway

Irreversible loss of circulatory function

Organs removed 2-5 minutes after cardiac arrest

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## Ischemia for donor organs

**DBD**



**DCD**



Frontiers Cardiovasc Med 2018  
University of Colorado

16

## Worlds First Human to Human Heart Transplant December 3<sup>rd</sup> 1967



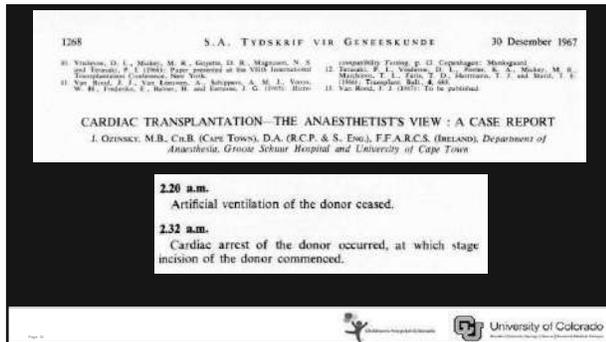
DENISE DARVALL



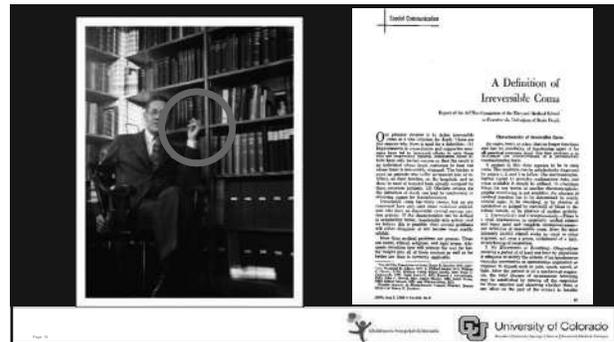
Jonathan van Wyk

University of Colorado

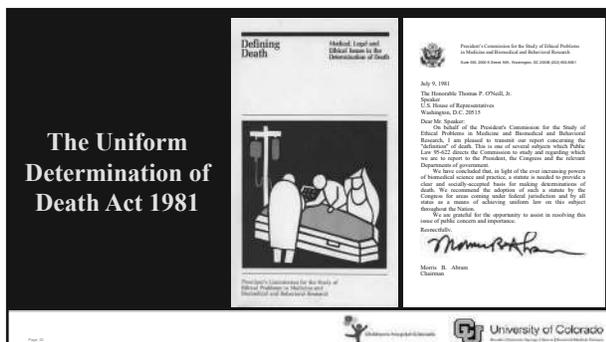
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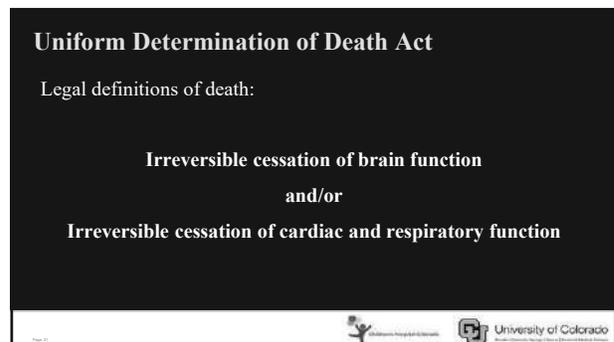
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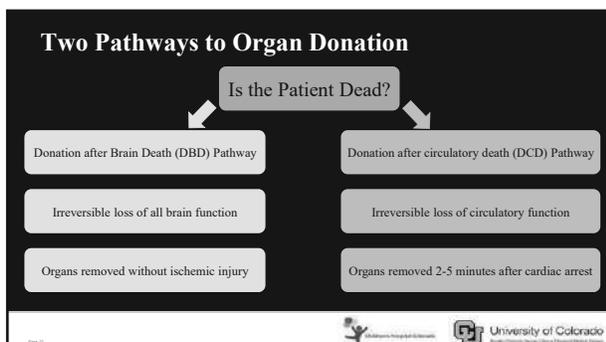
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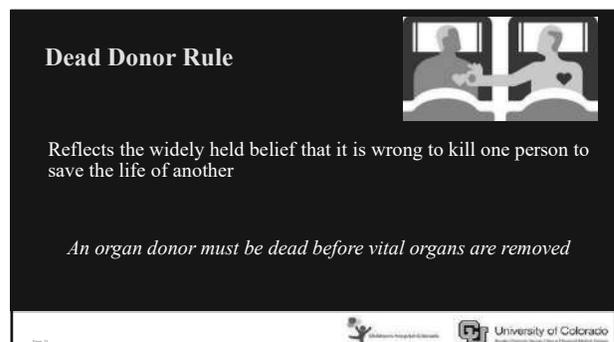
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### Heart stops – now what?

- 1997 Institute of Medicine (IOM) suggested that 5 minutes should elapse between cardiocirculatory death and organ retrieval
- 2000 IOM suggested that empirical data indicates that cardiopulmonary arrest becomes irreversible in a shorter time interval – less than 60 seconds
- Society for Critical Care Medicine recommends waiting 2 - 5 minutes

**Lazarus Phenomenon**



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Vincent Van Gogh The resurrection of Lazarus      Lazarus' first tomb in Bethany – his second tomb was in Cyprus



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Health Sciences Center, Denver, Colorado

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### What happens if the heart doesn't stop?

- Heart donation: circulatory death must occur < 30 minutes of extubating patient
- Other organ donations: circulatory death must occur < 1 hour of extubating patient
- After these time periods, the patient is taken back to the ICU for further comfort care and is no longer eligible to donate their organs



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Health Sciences Center, Denver, Colorado

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American Society of Anesthesiologists®

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**Statement on Controlled Organ Donation After Circulatory Death**  
 Committees of Origin: Critical Care Medicine, Ethics and Transplant Anesthesia  
 (Approved by the ASA House of Delegates on October 25, 2017)



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Health Sciences Center, Denver, Colorado

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### Future State

<b>DBD</b>	
<b>DCD</b>	
<b>DCD +</b>	



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### Future State?

- 3-D Printing organs
- Growing organs in the lab
- Gene editing animals

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### Take Home Messages.....

1. Death is difficult to define
2. DCD offers another pathway to organ donation which
  - a. Helps fulfill the wishes of the patient / family to be a donor
  - b. Increases the number of available organs
3. The primary team, usually the intensivist, should care for the patient during the dying and death process.

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**“If one subject in health law and bioethics can be said to be at once well settled and persistently unresolved, it is how to determine that death has occurred.”**

Alexander M. Capron, LL.B., Executive Director, President's Commission 1981

*New England Journal of Medicine (2001) 344:1244.*

University of Colorado

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### Thank you

Mark.Twite@childrenscolorado.org

University of Colorado

40

# Perioperative DNR

Lawrence I Schwartz, MD  
Associate Professor, Pediatric Anesthesia  
Children's Hospital Colorado, University of Colorado  
CRASH 2019  
February 27, 2019

1

## Objectives

- Describe the components of Do Not Resuscitate orders.
- Understand goals/values-oriented approach to discussing DNR with patients presenting to the OR.
- Discuss strategies for the anesthetic management of patients with active DNR orders.

2

M. William Shakspeare:  
*HIS*  
True Chronicle Historie of the life and  
death of King L. A. A. and his three  
Daughters.  
*With the unfortunate life of Edgar, sonne  
and heire to the Earle of Gloster, and his  
fall from and a famous humor of  
Tom of Beilman:*  
*As it was playd before the Kings Maiestie at Whitehall upon  
I. September night in Christmas time.*  
*By Iohn Maitheus Inuenter playd vnder the Countesse  
on the Swan-ticke.*

L. O. N. O. N.  
Printed by Iohn Iones at the Signe of the Plume in Pauls  
Church-yard at the Signe of the Plume in Pauls  
Church-yard at the Signe of the Plume in Pauls  
Church-yard at the Signe of the Plume in Pauls

<https://youtu.be/MhaH-QFiXe47t=10293>

3

Earl of Kent: Vex not his ghost. O, let him pass, he hates him  
That would upon the rack of this tough world  
Stretch him out longer.

Edgar: He is gone indeed.

Earl of Kent: The wonder is he hath endur'd so long,  
He but usurp'd his life.

Edgar: The weight of this sad time we must obey,  
Speak what we feel, not what we ought to say:  
The oldest hath borne most; we that are young  
Shall never see so much, nor live so long.

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Visit <http://www.playshakespeare.com/licensing> for details.

4

## What are your thoughts and feelings about perioperative DNR?

5

## History of CPR & DNR

- CPR originally described in 1960
  - Witnessed, closed-chest
  - Any patient with cardiac arrest in the hospital
- Sham resuscitations, "Slow Code"
- 1974: AMA recommended that decisions to forgo CPR be documented – explicit DNR policies followed by 1976 in Boston
- 1983: President's Commission for the Study of Ethical Problems in Medicine
  - Presumed to have implicit consent for CPR
  - All patients were "full code" unless otherwise stated

**CPR became the only medical therapy that required a MD order to withhold**

6

### DNR in the OR

- Pre 1990's DNR orders routinely suspended in the perioperative period
- Decisions left to anesthesiologists and surgeons
- Concerns raised
  - Patient autonomy
  - Right to self-determination
- American Society of Anesthesiologist
  - 1993 First guidelines on DNR in the OR



7

### Ethical Guidelines for the Anesthesia Care of Patients with Do-Not-Resuscitate Orders or Other Directive That Limit Care

ASA Ethics Committee

- First adopted 1993
- Last amended in 2013, & reaffirmed October 17, 2018

Required reconsideration  
Patient-centered shared decision making

8

### Biomedical Ethics

- Autonomy
- Beneficence
- Nonmaleficence
- Justice/Fairness

9

### Autonomy

- Fundamental to DNR orders
- Requires that patients are informed about condition and options
- Education is key – but barriers exist
  - Time constraints
  - Baseline knowledge
  - Illness
  - Cultural, religious, spiritual backgrounds
- Be aware of one's own biases



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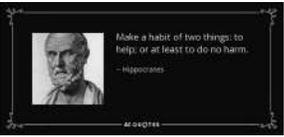
### Beneficence

- Do good
- Medical treatment should bring some benefit
- Realistic calculation vs. idealistic

11

### Nonmaleficence

- Do no harm
- We do not want to cause undue pain and suffering
- In the OR
  - Trying to save a life vs.. hastening death



12

### Justice

- The limits of health care resources
- DNR can save resources, but who decides.
- 1990 Patient Self-Determination Act in response to variable patterns of DNR ordering

13

### Back to the OR

- 79 year-old-woman, stage IV metastatic non-small cell lung cancer
- Hospice care
- Increased hip pain
- Imaging → impeding hip fracture secondary to metastatic disease
- Offered ORIF in hopes of restoring limited mobility and pain relief
- Adamant: no CPR. Declines vasopressors and intubation.

Scott & Garvin, Anesthesiology Clin, 2012

**Negative Rights vs.. Positive Right**

14



15

### DNR in the OR

- CPR is generally very effective in our hands
  - Witnessed
  - Reversible causes
  - Rapid ROSC
- We don't usually have a close relationship with the patient
- Time
- We can cause instability with routine care
  - Can lead us to cut corners with dosing
- Culture
  - "What happened" vs. "What did you do"

16

### ASA Guidelines

- Automatic suspension of DNR is unethical due to patient's right to self-determination
- Communication & Documentation – two way street
  - Face-to-face
- 3 paths
  - Full Attempt at Resuscitation
  - Limited Attempt at Resuscitation – procedurally defined
  - Limited Attempt at Resuscitation – patient goal defined

17

### Limited Resuscitation

<p><b>Procedure-Directed</b></p> <ul style="list-style-type: none"> <li>• Patient/surrogate can choose which procedures are permissible, which are refused</li> <li>• Anesthesiologist must educate patient/surrogate which procedures are essential to successful anesthesia, which are not</li> </ul>	<p><b>Goal/Value-Directed</b></p> <ul style="list-style-type: none"> <li>• Pt. allows operative team to use clinical judgment in determining appropriateness of resuscitation measures.</li> <li>• Must align with patient's goals for the procedure and their end of life</li> </ul>
---	---

18

19

Goal/Value oriented approach to resuscitative intervention

- Treating an easily reversible anesthetic cause of hypotension
- Providing a safe anesthetic with extubation
- Ensuring comfortable anesthesia without recall
- Treating an arrest due to primary disease
- Risk of long term intubation, or ICU stay
- Risk of neurologic injury
- Discharge to home

20

Goal/Value directed DNR

- 79 year-old-woman, stage IV metastatic non-small cell lung cancer
- Hospice care
- Increased hip pain
- Imaging → impeding hip fracture secondary to metastatic disease
- Offered ORIF in hopes of restoring limited mobility and pain relief
- Adamant: no CPR. Declines vasopressors and intubation.
- Wants to attend granddaughter's wedding

Scott & Garvin, Anesthesiology Clin, 2012

21

Limited Resuscitation

<p><b>Procedure-Directed</b></p> <ul style="list-style-type: none"> <li>• Clear communication</li> <li>• Checklist</li> <li>• Faster</li> <li>• Less flexibility</li> </ul>	<p><b>Goal-Directed</b></p> <ul style="list-style-type: none"> <li>• Flexible</li> <li>• Can more readily deal with the unexpected event</li> <li>• Balanced approach</li> <li>• Must establish a deeper relationship</li> <li>• Ethical and legal concerns</li> </ul>
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22

Guidelines

- Post-operative care. Reinstatement of DNR
- Involvement of the primary physician
- Establish liaison from Dept. of Anesthesiology
- Conflict of moral views
  - Non-judgmental fashion
  - Finding alternative care in timely fashion
  - Conflict of general standards of care

23

How to start?

- Ask permission
- Start with what they know
- Short sentences
- Allow silence
- Expect any emotion
- Prepare for next steps

Chandrakantan, Anesthesiology Clinics, 2016  
Adapted from Morrison, Anesthesiology, 2015

24

### Pediatrics

- Are kids different?
- Survey 1995
  - 107 Anesthesiologists
  - 69% would honor DNR for palliative procedure
  - 46.7% would honor DNR for elective surgery
  - Should procedures be withheld
    - PPV, Vasoactive Rx, CPR, ETT – no 71-85%
    - Defibrillation 42% “no”



Fallat ME, Pediatrics, 2004

25

### Pediatrics

- The ethics are essentially the same
- Guidelines from AAP, Sections of Surgery and Anesthesiology, Committee on Bioethics
  - Fallat & Hardy, Pediatric, 2018
- Some unique aspects
  - When to discuss with the child
  - Parents as surrogate decision makers
  - What the parent wants vs.. What is in the child’s best interest

26

### How do patients feel about it?

- Two main themes regarding institution and intention of DNR
  - Avoiding financial and emotional costs for themselves and their families
  - “being ready to die.”

Clemency, Anesth Analg, 1997

27

### How do patients feel about it?

- 15% of patients with DNR will undergo surgery
  - LaPluma, Arch Intern Med, 1988
- 83% would agree to some type of surgery
  - Avoid pain
  - Improve quality
  - Unrelated to terminal disease
    - Clemency, Anesth Analg, 1997
- Nearly all want to discuss perioperative DNR...and they need to do so
  - Clemency, Anesth Analg, 1997

28



**Rather than perceiving that [we] are doing nothing,  
 something has indeed been done;  
 the wishes of the patient have been respected,  
 their autonomy has been preserved  
 and they have been allowed to dies with dignity**

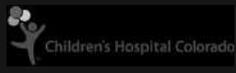
Ewanchuk, Critical Care, 2006

29

# Thursday

# Update on Pediatric Anesthesia

Patrick Fernandez, MD  
Assistant Professor  
Department of Anesthesiology | University of Colorado School of Medicine  
Section of Pediatric Anesthesiology | Children's Hospital Colorado  
February 28, 2019



1

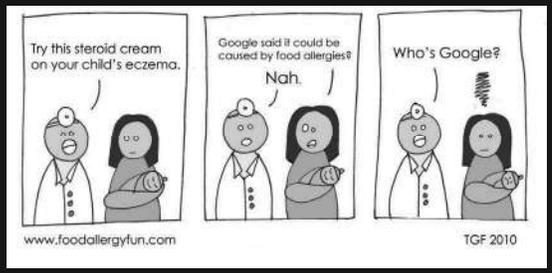
## Outline

- > Perioperative management of the food allergic pediatric patient
- > "Child friendly" preoperative NPO guidelines & RSI
- > Management of button battery ingestion
- > Update on pediatric craniofacial reconstruction

2

## No Disclosures . . .

3



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## The food allergic pediatric patient . . .



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Finding a Path to Safety in Food Allergy  
Highlights of the Consensus Report

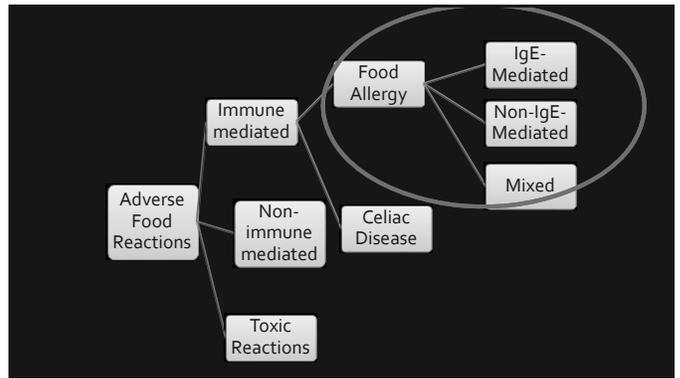
"There is no estimate of true prevalence of food allergy in the U.S."  
The National Academies of Science-Engineering-Medicine  
November 2016

6

### Emily, a food allergic pediatric patient . . .

- History of multiple food intolerance
- History of anaphylaxis to eggs
- Family history of malignant hyperthermia
- Propofol was avoided during anesthetic for MRI
- Pt had concerning bradycardia during that anesthetic

7



8

Most Common	Likely Outgrown by Adulthood	Likely Lifelong
Egg		
Fish		
Milk		
Peanut		
Shellfish		
Soy		
Tree nuts		
Wheat		

Wasserman, S and Watson, W. Food Allergy. Allergy, Asthma & Clinical Immunology. 2011

9

Most Common	Likely Outgrown by Adulthood	Likely Lifelong
Egg	✓	
Fish		
Milk	✓	
Peanut		
Shellfish		
Soy	✓	
Tree nuts		
Wheat	✓	

Wasserman, S and Watson, W. Food Allergy. Allergy, Asthma & Clinical Immunology. 2011

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Most Common	Likely Outgrown by Adulthood	Likely Lifelong
Egg	✓	
Fish		✓
Milk	✓	
Peanut		✓
Shellfish		✓
Soy	✓	
Tree nuts		✓
Wheat	✓	

Wasserman, S and Watson, W. Food Allergy. Allergy, Asthma & Clinical Immunology. 2011

11

Most Common	Immunodominant Allergens
Egg	Ovomucoid, Ovalbumin, Ovotransferrin, Lysozyme
Milk	Caseins (a, b, k, g) & Whey (lactoglobulins, immunoglobulin & lactoferrin)
Peanut	Cupin, Conglutin, Profilin
Shellfish	Tropomyosin, Arginine kinase, Myosin light chain, Sarcoplasmic calcium-binding protein
Soy	Contain allergens belonging to all categories of protein superfamilies
Wheat	Glutenins, gliadins, profilin

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### IODINE ALLERGY AND SEAFOOD = MYTH!

Reaction to iodinated media is NOT IgE-mediated and NOT due to iodine

Contact dermatitis is NOT triggered by iodine

Protein components of seafood are responsible for allergy NOT iodine

### PERHAPS THINK ABOUT PROTAMINE

"patients with a history of allergy to fish may develop hypersensitivity reactions to protamine . . . to date no relationship has been established between allergic reactions to protamine and fish allergy"

19

### Propofol



... In addition to the active component . . . soybean oil, glycerol, egg lecithin . . .

... 20% soybean oil, egg yolk phospholipids, glycerin . . .

20

### Propofol



... In addition to the active component . . . soybean oil, glycerol, egg lecithin . . .

... 20% soybean oil, egg yolk phospholipids, glycerin . . .

**NOT PROTEINS**

21

### Package Inserts

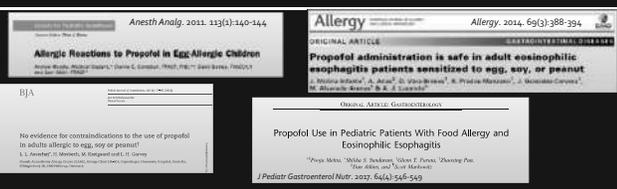


... contraindicated in patients with allergies to eggs, egg products, soybeans or soy products."

Contraindications: ". . . patients with disturbances of fat metabolism . . . pathologic hyperlipemia, lipid nephrosis or acute pancreatitis . . ."

22

### Egg, soy and peanut allergy . . .



Propofol is safely used in patients with allergy to egg, soy and peanuts

The practice of choosing alternatives to propofol in patients with these food allergies is not evidence based and should be reconsidered

23

### Considering Emily's food allergy . . .

No concern for food allergy & anesthesia

Education of patients

- Anesthetic need not be altered
- Atopic patients are at risk
- Reasonable concessions considered

24



25

### Nil per os (NPO) rules for clear liquids

*Anesthesiology*, 2017, 126:376-393

**PRACTICE PARAMETERS**

**Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures**

*An Updated Report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration\**

"The purposes of these guidelines are to provide direction . . . related to preoperative fasting . . . to **reduce the risk of pulmonary aspiration** and to reduce the severity of complications related to perioperative pulmonary aspiration."

26

### Still 2-4-6-8 . . .

Ingested Material	Minimum Fasting Period (Healthy patients undergoing elective procedures)
Clear liquids	2 hr
Breast milk	4 hr
Infant formula, nonhuman milk, "light meal"	6 hr
Fried/fatty food or meat	8 hr

27

### European Guidelines . . . February 2018

" . . . unless there is a contraindication, it is safe and recommended for all children able to take **clear fluids**, to be **allowed and encouraged to have them up to one hour** before elective general anesthesia."

*Pediatric Anesthesia*, 2018, 28:411-414

28

### Risk of pulmonary aspiration . . . U.K.

- Aspiration is rare
  - Incidence 0.07-0.1 %
- Sequelae are rarely severe or long lasting

29

### Morbidity is low . . .

- 2/10,000 incidence
- "severe deterioration" in 5 cases
- All made full recovery

30

### Risk of pulmonary aspiration . . . U.S.A

**Aspiration is rare**

- Incidence 1/10,000

**Similar despite NPO status**

**Major Adverse Events and Relationship to Nil per Os Status in Pediatric Sedation/Anesthesia Outside the Operating Room**

*A Report of the Pediatric Sedation Research Consortium*

Michael L. Beach, MD, PhD, Daniel M. Cohen, MD, Susan M. Gilkether, BS, Joseph F. Cravero, MD, Anesthesiology, 2016; 124(1):80-88

31

### What influences risk?

Patient Factors	Anesthetic Factors
<ul style="list-style-type: none"> <li>❖ Full stomach</li> <li>❖ Bowel obstruction</li> <li>❖ Abdominal pain</li> <li>❖ Trauma</li> <li>❖ Obesity</li> <li>❖ Esophageal pathology</li> <li>❖ Renal failure</li> <li>❖ Diabetes</li> </ul>	<ul style="list-style-type: none"> <li>❖ Opioids</li> <li>❖ Appropriate fasting</li> <li>❖ Airway management</li> <li>❖ Anesthetic technique</li> </ul>

32

### What influences risk?

Patient Factors	Anesthetic Factors
<ul style="list-style-type: none"> <li>❖ Full stomach</li> <li>❖ Bowel obstruction</li> <li>❖ Abdominal pain</li> <li>❖ Trauma</li> <li>❖ Obesity</li> <li>❖ Esophageal pathology</li> <li>❖ Renal failure</li> <li>❖ Diabetes</li> </ul>	<ul style="list-style-type: none"> <li>❖ Opioids</li> <li>❖ <b>Appropriate fasting</b></li> <li>❖ Airway management</li> <li>❖ Anesthetic technique</li> </ul>

33

### Actual fasting times

12hrs for solids and nearly 8 hrs for liquids

Pediatric Anesthesia, 2011; 21:964-968

NPO > than recommended 70% of cases

J of Pediatric Surgery, 2016; 51(8): 1298-1302

**Unnecessarily Long!**

62% fasted > 4 hours for clear liquids

Anaesth Intensive Care, 2016; 44(1): 107-110

34

### Consequences . . .

Hypoglycemia
Metabolic acidosis
Dehydration
Cardiovascular instability
Discomfort
Grumpiness
Post-op insulin resistance
Emergence delirium

35

Accepted: 15 March 2018  
DOI: 10.1111/pan.13381

**WILEY** Blackwell Publishing

**RESEARCH REPORT**

Correlation between duration of preoperative fasting and emergence delirium in pediatric patients undergoing ophthalmic examination under anesthesia: A prospective observational study

Pediatric Anesthesia, 2018; 28:547-551

- ❖ Eye exams under anesthesia
- ❖ Pediatric Anesthesia Emergence Delirium scale (PAED)
- ❖ Prolonged preop fasting → patient anxiety → emergence delirium

36

Accepted: 15 March 2018  
DOI: 10.1111/pan.13381

RESEARCH REPORT

WILEY *Pediatric Anesthesia*

Correlation between duration of preoperative fasting and emergence delirium in pediatric patients undergoing ophthalmic examination under anesthesia: A prospective observational study  
*Pediatric Anesthesia* 2018; 28:547-551

- ❖ Mean clear liquid fasting 6.3hrs!
- ❖ PAED score at 15 & 20 minutes correlated with fasting duration

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### "Choosing Wisely" in Pediatric Anesthesia

Accepted: 16 March 2018  
*Pediatric Anesthesia* 2018; 28(7):588-596  
DOI: 10.1111/pan.13380

SPECIAL INTEREST ARTICLE

WILEY *Pediatric Anesthesia*

Choosing Wisely in pediatric anesthesia: An interpretation from the German Scientific Working Group of Paediatric Anaesthesia (WAKKA)

Karin Becke<sup>1</sup>, Christoph Eick<sup>2</sup>, Claudia Hübner<sup>3</sup>, Martin Jähde<sup>4</sup>, Andreas Machotta<sup>5</sup>, Markus Schreiber<sup>6</sup>, Robert Sämpelman<sup>7</sup>

"Perioperative fasting should be safe and **child-friendly** with shorter real preoperative fasting times . . . In future guidelines, shorter fasting for light meals/formula milk (4 hours) and clear fluids (1 hour) should be considered"

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### Liberal fluid fasting . . .

30 minutes for clear fluids

4 hours for breast milk/formula & milk-based products

6 hours for solids

Patients are assessed by anesthesiologist

Andersson H et al. *Pediatric Anesthesia*. 2018; 28:46-52

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### Liberal fluid fasting . . .

↑ Risk of prolonged fasting

- ❖ Age < 3 years old
- ❖ First case of the day

	6-4-2 Fasting	6-4-0 Fasting
Median clear liquid fasting	4 hrs	1 hr
Fasting > 6 hrs	34.8 %	6.3 %
Fasting > 12 hrs	15.2 %	3.1 %

Andersson H et al. *Pediatric Anesthesia*. 2018; 28:46-52

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### Impact on gastric content . . .

- ✓ Liberal fasting → shorter fasting duration
- ✓ No difference in pH of gastric contents
- ✓ No difference in residual gastric volume

BJA

Liberal fluid fasting: impact on gastric pH and residual volume in healthy children undergoing general anaesthesia for elective surgery

A. R. Schmidt<sup>1</sup>, C. P. Buehler<sup>1</sup>, Ch. Rauh<sup>1</sup>, R. Wiener<sup>1</sup>, R. Klaghofer<sup>1</sup>, M. Hentschger<sup>1</sup>, M. Weiss<sup>1</sup> and A. Schmitt<sup>2</sup>

<sup>1</sup>Department of Anaesthesia and Children's Research Center, University Children's Hospital, Zurich, Switzerland; <sup>2</sup>Division of Clinical Chemistry and Biochemistry, University Children's Hospital, Zurich, Switzerland; <sup>3</sup>Department of Paediatrics and Paediatric Surgery, University Hospital, Zurich, Switzerland

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### Benefits of "child friendly" NPO times

Proven Benefit	Likely (possible) Benefit
<ul style="list-style-type: none"> <li>&gt; ↓ preoperative fasting times</li> <li>&gt; ↓ incidence of unnecessarily prolonged fasting</li> <li>&gt; ↓ thirst, hunger &amp; anxiety</li> </ul>	<ul style="list-style-type: none"> <li>❖ ↓ perioperative hypoglycemia</li> <li>❖ Hemodynamic stability</li> <li>❖ ↓ post-op insulin resistance</li> <li>❖ ↓ emergence agitation</li> </ul>

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### Summary: Child Friendly NPO

PRO	CON
<ul style="list-style-type: none"> <li>❖ MOST children are starved longer than necessary</li> <li>❖ The stomach processes contents rapidly</li> <li>❖ No good evidence that current NPO rules are protective</li> <li>❖ Aspiration is rare</li> </ul>	<ul style="list-style-type: none"> <li>❖ Maybe this goes too far . . .</li> <li>❖ One size does NOT fit all</li> <li>❖ Study power and safety?</li> <li>❖ If it isn't broken . . .</li> </ul>

British Journal of Anaesthesia, 2018, 120(3): 469-474

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### Pediatric RSI: Time for a different technique?

CLASSIC RSI . . .	"BEST PRACTICE" RSI . . .
<ul style="list-style-type: none"> <li>❖ Aspiration with anesthesia still occur</li> <li>❖ We are preventing aspiration</li> <li>❖ Cricoid is easy and effective (ca 1961)</li> </ul>	<ul style="list-style-type: none"> <li>❖ Yeah but how frequent &amp; how significant?</li> <li>❖ Are we?</li> <li>❖ Really?</li> </ul>

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### Pediatric RSI: Time for a different technique?

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### Pediatric RSI: Time for a different technique?

J Emerg Nurs 2009, 35:11	<ul style="list-style-type: none"> <li>• Not sure or wrong about pressure</li> <li>• Most agreed CP training was poor</li> </ul>
J Trauma 2010, 69:1182	<ul style="list-style-type: none"> <li>• 10 different CP techniques</li> <li>• Frequently done incorrectly</li> </ul>
Pediatr Anesth 2004, 14:43	<ul style="list-style-type: none"> <li>• Incorrectly done, CP may lead to damage and/or airway obstruction</li> </ul>

**Evidence-Based Clinical Update**

No evidence for decreased incidence of aspiration after rapid sequence induction

[Aucune donnée probante concernant l'incidence réduite d'inhalation après l'induction en séquence rapide]

David T. Nallipati MD MCh, Edward T. Crosby MD MCh\*

**"An absence of evidence from RCTs suggests the decision to use RSI . . . Can neither be supported nor discouraged. . ."**

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### Pediatric RSI: We can all agree . . .

- Pre-oxygenation is good
- Rapid drug administration → DO NOT fear Sux
- Consider "modified" RSI
- +/- cricoid pressure

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### Button Battery Ingestion Update



**Section on Anesthesiology & Pain Medicine**  
NEWSLETTER Fall 2018  
American Academy of Pediatrics  
http://myaaf.com/AAPSGA

SOA Newsletter—Fall 2018 / Page 5  
Updated Management Guidelines on Button Battery Ingestion in Children  
Debrah Chatterjee, MD, FAAP, Monica A. Hoagland, MD, Richard J. Ing, MBSCh FCA(SA), Department of Anesthesiology, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO



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### Button Battery . . . Background

- ~ 3500 ingestions/year
- 7x ↑ in complications and death
- 2006: 20-mm, 3-volt batteries



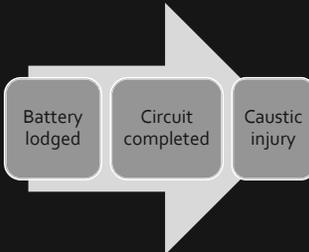
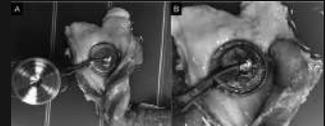
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### Button Battery . . . Background

Death	Major Complication
59 children	231 cases
All < 5 years of age	Esophageal perforation or stricture
80% aorto-esophageal fistula	Tracheoesophageal fistula
	Vocal cord paralysis
	Mediastinitis

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### Button Battery . . . Pathophysiology

Jatana KR. *Laryngoscope* 2017

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### Button Battery . . . Pathophysiology



**Three Ns**  
Negative  
Narrow  
Necrotic

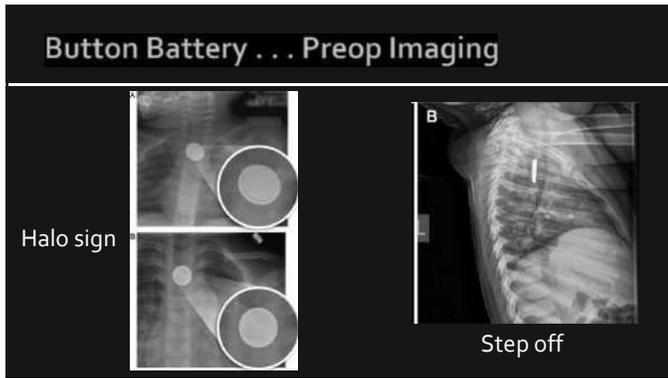
Courtesy: Jatana KR. Nationwide Children's Hospital

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### Button Battery . . . Preop Management

- Injury severity**
  - Timing
  - Orientation
  - Size/voltage
  - Age < 5 years
- Presentation**
  - Dysphagia
  - Drooling
  - Cough
  - Bleeding
- Evaluation**
  - X-ray halo sign & step off

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### Button Battery . . . Intraop Management

<b>MAIN OR</b> <ul style="list-style-type: none"> <li>❖ Stable patient</li> <li>❖ Low risk patient</li> <li>❖ Gastroenterologist or general surgeon</li> </ul>	<b>CATH LAB/CARDIAC OR</b> <ul style="list-style-type: none"> <li>❖ High-risk/unstable</li> <li>❖ Sentinel bleed</li> <li>❖ Cardiovascular surgeon or interventional cardiologist available</li> </ul>
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### Button Battery . . . Postop Management

<b>Ongoing Damage</b> Days to weeks	<b>Serial Imaging</b> CT scan or MRI
--	---

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### Button Battery Ingestion . . . Mitigation

pH 2.4

Pepsi® Water ReaLemon®

Coke® Saline Control Orange Juice

pH 3.3

*Jatana KR, et al. Laryngoscope 2017*

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### Button Battery Ingestion . . . Mitigation

A Saline B Honey C Carafate

*Anfang RR, et al. Laryngoscope 2018*

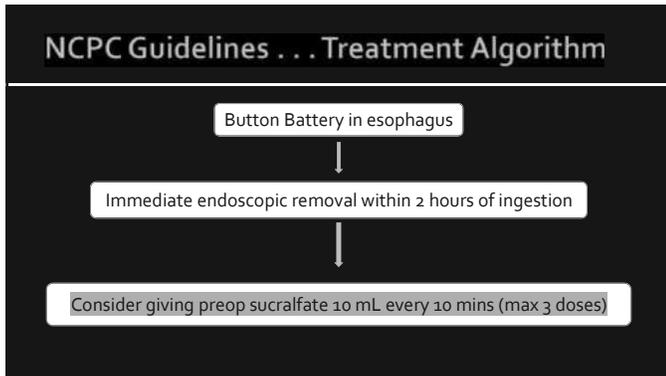
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### NCPC Guidelines . . . Prehospital

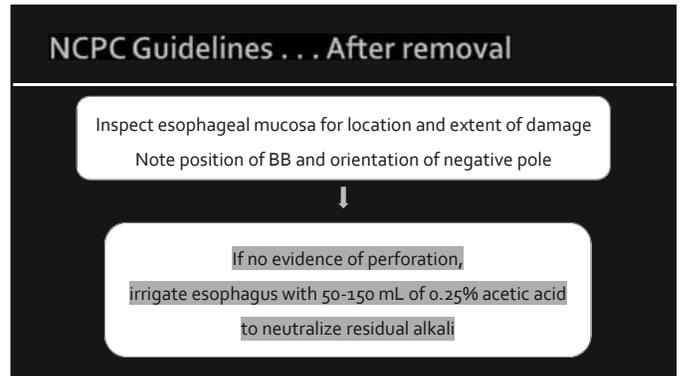
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    graph TD
      A[Witnessed or suspected BB ingestion] --> B[Proceed immediately to ED]
      B --> C[Do not induce vomiting]
      C --> D[Patient ≥12 months old AND lithium battery ingested within 12 hours]
      D --> E[Give honey 10 mL every 10 minutes (max 6 doses)]
      E --> F[Use commercial honey, rather than specialized or artisanal honey]
    
```

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61



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### Button Battery Ingestion . . . Take Home

- ❖ CXR: halo & step off
- ❖ Negative/Narrow/Necrotic
- ❖ Recognize sentinel bleed
- ❖ Emergent removal
- ❖ Active surveillance post-op
- ❖ Mitigate: honey/sucralfate



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### Pediatric Craniofacial Reconstruction Update

- Massive blood loss & transfusion
- Hypovolemic cardiac arrest
- Hyperkalemia
- Coagulopathy
- Transfusion reactions
- Venous air embolism
- Difficult airway
- Difficult vascular access



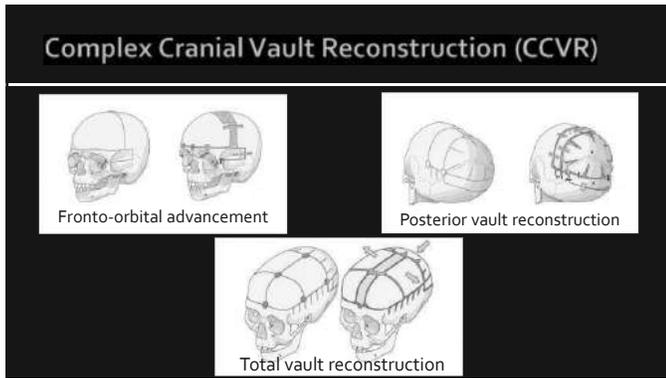
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### Leveraging Multicenter Data

- ❖ Formed in 2011
- ❖ Pediatric Craniofacial Perioperative Surgery Registry
- ❖ United States, Canada, Columbia and Mexico
- ❖ 7 publications since 2017



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### Benchmarking data

**CCVR Procedures**

- ❖ Anterior vault/FOA 64%
- ❖ Mid/Posterior vault 27%
- ❖ Total vault 8%
- ❖ First craniofacial surgery 89%

**Perioperative Outcomes and Management in Pediatric Complex Cranial Vault Reconstruction**  
 A Multicenter Study from the Pediatric Craniofacial Collaborative Group

Paul A. Sholler, MD, Susan M. Goebel, M.D., FRCP(C), Franklin R. Clasko, M.D., Charles M. Haberman, M.D., M.D.P.C., Peter M. Mearns, M.D., Brian K. Pinsky, M.D., M.B.A., Tharal D. Nigam, M.D., Ingrid Lee, M.D., Marjorie P. Kwan, B.S., M.D., M.S., Peter Simuk, M.D., and the Pediatric Craniofacial Collaborative Group

Anesthesiology, 2017, 126:276-287

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### CCVR. . . Vascular access

- 95% ≥ 2 peripheral IVs
- 99% arterial line
- 12% central line

Anesthesiology, 2017, 126:276-287

69

### CCVR. . . Other monitors

**PRECARDIAL DOPPLER**

21%

**THROMBOELASTOGRAPHY**

7%

Anesthesiology, 2017, 126:276-287

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### CCV. . . Blood conservation

Modality	% of cases	Conclusion
Acute normovolemic hemodilution	< 0.001 (1 case total)	Not used
Preoperative erythropoietin	0.005% (7 cases total)	Rarely used
Cell saver	16%	?Limited by cost and availability
Antifibrinolytics (TXA)	63%	Should be used more

Anesthesiology, 2017, 126:276-287

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### CCVR. . . Blood transfusion

- 94% transfusion rate
- 28% > 40 mL/kg
- 10% > 60 mL/kg
- 5% > 80 mL/kg

Anesthesiology, 2017, 126:276-287

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### Transfusion . . . Predictive factors

↑ INTRAOP TRANSFUSION (ML/KG)	↓ INTRAOP TRANSFUSION (ML/KG)
<ul style="list-style-type: none"> <li>Decreased weight</li> <li>Greater ASA physical status</li> <li>Longer surgery</li> <li>Intraop vasopressor use</li> <li>Intraop cardiorespiratory complication</li> <li>Lack of antifibrinolytic use</li> </ul>	<ul style="list-style-type: none"> <li>Increased weight</li> <li>Lower ASA physical status</li> <li>Shorter surgery</li> <li>Cranial distractor placement</li> </ul>

Can J Anesth. Accepted for Publication December 2018.

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### Transfusion . . . Non-predictive factors

- Sex, race, ethnicity
- Preop erythropoietin
- Syndromic/multisuture synostosis
- Redo procedures

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### Antifibrinolytic safety . . .

Pediatric Anesthesia 2017, 27:373-381

**RESEARCH REPORT**  
Safety of antifibrinolytics in cranial vault reconstructive surgery: a report from the pediatric craniofacial collaborative group  
Susan M. Goobie<sup>1</sup>, Franklin P. Clavito<sup>2</sup>, Chris D. Glover<sup>3</sup>, Henry Huang<sup>4</sup>, Drisaya K. Reddy<sup>5</sup>, Allison M. Fernandez<sup>6</sup>, David Zurakowski<sup>7</sup>, Helle Ovesen<sup>8</sup>, Paul A. Brinkler<sup>9</sup> & the Pediatric Craniofacial Collaborative Group\*

- o 0.6% incidence of post of seizure
- o No difference in seizure related to antifibrinolytic use
- o 1 instance of postop DVT
- o Use is likely safe, but caution in high-risk patients and avoid high doses

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### Endoscopic vs Open Repair . . .

**What?** Most types of craniosynostosis

**Who?** < 3 months old

↓ Morbidity & Mortality! AND ↓ health care cost!

**Endoscopic → Decreased**

- ❖ Blood product exposure
- ❖ Post-op intubation
- ❖ ICU utilization
- ❖ Hospital length of stay

Anesthesia & Analgesia 2018, 116(3):68-875

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### Take home points . . . CCVR

- Central venous access likely unnecessary
- Certain perioperative factors predict increased blood transfusion
- Use antifibrinolytics → TXA: 10 mg/kg bolus over 10 min → 5 mg/kg/hr during surgery
- Future developments? → Cell saver use?, Endoscopic-assisted repairs?
- More to come from the PCCG

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### Thank You!

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# SEEING KETAMINE IN A NEW LIGHT

**BobbieJean Sweitzer, M.D., FACP**  
**Professor of Anesthesiology**  
**Director of Perioperative Medicine**  
**Northwestern University**

I have no disclosures

1

## LEARNING OBJECTIVES

*At the conclusion of this activity, participants should be able to:*

- Understand the role of ketamine as an anesthetic
- Understand the role of ketamine as a sedative
- Use ketamine as an adjunct for analgesia
- Incorporate ketamine into your practice

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## Off-Label Use

**Ketamine FDA-Approved**

- General anesthesia
- Procedural sedation

**Ketamine NOT FDA-Approved**

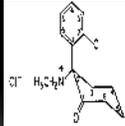
- Acute postoperative pain
- Psychiatric disease



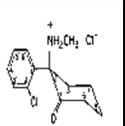
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## KETAMINE

- Developed in search of an “ideal anesthetic”
- Introduced as a dissociative anesthetic in 1964
- Phencyclidine derivative
- Only “total anesthetic in a bottle”
- Hypnosis
- Analgesia
- Amnesia
- Immobility
- Inexpensive



S<sub>2</sub>(+)-Ketamine hydrochloride



R<sub>1</sub>(-)-Ketamine hydrochloride

4

## KETAMINE AS A RECREATIONAL DRUG

- WAS the most common reason to burglarize veterinarian practices; now its tramadol
- “Special K” on the streets
- How bad can a drug be if it is used recreationally???

**Pet Connection: Opioid Addicts Score Drugs From the Local Vet**



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## MECHANISM OF ACTION

- Non-competitive NMDA receptor antagonist
- Partial opioid receptor agonist
- Short distribution and elimination (half-life 2 ½ hrs)
- LOW DOSE maximizes benefits; decreases side effects
- Adjunct to opioids, sedatives or local anesthetics
- Improves safety of sedation
- Modulates opioid tolerance
- Prevents development of increased pain sensitization

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### KETAMINE MODULATION OF PAIN

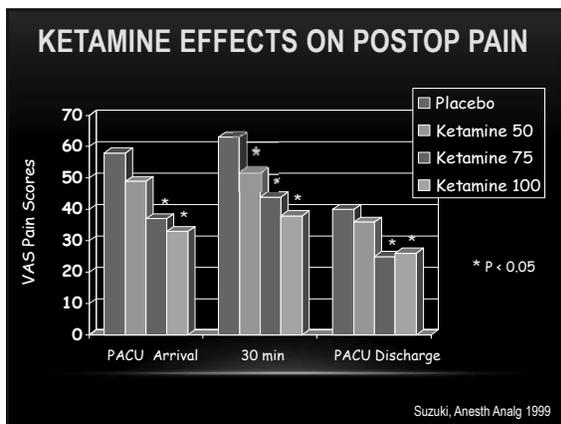
- NMDA receptor antagonism
- Interferes with pain transmission in the spinal cord
- Results in analgesia
- Prevents central sensitization in dorsal horn neurons
- Inhibits nitric oxide synthase → lowers the production of nitric oxide (involved in pain perception)
- Further contributes to analgesia

J Pain Symptom Management 2011;41:640-49 NMDA (excitatory) receptor-channel complex.

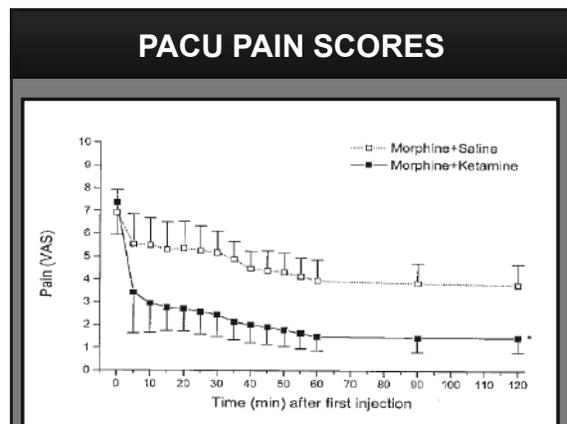
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### PHYSIOLOGY OF PAIN

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### OPIOIDS

- Respiratory depression
- Cardiovascular depression
- Nausea & vomiting
- Postoperative ileus
- Urinary retention
- Pruritus
- Sedation & dizziness
- Tolerance & dependence

↓ Pain 30%

↑ Side effects 80%

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### LOW DOSE KETAMINE COMPARED TO OPIOIDS

- No tolerance
- Less sedation
- Less N/V
- Less urinary retention
- No delayed gastric emptying
- No prolonged ileus or constipation
- Less respiratory depression

THIS?

Or, THIS?

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**Perioperative ketamine for acute postoperative pain (Review)**

Bell RF, Dahl JB, Moore RA, Kalso EA

<http://www.thecochranelibrary.com>

**Authors' conclusions**

Ketamine in subanaesthetic dose (that is a dose which is below that required to produce anaesthesia) is effective in reducing morphine requirements in the first 24 hours after surgery. Ketamine also reduces postoperative nausea and vomiting. Adverse effects are mild or absent.



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**KETAMINE**

- Can be given IV, SC, IM, epidural, intrathecal, intraarticular, intranasal, oral and topically
- Attenuates sevoflurane induced emergence agitation in pediatric patients
- Has anti-inflammatory effects
- May have anti-tumor effects
- Neuroprotective effects
- Prevents post-anesthesia shivering
- As co-induction agent: stable hemodynamics, reduced pain of propofol injection



Paediatr Anaesth. 2008;18:1114-5  
Acta Anaesthesiol Belg. 2011;62:33-6  
Br J Anaesth 2011;107: 123-6

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**THE EFFECT OF KETAMINE VERSUS FENTANYL ON THE INCIDENCE OF EMERGENCE AGITATION AFTER SEVOFLURANE ANESTHESIA IN PEDIATRIC PATIENTS**

Table 3  
Incidence of emergence agitation

Ketamine 0.5 mg/kg				
Group	K (n=40)	F (n=40)	C (n=40)	P
<b>Four point scale</b>				
Score 1	32 (80)	30 (75)	6 (15)	
Score 2	2 (5)	3 (7.5)	17 (42.5)	
Score 3	6 (15)	7 (17.5)	12 (30)	
Score 4	0 (0)	0 (0)	5 (12.5)	
<b>Emergence agitation</b>				
3+4	6 (15)	7 (17.5)	17 (42.5)*	<0.001

Agitation score: 1 – Asleep; 2 – Awake but calm; 3 – Agitated but consolable; 4 – Severely agitated and inconsolable. Values are presented as number (n) or percentage (%). \*Significantly different compared to other two groups (P<0.05)

Saudi J Anaesth 2013;7(4): 392-398

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**PREMEDICATION WITH KETAMINE IS MORE EFFECTIVE THAN MIDAZOLAM IN PREVENTING EMERGENCE AGITATION AFTER SEVOFLURANE ANESTHESIA IN CHILDREN**

Incidence of emergence agitation<sup>a</sup> following sevoflurane anaesthesia in children undergoing ophthalmic surgery, stratified by study drug.

Time after arrival at PACU, min	Midazolam group n = 34	Ketamine group n = 33
0	8 (23.5)	8 (24.2)
10	6 (17.6)	0 (0.0)*
20	4 (11.8)	0 (0.0)*
30	0 (0.0)	0 (0.0)
Overall (0-30)	15 (44.2)	11 (33.3)

Ketamine 1 mg/kg

J Int Med Res 2016;44(2):258-266

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**INTRAOPERATIVE USE OF KETAMINE**

- Maintenance of respiratory drive
- Airway patency
- Deep sedation without need for supplemental O<sub>2</sub>
  - Advantages for facial, airway & OBA procedures
- Analgesia
- Amnesia
- Immobility
- Reduced opioid requirements/tolerance

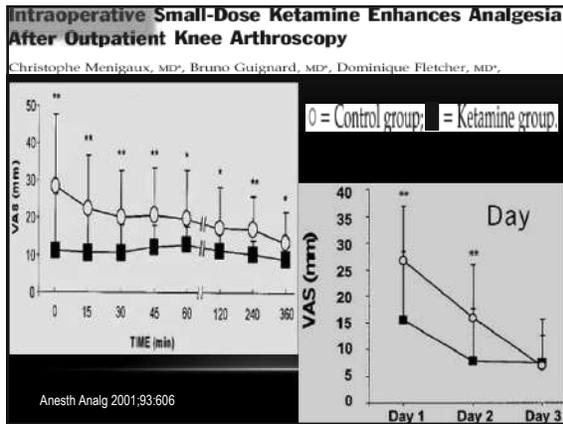
**Reduces secondary hyperalgesia**  
**Prevents central sensitization from peripheral pain**

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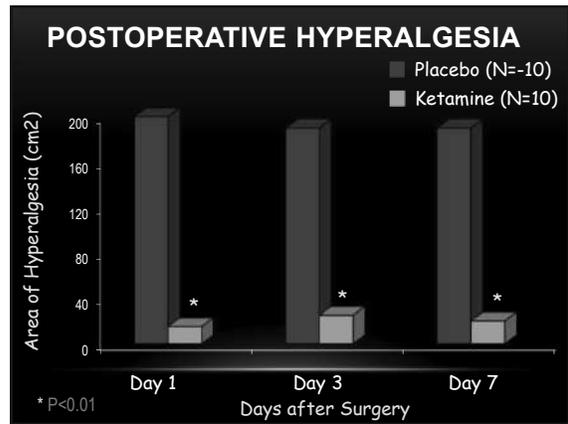
**POSTOPERATIVE BENEFITS OF INTRAOPERATIVE KETAMINE**

- Maintenance of respiratory drive
- Airway patency
- Analgesia
- Reduced opioid requirements
- Reduced postoperative pain
- Less PONV
- Euphoria

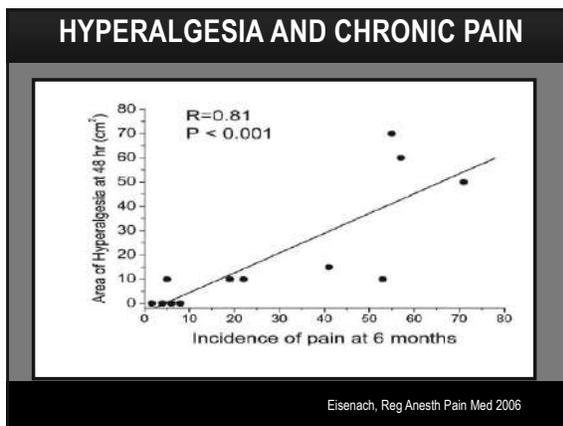
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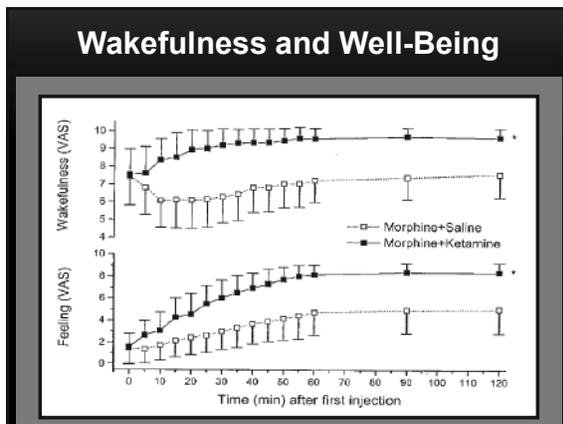


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### PSYCHOTROPIC EFFECTS

- Floating
- Dreams
  - Frightful
  - Euphoria
  - Hyper-alert
  - Vivid dreams
    - Often colorful
    - Often with religious overtones
- Near death experience
- Distorted perception
- Hallucinations
- Psychosis
- Talkative
- Wakefulness

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### NON ANESTHETIC/ANALGESIC USES

- Incidental antidepressant effect observed with chronic pain Rx
- Early study- Rapid antidepressant effect of ketamine within hours
  - Dose 0.5 mg/kg in 45 minutes
  - Saline vs ketamine infusions
- Later studies for both unipolar and bipolar depression
  - 24 hours after infusion: 25%-70% patients respond
  - 72 hours after infusion: 14%-50% patients respond
- Antidepressants take days-weeks to be effective
- ECT takes days to work

Biol Psychiatry 2000;47:351-4  
 Arch Gen Psychiatry 2006;63:856-64  
 Biol Psychiatry 2012;72:537-47  
 Front Pharmacol 2013;4:161

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### Obsessive compulsive disorders

- Near constant obsession responds to ketamine
  - Effect within 24 hours
  - lasts 7 days
- Refractory OCD responds immediately
  - lasts 24 hours

### Post-traumatic stress disorders

- 41 patients in randomized, double blind, crossover study
- Ketamine vs midazolam
- PTSD symptoms reduced in ketamine group at 24 hrs, lasting 7 days

• Neuropsychopharma 2013;38:2475-8  
 • Biol Psychiatry 2012;72: 964-70  
 • JAMA Psychiatry 2014;71:681-8  
 • JAMA 2014;312:327

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### MAC/SEDATION CHALLENGES INCLUDE:

- Safety
  - Hemodynamic stability
  - Airway maintenance
  - Adequate oxygenation
  - Adequate ventilation (normocarbica)
  - Immobile patient
- Expectations
  - Analgesia
  - Amnesia
  - Immobile patient

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### PROPOFOL FOR MAC

- Respiratory depression
- Cardiovascular depression
  - Decreases cardiac output
- Decreases blood pressure
- Pain on injection
- Disinhibited state
- Increased movement
- **No analgesia**

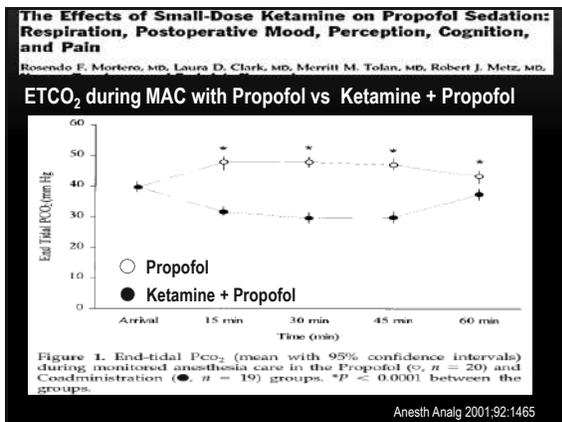


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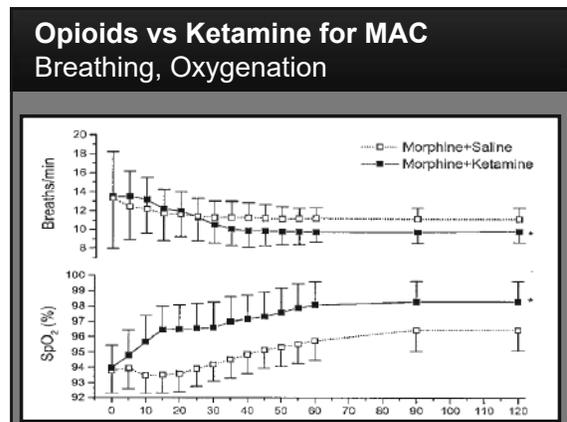
### KETAMINE FOR MAC

- Stimulates ventilation
- Enhances airway patency
- Analgesia
- Amnesia
- Immobility
- Enhances hemodynamics
  - Increases heart rate
  - Increases blood pressure
  - Increases cardiac output

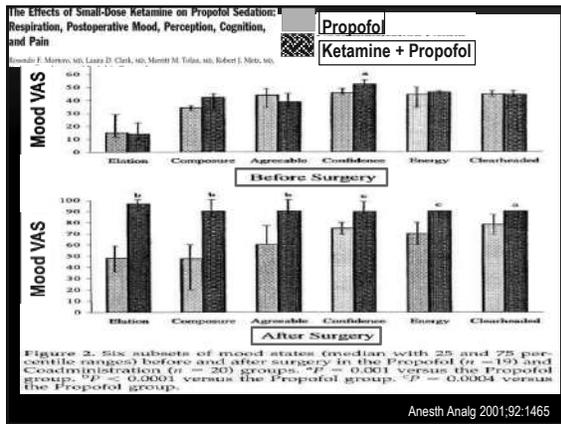
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29



30



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### KETAMINE + PROPOFOL = KETAFOLO

- Wide range of ketamine:propofol of ratio reported in literature
- 1:10 or 2:10 ratio of ketamine and propofol combined
- Balancing of hemodynamic effects
  - Propofol depresses cardiac function, lowers BP and HR
  - Ketamine is a sympathomimetic and augments cardiac contractility, BP and HR
- Ease of a single infusion

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### DOSING FOR SEDATION (OR ADJUNCT TO GENERAL ANESTHESIA)

- Ketamine
  - Bolus- 0.5 mg/kg (500 mcg/kg)
  - Infusion- 3-5 mcg/kg/min
- Ketafol
  - 1:10 ratio of Ketamine:Propofol
  - Bolus: 250-500 mcg/kg using propofol setting (25-50 mcg/kg of ketamine)
  - Infusion: 25-75 mcg/kg/min using propofol setting (2.5-7.5 mcg/kg/min of ketamine)
- Ketafol is like doubling the concentration of propofol

33

### IDEAL CANDIDATES FOR KETAMINE (OR KETAFOLO)

- Sleep apnea
- Tolerance to opioids
- Chronic pain
- High-risk for chronic pain procedures
- Concern about awareness
- Inability to use oxygen (fire hazard)
- Difficult airway sedation cases
- High risk PONV
- Severe asthma

34

### Multimodal Anesthesia

- Propofol
- Opioids
- Benzodiazepines
- Beta-blockers
- Inhalational agents
- Lidocaine infusions
- Ketamine (low-dose)

35

### MULTIMODAL SEDATION

- Propofol
- Opioids
- Benzodiazepines
- Ketamine (low-dose)

36

### MULTIMODAL ANALGESIA

- Opioids
- NSAIDs
- COX-2 inhibitors
- Gabapentin
- Acetaminophen
- Steroids
- Peripheral nerve blockade
- Local anesthetic injection
- Ketamine (low-dose)



37

### SUMMARY- KETAMINE

- Effective sedative when used in low doses
  - Especially when combined with propofol
- Decreased PONV, sedation and hypoventilation
- Effective analgesic in low doses
- Significantly improves pain scores (acute & chronic)
- Reduces opioid requirements by 40%-60%
- Minimal psychomimetic effects



38

**Pediatric Anesthesia Panel**  
**CRASH 2019**

Debnath Chatterjee, MD  
 Patrick Fernandez, MD  
 Lawrence Schwartz, MD

1

Disclosures

None

2

**Tonsillectomy and OSA**

A 7-year-old obese girl with sleep-disordered breathing is scheduled for tonsillectomy and adenoidectomy. She has a h/o ADHD and poor school performance. She had a sleep study which showed an Apnea Hypopnea Index of 28 events/h

3

**Preoperative Evaluation**

How is pediatric OSA different from adult OSA?  
 What are you looking for in the sleep study?

4

**Pediatric Obstructive Sleep Apnea**

Sleep disordered breathing

Primary snoring → Upper airway resistance syndrome → Obstructive sleep apnea syndrome

Recurrent episodes of partial or complete obstruction during sleep → Hypoxemia, Hypercapnia, Sleep disruption

1-4% of all children have OSA  
 Snoring is not synonymous with OSA

5

**Pediatric vs. Adult OSA**

	Children	Adults
<b>Presentation</b>		
Age	2-6 year peak	Increased elderly
Gender	M= F	M > F
Obesity	Few	Most
Tonsils& adenoids	Often enlarged	Rarely enlarged
Daytime sleepiness	Less common	More common
<b>Sleep</b>		
Sleep architecture	Usually normal	Decreased delta & REM
Arousals	May not be seen	At end of each apnea
<b>Treatment</b>		
Surgical	Definitive	Minority
Medical (CPAP)	Selected patients	Most common

6

### Pediatric OSA Grading

Severity	AHI Scores	Descriptors	O <sub>2</sub> nadir
Mild	1-5	SpO <sub>2</sub> < 90% for 2-5% of sleep time	> 92
Moderate	5-9	SpO <sub>2</sub> < 90% for 5-10% of sleep time	
Severe	>10	SpO <sub>2</sub> < 90% for > 10% of sleep time	< 80

Schwengel DA. Anesthesiology Clin 2014

7

- ### Indications for PSG in Children
- Obesity
  - Down's syndrome
  - Craniofacial abnormalities
  - Neuromuscular disorders
  - Sickle cell disease
  - Mucopolysaccharidoses
- AAO-HNS CPG on Tonsillectomy in Children. 2019

8

### Case continues

Following inhalational induction and intubation, the patient is being maintained with sevoflurane, O<sub>2</sub> & air.

What are your options for pain control in this patient?

Would you extubate awake vs. deep?

Would you admit this patient?

9

- ### Intra-op Analgesic Options
- Fentanyl
    - 0.5- 1 mcg/kg, titrated to RR
  - Dexmedetomidine
    - 0.5-1 mcg/kg
  - Dexamethasone
    - 0.5 mg/kg, up to max 10 mg IV
  - Acetaminophen- IV

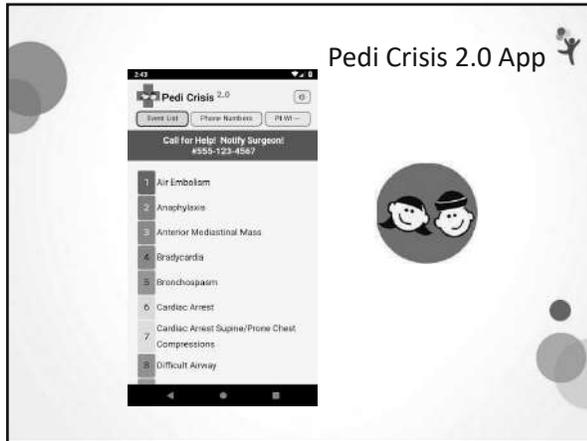
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- ### Post Discharge Medications
- Alternating Acetaminophen & ibuprofen q 3 hours
  - Acetaminophen 10-15 mg/kg q 4-6 hours
    - max- 75 mg/kg/day or 4 grams
  - Ibuprofen 5-10 mg/kg q 6-8 hours
    - After 3 hours post op
  - Oxycodone 0.05 mg/kg q 6 h for patients > 5 years
  - NO CODEINE, tramadol and hydrocodone
  - Ultra-rapid metabolizers CYP450 2D6 pathway

11

- ### Overnight Admission Criteria
- Children < 3 years of age
  - Severe OSA
  - Comorbidities
    - Down syndrome
    - Cardiac complications of OSA
    - Neuromuscular disorders
    - Failure to thrive
    - Craniofacial anomalies
    - Obese children
- AAO-HNS CPG on Tonsillectomy in Children. 2019

12



13

### Hypospadias

An 18-month-old boy, who weighs 10 kg is scheduled for hypospadias repair. He was born at term and is otherwise healthy.

Would you supplement GA with a regional block?

Are there any concerns with a caudal?

14

### Caudal Controversy

Associated between caudal and increased risk of postop surgical complications in hypospadias repair  
 Taicher BM, et al. *Pediatr Anesth* 2017  
 13 – fold increase in urethrocutaneous fistula (5.6%, n=22)

Caudal, hypospadias and urethrocutaneous fistula:  
 Does association mean causality?  
 Polaner DM. *Pediatr Anesth* 2017 : Statistical issues

Cause and Effect versus Confounding?  
 Braga LH, *J Urology* 2017  
 Hypospadias severity and not type of block increased comps

15

### Caudal Block

You proceed to perform a caudal block with 10 cc of bupivacaine 0.125% with epinephrine.

Is there a role for test dose?

Following administration of LA, you notice ST elevation on EKG, hypotension and bradycardia.

How would proceed?

16

### Test Dose

- Epinephrine 0.5 mcg/kg
- Increase in HR of > 10 bpm or SBP > 15 mm Hg
- Low sensitivity in children
- Prior administration of atropine
- Changes in T wave amplitude
- Administer LA in 0.1-0.2 ml/kg aliquots with an observation time of 60-90 s after each injection

Tobias JD. *Anesth Analg* 2001

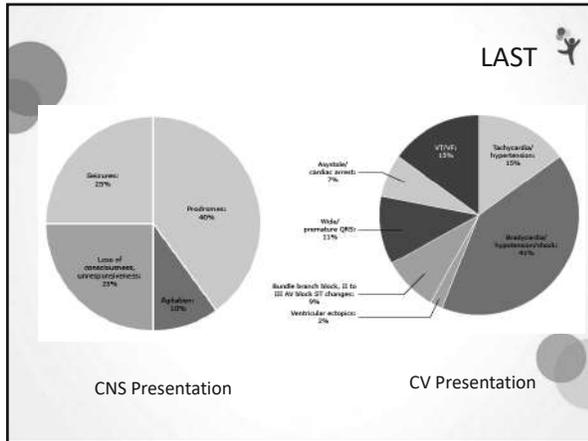
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### Caudal Block

Following administration of LA, you notice ST elevation on EKG, hypotension and bradycardia.

How would proceed?

18



19

**LAST**

Pharmacologic Treatment of LAST is Different from Other Cardiac Arrest Scenarios

- \* **Reduce** individual epinephrine boluses to  $\leq 1$  mcg/kg
- \* **Avoid** vasopressin, calcium channel blocks, beta blockers, or other local anesthetics

20

**LAST**

Stop injecting local anesthetic and call for help

Consider lipid emulsion therapy at the first sign

- Call for the LAST Rescue Kit
- Alert the nearest cardiopulmonary bypass team

**Airway management**

Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary

**Control seizures**

- Benzodiazepines preferred
- Avoid** large doses of propofol, especially in hemodynamically unstable patients

Treat hypotension and bradycardia — **If pulseless, start CPR**

21

**LAST**

Lipid Emulsion 20% (Precise volume and flow rate are not crucial)	
Greater than 70 kg patient	Less than 70 kg patient
<b>Bolus 100 mL Lipid Emulsion 20%</b> rapidly over 2-3 minutes	<b>Bolus 1.5 mL/kg Lipid Emulsion 20%</b> rapidly over 2-3 minutes
<ul style="list-style-type: none"> <li>Lipid emulsion infusion 200-250 mL over 15-20 minutes</li> </ul>	<ul style="list-style-type: none"> <li>Lipid emulsion infusion <math>\sim 0.25</math> mL/kg/min (ideal body weight)</li> </ul>
<b>If patient remains unstable:</b>	
<ul style="list-style-type: none"> <li>Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (1.2mL/kg)</li> <li>Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., &gt; 30 minutes)</li> </ul>	

22



23

## Pectus excavatum repair . . .

An otherwise healthy 15 year-old, 53 kg male is scheduled to undergo minimally invasive surgical repair of pectus excavatum (Nuss procedure). The patient denies chest pain or shortness of breath but complains of increasing fatigue over the past 6 months.

- Opioid crisis and multimodal analgesia
- Options for pain management
- Foley catheter needed with thoracic epidural?

1

## Pectus . . . Opioid crisis

- Death from prescription opioids ↑ 4x since 1999
- Past decade
  - > 200,000 poison center calls for pediatric opioid exposure
  - Doubling of pediatric opioid-related hospital admissions
- National standard to limit outpatient opioid prescriptions to 7-day
- Multimodal analgesia is KEY

2

## Pectus . . . Perioperative analgesia

- IV opioid PCA
- Regional analgesia
  - Thoracic epidural (PCEA vs continuous only)
  - Peripheral blocks/catheters: Paravertebral, erector spinae plane
- Multimodal approach: Regional + NSAIDs + NMDA blockers +  $\alpha_2$ -agonists . . .
- Cryoanalgesia?

3

## Pectus . . . Foley for thoracic epidural

- Why place one?
  - Concern for urinary retention due to epidural opioid
  - Less patient distress to place when under GA for surgery
- Why not place one?
  - Pt discomfort
  - Risk of iatrogenic UTI

4

## Arm fracture . . .

12 year old male presents for open reduction and internal fixation of right supracondylar humerus fracture following a fall at the trampoline park.

- Airway management: Intubate vs LMA?
- Brachial plexus block and concern for acute compartment syndrome

5

## Arm fracture . . . Airway management

- LMA vs ETT . . .
  - Patient positioning . . . Prone?
  - Full stomach → Taking opioids
  - Length of procedure?

6

## Arm fracture . . . Regional anesthesia

- Can compartment syndrome be masked?
  - Case reports suggest regional anesthesia may delay diagnosis
- Can RA facilitate diagnosis?
  - "Pain out of proportion"
- Still controversial
  - Anterior compartment of lower extremity is highest risk

Things to consider . . .
Reduce LA concentration (0.1 – 0.25%)
Limit continuous infusions to 0.1%
Think carefully with higher risk surgeries
Careful follow-up/adequate vigilance
Do not delay evaluation if compartment syndrome is suspected

**CRASH 2019**

The Relationship Between Wellness, Resilience and Quality  
Alison Brainard MD, Norah Janosy MD, Melanie Donnelly MD  
February, 2018

1

**Objectives**

- Understand burnout – the features, risk factors, signs and symptoms
- Understand the connection between provider wellness, quality and safety culture
- Experience resilience techniques that are shown to decrease burnout and increase resilience
- Investigate the national and regional available resources surrounding quality improvement and wellness
- Develop an unexpected event algorithm for your own institution
- Using the tools, develop an outline of an initial PDSA cycle meant to address the problem of burnout

2

**Overview**

3



4

**Acknowledgments**



Jenny Reese, MD



Abbie Beacham, PhD



Resilience Program



Vesna Jevtovic-Todorovic, MD, PhD, MBA

5

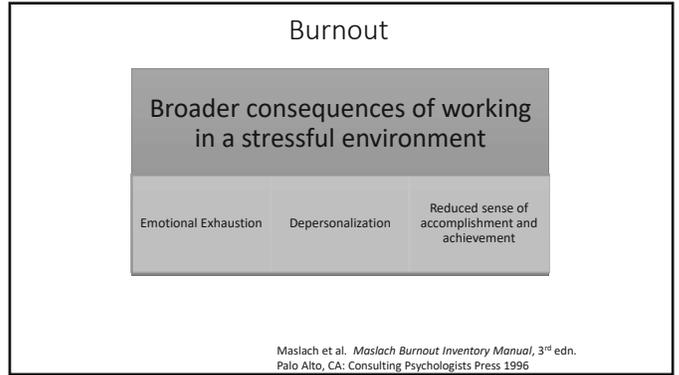
How do you **define** burnout?



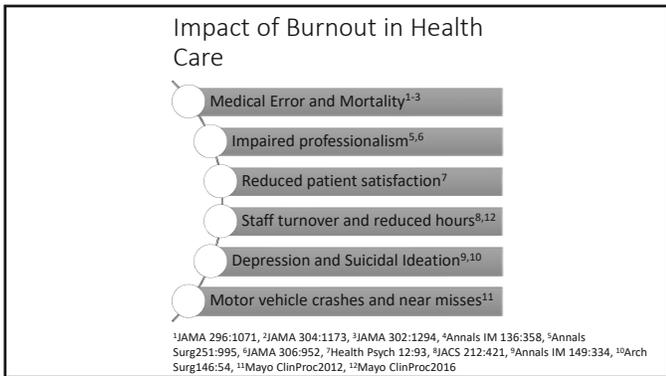
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“Burnout is the sum total of hundreds of tiny betrayals of purpose, each one so minute that it hardly attracts notice.”  
 – Richard Gunderman, MD, PhD

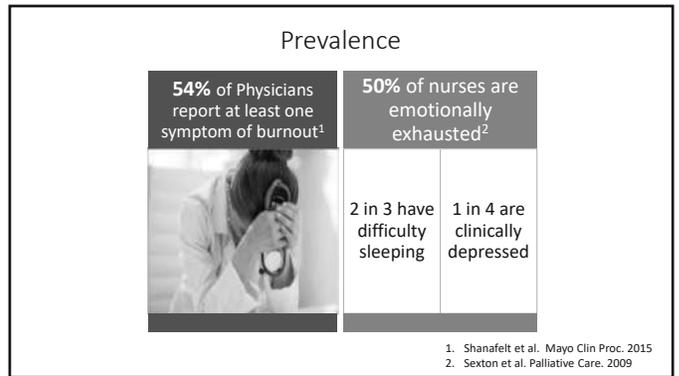
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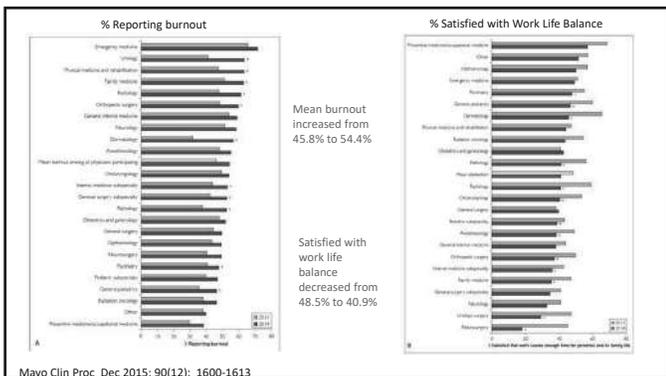
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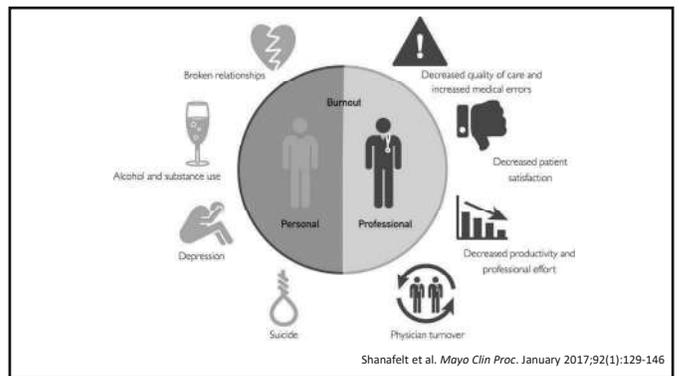
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13

What is a “second victim”?

First described by Albert Wu in 2000

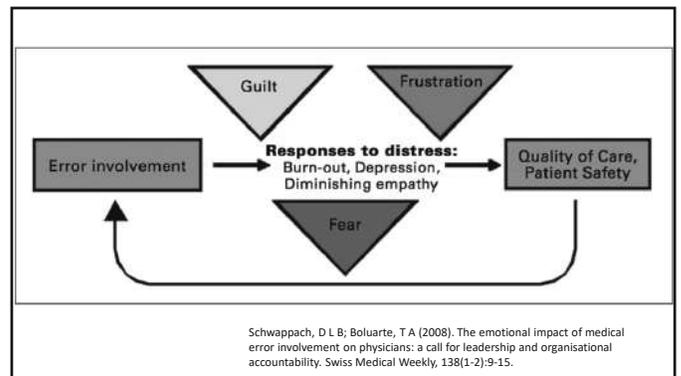
“... although patients are the first and obvious victims of medical mistakes, doctors are wounded by the same errors: they are the second victims.”

14

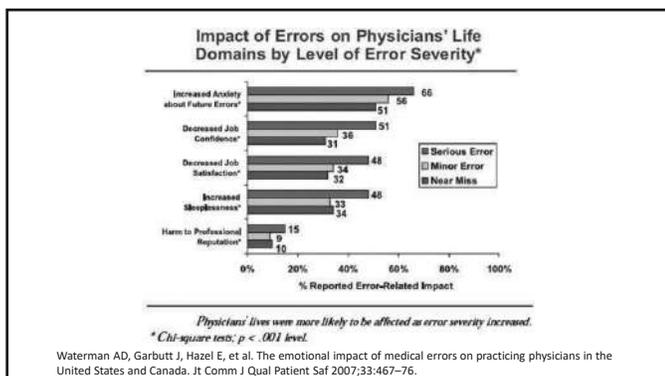
Formal definition:

- “A health-care provider involved in an unanticipated adverse patient event, medical error and/or a patient-related injury who becomes victimized in the sense that the provider is traumatized by the event.” (Scott et al., 2009)

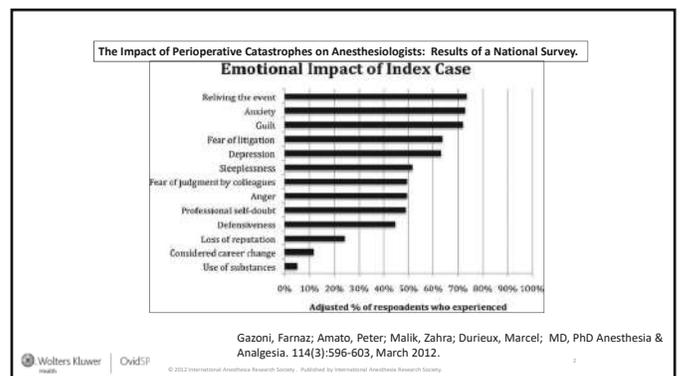
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What happens at your institution?

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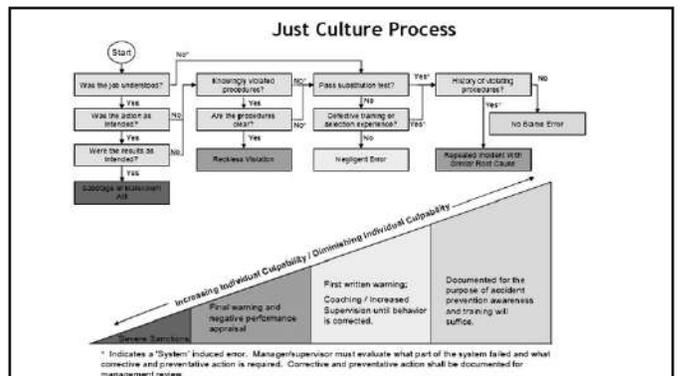


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So now what....

- We know that burnout is an adverse outcome for health care providers which we need to address
- Lets figure out what how to approach this problem in a systematic way....

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22

First steps.....

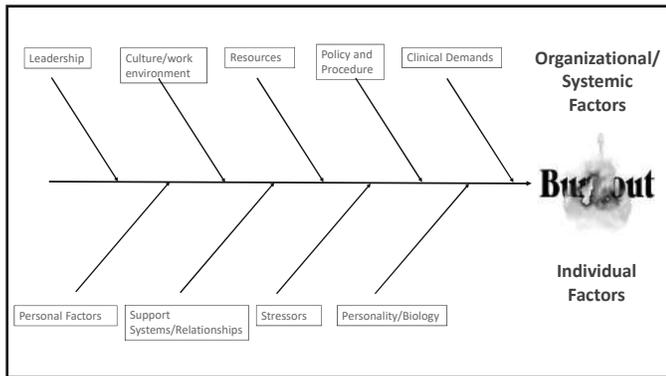
- Step 1: Overall what is our goal...
  - reduce burnout in ourselves and colleagues, focus on improving provider wellness in achievement of the quadruple aim in healthcare, etc
- Step 2: Literature Review to better understand the problem

23

Step 3: What is current culture surrounding this problem and provide a better definition of the problem.

- Define problem better:
  - What is the problem exactly and why is it a problem?
  - → what is burnout and why do you consider it a problem at all?
  - What is the evidence that this is a problem, local or based on literature?
  - Who are the stakeholders who may have something to gain or lose by addressing this problem?

24



25

Next....

- So...
  - 1-we know the problem,
  - 2-we have some literature about the problem
  - 3-we have engaged our stakeholders in defining what factors contribute to the problem...
- **What do we want to do to fix the problem....or at least begin to address the problem....**

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Step 5: SMART AIM

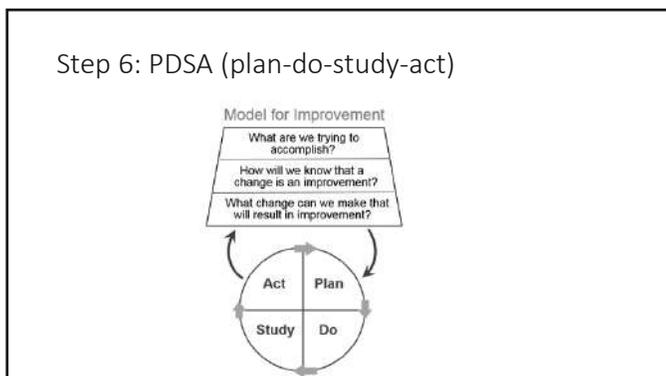
- **Specific, Measurable, Achievable, Relevant and Time based**
- To do this we need to figure out:
  - What changes can we make which will result in improvement of the problem based on what we have discovered about the problem and the literature?
  - How will we measure success? What outcome will you use? – more to come....

27

SMART AIM

- We will increase “mindfulness” by doing 30 minute experiential mindfulness exercises before work once a week for 8 weeks. We will evaluate the impact of this intervention by measuring the Cognitive and Affective Mindfulness Scale (CAMS-R) before and after the intervention.

28



29

How can we measure success in the arena of wellness and burnout?

30



31

### Subjective Rating of Sleep Quality

Please rate your sleep quality over the previous month

0 Very Good      1      2      3 Very Bad

Byssse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*, 28, 193-213.

32

### Perceived Stress Scale- 10 Item

Instructions: The questions in this scale ask you about your feelings and thoughts during the last month. In each case, please indicate with a check how often you felt or thought a certain way.

33

### MINI-Z BURNOUT SURVEY

AMA STEPS

<https://www.stepsforward.org/modules/physician-burnout-survey>

34

### What is Resilience?

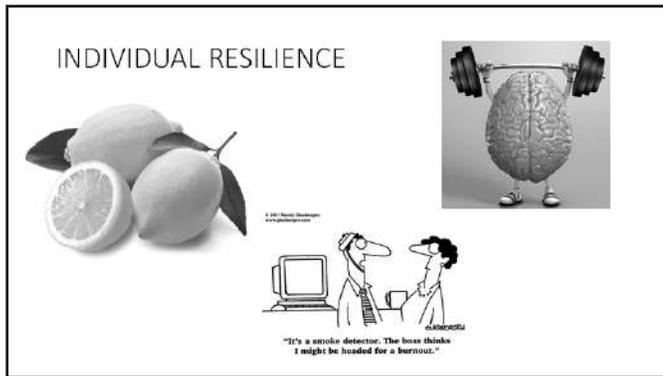
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### Resilience

- Resilience is the process of negotiating, managing and adapting to significant sources of stress or trauma.
- Assets and resources within the individual, their life and environment facilitate this capacity for adaptation and “bouncing back” in the face of adversity.
- Across the life course, the experience of resilience will vary.

Windle et al. A methodological review of resilience measurement scales. *Health and Quality of Life Outcomes* 2011, 9:8.

36



37



38



39

# Friday

## PERIOPERATIVE EVALUATION AND ANESTHETIC MANAGEMENT OF PATIENTS WITH CARDIAC DISEASE FOR NON-CARDIAC SURGERY

BobbieJean Sweitzer, MD, FACP  
 Professor of Anesthesiology  
 Director, Perioperative Medicine  
 Northwestern University, Chicago IL  
[bobbie.sweitzer@northwestern.edu](mailto:bobbie.sweitzer@northwestern.edu)  
**I have no disclosures**

1

### WHICH PATIENT IS AT HIGHEST RISK?

1. 70 yo asymptomatic patient with history of heart failure with recent echocardiogram with EF 28%
2. 55 yo with previous history of myocardial infarction with fixed defect on nuclear medicine stress test 3 wks ago
3. 60 yo with stable angina ~once/month if he "hurries upstairs"

2

**Circulation** JACC VOL. 64, NO. 22, 2014  
 DECEMBER 9, 2014:e77-137 American Heart Association

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

although perioperative risk-prediction models place greater emphasis on CAD than on HF, patients with active HF have a significantly higher risk of postoperative death than do patients with CAD.

the 30-day postoperative mortality rate was significantly higher in patients with nonischemic HF (9.3%), ischemic HF (9.2%), and atrial fibrillation (AF) (6.4%) than in those with CAD

3

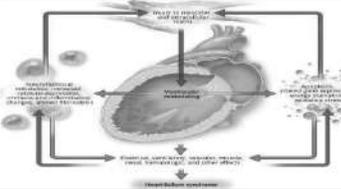
### PERIOPERATIVE RISK OF HF

- ❖ Surgical survival worse
  - ❖ with HFrEF (systolic dysfunction) <30% *versus* HFREF ≥30%
  - ❖ with HFrEF > HFpEF (diastolic dysfunction)
  - ❖ with HFpEF > without HF
- ❖ Mortality and Morbidity
  - Highest in patients with **symptomatic** HF (49%)
  - **Asymptomatic** HFrEF (23%)
  - **Asymptomatic** HFpEF (18%)
  - Normal LV function (10%)

Kazmers AJ. Vasc Surg 1988;8:307  
 Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). Eur Heart J 2012;33:1750  
 Flu W-J. Anesthesiology 2010;112:1316

4

## HEART FAILURE



- ❖ 2/3 of patients with HFrEF have CAD
- ❖ Diabetes, hypertension contribute
- ❖ 1/3: genetic causes, viral infection (often unrecognized), alcohol abuse, chemotherapy
- ❖ 50% of HF patients have HFpEF
- ❖ Hypertension #1 cause of HFpEF

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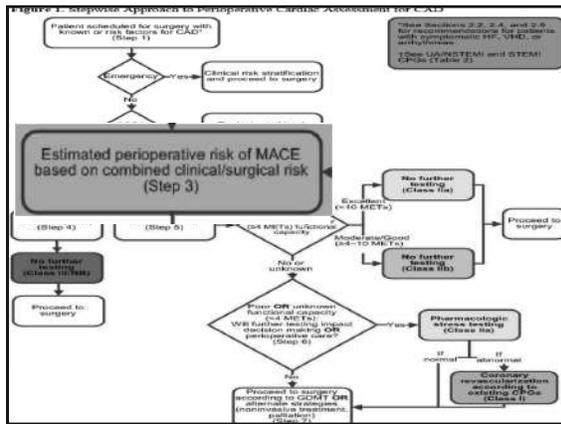
**Circulation** Circulation. 2014;130:e278-e333 American Heart Association

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Assessment of LV function	
It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of LV function	IIa
It is reasonable for patients with HF with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function	IIa
Reassessment of LV function in clinically stable patients may be considered	IIb
Routine preoperative evaluation of LV function is not recommended	III: No Benefit

6





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### 3. Calculation of Risk to Predict Perioperative Cardiac Morbidity

#### 3.1. Multivariate Risk Indices: Recommendations

- <http://www.riskcalculator.facs.org/>
- <http://www.surgicalriskcalculator.com/miorcardiacarrest>
- RCRI (6 predictors)
  - Major surgery (thoracic, intra-peritoneal, suprainguinal vascular)
  - Diabetes requiring insulin
  - Creatinine  $\geq 2.0$  mg/dL
  - Cerebrovascular disease
  - Heart failure
  - Ischemic heart disease

Smoking  
Gender  
Hypercholesterolemia  
Hypertension  
Family history  
Abnormal ECGs

- 0-1 predictor(s): low risk of MACE
- $\geq 2$  predictors: elevated risk of MACE

JACC. 2014;64:e77-e137.

14

**Estimate risk of perioperative myocardial infarction or cardiac arrest.**

Age:

Creatinine:

ASA Class:

ASA 1 = Normal healthy patient  
 ASA 2 = Patients with mild systemic disease  
 ASA 3 = Patients with severe systemic disease  
 ASA 4 = Patients with severe systemic disease that is a constant threat to life  
 ASA 5 = Moribund patients who are not expected to survive without the operation

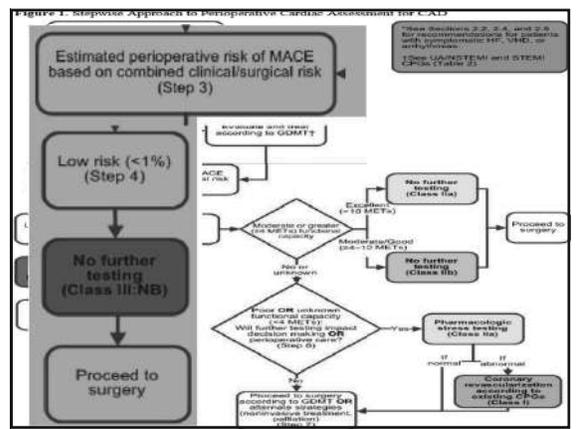
Preoperative Function:

Procedure:

**Gupta Perioperative Cardiac Risk**

**Estimated risk of perioperative myocardial infarction or cardiac arrest: 0.18 %.**

15



16

**Circulation** | American Heart Association

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

**Low risk: <1% risk of MACE\***

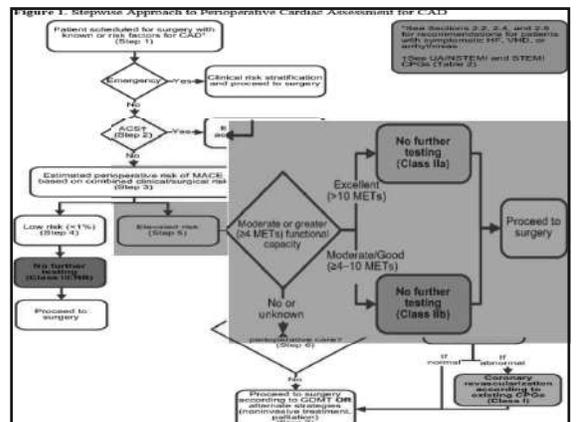
**Class III: No Benefit**

1. For patients with a low risk of perioperative MACE, further testing is not recommended before the planned operation (34, 35). (Level of Evidence: B)

- No ECG
- No stress testing
- No echocardiography
- No cath

JACC. 2014;64:e77-e137.

17



18

### MANY PATIENTS WHO DIE POSTOPERATIVELY ARE SUBJECTIVELY JUDGED AS LOW-RISK BEFORE SURGERY

- Measurement of exercise tolerance (METs) before surgery
- Participants ≥40 years with ≥1 risk factor for CAD or known CAD and major non-cardiac surgery (n=1399)
- Outcomes: Death or MI within 30 days of surgery and at 1 year
- Subjective rating of preoperative functional capacity
  - Anesthesiologists in the preop clinic or on the DOS asked to make a subjective judgment of participants' functional capacity after assessing their usual preop history
- Cardiopulmonary exercise testing
  - Measured peak O<sub>2</sub> consumption
- Duke Activity Status Index (DASI) questionnaire
- N-terminal pro-B-type natriuretic peptide (NT pro-BNP)

Lancet 2018;391:2631-2640

19

### CONCLUSIONS

- Subjective assessment of functional capacity should not be used
- This common practice does not accurately identify patients with poor fitness or increased risk for postop morbidity & mortality
- Objective measures (DASI questionnaire & NT-pro-BNP & perhaps CPET) can predict complications after major non-cardiac surgery

Can you:	Points
1. Take care of yourself, that is, eat, dress, bathe or use the toilet?	2.75
2. Walk indoors, such as around your house?	1.75
3. Walk 200 yards on level ground?	2.75
4. Climb a flight of stairs or walk up a hill?	5.50
5. Run a short distance?	8.00
6. Do light work around the house like dusting or washing dishes?	2.70
7. Do moderate work around the house like vacuuming, sweeping floors, or carrying groceries?	3.50
8. Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?	8.00
9. Do yard work like raking leaves, weeding or pushing a power mower?	4.50
10. Have sexual relations?	5.25
11. Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a ball?	6.00
12. Participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	7.50

Lancet 2018;391:2631-2640; Am J Cardiol 1989;64:651

20

**Class IIa**

1. It is reasonable for patients who are at an elevated risk for noncardiac surgery and have poor functional capacity (<4 METs) to undergo noninvasive pharmacological stress testing (either dobutamine stress echocardiogram [DSE] or pharmacological stress MPI) if it will change management (183-187). (Level of Evidence: B)

**Class III: No Benefit**

1. Routine screening with noninvasive stress testing is not useful for patients undergoing low-risk noncardiac surgery (165, 166). (Level of Evidence: B)

- The presence of moderate to large areas of myocardial ischemia is associated with increased risk of perioperative MI and/or death.
- A normal study for perioperative MI and/or cardiac death has a very high negative predictive value.
- The presence of an old MI identified on rest imaging is of little predictive value for perioperative MI or cardiac death.

JACC. 2014;64:e77-e137.

21

### Non-invasive cardiac stress testing before elective major non-cardiac surgery: population based cohort study

Durrant N, Wijeyesundera, lecture 18.3 W Scott Beattie, B Fraser Elliot chair in cardiac anaesthesia 2 Penn

**Revised Cardiac Risk Index**

1. High risk surgery: thoracic, intra-peritoneal, suprainguinal vascular
2. Ischemic heart disease
3. Heart failure
4. Cerebrovascular disease
5. Diabetes mellitus
6. Renal insuff (Cr ≥2)

Fig 2 | Association of preoperative stress testing with one year survival in the subgroup. These benefits largely applied to patients who were at high risk for cardiac complications on the basis of three or more clinical risk factors. In contrast, stress testing was associated with only minor benefits for intermediate risk patients (one or two risk factors) and with harm in low risk individuals.

BMJ 2010;340:5526

22

### Overuse of Preoperative Cardiac Stress Testing in Medicare Patients Undergoing Elective Noncardiac Surgery

Kristin M. Sheffield, PhD,\* Patricia S. McAdams, BA,\* Jaime Benavente-Gampel, MD,\* James S. Gooswin, MD.

nearly one third of imaging tests were for patients in whom such testing is rarely appropriate.

risk for cancer due to ionizing radiation related to stress MPI (mean effective dose, 16.9 mSv per examination) was estimated to be 1 radiation-related cancer per 1230 MPIs

would result in 491 patients per year developing cancer later in their lifetime.

Ann Surg. 2013;257:73.  
Ann Intern Med. 2014;161:482.

23

### OUR PREOCCUPATION WITH CORONARY LUMINOLOGY: THE DISSOCIATION BETWEEN CLINICAL AND ANGIOGRAPHIC FINDINGS IN ISCHEMIC HEART DISEASE

CIRCULATION 1995;92:2333

- Overestimation of lumen gain angiographically after angioplasty
- Angiographically unrecognized left main disease

X-ray beam

24

**Circulation** American Heart Association

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

**The 12-lead ECG**

Preoperative resting 12-lead ECG is reasonable for patients with known coronary heart disease or other significant structural heart disease, except for low-risk surgery	IIa
Preoperative resting 12-lead ECG may be considered for asymptomatic patients, except for low-risk surgery	IIb
Routine preoperative resting 12-lead ECG is not useful for asymptomatic patients undergoing low-risk surgical procedures	III: No Benefit

**What about a preoperative ECG for a baseline??**

JACC 2014; 64 : e77-137

25

*Vasc Surg*, 2013 Jan 57(1):119-72. doi: 10.1016/j.jvs.2012.06.004. Epub 2012 Sep 10.

**Prognostic value of 12-lead electrocardiogram and peak troponin I level after vascular surgery.**

Garcia S<sup>1</sup>, Marston N, Sandoval Y, Plerpoint G, Adalog S, Glines J, Santilli S, McFalls EO.

- High risk patients: routine ECG and troponins measured
  - 40% had elevated troponin levels
  - Only 6% had ischemia on ECG
  - Elevations in troponins predicted death at 1 year; ECGs did NOT

- "The current use of ECGs may have developed as a method to screen for MI when little else was routinely available."
- "A standard age or risk factor cutoff for use of preoperative electrocardiographic testing has not been defined."
- "Likewise, the optimal time interval between obtaining a 12-lead ECG and elective surgery is unknown."

JACC 2014; 64 : e77-137

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**THE VALUE OF ROUTINE PREOPERATIVE ELECTROCARDIOGRAPHY IN PREDICTING MYOCARDIAL INFARCTION AFTER NONCARDIAC SURGERY**

- 2967 non-ambulatory, noncardiac surgery pts > 50 yrs
- Preoperative ECG in 80% of patients
- 45% ECGs with at least one abnormality
- Bundle branch blocks (RBBB & LBBB) on the preop ECG were related to POMI & death
- Did not improve prediction beyond risk factors identified on patient history

CMS (Medicare and Medicaid) does NOT reimburse for *preoperative, or age-based ECGs*

van Klei, WA . Ann Surg 2007;246:165-170

27

**Society Guidelines**

**Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery**

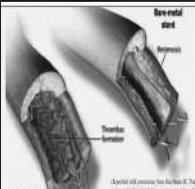
- Strong recommendations include:
  - Measure BNP or NT-proBNP before surgery for:
    - Patients ≥65 years old
    - Patients 45-64 years of age with significant CV disease or a Revised Cardiac Risk Index >1
  - Smoking cessation for ALL patients
- Recommend against performing (preoperatively):
  - Resting echo
  - Stress test
  - Angiography
  - CPET

Duceppe E. Can J Cardiol 2017;33:17  
 Ryding ADS. Anesthesiology 2009;111:311  
 Rodseth RN. JACC 2014;63:170

28

**Mounting Evidence for Lack of PCI Benefit in Stable Ischemic Heart Disease**

What More Will It Take to Turn the Tide of Treatment?  
 Perioperative coronary revascularization can cause harm and does not improve clinical outcomes, even in high-risk patients.



"Interventional cardiology is doing *cosmetic surgery* on coronary arteries, making them look pretty, but it's not treating the underlying biology of these arteries," (Dr. Ozner, author of "The Great American Heart Hoax" who received the 2008 AHA Humanitarian Award)

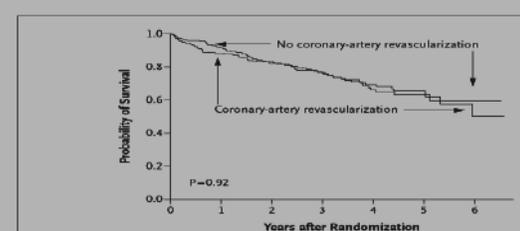
Ann Intern Med. 2010;152:47-51  
 Arch Intern Med. 2012;172:

29

**The NEW ENGLAND JOURNAL of MEDICINE**

**CORONARY-ARTERY REVASCULARIZATION BEFORE ELECTIVE MAJOR VASCULAR SURGERY (CARP)**

MCFALLS E. 2004; 351:2795



No. at Risk	0	1	2	3	4	5	6
Revascularization	226	175	113	65	18	7	
No revascularization	229	172	108	55	17	12	

30

### 6.1. Coronary Revascularization Before Noncardiac Surgery: Recommendations

**Class III: No Benefit**

- It is not recommended that routine coronary revascularization be performed before noncardiac surgery exclusively to reduce perioperative cardiac events (116). (Level of Evidence: B)

**CABG can prolong life and reduce angina in select populations (left main, 3 vessel disease)**

PCI should be limited to:

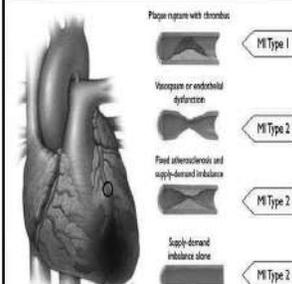
- L main disease if CABG too high
- Unstable CAD (imminent risk of infarction)
- STEMI or non-ST elevation ACS

JACC. 2014; 64: e77-137

31

### WHY DOES MEDICAL MANAGEMENT MAKE SENSE AND REVASCULARIZATION DOESN'T?

Medical management stabilizes plaques, prevents thrombosis and supply-demand mismatch



- Most non-periop events due to plaque rupture/thrombosis
  - Type 1 MI
  - Most common in vessels with 40%-70% blockage
- Most periop events 2nd supply-demand mismatch
  - Type 2 MI
  - Frequently NOT critical stenoses
  - Commonly: <70% blockage

32

Circulation  
JACC VOL. 64, NO. 23, 2014  
DECEMBER 9, 2014:e77-137  
American Heart Association

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

(302). The combination of aspirin, beta blockers, and statin therapy was associated with better 30-day and 12-month risk reduction for MI, stroke, and death than any of the 3 medications independently.

302. Lau WC, Froehlich JB, Jewell ES, et al. Impact of adding aspirin to beta-blocker and statin in high-risk patients undergoing major vascular surgery. *Ann Vasc Surg.* 2013;27:537-45.

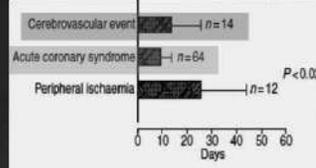
33

Low-dose aspirin for secondary cardiovascular prevention — cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation — review and meta-analysis

W. BURGER, J.-M. CHEMISNUS, G. D. KNEISSL, & G. BECKER

- Reviewed 41 studies/ 50,000 patients
- ASA withdrawal precedes 10.2% of acute CV events

Rebound effect with increased platelet activity with aspirin withdrawal 8-12 days after stopping



Hyper-coagulable states:

- Surgery
  - Decreased fibrinolysis
  - Inflammation
  - Increased platelet adhesiveness
- Pathologies
  - (Cancer, diabetes, obesity, infection)

J Intern Med 2005;257:399-414

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ORIGINAL ARTICLE

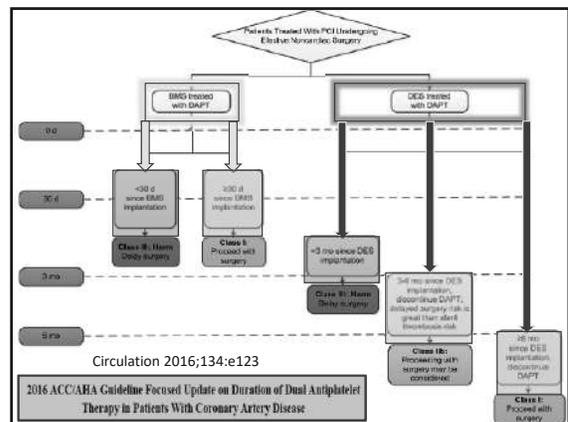
### Aspirin in Patients Undergoing Noncardiac Surgery

P. J. Devereaux, M. Mroczkowska, D. I. Sessler, K. Leslie, P. Alonso-Coello, A. Kurz

Table 1. Characteristics of the Patients at Baseline.\*

Characteristic	Aspirin (N=4998)	Placebo (N=5012)
Eligibility criteria met — no. (%)		
History of vascular disease	1636 (32.7)	1635 (32.6)
Coronary artery disease	1153 (23.1)	1115 (22.2)
Peripheral arterial disease	438 (8.8)	427 (8.5)
Stroke	250 (5.0)	292 (5.8)
Other medical history — no. (%)		
History of coronary-artery bypass grafting	241 (4.8)	240 (4.8)
History of percutaneous coronary intervention	234 (4.7)	236 (4.7)
Bare metal stent	128 (2.6)	127 (2.5)
Drug eluting stent	54 (1.1)	65 (1.3)
Unknown stent type	29 (0.6)	24 (0.5)

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**2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease**

Recommendations for Duration of DAPT in Patients With SHD		
COR	LOE	Recommendations
I	A	In patients with SHD treated with DAPT after BMS implantation, P2Y <sub>12</sub> inhibitor therapy (clopidogrel) should be given for a minimum of 1 month. <sup>64,65</sup>
I	B-R <sup>66</sup>	In patients with SHD treated with DAPT after DES implantation, P2Y <sub>12</sub> inhibitor therapy (clopidogrel) should be given for at least 6 months. <sup>11,12,23,26,67</sup>

**Continue aspirin, 75-100 mg for ALL patients with stents if at all possible**

Recommendations for Duration of DAPT in Patients With ACS Treated With PCI		
COR	LOE	Recommendations
I	B-R	In patients with ACS treated with DAPT after BMS or DES implantation, P2Y <sub>12</sub> inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) should be given for at least 12 months. <sup>6,68-69,70,86-88</sup>

Circulation 2016;134:e123.

37

♦ Statin users have 5-fold reduced risk of 30-day death  
 ♦ Vascular surgery patients on statins have 57% lower chance of perioperative MI or death at 2-yr follow-up

Heeschen, Circulation 2002  
 Collard, J Thorac Cardiovasc Surg 2006  
 Schouten, Am J Cardiol 2007  
 Le Manach, Anesth Analg 2007

38

**MYOCARDIAL INJURY IN NONCARDIAC SURGERY (MINS) THE ROLE OF POSTOPERATIVE TROPONINS**

- Myocardial injury is the most common cause of death during the 30 days after noncardiac surgery
- Only 14% of patients will have chest pain
- 65% are clinically silent (no symptoms at all)
- Mortality is similar with and without symptoms
- 30 day mortality with troponin elevation is 10%
  - A 5-fold increase from background risk
- In surgical patients ≥45 years of age the NNT is only 15

Peak Troponin (ng/mL)	30-Day Mortality (%)	Time to Death (d)
<0.01	1	—
0.02	4	13
0.03-0.29	9	9
≥0.3	17	6

Sessler D. Anesth Analg 2016;123:359

39

**Relationship between Intraoperative Hypotension, Defined by Either Reduction from Baseline or Absolute Thresholds, and Acute Kidney and Myocardial Injury after Noncardiac Surgery**

**AVOID HYPOTENSION!!!!**

Anesthesiology 2017;126:47-65

40

**Society Guidelines**

**Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery**

Emmanuelle Duceppe, MD,<sup>a,b,c</sup> Joel Parlow, MD, MSc (Co-chair),<sup>d</sup> Paul MacDonald, MD,<sup>e</sup>

- Measuring daily troponin for 48-72 hrs postop in patients with:
  - PREOP elevated NT-proBNP/BNP
  - If NO PREOP measurement of NT-proBNP/BNP those with:
    - RCRI ≥1
    - Age 45-64 with significant CV disease
    - Age ≥65
- Initiation of long term aspirin and statin in those having MINS or infarction after surgery

Duceppe E. Can J Cardiol 2017;33:17

41

**The Use of Antiplatelet Therapy in the Outpatient Setting: Canadian Cardiovascular Society Guidelines**

2005

Use of NSAIDs in patients on ASA

All NSAIDs and coxibs should be avoided in patients at increased cardiovascular risk (Class III, Level A).

Individuals taking ASA for vascular protection should avoid the concomitant use of traditional (non-coxib) NSAIDs (Class III, Level C).

- The FDA specifically recommended taking the lowest effective NSAID dose for the shortest period of time

In July 2015, the FDA strengthened its warning about NSAID use to emphasize that patients taking NSAIDs are at greater risk for heart attack or stroke.

Can J Cardiology 2011;27:S1-S59

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**The Thrombotic and Arrhythmogenic Risks of Perioperative NSAIDs**  
 Neal Stuart Gerstein, MD,<sup>1</sup> Wendy Hai,<sup>2</sup> *Journal of Cardiothoracic and Vascular Anesthesia*, Vol 28, No 2 (April), 2014; pp. 363

**NSAID Use and Association with Cardiovascular Outcomes in Outpatients with Stable Atherothrombotic Disease**  
 Payal Kohli, MD,<sup>3</sup> Ph. Gabriel Steg, MD,<sup>3</sup> Christopher P. Cannon, MD,<sup>1,4</sup> *The American Journal of Medicine* (2014) 127, 53

**Cardiovascular Risk**

- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See WARNINGS.)
- Voltaren® (diclofenac sodium enteric-coated tablets) is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

**Cardiovascular Risk**

- CELEBREX may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See WARNINGS and CLINICAL TRIALS).
- CELEBREX is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

**CONCLUSION:** Among patients with stable atherothrombosis, NSAID use is associated with a higher risk of myocardial infarction, stroke, and hospitalizations for both ischemia and heart failure.

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**SUMMARY**

- Heart failure, valvular abnormalities and atrial fibrillation pose higher perioperative risk than CAD
- Risk reduction best accomplished with drugs not stents
- Benefits of aspirin, statins, beta blockers
- Optimal anesthetic management and monitoring lowers risk
- Attention to postoperative care!

44

# Volatile Anesthetics and Climate Change: How You Can Make a Difference

David Abts, MD  
Assistant Professor, University of Colorado School of Medicine  
Department of Anesthesiology  
Denver Health Medical Center

March 1<sup>st</sup>, 2019

## Goals

- Gain an understanding of the environmental impact of aspects of our anesthesia practice
- Address some clinical concerns of sevoflurane use
- Cost: does it play a role?
- Future directions in anesthesiology and healthcare at large

## Global Climate Change

- Prominent in recent news cycles
- Will most likely only to continue to grow in profile and importance

The New York Times

### Major Climate Report Describes a Strong Risk of Crisis as Early as 2040



DOOMSDAY Published October 8

## Terrifying climate change warning: 12 years until we're doomed



(AP Photo/Sergei Chuzankov) (The Associated Press)

Foxnews.com, 10/8/2018

- Intergovernmental Panel on Climate Change (IPCC)
- Group of UN-commissioned scientists to advise world leaders
- Report findings
  - Many climate change catastrophes are likely to be realized at 1.5 degree C rise
  - Likely to happen by 2040
  - To prevent, global greenhouse gas emissions must be reduced by 45% from 2010 levels by 2030

1) Davenport, Coral. Major Climate Report Describes a Strong Risk of Crisis as Early as 2040. New York Times. Oct 7, 2018.

## Global Warming Potentials

- $GWP_{100}$  = measure of gas' ability to trap heat compared with  $CO_2$  over 100 year time horizon
- Sevoflurane 130
- Isoflurane 510
- Desflurane 2540
- $N_2O$  298
- $CO_2$  1

## Background

- Montreal Protocol 1987
  - Commitment to reduce ozone-depleting gases
  - After 1985 discovery of hole in ozone layer
- Kyoto Protocol 1997
  - Commitment to reduce greenhouse gases
- Volatile anesthetics and  $N_2O$  deemed medically necessary
- No regulation regarding their use and disposal
- OSHA standards for occupational exposure
- Vented directly to atmosphere once they leave hospital

- Definitions
  - ODP = Ozone depleting potential
  - GWP = Global warming potential
- $GWP_{(t)}$  = Warming potential relative to  $CO_2$  for specified time period

### Laboratory Investigations

#### Volatile anaesthetics and the atmosphere: atmospheric lifetimes and atmospheric effects of halothane, enflurane, isoflurane, desflurane and sevoflurane

T. Langbein<sup>1\*</sup>, H. Sonntag<sup>1</sup>, D. Trapp<sup>1</sup>, A. Hoffmann<sup>2</sup>, W. Malm<sup>2</sup>, E.-P. Roth<sup>2</sup>, V. Mors<sup>2</sup> and R. Zeller<sup>2</sup>

<sup>1</sup>Department of Anaesthesia, Georg-August-Universität, D-37075 Göttingen, Germany; <sup>2</sup>Institute for Physical and Theoretical Chemistry, Universität-GH-Essen, D-45117 Essen, Germany

- BJA 1999
- Built on original work from Brown and Colleagues (1989) for estimating atmospheric lifetimes of halogenated anesthetics
- Atmospheric lifetime believed to be the basis for a gas' ODP and GWP
- Calculations based on experimental models of gas degradation due to hydroxyl radical and photolysis
- First time ODP and GWP calculated for volatile anesthetics

2) Langbein, T. et al. Volatile anaesthetics and the atmosphere: atmospheric lifetimes and atmospheric effects of halothane, enflurane, isoflurane, desflurane and sevoflurane. British Journal of Anaesthesia 82 (1): 66-73 (1999).

British Journal of Anaesthesia 109 (5): 766-6 (2012)  
Advance Access publication 8 October 2010 • doi:10.1093/bja/aee259

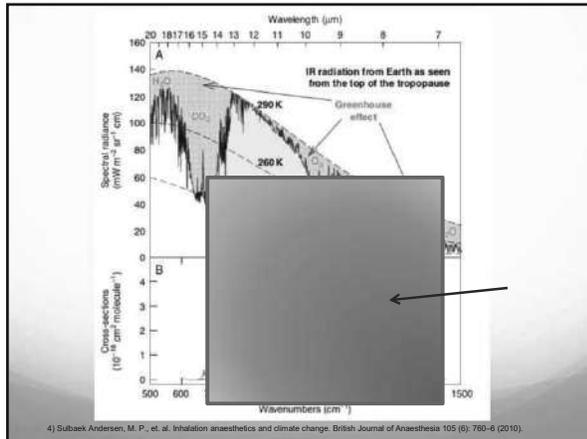
### CLINICAL PRACTICE

#### Inhalation anaesthetics and climate change<sup>†</sup>

M. P. Sulbaek Andersen<sup>1\*</sup>, S. P. Sander<sup>1</sup>, O. J. Nielsen<sup>2</sup>, D. S. Wagner<sup>3</sup>, T. J. Sanford Jr<sup>4</sup> and T. J. Wallington<sup>5</sup>  
<sup>1</sup>Jet Propulsion Laboratory, California Institute of Technology, 4800 Oak Grove Drive, Mail Stop 181-901, Pasadena, CA 91109, USA  
<sup>2</sup>Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark  
<sup>3</sup>Department of Clinical Sciences, College of Pharmacy, University of Michigan, 428 Church Street, Ann Arbor, MI 48109-1065, USA  
<sup>4</sup>Department of Anesthesiology, University of Michigan Medical School, 1500 East Medical Center Drive, Ann Arbor, MI 48109-5048, USA  
<sup>5</sup>Systems Analytics and Environmental Sciences Department, Ford Motor Company, Mail Drop RBC-2122, Dearborn, MI 48121-2053, USA  
Corresponding author. E-mail: mads@sulbaek.dk

- BJA 2010
- Experimentally measured the IR spectra of the volatile anesthetics
- Further refined the calculated GWPs for the common volatile anesthetics

- Calculated halogenated anesthetic contribution to radiative forcing of climate change
  - Atmospheric window = Spectra of IR radiation *leaving* earth's surface
  - Radiative forcing = absorption spectra of a gas in earth's atmospheric window → imbalance between IR radiation entering and leaving earth's atmosphere
- Radiative forcing is dependent on the wavelength of gases' absorption features
- Set the stage for further atmospheric studies to follow



## General Anesthetic Gases and the Global Environment

Yumiko Ishizawa, MD, MPH, PhD

- 2011 A&A, Massachusetts General Hospital
- Escalated concern for ecotoxicological consequences of our common anesthetic gases
- Although erroneous on the subject of halogenated anesthetics (claimed all depleted ozone), brought attention to the dual ozone-depleting and global warming potential of N<sub>2</sub>O
- Also brought attention to scale at which N<sub>2</sub>O is used → 20 tons at MGH in 2006, 35,000 tons nationally in healthcare sector

5) Ishizawa, Y. General Anesthetic Gases and the Global Environment. *Anesthesia and Analgesia*. January 2011 • Volume 112 • Number 1.

## Assessing the Impact on Global Climate from General Anesthetic Gases

Mads P. Subbaek Andersen, PhD,\* Ole J. Nielsen, PhD,† Timothy J. Wallington, PhD,\*† Boris Karpichev, PhD,\* and Stanley P. Sander, PhD\*

- 2012 A&A in response to 2011 Ishizawa article
- Most up to date science on the GWP, radiative forcing and ODP of our volatile anesthetics, including N<sub>2</sub>O
- Reintroduced graph of absorption spectra of volatile anesthetics in context of “atmospheric window”

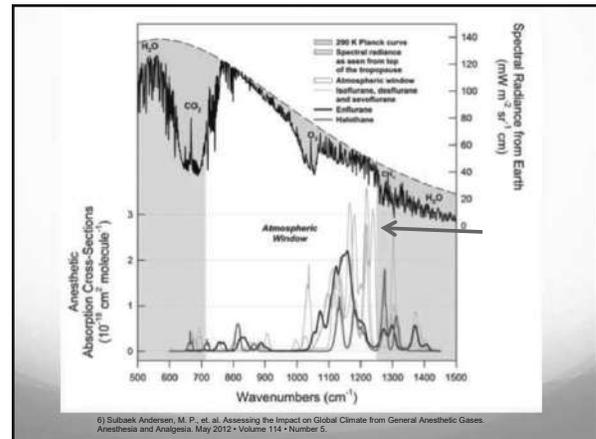


Table 1. Summary of Radiative Properties, Atmospheric Lifetimes, and Global Warming Potentials for Nitrous Oxide and the Halogenated Anesthetic Gases

Compound	Atmospheric lifetime (y)	Radiative efficiency (W m <sup>-2</sup> ppb <sup>-1</sup> )	GWP	
			100y	100y time horizon
Nitrous oxide, N <sub>2</sub> O	114 <sup>8</sup>	0.00303 <sup>8</sup>	153 <sup>8</sup>	153 <sup>8</sup>
Halothane, C <sub>2</sub> HClBr	1.9 <sup>9</sup>	0.185 <sup>9</sup>	20 <sup>9</sup>	20 <sup>9</sup>
Enflurane, C <sub>2</sub> HFC <sub>2</sub> ClO <sub>2</sub> F	4.3 <sup>9</sup>	0.447 <sup>9</sup>	210 <sup>9</sup>	210 <sup>9</sup>
Isflurane, C <sub>2</sub> HClOCHF <sub>2</sub>	3.2 <sup>11</sup>	0.453 <sup>11</sup>	160 <sup>11</sup>	160 <sup>11</sup>
Desflurane, C <sub>2</sub> HClOCHF <sub>2</sub>	14 <sup>7</sup>	0.469 <sup>11</sup>	130 <sup>7</sup>	130 <sup>7</sup>
Sevoflurane, C <sub>2</sub> H <sub>2</sub> ClOCH <sub>2</sub> F	1.1 <sup>1</sup>	0.351 <sup>11</sup>	40 <sup>7</sup>	40 <sup>7</sup>

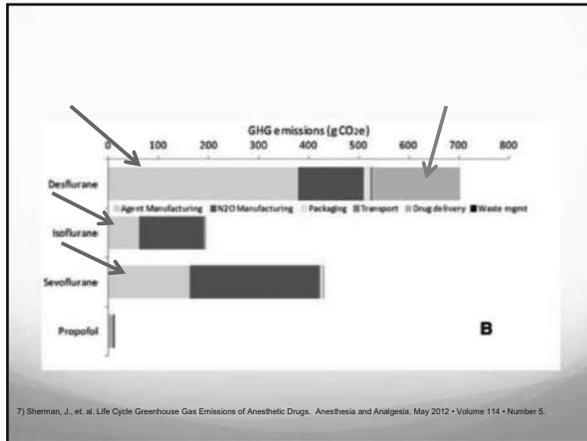
6) Subbaek Andersen, M. P., et al. Assessing the Impact on Global Climate from General Anesthetic Gases. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5.

## Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs

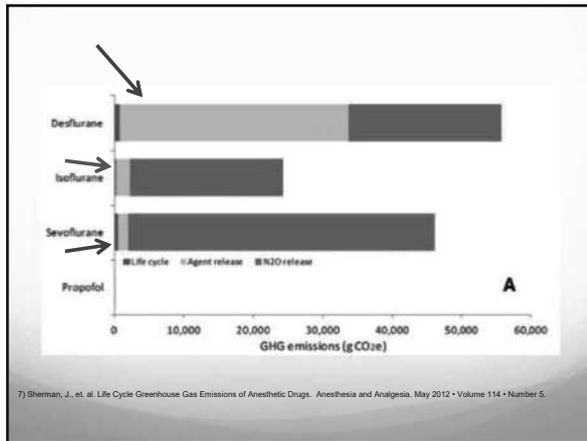
Jodi Sherman, MD,\* Cathy Le,† Vanessa Lamers,†† and Matthew Eckelman, PhD§

- 2012 A&A Study to examine the life cycle climate change impacts of 5 anesthetics drugs: Isoflurane, Desflurane, Sevoflurane, Nitrous oxide, Propofol
- Cradle to grave approach used, examining resource extraction, drug manufacturing, transport to healthcare facilities, drug delivery to the patient, and disposal/emission to the environment
- At each stage energy, material inputs and emissions were considered.

7) Sherman, J., et al. Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5.



- Emissions are calculated in CO<sub>2</sub> equivalents
  - Fresh gas flows are assumed to be 1L/min for desflurane and isoflurane, 2L/min for sevoflurane
  - N<sub>2</sub>O is assumed to be administered in a 60% concentration
- 7) Sherman, J., et al. Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5.



- Life cycle GHG emissions for desflurane are 15x those of isoflurane and 20x those of sevoflurane
  - Isoflurane and sevoflurane have similar GHG emission profiles in O<sub>2</sub>/air mixture – largely due to higher FGF rates in this analysis.
  - When co-administered with N<sub>2</sub>O emissions for isoflurane increase by 65% and those for sevoflurane increase by 900%
- 7) Sherman, J., et al. Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5.

**AGU PUBLICATIONS**  
**Geophysical Research Letters**

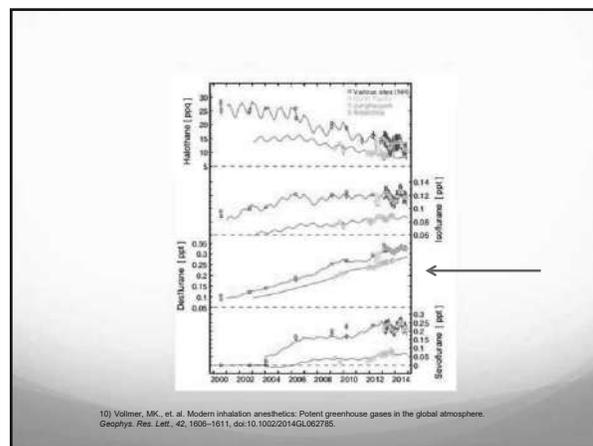
**RESEARCH LETTER**  
10.1002/2014GL024726

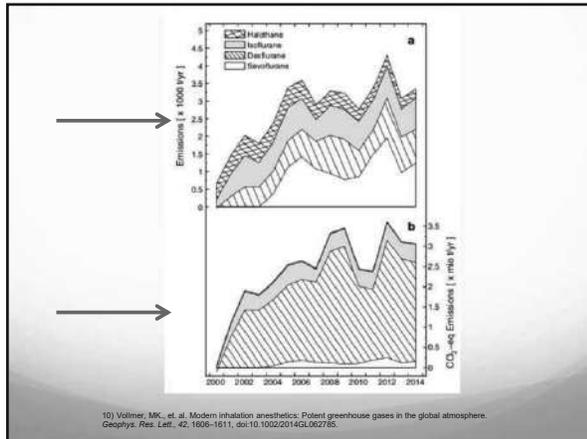
**Modern inhalation anesthetics: Potent greenhouse gases in the global atmosphere**  
Maurice H. Sittler<sup>1</sup>, Tom Sisk Rieker<sup>1</sup>, Matt Ripley<sup>1</sup>, Doris Hofbauer<sup>2</sup>, Matthias Hübner<sup>3</sup>, Felten Schoenenberger<sup>4</sup>, and Stefan Reimann<sup>1</sup>

<sup>1</sup>Laboratory for Air Pollution and Environmental Technology, Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf, Switzerland; <sup>2</sup>Human Policy Research Institute, HKUST, Kowloon, Hong Kong; <sup>3</sup>Institut für Umweltwissenschaften, University of Bern, Bern, Switzerland; <sup>4</sup>Research Institute for Air Quality, Zurich, Switzerland

- 2015 study examining the atmospheric content of halogenated volatile anesthetics
- First study to estimate global warming contribution from each agent using “top down” analysis
- Air samples drawn from 4 locations: icebreaker research vessel in the north Pacific, South Korea Antarctic station, Jungfrauoch Observatory (Switzerland), Dubendorf (suburban Zurich) from 2000-2014

10) Vulliamy, M.K., et al. Modern inhalation anesthetics: Potent greenhouse gases in the global atmosphere. *Geophys. Res. Lett.*, 42, 1606–1611, doi:10.1002/2014GL024726.





- Collectively, volatile anesthetics can have an appreciable impact on radiative forcing
- In 2014, by this measurement, approximately 3.1 million tons of CO<sub>2</sub> equivalents were released into the atmosphere
- Of which, approximately 80% was due to desflurane

10) Volmer, MK, et al. Modern inhalation anesthetics: Potent greenhouse gases in the global atmosphere. *Geophys. Res. Lett.* 42, 1606-1611, doi:10.1002/2014GL02785.

**Table. One hour of anesthetic is like driving a car [how many?] miles.<sup>a</sup>**

Dose (1-MAC-hr)	Sevoflurane 2.2%	Isoflurane 1.2%	Desflurane 6.7%	N <sub>2</sub> O <sup>b</sup> 0.6 MAC-hour
0.5 L/min	—	4	93	29
1.0 L/min	4	8	186	57
2.0 L/min	8	15	378	112
5.0 L/min	19	38	939	282
10.0 L/min	38	74	1,876	564

<sup>a</sup> Assumes EPA 2012 fuel efficiency average of 23.9 miles per gallon.  
<sup>b</sup> Because N<sub>2</sub>O cannot be delivered at 100%, the more typical percentage of 60% is used. In combination, 0.6 MAC-hour of N<sub>2</sub>O would be added to 0.4 MAC-hour of a volatile.  
 EPA, Environmental Protection Agency; MAC, minimal alveolar concentration; N<sub>2</sub>O, nitrous oxide

14) *Anesthesiology News*, April, 2017.

## Healthcare Sector

- How significant are greenhouse gas emissions in context of the healthcare sector?
- How significant is the healthcare sector in terms of total national emissions?

### RESEARCH LETTER

#### Estimate of the Carbon Footprint of the US Health Care Sector

- 2009 JAMA
- First attempt to estimate the carbon footprint of the US healthcare sector
- GHG emissions estimated using 2007 data on health expenditures published by the National Health Accounts Team
- In 2007 US healthcare sector accounted for 16% of GDP and 8% of GHG emissions
- For comparison, in 2004 NHS accounted for 3% of total UK CO<sub>2</sub> emissions

3) Chung, JW, et al. Estimate of the Carbon Footprint of the US Health Care Sector. *JAMA*, November 11, 2009—Vol 302, No. 18.

### RESEARCH ARTICLE

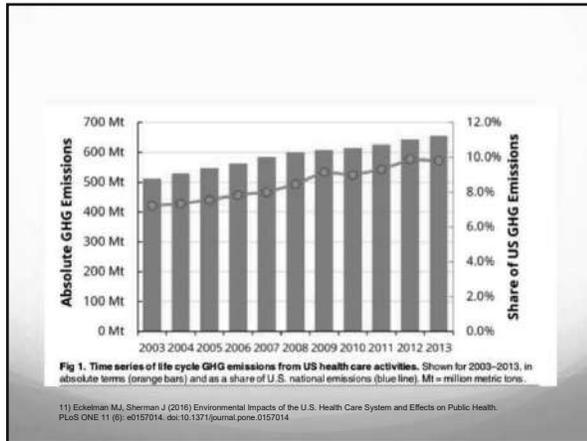
#### Environmental Impacts of the U.S. Health Care System and Effects on Public Health

Matthew J. Eckelman<sup>1\*</sup>, Jodi Sherman<sup>2</sup>

<sup>1</sup> Department of Civil and Environmental Engineering, Northeastern University, Boston, Massachusetts, United States of America; <sup>2</sup> Department of Anesthesiology, Yale School of Medicine, New Haven, Connecticut, United States of America

- As of 2013, the US healthcare sector responsible for 10% of US GHG emissions
- US healthcare emissions responsible for 400,000+ DALYs lost
- Comparable impact to scope of preventable in-hospital deaths

11) Eckelman MJ, Sherman J (2016) Environmental Impacts of the U.S. Health Care System and Effects on Public Health. *PLoS ONE* 11(6): e0157014. doi:10.1371/journal.pone.0157014



## Operating Room Carbon Footprint

**The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems**

Andrew MacNeill, Robert Lippert, Carl Brown

- 2017 study published in The Lancet
- Examined the carbon footprint of the OR for three different hospitals in different healthcare systems for the year 2011
- Vancouver, Canada
- Minneapolis, USA
- Oxford, England

- Study included three scopes
  - Scope 1: GHG emissions attributable to volatile anesthetics
  - Scope 2: GHG emissions attributable to energy consumption of the ORs
  - Scope 3: GHG emissions attributable to supply chain and waste
- 12) MacNeill, AJ, et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. Lancet Planet Health 2017; 1: e381-88

	Volume purchased (L/year)			CO <sub>2</sub> e (kg/year)		
	VGH	UMMC	JRH	VGH	UMMC	JRH
<b>Desflurane</b>	535.7	532.8	0	1983.073	1972.412	0
<b>Isosulfurane</b>	34.2	126.4	222	26.297	135.636	170.314
<b>Sevoflurane</b>	132	315.5	217	24907	21.793	40.898
<b>Total</b>	-	-	-	20342.77	2129.841	211.212

CO<sub>2</sub>e calculated using 100-year Global Warming Potential (GWP<sub>100</sub>) values of 2540 for desflurane, 510 for isoflurane, and 130 for sevoflurane. \*VGH=Vancouver General Hospital. CO<sub>2</sub>e=CO<sub>2</sub> equivalents. UMMC=University of Minnesota Medical Center. JRH=John Radcliffe Hospital.

**Table 1: Annual greenhouse gas emissions from volatile anaesthetics**

12) MacNeill, AJ, et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. Lancet Planet Health 2017; 1: e381-88

	Energy (MWh/year)			CO <sub>2</sub> e (kg/year)		
	VGH	UMMC	JRH	VGH	UMMC	JRH
<b>Heating</b>	2538	2204	6971	534340	610702	2283426
<b>Cooling</b>	66	357	1312	1523	195629	787149
<b>Ventilation</b>	449	1062	2045	20317	581938	1104386
<b>Lighting*</b>	236	177	313	5423	96959	169189
<b>Plug-loads</b>	113	56	-	2591	30535	-
<b>Total</b>	3382	3856	10641	534194	1515763	4344150

CO<sub>2</sub>e=CO<sub>2</sub> equivalents. VGH=Vancouver General Hospital. UMMC=University of Minnesota Medical Center. JRH=John Radcliffe Hospital. \*At VGH and UMMC, theatre submetering included plug-loads and surgical spotlights, but not overhead lighting; overhead lighting is reported separately based on lighting audits at JRH; all lighting was captured in theatre submetering, hence only one value is reported for both lighting and plug-loads.

**Table 2: Annual operating theatre energy requirements and greenhouse gas emissions**

12) MacNeill, AJ, et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. Lancet Planet Health 2017; 1: e381-88

	Waste (kg/year)			CO <sub>2</sub> e (kg/year)		
	VGH	UMMC	JRH	VGH	UMMC	JRH
Municipal solid waste	111 255	105 975	83 060	438 167	423 060	327 122
Hazardous waste	21 933	9374	81 121	63028	26 938	233123
Reusable textiles	178 176	87320	33597	53 336	52 248	12 459
Fluid waste	15 526	—	15 525	194	—	194
Sharps	1793	1076	9698	4913	2980	44229
Cytotoxic waste	902	598	—	4114	2728	—
Recycling†	30 991	10 154	4620	85 264	26 913	11 445
Domestic waste	—	—	993	—	—	2322
Transport‡	1855	1818	1484	1421	1393	1227
<b>Total</b>	<b>360 576</b>	<b>214 797</b>	<b>228 615</b>	<b>662 436</b>	<b>516 260</b>	<b>632 574</b>

CO<sub>2</sub>e=CO<sub>2</sub> equivalents. VGH=Vancouver General Hospital. UMMC=University of Minnesota Medical Center. JRH=John Radcliffe Hospital. †Except transport where the units are km/year. ‡Recycling excludes cardboard, plastic, and surgical blue wrap (polypropylene) at UMMC, versus cardboard and plastic only at VGH and UMMC, production emissions factors used were 3.038 kg CO<sub>2</sub>e/tonne for cardboard, 11.79 kg CO<sub>2</sub>e/tonne for average plastics, and 125.4 kg CO<sub>2</sub>e/tonne for polypropylene, net emissions with recycling were -240 kg CO<sub>2</sub>e/tonne for cardboard, -282 kg CO<sub>2</sub>e/tonne for average plastics, and 12 kg CO<sub>2</sub>e/tonne for polypropylene. ‡Assuming 7.25 miles per gallon average fleet fuel efficiency (Natural Resources Canada).

**Table 3: Annual waste volumes and greenhouse gas emissions due to surgical consumables**

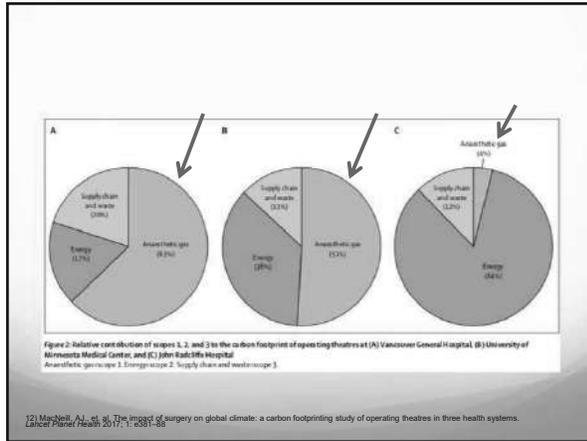
12) MacNeill, A.J., et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. *Lancet Planet Health* 2017; 1: e381-88

	VGH	UMMC	JRH
Scope 1	2 034 277	2 129 841	2 112 121
Scope 2	534 194	1 515 763	434 415
Scope 3	650 436	536 260	632 574
<b>Total</b>	<b>3 218 907</b>	<b>4 181 864</b>	<b>5 187 936</b>

CO<sub>2</sub>e=CO<sub>2</sub> equivalents. VGH=Vancouver General Hospital. UMMC=University of Minnesota Medical Center. JRH=John Radcliffe Hospital

**Table 4: Total annual operating theatre greenhouse gas emissions (kg CO<sub>2</sub>e/year)**

12) MacNeill, A.J., et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. *Lancet Planet Health* 2017; 1: e381-88



12) MacNeill, A.J., et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. *Lancet Planet Health* 2017; 1: e381-88

- Study highlights importance of energy grid composition
- For North American hospitals, *volatile anesthetics were largest contributors to GHG emissions by far*
  - 10x that of JRH in England
  - With 1/3 fewer cases performed
  - ~ 20k cases at UMMC and VGH, ~30k cases at JRH
  - Disparity can be accounted for by preferential use of desflurane at North American sites

12) MacNeill, A.J., et al. The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. *Lancet Planet Health* 2017; 1: e381-88

## Volatile Anesthetic Lifespans

- Sevoflurane 1.1 years
- Isoflurane 3.2 years
- Desflurane 14 years
- N<sub>2</sub>O 114 years

## Global Warming Potentials

- GWP<sub>100</sub> = measure of gas' ability to trap heat compared with CO<sub>2</sub> over 100 year time horizon
- Sevoflurane 130
- Isoflurane 510
- Desflurane 2540
- N<sub>2</sub>O 298



## Sevoflurane

- Advantages
- Disadvantages
- Cost?

- Advantages
  - Smallest environmental burden defined by GWP and atmospheric lifetime
  - Instances of clinical advantage
    - Mask induction, pulmonary disease, etc

- Disadvantages
  - 2L/min minimum flow requirement, right?
  - Compound A – induced nephrotoxicity, right?

- Sevoflurane approved for use by FDA in 1995
- Product insert/FDA website

### WARNINGS

Although data from controlled clinical studies at low flow rates are limited, findings taken from patient and animal studies suggest that there is a potential for renal injury which is presumed due to Compound A. Animal and human studies demonstrate that sevoflurane administered for more than 2 MAC-hours and at fresh gas flow rates of < 2 L/min may be associated with proteinuria and glycosuria.

15) Utane (sevoflurane), Volatile liquid for inhalation, AbbVie Inc. 2017.

- This is the evidence for their recommendation

Sevoflurane may be associated with glycosuria and proteinuria when used for long procedures at low flow rates. The safety of low flow sevoflurane on renal function was evaluated in patients with normal preoperative renal function. One study compared sevoflurane (N = 98) to an active control (N = 90) administered for  $\geq 2$  hours at a fresh gas flow rate of  $\leq 1$  Liter/minute. Per study defined criteria, one patient in the sevoflurane group developed elevations of creatinine, in addition to glycosuria and proteinuria. This patient received sevoflurane at fresh gas flow rates of  $\leq 800$  mL/minute. Using these same criteria, there were no patients in the active control group who developed treatment emergent elevations in serum creatinine.

15) Utane (sevoflurane), Volatile liquid for inhalation, AbbVie Inc. 2017.

### Nephrotoxicity of Sevoflurane Versus Desflurane Anesthesia in Volunteers

Edmond I Eger II, MD\*, Donald D. Koblin, PhD, MD\*, Terri Bowland, BS\*, Pompiliu Ionescu, MD\*, Michael J. Laster, DVM\*, Zexu Fang, MD\*, Diane Gong, BS\*, James Sonner, MD\*, and Richard B. Weiskopf, MD\*†‡

Departments of \*Anesthesia and †Physiology and the ‡Cardiovascular Research Institute, University of California San Francisco, California

- 1997 A&A
- Study of 12 healthy volunteers
- ½ to receive 8hr desflurane anesthetic, ½ to receive 8hr sevoflurane anesthetic, then switch (1.25 MAC)
- 7 volunteers completed study
- Variety of laboratory tests run day of experiment and several days after to assess renal integrity

31) Eger et al. Nephrotoxicity of Sevoflurane vs Desflurane Anesthesia in Volunteers. *Anesth Analg* 1997; 84:160-168.

- Some sevoflurane volunteers demonstrated renal microinjury
  - Elevations in urine albumin, glucose, alpha-GST, pi-GST
- Neither anesthetic affected serum Cr or BUN
- Neither anesthetic affected volunteers' ability to concentrate urine in response to vasopressin

31) Eger et al. Nephrotoxicity of Sevoflurane vs Desflurane Anesthesia in Volunteers. *Anesth Analg* 1997; 84:160-168.

## In General

- Studies demonstrating compound A-mediated renal injury
  - Animal studies evaluated compound A directly, not sevoflurane
  - Human studies have all been small with a variety of confounding variables

*British Journal of Anaesthesia* 1995; 74: 667-669

### Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime

H. BITO AND K. IKEDA

- 1995 BJA
- 24 ASA 1-2 patients undergoing typanoplasty
- Sevoflurane/N<sub>2</sub>O anesthesia administered
- Compound A measured in circuit at different time points
- Patients randomized to 1L/min, 3L/min, 6L/min flows

16) Bito, H., Ikeda, K. Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime. *British Journal of Anaesthesia* 1995; 74: 667-669.

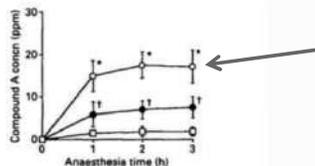


Figure 1. Comparison of concentrations of compound A at fresh gas flows of 1 (○), 3 (●) and 6 (□) litre min<sup>-1</sup> (mean, SD). \* P < 0.05 vs 3 litre min<sup>-1</sup> and 6 litre min<sup>-1</sup>; † P < 0.05 vs 6 litre min<sup>-1</sup>. n = 8 in each group.

	Maximum compound A concn (ppm)	Corresponding end-tidal sevoflurane concn (%)	Maximum temperature of soda lime (°C)
1 litre min <sup>-1</sup>	19.7 (4.3)*	2.0 (0.3)	44.6 (1.5)*
3 litre min <sup>-1</sup>	8.1 (2.7)†	1.9 (0.3)	37.0 (4.4)†
6 litre min <sup>-1</sup>	2.1 (1.0)	1.8 (0.3)	29.1 (5.1)

16) Bito, H., Ikeda, K. Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime. *British Journal of Anaesthesia* 1995; 74: 667-669.

### Effects of Low-flow Sevoflurane Anesthesia on Renal Function

#### Comparison with High-flow Sevoflurane Anesthesia and Low-flow Isoflurane Anesthesia

Hirohichi Bito, M.D.,\* Yukako Ikeuchi, M.D.,† Kazuyuki Ikeda, M.D., F.R.C.A.‡

- Anesthesiology 1997
- 48 ASA 1-2 patients undergoing gastrectomy for gastric CA enrolled
- Randomized to either low-flow sevo (1L/min), high-flow sevo (6-10L/min), low-flow iso (1L/min)
- Baralyme CO<sub>2</sub> absorbant used (glass balls in high-flow sevo group), compound A concentrations measured throughout the case
- Blood samples obtained pre-op and on POD 1-3 to measure BUN/Cr
- 24hr Urine samples obtained pre-op and on POD 1-3 to measure Cr, N-acetyl-B-D-glucosaminidase (NAG), alanine aminopeptidase (AAP)

17) Bito, H., et al. Effects of Low-Flow Sevoflurane Anesthesia on Renal Function: Comparison with High-Flow Sevoflurane Anesthesia and Low-Flow Isoflurane Anesthesia. *Anesthesiology* 1997; 86: 1231-7.

17) Bito, H., et al. Effects of Low-Flow Sevoflurane Anesthesia on Renal Function: Comparison with High-Flow Sevoflurane Anesthesia and Low-Flow Isoflurane Anesthesia. *Anesthesiology* 1997; 86: 1231-7.

- Average concentration of compound A in low-flow sevo group 20ppm, which trended down over time
- Average case duration ~ 6hrs
- **No differences amongst groups postoperatively**
  - BUN decreased in all groups
  - Cr decreased POD 3 in sevo groups, not in iso group
  - CrCl increased in all groups
  - 24hr urinary NAG and AAP excretion increased in all groups

### The Effects of Prolonged Low-Flow Sevoflurane Anesthesia on Renal and Hepatic Function

Ryoji Obata, MD, Hiromichi Bito, MD, Morihiro Ohmura, Goroku Moriwaki, MD, Yukako Ikeuchi, MD, Takasumi Katoh, MD, and Shigehito Sato, MD  
Department of Anesthesiology and Intensive Care, Hamamatsu University School of Medicine, Hamamatsu, Japan

- A&A 2000
- 30 ASA 1-2 patients with head & neck CA scheduled to undergo surgery > 10hrs
- Randomized to low-flow sevo (1L/min), high-flow sevo (6-10L/min), low-flow iso (1L/min)
- Baralyme CO<sub>2</sub> absorbant used (glass balls in high-flow sevo group), compound A concentrations measured throughout the case
- Blood samples obtained pre-op and on POD 1-3, 5 to measure BUN/Cr, LFTs
- 24hr Urine samples obtained pre-op and on POD 1-3, 5 to measure Cr, N-acetyl-B-D-glucosaminidase (NAG), albumin, protein, glucose

18) Obata, R., et al. Effects of Prolonged Low-Flow Sevoflurane Anesthesia on Renal and Hepatic Function. *Anesth Analg* 2000; 91:1262-8.

18) Obata, R., et al. Effects of Prolonged Low-Flow Sevoflurane Anesthesia on Renal and Hepatic Function. *Anesth Analg* 2000; 91:1262-8.

- Average case duration 18 hrs (10-24hrs)
- Average compound A concentration in low-flow sevo group was 26ppm at 2hr
- Average AUC for compound A in low-flow sevo group 277ppm-hr (renal injury surmised to occur at 150-342ppm-h based on rat model)
- No increases in Cr, no decreases in CrCL,
  - **No differences amongst groups**
- Increases in urinary excretion of protein, albumin, glucose, NAG, in all groups,
  - **No differences amongst groups**

### Compound A and carbon monoxide production from sevoflurane and seven different types of carbon dioxide absorbent in a patient model

C. KEIJZER<sup>1</sup>, R. S. G. M. PEREZ<sup>2</sup> and J. J. DE LANGE<sup>2</sup>  
<sup>1</sup>Department of Anesthesiology and Intensive Care, Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital and <sup>2</sup>Department of Anesthesiology, VU University Medical Center, Amsterdam, the Netherlands

Acta Anaesthesiologica Scandinavica 2007

- 7 different modern CO<sub>2</sub> absorbants tested in a patient model under desiccated and normally hydrated conditions
- Sevoflurane administered at FGF 0.5L/min for 3 hrs

19) Keijzer, C., et al. Compound A and carbon monoxide production from sevoflurane and seven different types of carbon dioxide absorbent in a patient model. *Acta Anaesthesiol Scand* 2007; 51: 31-37.

Compositions of carbon dioxide absorbents tested.					
CO <sub>2</sub> absorbent	Ca(OH) <sub>2</sub> (%)	KOH (%)	NaOH (%)	LiOH (%)	H <sub>2</sub> O (%)
Drägerisorb 800 plus <sup>®</sup>	82	0.003	2	-	16
Melisorb <sup>®</sup>	91	0.003	3	-	16
Spherasorb <sup>®</sup>	84.5	0.003	1.5	-	14
Amsorb <sup>®</sup>	83.2	-	-	-	14.4
LeRo Sorb <sup>®</sup>	84	-	-	-	16
Suvena <sup>®</sup>	79.5	-	-	-	17.5
Lithium hydroxide	-	-	-	99	1

28ppm-hr

Areas under the curve (AUCs, p.p.m. min) of compound A (CA) and carbon monoxide (CO) based on the mean concentrations from the duplicate experiments of each desiccated and normally hydrated carbon dioxide absorbent used in combination with sevoflurane 0.8%.

CO <sub>2</sub> absorbent	AUC-CA-d	AUC-CA-t	AUC-CO-d	AUC-CO-t
Drägerisorb 800 plus <sup>®</sup>	353	1228	4518	0
Melisorb <sup>®</sup>	327	1228	1452	0
Spherasorb <sup>®</sup>	294	301	1866	0
LeRo Sorb <sup>®</sup>	0	0	0	0
Suvena <sup>®</sup>	0	0	0	0
Amsorb <sup>®</sup>	2937	0	0	0
Lithium hydroxide	396	0	0	0

d, desiccated absorbent; t, normally hydrated absorbent.

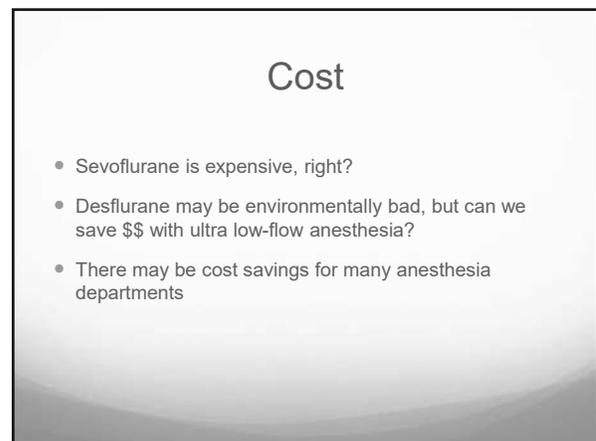
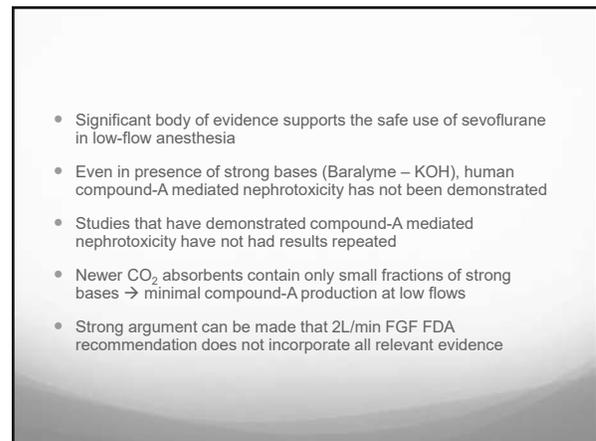
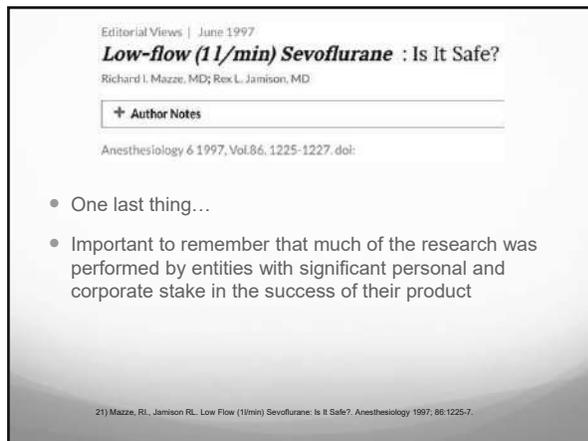
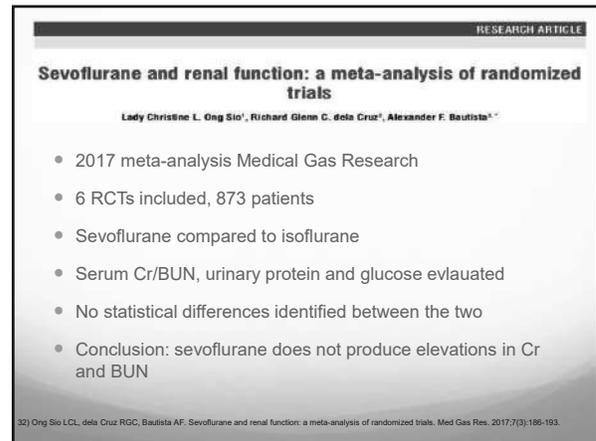
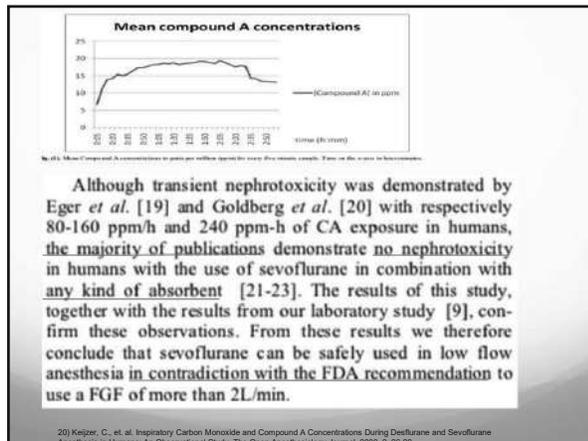
19) Keijzer, C., et al. Compound A and carbon monoxide production from sevoflurane and seven different types of carbon dioxide absorbent in a patient model. *Acta Anaesthesiol Scand* 2007; 51: 31-37.

### Inspiratory Carbon Monoxide and Compound A Concentrations During Desflurane and Sevoflurane Anesthesia in Humans: An Observational Study

Christiaan Keijzer<sup>1,2</sup>, Roberto S.G.M. Perez<sup>2</sup> and Jaap J. De Lange<sup>2</sup>

- 2008
- 40 patients ASA 1-3 randomized to either sevoflurane or desflurane anesthesia
- Cases lasted at least 90 minutes
- FGF maintained at 0.5L/min – 1L/min
- Compound A measured in circuit throughout case

20) Keijzer, C., et al. Inspiratory Carbon Monoxide and Compound A Concentrations During Desflurane and Sevoflurane Anesthesia in Humans: An Observational Study. *The Open Anesthesiology Journal* 2008; 2: 20-25.



## Cost of anaesthesia

- 1992 Dion published an equation in the CJA for calculating the costs of volatile anesthetics in clinical use
- 1993, Loke and Shearer published an equation in CJA for calculating cost per MAC hour and a method for establishing cost equivalency

22) Loke, J., Shearer W. The Cost of Anaesthesia. Canadian Journal of Anaesthesia. 1993; 472-474.

$$S\dot{X}_{\text{liquid agent}} = C_{\text{liquid agent}} \times \dot{V}_{\text{gas}} \times 60 \text{ min} \\ \times \frac{\text{MAC}_{\text{agent}}}{100\%} \times \frac{W_{\text{mol agent}}}{\rho_{\text{liquid agent}}} \times \frac{P_{\text{Bar}} \times 10^{-3} \cdot \text{m}^3 \cdot \text{L}^{-1}}{R \times T}$$

$S\dot{X}_{\text{liquid agent}}$  is the MAC-hour cost of agent (\$),  
 $C_{\text{liquid agent}}$  is unit cost (\$ · ml<sup>-1</sup>) of liquid agent,  
 $\dot{V}_{\text{gas}}$  is the fresh gas flow (L · min<sup>-1</sup>),  
 $\text{MAC}_{\text{agent}}$  is the agent's minimum alveolar concentration (%),  
 $W_{\text{mol agent}}$  is the agent's molecular weight (g · mol<sup>-1</sup>),  
 $\rho_{\text{liquid agent}}$  is the agent's liquid density (g · ml<sup>-1</sup>),  
 $P_{\text{Bar}}$  is the atmospheric pressure (Pa),  
 $R$  is the ideal gas constant (8.314 J · K<sup>-1</sup> · mol<sup>-1</sup>) and  
 $T$  is the temperature of the gas (K)

22) Loke, J., Shearer W. The Cost of Anaesthesia. Canadian Journal of Anaesthesia. 1993; 472-474.

- Assuming everyone still uses 2L/min FGF sevoflurane, is there cost savings to using low-flow desflurane?
- Where is the break even point for the two gases?
- \$MAC hour<sub>des</sub> = \$MAC hour<sub>sevo</sub>

- $\frac{[(\text{MAC}\%)_d](\text{FGF}_d)(\text{MW}_d)(\$/\text{ml}_d)(60\text{min})}{(R)(T_d)(d_d)} = \frac{[(\text{MAC}\%)_s](\text{FGF}_s)(\text{MW}_s)(\$/\text{ml}_s)(60\text{min})}{(R)(T_s)(d_s)}$
- Desflurane
  - MAC = 6%
  - MW = 168
  - T = 312 K (39 C)
  - Density (liquid) = 1.44 g/ml
- Sevoflurane
  - MAC = 2%
  - MW = 200
  - T = 294 K (21 C)
  - Density (liquid) = 1.51 g/ml

- Denver Health
  - Sevoflurane = \$X/ml
  - Desflurane = \$2.25X/ml
- FGF<sub>d</sub> = 0.36 L/min

- UCH
  - Sevoflurane = \$X/ml
  - Desflurane = \$1.86X/ml
- FGF<sub>d</sub> = 0.43 L/min

- VA
  - Sevoflurane =  $\$X/ml$
  - Desflurane =  $\$1.73X/ml$
- $FGF_d = 0.47 \text{ L/min}$

- Childrens Hospital Colorado
  - Sevoflurane =  $\$X/ml$
  - Desflurane =  $\$2.1X/ml$
- $FGF_d = 0.38 \text{ L/min}$

- Denver Health's annual volatile anesthetic budget is approximately \$300k
- January – September 2017
  - \$236,097
- January – September 2018
  - \$110,685
- This represents 53% savings 2018 over 2017 and 51% under projected annual budget
- Only intervention was majority of providers switching to sevoflurane as "default" volatile about 1/1/2018 (with 2L/min FGF as practice habit)

**Economic and Environmental Considerations During Low Fresh Gas Flow Volatile Agent Administration After Change to a Nonreactive Carbon Dioxide Absorbent**

Richard H. Epstein, MD, CPHIMS,\* Franklin Dexter, MD, PhD,† David P Maguire, MD,\* Niraj K. Agarwalla, DO,‡ and David M. Gratch, DO\*

- 2016 Anesthesia & Analgesia
- Thomas Jefferson University
- Department of Anesthesia changed from Sodalime (NaOH containing) CO<sub>2</sub> absorbers to Litholyme (non-compound A forming) CO<sub>2</sub> absorbers
- All department providers instructed to reduce their FGFs during sevoflurane anesthetics to 1.25L/min, or less

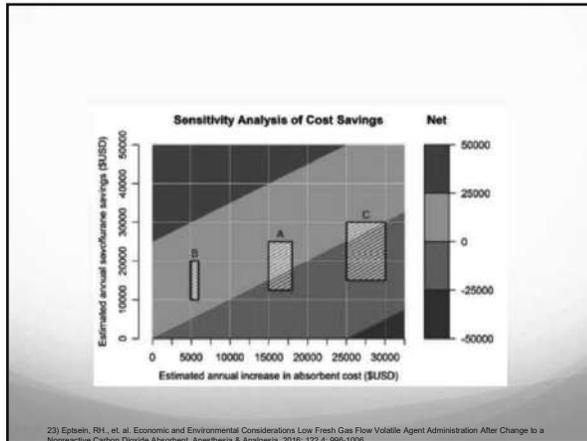
23) Epstein, RH, et al. Economic and Environmental Considerations Low Fresh Gas Flow Volatile Agent Administration After Change to a Nonreactive Carbon Dioxide Absorbent. Anesthesia & Analgesia. 2016; 122:4: 996-1004.

- Hypothesis tested
  - The cost savings from reduced sevo consumption would modestly exceed the incremental cost of premium CO<sub>2</sub> absorbent

23) Epstein, RH, et al. Economic and Environmental Considerations Low Fresh Gas Flow Volatile Agent Administration After Change to a Nonreactive Carbon Dioxide Absorbent. Anesthesia & Analgesia. 2016; 122:4: 996-1004.

- Savings on sevo administration ended up cost neutral with extra cost of litholyme absorbent
  - Attributed to practice inertia (providers not reducing their flows to goal)
  - Imprecision in sevoflurane ordering (lag time, extra storage)
- Did prove to be at least cost neutral

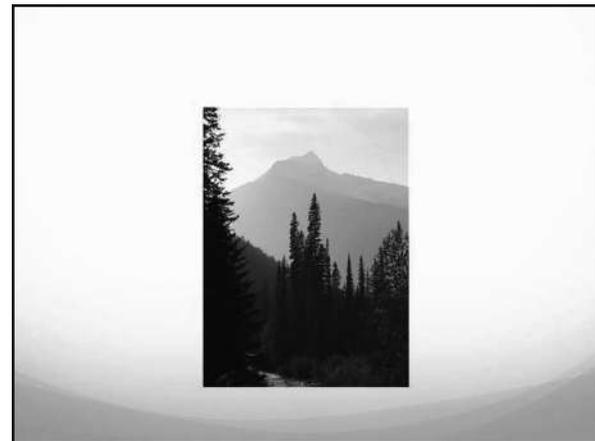
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	Scenario A	Scenario B	Scenario C
Current sevoflurane annual cost	\$200,000	\$300,000	\$100,000
Current intraoperative FGF (L/min)	2.00	2.25	2.50
Expected intraoperative FGF (L/min)	1.50	1.80	1.50
FGF reduction (%)	25.0	30.0	40.0
Minimum realized reduction in sevoflurane consumption as a fraction of intraoperative FGF reduction (%)	25.0	25.0	25.0
Maximum realized reduction in sevoflurane consumption as a fraction of intraoperative FGF reduction (%)	50.0	50.0	60.0
Current annual absorbent cost purchased (1 bag/canister)	\$15,000	\$18,750	\$12,000
Current annual absorbent bags purchased (1 bag/canister)	3000	3750	1500
Current average cost/bag	\$4.00	\$5.00	\$8.00
New refill average cost/bag	\$10.00	\$15.00	\$12.00
Relative CO <sub>2</sub> absorbing capacity (new/old)	1.2	1.5	1.2
Minimum estimated percentage reduction in bags purchased due to enhanced absorbing capacity of new absorbent (N <sub>2</sub> O)	0	50	0
Maximum estimated percentage reduction in bags purchased due to enhanced absorbing capacity of new absorbent (N <sub>2</sub> O)	100	100	100
Maximum absorbent bags purchased	3000	3000	1500
Minimum absorbent bags purchased	2500	2500	1250
Minimum sevoflurane savings	\$12,500	\$18,000	\$10,000
Maximum sevoflurane savings	\$25,000	\$30,000	\$20,000
Minimum additional absorbent cost	\$15,000	\$25,000	\$5,000
Maximum additional absorbent cost	\$18,000	\$30,000	\$6,000

23) Epstein, RH, et al. Economic and Environmental Considerations Low Fresh Gas Flow Volatile Agent Administration After Change to a Noninertive Carbon Dioxide Absorbent. *Anesthesia & Analgesia* 2016; 62:4: 596-599.

- While multiple factors determine overall cost, it is likely that for many institutions, transitioning away from preferential desflurane use represents potentially significant cost savings
- It can be fairly simple to calculate cost savings, or cost neutrality should an institution decide to optimize its OR carbon footprint



- ### Counter Argument
- “Drop in the bucket”
  - Patient safety
  - I’ll practice how I want to

- ### A Different Perspective on Anesthetics and Climate Change
- A&A Editorial 2013
  - “The overall contribution of inhalational anesthetics to greenhouse gas emissions is miniscule...” approximately 0.01% of that of the CO<sub>2</sub> released by global fossil fuel combustion.”
    - This comes from a study which extrapolated the emissions from University of Michigan to global emissions
    - Little des used at UM (6L), did not account for N<sub>2</sub>O, did not account for life cycle assessments
  - “We believe the notion that miniscule impact on the environment compares with clinical issues such as cardioprotection, airway irritability, rapidity of recovery, and cost is inappropriate.”
- 24) Mychaskiw, G. Eger, EI. A Different Perspective on Anesthetics and Climate Change. *Anesthesia and Analgesia* 2013; 116:3: 734-5.



## Future Directions

- N<sub>2</sub>O destruction
- Waste anesthetic gas reclamation
- Novel volatile anesthetics
- Common sense strategies for personal practice

### Decreased emission of nitrous oxide from delivery wards—case study in Sweden

- N<sub>2</sub>O
- N<sub>2</sub>O can be catalytically split → N<sub>2</sub> + O<sub>2</sub>
- Commercial system for this exists (Anesclean®)
- System employed on L&D ward at Karolinska University Hospital, Stockholm Sweden
- 95% of collected N<sub>2</sub>O catalytically destroyed
- LCA showed GHG benefit to system

25) Ek, M., Tius, K. Decreased emission of nitrous oxide from delivery wards – case study in Sweden. *Mitig Adapt Strateg Glob Change* (2008) 13:809-818.

- Waste anesthetic gas (WAG) reclamation
- Blue-Zone Technologies (Toronto, ON) produces a system → Deltasorb®, Centralorb® to capture VAs at the level of the machine, or central HVAC system
- Allow for desorption of halogenated agents as liquids for potential processing and reuse.
- System in place in some Canadian hospitals
- Not yet FDA approved

26) Barock, B., Sooy, F. WAG Treatment and CO<sub>2</sub> Absorbers: New Technologies for Pollution and Waste Prevention. *ASA Monitor* 2018; 82:4-12-14.

- Novel Volatile Anesthetics
- Xenon
- Noble gas with profound analgesic effects, neuroprotection, hemodynamic stability, low blood-gas partition coefficient
- No known detrimental ecotoxicological effects
- Limited by high cost and energy consumption of fractional distillation of liquid air
- Use would only be possible in closed circuit system with reclamation of gas

5) Ishizawa, Y. General Anesthetic Gases and the Global Environment. *Anesthesia and Analgesia*, January 2011 • Volume 112 • Number 1.

- Managing fresh gas flows
- Aim for 1L/min FGF if using sevoflurane for maintenance of anesthesia
- If using isoflurane or desflurane, aim for closed-circuit maintenance of anesthesia
  - Calculate O<sub>2</sub> consumption ~5ml O<sub>2</sub>/kg/min
  - Minimum FGF = O<sub>2</sub> consumption (O<sub>2</sub> flow + 21% air flow) + leaks
- During intubation, reduce FGF to zero
- Turn vaporizer off before increasing FGF for emergence

27) Feldman, J. Managing Fresh Gas Flow to Reduce Environmental Contamination. *Anesthesia and Analgesia*, 2012; 114:5-1093-1101.

- According to US Energy Information Administration, healthcare sector is second largest energy consumer
  - Inpatient facility, notably perioperative care, consuming the most
- As physicians we have been called to a life of stewardship
- As anesthesiologists, we have the ability to expand our advances in patient safety and individual outcomes to include the world we live in
- We are uniquely positioned for leadership in the area of sustainability

28) Sherman, J. Ryan, S. Ecological Responsibility in Anesthesia Practice. *International Anesthesiology Clinics*. 2010; 48:3:139-151.

- Topics covered today have covered the value of "greening" operating rooms
- The OR is an area for significant impact and savings
- Implementing these strategies has the ultimate goal of affecting the "triple bottom line" → patient safety, community health, cost reduction

29) Kagoma, Y., et. al. People, planet and profits: the case for greening operating rooms. *CMAJ*. 2012; 184(17):1905-1911.

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## Some Good News

- In 2018, Denver Health reduced its volatile anesthetic associated GHG emissions by ~80%
- Overall perioperative GHG emissions were reduced by approximately 40%
- We have almost reached our 45% reduction in carbon emissions!

## Summary

- Differences exist amongst anesthetics regarding environmental impact
  - Sevoflurane > Isoflurane >>> N<sub>2</sub>O >>>>>>> Desflurane
- Safety concerns about sevoflurane haven't been supported by research
- Significant cost savings are likely with reduction in desflurane use
- Anesthesia is uniquely positioned to impact health from patient to global level through our decision making

## Thank You

- Special thanks
  - Lisa Chirico
  - Clark Lyda
  - Mario Villasenor
  - April Ort
  - Paul Scott

## Resources

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- 3) Chung, JW, et. al. Estimate of the Carbon Footprint of the US Health Care Sector. *JAMA*, November 11, 2009—Vol 302, No. 18.
- 4) [https://doi.org/10.1093/bja/aax303](#) Andersen, M. P., et. al. Inhalation anaesthetics and climate change. *British Journal of Anaesthesia* 105 (6): 760-6
- 5) [https://doi.org/10.1093/bja/aax303](#) Kagoma, Y. General Anesthetic Gases and the Global Environment. *Anesthesia and Analgesia*. January 2011 • Volume 112 • Number 1
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- 7) [https://doi.org/10.1093/bja/aax303](#) Kagoma, Y., et. al. Life Cycle Greenhouse Gas Emissions of Anesthetic Drugs. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5
- 8) Kagoma, Y., et. al. People, planet and profits: the case for greening operating rooms. *CMAJ*, November 20, 2012, 184(17).
- 9) Mankes, RF. Propofol Wastage in Anesthesia. *Anesthesia and Analgesia*. May 2012 • Volume 114 • Number 5.
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- 11) Environmental Impacts of the U.S. Health Care System and Effects on Public Health. PLoS ONE 11 (6): 1-11. doi:10.1371/journal.pone.0158738
- 12) The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems. Lancet 2017; 391: 1037-38
- 13) Landrigan, P.J., et al. The Lancet Commission on pollution and health. Lancet 2018; 391: 462-512.
- 14) Anesthesiology News. April, 2017.
- 15) Ultane (sevoflurane). Volatile liquid for inhalation. AbbVie Inc. 2017.
- 16) Effect of sevoflurane concentration of degradation products generated by reaction between sevoflurane and soda
- 17) Effects of Sevoflurane Anesthesia on Renal Function: Comparison with High-Flow Sevoflurane Anesthesia and Low-Flow Sevoflurane Anesthesia. Anesth Analg 2000; 91:1262-8.
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- 32) Ong Sio LCL, dela Cruz RGC, Bautista AF. Sevoflurane and renal function: a meta-analysis of randomized trials. Med Gas Res. 2017;7(3):186-193.

