# Table of Contents

Acknowledgements........................................................................................................1  
Course Information Sheet.............................................................................................3  
Course Program...........................................................................................................7  
Daily Evaluations.........................................................................................................13  
General Evaluation.....................................................................................................35  

## Handouts

### Sunday – February 24

What’s New in OB Anesthesia from 2007? (Hawkins).................................................37  
Updates on Postoperative Analgesia and Outcomes (Liu)...........................................59  

### Monday – February 25

Ultrasound Guided Regional Anesthesia and Analgesia (Liu)..................................65  
What’s Changing in Obstetric Anesthesia Practice? (Hawkins)....................................67  

### Tuesday – February 26

The OR Pharmacy (Henthorn)....................................................................................81  
Pediatric Anesthesia in 2008 (Agarwal)......................................................................91  

### Wednesday – February 27

Neuroanesthesia: Awake Procedures in Neurosurgery (Sloan)..............................111  
Sedation – What’s New for Anesthesiologist and Non-Anesthesiologist (Maurer)......119  
Propofol Infusion Syndrome: What Do We Know, Why Does It Happen and When Should I Worry (Polaner)..........................................................127  
Platelet Function, Coagulation, and the Effects of Cardiopulmonary Bypass (Weitzel)..............................................................................................................133  
Accreditation in the USA and National Patient Safety Goals (Maurer).........................145  

### Thursday – February 28

New Modes for Ventilation in the Operating Room: Do They Matter (Polaner)....155  
Prophylactis Perioperative Beta-Blockers (Gravlee)..................................................163  
Neuroanesthesia: Intracranial Aneurysms and AVMs: IR or OR? (Sloan)...............169  
Update on Perineural Analgesia: Focus on Lower Extremity (Liu).............................177  
Perioperative Nerve Damage: Prognosis and Prevention (Janik)..............................179
Friday – February 29
Cardiac Anesthesia Update (Gravlee)..............................................................195
Critical Care Updates (Wischmeyer).................................................................205

WORKSHOPS

Monday – February 26

Comprehensive Airway Management.
   Fiberoptic Airway Management (Lane)..........................................................233

Challenges in Ambulatory Anesthesia
   The Association of OSA with Chronic Medical Disorders and the
   Effects of CPAP (Maurer)..............................................................................245

TEE Course Part 1
1. Continuity Equation (Seres)........................................................................249
2. Prominal Isovelocity Surface Area (Seres)..................................................255
3. Clinical Application of Real Time 3D TEE (Seres).........................................261
4. Diastolic Function (Seres).............................................................................265
5. Systolic Function (Seres)..............................................................................269
6. Important TEE Parameters in Clinical Practice (Seres).............................275
7. Mitral Stenosis (Seres)..................................................................................285

Tuesday – February 27

Comprehensive Airway Management
   Fiberoptic Airway Management (Lane)..........................................................233

Challenges in Ambulatory Anesthesia
   The Association of OSA with Chronic Medical Disorders and the
   Effects of CPAP (Maurer)..............................................................................289

Pediatric Controversies
   Pediatric Controversies (Agarwal, Clark).....................................................295

TEE Course Part 2.............................................................................................249

Wednesday –February 28

TEE Course Part 3
1. The Anatomy and Function of the Normal Aortic Valve (Puskas).............297
2. Evaluation of Aortic Stenosis (Puskas)..........................................................315
3. Evaluation of Aortic Regurgitation (Puskas)................................................329
Disclosure of Commercial Interest

Colorado Review of Anesthesia
February 24-29, 2008
Vail, Colorado

As a sponsor accredited by the Accreditation Council for Continuing Medical Education, the University of Colorado School of Medicine must insure balance, independence, objectivity, and scientific rigor in all its sponsored educational activities. All speakers/contributors participating in a sponsored activity are expected to disclose to the accredited provider any significant financial interest or other relationship(s) involving themselves or their spouse/partner within the last 12 months with any proprietary entity producing health care goods or services related to the content of the activity. The intent of this disclosure is not to prevent a speaker with a significant financial or other relationship from making the presentation, but rather to identify and resolve any conflicts of interest that may control the content of the activity. It is also intended that any potential conflict be identified openly so that the listeners have a full disclosure of the facts and may form their own judgments about the presentation. It remains for the audience to determine whether the speaker's interests or relationships may influence the presentation with regard to exposition or conclusion.

All faculty have reported no commercial affiliation associated with this conference.

Faculty do not intend to reference off-label/unapproved uses of products or devices in their presentations.
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<tr>
<th>CRASH 2008 ACKNOWLEDGEMENTS</th>
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* Bronze Sponsorship
IMPORTANT! PLEASE READ

WELCOME TO CRASH 2008!

We encourage you to take five minutes to read this Orientation Packet prior to the start of CRASH 2008.

1. CME Certificates – You should have received your certificate during the registration process. If you did not, please take all the materials you were given and return to the CRASH desk. Above the perforation is the actual certificate which you keep. Below the perforation is the form that you must complete, sign, and return to us for your certificate to be valid. If you have any questions, please check at the CRASH desk. Place your completed sign-in sheet (the bottom portion of your certificate) in one of the evaluation boxes after your final session.

2. Opening Reception – Please plan to attend the Opening Reception hosted by Dr. Henthorn on Sunday night, **February 24**. This will be held between **6:00 and 8:00 PM**, in the pre-function exhibitor area. All members of your family are welcome. There will be a room adjacent to the reception with children's videotapes running.

3. Questions or Problems - Please contact Beverly Janik, Anne Caulfield, Joann Bauer, Russ Ingram, Dr. Rita Agarwal, Dr. Joy Hawkins, or Dr. Daniel Janik with any questions or problems. Our nametags have ribbons that say Committee with “Ralphie” stickers and we spend a LOT of time at the CRASH registration desk.

4. For your family, partners-stuck-back-at-home, house-sitters or other people needing to find you, the **phone number for messages is (970) 477-5630**. All messages will be displayed on the bulletin board which is located next to the CRASH registration desk.

5. Limited Seating – Since we will again approach the seating limit of the large conference room, please:
   * do not bring children to the lectures or workshops. The presence of children has been cited as a problem by participants at previous CRASH conferences and we ask your help in this matter. The lecture/workshop areas are for paid participants only. Should your family need to contact you, have them call **(970) 479-5011** and leave a message.

6. Workshops – Regional Anesthesia, Comprehensive Airway, all TEE workshops, which offers TEE CME Certificate, and Challenges in Ambulatory Anesthesia require a fee. If you wish to attend a workshop, please check at the CRASH desk for space available and payment. You may attend the OB controversies and Pediatric Controversies for free but signup is required!

7. Complimentary Breakfast – This year we ask each participant and their paying guest to wear a purple wrist band mark with CRASH to denote paying guest and participants for meals served by CRASH. Each morning’s breakfast will begin at 6:30 a.m. and will close at 8:00 a.m.
participants. The Guest Breakfast will run from 7:00-8:30am but the hot items will not be available after 8:00am.

• A seating area for family and friends who have paid the guest fee will be available in Salons C/D. This room will also have high chairs and booster chairs for the kids.

8. **Afternoon Refreshments** - Are available from 4:00–5:30p.m. These are not meant to be dinner, but rather a sustaining refreshment to tide you over. The afternoon sessions begin at 4:30. Refreshments are for paid participants only – *guest fees do not cover afternoon refreshments*.

9. **Break** – There will be a ten minute break between the first and second lectures each morning and each afternoon. When you hear the Bell, the next lecture will begin in 3 minutes.

10. **NASTAR Race** - Will be held Wednesday, **February 27th**. This year we are only offering one race time – 1:00 p.m. This activity is complimentary for you and your guests. No matter what your level of skiing, we encourage you to take your 2 runs through the gates. It’s WAY COOL! All racers will need to sign a waiver card available at the registration desk.

11. **CRASH Banquet** – In our continued cost savings efforts, we have decided not to host the CRASH Banquet this year. We felt the time would be better utilized by offering CME credits. Please let us know your thoughts.

12. **Friday Morning Raffle** - Once again we will hold a raffle at the very end of the very last talk on the very last day of the conference. We will be giving away medical books. You must be **IN ATTENDANCE** at the very end of the very last talk on the very last day of the Conference to be eligible.

13. **Evaluations** – Evaluation forms are in your syllabus. Baskets will be furnished at the back of the conference room for your completed evaluation forms; if you have other ideas or concerns, let one of us know or write them down and put them into one of those baskets.

14. **Trivia Questions** – Due to continued public demand, we are again offering the trivia questions. The answer sheet is on the bottom of each eligible session’s daily evaluation and the questions will be projected on the big screen in the main room and on the Announcements Bulletin Board. A winner will be chosen from the correct answers at the close of each eligible session so mark those answers and turn in those forms! Be sure to write your name on the answer portion of your evaluation sheet.

**HAVE FUN, PLAY SAFELY, DRINK LOTS OF WATER, AND USE PLENTY OF SUNSCREEN.**

**DO NOT HESITATE TO ASK DR. AGARWAL, DR. HAWKINS, DR. JANIK, or BEVERLY, RUSS, OR ANNE FOR ASSISTANCE:**

**OUR PHONE NUMBER IS (970) 477-5630**
VAIL RESTURANT

DISCOUNTS FOR CRASH ATTENDEES

Billy's Island Grill 10%

Blue Tiger 15%

Centre V 10%

Montauk's Seafood Grill 10%

Ocotillo 10%
CRASH 2008 PROGRAM

Sunday – February 24

9:00am-8:00pm  Registration

3:30–4:30 p.m.  What’s New in OB Anesthesia for 2007?  
Joy Hawkins MD

4:30–5:30 p.m.  Updates on Postoperative Analgesia and Outcomes  
Spencer Liu MD

5:30-6:00 p.m.  Question and Answer Session  
Hawkins and Liu

6:00-8:00  Opening Reception

Monday – February 25

6:30-7:00 a.m.  Continental Breakfast/View Exhibits

7:00-8:00 a.m.  Ultrasound Guided Regional Anesthesia and Analgesia  
Spencer Liu MD

8:00-9:00 a.m.  What’s Changing in Obstetric Anesthesia Practice?  
Joy Hawkins MD

9:00-9:30 a.m.  Question and Answer Session  
Liu and Hawkins

9:30 a.m.  View Exhibits; Recess
Monday – February 25 (continued)

4:00-5:30 p.m. View Exhibits; Refreshments

4:30-7:00 p.m. WORKSHOPS
Regional Anesthesia
John Armstrong MD; Christopher Ciarallo MD; Sunil Kumar MD; Jason, Ramirez MD; Ronald Valdivieso MD

4:30-5:45 p.m. Comprehensive Airway Management
& Howard Miller MD; Daniel J. Janik MD; David Polaner MD;
5:45-7:00 p.m. Geoffrey Lane MB; Thomas Henthorn MD

4:30-7:00 p.m. Practical TEE for Anesthesiologist Part 1
1. Important Principles of Ultrasound for clinical application of the TEE
   Tamas Seres MD
2. Two and 3 Dimensional Images
   Nathaen Weitzel
3. Clinical application of 3D TEE,
   Tamas Seres MD, Nathaen Weitzel MD
4. Evaluation of Left Ventricular Systolic Function
   Tamas Seres MD

4:30-5:45 p.m. OB Controversies in Anesthesia
Joy Hawkins MD, Brenda Bucklin MD

5:45-7:00 p.m. Challenges in Ambulatory Anesthesia
The Association of OSA with Chronic Medical Disorders and the Effects of CPAP
Walter Maurer MD
Roger Mattison MD

Tuesday – February 26

6:30-7:00 a.m. Continental Breakfast/View Exhibits

7:00-8:00 a.m. The OR Pharmacy
Thomas Henthorn MD

8:00-9:00 a.m. Pediatric Anesthesia in 2008
Rita Agarwal MD, FAAP

9:15-9:30 a.m. Question and Answer Session
Henthorn and Agarwal

9:30 a.m. View Exhibits; Recess
Tuesday – February 26 (continued)

4:00-5:30 p.m.  View Exhibits; Refreshments

4:30-5:45 p.m.  WORKSHOPS
 Regional Anesthesia
    John Armstrong MD; Sunil Kumar MD; Jason, Ramirez MD;
    Christopher Ciarallo MD; Ronald Valdivieso MD

4:30-5:45 p.m.  Comprehensive Airway Management
    &
    Howard Miller MD; Daniel J. Janik MD; David Polaner MD;
    Geoffrey Lane MB; Thomas Henthorn MD

4:30-7:00 p.m.  Practical TEE for Anesthesiologist Part 2
    1. Evaluation of Left Ventricular Diastolic Function
       Tamas Seres MD
    2. The Anatomy and Function of the Normal Mitral Valve
       Fadi Nasrallah MD
    3. Evaluation of Mitral Stenosis
       Tamas Seres MD
    4. Evaluation of Mitral Regurgitation
       Fadi Nasrallah MD

4:30-5:45 p.m.  Pediatric Controversies
    Rita Agarwal MD, FAAC; Randy Clark MD

5:45-7:00 p.m.  Challenges in Ambulatory Anesthesia
    Walter Maurer MD and Roger Mattison MD

Wednesday – February 27

6:30-7:00 a.m.  Continental Breakfast/View Exhibits

7:00-8:00 a.m.  Neuroanesthesia: Awake Procedures in Neurosurgery
    Tod Sloan MD, PhD, MBA

8:00-9:00 a.m.  Sedation - What's New for Anesthesiologist and
    Non-Anesthesiologist?
    Walter Maurer MD

9:00-9:30 a.m.  Question and Answer Session
    Sloan and Maurer

9:30 a.m.  View Exhibits; Recess
Wednesday – February 27 (continued)

9:45-12:00 p.m.  **Practical TEE for Anesthesiologist Part 3**
1. **The Anatomy and function of the Normal Aortic Valve**
   Fadi Nasrallah MD
2. **Evaluation of Aortic Stenosis**
   Ferenc Puskas MD, PhD
3. **Evaluation of Aortic Regurgitation**
   Ferenc Puskas MD, PhD

1:00 p.m.  **NASTAR Race**

4:00-5:30 p.m.  View Exhibits; Refreshments

4:30-5:15 p.m.  **Propofol Infusion Syndrome: What Do We Know, Why Does It Happen and When Should I Worry**
   David Polaner MD

5:15–6:00 p.m.  **Platelet Function, Coagulation, and the Effects of Cardiopulmonary Bypass**
   Nate Weitzel MD

6:00-6:45 p.m.  **Accreditation in the USA and National Patient Safety Goals**
   Walter Maurer MD

6:45-7:00  **Question and Answer Session**
   Polaner, Weitzel, Maurer

Thursday – February 28

6:30-7:00  Continental Breakfast/View Exhibits

7:00-8:00 a.m.  **New Modes for Ventilation in the Operating Room: Do They Matter**
   David Polaner MD

8:00-9:00 a.m.  **Prophylactic Perioperative Beta-Blockers**
   Glenn Gravlee MD

9:00-9:30 a.m.  **Questions and Answers**
   Polaner and Gravlee

9:30 a.m.  View Exhibits/Recess
Thursday – February 28 (continued)
4:00-5:30 p.m.  View Exhibits; Refreshments

4:30-5:15 p.m.  Neuroanesthesia: Intracranial Aneurysms and AVMs: IR or OR?
                Tod Sloan MD, PhD, MBA

5:15 - 6:00 pm. Update on Perineural Analgesia: Focus on Lower Extremity
                Spencer Liu MD

6:00 – 6:45 p.m. Perioperative Nerve Damage: Prognosis and Prevention
                 Daniel Janik MD

6:45 – 7:00 p.m. Questions and Answers
                 Sloan, Liu, and Janik

Friday – February 29

6:30-7:00 a.m. Continental Breakfast/View Exhibits

7:00-8:00 a.m. Cardiac Anesthesia Update
                Glenn Gravlee MD

8:00 - 9:00 a.m. Critical Care Updates
                 Paul Wischmeyer MD

9:00 – 9:30 a.m. Questions and Answers
                 Gravlee and Wischmeyer

9:30  Lottery: Giving out books
      must be present to win!

9:45  Adjourn
Please rate each subject and speaker:

1 - Below Expectations  2 - Met Expectations  3 - Exceeded Expectations

LECTURES
3:30-4:30 p.m.
What’s New in OB Anesthesia?  Joy Hawkins

_________ Please rate this Subject, Would you like to see this topic repeated? Y/N
_________ Please rate this Speaker. Would you like to see this speaker repeated? Y/N
_________ Please rate effectiveness of AV
_________ Please rate quality of handout

Comments: ______________________________________________________________________________

4:30-5:30 p.m.
Updates on Postoperative Analgesia and Outcomes  Spencer Liu

_________ Please rate this Subject, Would you like to see this topic repeated? Y/N
_________ Please rate this Speaker. Would you like to see this speaker repeated? Y/N
_________ Please rate effectiveness of AV
_________ Please rate quality of handout

Comments: ______________________________________________________________________________

Answer to Sunday Afternoon’s Trivia Question:

Name: _________________________________________________________________________

Circle One

A  B  C  D
Please rate each subject and speaker:
   1 - Below Expectation   2 - Met Expectation   3 - Exceeded Expectation

LECTURES

7:00 – 8:00 a.m.

Ultrasound Guided Regional Anesthesia and Analgesia

Spencer Liu

(_______) Please rate this Subject.  Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.  Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

8:00-9:00 a.m.

What’s Changing in Obstetric Anesthesia Practice?

Joy Hawkins

(_______) Please rate this Subject.  Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.  Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

Answer to Monday Morning’s Trivia Question:

Name: ____________________________

Circle One

A    B    C    D
Please rate each subject and speaker:

1 - Below Expectation   2 - Met Expectation   3 - Exceeded Expectation

7:00 – 8:00 a.m.

**The OR Pharmacy**

______ Please rate this Subject, Thomas Henthorn
______ Please rate this Speaker.
______ Please rate effectiveness of AV
______ Please rate quality of handout

Comments: ________________________________________________________________

8:00-9:00 a.m.

**Pediatric Anesthesia in 2008**

______ Please rate this Subject, Rita Agarwal
______ Please rate this Speaker.
______ Please rate effectiveness of AV
______ Please rate quality of handout

Comments: ________________________________________________________________

Answer to Tuesday Morning’s Trivia Question:

Name: ________________________________________________________________

Circle One

A  B  C  D
Please rate each subject and speaker:

1 - Below Expectation  2 - Met Expectation  3 - Exceeded Expectation

7:00 – 8:00 a.m.

Neuroanesthesia: Awake Procedures in Neurosurgery
Tod Sloan

(_______) Please rate this Subject, Would you like to see this topic repeated? Y/N

(_______) Please rate this Speaker, Would you like to see this speaker repeated? Y/N

(_______) Please rate effectiveness of AV

(_______) Please rate quality of handout

Comments: ___________________________________________________________________________

8:00 – 9:00 a.m.

Sedation: What’s New for Anesthesiologist and Non-Anesthesiologist?
Walter Maurer

(_______) Please rate this Subject, Would you like to see this topic repeated? Y/N

(_______) Please rate this Speaker, Would you like to see this speaker repeated? Y/N

(_______) Please rate effectiveness of AV

(_______) Please rate quality of handout

Comments: ___________________________________________________________________________

Answer to Wednesday Morning’s Trivia Question:

Name: _________________________________________________________________

Circle One

A  B  C  D
Please rate each subject and speaker:

1 - Below Expectation  2 - Met Expectation  3 - Exceeded Expectation

4:30-5:15 p.m.

**Propofol Infusion Syndrome in the OR: What Do We Know, Why Does It Happen and When Should we Worry**

David Polaner

(_______) Please rate this Subject,            Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.            Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

5:15-6:00 p.m.

**Platelet Function, Coagulation, and the Effects of Cardiopulmonary Bypass**

Nathaen Weitzel

(_______) Please rate this Subject,            Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.            Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

6:00-6:45 p.m.

**Accreditation in the USA and National Patient Safety Goals**

Walter Maurer

(_______) Please rate this Subject,            Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.            Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

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**Answer to Wednesday Afternoon’s Trivia Question:**

Name: ____________________________________________________________________

Circle One

A  B  C  D
CRASH 2008
Daily Evaluation
THURSDAY MORNING
LECTURES

Please rate each subject and speaker:

1 - Below Expectation  2 - Met Expectation  3 - Exceeded Expectation

7:00-8:00 a.m.

New Strategies for Ventilation in the OR:    David Polaner
Do They Make a Difference

(_______) Please rate this Subject,                Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.                Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

8:00-9:00 a.m

Beta-Blocker Perioperative Prophylaxis    Glenn Gravlee

(_______) Please rate this Subject,                Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker.                Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

Answer to Thursday Morning’s Trivia Question:

Name: ____________________________________________

Circle One

A    B    C    D
Please rate each subject and speaker:

1 - Below Expectation   2 - Met Expectation   3 - Exceeded Expectation

4:30-5:15 p.m
Neuroanesthesia: Intracranial Aneurysms and AVMs: IR or OR? Tod Sloan
(_______) Please rate this Subject, Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker. Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout
Comments: ______________________________________________________________________________

5:15-6:00 pm
Update on Perineural Analgesia Spencer Liu
(_______) Please rate this Subject, Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker. Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout
Comments: ______________________________________________________________________________

6:00 – 6:45 p.m.
Peri-operative Nerve Damage: Diagnosis, Follow-up, and Prevention Daniel Janik
(_______) Please rate this Subject, Would you like to see this topic repeated? Y/N
(_______) Please rate this Speaker. Would you like to see this speaker repeated? Y/N
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout
Comments: ______________________________________________________________________________

Answer to Thursday Afternoon’s Trivia Question:

Name: ____________________________________________________________

Circle One
A       B       C       D
Please rate each subject and speaker:

1 - Below Expectation  2 - Met Expectation  3 - Exceeded Expectation

7:00-8:00 a.m.
Cardiac Anesthesia Update
Glenn Gravlee
(_______) Please rate this Subject,
(_______) Please rate this Speaker.
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

8:00-9:00 a.m.
Critical Care Updates
Paul Wischmeyer
(_______) Please rate this Subject,
(_______) Please rate this Speaker.
(_______) Please rate effectiveness of AV
(_______) Please rate quality of handout

Comments: ______________________________________________________________________________

Answer to Friday's Trivia Question:

Name: ________________________________________________________________________________

Circle One
A  B  C  D
# CRASH 2008

**Workshop Evaluations**

**MONDAY AFTERNOON**

Please rate each subject and speaker:

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<th>Subject</th>
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<td>John P. Armstrong, MD</td>
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<td>Christopher Ciarallo</td>
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<td>Jeffrey Galinkin, MB, FRCA</td>
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<td>Tamas Seres, MD</td>
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<td><strong>OB Controversies</strong></td>
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<td><strong>Challenges in Ambulatory Anesthesia</strong></td>
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<td>Walter Maurer, M.D</td>
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What was your impression of this workshop and how it was run? ____________________________________________
### CRASH 2008

**Workshop Evaluations**

**TUESDAY AFTERNOON**

Please rate each subject and speaker:

<table>
<thead>
<tr>
<th>Subject</th>
<th>Rating</th>
<th>Facilitator</th>
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<tr>
<td>Regional Anesthesia</td>
<td>(_______)</td>
<td>John P. Armstrong, MD</td>
<td>(_______)</td>
<td>Christopher Ciarallo, MD</td>
<td>(_______)</td>
<td>Sunil Kumar, MD</td>
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<td>Comprehensive Airway Management</td>
<td>(_______)</td>
<td>Jeffrey Galinkin, MD</td>
<td>(_______)</td>
<td>Thomas Henthorn, MD</td>
<td>(_______)</td>
<td>Daniel J. Janik, MD</td>
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<tr>
<td>TEE Course - Part 2</td>
<td>(_______)</td>
<td>Tamas Seres, MD</td>
<td>(_______)</td>
<td>Fadi Nasrallah, MD</td>
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<td>Pediatric Controversies</td>
<td>(_______)</td>
<td>Rita Agarwal, MD, FAAP</td>
<td>(_______)</td>
<td>Randall M. Clark, MD</td>
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What was your impression of this workshop and how it was run? ____________________________________

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**Please rate this Subject**

**Please rate this Facilitator**
Please rate each subject and speaker:

1 - Below Expectation  2 - Met Expectation  3 - Exceeded Expectation

WORKSHOPS
9:45-12:00 noon

**TEE Course - Part 3**
Ferenc Puskas, PhD, MD

(_______) Please rate this Subject
(_______) Please rate this Facilitator

What was your impression of this workshop and how it was run? _________________________________________

______________________________________________________________
**Course Evaluation**

We are pleased that you chose to visit us in Vail. Please take a few minutes and give us your comments regarding the program. We read each evaluation and will use them to help us plan next year’s meeting.

**Are you a:**

- _____ Physician in Practice
- _____ CRNA/RN/PA
- _____ Resident in Training
- _____ Retired Physician
- _____ Other (specify)____________________

**If you are working, how long have you been in practice?**

- _____ In training
- _____ < 10 years
- _____ > 10 years

**What setting do you primarily practice in?**

- _____ Academic Institution
- _____ Large Urban Hospital
- _____ Small Urban Hospital
- _____ Large Rural Hospital
- _____ Small Rural Hospital

**What percentage of your practice are the following areas?**

- _____ Cardiovascular Anesthesia
- _____ Vascular/Thoracic (non-hearts)
- _____ Obstetrics
- _____ Pediatrics
- _____ Ambulatory
- _____ Trauma
- _____ Critical Care
- _____ Pain
- _____ Other _______________________

**What is your overall impression of the program? (Circle one)**

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**Specifically, how satisfied were you with:**

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<td>Course Management</td>
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**What topics were covered well this year?**

**What topics were not covered well this year?**

**What topics would you like to see at future meetings?**

**Was the course content educational, fair, balanced, and free of commercial bias?**

<table>
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<td>Do you plan to change/alter your practice habits as a result of</td>
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<td>Do you plan to return to future CRASH Conferences?</td>
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<td>If PALS was offered would you be interested in taking the course?</td>
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<td>Would you like to see Poster Presentations at this Conference?</td>
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<td>Do you like the Trivia questions?</td>
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What’s New in Obstetric Anesthesia from 2007?
Joy L. Hawkins, MD

“Research is to see what everybody else has seen, and to think what nobody else has thought.” *

Policies and Procedures
• New ASA guidelines: Obstetric Anesthesia, Neuraxial Opioids
• New from ACOG: Antithrombotic Therapy, Cesarean on Request
• Medicaid coverage for obstetric services
• Disparities in utilization of epidural analgesia
• Team training results
• A good clinical update / overview of obstetric anesthesia

Labor Analgesia
• Parenteral opioid analgesia
• Physiologic changes in the mother, fetus and father
• Technical aspects of placing neuraxial anesthetics
• Technical aspects of maintaining neuraxial anesthesia
• Choice of local anesthetic for labor analgesia
• Progress of labor with and without neuraxial analgesia

Cesarean Delivery
• General anesthesia: fetal responses, difficult airways
• Management issues for spinal anesthesia for cesarean
• Intraoperative issues: warming the mother, uterine exteriorization versus in situ repair, antibiotic timing
• Postoperative pain management: DepoDur™, opiate dependence, FDA concerns over codeine and breast-feeding
• Treating side effects; itching and nausea

Anesthetic Complications
• Anesthesia-related maternal mortality; results from the Doctor’s Company and from Michigan
• Epidural abscess and hematoma in acute pain management
• Postpartum headache work-up; common and uncommon causes
• Elevated temperature associated with epidural analgesia for labor
• Anesthetic neurotoxicity in the fetus and newborn
• Pharmacokinetics of anesthetic transfer to human breast milk

The Fetus and Newborn
• Intrapartum management of fetal heart rate patterns
• Pregnancy issues and longterm newborn outcomes
• Management at delivery: cord clamping, meconium-stained fluid, head trauma vs mode of delivery
• Amniotic fluid analysis and stem cell recovery
• Preterm labor: prevention, steroids, treatment choices
• Outcome of preterm newborns
• Caring for bereaved parents during and after delivery

Obstetric Complications
• Choosing a cesarean over a trial of labor; risk benefit calculations
• Obesity: influence on progress of labor and risk of stillbirth
• Peri-partum hemorrhage: obstetric management, interventional radiology techniques, cell salvage and Factor VII use
• Preeclampsia: pathophysiology, biomarkers for early diagnosis, prevention, treatment and complications
• Pregnancy-related co-morbidities predict later health issues
• Spinal anesthesia for version
• Rare pregnancy-related morbidities and anesthetic management

* Albert Szent-Gyorgyi
Policies and Procedures

- In April 2007 the updated ASA Practice Guidelines for Obstetric Anesthesia were published. The Summary of Recommendations is on pages 852-3 with explanations of the literature used and Task Force’s conclusions in the text. Some new items in the document include: having a communication system in place between obstetric providers, anesthesia personnel and nursing, further NPO guidelines (to include allowing clear liquids) and aspiration prophylaxis, lack of effect of neuraxial analgesia on the progress of labor, use of pencil point needles for spinal and CSE procedures, PCEA, preload and pressors, and management of emergencies such as hemorrhage, failed airway and cardiac arrest. The recommendations are evidence-based as much as possible. An editorial summarizes the process and conclusions.

- The ASA House of Delegates approved “Practice Guidelines for the Prevention, Detection and Management of Respiratory Depression Associated with Neuraxial Opioid Administration” at their meeting in October 2007. Most of their provisions are in line with the way we use neuraxial opioids on L&D, but one recommendation for detection states: “In the case of single-injection neuraxial lipophilic opioids (e.g. fentanyl), continual monitoring should be performed for a minimum of 2 hr following administration.” Continual is not how we typically monitor after spinal opioids for labor analgesia, and certainly not for 2 hours.

- Embolism (thrombotic, amniotic fluid and air) has been the #1 cause of maternal death in the United States for many years. ACOG published two documents this year with guidelines for prevention and treatment of DVT and pulmonary embolism. The ACOG Practice Bulletin for “Prevention of Deep Vein Thrombosis and Pulmonary Embolism” has a section on Anesthesia Concerns on page 434 which states that neuraxial anesthesia should be delayed until 12-18 hours after the last dose, and that catheters should be removed in the same time frame. After catheter removal, the next dose of LMWH should be delayed for 2 hours. These are consistent with ASRA guidelines. The second document, “Antithrombotic therapy and pregnancy: consensus report and recommendations for prevention and treatment of venous thromboembolism and adverse pregnancy outcomes” states: If the patient labors before the ASA time limits [those noted above], then aggressive use of an IV narcotic provides safe and satisfactory analgesia, and general anesthesia may be used for cesarean delivery if necessary…. Data from several small studies have demonstrated no increased risk of major bleeding with surgical procedures, operative vaginal delivery, and cesarean delivery in patients treated with LMWHs (prophylactic and full anticoagulation doses). The consensus panel recommendations for regional anesthesia also follow the ASRA guidelines. These are both excellent well-referenced documents.

- ACOG continues to wrestle with cesarean delivery on maternal request, defined as a primary cesarean delivery in the absence of any medical or obstetric indication. A Committee Opinion published in 2007 states that potential risks include longer hospital stay, increased risk of respiratory
problems for the baby, and greater complications in subsequent pregnancies. They also state it should not be motivated by the unavailability of effective pain management. It should not be performed before 39 weeks and is not recommended for women desiring several children.

- A study was done to estimate the association between changes in professional liability premiums for obstetricians and the primary cesarean delivery rates. They found that for each annual $10,000 increase in premium, the cesarean rate increased by 15.7 per 1000 nulliparous women. Are medico-legal pressures influencing obstetricians to perform procedures that may not be clearly medically necessary?

- A review of emergency Medicaid expenses in North Carolina found that childbirth and pregnancy complications were responsible for the major part of emergency Medicaid spending for undocumented and recent immigrants. These programs generally fail to cover routine check-ups (or contraceptive care such as postpartum tubal ligation), despite the fact that other studies have shown taxpayers can save $3 for every $1 spent on prenatal care.

- A review of the New York State Perinatal Database questioned whether race and ethnicity are associated with the undertreatment of pain in pregnant women. They found Hispanic and black patients were less likely to receive epidural analgesia than non-Hispanic whites (O.R. 0.85 and 0.78 respectively), and that patients without insurance were least likely to receive epidural analgesia (O.R. 0.76). However, black patients with insurance were no more likely than white patients without insurance to receive epidural analgesia (O.R. 0.69 versus 0.66). An accompanying editorial notes the literature supports that pain complaints (in all settings) of racial and ethnic minorities, women, and elderly persons are often unheard, that minorities are less likely to have their pain assessed, and that when they do they often receive less pain medication than white patients.

- Teamwork training based on crew resource management has been studied in several settings such as the emergency room and L&D to see if patient outcomes can be improved. A comparison of 7 hospitals with and 8 hospitals without intervention in the form of teamwork training on L&D found no difference in outcome as measured by the “Adverse Outcome Index”. Interestingly, about 8% of deliveries in both arms had an adverse outcome, although it ranged from 4-16.5% of deliveries across all hospitals. Why the range in incidence of adverse outcomes between hospitals??

- An excellent clinical update on obstetric anesthesia was published in the Lancet. It’s a good review for obstetric personnel and others wanting a brief overview.

**Labor Analgesia**

- In response to concerns for fetal safety raised by a drug company, ACOG issued a Committee Opinion on “Nalbuphine Hydrochloride Use for Intrapartum Analgesia”. The drug company insert states that “Fetal death
has been reported where mothers received Nubain during labor and delivery”, however ACOG states “data are insufficient to recommend any changes in nalbuphine hydrochloride administration at this time.” There is nothing new in the insert that hasn’t been known for some time, e.g. fetal bradycardia, sinusoidal FHR pattern.

- A letter emphasizes the difficulties using remifentanil for IV labor analgesia because of wide variation in dose, the episodic nature of labor pain, and the potency and rapidity of action. Certainly immediate availability of anesthesia personnel is necessary when it is used, as illustrated by their case report of a maternal respiratory arrest resulting in emergency cesarean delivery. A study comparing different regimens to administer remifentanil during labor found fewer side effects when the bolus dose was kept constant (0.25 μg/kg) while the background infusion was increased as needed (0.025-0.1 μg/kg/min). Increasing the bolus dose to improve pain relief caused more sedation and comparable pain scores. No respiratory depression was seen with comparable saturations.

- A study in rats tested whether estrogen enhanced painful responses to uterine cervical distension. Estrogen increases the excitatory transient receptor potential-1 channel (TRPV-1), raising the possibility that pain from the cervix could be enhanced by estrogen and reduced by antagonists of TRPV-1.

- The ASA Practice Guidelines for Obstetric Anesthesia allow for intake of clear liquids in uncomplicated labor, but what about gastric emptying of the obese pregnant woman? In a group of obese (mean BMI 41), term, non-laboring pregnant women, gastric emptying was no different after ingestion of 50 or 300ml water, and gastric antral volume after 300ml was similar to baseline fasting.

- Is the fetal bradycardia sometimes seen after CSE due to changes in fetal oxygen saturation? Fetal SpO2 was measured in 8 women receiving spinal sufentanil 5mcg and Bupivacaine 2.5mg. No changes in FHR or fetal saturation were seen. Fetal saturation was about 50% before and after CSE.

- A retrospective study looked at use of epidural analgesia and the risk of acute postpartum urinary retention in 1994 women. A longer second stage, use of systemic narcotics, perineal laceration and instrumental delivery all strongly predicted urinary retention (O.R. 1.63-2.62). Epidural analgesia showed a trend toward an association, but the effect was likely due to the influence of other obstetric variables.

- What are fathers’ attitudes toward labor with their first child with or without epidural analgesia? Fathers whose partners did not receive epidurals felt their presence as troublesome and unnecessary. Maternal analgesia with an epidural increased paternal feelings of helpfulness and was associated with greater involvement and less anxiety and stress.

- Ultrasound imaging using a transverse approach can help identify the midline for an epidural placement, the distance from the skin to the epidural space, and the intervertebral space. Using this information, the success of the initial insertion point chosen was 92% with no need to redirect in 74%. 

Correlation with depth was 0.881. This could be a useful technique in difficult situations such as obesity.

- Previous work has shown that using lidocaine with epinephrine (found in most epidural kits as the test dose ampule) for skin infiltration decreases superficial bleeding. A new study confirmed that finding and also showed that addition of bicarbonate decreased pain during skin infiltration from a VAS score of 3.6 to 2.6.xxii

- A new device, the Episure™ Syringe, may provide a reliable, objective endpoint for loss of resistance in identifying the epidural space.xxiii In laboratory, animal and clinical studies, the authors found the spring-loaded syringe correctly located the epidural space in all patients with no accidental dural punctures or false LORs encountered.

- We continue to look for the optimal way to maintain epidural analgesia in labor. A new study compared 3 methods: continuous infusion, PCEA with a background infusion and PCEA with demand-dose only.xxiv They found the total dose of drug administered was lowest in the demand-only group, but there were no other differences in pain scores, motor block, delivery outcome, satisfaction scores, or maternal or neonatal outcome between the three groups. Interestingly, there was no difference in the number of staff interventions between the groups, a commonly cited advantage of PCEA.

- A novel method using PCEA with mandatory boluses (5ml demand dose + 5ml hourly bolus) versus PCEA with a continuous basal infusion (5ml demand dose + 5ml/hour basal infusion) found benefits to the mandatory bolusesxxv: less total drug administered, less need to self-administer boluses, and a longer time to the first self-administered bolus after CSE. There was no difference in pain scores or side effects. The authors speculate that boluses provide better spread in the epidural space than a continuous infusion of the same amount.

- Several studies were done this year comparing the local anesthetics most commonly used for labor analgesia: bupivacaine, ropivacaine and levobupivacaine. In the first, the ED50 for developing motor block when given intrathecally was compared between the 3 drugs.xxvi The doses were 5.8mg for ropivacaine, 4.8mg for levobupivacaine, and 3.4mg for bupivacaine. In the second study, the MMLAC (minimum local anesthetic concentration producing motor block) for epidural administration was found to be 0.34% for R, 0.30% for L, and 0.26% for B.xxvii In other words; the same motor blocking hierarchy was found for both spinal and epidural administration. Another study compared the intrathecal dose needed for complete labor analgesia when combined with 1.5μg sufentanil.xxviii The ED95 of bupivacaine was 3.3mg, for levobupivacaine and ropivacaine were 4.8mg, again showing that bupivacaine is more potent than the other two local anesthetics. But the bottom line is, does it make a difference in maternal or neonatal outcome? No. When nulliparous women at term were randomized to epidural B, L, or R, there was no difference in operative delivery rate, duration of first or second stage of labor, total dose of LA received per hour of labor, or neonatal outcome.xxix Of course, levobupivacaine is no longer available in the U.S., but
any of these local anesthetics can be used safely and effectively for labor analgesia with appropriate dose adjustments.

- Although simmering down, the “epidural analgesia versus progress of labor” issue is still contentious in some institutions. A systematic review and meta-analysis of early epidural versus parenteral opioids or late epidural placement included 3,320 nulliparous women and found the following: 1) cesarean delivery rates (OR 1) and instrumental vaginal delivery rates (OR 1) were similar in the two groups, 2) neonates in the early epidural group had higher pH values and received less naloxone, 3) those receiving parenteral opioids or a late epidural had more instrumental vaginal deliveries for nonreassuring fetal status, worse indices of neonatal wellness and lower quality of maternal analgesia. Although not yet published in manuscript form, a follow-up to Wong’s 2005 NEJM study of early versus late neuraxial analgesia, now in nulliparas undergoing induction (a high risk group for failure to progress), was presented in abstract form. Again, they found placement of CSE at 2cm (versus parenteral hydromorphone) in women undergoing induction did not increase cesarean delivery rate. In addition, the CSE group had lower pain scores (1 vs 5) and less nausea and vomiting (8% vs 34%). There was no difference in length of labor or neonatal condition.

Cesarean Delivery

- General anesthesia is used in less than 10% of cesareans in the U.S., but is still a valuable technique in many obstetric situations. When general anesthesia must be used for a preterm fetus, either for non-obstetric surgery or for cesarean delivery, what are the fetal responses? Instrumented preterm pregnant sheep were monitored before, during and after general anesthesia with thiopental, midazolam and isoflurane. Fetal SaO2, cerebral oxygenation and cerebral blood flow were unchanged during anesthesia, while fetal mean arterial pressure decreased, indicating the cerebrovasculature can maintain constant oxygenation and flow even if fetal MAP falls significantly.

- Airway management is our big concern during general anesthesia. The Airtraq® disposable intubating laryngoscope was used in a case series of morbidly obese (BMI 38 and 44) parturients undergoing cesarean after failed standard laryngoscopy and attempted bougie placement. There was good visualization of the glottis in all cases. Another case report describes a parturient with Treacher-Collins Syndrome who required emergent cesarean after cord prolapse (no preanesthesia consult had been obtained!). A LMA-Fastrach™ was placed successfully for the cesarean with subsequent spontaneous ventilation, although intubation could never be achieved.

- The management of spinal anesthesia for cesarean continues to be fine-tuned. Preload with 6% hydroxyethyl starch reduces the incidence of hypotension over preloading with crystalloid, but what are the effects on coagulation? TEG values (r and K) were prolonged after the colloid although they remained in normal range. There were no differences after
crystalloid preload. Does speed of injection matter when using hyperbaric bupivacaine for elective cesarean? Injection of 12mg hyperbaric 0.75% bupivacaine in 4 seconds or 40 seconds produced no difference in spread, hypotension or nausea. Adding just 2.5μg sufentanil to bupivacaine for cesarean had a significant local anesthetic sparing effect compared to IV sufentanil in the same dose. The ED50 (not ED95!) was 6.3mg in the control group, 5.2mg with IV sufentanil, and 3.0mg with spinal sufentanil. A previous study found rostral spread of spinal levobupivacaine was less when phenylephrine was used as a pressor versus ephedrine. The authors repeated the study with spinal bupivacaine and found no difference in block height when the two pressors were used, however the incidence of fetal acidosis was higher (7.32 with phenylephrine versus 7.2 with ephedrine) and Apgar scores were lower in the ephedrine group. Yet more evidence that phenylephrine should be our pressor of choice in most situations during cesarean.

- The utility of forced air warming during cesarean under spinal anesthesia was tested, with no difference in the incidence of core hypothermia (53% of warmed versus 67% of unwarmed, NS) or shivering. Note that hypothermia (< 35.5 C) was very common in all their patients!
- Obstetric technique can influence our anesthetic management. Uterine exteriorization versus in situ repair by the obstetrician increases postoperative pain significantly after general anesthesia, although postoperative fever, wound infection and hemoglobin are similar. Another study showed that exteriorization increased nausea, vomiting and tachycardia during cesarean under spinal, and concluded uterine repair should be done in situ where possible.
- Traditionally antibiotics have been administered after cord clamp during cesarean section. A prospective randomized double-blind study found that cefazolin administered before skin incision decreased infectious morbidity (RR = 0.4) and endometritis (RR=0.2) in parturients, versus giving antibiotics at cord clamping. There was no increase in neonatal septic workups or complications.
- Optimizing postoperative pain management after cesarean is important for early mobilization and neonatal care. Extended-release epidural morphine, DepoDur™, provides superior pain relief in women from the 24-48 hour time period when traditional neuraxial morphine would have worn off. Although no increase in adverse events was found, the package insert recommends 48 hours of nursing monitoring which may be problematic. Although the extended release formulation cannot be given with local anesthetics or as part of a spinal anesthetic, if a CSE is used for a projected longer procedure (3rd or more cesarean, obesity, etc.) or if an epidural from labor is used, DepoDur™ becomes a practical alternative for a select group of parturients.
- What about postpartum analgesia for women maintained on methadone? A study of women in the methadone maintenance program versus control women found no difference in intrapartum analgesia or in analgesic use after vaginal delivery. However, after cesarean delivery pain scores were
significantly higher (5.3 versus 3.0 in controls) and opiate use was 70% greater. Unfortunately for study purposes (and patient comfort!), neuraxial morphine was used only at the discretion of the anesthesiologist and was not consistent.

- Following a report of the death of a healthy breast-feeding baby whose mother was taking codeine for episiotomy pain (Lancet 2006;368:704), the U.S. FDA issued a Public Health Advisory. The mother’s blood level of morphine was abnormally high after just small doses of codeine, and she was found to be an ultra-rapid metabolizer of codeine. ACOG advises physicians and mothers to let the infant’s pediatrician know codeine has been prescribed and to alert the mother to signs of possible overdose in her baby.

- Side effects of neuraxial opioids can be troublesome to parturients. Nalbuphine is commonly used to treat neuraxial morphine-induced itching, and an animal study has shown that butorphanol has similar efficacy at attenuating itching without reducing morphine analgesia. Their work also showed that partial mu and kappa opioid agonist actions contribute to its effectiveness.

- Several studies looked at treatments for nausea during and after neuraxial anesthesia for cesarean. Intraoperative oxygen administration did not reduce the incidence or severity of nausea or vomiting in the operating room or 24 hours postoperatively. Similarly, prophylactic granisetron 1mg did not reduce post-delivery nausea or vomiting during cesarean under spinal anesthesia. In contrast, transdermal scopolamine placed after delivery during cesarean under spinal anesthesia (with intrathecal morphine) was more effective than placebo in reducing nausea and vomiting, with greatest effectiveness at 6-24 hours. Its use was associated with more dry mouth and blurry vision however. This may be a useful technique for patients at very high risk of PONV or who have not responded to traditional anti-emetics.

### Anesthetic Complications

- The Doctors Company reported on 22 anesthesiology claims filed after maternal cardiac arrests on labor and delivery wards between 1998 and 2006. Outcomes were poor: 10/22 died, 11 had anoxic brain damage, and only 1 left the hospital intact. Thirteen cases were respiratory arrests following epidurals or spinals – 8 following labor epidural placement with unintentional subarachnoid blocks (all occurred within 30 minutes of placement) and 5 during spinal anesthetics for cesarean. None of the cases had audible alarms on the monitors at the time of arrest, making delay in response likely. In 7 cases resuscitation of the mother was delayed when the decision was made to move to the operating room to facilitate delivery, or because airway equipment was not available in the labor room. The one woman who survived intact had ventilation with an Ambu begun immediately and the obstetrician delivered the baby within minutes of the arrest, indicating any delay in ventilation and/or pressure support of the mother is crucial.
Seven cases involved postpartum hemorrhage with delay in diagnosis and/or treatment with blood products. These were often system issues involving communication, but the anesthesia care contributed to the arrest. Two cases involved preeclampsia, with arrest occurring at induction of anesthesia – one spinal and one general. Hypovolemia might have been involved. Only one case involved general anesthesia with loss of the airway.

- A review of maternal deaths in Michigan found that 8 of 855 deaths were anesthesia-related and in another 7 anesthesia contributed. All of the anesthesia-related deaths occurred during emergence (not induction) or recovery from general anesthesia and involved hypoventilation or airway obstruction. Obesity and African-American race were common factors associated with these deaths. In 3 cases inadequate supervision was an associated factor; two in which the CRNA was supervised by the operating obstetrician and one in which the anesthesiologist was absent for emergence from general anesthesia. All these cases raise the question of appropriate PACU management after general anesthesia and additional monitoring for obese patients at risk for sleep-obstructed breathing. An accompanying editorial notes that each anesthesia practice must establish protocols that reduce risks associated with emergence from general anesthesia and during recovery (which PACU should we use after general anesthesia for cesarean; main O.R. or L&D?) and address risks associated with obesity and obstructive sleep apnea.

- Great Britain published their “Confidential Enquiry into Maternal and Child Health, Saving Mother’s Lives, 2003-2005”, the seventh report from the United Kingdom. The found 6 direct anesthetic deaths: 4/6 involved obese women having general anesthetics, 3/6 of these women suffered postoperative respiratory failure, 1/6 was local anesthetic toxicity when a bupivacaine infusion was mistakenly attached to an IV line during labor, and 1/6 was a hemotorax following central line placement for urgent cesarean. In another 31 cases anesthesia care contributed. These were related to unrecognized or under-managed co-morbidities or peripartum hemorrhage. Their recommendations focus on protocols for management of morbidly obese women including antepartum anesthetic consultation, experienced practitioners (not just trainees) for care of morbidly obese women, better blood pressure control in severe preeclampsia, and better recognition and aggressive management of obstetric hemorrhage. The CEMD reviews are superb for the level of detail about the cases they are able to retrieve.

- Two centers reviewed their data on epidural hematoma or abscess in their Acute Pain Service databases (these are not obstetric patients). Each group reviewed about 8000 cases over a several year period. The incidence of hematoma was 1:4105 versus 1:2700 (between studies) and the incidence of epidural abscess was 1:1368 versus 1:1350 for an overall incidence of neuraxial complication of 1:1026 or 0.1%. They recommend early MRI in patients with concerning symptoms. They performed 32 scans to diagnose 8 lesions, but only one patient required surgical decompression and there were no long term neurological sequelae – good outcomes! An accompanying
letter emphasizes that chlorhexidine is the preferred solution for skin preparation. Although not obstetric patients, these reviews should be mandatory reading for those who provide neuraxial blocks.

- A review of postpartum headaches reminds us that not all headaches are related to an anesthetic. They remind us that tension and migraine headaches are the most common postpartum headaches and that severe preeclampsia/eclampsia should be considered if hypertension is present. Cerebral imaging is necessary if neurologic deficits are present or when the headache fails to respond to treatment of the presumed cause. Intracranial venous thrombosis is rare but potentially fatal, and can mimic postdural puncture headache with a postural component. Consider imaging if the character of the headache changes, blood patch does not provide improvement, there are thrombophilic risk factors, or neurologic exam is suggestive of more severe intracranial pathology. A case report describes posterior reversible encephalopathy syndrome after postdural puncture headache following spinal anesthesia for cesarean. After 4 days of conservative treatment for presumed PDPH she deteriorated, was diagnosed with vasospasm after extensive work-up, and responded completely to magnesium sulfate!

- The perplexing problem of maternal fever associated with epidural analgesia for labor remains unsolved, but a recent study elucidates its presentation. They found that that a minority of women will develop hyperthermia, but those who do so develop it in the first hour after epidural exposure and then have a rise of 0.33 degrees F per hour. Hyperthermia appears to be an abnormal response in a small subset of women at term. The immediate increase suggests an inflammatory response, perhaps due to a polymorphism increasing levels of a pro-inflammatory cytokine.

- The question of anesthetic neurotoxicity in neonates is usually referred to as a pediatric anesthesia problem, but providing anesthesia for non-obstetric surgery involves a fetus potentially at risk of exposure. On March 29, 2007 the FDA Anesthetic and Life Support Drugs Advisory Committee held a hearing on the studies reporting neurodegenerative changes in juvenile animals exposed to anesthetic drugs. Many anesthesiologists testified on the need for more research. An excellent review article summarizes the literature to date, noting that both NMDA receptor antagonists (eg. ketamine) and GABA potentiating agents are potentially neurotoxic to the developing brain, but that a lack of information precludes the ability to designate any one anesthetic agent or regimen as safer than another. An editorial notes that “Until further empirical evidence becomes available, such as from noninvasive neuroimaging of cell death after anesthesia in human infants or identifying a behavioral ‘phenotype’ after anesthetic exposure in infancy, changing clinical practices based on these animal data are premature.” Suggestions for possible research approaches in humans are outlined in several letters to the editor. Until then we are faced with falling back on “avoid hypoxia and hypotension”!
• Women may be worried about breast-feeding after a cesarean or postpartum tubal ligation done under general anesthesia because of concerns for drug exposure to their neonate. A study on lactating women looked at the pharmacokinetics of midazolam, propofol and fentanyl transfer to breast milk. The authors found that the amount of drug excreted into milk within 24 hours of surgery is extremely small and unlikely to affect a healthy term infant.

The Fetus and Newborn

• Interpretation and management of intrapartum fetal heart rate patterns can be subjective and differ between obstetric practitioners. An algorithm for management of fetal heart rate patterns and their relationship to fetal acidemia may help standardize obstetric management. With the goal of minimizing newborn infant acidemia, without excessive obstetric intervention, 134 FHR patterns were identified and assigned a score based on risk of acidemia or low Apgar score. The management recommendations also include whether the anesthetist should be informed and/or present at the bedside.

• Several studies point out that even seemingly minor perturbations in maternal variables or habits can adversely impact the fetus and newborn. For example, blood glucoses that are elevated but still within normal range (75 versus 105 mg/dL) can increase risks of macrosomia, first time cesarean delivery, and newborn low blood glucose and elevated insulin levels. Fetal heart rate patterns (rate and variability) from 20-38 weeks predict performance on a standardized developmental exam at 24 months and language skills at 30 months. Smoking just half a pack of cigarettes a day increases the risk of a newborn having extra, missing or webbed fingers of toes by 30%. The risk of birth defects in women with depression who take SSRIs is controversial, and two recent studies indicate that although risks cannot be completely excluded, they are exceedingly low and any associated defects are rare. An accompanying editorial points out that “…patients and physicians alike would prefer it if there were clear lines separating ‘risk’ and ‘no risk’ and if all studies gave consistent results pointing in the same direction. Unfortunately, this is often not the case…”

• Similarly, there are a number of seemingly minor maneuvers at the time of delivery that can impact the newborn. A study of late versus early clamping of the umbilical cord in full term neonates found that delaying clamping for 2 minutes following birth is beneficial even into infancy. Hematocrit and iron stores were improved at 6 months, and although neonates were at risk of asymptomatic polycythemia, the condition appeared benign. An accompanying editorial notes that 1) this is a meta analysis rather than an RCT, 2) that delivery personnel should prioritize resuscitation (if needed) over delayed clamping, and 3) that nutritional guidance and iron supplementation should still occur.
An ACOG Committee Opinion on “Management of Delivery of a Newborn With Meconium-Stained Amniotic Fluid” notes that: “…infants with meconium-stained amniotic fluid should no longer routinely receive intrapartum suctioning. If meconium is present and the newborn is depressed, the clinician should intubate the trachea and suction meconium and other aspirated material from beneath the glottis.”

A radiology study did MRI scans on 88 term newborns about 3 weeks after vaginal delivery and found small brain hemorrhages in 25%. The researchers point out that they did not occur in babies born by cesarean, but that they did not seem to be clinically significant. It may help with medicolegal liability to know that these hemorrhages are “normal” after vaginal delivery and do not signify pathology or trauma. An unrelated study found that serious fetal trauma (cranial bleed or fracture, brachial plexus injuries, facial trauma, other fractures) was reduced with cesarean delivery, with or without labor.

Breast-feeding has many short-term advantages (eg, fewer ear infections), but also seems to reduce obesity and heart disease later in life. Researchers found that babies who are nursed for one month or longer have a lower BMI and higher levels of HDL cholesterol in mid-adulthood than their bottle-fed counterparts. Children with a version of the gene FADS2 have a 7-point higher IQ score when breast fed than children without the gene variant. An example of nature working through nurture!

An excellent review of what we know (and don’t know) about the mechanisms that instigate parturition in humans highlights new and ongoing research.

The prevention and treatment of preterm labor and delivery remains elusive and frustrating. In two studies, progesterone failed to prevent preterm birth in women with twin gestations (RR 1.1), but reduced the rate of spontaneous early preterm delivery in women with a short cervical length (RR 0.56). An accompanying editorial notes that who progesterone should be used for, how it should be used, and what if any long-term effects there might be on these children remain to be seen. There are at least 14 ongoing trials of progesterone involving women with high-risk pregnancies recruiting more than 5000 women. Two separate groups looked at the impact at 2-3 years of age of repeat doses of corticosteroids for lung maturity during preterm labor. Neither found evidence of differences in body size measurements, blood pressure, or neurocognitive abilities (blindness, deafness or cerebral palsy) among these children. The editorial points out that the non-significant increase in cerebral palsy in the repeat dosage group warrants caution and informed consent for the parents.

As yet there is no optimal drug to treat preterm labor when it occurs. A comparison of magnesium to nifedipine for acute tocolysis found nifedipine had fewer maternal adverse effects (lethargy, dizziness, nausea or vomiting) and similar effectiveness as measured by delay of delivery, gestational age at delivery and neonatal outcomes. Babies in the magnesium group spent longer in the NICU (8.8 versus 4.2 days). Nifedipine (20mg PO q 4-6 hours) is much easier to use and tolerate than magnesium 2gm/hr as an IV infusion. A trial of nitroglycerin patch versus placebo for preterm labor found the
nitroglycerin-treated infants had reduced morbidity and mortality (RR 0.29) and reduced birth prior to 28 weeks (RR 0.50). An excellent review article reviews current drug therapy for prevention of preterm labor. Anesthesiologists should be familiar with the dosing regimens for these drugs and their side effects. If tocolysis fails and preterm delivery is inevitable, these patients may require an anesthetic for delivery.

- What about outcome for very preterm infants? In support of regionalization of obstetric services, mortality rates for infants <1500 grams were lowest in hospitals with NICUs that had high level of care (Level 3) and high volume of these infants (>100). Unfortunately, less than 25% of very low birth weight infants are born in such hospitals, and that percentage has declined over the last 10 years. The authors recommend the merging of existing smaller NICUs.

- Infants less than 1500 grams at birth have insulin resistance. When they are young adults, they continue to show insulin resistance, glucose intolerance and higher blood pressures than those born at term.

- Our Neonatology colleagues have become so good at what they do, we hardly worry about the implications for mildly premature infants at 34-36 weeks. However, mortality rates are 6 times higher in the first week and 3 times higher at one year for infants born at 34-36 weeks than those born at >37 weeks.

- Sadly, families sometimes must deal with a perinatal death. A review of families’ experiences included comments about analgesia during labor. Negative experiences included inadequate pain control during labor and feeling sedated during delivery. Sedatives are not a recommended treatment for grief reactions, but unfortunately 41% of patients reported their physicians had prescribed such medications. We can help these families by providing neuraxial analgesia when requested.

Obstetric Complications

- Obstetricians continue to debate the risk benefit calculations of a scheduled cesarean versus a trial of labor. An excellent editorial outlines the reasons we now have a 30% cesarean rate in the U.S. (abandonment of breech vaginal deliveries, decreased forceps/vacuum rates, studies showing that repeat cesarean has fewer major complications and better perinatal outcome, the malpractice crisis, etc.) and concludes that we need to decide on the level of risk currently considered acceptable given the large number needed to treat to avoid one adverse neonatal outcome. In contrast, several studies show that elective cesareans carry higher risks including longer hospital stays (4.3 vs 2.4 days for a planned vaginal birth), higher costs ($4372 vs $2487)
An accompanying piece in the New York Times notes that in general, cesarean delivery tends to be modestly more safe for the baby while more risky for the mother. What obstetricians think about cesarean delivery on maternal request, i.e. no medical or obstetric reason for the surgery? A survey of ACOG fellows found that many are seeing an increased demand for cesareans on request in their practices, but most feel the risks outweigh the benefits. An Australian review of 8,725 women who had a cesarean delivery for their first birth compared to 27,313 women who had a vaginal first birth found prior cesarean delivery was associated with increased risks in the subsequent pregnancy. Stillbirth, preterm birth, SGA, emergency cesarean, placental abnormalities, uterine rupture and malpresentation were all significantly more common in the cesarean group. This information should help in counseling women considering an elective primary cesarean delivery. As noted earlier (reference #6), ACOG has a Committee Opinion on how to counsel patients who are considering an elective primary cesarean for themselves.

What about VBAC? Two studies published in 2007 attempted to find the “Holy Grail” – how to predict who will be successful in their attempt at vaginal delivery and who is destined to fail. In the first study, a retrospective chart review of 25,005 patients at both community and academic hospitals with previous cesareans found that 75% of those who attempted VBAC succeeded. Variables that predicted success were prior vaginal birth and young maternal age (<20 years). The second paper was a prospective study at only academic hospitals of 11,856 women who attempted VBAC. The 73% who succeeded were younger, had a lower BMI at first prenatal visit, were white, had a history of prior vaginal birth, and had a nonrecurrent indication for their prior cesarean. The findings in both studies were remarkably similar despite different design and study populations. Both showed that obese, older minority women who have histories of cesarean delivery for labor abnormalities and no prior vaginal births are less likely to be successful in a trial of labor (<50%). Not surprisingly, women with one prior cesarean attempting VBAC have a lower likelihood of vaginal delivery with induction versus spontaneous labor, especially if they have an unfavorable cervix.

Maternal obesity leads to management issues for both obstetricians and anesthesiologists. Nulliparous women with a BMI > 35 in the first trimester had an increased rate of cesarean delivery following onset of spontaneous labor at term when compared to women with BMI < 25 (OR 3.8). The risk for stillbirth increased in a dose-dependent fashion with increases in BMI; OR 1.9 for BMI > 40. Obese black mothers experienced more stillbirths than their white counterparts, another racial disparity in obstetric outcomes.

A number of strategies for management of peripartum hemorrhage are evolving. Women with a placenta previa will have increasing morbidity (coagulopathy, hysterectomy, pulmonary edema) with an increasing number of prior cesarean deliveries. In contrast, newborn outcome was not affected...
by number of prior cesareans. A case report describes a woman with one prior cesarean who presented at 14 weeks gestation with massive (4L) intra-abdominal bleeding. On laparotomy there was placenta percreta with trophoblastic tissue protruding through the prior uterine incision. The decision was made to continue the pregnancy, and an uncomplicated cesarean hysterectomy was performed at 34 weeks after iliac artery embolization. Mother and baby did well! A review of 30 planned and 35 emergent cesarean hysterectomies found (not surprisingly) more complications, ICU admissions, greater blood loss and more transfusion in the emergent group. Anticipating cesarean hysterectomy allows for planning to reduce blood loss, presence of surgical specialists and interventional radiologists, and expanded operative instrument sets. Using uterine compression sutures may reduce the need for hysterectomy during severe postpartum hemorrhage, and also preserves subsequent fertility if desired.

- Interventional radiology techniques can be life-saving, but the indications for its use are still evolving. A case series describes successful management of three women who strongly desired continued fertility but were at risk for hysterectomy due to hemorrhage. All were delivered in the I.R. suite after prophylactic placement of balloon occlusion catheters. In contrast, a case report of placenta percreta managed with prophylactic balloon occlusion of the internal iliac arteries resulted in the mother developing an ischemic leg due to a large thrombus of the common and external iliac artery, requiring an emergent thrombectomy in the operating room. Also discouraging is a case control comparison of cesarean hysterectomy with or without prophylactic placement of intravascular balloon catheters for placenta accreta that showed no improvement in outcome as measured by blood loss, blood products given, or postoperative days in the hospital. Clearly a large prospective RCT is needed.

- Although use of cell salvage for postpartum hemorrhage is controversial for other reasons (contamination, AFE exposure), how likely is it to reduce the need for allogenic RBC transfusion? A review of cesarean delivery patients who required transfusion estimated that at best 25% of patients could have completely avoided allogenic RBC transfusion, although transfusion could have been reduced in 49%. Cell salvage may be useful when religious or cultural beliefs, atypical antibodies, or shortages of blood limit the availability of banked blood.

- Recombinant Factor VIIa (NovoSeven®) seems to have an evolving role in managing postpartum hemorrhage as evidenced by several studies in 2007. A case report describes use of factor VIIa to treat DIC following amniotic fluid embolism. After about 6 liters of blood loss, 60 mcg/kg was given with clinical improvement of bleeding within 10 minutes. Another case series of 4 patients given 70-85 mcg/kg factor VIIa for peripartum hemorrhage unresponsive to oxytocics and blood product replacement notes that guidelines are needed to define dosing and provide a cost analysis. They note that other authors estimate cost neutrality when 14 units of PRBC have
been transfused. A European registry identified 113 women with data available who received factor VIIa over a 4-year period. Their data showed rapidly increasing use over the period of time studied. They found marked improvement in over 80% of women after treatment, with very few adverse effects, but there was no control group. Despite the “success” of treatment, 5/113 died, 82/113 were admitted to ICU and 33/113 needed hysterectomy. Both a pro-con debate and a review article on the use of recombinant factor VIIa in massive postpartum hemorrhage note that the window to do a randomized controlled trial in this setting is probably closed because of the rarity of such hemorrhage, the difficulty in recruiting patients and gaining consent in an emergency situation, and because the published literature of case reports has been overwhelmingly positive.

- Preeclampsia (PEC) remains an enigma with significant associated morbidity, but the pathophysiology is becoming clearer, and biomarkers are exciting new tools. Although not an autoimmune disease, preeclampsia mimics many features typically seen in autoimmune diseases, allograft rejection and graft-versus-host disease including clinical and laboratory characteristics. Recent work suggests a key role for altered expression of placental antiangiogenic factors, soluble Flt1 and soluble endoglin. They are secreted by the placenta and increase in the maternal circulation weeks before the onset of preeclampsia, producing systemic endothelial dysfunction such as hypertension, proteinuria and the other systemic manifestations of PEC. A systematic review of the literature on elevated sFlt-1 and reduced placental growth factor (PIGF) predicting preeclampsia concluded that third-trimester increases in sFlt-1 with decreases in placental growth factor levels are associated with severe preeclampsia. Whether they can be used for screening is unclear, and prospective studies are needed to determine their clinical usefulness. Those studies are now starting to appear. A comparison of soluble sFlt-1 and soluble endoglin levels in gestational hypertension, chronic hypertension, preeclampsia and normal pregnancies found a high sensitivity and specificity in differentiating women with preeclampsia from those with other hypertensive diseases during pregnancy. An accompanying editorial notes flaws in the study, but outlines ways in which information of this kind will be useful to clinicians: ruling out the disease in suspected cases, identifying women with mild disease who will progress to severe, identifying women whose PEC will produce adverse pregnancy outcome, and predicting women at risk for subsequent preeclampsia. In two other studies, women with at least one high risk factor for developing preeclampsia (diabetes, chronic hypertension, kidney disease, etc.) had sFlt1, PIGF and their ratio followed through pregnancy, and researchers were able to predict development of early and late-onset preeclampsia.

- An excellent clinical review looks at “Imitators of Severe Preeclampsia” such as TTP, hemolytic uremic syndrome, acute fatty liver of pregnancy, and acute exacerbation of SLE and discusses their differentiation, management, and counseling during pregnancy.
• Prevention of preeclampsia in high risk women has included trials of aspirin, calcium, vitamin C and other therapies. A recent trial of antioxidant supplementation with both vitamins C and E or placebo found no reduction in the rate of preeclampsia in women who were high risk due to chronic hypertension and/or prior preeclampsia.\textsuperscript{c\textsubscript{x\textsuperscript{iv}}}

• Women who increase their BMI from normal weight to obese between pregnancies increase their risk of preeclampsia significantly.\textsuperscript{c\textsuperscript{xxv}} For example, changing from underweight to obese OR 5.6 for preeclampsia (from a baseline rate of 2% overall), from normal to obese OR 3.2, and from overweight to obese was OR 3.7.

• Magnesium remains the mainstay of obstetric management for seizure prophylaxis to prevent preeclampsia from progressing to eclampsia, but it can cause significant toxicity to the mother and has unpleasant side effects even without toxicity. Since the major complications of preeclampsia occur in the severe forms of the disease, should magnesium therapy be used in mild forms of the disease? A decision analytic model of magnesium therapy or no magnesium for mild preeclampsia found that either approach is acceptable, with the strategies essentially equivalent in aggregate maternal and neonatal outcomes.\textsuperscript{c\textsuperscript{xxvi}} When severe preeclampsia develops remote from term (24-32 weeks gestation), the obstetrician is faced with morbidity to the mother if delivery is delayed, and to the fetus if delivery is expedited. An algorithm has been developed to help clinicians select appropriate candidates for expectant treatment, criteria for maternal-fetal monitoring, and targets for delivery.\textsuperscript{c\textsuperscript{xxvii}}

• A growing literature indicates that pregnancy is a form of “stress test” that may predict later health issues in the mother. For example, post-menopausal women who had preeclampsia decades earlier were 57% more likely to have coronary calcification on CT.\textsuperscript{c\textsuperscript{xxviii}} Women with increased pre-pregnancy BMI were more likely to develop hypertension during pregnancy (OR 5.5 for BMI > 30), and those women had higher mortality rates 30 years later (OR 2.9 for obese women who had hypertension during pregnancy versus obese women who had not been hypertensive).\textsuperscript{c\textsuperscript{xxix}} At 21 years after delivery, women who had hypertension during pregnancy were twice as likely to have diabetes as those who had not been hypertensive.\textsuperscript{c\textsuperscript{xxx}} These studies all recommend better long term follow-up of these women.

• Anesthesia/analgesia has been used in several studies to improve the success rate of external cephalic version for breech presentation at term without conclusive results or recommendations. An RCT of 70 nulliparous women who received 7.5mg spinal bupivacaine or no analgesia for version found that spinal anesthesia significantly increased the success rate (67% versus 32%), allowing for a trial of labor for vaginal delivery.\textsuperscript{c\textsuperscript{xxxi}}

• Maternal co-morbidities can be associated with the pregnancy or exacerbated by pregnancy. A case series of 4 women with cardiomyopathy describes their cesarean delivery management by CSE or general anesthesia with invasive monitoring.\textsuperscript{c\textsuperscript{xxxii}} One woman required emergent heart transplant in the postpartum period with decompensation to an EF of 9%! A review of 3 cases of acute fatty liver of pregnancy (AFLP) notes that maternal and fetal mortality
are significant and that anesthetic management is complicated by coagulopathy and hepatic failure.\textsuperscript{cxxxiii} A review of HIV infected mothers who underwent cesarean delivery found they were more likely to have postpartum endometritis (12\% vs 6\%), require transfusion (4\% vs 2\%), develop sepsis (1.1\% vs 0.2\%) or pneumonia (1.3\% vs 0.3\%), or to die (0.8\% vs 0.1\%).\textsuperscript{cxxxiv} A case report describes a woman who had a seizure on emergence from general anesthesia for cesarean.\textsuperscript{cxxxv} An MRI revealed a giant unruptured left internal carotid aneurysm with mass effect on the frontal lobe. Consultation with neurosurgery resulted in her discharge with planned follow-up 4 weeks later in their clinic, but one day after discharge she presented to the ER with an acute bleed and died several days later. Should management of cerebral aneurysms or AVMs be expedited in the peripartum period? Finally, ACOG published a Practice Bulletin on clinical management guidelines for hemoglobinopathies in pregnancy, including sickle cell disease and the thalassemias.\textsuperscript{cxxxvi} Anesthetic issues are similar to those in non-pregnant patients.

And that’s all until next year!
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Provision of high quality postoperative analgesia has become recognized as an important perioperative goal. The potential to modify major postoperative complications by providing high quality postoperative pain control has been a popular area for investigation in the past decade with over 3,800 clinical trials indexed in the National Library of Medicine’s Medline database (through June, 2006). Despite the popularity of the topic, consensus on effects of acute postoperative pain control on outcomes remains controversial. A key component of this controversy is the need for large patient numbers in any individual clinical trial due to the relatively low incidences of major postoperative morbidity. For example, an observational meta-analysis in 2003 of 176 studies enrolling more than 205,000 subjects undergoing the traditionally “high risk” procedure of coronary artery bypass surgery reported a mortality rate of ~1.7% (1). The same has become true for “high risk” populations such as the elderly. Random 5% sample of Medicare insurance claims (1997-2001) collected postoperative data from 68,726 patients undergoing a variety of surgical procedures and noted a 30 day mortality rate of 2.5% (2). Such modest incidences require approximately 4,600 patients in a single, randomized, controlled trial (RCT) to be able to detect a 50% reduction in incidence from 2% to 1%. Even the highest reported rates of postoperative morbidity, such as pulmonary complications after thoracic or abdominal surgery (23-36% incidence), would require approximately 100 patients per group to detect a 50% reduction (3-5). Very few individual RCTs currently exist to definitively answer such questions. A systematic review examined all major studies from the past decade to review the evidence for impact of postoperative analgesia on major outcomes.

Table 1. Included Articles that Examined Effects of Epidural Analgesia on Postoperative Mortality and Morbidity

<table>
<thead>
<tr>
<th>Study (Reference)</th>
<th>N</th>
<th>Surgical procedure</th>
<th>Mortality (%)</th>
<th>Cardiovascular complication (%)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Epidural</td>
<td>Control</td>
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<td>Retroactive</td>
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<tr>
<td>Rogers 2010 (9)</td>
<td>995</td>
<td>Spinal</td>
<td>1.7</td>
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<td>Caudal</td>
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<td>4.0</td>
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<td>Liu 2004 (8)</td>
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<td>Spinal</td>
<td>0.7</td>
<td>0.5</td>
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<tr>
<td>Rusiniak 2005 (6)</td>
<td>1375</td>
<td>Spinal</td>
<td>1.1</td>
<td>4.4</td>
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<tr>
<td>Roche 2010 (11)</td>
<td>1034</td>
<td>Spinal</td>
<td>1.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Weenink 2010 (12)</td>
<td>1111</td>
<td>Spinal</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Others 2001 (10)</td>
<td>1289</td>
<td>Spinal</td>
<td>1.1</td>
<td>4.4</td>
</tr>
<tr>
<td>Total RCT</td>
<td>884</td>
<td>Spinal</td>
<td>0.7</td>
<td>0.5</td>
</tr>
</tbody>
</table>

- RR = relative risk; M = mortality; S = surgical; H = heart rate; COP = chronic obstructive pulmonary disease; CVD = cardiovascular disease; IRR = incidence reduction rate; NRI = net reclassification improvement; NS = not significant; NID = not applicable
- *Statistically significant; †Significantly different from no epidural group
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### Table 1. Included Articles that Examined Effects of Epidural Analgesia on Postoperative Morbidity

<table>
<thead>
<tr>
<th>Study (Reference)</th>
<th>N</th>
<th>Surgical procedure</th>
<th>Respiratory Failure (%)</th>
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<td>Alencar et al.</td>
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<td>9/10</td>
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</tr>
<tr>
<td>Cho et al. (3)</td>
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Copyright restrictions apply.

### Table 2. Included Articles that Examined Effects of Epidural Analgesia on Postoperative Morbidity

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Copyright restrictions apply.
Conclusion and Future directions

Overall, there is insufficient evidence to confirm or deny the ability of postoperative analgesic techniques to affect major postoperative mortality or morbidity. Epidural analgesia with local anesthetics has the greatest theoretical potential to affect outcome and correspondingly has been the most thoroughly investigated technique. The majority of evidence favors an ability of epidural analgesia to reduce postoperative cardiovascular and pulmonary complications after major vascular surgery and in high-risk patients. This finding may become irrelevant due to rapid conversion of major surgery to minimally invasive techniques (e.g.,
endoluminal abdominal aortic repair) that have less risk of complications (7). There is also consistent evidence that epidural analgesia with local anesthetics is associated with faster resolution of postoperative ileus after major abdominal surgery. Again, this finding may also become irrelevant with adoption of laparoscopic techniques and multi-modal fast track programs for abdominal surgery (8). There is no current evidence that peri-neural analgesia, continuous wound catheters using local anesthetics, IV PCA with opioids, or addition of multimodal systemic analgesics have any clinically significant beneficial effect on postoperative complications.

With the increasing safety of surgical procedures, it may be time to increase the scope of definition of “outcomes” of interest. As mortality and major morbidity become increasingly uncommon, perhaps it will be appropriate to focus more upon patient oriented outcomes. These “nontraditional” outcomes are assessed from the patient’s perspective which mirrors the increasing importance of patient-oriented assessments in other areas of medicine and increasing consumerism in health care (9). Domains typically include quality of postoperative recovery including analgesia and side effects, patient satisfaction, and quality of life (10). Interestingly, patients are often more concerned about these common, low morbidity outcomes, whereas anesthesiologists are often more concerned about major complications that are increasingly uncommon (9).
References


Regional anesthesia has evolved from the purview of surgeons with intimate knowledge of specialized anatomy to increasingly widespread use in the specialty of Anesthesiology. The path of the operator from surgeon to regional anesthesia artist to increasingly typical practitioner has been aided by technology. Needles for regional anesthesia evolved into smaller needles with blunter tips to aid in detecting tissue and fascial layers. The introduction of nerve stimulators and specialized insulated needles was a tremendous advancement in the ability to functionally apply 3-D anatomy for regional anesthesia. This technology has further evolved with the introduction of stimulating perineural catheters that allow real time assessment of functional placement of the catheter prior to use.

Now, another new technology has burst to the forefront and offers potential to further simplify and improve application of regional anesthesia. Improved technology in portable ultrasound has changed the imaging of neural and perineural structures from fuzzy Rorschach type blots to very crisp and clear images. Certainly, ultrasound guided blocks are fun, but what is the current evidence for superiority?

**Efficacy:** In theory, direct visualization of peri-neural and neural structures should allow for faster and better blocks. After all, “Seeing is believing”. On the other hand, a practitioner skilled with nerve stimulator, paresthesia, or transarterial techniques has equally excellent success rates for brachial plexus anesthesia. Can technology really improve the operator?

Current RCTs do suggest that ultrasound guided blocks decrease the number of needle passes and perhaps onset time when compared to single injection nerve stimulator guided blocks. Reduction in onset times is typically < 7 minutes and may not occur when compared to multiple stimulation nerve block techniques. One can also debate the economic value of this modest time savings. Most interestingly, consistent evidence for increased overall block success is lacking. In all likelihood, very similar efficacy can be achieved by a practitioner skilled in either technique, just as a skilled aneaesthetist can use either intravenous or volatile agents to achieve a smooth and rapid ambulatory anesthetic. In the preceding sentence, the term “skilled” was used as a requisite for equivalence between techniques. Does ultrasound increase the rate of skill acquisition? That probably depends on if a formal program is created. Ultrasound is a relatively sophisticated technology and requires knowledge in addition to human anatomy. In a similar fashion to TEE, important topics include ultrasound equipment, knobology, physics, scanning skills, and image interpretation. Important techniques include needle tracking both in and out of plane and imaging spread of local anesthetic. Acquisition of all these skills takes time. Finally, there has been some debate as to whether investment in
proficiency in ultrasound guided blocks is an advantage or disadvantage for joining a practice, especially one without easy access to sophisticated ultrasound devices.

**Safety:** In theory, direct visualization of peri-neural and neural structures should allow for less risk of direct needle trauma to the nerve. Clearly many non-imaged guided blocks are to some extent intra-neural or intra-epineurium. Animal and human studies suggest that one can satisfactorily view intra-neural injection, which may improve safety. But is intra or epineurium injection really a problem? The very rare incidence of permanent nerve injury with any technique suggests that either nerves are very resilient or we are consistently very lucky. Due to the infrequency of permanent nerve injury after regional anesthesia, this will likely be a very difficult question to answer and either very large databases will need to be created or more common surrogate measures will have to be substituted (a la ST segment changes vs myocardial infarction for the cardiac literature). On the other hand, there are more subtle potential safety benefits. For example, use of ultrasound has revitalized the supraclavicular block for upper extremity surgery. Despite excellent clinical block characteristics (superficial anatomy, rapid onset, small local anesthetic dose requirement, dense anesthesia), this block had been previously ignored due to concerns for vascular injury and pneumothorax. Use of ultrasound allows consistent direct visualization of the actual brachial plexus and more importantly of structures to avoid (vessels and pleura). In fact, this may be the only block needed for the entire upper extremity and shoulder, as a large enough dose converts this block to a “low” interscalene block suitable for surgery. Thus, ability to perform a simple and superior technique due to reduced risk from imaging may in itself be an important safety accomplishment.

Future: The debate over value of ultrasound is likely to continue until the technology becomes too cheap, easy to use, and available to argue. For example, no one really cares now if an axillary block is performed with nerve stimulator vs paresthesia, vs fascial click technique, as nerve stimulators are ubiquitous. Until then, there is plenty of work to be done to determine relative efficacy, safety, and best means of training for this new technique.

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1. RAPM 2002;27:402
3. Anesth Analg 1999;88:1053
4. Anesth Analg 2007;1265
6. RAPM 2004::29:544
7. ASRA Newsletter, May 2007:6
10. Anesthesiology 2002:97:1274
WHAT’S CHANGING IN OBSTETRIC ANESTHESIA PRACTICE?

Joy L. Hawkins, M.D.
University of Colorado SOM
Denver, CO
(“I have nothing to disclose.”)

INTRODUCTION

Many of the concepts and techniques we thought we knew and understood are being re-examined and our clinical practices are changing as a result.

For example……………

TOPICS TO COVER

• Preventing hypotension; pressors and fluids
• Spinals in preeclampsia
• CSE versus CLE
• Impact of early epidurals on progress of labor
• Epidural analgesia causing maternal fever
• Adverse effects of maternal O₂ supplementation
• LMA as a rescue device during cesarean
• Use of Interventional Radiology for hemorrhage
• “Best” anesthetic for surgery during pregnancy

Which pressor produces the best outcome for mother and baby when treating hypotension due to spinal anesthesia?

Phenylephrine.

CHOICE OF PRESSOR

After spinal anesthesia for elective C/S, parturients received ephedrine infusion with or without phenylephrine. The combination (E+P) group had:
• less hypotension (37 vs. 75%)
• less need for supplemental ephedrine
• higher umbilical artery pH

Anesthesiology 2001; 95:668

“If physicians would read two articles per day out of the six million medical articles published annually, in one year, they would fall 82 centuries behind in their reading.”

**CHOICE OF PRESSOR**

Women having an elective C/S under spinal anesthesia were randomized to ephedrine or metaraminol infusions.
- The \( \alpha \)-agonist provided closer control of maternal systolic pressure.
- Umbilical pH was higher after an \( \alpha \)-agonist.
- Uterine artery pulsatility by Doppler was similar in both groups.

*Anesthesiology 2001; 95:307*

**CHOICE OF PRESSOR**

- Women were randomized to receive ephedrine, phenylephrine or a mixture during spinal anesthesia for cesarean.
- Giving phenylephrine *alone* produced the best fetal pH and the least amount of nausea and vomiting in the mother. Adding ephedrine offered no advantage.

*Anesthesiology 2002;97:1582*

**CHOICE OF PRESSOR**

Should we avoid using high doses of \( \alpha \)-agonists? What is the optimal BP we should target after regional anesthesia? Should we allow BP to fall 20% before treating?

Women (n=75) receiving spinal anesthesia for elective cesarean delivery were randomized to receive enough phenylephrine to keep their blood pressure at 100%, 90% or 80% of baseline.

(cont.)

**CHOICE OF PRESSOR**

When BP was kept at 100% of baseline, patients had:
- the fewest episodes of “hypotension”
- the highest fetal umbilical pH values
- the fewest episodes of maternal N&V

This *despite* receiving the highest doses of phenylephrine (mean dose 1520\( \mu \)g).

*Br J Anaesth 2004;92:469*

**CHOICE OF PRESSOR**

“Keep the pressure up and don’t spare the vasoconstrictors” (editorial)
- Ephedrine’s \( \beta \) activity may adversely affect the fetus by increasing its metabolic rate.
- Using \( \alpha \)-agonists does not cause vasoconstriction, it returns status to normal.
- Maternal sensitivity to vasoconstrictors is decreased in pregnancy; this may also protect the fetus.

*Br J Anaesth 2004;92:459*

**CHOICE OF PRESSOR**

A meta analysis of 27 studies reporting neonatal acid-base status with different types of anesthesia:
- Cord pH was lowest using spinal compared to general (1272 subjects) or epidural (828 subjects).
- In addition, base deficit was significantly higher with spinal than general or epidural anesthesia.
- Regression analysis \( \rightarrow \) larger doses of ephedrine. Use phenylephrine in preference as your pressor.

*Anaesthesia 2005;60:636*
CHOICE OF PRESSOR

Summary: Clinical studies in humans have consistently shown that use of α-agonists (phenylephrine) produces better umbilical arterial pH values and less maternal nausea than ephedrine. Ephedrine may ↑ fetal oxygen consumption, thereby ↓ overall oxygen delivery.

Will adequate preload prevent maternal hypotension after spinal or epidural anesthesia for cesarean delivery?

No.

PRELOAD

- Women randomized to 20ml/kg versus no preload had similar episodes of hypotension (71 vs 55%) after spinal for cesarean.
  Anesthesiology 1993;79:262
- Women randomized to 10, 20, or 30ml/kg crystalloid preload had a similar incidence of hypotension and ephedrine use. However, COP decreased significantly after larger volumes.
  Anest Analg 1996;83:299

- A Cochrane Systematic Review of spinal anesthesia for cesarean included 75 trials and 4624 women. No intervention eliminated the need to treat hypotension. However, the incidence is reduced by:
  - Administering IV fluids (RR 0.78 for crystalloids and 0.68 for colloids)
  - Ephedrine or phenylephrine use (RR 0.51 or 0.27)
  - Lower limb compression (RR 0.69)
  CD002251, online October 2006

Is spinal anesthesia for cesarean delivery safe and appropriate for women with severe preeclampsia?

Yes.

SPINALS IN PREECLAMPSIA

Several small retrospective studies showed no difference in the incidence of hypotension or maternal or fetal outcome when comparing spinal to epidural anesthesia.

Obstet Gynecol 1995;86:193
Anesthesiology 1999;90:1276
IJOA 1999;8:85
**SPINALS IN PREECLAMPSIA**

- Women with severe preeclampsia (BP $\geq$ 160/110) were compared to healthy women having spinal anesthesia for C/S.
- Severely preeclamptic patients had less hypotension than healthy women (17% vs 53%), despite receiving less fluid preload and a larger dose of spinal bupivacaine.

  Anesth Analg 2003;97:867

**CSE IN PREECLAMPSIA**

Can a lower dose of spinal anesthetic be used?

- 46 women received a combined spinal-epidural anesthetic for cesarean using 7.5mg bupivacaïne and 25$\mu$g fentanyl. Four needed additional epidural 2% lidocaine to attain a T4 level.
- There were modest hemodynamic changes and no adverse neonatal effects.

  Reg Anesth Pain Med 2001;26:46-51

**SPINALS IN PREECLAMPSIA**

- Is the decrease in hypotension due to preeclamptic factors or a smaller uterus?
  - During spinal anesthesia for cesarean, preeclamptic patients had less hypotension (RR 0.6) and required less ephedrine (10mg vs 16mg) than parturients with preterm pregnancies.

  Anesth Analg 2005;101:869

**SPINALS IN PREECLAMPSIA**

In a randomized trial, spinal and epidural anesthesia were compared in severely preeclamptic patients with clinically insignificant differences.

- Hypotension was more frequent with spinal (51 vs 23%), but duration was short ($\leq$ 1 min).
- There was more ephedrine used with spinal (6 vs 0 mg), but hypotension was easily treated.
- Neonatal outcomes were similar in both groups.

  Anesth Analg 2005;101:862

**Is CSE analgesia less successful than epidural analgesia?** No, more.

**Are complications more common after CSE than epidural analgesia?** No.
CSE versus CLE
In a retrospective review of 12,590 neuraxial labor analgesia blocks:

<table>
<thead>
<tr>
<th></th>
<th>CLE</th>
<th>CSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall failure rate</td>
<td>14%</td>
<td>10%</td>
</tr>
<tr>
<td>Inadequate analgesia</td>
<td>8.4%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Needed replacement</td>
<td>7.1%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Wet tap</td>
<td>1.4%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>


CSE versus CLE
Comparing ~1100 parturients who received CSE with ~1100 parturients receiving CLE, there were no differences in:
- labor progress and outcome
- failed epidural catheters
- accidental dural puncture
- PDPH
- epidural blood patch

Anesthesiology 2001; 95:913

Is there evidence that regional analgesia for labor negatively impacts delivery outcome in spontaneously laboring patients?
Less and less.

PROGRESS OF LABOR
A natural experiment...in one year the use of epidural analgesia for labor increased from 1→84%. There was no change in:
- overall C/S rate
- C/S for dystocia rate
- instrumental delivery rate
- duration of first stage of labor
Second stage duration (pushing) was increased by 25 minutes.

Am J Obstet Gynecol 2001; 185:128

PROGRESS OF LABOR
242 nulliparous women were randomized to IV PCA fentanyl or epidural for analgesia:
- No difference in cesarean delivery rate.
- No difference in forceps delivery rate.
- In the epidural group the second stage was 23 minutes longer but pain and satisfaction scores were better.
- In the IV PCA group, there was more maternal nausea and sedation and more need for active newborn resuscitation or naloxone.

Anesth Analg 2004;99:1532

PROGRESS OF LABOR
2703 nulliparous women were randomized to epidural analgesia or IV meperidine. There was no difference in cesarean delivery rate. However, patients in the epidural group had:
- Increased oxytocin use.
- Longer first stage (~30 minutes) and second stage (~13 minutes) of labor.
- More forceps deliveries (13 vs 7%).
- More fevers**.

Anesthesiology 2004;100:142

71
PROGRESS OF LABOR

A systematic review of seven randomized controlled trials involving 2962 nulliparous women compared low dose epidural infusions with parenteral opioids:

**Conclusions:**
1. Epidural infusions with low concentration local anesthetics are unlikely to increase the risk of cesarean section in nulliparous women.

PROGRESS OF LABOR

2. Although epidural analgesia is associated with an ↑ risk of instrumental vaginal delivery, operator bias cannot be excluded.

3. Epidural analgesia is associated with a longer second stage of labor (mean 15 minutes) and ↑ oxytocin requirements, but the importance of these is unclear as maternal analgesia and neonatal outcome may be better with epidural analgesia.

BMJ 2004;328:1410

When a woman has severe pain in early labor, will neuraxial analgesia adversely impact progress of labor? No.

**Is one neuraxial technique better than another in this setting?**
Maybe.

EARLY ANALGESIA

750 nulliparous women, spontaneous labor, < 4cm were randomized to receive spinal fentanyl (ITF) or IV hydromorphone for analgesia.

• Pain scores were lower after ITF (2 vs 6).
• Rates of C/S were no different (18 vs 21%).
• Time to complete dilation (duration of first stage of labor) was 90 minutes shorter in the ITF group.
• Newborn outcome (Apgar < 7) was worse after parenteral medications.

NEJM 2005;352:655

EARLY ANALGESIA

Are there differences in progress of labor between intrathecal and epidural techniques?

• 100 nulliparous patients < 5 cm were randomized to conventional epidurals or combined spinal-epidural (CSE) analgesia with spinal sufentanil.
• Patients receiving spinal analgesia dilated faster (2.1 vs. 1 cm/hr, p = 0.0008).
• 10% of spinal analgesia patients (vs. none in the epidural group) had very rapid dilation > 5 cm/hr.

Anesthesiology 1999; 91:920

EDITORIAL: “The common belief…that a laboring woman is “not ready yet” for epidural analgesia forces women to endure hours of extra pain…the findings …make it clear that safe, effective pain relief with the use of regional anesthetics should not be withheld simply because an arbitrary degree of cervical dilatation has not yet been achieved.”

NEJM 2005;352:718
EARLY ANALGESIA

- Randomized controlled trial of 449 term, nulliparous women: early epidural < 3cm dilation versus late epidural when > 4cm.
- Mean dilation was 2.4 vs 4.6 cm at placement.
- Rates of cesarean were no different (13 vs 11%).
- Labor was 42 minutes shorter in the early group.
- Women preferred early epidural analgesia.

EDITORIAL: “No longer should a patient be made to feel guilty about her wish for pain relief early in labor, powerless in her choices or conflicted about the consequences of such a choice….What a concept – pain relief of real pain when requested. We all should now feel comfortable supporting this position for the patient in labor.”

Am J Obstet Gynecol 2006;194:598

PROGRESS OF LABOR

ACOG Committee Opinion #339: Analgesia and Cesarean Delivery Rates

“Neuraxial analgesia techniques are the most effective and least depressant treatments for labor pain….more recent studies have shown that epidural analgesia does not increase the risks of cesarean delivery….the fear of unnecessary cesarean delivery should not influence the method of pain relief that women can choose during labor.”

Obstet Gynecol 2006;107:1487

BREAST-FEEDING

What is in the lactation literature?

“….recommend a reduction in the use of epidural analgesia to enhance breastfeeding.”

J Human Lactation 1996;13:131

“Women in this cohort who had epidurals were less likely to fully breastfeed their infant in the few days after birth and more likely to stop breastfeeding in the first 24 weeks.”

Int Breastfeeding Journal 2006;1:24

Does the use of epidural analgesia for labor adversely affect breast-feeding?

Probably not, but the evidence is still out.
**BREAST-FEEDING**

- Two studies have now correlated epidural fentanyl with ↓ rates of breast-feeding. Women who received > 150 μg fentanyl during labor had more difficulty with breast-feeding on postpartum day 1 and at 6 weeks.
- However, advantages of including fentanyl are improved analgesia and ↓ motor block.
- Recommendations: Avoid boluses of fentanyl if possible and provide more intervention by lactation consultants for high risk women.

BJOG 2005;112:927
Anesthesiology 2005;103:1211

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**Does the use of spinal or epidural analgesia for labor increase the incidence of back pain in parturients?**

No, but childbirth does.

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**BACK PAIN**

A survey of women during pregnancy found:
- 69% had back pain.
- 58% said pain disturbed their sleep and interfered with daily activities.
- 30% had stopped at least one activity.
- Only 32% had told their caregiver, and only 25% of caregivers prescribed treatment.

Obstet Gynecol 2004;104:65
Document pre-existing back pain in your preop!

---

**BACK PAIN**

Why do some parturients choose not to receive epidural analgesia for labor?

- 23% Desire for “natural” childbirth
- 20% Fear of back pain
- 17% Told by their obstetrician it was “too late” (all were in labor at least 90 minutes longer)
- 10% Fear of needle or side effects
- 0% Lack of pain

33% received their information on labor analgesia from family, friends, or magazines, yet all had prenatal care.

---

**BACK PAIN**

Over 600 nulliparous women were randomized to receive IV meperidine or epidural analgesia for labor. Six months later, 83% replied to a questionnaire:
- 50% reported backache in meperidine group
- 48% reported backache in epidural group

Br J Anaesth 2002;88:466

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**Are women who have labor epidural analgesia more likely to have an ↑ temperature?** Yes.

Is it associated with increased rates of infection in the mother or neonate? No.

Can an elevated maternal temperature cause fetal/newborn complications? Possibly.
AAP NEWS RELEASE

"The new study says that epidurals can cause fevers in mothers during childbirth, which in turn, causes doctors to test newborns for blood and tissue infections (sepsis), and to treat the newborns with antibiotics."

"However, babies of women who received an epidural were not more likely to actually have infections, which was very rare in both groups."

AAP NEWS RELEASE

"The authors conclude that women and their doctors should discuss the possible consequences of fever resulting from epidural use when deciding what method of pain relief to use during labor."

Pediatrics 1997

EPIRUDRALS AND FEVERS

Why are epidurals associated with fevers?

- Selection bias (epidurals are used more often in long labors with prolonged rupture of membranes and more cervical exams)
- No sweating below the sympathectomy
- No hyperventilation with contractions
- Increased shivering

Does CLE ↑ inflammatory mediators? Do parenteral opioids suppress febrile responses?
EPIDURALS AND FEVERS

A comparison of maximum temperature in women who delivered before epidural analgesia was available (1% usage) and after it was available (83% usage) found the incidence of maternal temperature > 38° increased from 0.6% to 11%, a twenty-fold increase.

Obstet Gynecol 2001;98:763

Could maternal hyperthermia harm the fetus?

• A study in neonatal rats found hyperthermia during hypoxia-ischemia increases susceptibility to brain injury, even if the insult is so mild it causes no injury by itself.

Am J Obstet Gynecol 2003;188:768

SUPPLEMENTAL OXYGEN

During spinal anesthesia for elective cesarean, mothers were randomized to room air, 2L/min nasal cannula, or 10L/min face mask.

• There was no difference in umbilical cord venous or arterial blood pO₂, pCO₂, pH, HCO₃ or base deficit.

Anesthesiology 2004;101:A1206

• When parturients were given oxygen by facemask during spinal anesthesia for C/S, maternal and fetal oxygenation modestly increased, although outcome was no different than a control group breathing air.

• However, markers of free radical activity were increased in mother and newborn. Hyperoxia is also known to reduce cerebral blood flow in the newborn.

Br J Anaesth 2002;88:18

Does oxygen supplementation, given routinely to the mother during regional anesthesia for cesarean delivery, benefit the fetus or newborn? Probably not.

Could it harm the fetus? Maybe.

SUPPLEMENTAL OXYGEN

Would supplementary oxygen protect the fetus if uterine incision-to-delivery is > 3 min?

Comparing room air, 40% or 60% oxygen given to the mother, fetal oxygenation was no different, even when U-D interval was prolonged.

Br J Anaesth 2004;92:518
SUPPLEMENTAL OXYGEN

Could depletion of intrinsic anti-oxidants from this free radical activity weaken a newborn’s ability to withstand ischemic insult, i.e. reperfusion injury after asphyxia, especially for compromised or preterm infants?

Br J Anaesth 2002;88:4 (editorial)

A meta analysis of trials comparing newborn resuscitation with 100% oxygen or room air (1302 newborns) found significant benefit to using air.

RR 0.71 (CI 0.54-0.94) for death in the first week and death at 28 days.

The authors recommend using air initially with oxygen as back-up if initial resuscitation fails.

Lancet 2004;364:1329

SUPPLEMENTAL OXYGEN

Does inflammation / infection make newborns more vulnerable to hypoxia?

In newborn piglets given endotoxin prior to a hypoxic episode, base deficit decreased more quickly.

But resuscitation with air was just as effective as 100% oxygen.

Am J Obstet Gynecol 2005;192:1172

Is the LMA an appropriate rescue device for a failed intubation in a parturient for cesarean delivery?

Yes.

LMA USE

The LMA was used in 1067 consecutive elective cesarean deliveries who were fasted and received ranitidine and antacid.

Excluded: reflux, obesity, difficult airway

There were no episodes of hypoxia, aspiration, regurgitation, laryngospasm or gastric insufflation.

Can J Anaesth 2001; 48:1117

LMA USE

During cesarean delivery for HELLP Syndrome the patient could not be intubated or ventilated. A ProSeal™ LMA was inserted and the stomach drained of 300ml. Postoperatively she was ventilated for 8 hours until stabilized, using the LMA.

Anesth Analg 2004;98:1467
LMA USE

During emergency cesarean delivery for fetal bradycardia the woman could not be intubated or ventilated. A #4 ProSeal™ LMA was inserted (twice), and controlled ventilation was used successfully for the procedure. A catheter was passed into the stomach.

Br J Anaesth 2004;92:144

Should interventional radiology techniques be an available option for the patient with potential or ongoing massive obstetric hemorrhage?

Absolutely.

INTERVENTIONAL RADIOLOGY

In a series of 12 patients treated for severe postpartum hemorrhage using selective uterine artery embolization, the success rate was 92%.

• One patient required hysterectomy.
• There were no maternal deaths.
• One patient has since had a normal pregnancy.


INTERVENTIONAL RADIOLOGY

A series of 7 patients had elective cesarean deliveries for accreta/percreta under epidural anesthesia following preoperative placement of intra-arterial balloon catheters.

• 3 required hysterectomy
• 2 required GETA because of uncontrolled bleeding due to percreta adherent to bladder.

Anesth Analg 2006;102:585

Is there a “best” anesthetic for surgery in pregnancy to protect the fetal brain from enhanced apoptosis? Unknown.

Do anesthetic drugs cause developing neurons to commit suicide? Possibly.

ANESTHETIC MECHANISMS

All currently used anesthetics act by one of two mechanisms:

• An increase in inhibition by stimulating GABA receptors, eg. benzodiazepines, IV induction agents, volatile anesthetics
• A decrease in excitation by depressing NMDA receptors, eg. N₂O, ketamine
SMALL ANIMAL STUDIES
Ethanol acts by both mechanisms: ↑GABA and ↓NMDA receptors. It triggers widespread apoptotic neurodegeneration in the developing rat brain. This period of development coincides with ~22 weeks gestation to several years of age in humans.
Science 2000;287:1056

SMALL ANIMAL STUDIES
In an attempt to simulate clinical practice:
• 7-day old rats (0-6 months in humans) received 6 hours of general anesthesia: midazolam, nitrous oxide, isoflurane.
• Animals had memory/learning impairments, apoptotic neurodegeneration, hippocampal synaptic function deficits.
J Neuroscience 2003;23:876

SMALL ANIMAL STUDIES
The clinical relevance is discussed in a pair of "point-counterpoint" articles.
Anesthesiology 2004;101:273,527

• Are the adverse effects attributable to the direct effects of anesthetics, or are they the result of factors we would not see clinically; eg. high doses over long periods, acidosis, hypoxia, starvation?

“If exposure of an immature mouse to the NMDA receptor antagonist/GABA-mimetic properties of ethanol at non-anesthetizing doses for 1 hour is sufficient to trigger neuro apoptosis, what are the chances that exposing an immature human to the NMDA receptor antagonist/GABA-mimetic properties of an anesthetic cocktail at doses that maintain a comatose state for several hours do not trigger neuro apoptosis?”
TRENDS in Pharmacological Science 2004;25:135

SURGERY IN PREGNANCY
A series of 235 patients requiring adnexal mass surgery during pregnancy compared general and regional anesthetic techniques.
• 30% preterm labor with regional
• 6% preterm labor with general
• Overall incidence of preterm labor in the surgery groups was 12% vs 3% in controls.
Increasingly we are learning that interventions made during the perioperative period, including, during anesthesia make significant differences in surgical outcomes. Anesthesiologists have taken a strong interest in examining these potential interventions with the idea that perioperative risk could be reduced and outcomes improved. Anesthesia providers have risen to this challenge by incorporating perioperative beta-blockers and timely administration of prophylactic antibiotics to their anesthetic regimens.

We will examine some of the pharmacologic interventions that are currently under discussion and investigation. Some of these may be among the drugs that we will all be getting from the OR pharmacy for our routine cases in the near future.

Beta Blockers

Significant risk exists for cardiac complications in patients having noncardiac surgery. The Revised Cardiac Risk Index by Lee and colleagues is that most widely used method for calculating this risk. They give one point each for the presence of high-risk procedure, history of ischemic heart disease, history of CHF, history of CVA, preoperative insulin or a serum creatinine of 2.0 or greater. The incidences of “major cardiac complications” (myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and/or complete heart block) with an index of 0, 1, 2, or 3 (or higher) were 0.4% 0.9%, 7% and 11% respectively. In a study of 200 noncardiac surgical patients at the SF VA, Mangano et al. showed that IV atenolol given at the time of discharge and continued (IV and oral) until discharge from the hospital significantly lowered mortality among the atenolol-treated patients versus those who were given placebo over the six months following hospital discharge (0 vs. 8 percent, P<0.001), over the first year (3 percent vs. 14 percent, P=0.005), and over two years (10 percent vs. 21 percent, P=0.019).

This set the stage for the ACC/AHA recommendations for perioperative beta blocker therapy. Most agree that Lee score of 2 or greater would merit initiation of perioperative beta blocker therapy (PBB). However, questions still remain: how long before surgery is PBB efficacious, is titration to a HR=60±5 necessary, and does pre-induction titration of PBB to HR make a difference in outcome? In addition, there is a lack of definitive data on this subject, specifically:

- Most trials are inadequately powered.
- Few randomized trials of medical therapy to prevent perioperative major adverse cardiac events (MACE) have been performed.
- Few randomized trials have examined the role of perioperative beta-blocker therapy, and there is particularly a lack of trials that focus on high-risk patients.
- Studies to determine the role of beta blockers in intermediate- and low-risk populations are lacking.
• Studies to determine the optimal type of beta blockers are lacking.
• No studies have addressed care-delivery mechanisms in the perioperative setting, identifying how, when, and by whom perioperative beta-blocker therapy should be implemented and monitored.

As a result Lee Fleisher and Marty London both now advocate that patients already on BB should remain on them through the perioperative period and vascular surgery patients at high risk for MACE (known CAD or history of CHF) should have PBB initiated if they are not already receiving BBs. The jury is still out those at low and intermediate risk.

**Statins**

Statins inhibit the rate-limiting step in biosynthesis of cholesterol. There is compelling evidence that chronic statin use decreases cardiovascular events. Traditionally, a statin is accepted as successful lipid-lowering therapy that reduces cardiovascular events over years. Recently, statins have been promoted as perioperative risk reduction strategies because of their short-term effects on endothelium-dependent vasodilation, coagulation, platelet aggregation, vascular plaque stability, and inflammation. Because perioperative myocardial infarctions (MI) occur equally from coronary stenosis and plaque rupture, statins are postulated to decrease perioperative cardiovascular complications.

While increasing cholesterol levels correlate with increasing risk of cardiovascular events, there is no threshold cholesterol level below which there is no occurrence of cardiovascular events. Accordingly, populations with low cholesterol levels still benefit from lipid-lowering therapy. A trial of primary prevention reported a 37% reduction (95% confidence interval 0.50–0.79; \( P < 0.001 \)) in the incidence of a first acute major coronary event in people taking a statin even with “normal” cholesterol levels.

Benefits from statins administered both immediately after acute coronary syndromes (ACS) and chronically in higher doses continue to be demonstrated. These benefits include reduced nonfatal MI at 2 years (hazard ratio 0.83, 95% CI 0.71–0.98). Retrospective studies of ACS and MI databases identify reduced cardiovascular morbidity and mortality when statins are administered within hours of ACS. This same benefit requires years to achieve if statins are started in a delayed fashion. This implies that patients should be on a statin after any perioperative cardiac event, if not preoperatively. Analysis of patients who took statins before hospitalization indicates that they are less likely to have ST segment elevation or a “large” infarct perioperatively. These same patients, however, have higher troponin levels and are more likely to die if statins are discontinued after ACS. In light of evidence for a “rebound” phenomenon, it is not advisable to discontinue statin therapy perioperatively in patients at risk for acute cardiac stress.

Statins inhibit the rate-limiting step for cholesterol synthesis by preventing conversion of HMGCoA to mevalonate. Statins also cause hepatocytes to increase LDL-receptor expression, increasing cholesterol uptake thus decreasing circulating cholesterol and apolipoprotein B levels. Alternate lipid-lowering agents appear to confer less reduction in
cardiovascular risk compared with statins, relative to the absolute reduction in cholesterol level. The hypothesis as to why statins reduce cardiovascular risk out of proportion to its lipid-lowering potential is that by blocking HMG-CoA reductase mevalonate is depleted as well as the subsequent isoprenoid intermediates. These isoprenoid intermediates are responsible for posttranslational modification of small intracellular signaling G-proteins that influence many intracellular signaling pathways (Ras, Rho, Rac).

**Vasomotor Effects**
LDL inhibits endothelium-dependent vasodilation through suppression of nitric oxide (NO). Statins prolong endothelial NO synthase activity via a non-cholesterol-lowering mechanism, likely related to the G-protein Rho pathway. Lovastatin decreases coronary vasoconstriction in response to acetylcholine and improves Holter monitor measured ST segment depression in patients with stable CAD. In hypercholesterolemic patients, enhanced myocardial perfusion is 6-fold greater in ischemic coronary segments than nonischemic coronary segments after 12 weeks of fluvastatin. Statins decrease expression of vasoconstrictors such as endothelin I and angiotensin II in animals. In animal models of MI a reduction in infarct size with as little as 3 days of pretreatment with atorvastatin was identified. Statin-treated animals exhibited better coronary relaxation, improved left ventricular wall motion scores, and required fewer therapeutic cardioversions. NO synthase inhibitors abolished theses protective effect of statins.

Simvastatin improves peripheral vascular function. Patients with claudication treated with crivastatin had longer pain-free periods and prolonged walking distance in at 6 months. Vasomotor improvement even occurred in normocholesterolemic subjects.

**Coagulation**
Tissue factor is expressed by endothelial cells, smooth muscle cells, and macrophages. Statins reduce thrombin-induced and lipopolysaccharide (LPS)-induced expression of tissue factor in a time- and concentration-dependent manner in both animals and humans. Interestingly, these effects occur before an alteration in lipid profile. Hypercholesterolemia increases platelet aggregation and statins normalize platelet function in familial hypercholesterolemia. No correlation was identified with LDL cholesterol or platelet cholesterol level changes, implicating a noncholesterol-mediated effect of statins.

Statins also affect the fibrinolytic side of the coagulation balance. Patients with CAD exhibit reduced levels of tissue plasminogen activator and elevated circulating plasminogen activator inhibitor (PAI)-1. Plasma PAI-1 is an independent risk factor for recurrent MI. In vitro data indicates that statins increase tissue plasminogen activator and decrease PAI-1 in endothelial cells (lovastatin), vascular smooth muscle cells (simvastatin), and macrophages (cervastatin).

**Coronary Plaques and Inflammation**
Pathologic studies indicate that deadly postoperative and occur with equal frequency from arterial stenosis and plaque rupture and the myocardium at risk does not correlate with the degree of feeding artery stenosis. This supports the conclusion that risk of coronary occlusion is related to both plaque composition and plaque size. Since statins reduce the inflammatory atherosclerotic process that leads to plaque instability MI from plaque rupture is reduced.

Statins may even affect sepsis-induced inflammation. Healthy normocholesterolemic men administered simvastatin (80 mg/d for 3 days) (versus placebo), given an intravenous injection of endotoxin (LPS), had reduced LPS-induced increases in monocyte chemoattractant protein 1, as well as other inflammatory markers. In a mouse model of cecal ligation and puncture, 18-hour pretreatment with statins prolonged survival 4-fold and survival even increased by 50% when statins were administered 6 hours after sepsis induction.

**Perioperative Studies**

Much indirect evidence from meta analyses, case-controlled retrospective cohort studies, and other observational studies all point to a large benefit from perioperative statin therapy both in terms of mortality and incident of MACE. To date only one randomized control trial has been conducted to examine the influence of statin therapy on perioperative cardiovascular complications. Durazzo et al. randomly assigned 100 patients to receive 20mg of atorvastatin or placebo for 45 days with vascular surgery performed on average 30 days after randomization. Within 6 months after vascular surgery, a 26.0% incidence of cardiac events was reported in the placebo group compared with 8.0% in those treated with atorvastatin. Interestingly, more patients in the placebo group took beta-blockers and had spinal anesthesia than in the statin group. This is also the only study to include normocholesterolemic patients, just over one third of patients in both arms. This study suggested that even short-term treatment with a statin could significantly reduce the incidence.

**Lidocaine**

Studies performed in vascular surgery patients to test whether epidural anesthesia resulted in fewer MACE than general anesthesia instead found that lower extremity graft patency was statistically significantly improved in those patients receiving epidural anesthesia for their vascular surgery. The authors speculated that graft patency could have been due to beneficial effects of the epidural’s sympathetic block or of a mild anticoagulant effect of the local anesthetic. Conversely the drug used for general anesthesia could have produced a deleterious effect of the vascular graft.

Excessive stimulation of the inflammatory and hemostatic systems plays a role in the development of postoperative ileus, ischemia-reperfusion syndromes (e.g. myocardial infarction), hypercoagulation syndromes (e.g. deep venous thrombosis) and pain; together, these represent a significant fraction of major postoperative disorders.
Epidurally administered local anesthetics prevent or modulate many of these processes and have been shown to have many beneficial effects for postoperative surgical patients.

However, many of these effects could also be ascribed to direct effects of the absorbed local anesthetics, thus the question arises whether intravenous local anesthetic could derive similar benefits.

Since:
1) Local anesthetics prevent excessive stimulation of the inflammatory response
2) Local anesthetics prevent postoperative thrombosis
3) Local anesthetics reduce postoperative ileus and duration of hospital stay
4) Local anesthetics are neuroprotective

Then intravenously or epidurally administered local anesthetics should demonstrate:
1) In comparison with general anesthesia, local anesthetics administered either epidurally or intravenously prevent excessive stimulation of the inflammatory response.
2) Postoperative thrombosis (due most likely to surgery-induced hypercoagulability) is significantly reduced after either epidural or intravenous local anesthetic administration, as compared with general anesthesia.
3) Postoperative ileus is reduced after either epidural or intravenous local anesthetic administration as compared with general anesthesia.
4) Length of stay in the postanesthesia care unit (PACU) and total hospital stay is reduced after either systemic or epidural application of local anesthetics, as compared with general anesthesia.
5) Postoperative cognitive dysfunction is reduced equally by either epidural or intravenous application of local anesthetics, as compared with general anesthesia without administration of local anesthetics.
To date there has been one placebo-controlled randomized trial to examine these hypotheses. In this study of 60 patients undergoing open colorectal surgery intravenous lidocaine (1.5 mg/kg loading and 2 mg/min infusion) significantly accelerated return of bowel function and shortened length of hospital stay by one day. No difference could be observed in daily pain ratings. Elevated plasma levels of IL-6, IL-8, complement C3a, and IL-1ra as well as expression of CD11b, L- and P-selectin, and platelet-leukocyte aggregates were significantly attenuated by systemic lidocaine.

These results are encouraging and may open an avenue for the benefits of local anesthetics in patients not wanting or in whom epidural analgesia is contraindicated. Further studies are needed to determine what the plasma concentration-response relationships are for these effects, how long the treatment needs to be implemented, what patient groups benefit, which local anesthetics are most efficacious, and what the potential side effects and toxicities need to be monitored for.

**Peripheral Opioid Antagonists**

By adding a methyl group to naltrexone Leon Goldberg, M.D., at the University of Chicago developed a polar compound that would be excluded from the central nervous system, but would be able to antagonize peripheral opioid receptors. Another drug, alvimopan is a large polar compound with opioid receptor specificity that is also in the FDA testing pipeline. The first indication being worked on for the New Drug Applications for both drugs is as a GI motility agent in patients taking opioids for acute or chronic pain and methadone maintenance. I suppose it could also be used to reverse an Imodium overdose.

It is now clear that there are other peripheral opioid receptors that we will learn more about now that there is a specific antagonist. Two that could have an impact on perioperative outcomes are ones that stimulate angiogenesis and stimulate bacterial growth. Recent studies in mice show that morphine in clinically relevant doses stimulates angiogenesis and breast cancer progression. So far only one study in humans found a much increased breast cancer recurrence rate in patients receiving morphine PCA vs those who received thoracic epidurals. Opioids may play an important role in the enhancement of breast and other cancer progression. Blocking or preventing these effects could be very important perioperatively.

Evidence exists that exogenous (as opposed to endogenous) opioids decrease the inflammatory and immune response to infection. In addition, bacteria express opioid receptors and exposure of bacteria to opiates induces increased bacterial virulence.

**Glucose**

There has been much discussion about perioperative glucose control stimulated by articles from Oregon on cardiac surgery and from Belgium on SICU patients. These studies seem to indicate that tight glucose control (between 80 and 120 mg/dl) with intensive insulin therapy is associated with better outcomes. The Belgian trial
convincingly showed that ‘diabetes of injury’ should be treated aggressively, demonstrating markedly reduced morbidity and mortality in a heterogeneous group of patients requiring mechanical ventilation after undergoing cardiac and other major surgery. However, studies aimed at replicating these results have found increased morbidity and mortality associated with low blood sugars and very little overall benefit. Until these issues are resolved, it is probably not warranted to institute tight glucose control in the perioperative period.

However, the topic of insulin resistance and increased perioperative morbidity remains an issue of great interest. Insulin resistance is a central feature of postoperative metabolism, resulting in decreased glucose uptake in skeletal muscle and adipose tissue, increased glucose release and hyperglycemia. It is most pronounced on the day after surgery and returns to preoperative levels within 3 weeks of open cholecystectomy. The development of whole-body insulin resistance is related to the magnitude of surgery and length of postoperative stay.

A group at the Karolinska in Stockholm have shown that postoperative insulin resistance can be prevented by providing a preoperative high carbohydrate drink. Provision of these carbohydrates 2–3 h prior to surgery acutely increases insulin sensitivity at the time of surgery (i.e. it triggers the so-called Staub–Traugott effect, or glucose facilitation), and this elevation of insulin action is then maintained postoperatively. Preliminary evidence indicates that preoperative carbohydrate treatment may improve immune function. In patients undergoing minor orthopedic procedures, carbohydrate treatment was shown to preserve levels of human leukocyte antigen (HLA)-DR expression on CD14+ monocytes 1 day after surgery compared with the control group of 10 patients, in whom HLA-DR expression decreased by roughly 25%. Expression of HLA-DR has been suggested as an index of immunocompetence in acute stress.

In a randomized study of 188 high-risk patients (American Society of Anesthesiologists grade III–IV) undergoing cardiac surgery with cardiopulmonary bypass to either preoperative oral carbohydrate treatment, placebo treatment or conventional overnight fast before surgery, carbohydrate treatment was found to significantly reduce the need for inotropic support during cardiopulmonary bypass weaning, in line with previous literature of preoperative intravenous glucose administration in cardiac surgery. All groups received the same amount of nutrition and plasma glucose concentrations were controlled using a variable intravenous insulin infusion.

These very preliminary studies do indicate that preoperative nutrition may become an important aspect of perioperative care. Since anesthesia providers typically ‘control’ preoperative fluids and solids, this arena could become an important part of anesthesia care in the future.
BIBLIOGRAPHY


New guidelines published in 2007

Rationale:
- Infective endocarditis is more likely to occur from frequent exposures to random bacteremia associated with daily activities than from procedures.
- Very few good randomized prospective studies to support efficacy of prophylactic antibiotics in preventing endocarditis.
- Prophylaxis may prevent an exceedingly small # of cases if any.
- Risk of antibiotic associated adverse events is greater than any benefit (if any)
- Maintenance or optimal oral hygiene may reduce incidence of bacteremia and is more important than prophylactic antibiotics
- The emergence of and increasing incidence of multi-drug resistant streptococcus viridans and enterococci, making the efficacy of current treatment recommendations suspect

Risk of IE after many surgical procedures is not well established
The risk of endocarditis, while real is extremely low.

Cardiac conditions associated with the highest risk of IE
- Prosthetic Valve or prosthetic material used for valve repair
- Previous IE
- Un-repaired cyanotic CHD, including palliative shunts and conduits
- CHD defects repaired with prosthetic material, during the first 6 months
- Repaired CHD with residual defects at the site of or adjacent to prosthetic material
- Cardiac transplant patients who develop valvopathy

Single dose of antibiotic should be delivered one hour prior to the procedure
May be delivered up to 2-3 hours after, if the dose is inadvertently not administered prior to the procedure.
The specific antibiotics are listed in table 2, as are the major changes (table 3)
The biggest change is: the number of procedures for which prophylactic antibiotics should be administered have been substantially reduced, with an emphasis on treating underlying infections prior to manipulations.
It is no longer necessary to give antibiotic prophylaxis prior to GI or GU procedures even for the conditions listed in Table 1. If they have a pre-existing infection, treat the infection.
Recommendations should be discussed with cardiologist pre-op, there is still considerable controversy and confusion over these recommendations

Anesthesia and Vaccinations
Do childhood vaccines prior to or immediately after anesthesia render them less effective?
Do childhood vaccines prior to immediately after anesthesia increase the child’s risk of an adverse reaction?
Would complications of vaccinations confuse post-operative assessment?
Should we postpone elective anesthesia or surgery in a child who has been recently vaccinated?
- There are no good answers to these questions; however 2 recent reviews, an editorial and several excellent letters to the editor try and bring some science and rationale to the issue.
  - Anesthesia and surgery have been shown in-vitro to cause immuno-modulation in adults (Table 5), and possible children.
  - Anesthesia and surgery may lead to impaired immune responses in-vivo in children and adults, however these findings are less clear and their significance are not known (Table 7). Most anesthesia related immune-suppression is short-lived (hours-a couple of days), while immune responses to vaccines may take days to months to fully develop.
There is a theoretical risk that anesthesia may render vaccines less effective or increase the risk of complications. There are a few case reports (primarily from the veterinary literature, but an occasional human case) that have shown decreased antibody titers in animals after immunization and surgery than would occur after immunization alone.

Vaccination reactions are not infrequent, usually mild, occur within 2-21 days, self limited, but may mimic commonly seen post-operative complications or side effects. There is no evidence that these reactions could delay diagnosis or treatment of a post-operative problem, or in was exacerbate post-operative complications.

The CDC has no policy regarding the timing of vaccinations and surgery.

There are recommendations from other countries’ national agencies to delay elective surgery for 2 days (inactivated vaccines) to 3 weeks (live attenuated species) if possible and to delay vaccination until several days to several weeks after surgery.

Short et al. conducted an international survey of members of the Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI) and the Society for Paediatric Anaesthesia of New Zealand and Australia (SPANZA). Sixty % of respondents would anesthetize a patient within 7 days of having received a live vaccine. Of the 40% who would not, the time they recommended for delaying surgery ranged from 7 days to 6 weeks. Many practitioners evaluated the patient’s physical status before deciding. If the patient had a low grade fever or other signs of distress they would postpone surgery, but would be proceed if the child seemed healthy.

All of the recent articles do recommend postponing elective anesthesia and surgery for 2 days after inactivated vaccines and 1-3 weeks after attenuated live vaccines, despite the lack of evidence.

Crowcraft and Elliman, in an impassioned and compelling letter felt that the risk of adding barriers to appropriate immunization far outweighed the risk of anesthesia and surgery in the recently immunized child. They argued vehemently that avoiding or postponing anesthesia in a recently immunized child was unnecessary, given the scant evidence on the subject. They also felt that recent anesthesia or surgery should not cause for delaying scheduled immunizations. If sufficient doubt exists regarding the efficacy of the immunization response, they argue that the vaccine should be repeated.

Anesthesia and Childhood Obesity

- The prevalence of pediatric obesity is rapidly increasing throughout the western world. One third of children in the US are considered overweight or at risk of becoming overweight.

- Co-morbidities that are common in obese adult patients are being seen in this population as well. These include hypertension, diabetes, dyslipidemia, cardiovascular disease, left ventricular hypertrophy, arthritis and certain types of cancers. LVH has been seen in children as young as 10, and is common in adolescents presenting for bariatric surgery.

- Obstructive sleep apnea (OSA) reactive airway disease, other sleep and respiratory problems are more common in these patients.

- Bariatric surgery for children and adolescents is becoming more widespread. The number of bariatric procedures in adolescents (age less than 18) increased 5 fold from 2000 to 2003. More than 100 institutions were performing these operations, the majority of whom were adult facilities.

- Two recent articles and several abstracts have sought to identify the incidence of complications in overweight and obese patients.

- The CDC has defined overweight children as those who are >95th % ile body weight and “at risk” , those who are between 85-95th % ile. (in adults BMI is still used, >30 is considered overweight and 25-30 “at risk”.) in 2005 10% of adolescents had a BMI > 40. The likelihood that an overweight child will become an obese adults increases as the child ages. Weight loss is less likely as the degree of adiposity rises. Incidence and severity of co-morbidities increases, as the duration of obesity increases.

- Patients appear to have a higher incidence of perioperative respiratory complications, although difficult ventilation and intubation did not seem to be a significant problem.

- Nafui and colleagues did find that patients with a high BMI undergoing adeno-tonsillectomy generated higher charges than their peers and have a higher incidence of getting admitted post-operatively.

- Interestingly many of the obese and morbidly obese patients in all these studies were assigned ASA status of 1 or 2. Inhaled induction was commonly used and patients were not found to have a greater risk of aspiration than non-obese patients.

- Cook-Sather measured gastric volumes/kg in patients who were obese and compared them to those were not. He compared gastric volume/actual body wt and gastric volume/ lean body weight. There was no difference in gastric volume/lean body weight in obese and non-obese patients. All their patients receive midazolam + acetaminophen prior to the induction of anesthesia, therefore their gastric volumes were higher than previously
reported (1ml/kg vs. 0.4ml/kg). All patients underwent a inhalational induction and the only evidence of vomiting on induction was in a non-obese child.

- Just as in adults, dosing should be based on “ideal” body weight, although lean body weight will increase with obesity. Anesthetic agents with low blood gas solubilities and short duration of action are ideal and facilitate emergence.

**What’s new in Pediatric Regional Anesthesia?**

**Peripheral Nerve Blocks**

- Ultrasound is gaining ground

- All the same pros and cons that apply to using the ultrasound in adult patients apply to pediatric patients. However since many peripheral nerve blocks in children are done while they are either heavily sedated or anesthetized, ultrasound potentially offers huge advantages in both safety and efficacy. At my own institution the number of peripheral nerve blocks being performed has dramatically increased in the year since we obtained our ultrasound machine (Thank you Doug Coursin!).

- There have been several studies that have examined the utility of ultrasound in pediatrics. The dose of local anesthesia required to achieve blockade are lower for the majority of the blocks studies; the onset time to sensory and/or motor block is less, and success rates may be higher. The advent of ultrasound has caused a resurgence of interest in both single shot peripheral nerve blocks and continuous catheter techniques in children.

- Ganesh et al from the Children’s Hospital of Philadelphia used their Regional Anesthesia Data Base to determine the safety and efficacy of continuous peripheral nerve blocks in children who were both outpatients and inpatients.
  - 217 patients (226 catheters), 112 were discharged home with the catheter in place.
  - Average age 13.7 years (range 4-16), all blocks placed with the aid of a nerve stimulator
  - Average duration of infusion was 48.4 hours
  - Solutions used were bupivacaine 0.125%, ropivacaine 0.1%, or 0.15%, at rates of 2-12ml/hour.
  - 4 complications (2.8%)
    - 3 patients with prolonged numbness that resolved spontaneously
    - One with superficial cellulitis requiring antibiotics
Dadure and colleagues compared the efficacy and side effects of continuous epidural block to continuous popliteal nerve block in children undergoing foot and ankle surgery.28

- Prospective randomized study with 59 children divided by block type and age (1-6 and 7-12 years)
- All blocks were placed after the induction of anesthesia
- Popliteal blocks were placed with the help of a nerve stimulator
- There were no block failures in either group
- All patients received a standard bolus of bupivacaine, lidocaine and epinephrine after the placement of the blocks.
- They received 0.2% ropivacaine at either 0.1ml.kg.hour (popliteal block) or 0.2ml/kg/hour (epidural block) for 48 hours

While both techniques provided excellent analgesia there was a higher rate of complications with the continuous epidural technique. These complications included: a higher incidence of pruritus, urinary retention, and nausea and vomiting and premature discontinuation of the local anesthetic due to technical problems. Patients did not receive narcotics with their local anesthetic and only received acetaminophen or nalbuphine for breakthrough pain, so it is unclear why patients in the epidural group had a higher incidence of nausea, vomiting and pruritus. Their incidence of technical problems with epidurals seems inordinately high.

Nerve stimulator technology has not yet gone the way of the dinosaur (and I for one hope that it doesn’t). Anatomical landmarks are often easier to find and use in children than they are in adults, local anesthesia spreads easily through tissue plains and although higher volumes of local anesthesia may be required, these blocks are fast and simple to do.21

**Epidural Anesthesia**

In 2007 Dr’s Llewellyn and Moriarty published the results of a 5 year National Audit from Great Britain and Ireland (2001-2005) to quantify the risks associated with epidural anesthetic techniques in children. This was the first large scale prospective study of its kind that included only epidural infusion analgesia. 21 sites with different levels of sub-specialization, and different volumes of cases volunteered to participate. A Monitoring Committee was established to oversee the effort. All volunteering centers submitted their data monthly. Inclusion criteria were all children who had an epidural catheter placed for post-operative pain management. The level at which the catheter was placed was recorded (caudal, lumbar, thoracic), as well as age, and type of incident if any. The incidents that were reported were: infection, drug errors, nerve injury, local anesthetic toxicity, spinal cord insult, post dural puncture headache, inadvertent spinal anesthesia, respiratory/cardiac arrest, concurrent events such as compartment syndrome and pressure sores. Incidents were graded from 1-3 depending on the severity and duration of the injury. Grade 1 was considered the most serious injury

- All but one child had their epidural catheter placed under general anesthesia. There were 6 reports of nerve injury in 9712 lumbar or thoracic epidurals. One of these was a 17 year old who was awake during the placement of his thoracic epidural.
- There were 10,633 epidurals performed, 96 incidents reported
  - 40 were associated events (pressure sores-33, compartment syndrome-4, spinal cord insult in patients undergoing spinal fusion)
  - There was a reduction in the number of incidents over the course of the audit with no Grade 1 incidents reported after 2003, although the overall activity remained constant throughout the study period.
  - There was a higher incidence of adverse events in neonates compared to other age groups, most related to drug errors and local anesthetic toxicity.
  - All tables below are modified from Llewellyn and Moriarty: The National Pediatric Epidural Audit. Pediatric Anesthesia 17 (6), 520-533

The Pediatric Regional Anesthesia Network (PRAN) database is an ongoing multi-institutional project directed by Drs David Polaner (Denver) and Lynn Martin (Seattle) and supported by the American Association of Pediatrics: Section on Anesthesiology and Pain Management and the Society for Pediatric Anesthesia. This project was set up to collect numerator and denominator information on the practice of regional anesthesia in infants and children and to learn about the incidence and nature of complications. Hopefully in the next few years we will have meaningful results to help guide our practices.
Although Nurse or Parent Controlled Analgesia (PNCA or PCA by proxy) has been in use in many hospitals for quite some time, very little has been published on either efficacy or side effects of these techniques. The recent Safety Alert from JCAHO advocating against this practice has not prevented the majority of institutions that provide this therapy for children from continuing to do so.

In a survey of the Society for Pediatric Anesthesia Members, 95% allowed PCA in children. Only 49% used PCA by proxy and of those who did, 88% allowed nurse bolus dosing, while 47% allowed parent bolus dosing. One significant difference between pediatric pain services and adult pain services was found to be in the use of monitoring. Over 80% of respondents reported using pulse oximetry and/or ECG and apnea monitoring during the time patients are receiving opioids.

Both PCEA and PCEA by proxy are being used at some institutions.
Anesthesia Toxicity

- In the past few years there has been an explosion of research and interest in anesthesia toxicity in various patient populations. While it is outside the scope of this lecture to discuss these in depth, I wanted to highlight a few of these findings.
- Propofol Infusion syndrome (refer to Dr Polaner’s lecture CRASH 2008)

Nitrous Oxide

- There is an excellent recent review that summarizes the effects of nitrous oxide on B12 and other metabolic pathways. 34
- Nitrous has long been known to cause hematological problems (thrombocytopenia, aplastic anemia, etc) when used for prolonged periods of time or in patients with chronic exposure. It has also been shown to cause polyneuropathy in susceptible patients. Such patients include those with methionine synthetase deficiency; Type III homocystinuria; patients with B12 deficiency; and those with single nucleotide polymorphisms (SNP) in the gene that is involved with the production of 5,10-methylenetetrahydrofolate reductase or MTHFR.
- These SNPs are common and have been reported in 12-57% of the general population. One is associated with mild homocystinemia another with pre-eclampsia. It is unknown if these missense mutations are associated with increased susceptibility to nitrous oxide toxicity, but there has been at least one case report of such an event.
- Nitrous oxide has been implicated in much of the recent research on anesthesia and neurotoxicity. It may have significant effects on cell death in both developing and aging brains.

Figure 1 Metabolic pathways affected by nitrous oxide Hatched bars, points of inhibition by nitrous oxide; MTHFR, methylene tetrahydrofolate reductase; Roman numerals, the three types of homocystinuria.

Volatile Anesthetics, other Sedative and Hypnotics

- Volatile anesthetics in conditions where one would normally be providing anesthesia care for a neonate or young infant have not been shown to cause neurotoxicity.
- However experimental studies in young rodents have shown evidence of accelerated apoptosis and possible neuro-developmental sequelae after exposure to volatile anesthetics or anesthetic cocktails. 34-41
- In many of these studies young mice or rats were exposed to several hours of anesthetic, in completely unmonitored conditions. Since no physiologic parameters were monitored (respiration, saturation, glucose,
hydration BP etc) it is unclear what role if any these factors had on apoptosis. The mice were found to have the greatest vulnerability during the time of greatest synaptogenesis or the “brain growth spurt”. In mice this occurs in the early postnatal phase (1-2 weeks of age). The brain growth spurt occurs from mid-gestation to several years after birth (24-26 months) in humans. Most of the experimental designs anesthetized the mice for 5-6 houts during this period of maximal synaptogenesis, a circumstance that would be highly unlikely in humans.

- All the volatile anesthetics, ketamine, midazolam, and other sedative/hypnotics even in sub-anesthetic concentrations have been shown to cause widespread neuro-degeneration in mice. It appears that a very fine balance between neuronal excitation and inhibition in the CNS is crucial, not only for neuronal survival, but for their proper maturation and functioning. Over-inhibition, just like over-excitation, may be toxic to a developing neuron, however the same agents that may cause over-inhibition of the neuronal system are also neuroprotective during both focal and global ischemia.

- The significance and applicability of these findings is not clear for humans. Certainly prolonged pain and stress of surgery have been associated with negative physiologic and behavioral consequences. Hopefully further research will elucidate whether these findings have any applicability to the human neonate.

Updates from 2007

(for more details refer to archived handouts on the CRASH website at http://www.cucrash.com/07handouts.htm

Cuffed ETT

- Recent MRI studies in spontaneously breathing children found that the narrowest part of the airway was at the vocal cords and not at the cricoid ring as has been previously thought. The airway was shown to be elliptical in these circumstances, not round as had been thought from cadaveric studies.46

- These anatomical findings support the utility of cuffed ETT in children

- Several recent studies have found that cuffed ETT decrease the # of intubation attempts and are associated with decreased air leak (↑ OR pollution, greater ability to use low fresh gas flows), and provide better protection from aspiration.47

- In a study of almost 600 PICU patients < 5 years of age, the use of a cuffed ETT was not associated with a greater incidence of post-extubation stridor, need for racemic epinephrine, treatment of subglottic stenosis, failed extubation or need for tracheotomy.48

  - Cuff pressures were checked every 8 hours
  - A significant # of patients were >1 month
  - In general the patients who were intubated with cuffed ETT were sicker and required longer intubations.

- Khine et.al recommend using the formula \[ \text{age}/4 + 3 \] to estimate cuffed tube size. They found that with this formula there was no difference in the incidence of post-intubation croup or need for racemic epinephrine treatment, when compared to patients receiving uncuffed ETT. They used the commonly used formula to calculate uncuffed ETT size (age/4 +4). 30% of their patients <2 yrs of age and 18% of patients >2 needed to have their uncuffed ETT replaced. Only 3 (n=251) patients with cuffed ETT had their tubes changed. The authors measured nitrous oxide concentrations 24 inches away from the patients mouth and found that when cuffed ETT were used the concentration was <10 ppm, but that when an uncuffed ETT was used more than half the cases had nitrous oxide concentrations > 25 ppm and 15% had concentrations > 300 ppm

<table>
<thead>
<tr>
<th>Nitrous Oxide Concentration (ppm)</th>
<th>&lt;10</th>
<th>11-25</th>
<th>26-299</th>
<th>&gt;300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncuffed ETT</td>
<td>19</td>
<td>6</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Cuffed ETT</td>
<td>39</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Values are no. of cases with measured nitrous oxide levels in the specified range.

- Cuff pressures are variable in children, and may increase during an anesthetic in which at least 50% nitrous oxide is being used. If nitrous oxide is being used in a patient with a cuffed ETT, either the cuff pressures should be checked regularly or the cuff should be inflated with a nitrous/air mixture.
Placing cuffed ETT in children can be a little more difficult. The cuff should be placed below the cricoid ring to avoid too much pressure on that structure; this may limit the amount of space in the trachea before mainstem intubation takes place.

Most authors recommend checking airway pressure prior to inflating the cuff and then only inflating the cuff until the leak is obliterated at ~ 20 cm H₂O.

New ultra thin walled cuffed ETT’s are now available and while they seem to be superior to the older tubes, experience with them in this country is still limited.

The American Heart Association in its 2005 PALS and ACLS resuscitation guidelines states that the use of cuffed tubes in infants and children is an acceptable practice.

Sleep Disordered Breathing

Sleep Disordered Breathing (SDB) is a continuum that ranges from normal breathing and oxygenation to chronic intermittent desaturation (CIND) and obstructive sleep apnea (OSA). In children it is commonly associated with adeno-tonsillar hypertrophy, craniofacial abnormalities and neuromuscular problems.

Children with OSA have a decreased CO₂ response curve, and a higher incidence of perioperative respiratory complications. Statham et.al found that children younger than 3 with OSA, had an incidence of peri-operative complication approaching 10%, compared to approximately 5% in children aged 3-5 years. This was despite the fact that the younger children had a lower incidence of co-morbid conditions.54

Chronic intermittent nocturnal oxygen desaturation to < 80% is associated with both an increased sensitivity to and a decreased need for opioids.

Emergence Agitation

Emergence Agitation (EA) is a disturbing phenomenon that can delay discharge from the PACU, cause injury to the child or caregiver, decrease parental satisfaction and potentially be associated with a higher incidence of prolonged negative behaviors, postoperatively.

The advent of short acting anesthetic agents with low blood gas solubility seems to have increased the interest in this unpleasant side effect.

There are a myriad of conflicting reports on the utility of various medications such as midazolam or techniques (converting to isoflurane) to prevent EA.

Good analgesia, fentanyl, dexmedetomidine, clonidine and propofol maintenance have consistently been shown to decrease the incidence of EA.55-58

Aouad and her colleagues recently studied the effects of a single dose of propofol 1mg/kg on emergence agitation, in children undergoing strabismus repair with sevoflurane anesthetic. The incidence of EA was reduced significantly from 47% to 19%. The time to removal of the LMA and emergence times were slightly longer in the propofol group, however discharge times were similar at approximately 34 minutes.58 This is a technique that seems to be very popular and effective in many institutions.
Table 1. Cardiac Conditions Associated With the Highest Risk of Adverse Outcome From Endocarditis for Which Prophylaxis With Dental Procedures Is Reasonable

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prosthetic cardiac valve or prosthetic material used for cardiac valve repair</td>
</tr>
<tr>
<td>Previous IE</td>
</tr>
<tr>
<td>Congenital heart disease (CHD)*</td>
</tr>
<tr>
<td>Unrepaired cyanotic CHD, including palliative shunts and conduits</td>
</tr>
<tr>
<td>Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure</td>
</tr>
<tr>
<td>Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)</td>
</tr>
<tr>
<td>Cardiac transplantation recipients who develop cardiac valvulopathy</td>
</tr>
</tbody>
</table>

*Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD.
† Prophylaxis is reasonable because endothelialization of prosthetic material occurs within 6 months after the procedure.

Table 2. Dental Procedures for Which Endocarditis Prophylaxis Is Reasonable for Patients in Table 1

All dental procedures that involve manipulation of gingival tissue or the peri-apical region of teeth or perforation of the oral mucosa

*The following procedures and events do not need prophylaxis: routine anesthetic injections through non-infected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa.

Table 3. Regimens for a Dental Procedure

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Regimen: Single Dose 30 to 60 min Before Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin</td>
<td>Adults: 2 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children: 50 mg/kg</td>
</tr>
</tbody>
</table>
Unable to take oral medication

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin OR Cefazolin or ceftriaxone</td>
<td>2 g IM or IV 50 mg/kg IM or IV</td>
</tr>
<tr>
<td>OR Cefazolin or ceftriaxone</td>
<td>1 g IM or IV 50 mg/kg IM or IV</td>
</tr>
</tbody>
</table>

Allergic to penicillins or ampicillin—oral

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalaxin OR Clindamycin OR Azithromycin or clarithromycin</td>
<td>2 g 50 mg/kg</td>
</tr>
<tr>
<td>OR Clindamycin OR Azithromycin or clarithromycin</td>
<td>600 mg 20 mg/kg</td>
</tr>
<tr>
<td>OR Clindamycin OR Azithromycin or clarithromycin</td>
<td>500 mg 15 mg/kg</td>
</tr>
<tr>
<td>OR Clindamycin OR Azithromycin or clarithromycin</td>
<td>1 g IM or IV 50 mg/kg IM or IV</td>
</tr>
</tbody>
</table>

Allergic to penicillins or ampicillin and unable to take oral medication

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin or ceftriaxone OR Clindamycin</td>
<td>600 mg IM or IV 20 mg/kg IM or IV</td>
</tr>
</tbody>
</table>

*Or other first- or second-generation oral cephalosporin in equivalent doses

†Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.

Table 4. Summary of Major Changes in Updated Document

We concluded that bacteremia resulting from daily activities is much more likely to cause IE than bacteremia associated with a dental procedure.

We concluded that only an extremely small number of cases of IE might be prevented by antibiotic prophylaxis even if prophylaxis is 100% effective.

Antibiotic prophylaxis is not recommended based solely on an increased lifetime risk of acquisition of IE.

Limit recommendations for IE prophylaxis only to those conditions listed in Table 3.

Antibiotic prophylaxis is no longer recommended for any other form of CHD, except for the conditions listed in Table 3.

Antibiotic prophylaxis is reasonable for all dental procedures that involve manipulation of gingival tissues or periapical region of teeth or perforation of oral mucosa only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).

Antibiotic prophylaxis is reasonable for procedures on respiratory tract or infected skin, skin structures, or musculoskeletal tissue only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from IE (Table 3).

Antibiotic prophylaxis solely to prevent IE is not recommended for GU or GI tract procedures.

Although these guidelines recommend changes in indications for IE prophylaxis with regard to selected dental procedures (see text), the writing group reaffirms that those medical procedures listed as not requiring IE prophylaxis in the 1997 statement remain unchanged and extends this view to vaginal delivery, hysterectomy, and tattooing. Additionally, the committee advises against body piercing for patients with conditions listed in Table 3 because of the possibility of bacteremia, while recognizing that there are minimal published data regarding the risk of bacteremia or endocarditis associated with body piercing.

Table 5 Side effects or complications of immunization and surgery

<table>
<thead>
<tr>
<th>Immunization (50)</th>
<th>Surgery (non-exhaustive list)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local</td>
<td>Local</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Inflammation (wound infection)</td>
</tr>
<tr>
<td>Pain</td>
<td>Postoperative pain</td>
</tr>
<tr>
<td>Immunization (50)</td>
<td>Surgery (non-exhaustive list)</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Granuloma and necrosis (uncommon)</td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy and abscess (exceptional)</td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>Systemic</td>
</tr>
<tr>
<td>Fever</td>
<td>Fever (sepsis)</td>
</tr>
<tr>
<td>Irritability</td>
<td>Irritability</td>
</tr>
<tr>
<td>Exanthema</td>
<td>Anesthesia-induced rash</td>
</tr>
<tr>
<td>Prolonged inconsolable crying (≥3 h)</td>
<td>Crying</td>
</tr>
<tr>
<td>Neurodeficiency</td>
<td>Postanesthesia agitation and confusion</td>
</tr>
<tr>
<td>Thrombocytopenic purpura</td>
<td>Septic petechiae</td>
</tr>
<tr>
<td>Anaphylaxis with shock like state</td>
<td>Septic shock</td>
</tr>
</tbody>
</table>


Table 6 *In vitro* effects of general anesthesia on adult immunity

<table>
<thead>
<tr>
<th>Anesthetic agent</th>
<th>Innate</th>
<th>Acquired cellular</th>
<th>Acquired humoral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopental</td>
<td>Inhibited bactericidal functions of leukocytes</td>
<td>Impaired lymphocyte's proliferation</td>
<td>Intact IgA, IgM, IgG production (64)</td>
</tr>
<tr>
<td></td>
<td>Impaired PMNs and monocytes functions Reduced LPS-recognition molecule CD14 on monocytes surface nitric oxide (NO) production reduced by inhibition of the NO synthase IL-1 receptor antagonist (IL-1ra) release is inhibited. IL-10 release is increased</td>
<td>Impaired TH1-cytokines production</td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>Impaired PMNs and monocytes functions Reduced LPS-recognition molecule CD14 on monocytes surface Cytokine release not impaired</td>
<td>Lymphocyte's proliferation not impaired&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>Reduced leukocyte endothelial transmigration Decreased NKCC Reduced IL-6 response</td>
<td>Impaired lymphocyte's proliferation</td>
<td></td>
</tr>
<tr>
<td>Sufentanil/alfentanil</td>
<td>Increased number of NK cells and NKCC</td>
<td>Increased number of CD8 T-cells</td>
<td>Intact B-cells proliferation (65)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Inhibitory effects on PMN functions Increase pro-inflammatory cytokines TNF-α, IL1-β and IFNγ&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Impaired lymphocyte's proliferation</td>
<td>Intact B-cells proliferation (66)</td>
</tr>
</tbody>
</table>

NK, Natural Killer cells; NKCC, NK cytotoxicity; IL, interleukin.

<sup>a</sup>Impaired in surgical intensive care patients in response to pokeweed mitogen (5). Adapted from Hunter (7) and Schneemilch (6).

<sup>b</sup>Mechanical ventilation within 2 h of exposure.

doi: 10.1111/j.1460-9592.2006.02120.x
<table>
<thead>
<tr>
<th>First author (publication date)</th>
<th>References</th>
<th>Number of patients</th>
<th>Age range</th>
<th>Type of anesthesia</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donovan (1973)</td>
<td>(17)</td>
<td>6</td>
<td>3–12 years</td>
<td>Not stated</td>
<td>↓ to PHA</td>
</tr>
<tr>
<td>Espanol (1974)</td>
<td>(18)</td>
<td>6</td>
<td>3–13 years</td>
<td>Inhalational or balanced</td>
<td>↓ to PHA</td>
</tr>
<tr>
<td>Puri (1979)</td>
<td>(12)</td>
<td>14</td>
<td>1–3 days</td>
<td>Inhalational</td>
<td>No overall differences in immune response pre- and postoperatively</td>
</tr>
<tr>
<td>Kurz (1983)</td>
<td>(19)</td>
<td>20</td>
<td>1–4 weeks</td>
<td>Balanced</td>
<td>decrease of T lymphocytes and increase in IgM concentrations in all age groups (steady IgA and IgG concentrations)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>25</td>
<td>2–12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>&lt;6 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>23</td>
<td>&gt;6 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puri (1984)</td>
<td>(20)</td>
<td>16</td>
<td>1–3 days and 2–11 years</td>
<td>Inhalational</td>
<td>Distinct mitogen-induced lymphoproliferation in neonates and children</td>
</tr>
<tr>
<td>Mollitt (1984)</td>
<td>(21)</td>
<td>50</td>
<td>Mean age 20 months</td>
<td>Inhalational</td>
<td></td>
</tr>
<tr>
<td>Mollitt (1986)</td>
<td>(22)</td>
<td>35</td>
<td>1 months to 12 years</td>
<td>Inhalational</td>
<td>lymphocyte alterations inversely age-related</td>
</tr>
<tr>
<td>Platt (1989)</td>
<td>(23)</td>
<td>22</td>
<td>1 months to 10 years</td>
<td>Inhalational</td>
<td>a</td>
</tr>
<tr>
<td>Hauser (1991)</td>
<td>(24)</td>
<td>31</td>
<td>3 months to 12 years</td>
<td>Balanced</td>
<td>No change</td>
</tr>
<tr>
<td>Puri (1992)</td>
<td>(25)</td>
<td>15</td>
<td>1–4 days</td>
<td>Inhalational</td>
<td>Variable lymphoproliferative response to a range of mitogens</td>
</tr>
<tr>
<td>Merry (1997)</td>
<td>(26)</td>
<td>21</td>
<td>36 weeks to 16 years</td>
<td>Not stated</td>
<td>No alterations in PMN chemotaxis and actin polymerization</td>
</tr>
<tr>
<td>Hansen (1998)</td>
<td>(27)</td>
<td>13</td>
<td>1.5–54 months</td>
<td>Balanced and epidural</td>
<td>No significant cytokine changes between pre- and post surgery</td>
</tr>
<tr>
<td>Mattila-Vuori (1999)</td>
<td>(28)</td>
<td>12</td>
<td>14–20 and 12–23 weeks</td>
<td>Balanced vs. inhalational</td>
<td>↓ to PWM</td>
</tr>
<tr>
<td>Mattila-Vuori (2000)</td>
<td>(29)</td>
<td>20</td>
<td>0.5–3 years</td>
<td>Balanced</td>
<td>a</td>
</tr>
<tr>
<td>Romeo (2002)</td>
<td>(30)</td>
<td>16</td>
<td>&gt;6 months</td>
<td>Balanced</td>
<td>Increased PMN and monocytes phagocytosis and oxidative burst</td>
</tr>
</tbody>
</table>
Vuori (2004)  (31)  51  2–12 years  Balanced  

End of anesthesia

PMN, polymorphonuclear (neutrophils); B, B-cells; NK, natural killer cells; ns, no significant; T_H, T-helper cells; T_C, T-cytotoxic cells.

Post surgical increase followed by a decrease.

Post surgical decrease followed by an increase.

Activated lymphocytes.

In nine patients.

PHA-induced response decreased in opioid group.


Llewellyn N, Moriarty A. The national pediatric epidural audit. Paediatr Anaesth. 2007 Jun; 17(6):520-33 (tables 8-10)

Table 8: Number and severity of adverse events during continuous epidural anesthesia

<table>
<thead>
<tr>
<th>GRADE 1</th>
<th>N</th>
<th>GRADE 2</th>
<th>N</th>
<th>GRADE 3</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural abscess</td>
<td>2</td>
<td>Drug error respiratory arrest</td>
<td>1</td>
<td>Drug error</td>
<td>10</td>
</tr>
<tr>
<td>Meningism</td>
<td>1</td>
<td>Drug error – seizure</td>
<td>1</td>
<td>Local infection</td>
<td>25</td>
</tr>
<tr>
<td>Postdural puncture headache</td>
<td>1</td>
<td>Local anesthetic toxicity</td>
<td>1</td>
<td>Postdural puncture headache</td>
<td>5</td>
</tr>
<tr>
<td>Drug error, resulting in cauda equina syndrome</td>
<td>1</td>
<td>Peripheral nerve injury</td>
<td>1</td>
<td>Inadvertent spinal anesthetic</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 9: Percentage and grade of incidents excluding drug errors and local anesthetic toxicity (all grades, n = 43)
<table>
<thead>
<tr>
<th>Age Group</th>
<th>Caudal</th>
<th>Lumbar</th>
<th>Thoracic</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>276</td>
<td>178</td>
<td>75</td>
<td>0.36</td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>476</td>
<td>838</td>
<td>412</td>
<td>0.21</td>
</tr>
<tr>
<td>1-8 years</td>
<td>140</td>
<td>2645</td>
<td>1351</td>
<td>0.26</td>
</tr>
<tr>
<td>&gt; 8 years</td>
<td>29</td>
<td>2565</td>
<td>1648</td>
<td>0.30</td>
</tr>
<tr>
<td>All</td>
<td>10633</td>
<td>43</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>

The incidence of severe events was 1:2000, moderate events 1:1100. One child had symptom (cauda equine after an overdose of LA in a neonate) one year post op (incidence 1:10,000)

Flag raising ceremony at the new Children’s Hospital 10/2007
<table>
<thead>
<tr>
<th>Insult</th>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infection</strong></td>
<td>1</td>
<td>Meningism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Permanent damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No permanent damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epidural abscess</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Permanent damage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No permanent damage</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Local sepsis requiring surgical treatment</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Local skin infection which requires nonsurgical treatment</td>
</tr>
<tr>
<td><strong>Nerve injury</strong></td>
<td>1</td>
<td>Definite peripheral or nerve root damage with no recovery (at one year follow-up)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Definite peripheral or nerve root damage whatever the duration with full late recovery (at one year follow-up)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Definite peripheral or nerve root damage whatever the duration with full recovery on discharge</td>
</tr>
<tr>
<td><strong>Drug error</strong></td>
<td>1</td>
<td>Drug error with actual harm to the child which remains present at discharge</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Drug error with harm caused to the child which is corrected</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Drug error with no actual harm caused to the child because corrective action taken/no adverse effects</td>
</tr>
<tr>
<td><strong>Local anesthetic toxicity</strong></td>
<td>1</td>
<td>Resulting in cardiac arrest and/or death</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Definite signs of serious local anesthetic toxicity requiring active treatment with no actual harm to the child</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Symptoms suspicious of local anesthetic toxicity not requiring active treatment and with no actual harm to the child</td>
</tr>
<tr>
<td><strong>Spinal cord insult</strong></td>
<td>1</td>
<td>Spinal cord insult 1 No recovery at time of discharge</td>
</tr>
<tr>
<td><strong>PDPH</strong></td>
<td>1</td>
<td>Postdural puncture headache requiring active in patient treatment including blood patching</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Postdural puncture headache requiring active in patient treatment but not blood patching</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Postdural puncture headache of short duration requiring simple analgesia, bed rest, fluids</td>
</tr>
<tr>
<td><strong>Inadvertent spinal anesthetic</strong></td>
<td>1</td>
<td>Recognized/unrecognized – serious sequelae leading to permanent damage</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Recognized/unrecognized – serious sequelae with no long term damage</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Recognized – no sequelae</td>
</tr>
<tr>
<td><strong>Respiratory/cardiac arrest</strong></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
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Anesthesia for Awake Craniotomies
Tod B. Sloan

Prior to modern inhaled anesthetic agents, many craniotomies were conducted using local anesthesia since field blocks or specific nerve blocks by the surgeon would allow a craniotomy and operation on an insensitive brain without the unfavorable intracranial effects of the anesthetics. With the introduction of isoflurane, craniotomies could be routinely conducted without adverse brain swelling as long as the inhaled concentration was kept below 1 MAC and other adjuncts (e.g. hyperventilation, mannitol, lasix, etc.) were used. However, the awake craniotomy under local anesthesia reemerged as surgeons operated on brain structures near sensitive or eloquent regions of the brain to provide maximal resection with minimal injury or for optimal placement of lesions or stimulators. For example, removal of seizure foci near speech centers, removal of tumors near the motor cortex, and placement of deep brain stimulators or lesions are situations where awake craniotomy allows a focused resection with minimal morbidity in these functional areas. This talk will focus on the aspects of the participation of anesthesiology in these procedures.

Overview – the Asleep-awake-asleep technique

In general, the anesthesia for these procedures can be done as monitored anesthesia care with local anesthesia and sedation similar to other MAC cases. However, frequently the procedures are long enough that this is difficult for the patients to tolerate. As a consequence most are done using an asleep-awake-asleep anesthetic. In the first stage the patient is heavily sedated such that they are asleep while preliminary procedures are done which are uncomfortable. These may include placement of a Foley catheter, placement of an arterial line, placement of the Mayfield head holder, placement of the local anesthesia on the scalp, and craniotomy to expose the cerebral cortex. During this stage the patient’s participation is not needed. In the next stage the patient must be awake as the surgeon will be interacting with the patient to determine the functional mapping of the brain and its location relative to the region of brain for resection. Once this is completed the third stage begins where the procedure is completed and patient participation is no longer needed so heavy sedation can be used.

Preoperative Considerations

In the preoperative evaluation the surgical team must evaluate the ability of the patient to cooperate with the awake portion of the procedure. In essence a mature motivated patient is key with the only contraindication is an uncooperative patient. Although often done in adults, children as young as 9-12 years old have undergone the procedure successfully. In addition to the usual preoperative anesthesia evaluation, the patient needs reassurance and clarity of the role of the anesthesiologist during the procedure. They need reassurance of the role of sedation during the sleep portions and reassurance of the presence and support
about Local Anesthesia

Although local scalp infiltration can be used for the limited burr hole needed for DBS placement, local anesthesia for craniotomy usually requires a “ring” infiltration around the scalp or specific blockage of the nerves which provide sensory innervation of the scalp (auriculotemporal, zygomaticotemporal, supraorbital, supratrochlear, lesser occipital and greater occipital nerves).\(^3\) The blocking of the specific nerves is both more effective and safer because the total dose of local anesthesia is smaller. Of note is that the addition of sodium bicarbonate to the local (2 cc of 8.4% to 30 cc lidocaine or 1 cc to 30 cc bupivicaine) reduces the discomfort of the injection and be helpful if the patient is not heavily sedated.

Choice of Anesthesia for the Asleep Portion

A variety of anesthesia techniques can be used for the asleep portion of the procedure. This includes the use of general anesthesia with endotracheal tubes, however, most individuals use infusion of sedative and analgesic medications. In particular, sedation with propofol and analgesia with remifentanil or the use of dexmeditomidine are popular. In these cases the medications can be stopped to allow the awake portion with good clear cognitive testing. Neuroleptic analgesia with droperidol and an opioid was frequently used in the past but newer agents have generally replaced its use.

As a sedative, propofol provides excellent sedative properties with fast recovery (usually awakening 15-20 minutes after cessation of the infusion). Occasionally irritation at the site of infusion can be a problem. It also has the advantage of being antiemetic which helps reduce the chance of nausea and vomiting with can occur during the awake portion. Typically infusion rates exceed 50 ug/kg/min during the asleep portion when effect site concentrations of the drug need to exceed 1-2 ug/ml.\(^4\) When the infusion is stopped, its rapid metabolism allows awakening within a reasonable period of time when the awake testing is desired.

Remifentanil has also become popular for the analgesic component of the anesthetic. Because of its rapid metabolism the effect can be increased or decreased rapidly as needed. Usually an effect site concentration of 2-2.5 ug/ml is targeted (0.01-0.05 ug/kg/min).\(^4\) Of particular note is that usually spontaneous breathing is used during the asleep portion so that the remifentanil can be titrated against respiratory rate. Often the remifentanil is not completely stopped during the awake portion since its supplemental analgesia can be advantageous as a supplement to the local anesthesia, especially in the temporal area of a craniotomy.
where local anesthesia may be problematic. Remifentanil has also been associated with muscle rigidity, postoperative shivering, and bradycardia (especially in patients who are beta blocked). Remifentanil has also been associated with muscle rigidly, postoperative shivering, and bradycardia (especially in patients who are beta blocked).  

The addition of dexmedetomidine to the anesthesia armamentarium has allowed it to be used as an effective supplement for these procedures. Although an occasional case is reported where testing is not possible at higher doses, it has been effective in infusion doses of 0.1-0.2 ug/kg/min following a loading dose of 1-2 ug/kg. Although not FDA approved for use outside the ICU where it is approved for sedation, it has been effectively used during awake craniotomies. Although it is metabolized a bit slower than propofol or remifentanil, it has been used very effectively by some individuals. Dex, through its action as a central alpha 2 stimulant, has both sedative and analgesic actions.

Further, the drug interacts with the brainstem to produce a sleep state that more closely mimics natural sleep. In the awake state the locus coerulus (LC) and pedunculopontine tegmental nuclei (PPTg) inhibit the ventrolateral preoptic nucleus (VPLO) such that the tuberomammillary nucleus (TMN) stimulates the brain to promote vigilance. Dex decreases the output of the LC which releases its inhibition of the VPLO allowing the VPLO to inhibit the TMN stimulation of the brain such that sleep is promoted. As such, cognitive function after awakening from Dex induced sleep is more normal. Another advantage of Dex is less respiratory depression. Since Dex cannot be used as a sole anesthetic agent due to side effects such as hypotension and bradycardia, it may require supplemental sedation during the asleep portion of the procedure (e.g. propofol 80-100 ug/kg/min). Occasionally a headache has been reported with Dex such that an infusion of remifentanil may be needed.

**Wake Testing**

The awake portion of the procedure is required so that the surgeon can test various areas of the brain to determine the functional nature of the tissue. Essentially they need to functionally map the regions of the brain near the area for surgical resection. This is usually done by stimulating a region and observing the clinical effect. For example, when mapping the motor cortex the stimulation may produce motion in a hand or leg and the patient can sense the motion much more effectively than observation by the anesthesiologist (although such mapping can be done in the anesthetized patient without muscle relaxants). Alternatively, stimulation can also block function such as stimulation of a speech area causing the patient to be unable to name an object which they see on a screen in front of them.

In its simplest form, functional mapping is often done preoperatively to identify the dominant hemisphere. Here, the WADA test is performed by injection of a sleep dose of sodium amytal into the internal carotid artery while the patient holds their arms up and talks. If the contralateral arm falls then the hemisphere is “asleep” and if the speech is lost then the injected side is the side of language dominance such that resection of a temporal lobe epileptic focus places speech areas at risk.

Although a large number of non-invasive techniques have been developed for functional mapping, electrocortical stimulation of the brain in an awake patient is the
This stimulation to induce speech arrest or errors in counting or naming can also be done extraoperatively using implanted grid electrodes which are also used to map seizure foci. However this technique is limited to stimulation of the cortical surface and does not allow stimulation testing of the sulcal depths which comprise as much as two-thirds of the cortical surface.10

The importance of testing during an awake craniotomy is shown by the fact that lesions (tumors and vascular abnormalities) may alter the traditional anatomic locations of structures10 and that the brain may shift during physiological changes (e.g. position, gravity, edema, carbon dioxide changes), craniotomy (which may account for as much as a 24 mm shift10), and effects such as retraction, CSF drainage, mannitol and lasix used to reduce brain swelling at craniotomy. In addition, some low grade tumors may have functional tissue within the tumor making maximal resection compete with minimizing functional impairment.10

Special Considerations in Specific Procedures: Epilepsy

Epilepsy affects approximately 0.55-1% of the population with 30-40% continuing to have seizures despite medications.2 For most of these patients the morbidity and mortality of a craniotomy is less than that of uncontrolled epilepsy. Unfortunately many of the seizure foci not associated with structural abnormalities such as tumors have their foci near the speech centers such that awake craniotomy is often indicated. Many of the epileptic foci lie near Wernickes' speech area in the dominant temporal lobe, Broca's speech area in the dominant frontal lobe and near the motor strip.

Unfortunately mesial temporal lobe epilepsy is the most common form of epilepsy and is the most refractory to medications.2 Of particular importance with this epilepsy is that the encoding and retrieval of memory which involve the hippocampus, amygdale and parahippocampal cortices makes awake testing critical.10 In one large trial 60% of patients were seizure free at 1 year after the procedure.11

Resection of the epileptic foci is usually accomplished with two surgical procedures. The first is done using routine general anesthesia and involves a craniotomy with placement of grid and depth electrodes. EEG recording is done between surgeries to localize the focus of the seizure and the patient returns for excision of the offending cortex. If the tissue is in the dominant hemisphere (i.e. speech is at risk) or near the motor cortex then an awake craniotomy is often done. The patient is usually in the lateral position with the dominant cortex to be tested up. Special considerations here are that a Foley catheter is usually used since mannitol and lasix may be needed during resection. An arterial line is often not used.

Motor Mapping

For abnormalities near the motor cortex, awake craniotomy can allow identification of the cortical motor areas. The patient is usually in a lateral position with the cortex to be tested in the upside. A Foley catheter is usually used due to the
frequent use of mannitol and lasix. If the lesion is a tumor an arterial line is frequently used.

The central sulcus can usually be identified in the asleep patient by the phase inversion of the SSEP recorded from the cortical surface and motor cortex mapping can be done using motor evoked potentials from cortex stimulation, however distortions in the brain anatomy make awake testing advantageous. In this case the brain is stimulated and the patient identifies motion in regions of the body. Alternatively the patient can perform a continuous task and stimulation of the brain indicate interruption of the task.

Placement of Deep Brain Stimulators for Movement Disorders

Anesthesia for the placement of deep brain stimulators is similar to the procedures above except that the movement disorders are very sensitive to anesthetic agents. Hence it is important to avoid benzodiazepines preoperatively and beta blocking agents as these may make awake testing difficult. In this case the patient is in a sitting position and an arterial line is usually not used. The procedures may be long so a Foley or condom catheter is usually indicated.

The procedure is usually done through a small burr hole and a motorized apparatus is attached to the skull with a trajectory for the electrode aimed at the target location (usually subthalamic nucleus, globus pallidus internus, or ventralis intermedius nucleus) based on stereotactic coordinates. A recording/stimulating electrode is advanced into the brain listening for characteristic electrical activity of the target neurons. In addition, the tremor of the patient is tested by stimulating the electrode tip to find the optimal placement. Of note is that the optic tract is just deep to the optimal location in the globus pallidus internus such that visual symptoms may be important. Hypertension appears to be a common problem with this procedure and outcomes are better if the systolic blood pressure is less than 140 mmHg (avoiding beta blockers as a treatment). Once the electrode is placed the patient returns for a second routine general anesthetic to place the generator in the chest (like a pacemaker) after a trial of use.

Complications

A variety of problems with the awake craniotomy technique have been reported including postural discomfort, agitation, dysphoria, disinhibition, claustrophobia, apnea, hypercarbia, venous air embolism, respiratory depression, airway obstruction, hemodynamic instability, vomiting, and pain. In general, the incidence of these is usually below 5% with the most common being seizures, excessive sedation, hypertension and nausea and vomiting.

Positioning and patient comfort are absolutely key. Liberal use of pillows and padding are important especially to insure no strain on the neck. Avoiding neck rotation and extension and a large roll behind their shoulder and back on the operative side can relieve tension on the neck. Warm blankets and warm air blankets are important in cold operating rooms and the use of cool air blown on the face is helpful if the patient becomes too warm. Access to the face and airway is paramount.
as is visual access of the patient to the anesthesiologist and pictures for speech testing. For DBS placement, access of the arms and legs is key for testing of motor function and tremor assessment during electrode positioning. If a urinary catheter is used, the use of lidocaine jelly as a lubricant can be helpful. If a catheter is not used, a condom catheter may be considered in a male patient since a full bladder can be very uncomfortable.

**Airway Considerations**

Management of the airway is one of the major challenges in these cases since free access is often limited during the craniotomy. Hence the careful titration of the sedative and analgesic components is important. Often a natural airway with supplemental Oxygen (i.e. nasal prongs) is sufficient for adequate ventilatory exchange during the asleep stages. However, many individuals use oral or nasal airways or LMA’s to maintain patent airways. These airway adjuncts have the advantage of easy insertion after draping and less violent awakening for the second stage. The LMA also has the advantage of some ability to augment ventilation if needed.

However, the use of endotracheal tubes and a more formal general anesthesia has also been used. In these cases general anesthesia is induced at the beginning of the procedure and the endotracheal tube is placed. Topical lidocaine is used in the airway to reduce the irritation and coughing on awakening when the endotracheal tube is removed over a tube exchanger. After the awake testing the exchanger is used to guide the replacement of the endotracheal tube for the last stage. The use of the endotracheal tube allows a secure airway with reduced aspiration risk and the capability of positive pressure ventilation for control of carbon dioxide which can be important for control of brain swelling. An endotracheal tube or LMA is also more commonly used in children undergoing these procedures.

Seizures during the procedure can occur either by spontaneous activation of a native foci (as during procedures for resection of an epileptic foci) or as a consequence of the irritation secondary to the stimulation of brain regions used during the functional testing (4.9%). Usually the seizure is stopped by the application of cold saline to the brain by the surgeon. This has the advantage of a quick recovery of cognitive function. However, if this is unsuccessful the anesthesiologist should be prepared to give a rapidly acting drug such as propofol or pentothal which will stop the seizure and allow a reasonable time for recovery to cognitive testing. Occasionally intubation and general anesthesia may be needed.

Control of Blood pressure is also another important consideration as the development of hematomas can complicate these procedures (1.1%), including the need for emergent reoperation. Currently we control the systolic blood pressure to below 140 mmHg during these procedures and postoperatively. The use of alpha and beta blocking medications is generally advantageous for the control of blood pressure as these produce minimal vasodilation of the brain since the blood vessels in the brain are less responsive to these agents. However, especially during deep brain stimulator placement when beta blocking agents may interfere with effective brain mapping, other agents may be indicated. Hydralazine, nicardipine, and sodium...
nitroprusside have been effectively used although the latter can produce a headache that can interfere with patient comfort.

Nausea during procedures can be problematic, especially if aspiration could occur. Medications utilized include dexamethasone, ondansetron and metoclopramide.

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SEDATION
What’s New for the Anesthesiologist and Non-Anesthesiologists?
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Cleveland Clinic Foundation, Cleveland, Ohio

Characteristics of the Continuum of Sedation (circa 1992)

<table>
<thead>
<tr>
<th>Conscious Sedation</th>
<th>Excessive Sedation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conscious</td>
<td>Unconscious</td>
</tr>
<tr>
<td>Cooperative</td>
<td>Non-responsive</td>
</tr>
<tr>
<td>Protective reflexes intact</td>
<td>Protective reflexes depressed</td>
</tr>
<tr>
<td>Airway patent</td>
<td>Airway unprotected</td>
</tr>
<tr>
<td>Spontaneous ventilation</td>
<td>Depressed ventilation</td>
</tr>
</tbody>
</table>

Now: A Continuum of Techniques
• Local by Surgeon without an Anesthesiologist
• Dense regional with or without sedation
• Partial field block with sedation
• Deep sedation with or without block
• Unconscious sedation/ analgesia
• General anesthesia - spontaneous respiration
• General anesthesia - neuromuscular blockade
• General anesthesia - circulatory arrest/bypass

“Definitions”
• Procedural Sedation = Moderate or Deep Sedation/ Analgesia
• Local Standby = Old term
• Conscious Sedation = Moderate Sedation
• MAC (Monitored Anesthesia Care) = “A continuum that can range widely and is not always predictable.”
• Light sedation, Just a “little” anesthesia, That white stuff, etc.

ASA Position on MAC
• http://www.asahq.org/publicationsAndServices/standards/23.pdf
• Involvement of an anesthesiologist
• Pre-procedure visit, care during the procedure, post-procedure care
• Potential and ability to convert to GA
• Differences from “conscious sedation”

MAC-Monitored Anesthesia Care as delivered ONLY by an anesthesia provider
• American Society of Anesthesiologists

“MAC involves monitoring of multiple physiologic parameters....anticipate the need to progress to general anesthesia. In addition, the possibility that the surgical procedure may become more extensive than originally thought, and/ or result in unforeseen complications.”
MAC Morbidity

- JAMA 1998 study by Cohen (JAMA 1988;260:2859-63)
  - 100,000 Anesthetics
  - Highest mortality with MAC = 208/100,000
- K. B. Domino in June 1997 ASA newsletter
  - ASA Closed Claims Project
  - 3791 closed malpractice claims
  - overall 2% were related to MAC

MAC - ASA Closed Claims

ASA Updated Reference Article on Sedation by Non-Anesthesiologists

- Original article was in 1995, updated in 2002.
- Anesthesiology 2002; 96: 1004-17
- www.asahq.org/publicationsAndServices/sedation1017.pdf

ASA and JCAHO “Definitions”

- Minimal Sedation (Anxiolysis) = Normal response to verbal commands. Cognitive function and coordination may be impaired. Airway, ventilation, and cardiovascular functions are unaffected.
- Moderate Sedation/ Analgesia (Conscious Sedation) = Purposeful response (not reflex withdrawal from painful stimulus) to verbal or tactile stimulation. No airway intervention. Adequate spontaneous ventilation. Cardiovascular function is usually maintained.
- Deep Sedation/ Analgesia = Purposeful response after repeated or painful stimulation. Airway intervention may be required. Spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.
- General Anesthesia = Unarousable even with painful stimulus. Airway intervention often required. Positive pressure ventilation may be required. Cardiovascular function may be impaired.
Propofol Package Insert

- July 2002 Revised Version
- Bottom of first page in bold type under “Warnings”
- “For general anesthesia or monitored anesthesia care (MAC) sedation, propofol should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure.”

Perils of Propofol

- No analgesia whatsoever. Only hypnosis. Adding narcotic yields synergistic effects.
- ED 50 and ED 95 very widely spaced. Thus the need for close titration for each and every patient based on frequent assessment of level of consciousness.
- Dis-inhibition makes “conscious” sedation very difficult, pushing the patient to deeper levels of sedation (close to GA).

Perils of Propofol continued

- When patients are deeply sedated they are candidates for developing laryngospasm and the need for emergent succinylcholine, mask ventilation, and intubation.
- Hypersalivation occurs in 12% of cases.
- Examine your governmental “Nursing Board” for any “scope of practice” statutes.
- Primary cardiac inhibitor and vasodilator, very problematic in the dry, NPO patient (especially with coexisting cardiac disease)

2004 ASA Statement on the “Safe Use of Propofol”

- Restates that sedation is a continuum and you must know how to do deep sedation to use propofol.
- Restates the warning on the FDA approved package insert.

Key Points in the ASA “Safe Use of Propofol”

- Defines “Rescue” from the next sedation level
  - Airway management.
  - Return to the previous level of sedation.
  - Halt the procedure until the patient returns.
- Outlines equipment needed for monitoring and training of personnel.
- Contains a joint statement by ASA & AANA.

Privileging for Sedation for Non-Anesthesia Providers

- Moderate
- Deep
Recent ASA Pronouncements
• 10/2006 at meeting of ASA House of Delegates in Chicago
• “Because of the significant risk that patients who receive deep sedation may enter a state of general anesthesia, privileges to administer deep sedation should be granted only to practitioners who are qualified to administer general anesthesia or to appropriately supervised anesthesia professionals.”

Gastroenterology and Propofol
Nurse Administered Propofol for Sedation (NAPS)
• 2004 - Joint statement from:
  – American College of Gastroenterology (ACG)
  – American Gastroenterological Association (AGA)
  – American Society for Gastrointestinal Endoscopy (ASGE)
  – Society for Gastroenterology Nurses and Associates (SGNA)
• The routine use of anesthesia providers for average risk patients for EGD and colonoscopy is not warranted.
• New CMS ASC payment system – 17% decrease in GI procedure reimbursement over 4 years.

Gastroenterology and Propofol (continued)
• GI physician-nurse teams using propofol for conscious sedation must be competent to do deep sedation and rescue from GA and severe respiratory depression.
• Must have a designated person other than the endoscopist to monitor and rescue.

Surgery Center of Southern Oregon
Medford, Oregon
• Since 1998 has trained 40 nurses in NAPS.
• “Perfect” safety record over 36,000 cases.
• ACLS and PALS certification.
• Nine written exam competency program.
• 10 case OR rotation covering induction, emergence, gases, paralytics, reversal agents
• Perform 3 successful LMA insertions.

NAPS training - continued
• Perform heart, lung, and airway assessments.
• Annual 5 hour airway class and written exam.
• Observe NAPS by an RN for one week.
• Administer NAPS under direction of surgeon and an RN
• Complete annual airway modules, clinical competency program, airway management class, perform a case observed by the medical director.

Supporting Documentation from Gastroenterology Literature
• 31 “Studies” demonstrate that this is safe.
• 9,152 cases of RN administered propofol with 7 cases of respiratory depression
• Seven years with 25,200 cases
  – 3 – Apnea
  – 3 – Laryngospasm
  – 1 - Aspiration
• 28,697 cases with 0.14% needing assisted ventilation (42 cases) with no intubation.
### Ethicon Endo-Surgery

**Propofol Sedation Delivery System**

- Now in FDA trials
- Intent is to deliver “Moderate Sedation” and NOT “Deep Sedation”
- System monitors HR, BP, SpO2, RR via ETCO2, & ARM with closed loop feedback
- ARM – Automated Responsiveness Monitor
- Patient can respond purposefully to verbal commands, no airway intervention, with adequate spontaneous ventilation.

### Safeguards in a Facility Sedation Protocol for Non-Anesthesiologists

- Training
  - Pharmacokinetics and pharmacodynamics.
  - Avoid sedation drips or pumps.
  - Ability to rescue from next level of sedation.
  - ACLS, Airway course for nurses and MD proceduralists.
- New AHA 4 hour “Airway Management” Course
  - “Designed for healthcare providers who must be proficient in using airway devices on adults in or out of hospital”
  - Bag-Mask Ventilation and Airway Adjuncts and LMA
  - Esophageal-Tracheal Combitube
  - ETT and ITD (Impedance Threshold Device)

- Documentation
  - OSA – ASA guideline and possible JCAHO 2008 NPSG.
  - Level of sedation (baseline, recording frequency).
  - SpO2, RR (ETCO2 ?), Responsiveness (Ramsay, OAAS), Airway intervention (chin lift, jaw thrust, nasal or oral airway, PPV by mask, LMA, OETT).

- Auditing/Oversight
  - Facility certifies and routinely reviews sedation site leadership (nurses and MDs)
  - CQI plans (volumes, events, code responders, training, equipment, space, nurse staffing, relationship to anesthesia department when sedation fails).
  - Random chart review
  - Unannounced observers from quality office

- Quality Improvement
  - Regular M&M conferences with nurses & MDs
  - P&T Committee or Pharmacy
  - Anesthesia representative on this committee
  - Restrict drugs to “approved” locations
  - Propofol (bolus, drip)
  - Brevital
  - Etomidate
  - Dexmedetomidine (drip)
  - Ongoing review of existing and new sedation drugs
Know the Nursing “Laws”

- Board of Nursing, Interpretive Guidelines
- Scope of Practice Issues
- Can – Administer medications for moderate sedation. Monitor the patient.
- Cannot – Accept duties “that would interfere with patient monitoring”. Administer medications to induce deep sedation.

Recent Developments at the Ohio Board of Nursing (9/07)

- Only Moderate Sedation (defined by ASA)
- Must have 2nd nurse monitoring the sedation
  - “The nurse …should not engage in activities that would divert attention from the patient.”
- Cannot “administer” deep sedation
  - “The nurse should not engage in activities that are the practice of anesthesia care… Therefore should not administer medications to induce deep sedation and/or anesthesia.”
Sedation
Advising Your Facility in Developing Guidelines
Walter Maurer, M.D.  maurerw@ccf.org

Links to Documents on ASA Website (as of 10/13/2007)

Privileging for Moderate Sedation (Non-Anesthesia Providers)
http://www.asahq.org/publicationsAndServices/standards/40.pdf

Privileging for Deep Sedation (Non-Anesthesia Providers)

Statement on the Safe Use of Propofol
http://www.asahq.org/publicationsAndServices/standards/37.pdf

ASA Position on MAC

Distinguishing MAC from Conscious Sedation
http://www.asahq.org/publicationsAndServices/standards/35.pdf

Continuum of Depth of Sedation

Sedation/ Analgesia for Non-Anesthesiologists
www.asahq.org/publicationsAndServices/sedation1017.pdf
Propofol infusion syndrome: what do we know, why does it happen, and when should I worry?

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The Children’s Hospital, Denver and University of Colorado School of Medicine

Soon after the introduction of propofol into clinical anesthesia practice, it began to be used as a sedative agent in the intensive care unit. Its use became widespread because it had unique pharmacological and pharmacokinetic properties that previously used agents lacked, and it rapidly became an important drug in the ICU armamentarium. Unlike previous agents used for sedation in the ICU, propofol is rapid in both onset and offset; when used as a continuous infusion it is possible to awaken a sedated patient within minutes for evaluation and return them to sleep in seconds. (Dexmedetomidine is currently perhaps the only agent that has similar characteristics, although offset may be slower after prolonged infusions, and its usefulness as an anticonvulsant is not as clear.) For patients with head injuries, for example, this allowed interval assessment of neurological status. Patients who were difficult to sedate with opioid and benzodiazepine combinations could be easily sedated with quick titration of drug level, yet still be awakened rapidly for extubation or for neurological evaluation. Although hemodynamic compromise may be seen in volume depleted patients or those with myocardial compromise, the use of this drug became common, first in pediatric critical care and then in adult ICU’s. Propofol was also shown to be a potent anticonvulsant that sometimes was effective in status epilepticus refractory to other agents.

In 1992, however, a disturbing case series appeared in the British Medical Journal reporting five children who developed intractable metabolic acidosis and fatal myocardial failure while receiving prolonged infusions of propofol for sedation in the ICU. These children all followed a similar clinical course, beginning with unexplained metabolic acidosis and lactic acidemia which was unresponsive to the administration of sodium bicarbonate, myoglobinuria and elevated serum CPK, renal failure, and hepatomegaly. They rapidly regressed to developing bradydysrhythmias and hypotension, soon followed by cardiovascular collapse and asystole or pulseless electrical activity (PEA). On laboratory and postmortem investigation, the victims exhibited lipemic serum, hepatomegaly and fatty infiltration of the liver and myopathic changes of cardiac and skeletal muscle. The complex of findings was soon termed propofol infusion syndrome (now commonly abbreviated PRIS, as “PIS” is apparently too risqué or vulgar for the medical literature!).

Following this initial report, other intensivists reported similar cases, and by 1999 there were at least 27 pediatric cases reported, as well as 14 adults. The mortality in these reports reached 85%; the only survivors had prompt institution of hemodialysis or hemofiltration. The primary risk factor for development of the syndrome was identified as a propofol infusion rate greater than 65mcg/kg/min for greater than 48 hours (the ICU literature usually describes infusion rates in mg/kg/hr-
I have converted them here to the units more familiar to anesthesiologists). A prospective randomized study of 327 pediatric intensive care patients that was sponsored by Astra-Zenica, the manufacturer of propofol, found that the mortality rate of patients receiving an infusion of the 1% propofol preparation was twice that of children receiving other drugs for sedation; those receiving a 2% preparation had a threefold increased mortality. Unfortunately, these data have never been published, and were distributed to US physicians in a letter from Astra-Zenica warning not to use propofol for prolonged sedation in the intensive care unit.

The initial reaction to these reports in the critical care community was highly contentious- editorials even appeared in the literature denying the existence of a problem.8 However, biochemical evidence for a putative mechanism of the syndrome has now been identified, and few now deny the existence of the “propofol infusion syndrome”.9 A prolonged infusion of propofol impairs free fatty acid utilization and mitochondrial activity, and an imbalance between energy demand and utilization may be a key pathogenic mechanism.9-14 One investigator likens the syndrome to the deterioration of a child with an inherited defect in b-oxidation, who is asymptomatic until starvation or infection creates conditions where fat metabolism is required for energy production.12

A specific disruption in fatty acid oxidation leading to impaired entry of long chain acylcarnitine esters into the mitochondria with failure of complex II of the respiratory chain has been shown in muscle biopsy of patients with the syndrome.14 This was concomitant with a rise in malonylcarnitine and C5 acylcarnitine levels in the blood. These levels can be normalized with the prompt institution of hemofiltration or hemodialysis. Impaired mitochondrial respiration has also been produced during propofol infusion in an isolated perfused guinea pig heart model.

It would seem to be a relatively simple matter to close the door on all of this by simply not using propofol for prolonged infusions in the ICU (and indeed, the package insert does list prolonged use as a relative contraindication). However, numerous case reports have now documented the propofol infusion syndrome during short-term infusions during anesthesia.15-23 It is unknown if these cases represent the unmasking of a sub-clinical mitochondrial disorder, the exacerbation of mitochondrial oxidative dysfunction mediated by the stress of surgery or injury, or the revelation of sub-clinical propofol infusion syndrome in susceptible individuals. In Burow’s case (reference 19), the patient was asymptomatic, and the lactic acidosis was discovered only because of delayed emergence and the incidental measurement of arterial blood gases. One patient received an infusion for only 4 hours, yet developed acidosis, dysrhythmias and signs of myocardial dysfunction that lasted several days despite an apparently otherwise uneventful procedure and anesthetic.23 The possibility of pharmacogenomic differences in individuals, particularly the existence of polymorphisms in mitochondrial respiration and electron transport, are important variables that may likely play a role in whether a patient is at risk.24 Several authors have postulated that the development of lactic acidosis may be an early warning sign for propofol infusion syndrome.20,25
As of 2007 there were 61 recorded cases of PRIS in the literature; of these, 20 children and 18 adults have died. Investigators have now begun to look beyond the overt full-blown PRIS cases with hopes of identifying early warning signs or risk factors that can identify subclinical cases. A paper by Wolf, who reported the case of a child with status epilepticus unresponsive to conventional anticonvulsants who was treated with propofol, is instructive. The authors recognized the risks and measured carbohydrate intake and C4 acylcarnitine levels daily. Although the child developed no signs or symptoms of propofol infusion syndrome, the C4 acylcarnitine levels rose steadily beginning on day 2 of the infusion despite increased carbohydrate intake, and by day 5 had reached 10x their baseline levels. This returned to normal when measured at a 6-month follow-up visit. These data suggest that even without the development of either overt biochemical or physiologic signs of propofol infusion syndrome, the perturbations of mitochondrial respiration are present during some prolonged infusions. The infusion rates used for this patient ranged from 75mcg/kg/hr (day one) to a maximum of 110mcg/kg/hr on day 4. These rates are considerably lower than used intraoperatively for anesthesia (average 150-250mcg/kg/min), so it would not be surprising that at anesthetic doses such findings might be seen over shorter time periods.

Since laboratory and animal data suggest that propofol does have a deleterious effect on mitochondrial electron transport and fatty acid oxidation, subclinical perturbation of cellular energetics might be far more common than previously thought. In a retrospective study of adults at Mayo who received prolonged TIVA with propofol for radiofrequency ablations 24% had unexplained acidosis, as compared with 8% of matched controls receiving general anesthesia with other agents for carotid endarterectomy. Although there are numerous methodologic problems with this study, subtle biochemical evidence of PRIS may be common if one looks carefully for it. On the other hand, it is possible that only some patients will be at risk. One can logically hypothesize that there may be a pharmacogenomic marker in those patients. Are there specific polymorphisms of mitochondrial respiration enzymes in patients who develop evidence of electron transport dysfunction during propofol anesthesia? Or are there are some patients who have polymorphisms in propofol's metabolic pathways that are different from those who do not develop the syndrome? These are unknown at this time, but we are now enrolling patients in a prospective study to try to answer these questions.

What should one do at this time? First, as with any rare drug complication, an index of suspicion is always helpful in making an early diagnosis. For cases under 2 hours, even with high rates of infusion, the incidence is apparently rare. For longer cases, especially using high infusion rates, it may be prudent to measure pH and lactate. The development of a lactic acidosis that cannot be explained by other causes should raise the question of early PRIS. More ominous warning signs include dysrhythmias, hypotension, and dark urine suggestive of myoglobinuria or other signs of rhabdomyolysis. Blood levels of C4 or C5 acycarnitine may be helpful in
confirming the diagnosis but this test is not commonly performed in a timely enough manner to aid in clinical decision-making.

Patients with long fasting times may be at increased risk. One should consider the addition of adequate carbohydrate substrate to intravenous fluids (4-8mg/kg/hr of glucose) if a long propofol anesthetic is considered. Additional lipid (intravenous fat emulsions for parenteral nutrition) should not be administered without adequate carbohydrate. Infusion rates should be minimized, perhaps with the addition of other drugs that reduce the propofol requirement (opioids, benzodiazepines, etc.).

References:


Overview

- Platelet physiology and review of general concepts in hemostasis
- Review of cell-based theory vs cascade theory on coagulation and its relation to platelet function.
- How does cardiac bypass affect platelet function?
- Possible therapies targeting platelet protection.

Platelet Function, Coagulation, and Effects of Cardiopulmonary Bypass.

Presented By:
Nathaen Weitzel MD

Platelet Physiology:

- Discoid shaped cells with 7-10 day lifespan.
- Contain both α and dense granules
- Activation can be maximal, or partial depending on degree of stimulus

Platelet Physiology:

- α-granules contain adhesive ligands, PF4 and coagulation factors including Factor V and VIII
- Dense granules contain calcium, ADP and serotonin, and require stronger signal for release

Hemostasis:

- Two types – Arterial and Venous
- Arterial bleeding is typically more concerning in perioperative setting.
- Arterial flow → high mechanical shear forces that oppose clot formation
- Platelet activation and adhesion represent the first line of defense.

Hemostasis cont.....

- The initiation of arterial hemostasis depends primarily on platelets.
- Requires platelet adhesion to subendothelial matrix (GPIbα, VWF)
- Activation and generation of stable platelet – platelet bonds
- Aggregation and recruitment of coagulation factors to direct development of a stable fibrin clot
Platelet Adhesion:

Initial platelet tethering  Platelet activation  Firm platelet adhesion


Platelet Activation:

- Activation induces the platelet to change shape and involves release of α-granules and / or dense granules
- Activators include: Fibrinogen, Collagen, Thrombin, ADP and “Cardiopulmonary bypass”
- Results of Activation:
  - Recruitment
  - Vasoconstriction
  - Release of messaging factors
  - Acceleration of fibrin formation
  - Clot protection

Activation:

- Basic structure of platelet plug is the platelet-ligand-platelet matrix
- Fibrinogen and VWF serve as links
- Both act to bind at GIIb/IIIa receptors, of which the resting platelet has 50,000
Thrombin and PARs:
- Aggregation begins once the initial platelet layer has formed. Platelet activators all act to recruit additional platelets and incorporate more fibrinogen.
- This is where aspirin and clopidigrel have their activity.

Recap:
- Discussed platelet physiology and covered basics of hemostasis
- Platelets form first line defense against arterial hemorrhage.
- Requires adhesion, activation and aggregation.
- This leads to interaction with coagulation factors and the dreaded coagulation cascade.

Coagulation cascade:
- Wait a minute, I thought this talk was about platelets?????
- I hope to show how platelets interact with the coagulation scheme, and how you can use this to evaluate bleeding problems in the OR.

Cell based model:
- Coagulation cascade now viewed more accurately as a series of proteolytic events localized to the activated platelet surface.
- Exposure and binding of various factors to the platelet allows a cascade of zymogen reactions eventually leading to thrombin and fibrin formation.
- Key point: Consider these reactions as occurring in the shelter of the platelet membranes.
Initiation Phase:

Factor VIIa bound to TF activates factor IX and also factor X. Factor Xa then activates factor V on the TF-bearing cell, complexes with factor Va, and converts a small amount of II to IIa.


Priming Phase:

Small amount of initial IIa activates platelets, causing release of a granule contents including factor V, activates factor V, activates factor XI, and activates factor VIII by cleaving it from vWF.


Propagation Phase:

Factor IXa generated by factor VIIa/TF binds to the activated platelets and subsequently activates factor X to Xa. The formation of the "tenase" complex, comprising factors VIIIa, IXa, and calcium ions on the platelet surface, leads to the large-scale generation of factor Xa.


Cell based model cont...

- Formation of the “Xase” complex is a key point in the cascade
- Provides kinetic advantage for Factor X activation-13 million fold more efficient
- Allows interaction of Factor Xa and Va in a protected platelet environment
- Tight geometry of matrix prevents “invasion” by TFPI, and Antithrombin (even with heparin)

Cell based model cont...

- End result → Thrombin Burst
- Thrombin cleaves fibrinogen to fibrin
- Platelet provides a foundation for protease / factor interactions.

Recap:

- Cell based coagulation theory:
  - Important changes incorporate the dependence of the entire cascade reaction on platelet activation and membrane signaling pathways.
  - Generation of tenase complex in contact with activated platelets allows for kinetically superior reaction times and improved clot formation.
Weitzel, Nathaen, MD        Platelet Function, Coagulation, and Effects of Cardiopulmonary Bypass.

Platelet Dysfunction and Bypass

- Who cares if the platelets are not working?
- If there is some bleeding we can just transfuse blood and platelets right?
- That is what the blood bank is for anyway.
- Well…..maybe this is not the best approach.

Problems with transfusion

- Speiss et al retrospectively analyzed data collected during 6 RCT’s evaluating aprotinin use with bypass.
- Results from logistic regression analysis demonstrated increased risk of stroke and death associated with platelet transfusion.

Transfusion 2004;44:4S-14

Effects of RBC transfusion

- Murphy et al recently published results from a large retrospective cohort study looking at both infectious outcomes and ischemic outcomes associated with transfusion.
- Results: Significantly increased risk of infection, ischemic outcomes, and death for those patients transfused.

Circulation 2007;116:2544-52

What causes platelet dysfunction?

- Platelet activation via interaction with cardiopulmonary bypass circuit.
- Mechanical shear from circuit
- Hemodilution (if extreme)
- Hypothermia
- Heparin induced platelet dysfunction

Cardiopulmonary Bypass:

- Artificial heart lung machine, requiring blood to be pumped through an extracorporeal circuit.
- Exposure to circuit causes coagulation defects, with platelet dysfunction considered a key player.
- Ironically, CPB causes both thrombosis and coagulation deficits
- Re-operation rates for bleeding are 2-6%.
Bypass induced platelet activation:

- **CPB activates platelets**
- Studies demonstrate α-granule release
- Activation allows platelet binding to subendothelium, bypass circuit, and circulating cells
- Potential loss of GPIIa/IIIb and GPIb receptors

Bypass induced platelet activation:

- Partial to complete activation causes shape changes and degranulation leading to weakened platelet pool and poor clot formation
- Receptor disruption leads to increased agonist concentrations to achieve activation post-bypass.
- End result is a thrombocytopenia and platelet dysfunction.

**Platelet membrane effects from CPB:**

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Effect of CPB (Reference No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPIIb/IIIa</td>
<td>Decreased [9]</td>
</tr>
<tr>
<td>GPI/IX/CX (thrombospondin)</td>
<td>Decreased [4]</td>
</tr>
<tr>
<td>GP Ib/IX</td>
<td>Decreased [8]</td>
</tr>
<tr>
<td>PS</td>
<td>Increased [6]</td>
</tr>
<tr>
<td>TSP</td>
<td>Decreased [11]</td>
</tr>
<tr>
<td>CD63(SNAREs)</td>
<td>Increased [8, 11]</td>
</tr>
</tbody>
</table>

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Weitzel, Nathaen, MD  Platelet Function, Coagulation, and Effects of Cardiopulmonary Bypass.
Hemodilution:
- Circuit prime is responsible for a significant dilution effect but most often insufficient to explain clotting defects.
- Platelet count reduction not entirely explained by hemodilution alone.
- Current theory involves platelet interactions with circuit and heparin induced dysfunction / activation.

Hemodilution
- Fibrinogen binds both circuit and platelets.
- Result → additional platelet sequestration along bypass circuit.
- Continuous low grade activation may preferentially act on younger / stronger platelets.
- This adds to the hemodilution effect, and reduces functional platelet pool.

Hypothermia and Platelets:
- Wolberg et al examined effects of hypothermia and coagulation.
  - Coagulation enzyme activity only mildly reduced at 33-36°C.
  - Significant reductions below 33°C.
  - However, both platelet adhesion and aggregation markedly reduced even at 33°C – 36°C.

- Study demonstrated that aggregatory function of platelets returned to normal in normothermic group (>35 °C) group by the next day, but in hypothermic group (28°C) function remained impaired beyond 24 hours.
- Also demonstrated that thrombocytopenia was increased in hypothermic group.

Heparin and Platelet Function:
- Heparin is the most common anticoagulant for CPB.
- Binds anti-thrombin speeding activity against thrombin, Factor Xa and IXa.
- Effective against systemic thrombin, but not necessarily surface bound thrombin, opening the possibility for platelet activation.

Heparin and Platelet Function:
- Sobel demonstrated direct heparin binding and dysfunction in 1991:
  - Studied blood samples from pts undergoing CPB.
  - Compared both in vivo and in vitro studies.
  - Demonstrated direct binding to platelets at GPIb site, thus disrupting ability to adhere via VWF – platelet interactions.

Heparin and Platelet Function:

- Issue: To little heparin → thrombin generation. Too much heparin → marked platelet dysfunction
- Future considerations will may look at use of different anticoagulants during bypass → possibly direct thrombin inhibitors or possibly hirudins to avoid some of the negative affects of heparin.

Protamine and Platelets:

- Protamine is reversal drug that forms 1:1 complex with heparin.
- Excess protamine can cause platelet dysfunction by inhibition of thrombin activation sites, as well as disruption of GPIb-VWF interaction

What else can we improve?

- Improved platelet protection.
  - Heparin Coated Circuits
  - Off Pump CABG
- Specific reversible platelet inhibitors
  - Iloprost
  - NO
  - PAR inhibitors

Clinical use of Heparin Coated CPB in CABG

- Prospective, RCT compared:
  - Standard heparin (ACT target 480)
  - Standard heparin + LMW heparin coated circuit (ACT target 480)
  - Low dose heparin + LMW heparin coated circuit. (ACT target 240)
- 243 total patients enrolled
Clinical use of Heparin Coated CPB in CABG

- Additional endpoints noted:
  - Reduction in measured levels of platelet activation (BTG)
  - Significant reduction in amount of blood transfused in study group.

2003 retrospective study of 1300 patients found similar results.
- Ovrum et al. Journal of Cardiothoracic Surgery 2003;18:140-146

Off Pump CABG
- By avoiding CBP, theoretically you can avoid the shear stress and activation previously discussed
- Lower Heparin doses required
- Less Hypothermia
- Elimination of Cross Clamping
- However- technically more difficult

Impact of Off-pump Coronary Artery Bypass Surgery on Postoperative bleeding: Current best available evidence
- 65 RCT’s evaluated, 19 specifically looked at blood loss and transfusion requirements.
- 9 of 19 trials showed significant reduction in transfusion rates.
- Remainder showed decreased or similar numbers between groups, but not statistically significant.
- Did not specifically evaluate platelet function.

Hemostasis in Off-pump compared to On-pump CABG: Prospective Randomized Study.
- Examined 31 patients in prospective, RCT for OPCAB vs CBP.
- Measured hemostatic parameters as well as markers of endothelial activation, but not platelet function.
- Results mixed.
Hemostasis in Off-pump compared to On-pump CABG: Prospective Randomized Study.

- No significant difference in intra-operative or post-operative bleeding.
- D-Dimer, platelet counts, VWF, and fibronectin all measured.
- Authors noted a trend toward reduction in markers of endothelial activation, but not significant.


Nitric Oxide and Iloprost

- NO, prostacyclin (PGI₂) and Iloprost (PGI2 analog) are potent platelet inhibitors both in vitro and in vivo.
- Can these be used to anesthetize the platelets during CPB?

Combined administration of nitric oxide gas and Iloprost during cardiopulmonary bypass reduces platelet dysfunction: a pilot clinical study.

- Pilot study to examine effects of NO and Iloprost on platelet function and hemostasis in CPB.
- Prospective RCT of 25 patients
- Control, NO, PGI2, and NO + PGI2
- Standard CPB. ACT of >400
- NO @ 20ppm and Iloprost (2ng/kg/min) given through pump.

Combined administration of nitric oxide gas and Iloprost during cardiopulmonary bypass reduces platelet dysfunction: a pilot clinical study.

- Decreased chest tube output with NO, and NO + Iloprost*
- Platelet aggregation well preserved with NO + Iloprost, along with reduction in markers for platelet activation.

PARs

- Signaling pathway for Thrombin
- Specific PAR antagonists exist, but are in preclinical trials
- Day et al conducted trial to examine effects of Aprotinin on PAR activity.
- Clinical Inhibition of the Seven-Transmembrane Thrombin Receptor (PAR1) by Intravenous Aprotinin During Cardiothoracic Surgery. Circulation 2004;110:2597-2600

Clinical Inhibition of the Seven-Transmembrane Thrombin Receptor (PAR1) by Intravenous Aprotinin During Cardiothoracic Surgery.

- 30 patients for elective CABG enrolled
- Either received Aprotinin (high dose) or saline infusion
- Examined thrombin formation, platelet aggregation, PAR-1 expression and function.
Clinical Inhibition of the Seven-Transmembrane Thrombin Receptor (PAR1) by Intravenous Aprotinin During Cardiothoracic Surgery.

Circulation 2004;110:2597-2600

Overall results:
- First trial to demonstrate thrombin activation via PAR-1 can be inhibited clinically.
- Result in net anti-thrombotic effect, but platelet activity for other activators is maintained (ADP, Collagen, Fibrin).
- Potential ability to block platelet activation during bypass, and preserve function post bypass.
- Aprotinin no longer available, but this study may pave the way for development of PAR inhibitors.

Desmopressin:  
- Synthetic vasopressin analogue
- Increases plasma levels of Factor IIIV, VWF and tissue plasminogen activator.
- Multiple studies have evaluated DDAVP with mixed results. Overall, studies do not justify use as prophylaxis against bleeding associated with cardiac bypass.

Desmopressin cont…
- Studies do support use in patients with vW disease, mild Haemophilia A, or platelet dysfunction with positive response to test dose.
- Dosing is 0.3 mcg / kg and should be re-dosed at 6 hours.

Concluding Remarks:
- Coagulation is extremely complex.
- Platelets play a key role.
- CBP markedly disrupts this process.
- Ideally one could give a quickly reversible platelet inhibitor during CBP, and reverse it along with heparin thus protecting the platelet function.
- There is not a simple answer.....

References:
- Paparella D. Interim Care Med 2004;30:1873-81.
Accreditation in the USA and National Patient Safety Goals

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Objectives of this Lecture

- Discuss Regulation and Accreditation in the Health Care Industry
- JCAHO as a Form of Accreditation
- Quality Improvement & Sentinel Events
- NPSG – National Patient Safety Goals
- How does this all morph into P4P?

Why do health care facilities need accreditation?

- Health care consumes a major portion of national GNP for the United States.
- The American people will NOT permit the expenditure of that much money without some sort of oversight and regulation.
- Accreditation provides some minimal "standards" which all health care facilities should adhere to and it should encourage those accredited to constantly improve their care of patients.
- To be effective, that oversight should be "independent" of those who are to be accredited.

The beginnings of Accreditation and Standardization

- 1917 – ACS develops the “Minimum Standards for Hospitals” (One Page!)
- 1918 – ACS begins on site inspections. Only 89 of 692 hospitals surveyed meet the minimum standards.
- 1926 – 1st standards manual, 26 pages
- 1951 – The ACP, AHA, AMA, and CMA join with the ACS to form the JCAH (Joint Commission on Accreditation of Hospitals)
- 1978 – JCAH changed to JCAHO (Joint Commission on Accreditation of Healthcare Organizations)
- 2007 – Now called TJC (The Joint Commission)

So how did JCAHO get so much power?

- The federal law which formed Medicare, required these expenditures be monitored, ensuring that the government got real value for the money spent. Thus they set out the COP (Conditions of Participation).
- Hospitals (very wisely) realized the advantage of paying for (and thus designing) this monitoring and compliance with the COPs, rather than having the federal government do it for them.

Medicare and JCAHO

- Thus in 1965 JCAHO applied for (and was granted) "deemed status". Thus if you passed JCAHO accreditation standards, you were “deemed” to be in compliance with the COPs.
- The federal government still monitors JCAHO through random CMS surveys (usually on the heels of a JCAHO survey) AND through periodic broad reviews of JCAHO by the OIG.
Why do I need JCAHO?

- To get paid by Medicare - CMS (i.e. “Deemed Status”).
- A requisite for other payers
- Useful for hospital marketing efforts
- Does provide an outside, unbiased, standardized, assessment of quality of care
- JCAHO standards focus on
  - Structure
  - Process
  - Outcome

Other Accreditation Options

- HFAP (Healthcare Facilities Accreditation Program) - American Osteopathic Assoc.
- State/ CMS Inspection
  - Not really “easier” (but is cheaper)
  - Certainly not standardized to national norms
  - Can be influenced by “local” politics
  - Lack of experience
  - Marketing this certification is problematic

Accreditation “outside” of Hospitals - ASCs

- Initially the hospitals did not want to share the blessing of accreditation and grant “credibility” to free standing ASCs as a safe way to have surgery – BIG MISTAKE!
- Thus the formation of the AAAHC which now accredits the vast majority of ASCs.

Accreditation of Office Based Surgery

- The American Society of Plastic Surgeons mandated that to be a member of ASPS, you MUST only do surgery in an accredited facility (Hospital, ASC, Office).
- Thus they formed the AAAASF to provide their members with accreditation for the surgery done in their offices.

2007 JCAHO Accreditations

- Hospitals = 4,252
- Long Term Care Facilities = 1,173
- Ambulatory Care Centers = 1,204
- Laboratory Services = 3,016
- Home Care = 3,416

2007 JCAHO Accreditations

- Behavioral Healthcare = 1,787
- Office Based Surgery = 288
- Critical Access Hospitals = 350
- International Facilities = 10
  - Outside USA
### JCAHO Competition (2002)
- State/CMS Accreditation = 300
- HFAP Facilities Accreditation = 150

### Current “Hot Topics”
- National Patient Safety Goals
- Medication Management
- Infection Control
- Staffing Effectiveness
- Emergency Preparedness
- HIPPA
- ED overcrowding, Pain Management, Medical Staff Standards

### Basic Format for JCAHO Standards and Measures
- **Structure Measures (the simplest)**
  - Presence of proper equipment
  - Logistical support
  - Availability of medications (pharmacy)
- **Process Measures (the most frequent)**
  - Preoperative evaluation
  - Patient informed consent
  - Adherence to sterile technique
  - Method for credentialing and privileging.
- **Outcomes Measures (the most difficult)**
  - Rate of postop infection
  - Rate of hospital admission of outpatient surgery
  - Rate of successful resuscitations.

### Sentinel Events
- “An unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof”
- 1995 - JCAHO starts collecting reportable sentinel events.
- 2002 - JCAHO began National Patient Safety Goals (NPSG) that were linked to these sentinel events.

### Types of 4473 Sentinel Events Since 1995
- Wrong site surgery = 13% (592)
- Suicide = 12% (555)
- OR/Post op complications = 12% (534)
- Medication error = 9% (416)
- Delay in treatment = 7% (336)
- Patient fall = 6% (257)
- Restraint injury = 4% (164)

### Types of 4473 Sentinel Events Since 1995
- Transfusion error = 2% (108)
- Anesthesia related = 1.8% (79)
- Fire = 1.5% (68)
- Ventilator injury = 1.1% (50)
- Resulting in death = 71% (3257)
Where does this data lead?

- Communication, training, and patient assessment are prime root causes.
- Thus these causes have spurred things like the “time out”, standardized patient handoffs, labeling of syringes, etc.
- Unfortunately the incidence of wrong site surgery, while initially improving, has now leveled off. Still at the top of the heap in SEs.

Why are we not complying with the “time out” procedure

- Are we committed to it?
- It has never happened to me?
- Are ALL the team members present?
  - Surgeon, Anesthesiologist, Nurse
- We are rushed and say “I agree”?
- Many other items “added” to T/O?
  - Implants, positioning, antibiotics, equipment, etc.
National Patient Safety Goals

- Published yearly since 2002.
- Derived from the sentinel event data.
- Some are “retired” because they are solved (not very likely).
- Some are transferred into the JCAHO standards themselves (more likely).
- Many have distinct “subheadings” added as the years pass.

2008 NPSG #1

- Improve the accuracy of patient identification with at least two patient identifiers.
  - Do you always ask the patient to spell their name AND give you their birth date?
  - Do you check those responses against hard copy?
  - Do you think the patient thinks less of you when you meet them and appear to “not know their name”?
  - Do you identify by room number or surgery?
  - Do you look on the “time out” as useful?

2008 NPSG #2A

- Effective communication – read back of verbal orders/results
  - Are you now ONLY using verbal orders out of necessity or still out of convenience?
  - Do you appear aggravated when a nurse wants to “read back” to you?
  - Are non-MDs writing “verbal” orders that are really “routine” orders?

2008 NPSG #2B

- “Do Not Use” abbreviations.
  - With zeros – “Lead, Don't Follow”
  - Daily instead of Q.D.
  - 2gm. MgSO4 vs 2gm. MSO4 or MS
  - ug vs mg

2008 NPSG #2E

- “Hand off” protocols – ability to ask and respond to questions.
  - Different hand-off protocols?
  - Lunch breaks vs taking over a case completely
  - Signing out to nurses in PACU
  - Resident vs Staff
  - Does Staff perform their hand-off in the OR and include the resident?

2008 NPSG #3D

- Labeling of medications
  - Syringes, IV bags (going to PACU)
  - Review of syringes done in “hand off”
  - Content of the label
    - Drug
    - Dose
    - Date (if not destroyed at end of case/day)
  - “Syringe Swap” still a major cause of adverse anesthesia events!!
2008 NPSG #3E (NEW)

- **Safe use of anticoagulants**
- Products involved in harmful errors
  - #3 = Heparin
  - #6 = Coumadin
  - #9 = Lovenox
- 4/17 deaths = enoxaparin (LMWH)
- Unit dose, premixed infusions, smart pumps with drug libraries, standard protocols, frequent INRs, dietary interactions.

2008 NPSG #7

- **Hand Washing Compliance**
- So simple to do, low cost, why has it taken us this long to recognize?
- ID field has known this for years.
- We really have to make it a habit.
- How often is your anesthesia machine or computer interface wiped with a disinfectant?
- Especially important for Staff to model this behavior as we go from “OR to OR”.

2008 NPSG #8

- **Reconcile patient medications**
- Has been extremely difficult to do?
- Who does this?
  - Nurses ? or Physicians ?
- Do you use generic or trade names?
- Encourage patients to carry a legible listing of medications, dose, frequency.

2008 NPSG #9

- **Implement a fall reduction program**
- Remember this was still 6% of all sentinel events.

2008 NPSG #13

- **Encourage patients AND families to be actively involved in their care.**
- The days of “the doctor should not be questioned” are definitely over.
- Probably one of the most important and least cost patient safety strategies.
- Need an easy “reporting strategy” for patients and their families.

2008 NPSG #15

- **Identify risks of patient suicide.**
- #2 on the list of SEs
- Second only to wrong site surgery!
2008 NPSG #16 (New)

- Recognition and Response to Changes in Patient’s Condition
- RRT (Rapid Response Teams)
- Different from a “Code Team”
- Warning signs occur 6 – 8 hours before
- Critical events in 4 - 17% of inpatients
- Probably staffed by ICU team members so that timely transfer to ICU can be accomplished if needed.

NPSGs that Did Not “Make the List”

- Obstructive Sleep Apnea screening.
  - This was considered immediately after the ASA published their guideline
- Remember that these NPSGs will probably very quickly move into the area of “Pay for Performance”.
- ASA must consider all the above when they embark on developing any new guidelines.

Other NPSGs?

- Influenza and Pneumococcal vaccine was moved from 2007 NPSG #10 into the standards manual.
- Reducing Pressure Ulcers was moved from 2007 NPSG #14 into the standards manual.
- Surgical Fires #11 in AHC only?

Future NPSGs

- “Anesthesia Awareness” or more accurately “Unanticipated Intraoperative Awareness” (SEA 32).
  - How has your facility responded?
- Use of IT in assisting accurate patient identification.
- Effect of Health Care Worker (HCW) fatigue on safe patient care. (look to airline and trucking industries)

How can you have input into the JCAHO standards?

- PTAC (Professional Technical and Advisory Committee)
- ASA
  - Two representatives on the Hospital PTAC
  - Jerry Cohen, Bob Lagasse
  - Two representative on the Ambulatory PTAC
  - Walter Maurer, Lance Lichtor
- SAMBA
  - Two representative on the Ambulatory PTAC
  - Tom Cutter, Peter Glass

Using Reporting of Quality Measures in P4P

- Anthem demands annual reporting of measures and an option to renegotiate if compliance falls below 70%.
  - Quality processes, behavioral medicine, obstetrical care, cardiac care, hospital credentialing, ED/asthma/pneumonia care, joint replacement, cancer care, CHF, AMI, patient safety
- Other purchasers and payers:
  - Requiring submission of data with rates made available to employees
  - Pay-for-performance schemes being devised such as forgoing co-pay if employee uses hospital or doctors with good “scores”
The Leapfrog Group

- By “The Business Roundtable” CEO group.
- To encourage large employers to recognize and reward health plans and hospitals that make breakthrough improvements in patient safety and quality.
- Using preferential referrals and “other” market reinforcements (like $$$$).

Initial Leapfrog “Leaps”

- Computerized Physician Order Entry (CPOE)
  - Elimination of 80% of preventable drug errors
- Intensive Care Physician Staffing (IPS)
  - CCM trained M.D. on site or tele-monitoring, or risk adjusted outcomes comparison
  - 29% mortality reduction (JAMA, 11/02)
- Evidence Based Hospital Referral (EHR)
  - Volume, process measures, outcomes
  - >30% mortality reduction - 7 complex treatments

27 NQF “Safe Practices” Adopted by Leapfrog

- Adequate staffing ♦
- Prevention of:
  - Surgical site infection (SSI) ♦
  - Pressure ulcers
  - DVT (Deep venous thrombosis) ♦
  - Tourniquet – ischemia/thrombosis ♦♦
  - Malnutrition ♦
  - Wrong Site, Wrong Surgery ♦
  - Central line sepsis ♦♦
  - Contrast induced renal failure
  - Aspiration

27 NQF “Safe Practices” Adopted by Leapfrog

- Anticoagulation services
- Document DNR orders ♦♦
- Hand washing ♦♦
- Flu vaccination of healthcare workers
- Identify high alert medications
- Medication unit dosing
- Perioperative beta blockers ♦♦
- Verbal order readback
- Pharmacists active in medication use
- Standardized abbreviations
- Prevent mislabeled radiographs

IHI “Save 100,000 Lives” What Is It?

- IHI Campaign to save 100K lives across the U.S.
  - 1600 volunteer hospitals (free to participate)
  - Using six evidence-based interventions
  - Participating hospitals commit to at least one intervention and send mortality data as the main measure of the campaign’s ‘success’
The Six Changes that Save Lives

- Rapid Response Teams
- Acute MI (e.g., aspirin, beta blockers, timely treatment)
- Ventilator Associated Pneumonia bundles (plus other complications) ♦♦
- Central Venous Line care to reduce infections (bundle of 5 practices) ♦♦
- Surgical Site Infection Prophylaxis ♦
- Prevention of Adverse Drug Events with patient medication reconciliation

SCIP Measures
Surgical Care Improvement Project

- Mortality within 30 days of surgery
- 30 day re-admission rates
- Within 30 days of discharge
  - Post-op wound infection
  - AMI
  - Cardiac Arrest
  - PE
  - DVT
  - Pneumonia

SCIP Measures (continued)

- Surgical Site Infections
  - % On-Time prophylactic antibiotics **
  - % Appropriate antibiotics *
  - % With 24 post-op antibiotics
  - % BS <200 for 24° pre-op and 48° post-op**
- Cardiovascular Events
  - % at risk patients receiving beta blockers**
- Venous Thromboembolism
  - % receiving prophylaxis for VTE**
- Respiratory Complications
  - % ventilators with HOB greater than 30 degrees**

APR-DRGs – A new method of accounting for co-existing disease

- “Attempt to enhance the accurate coding of comorbid conditions so as to more accurately compare outcomes as displayed on public report cards.”
- System was developed by 3M.
- Is applied to “All Payers”, not just Medicare.
- 4 levels of “Severity of Illness” for each DRG.
- These are used to develop a “Risk of Mortality” score.

Who is using APR DRGs

- AHRQ (The Agency for Healthcare Research and Quality)
- HealthGrades
- US News and World Report
- Used in state-based performance reporting
  - 33 state agencies use APR-DRGs

Example: Usage of beta blockers following a heart attack

Map Source: John H. Wennberg
Clinical Research Roundtable/Institute of Medicine 2000

Great variation exists in the quality of health care people receive
Variation in care quality contributes to health care cost increase

NOTE: According to the American College of Cardiology the use of beta blockers following a heart attack should be 100% for all eligible patients without contraindications.
“Pay for Performance” Terms

- Value = quality/cost
- Efficiency = cost
- Provider: individual or group
- Pay for Performance (P4P): provider gets bonus for high scores on quality indicators
- Pay for Value (P4V): provider gets bonus for high scores on quality and efficiency indicators
- Not true P4P, but relevant:
  - Financial incentives for higher productivity, lower resource utilization, etc.
  - Gainsharing: Providers share in cost savings that they help to achieve. Alignment of incentives.

Results of a few major P4P initiatives (over 100 now running)

- **Bridges to Excellence**
  - Several large employers, health plans, provider groups
  - Grant from RWJ Foundation
  - Boston, NY, Cincinnati, Louisville
  - Physician Office Link, Diabetes Care and Cardiac Care Link
  - 500 physicians split $1 million in 2004
  - Implementation of processes related to patient safety and quality of care.

- **CMS/Premiere**
  - 270 hospitals, high performers on core measures split $7 million per yr, worst are penalized
  - 1st year: Median improvement in single composite quality score of 7.5%; composite quality score for heart failure improved 12%

More Results

- **Integrated Healthcare Association of CA**
  - Coalition of 6 health plans, 7 million enrollees, 5 years
  - 24,000 PCPs split $50 million in 2003
  - Evidenced based performance goals:
    - Clinical measures
    - Patient Experience (placed on public internet)
    - Investment in IT
    - 35K more mammograms, 10K more immunizations for children .....
New modes of ventilation in the operating room- do they matter?
David M. Polaner, MD, FAAP
Associate Professor of Anesthesiology
The Children’s Hospital, Denver and University of Colorado School of Medicine

In the not very distant past, intraoperative ventilation was a fairly simple matter, in no small part because of the lack of sophistication of the ventilators on our anesthesia machines. In the last decade, an odd phenomenon has emerged, whereby the machines have increased in sophistication while the anesthesiologist’s use of the new modes and features have not. Do new insights into how to ventilate patients in the operating room make any difference in their care and their outcomes, or are these additional modes and concepts just another set of gimmicks that Datex-Ohmeda and Draeger use to sell new machines? Is this stuff really any better for the average patient than the “conventional” volume ventilation scheme with 10-12ml/kg at a rate of 8 and no PEEP that we have commonly used for the past 3 decades? I will argue that these new modes are, in fact, significant improvements on the old way of doing things. We will examine different aspects of intraoperative ventilation: ventilation modes (pressure vs. volume, pressure support); PEEP, recruitment and atelectasis; and tidal volumes and lung injury, and try to ascertain their place and value.

Ventilation modes: pressure vs. volume ventilation

Pressure and volume ventilation are in reality not different modes of ventilation (they are both controlled modes), but rather are different variables of control within that mode. With volume ventilation, a preset volume of gas is delivered to the patient over a time determined by the clinician (the inspiratory time \(T_i\) or, on some machines, the I:E ratio). Note that the \(T_i\) on those machines varies with the set respiratory rate, an issue that can prove problematic at both high and low rates, if not compensated for by the anesthesiologist.

Once that volume of gas has been delivered, the flow ends, and (passive expiration is allowed to occur. Note that this pattern (as is depicted in the figure) is described as accelerating flow. Gas flow accelerates over the course of inspiration and full lung inflation is not reached until its end. Thus, the time that the alveoli are completely inflated and the lung is fully exchanging gas is short compared with the \(T_i\). With volume controlled ventilation, the patient is guaranteed to receive the set volume, but airway pressure will increase in response to decreased lung or chest wall compliance, increased airway resistance or anything else that restricts the delivery of that volume of gas, potentially subjecting the patient to high airway pressures. Volume ventilation may be a better guarantee of “even” or consistent breath-to-breath ventilation in a patient with rapidly changing compliance, but without some of the newer alterations to this mode.
(pressure regulated volume control, where volume targets are reached with limits on inspiratory pressure and decelerating flow patterns are generated—a “hybrid” mode combining the best aspects of both volume and pressure ventilation) it has distinct disadvantages.

During pressure-limited ventilation, the flow characteristics of the ventilator are different. As soon as the inspiratory valve opens, the circuit is pressurized to the set peak inspiratory pressure. This pressure is then held for the duration of the set $T_i$. Gas flow is initially high and then diminishes over the course of the inspiratory phase of the breath. This is a decelerating flow pattern. Note that in this pattern, the alveoli are held in full inflation for a longer percentage of $T_i$ (figure to the left). Note also the superimposed pressure volume curves in the figure. While both breaths reach the same volume (integration of the area under the curve), the peak inspiratory pressure is lower for the pressure cycled breath. The same volume can be achieved with lower pressure in this mode. Thus with pressure cycled ventilation we can (1) keep the alveoli fully inflated for a longer portion of the inspiratory phase of the breath, enhancing both gas exchange and lung inflation (2) achieve equal volumes with lower inflating pressures. This mode requires that the anesthesiologist monitor exhaled volumes and minute ventilation to ensure that consistent ventilation is being delivered in the face of changes in compliance or resistance (more about this later and what it may mean).

**Pressure support ventilation**

Pressure support is a new addition to operating room ventilators, but has many applications during anesthesia. This mode was originally introduced to assist ventilation in awake patients with respiratory insufficiency so that they could “control the ventilator” instead of the reverse. In this manner, synergy between ventilator and patient could be easily achieved. In the operating room, pressure support has a different role. Before understanding how and why pressure support is useful, we should look at why one should even consider permitting spontaneous ventilation under anesthesia.

Classic research done by Allison Froese more than 30 years ago demonstrated that the diaphragm effectively compensates for the increased load of the abdominal contents that press up against it in the spontaneously breathing supine subject. The mechanically ventilated paralyzed diaphragm, however, moves mostly against its path of least resistance—the nondependent regions where there is the least load (that is, there is less abdominal pressure resisting the displacement of the diaphragm). Thus, under conditions of mechanical ventilation in the supine patient, dependent lung regions receive less ventilation, but because of gravitation effects, receive more blood flow. This worsens ventilation perfusion matching (a problem that is exacerbated by the blunting of HPV by inhaled anesthetics), decreases FRC and promotes atelectasis at the lung
bases. Although my explanation here is a somewhat simplified mechanistic approach (see Froese, Anesthesiology 70:887-890, 1989 for a discussion of some of the limitations and caveats to her original work, including the importance of the differential contributions of the costal and crural regions of the diaphragm, which act as two distinct muscles), the basic suppositions regarding the effects of paralysis, positive pressure ventilation in the supine position and respiratory mechanics remain sound to this day. In a recent retrospective of her classic paper, Froese writes

Active contraction of the diaphragm definitely expands dependent lung regions better than a passive imposed breath of similar volume in supine and lateral decubitus positions. In fact, an actively “stiffened” diaphragm can make supine regional lung volumes and ventilation more homogeneous. Conversely, prolonged mechanical ventilation of the diseased lung in the supine position is characterized by loss of aeration in dependent regions.....The spontaneously contracting diaphragm preserves dependent lung volume and ventilation better than any passively imposed pressure pattern yet devised.2

Therefore, from a physiologic standpoint there are significant benefits to spontaneous ventilation. However, when allowed to breathe on their own, our patients often will hypoventilate when adequate depths of anesthesia are achieved. Furthermore, we impose additional burdens of work of breathing when we place endotracheal tubes and LMA’s in their airways. How can we achieve the benefits of spontaneous ventilation without hypoventilation? The answer is pressure support. With pressure support ventilation the patient’s spontaneous breath- that is, the sensing of negative pressure or gas flow in the inspiratory limb of the breathing circuit- triggers the ventilator to deliver positive pressure augmentation to the patient’s own spontaneous breath. The operator can set the trigger threshold level for the inspiratory flow rate at which that breath is sensed. Too low, and any chest wall motion will trigger a breath; too high and smaller breaths will be missed. For most adults, a threshold of 1L/min will be adequate, while children will usually require a lower setting of 0.2-0.6 L/min. Pressure support levels are set in cmH2O, usually as delivered pressure over PEEP. This should be adjusted to deliver a desired tidal volume (usually about 6 ml/kg).

Pressure support has proven especially useful with supraglottic airway devices like the LMA. Pressure support ventilation was shown to deliver more effective gas exchange than CPAP, as measured by ETCO2, SpO2 and exhaled tidal volumes (VT0). CPAP alone will only reduce the work of breathing through an LMA by improving upper airway patency, while the addition of pressure support can augment ventilation itself as well as assist in overcoming resistance from the breathing circuit and airway device.3 Pressure support has also been shown to speed inhalation induction of anesthesia.4 Unlike controlled ventilation, it is usually well tolerated during light levels of anesthesia.

**PEEP, atelectasis and recruitment maneuvers:**
PEEP is the primary means of maintaining alveolar recruitment and returning FRC towards awake values during controlled ventilation in the anesthetized patient. Atelectasis is a common complication of anesthesia and is, in combination with airway closure (when closing volume is greater than the end-expiratory lung volume), the cause of 75% of the deterioration of PaO2 that may occur during general anesthesia. Atelectasis causes a reduction of FRC and ventilation perfusion mismatch or intrapulmonary shunt, especially in concert with blunting of HPV from anesthesia. Airway closure can be injurious to the lungs, resulting in both inflammatory changes (infiltration with PMN’s, elaboration of inflammatory mediators) and disruption of lung architecture (alveolar, epithelial and smooth muscle injury). There is evidence that part of what we call ventilator induced lung injury (VILI) may result from repeated opening and collapse of alveoli. This may be because the stresses induced on the alveolar walls are of sufficient magnitudes to cause structural damage. The transmural force on the alveolus to reopen atelectatic areas has been measured at 100cmH2O. Application of appropriate levels of PEEP can prevent the loss of FRC and homogeneity of ventilation in ventilated and paralyzed patients.

PEEP has effects on optimizing pulmonary blood flow as well as distribution of ventilation. PEEP has been shown to improve respiratory function, as measured by lung volumes, respiratory system elastance, pressure volume curves, and intra-abdominal pressure, in obese paralyzed and anesthetized patients. This study did not find a benefit in non-obese subjects, but other investigators have found that PEEP prevents derecruitment and optimizes lung mechanics in normal healthy patients during general anesthesia. Furthermore, PEEP was able to prevent atelectasis even in patients receiving high concentrations of oxygen (which promotes absorption atelectasis). CPAP, when applied during induction, may help to prevent the development of atelectasis. Excessive PEEP, of course, has potentially deleterious effects, including reduced cardiac output and pulmonary hyperinflation, so the lowest possible PEEP that prevents collapse should be used.

How do we know when atelectasis is occurring? Some clinical measurements and hints are relatively easy to use, and give us clues as well as to how to set PEEP to help reduce atelectasis after recruitment. One of the first signs that there is atelectasis should come from the physiological data cited above regarding the cause of hypoxemia. Rather than profound desaturation, a decline in SpO2 to the low 90’s may be an early manifestation. Concomitant with the fall is SpO2, there may be a change in compliance. If pressure limited ventilation is being used, one will notice a fall in exhaled tidal volume (VTe); with volume cycled ventilation, the peak pressures will rise. If your anesthesia monitor can generate pressure volume loops and calculate quasi-static compliance, the changes will be obvious (see figure on right; the larger outer loop is the...
reference or baseline loop while the inner smaller loop shows loss of compliance). This is a sign that alveolar collapse is occurring, and intervention with a recruitment maneuver is indicated.

There have been several methods described to perform recruitment; all are predicated on the need to transiently increase peak pressure to 30-40cmH$_2$O for a brief period, followed by returning to normal ventilator settings but with PEEP set at a higher value to prevent de-recruitment. One simple method involves setting the peak inspiratory pressure on the ventilator to 30-40cmH$_2$O, raising the PEEP so that the $P$- the difference between PIP and PEEP- is the same as before the recruitment maneuver, and holding this setting for about 5 breaths. When you return to normal ventilator settings, raise the PEEP by 2 cmH$_2$O. Alternatively, a manual vital capacity breath can be given and inspiration sustained for 20-30 seconds. When the breath is released, the airway pressure must not be allowed to fall below the new (higher) PEEP value.

**Low volume ventilation and “lung protective” strategies:**

The strategy of ventilation for patients with acute respiratory failure, especially ARDS, has changed dramatically in the last decade. Beginning with the studies of Amato, and subsequently corroborated by the multicenter collaborative ARDSNet trial, it is now generally accepted that some of the cause of VILI is overdistension of relatively normally compliant lung units. The shift from high (or what we might term “conventional”) tidal volumes of 10-12 ml/kg to 6ml/kg as target volumes has resulted in a dramatic fall in morbidity and mortality in ARDS. Additionally, data from Slutsky and others now implicate “volutrauma” as a potential cause of extrapulmonary organ injury, due to the liberation of inflammatory mediators and eicosanoids from the lung as a result of VILI. These substances enter the circulation, where they can then produce injury to distant organs such as the kidney. However, are these data applicable to our patients in the OR with normal lungs? Does short term ventilation with high tidal volumes and inadequate PEEP in patients without pre-existing lung injury during anesthesia lead to either lung injury or the potential for systemic inflammatory responses?

There are (to simplify matters) two mechanisms by which overdistension of the lungs may cause injury. The first is physical injury to the lung parenchyma- the shear stresses on alveolar walls can disrupt the architecture of the lung, harming the alveolar walls, the junctions between alveoli, the endothelium and the various cells that make up the functioning lung units. This has an effect on more than the actual structural integrity of the lung, because these cells have functions beyond gas exchange (surfactant production, etc.). Permeability pulmonary edema may also result from injury to the pulmonary microvasculature. The second mechanism of injury is mechanotransduction-overstretch and injury to lung cells, including intrapulmonary macrophages, may cause the release of cytokines and inflammatory mediators into the alveolar milieu and central circulation and promote cell injury, apoptosis, and activation of the inflammatory cascade.
There are two studies that compared low volume ventilation (6ml/kg with PEEP) to high volume ventilation (12-15ml/kg, no PEEP) in patients without pre-existing lung disease receiving anesthetics lasting less than 3 hours. The investigators did not detect differences in the levels of inflammatory mediators measured in blood or tracheal aspirate. They speculate that there needs to be a “priming” of the lung in order to be susceptible to this kind of injury, either by sepsis, pre-existing lung disease, or another systemic inflammatory state. However, a very recent study found significantly increased levels of some proinflammatory mediators as well as migration of inflammatory cells into the alveoli (measured with bronchoalveolar lavage (BAL), a better technique than tracheal aspirates) of patients without pre-existing lung disease who underwent prolonged anesthetics (>5 hours) with high volume (12ml/kg) ventilation as compared with low volume and PEEP. Another well controlled study of patients without pre-existing lung injury undergoing long operations compared low volume ventilation with PEEP with high volume ventilation and no PEEP and found that the high volume group had an increase in procoagulant changes in BAL fluid that was prevented in the low volume/ PEEP group. Deposition of fibrin within the alveoli may compromise pulmonary function, and is commonly seen in patients with ARDS, pneumonia, and sepsis. It is especially interesting to note that the seminal laboratory studies that first suggested that high ventilatory volumes and lack of PEEP produced volutrauma were done in animals without lung injury and ventilated for short periods of time.

Even though short-term ventilation with high volumes has not been found to be injurious, one must consider the suggestion by nearly all investigators (including those that did not find differences between low and high volume groups) that VILI may require a “primed” lung- a “two hit” hypothesis for the development of injury. One cannot predict the occurrence of adverse events during surgery and anesthesia (or always detect subclinical conditions that exist prior to surgery) that may provide conditions that make the patient susceptible to injury from high volume ventilation strategies. Furthermore, it is possible that the high volume ventilation may provide the “first hit” and that complications following the anesthetic may produce the “second hit”, thereby inducing an acute lung injury in the postoperative period. Low volume ventilation does not increase atelectasis as compared with traditional Vt in anesthetized patients without lung injury. Since there appear to be no negative effects of low volume ventilation, I can think of little reason not to adopt it as a routine strategy.

References:

2. Froese AB: Gravity, the belly, and the diaphragm: you can’t ignore physics. Anesthesiology 2006; 104: 193-6
among the face mask, laryngeal mask airway and endotracheal tube. Anesth Analg 2000; 91: 1381-8


Prophylactic Perioperative Beta Blockers: Pro

Glenn Gravlee
UCD & HSC
Denver

Beta-blockers are Good

• Prospective Studies
• Retrospective studies and meta-analyses
• ACC/AHA 2006 Beta-blocker update
• Conclusions and recommendations

Prophylactic β-blockers
What started the buzz?
• McSPI group – late 90s
• 200 general surgery Pts with cardiac risk factors randomized to atenolol from day of surgery to 7 days post-op
• Atenolol: lower incidence of ischemia by Holter monitoring (24% vs 39%)
• ND in periop MI or mortality, but decreased mortality in subsequent 6 mos (1% vs 10%)
  – Wallace A et al. Anesthesiology 1998;88:7-17

Prophylactic β-blockers
The buzz gets louder
• Poldermans et al., NEJM 1999;341:1789-4
• Vascular surgery: 112 Pts with new RWMAs on Dobut Stress Echo randomly assigned to bisoprolol or placebo
• Rx begins 7 days or more pre-op, continues to 30 days post-op
• Resting HR < 60 pre-op, <80 intra- and post-op

Results – Poldermans et al.

• Reduced cardiac death: 3.4% vs 17%
• Reduced nonfatal MI: 0% vs 17%

NEJM 1999; 341:1789

Beta-blockers are Good

• Prospective Studies
• Retrospective studies and meta-analyses
• ACC/AHA 2006 Beta-blocker update
• Conclusions and recommendations
2003 Meta-analysis of 11 trials
Stevens RD, Anesth Analg 2003;97:623
- (Not all trials were randomized or blinded)
- Noncardiac surgery
- Decreased ischemic episodes, nonfatal MIs, and cardiac death
- Number needed to treat to
  - Prevent MI = 23
  - Prevent cardiac death = 32

Peri-op beta-blockers for M&M Prevention: Systematic Review and Meta-analysis
Wiesbauer et al., A&A 2007;104:27-41
- 69 Randomized Trials met criteria (all but 24 were Cardiac Surgical Pts only)
- Principal findings for noncardiac surgery:
  - Reduced ischemia (OR 0.38 [0.21-0.69])
  - No difference in arrhythmias, mortality, MI, or length of hospital stay

Reduced myocardial ischemia and/or Enzyme release: Good enough for me
- True: Most perioperative ischemia doesn’t lead to MI, VT/fib, CHF
- Yet most periop MI is preceded by sustained ischemia – the link will eventually emerge
- So: oversensitive marker that has a low Positive Predictive Value, but it identifies a group at increased risk that probably benefits from β-blockade

Systematic Review and Meta-analysis
Wiesbauer F, Anesth Analg 2007;104:27-41
- Noncardiac Surgery MI Category: 12 of 69 clinical trials reviewed (45-921 Pts)
- Drugs: Metoprolol 5, Atenolol 2, Esmolol 1, Propranolol 1, Bisoprolol 1, Esm/metop 1, aten/labet/oxpren 1
- Surgery type: Vascular 5, “noncardiac” 3, lung 1, Ortho or intra-abd 1, total knee 1, General or Vasc 1,

βBs with mixed results
Lindenauer PK, NEJM 2005;353:349-61
- Retrospective review of 700K noncardiac surgery Pts at 329 US hospitals
- Retrieved data on βBs given within 2 days of hospitalization vs none
- Propensity scoring to reduce confounding factors
- Used a cardiac risk index score to assess effect of βBs on outcomes
βBs with mixed results
Lindenauer PK, NEJM 2005;353:349-61

- Pts with risk index of 3 or higher (Hx CAD, Hx CVD, Renal insuffic., DM, or high-risk surgery all = 1) were less likely to die in the hospital if they received βBs
- Pts with risk index of 1 or 2: no difference
- Pts with Risk index of 0: more likely to die if given a βB
  - But why did they get a βB? Complication perhaps?

Beta-blockers are Good

- Prospective Studies
- Retrospective studies and meta-analyses
- ACC/AHA 2006 Beta-blocker update
- Conclusions and recommendations

Strength of Recommendation
- Class I: Strong evidence of usefulness and efficacy, benefit >> risk (do it)
- Class II: Conflicting evidence
  - IIA: Weight of evidence favors (reasonable)
  - IIB: Less well established (consider it)
- Class III: Evidence/general agreement for lack of usefulness/efficacy, possibility for harm (don’t do it)

Quality of Evidence
- Level A: Multiple (3-5) population risk strata evaluated, multiple randomized trials, general consistency of direction and magnitude of effect
- Level B: Limited (2-3) population risk strata evaluated, single rand. trial or non-randomized trials
- Level C: Very limited (1-2) population risk strata evaluated, consensus of experts or case studies

Perioperative Beta Blockers
Class I Recommendations
- Continue βBs if on them for ACC/AHA Class I indications (ang, arrhyth, HT, etc.)(C)
- Give them to vasc surg Pts at high cardiac risk as a result of ischemia found on pre-op testing (B)

Perioperative Beta Blockers
Class IIa Recommendations
- Vasc Surgery plus known CAD (B)
- Vasc Surgery plus high cardiac risk (mult risk factors) (B)
- Intermed or Hi-risk nonvasc surgery plus known CAD or high card. Risk (B)
Perioperative Beta Blockers
Class IIb Recommendations
• Intermediate or High-risk procedure PLUS Intermediate Cardiac Risk (1 factor) (C)
• Vascular surgery with low cardiac risk who aren’t currently taking BBs

AHA/ACC 2006 βB Update
Their commentary
• Inadequate # randomized trials, often underpowered, often unblinded, highly variable Pt populations
• Titration of therapy (target HR) insufficiently established
• Optimal βBs or βB-subtypes not established
• Implementation timing, route, monitoring, and duration not well-established

Beta-blockers are Good
• Prospective Studies
• Retrospective studies and meta-analyses
• ACC/AHA 2006 Beta-blocker update
• Conclusions and recommendations

5 Commandments for using beta-blocker prophylaxis for QI or P4P
• I. Thou shalt only use Class I indicators to judge deficiency
  – Continuation in Pts taking β-blockers for angina, arrhythmias, hypertension, or other ACC/AHA Class I guidelines
  – Initiation in vascular surgery Pts at high cardiac risk as judged by finding ischemia on pre-op testing
• Corollary A: If you don’t want to be deficient, don’t test for ischemia pre-op in vascular surgical patients
• Corollary B: Corollary A will work better if you have a low threshold for pre-op β-blockers in leg revasc.

5 Commandments for β-blocker prophylaxis – (cont.)
• II. Thou shalt not penalize a physician for failing to implement indicated β-blockers prior to the day of surgery
  – It’s likely best to initiate blockade at least several days pre-op, but the jury is out

5 Commandments for β-blocker prophylaxis – (cont.)
• III. Thou shalt not give demerits for prophylactic β-blockers unless used for a Class III “indication”
  – Pts who have contraindications to β-blockers
  – This leaves room for judgment in Class IIa indications: Vasc surg plus stable CAD, Vasc surg plus multiple risk factors, Intermediate or high risk surgery plus multiple risk factors
5 Commandments for β-blocker prophylaxis – (cont.)

IV. Thou shalt not penalize a physician for failing to reach a target pre-op HR (e.g., <60) when (indicated) β-blockers are used

– It’s probably good to reach a target resting HR, and 60 is as good as any, but it’s only substantiated by one controversial study
– It’s probably MORE IMPORTANT to avoid perioperative tachycardia (HR >90 (?) in Pts with CAD or strong CAD risk factors). If Pt cardiac stress tested: avoid ischemic threshold

V. Thou shalt neither honor nor condemn physicians who use prophylactic β-blockers for Class IIb indications:

– Intermediate or high-risk procedures with a single clinical risk factor
– Vascular surgery Pts with low cardiac risk who are not taking β-blockers chronically

Poor man’s approach to Prophylactic Peri-operative Beta-blockade

Give Beta-blockers in the following clinical settings:

• [Assuming no contraindication]
• Vascular surgery below the diaphragm
• Symptomatic CAD
Step 1. Patient undergoing high-risk surgical procedure (e.g., intraperitoneal procedure, intra-thoracic procedure, suprainguinal vascular procedure)

Step 2: Does patient have any one of the following:
- Patient currently receiving a beta blocker as an outpatient
- History of coronary disease, which includes any one of the following: clinical history of myocardial infarction or angina, positive stress test (symptoms or not), presence of pathological Q waves on EKG, or prior CABG or PCI.
- History of peripheral vascular disease, which includes any one of the following: known carotid artery disease (for example: obstructive plaque, transient ischemic attack or cerebrovascular disease), prior endarterectomy, known thoracic or abdominal aneurysm, previous AAA repair, prior or planned peripheral vascular bypass, confirmation by doppler studies, or strong history of claudication.

Yes, one criterion are met

No criteria are met

Patient not a candidate for peri-operative beta blocker use

Step 3. Evaluate for absolute contraindications

- Cardiac conduction anomalies (e.g., 2nd or 3rd degree AV heart block in the absence of a pacemaker).
- Severe aortic stenosis (i.e., gradients > 50 mmHg or aortic valve area < 0.85 cm²).
- Resting heart rate less than 60 beats/minute or a systolic blood pressure less than 100 mmHg.
- Symptoms of heart failure or an ejection fraction < 35%.
- Evidence of pulmonary edema.
- Evidence of right ventricular dysfunction (greater than moderate)

Yes one or more are met

Page Cardiology Fellow

No criteria are met

Step 3. Evaluate for relative contraindications

1. Severe COPD
2. Severe reactive airway disease
3. Pulmonary hypertension

Yes one or more is met

Consider lower dose of metoprolol or esmolol (refer to pre operative order set)

No criteria are met

Refer to Pre/Post-operative beta blocker order set
Intracranial Aneurysms and AVMs: To IR or not to IR?
Tod Sloan

The advent of the detachable Gugleilmi coil and other advances in interventional radiology has made the interventional approach to intracranial vascular lesions a viable alternative to intracranial surgery. Further, although controversial, the International Subarachnoid Aneurysm Trial has indicated that the interventional approach may be associated with less morbidity than intracranial surgery for some patients such that the IR approach is commonly used in many institutions. Finally a new breed of neurosurgeon/interventionalists is emerging. This review will focus on the impact of the IR techniques on the practice of anesthesiology for intracranial aneurysms and arterio-venous malformations.

Intracranial Aneurysms

Intracranial aneurysms are not uncommon with incidental findings on MRI of 1.8% in adults\(^1\) and 0.2-9.9% by other means.\(^2\) Aneurysms over 10 mm in diameter often rupture presenting as subarachnoid hemorrhage (SAH) with the “worst headache of my life” where this is the leading cause (85%) of SAH. SAH occurs in 5-10 per 100,000 person years accounting for 25% of cardiovascular deaths since 25-50% of these patients die and many of the rest are substantially debilitated. Studies show that 63% of patients die after SAH; 61% within the first 2 weeks. Death is usually the result of a devastating SAH, rebleeding or delayed cerebral ischemia (including that from vasospasm).

For incidentally discovered aneurysms the annual rupture rate is 0.5-2%. Occasionally prodromal headaches (warning leaks) occur, but are misdiagnosed as migraine or sinus headaches. Aneurysms can also present due to mass effect (e.g. third nerve palsy), or as embolic stroke due to embolization of a thrombus formed in the aneurysm.

The most common location of aneurysms is at the branching of intracranial arteries. Those located at the basilar tip, vertebrobasilar or posterior cerebral distribution have a higher chance of bleeding. Rupture is usually caused by excessive wall strain (T) as promoted by the transmural pressure (P) (mean arterial pressure minus extra aneurysm pressure – usually CSF pressure) and as calculated by the Law of Laplace \(T=P*\frac{R}{2}\) assuming the wall thickness is unchanged. Here, as the aneurysm expands the limits of wall elasticity are exceeded and the aneurysm ruptures. In some, the wall stabilizes and “giant” aneurysms can be formed. Hypertension, activities involving valsalva and emotional strain increase the rupture rate by acute changes in wall strain.

The etiology of aneurysms includes an inherited tendency as well as an association with various connective tissue disorders (Ehlers-Danlos syndrome type IV, adult polycystic kidney disease, fibrous dysplasia, neurofibromatosis type 1, Marfan Syndrome and AVMs. Factors which are associated with increase risk of SAH include male gender when < 50 years, female gender when > 50 years, age (mean age rupture 52 years with increased risk above this), pregnancy (especially...
30th to 40th week and postparum), cigarette smoking, hypertension, and moderate to heavy alcohol consumption. It is currently believed that there is a genetic predisposition to aneurysm formation, likely through the inheritance of mitochondrial DNA.3

With SAH common symptoms besides headache include nucal rigidity and headache form meningeal irritation, focal neurological deficits, and alterations in mental status. These symptoms have led to the grading system of Hunt and Hess and more recently that of the World Federation of Neurological Surgeons which helps assess neurological injury and probable outcome.

The timing of the management of ruptured aneurysms has been a source of controversy in the past.4 The controversy results from the attempt to control the complications of rebleeding, vasospasm, and surgical morbidity that result following the initial rupture. Early surgery (3-4 days) has been prompted to reduce rebleeding which occurs within 2 weeks post rupture in 15-20% of patients and has an associated rate of 70-80% mortality. Early surgery has also been advocated to remove the extravascular blood products from the SAH that are thought to contribute to the incidence of vasospasm and its associated morbidity. However, surgery within a few days post SAH has also been thought to place the brain at risk due to the ischemia and altered physiology that results from the SAH. As such, controversy has developed between early (3-4 days) or late surgery (after 8 days); with few advocates for surgery in the intermediate period (5-8 days) when bleeding and vasospasm is particularly a problem. Few studies of early versus late surgery have been done and it is not clear if early or late surgery does make a difference (however surgery in the middle period is worse).5 Hence most surgeons operate 3-4 days after a SAH in good grade patients. It should be noted that some patients may require very early surgery due to the mass effect or raised ICP that occurs as a consequence of a large SAH.

**Choice of Management Surgical Clipping or Interventional Radiology?**

The International Subarachnoid Aneurysm Trial (ISAT) was a study in 2002 of good grade aneurysms (WFNS 1 and 2) where surgeons elected to have these patients randomized to IR coiling or surgical clipping.6,7 The study has been considered controversial due to patient selection, but the end result is that most feel that coil and surgery offer safe alternatives; each with advantages and disadvantages. Coiling has the advantage of a less invasive procedure than craniotomy, but not all aneurysms are amenable to coiling and rebleeding can be a problem if inadequate thrombosis is achieved. Endovascular coiling can be safely done within hours after aneurysm rupture. Complete obliteration of an aneurysm can usually be accomplished in 57-85% of cases if the neck is < 4 mm in diameter.8 Surgery has the advantage of definitive obliteration but the procedure carries more morbidity due to its invasive nature, especially in the first few days after SAH. Similarly, studies of rerupture rates after clipping or coiling also tend to suggest both techniques have advantages and disadvantages such that the choice should be based on the patient and aneurysm characteristics.9
As a result coiling or clipping are selected based on the local availability of the techniques and the specific aneurysm and patient characteristics. For example, patients at very high risk for cerebral morbidity may fare better with coiling. Patients with large SAH may require surgical approach to remove the hematoma. Aneurysms with very complex shapes and wide necks, fusiform aneurysm, when vessels arise near the aneurysm neck, on in patients with difficult vascular access to the aneurysm may not be amenable to coiling. Some authors also recommend surgery for large or giant aneurysms, MCA aneurysms, blister aneurysms and aneurysms associated with SAH. Coiling is recommended for basilar tip and trunk aneurysms, patients with subacute stage of SAH and those associated with medical complications that increase the risk of surgery. Many consider coiling the best alternative for unruptured aneurysms if they are amenable to coiling. In general, morbidity is lower with coiling but permanent occlusion of the aneurysm is better with surgery.

**Intraoperative Management During Aneurysm Surgery**

Perhaps the key management objective during surgery is blood pressure control. In particular, avoiding hypertension which can promote aneurysm rupture and bleeding with events such as induction, intubation, placement of the Mayfield headholder (pins), and skin incision. During the procedure, and particularly during temporary clipping, the maintenance of a controlled blood pressure (usually in the patient’s normal range) helps keep the brain perfused (especially if SAH has disturbed normal tissue perfusion). The days of deliberate hypotension for clipping have been replaced by “deliberate normotension” with temporary clipping being used to reduce the tension in the aneurysm and reduce the risk of rupture. If antihypertensive agents are needed to control blood pressure usually beta and alpha blockers are preferred (e.g. labetolol) since these agents do not vasodilate the brain aggravating brain swelling. Neosynephrine is often utilized for increasing blood pressure since it does not vasoconstrict the cerebral vessels potentially aggravating ischemia.

One special circumstance of blood pressure control is with patients who have vasospasm. In this case they may be undergoing “triple H” therapy with hypervolemia, hemodilution and hypertension; maintenance of the blood pressure at the target pressure will be important unless it needs to be reduced for the procedure. Another special consideration is the presence of CSF drains for the hydrocephalus that occurs when blood blocks the CSF drainage or when a drain is placed for decompression of the ventricles to improve the surgical exposure during an aneurysm clipping. The key issue here is to avoid opening the CSF drain at a time when a sudden CSF pressure drop could promote aneurysm rupture by a sudden increase in the transmural pressure (i.e. wait until the dura is opened. Otherwise the usual considerations for a craniotomy apply including management of glucose and brain swelling.

Brain protection during aneurysm clipping and coiling has received a lot of attention over the years since interruptions in cerebral blood flow during clipping (especially temporary clipping) may place the brain at risk. This is particularly true if
SAH has disrupted autoregulation or vasospasm is present. Laboratory studies suggest hypothermia, metabolic suppression (e.g. barbiturates), ischemic preconditioning (recombinant erythropoietin), hyperbaric oxygen, diazoxide, statins, and antibiotics are among the considerations. At present no clear methods have shown clear benefit and the recent IHAST study has suggested that even mild hypothermia is without clear benefit in good grade patients with SAH.\textsuperscript{11} We do know that preoperative nimodipine use in SAH, management of the glucose level and treatment of hyperthermia appear to be advantageous as does judicious mild hypertension during temporary clipping to improve collateral flow.

It is worth noting that patients who undergo surgical clipping or interventional approaches to aneurysm obliteration may have a transient neurological deficit recur. Here, a neurological deficit which developed with the SAH and resolved may recur with anesthesia. It is not clear why the repair or “rewiring” mechanism is reversed by anesthesia, but it is a well known effect.\textsuperscript{12}

**Management of Aneurysms in Interventional Radiology**

Anesthesia management during aneurysm coiling in interventional radiology has several anesthetic concerns.\textsuperscript{12} These include immobility (so that an x-ray can be taken for subtraction of subsequent films to highlight areas where contrast material is injected), management of anticoagulation, rapid recovery to allow neurological assessment, medical management of the patient, management of unexpected allergic reactions to the contrast material, management of sudden intracranial vascular rupture, and self protection from radiation. As such general anesthesia with neuromuscular paralysis and controlled ventilation through an endotracheal tube is usually chosen. Normocapnea or mild hyperventilation is usually chosen unless hyperventilation is required for control of elevated ICP. Nitrous oxide is avoided since it will enlarge small air bubbles which may be injected inadvertently during the catheterization.

A variety of agents are used to provide anticoagulation for these procedures. With heparin (70 units/kg) the target is an ACT 2-3 times baseline. Alternatives to heparin include thrombin inhibitors such as lepirudin and bivalirudin. Alternatively antiplatelet agents can be used. Anticoagulation is often reversed at the conclusion of the IR procedure unless permanent devices such as stents remain in the vasculature. Of note is that some antiplatelet agents (e.g. abciximab glycoprotein IIb/IIIa receptor agonist) are long acting and may increase the likelihood of major bleeding. Some agents (e.g. ticlodipine and clopidogrel) permanently alter the platelets ADP receptors.

In the event of a vascular rupture during coiling, the heparin needs immediate reversal (1 mg protamine per each 100 units heparin given) and mild hypotension may be indicated. Desmopressin has been reported to shorten the prolonged bleeding time of patients taking aspirin and ticlodipine. In addition, since ICP may rise, mannitol, 15 degree head up tilt, and ventriculostomy may be indicated. Seizures may also occur post rupture either as a reaction to the contrast or secondary to cerebral ischemia.
If vasospasm occurs then papaverine or calcium channel blockers (nicardipine or verapamil) may be injected or balloon angioplasty performed. Complications of papverine include monocular blindness, mydriasis, seizures, transient increase in ICP, hypertension, tachycardia and paradoxical worsening of vasospasm. Deliberate hypertension (usually using phenylephrine) to 20-30% above baseline may also be indicated. Similarly, if a vascular occlusive problem occurs then hypertension may be indicated to improve collateral blood flow as observed by the x-ray studies.

**Intracranial AVMs**

Cerebral AVMs consist of a tangle of vessels (a nidus) which connects one or more arterial feeders to one or more venous vessels and have an incidence of 0.5%. Some patients have one or more aneurysms within the nidus. Aneurysms may exist in the nidus. The etiology is thought to be congenital. About 12% are symptomatic with bleeding being the most common presentation. If the mass of blood vessels is sufficiently large (e.g. venous engorgement), and/or bleeding is marked, symptoms may also result from raised intracranial pressure. This bleeding is usually a low pressure venous bleed that is intraparenecymal or intraventricular so it is unlikely to present as a SAH. The chance of death after rupture is 10-15%. Seizures, headache or focal neurologic symptoms are the other major forms of presentation.

The treatment of AVMs depends on the size, location, and vascular pattern of the AVM and on the age and medical condition of the patient. In general, the goal is the restoration of normal blood flow to the cerebral tissue that may have its blood flow reduced by the “steal” through the AVM, treatment of seizures related to the AVM, and prevention of future bleeding. This vascular steal can lead to ischemia with associated focal neurological deficits or seizures.

Options for treatment include surgical resection, radiosurgery, and embolization of materials by interventional methods. Radiosurgery is often used when the location is difficult to approach surgically (e.g. brainstem, corpus callosum, basal ganglia, internal capsule, thalamus), especially if the AVM is small (< 3 cm). Embolization may be curative if the blood flow through the AVM is sufficiently occluded, but most often the management involves both interventional techniques and surgery.

The management of AVMs in most cases is actually a dual role of Interventional Radiology and surgical resection. In past years the AVM was taken to the OR and resected, but the outcomes were less than desirable. First, blood loss could be excessive due to the marked vascularity and, as such, deliberate hypotension was frequently used. However, because the AVM served as a bypass shunt to cerebral tissue, intraoperative hypotension caused further ischemia and cerebral injury to the bypassed tissue. Postoperatively, with the bypass removed, the previously bypassed tissue now had a marked increase in cerebral blood flow that it was not used to. This tissue, because of the ischemia related to the bypass, had abnormal autoregulation and this sudden increase in blood flow resulted in marked interstitial edema postoperatively (termed normal perfusion pressure breakthrough”). Alternatively, loss of the previous venous drainage in the AVM could lead to higher
venous pressures in the tissue such that this contributed to tissue swelling. This postresection edema could be a "malignant edema" resulting in substantial injury in its own right.

The resolution of these problems were solved for most AVMs by the use of interventional occlusion prior to surgical resection. Hence, prior to surgery the interventional placement of materials to reduce the blood flow through the AVM (often polyvinyl alcohol particles) was done. This restored the normal blood flow to the bypassed ischemic tissue so that the postoperative edema was reduced. It also reduced the vascularity of the AVM so that intraoperative bleeding was reduced and the anesthesia management could avoid hypotension and keep the blood flow to the cerebral tissue in the normal range.

In IR, the goal is a progressive occlusion of the blood flow through the AVM and care taken to avoid embolization of the glue into the draining vein which could result in venous outflow obstruction or pulmonary glue embolization. Two major approaches to anesthesia apply. The older technique was to use MAC or neuroleptic anesthesia so that the neurological examination could be conducted during embolization to detect when the major AVM flow was occluded and emboli were beginning to encroach on functional brain. When this is done SAFE (super selective anesthesia functional examination) can be conducted as well. Here, a small amount of a barbiturate can be given through the interventional catheter to determine functional brain tissue in the down stream area. This is similar to the Wada test used to look for hemispheric dominance.

Currently, general anesthesia similar to that described for aneurysm coiling is used since x-ray techniques are far more advanced. The considerations mentioned above regarding immobility also apply here.

Some special considerations apply to AVM which are not applicable to aneurysms. For example, the induction of hypercapnea can promote venous outflow from the cerebral venous system to help minimize the risk for inadvertent movement into the intracranial compartment. This situation applies especially to dural AVMs, extracranial AVMs, and during embolization of carotid-cavernous sinus fistulas. Of note is that one embolization material termed "Onyx" (ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide) which precipitates on injection and can lead to a characteristic odor in the patients breath such that nausea and distress may occur on awakening.

In some cases deliberate hypotension or induced bradycardia may be indicated with the injection of some cyanoacrylate "glues" which polymerize immediately on contact with blood. In this case a "flow arrest" allows the glue to set in the feeding arteries. A variety of methods have been used, including a sinus arrest using adenosine.

Once the AVM has been embolized and time given for the brain to adjust to the new blood flow, surgery can be performed. Similar to all craniotomies, including aneurysm clippings above, brain relaxation and glucose management are also important. Also similar to surgical clipping of aneurysms, temporary clips may be used in AVM resections. As such maintenance of normal blood pressure and intermittent pressure elevation (to improve collateral blood flow) or reduction may be used. Despite embolization, the management during the surgical resection must
include preparations for excessive bleeding and cerebral edema. Katayama has advocated the use of jugular bulb venous oxygenation monitoring to measure the shunt blood flow since the removal of the shunt will reduce venous oxygenation. In order to avoid hemorrhage or cerebral edema post surgery, normotension and euvolemia are usually recommended.

References


Update on perineural analgesia: Focus on lower extremity

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Introduction: Lower extremity surgery is particularly amendable to regional anesthesia and analgesia techniques, and perineural catheters offer the opportunity to extend potential benefits from single shot blocks for lower extremity surgery.

Lower extremity surgery
Prospective clinical trials support the use of continuous femoral analgesia after total knee replacement. Continuous femoral analgesia provides comparable or better analgesia with fewer side effects than IV PCA and epidural analgesia for at least the first 48 hours after surgery. The improved analgesia provided by continuous femoral nerve blocks resulted in faster short-term functional recovery of knee flexion during rehabilitation than IV PCA, but without significant differences between the two groups after 6-12 weeks. Use of a single shot femoral nerve block will also confer many of the same advantages without necessitating a burden on an Acute Pain Service. Patients undergoing outpatient lower extremity surgery have also been recently studied. Use of femoral perineural analgesia after ambulatory ACL repair leads to more consistent hospital discharge, less unplanned admission, and substantial cost savings. Popliteal fossa catheters also appear to be useful for ambulatory foot and ankle surgery patients. Thirty patients were randomized to receive either saline or 0.2% ropivacaine with a disposable infusion pump via a popliteal fossa catheter. During the infusion period, patients receiving ropivacaine had better analgesia, used less oral opioid, had less nausea, sedation, and pruritus, and better sleep patterns. Use of a popliteal fossa catheter may also improve ability to perform outpatient lower extremity surgery. A similar study enrolling 24 patients observed similar benefits and was able to discharge more patients on the same day with 0.25% bupivacaine (40%) vs saline infusions (0%). Popliteal catheters may also allow earlier resumption of activities of daily living for ambulatory surgery patients after foot and ankle surgery.

Update on Techniques: Use of high frequency linear arrays is also helping to improve visualization of femoral and sciatic nerves. Case series have described the successful use of ultrasound to guide femoral and popliteal blocks, and direct visualization may also improve catheter placement. Current controversies include whether ultrasound offers advantages in terms of efficacy and safety and whether ultrasound is better as a stand alone technique or combined with nerve stimulation. Stimulating catheters have also been used for continuous femoral and sciatic catheters (66 patients) with good success and similar stimulating characteristics as upper extremity placement. However when compared to non-stimulating catheters in patients undergoing continuous femoral analgesia after major knee surgery (TKR and ACL repair), efficacy of stimulating catheters was not different from regular femoral nerve catheters. Use of stimulating...
catheters for popliteal analgesia after foot surgery has also not been demonstrated to offer significant advantages over conventional non-stimulating catheters. Several recent RCTs have examined different techniques for continuous perineural analgesia for total knee replacement. Use of the posterior psoas compartment technique had been proposed to produce better block of the lumbar plexus than the femoral 3 in 1 approach. However, a RCT examining 3 in 1 (femoral) catheters vs psoas compartment (posterior) approach observed no differences in pain scores or analgesic consumption. Thus, the techniques appear equivalent with the femoral approach probably being technically easier. Within the femoral approach, a RCT has compared use of a nerve stimulator vs the loss of resistance fascia iliaca technique for placement of non-stimulating catheters. The fascia iliaca technique was equally effective and required less time than the nerve stimulator technique.

**Risks:** One prospective survey of 211 femoral catheters noted a 1.4% incidence of infectious complications and a 0.4% incidence of neurological complications after 12 months. Another recent survey of 1,416 patients receiving a variety of perineural catheters reported a 0.21% incidence of temporary neural injury and 0.07% incidence of abscess formation.

**AGENTS FOR CONTINUOUS PERINEURAL ANALGESIA**

**Local Anesthetics**

Lidocaine, bupivacaine, and ropivacaine have all been used as the primary local anesthetic for continuous plexus analgesia, with bupivacaine and ropivacaine being the most commonly used agents. The use of bupivacaine (0.1% to 0.25%) typically does not result in toxic blood levels when used for postoperative analgesia for 24-72 hours in current regimens. Typical venous total bupivacaine levels during continuous brachial plexus analgesia are 0.5-1.0 mcg/ml and during continuous lumbar plexus analgesia are 0.5-1.8 mcg/ml, whereas levels greater than 2 mcg/ml are considered toxic. In addition to local anesthetics, analgesic regimens may include clonidine or opioids. However, efficacy of these additives has not been demonstrated.

**Delivery of continuous plexus analgesia**

RCTs indicate that use of a background infusion + PCA provides superior analgesia, reduces local anesthetic consumption, and improves patient satisfaction when compared to infusion or PCA only administration for continuous popliteal analgesia. RCTs indicate similar findings in femoral catheters for PCA delivery but do not support the addition of a background infusion for femoral analgesia.

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ii Anesth Analg 2006:102:1234-9
iii Anesth Analg 2005:100:1822
iv Anesthesiology 2004:100:697
v Anesth Analg 2003:97:1303
vi Anesthesiology 2006:105:566
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ix CJA 2004:5:45
x RAPM 2003:28:309
Perioperative Nerve Damage: Diagnosis, Prognosis, and Prevention

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Overview

- Incidence
- ASA Closed Claims Project Data
- Etiology
- Types of Injury
- Pre-disposing Factors
- Electrophysiologic Testing
- Diagnosis
- Recommendations
- Postoperative Visual Loss (POVL)

Incidence

- Perioperative:
  Dhuner (1950) – 31/31,000 (0.1%)  
  Parks (1973) – 72/50,000 (0.14%)  
  Thompson (1988) – 30/26,167 (0.11%)

- Regional:
  Ulnar Nerve – 1/3005 Regionals, 1/2518 GETA  
  Spinal – 1/10,098 (Vandam, 1960)  
  24/40,640 (Auroy, 1997)  
  Epidural – 3/4227 (DeLeon-Casasola, 1994)  
  6/30,413 (Auroy, 1997)  
  Axillary – 0.2 – 19% (Ben-David, 2006)

ASA Closed Claims Project

- Database of 4183 Closed Claims
  Companies representing 50% of Anesthesiologists
- Nerve Damage in 670 Cases (16%)
  Ulnar 28% - (85% GETA)
  Brachial Plexus 20% - (16% Regional)
  Lumbosacral Root 16% - (93% Regional)
  Spinal Cord 13% - (58% Regional)
  Sciatic 5%
  All Others 46%


ASA Closed Claims Project (cont.)


<table>
<thead>
<tr>
<th>% Male</th>
<th>% Female</th>
<th>Median Age (y)</th>
<th>Age Range (y)</th>
<th>% of Total</th>
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<td>61</td>
<td>38</td>
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<tr>
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<td>67</td>
<td>48</td>
<td>44</td>
<td>1-80</td>
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<td>22</td>
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<td>58</td>
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<tr>
<td>All others (n = 156)</td>
<td>42</td>
<td>58</td>
<td>42</td>
<td>5-81</td>
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</tbody>
</table>

* P ≤ 0.01 versus non-nervous damage claim.
** P ≤ 0.05 versus non-nervous damage claim.

Claims for Nerve Injury Over Time


% of nerve damage claims by year
ASSA Closed Claims Project (cont.)
Cheney, et. al. Anesthesiology 90(4), April 1999, pp 1062-9

Primary Anesthetic Technique

- General
- Regional

% of Claims in group

Possible mechanism stated
Onset of symptoms
Immediate
Delayed
Unilateral
Bilateral
Lower body regional/USAC anesthetic

Multiple associated factors were noted in some cases.

Ulnar Neuropathy
Cheney FW et al, Anesthesiology 1999; 90(4): 1062-69

Ulnar Neuropathy
Warner MA et al, Anesthesiology 1994; 81:1332-40

Fig. 1. Distribution of patients with ulnar neuropathy by time from conclusion of the procedure to onset of first symptoms. The onset of symptoms was first noted more than 24 h after the procedure in more than one half of all patients. PAMI = postanesthetic recovery unit.

Ulnar Neuropathy
Warner MA et al, Anesthesiology 1999; 90(1): 54-59

- 7/1502 Patients = 0.46% incidence
- Non-cardiac surgery
Ulnar Neuropathy – Outcome
Warner MA et al, Anesthesiology 1994; 81:1332-40

- Of 1,129,692 non-cardiac patients, 0.036% developed persistent neuropathy lasting > 1 year
- Of 382 patients surviving > 1 year, 53% had complete recovery
- Other 47% had persistent pain and/or deficits
- 80% of sensory neuropathies had complete recovery vs. 35% with mixed motor/sensory neuropathy

Ulnar Neuropathy
Why Men?

- Ulnar nerve and posterior recurrent ulnar artery pass posteromedially to the tubercle of the coronoid process and are covered by skin, subcutaneous tissue, and aponeurosis of flexor carpi ulnaris
  - Tubercle is larger in men than women
  - Men have less adipose tissue overlying ulnar nerve at elbow (women have 2-19 times more)

Warner MA, Mayo Clinic Proceedings 1998; 73: 567-574

Ulnar Neuropathy
Prielipp RC et al, Anesthesiology 1999; 91: 345-54

- 50 Volunteers with forearm in three positions

Ulnar Neuropathy
Prielipp RC et al, Anesthesiology 1999; 91: 345-54

- 50 Volunteers with the forearm in three positions

Ulnar Neuropathy
Prielipp RC et al, Anesthesiology 1999; 91: 345-54

- Supination yielded lowest pressures at all positions

Ulnar Neuropathy
Prielipp RC et al, Anesthesiology 1999; 91: 345-54

- **A**
  - P < 0.001 by Mann-Whitney U test (supine vs. pronated and neutral)
  - P = 0.23 by Mann-Whitney U test (pronated vs. neutral)

- **B**
  - 30°
  - 60°
  - 90°
Ulnar Neuropathy
Prielipp RC et al, Anesthesiology 1999; 91: 345-54

- 16 Male volunteers

Ulnar Neuropathy - Am I Always at Fault?
Stewart JD and Shantz SH, Can J of Neurol Sci 2003; 30: 15-19

- Warner 1994: only 9% of initial symptoms noted in PACU
- Mechanism of injury noted only 6% (Kroll 1990) or 9% (Cheney 1999) of claims for Ulnar neuropathy; care deemed to have "met standard" in majority of cases
- Frequency and severity of Ulnar neuropathy unchanged over 20 years despite use of protection (Warner 1999)
- Stoelting (1993) noted no evidence that padding or positioning arms as recommended decreased incidence of injury
- Warner (2000) noted neuropathy occurs at the same rate in hospitalized patients who have not undergone surgery and anesthesia
- So – the answer is NO!

Median Nerve Neuropathy
Warner MA et al, Anesthesiology 1999; 90(1): 54-59

- Study of 1502 surgical patients
- 20 (1.3%) had symptoms of Carpal Tunnel Syndrome in perioperative period
- All had similar symptoms within 5 years preceding surgery
- Symptoms were transient
- Suspected causes: immobilization, tight bands near wrist, hyperextension, IV fluids resulting in edema under the transcarpal ligament

ASA Closed Claims Project (Cont.)

- Conclusions:
  1. Proportion of claims for nerve injury constant
  2. Proportion of claims for ulnar nerve decreased (most common)
  3. Proportion for spinal cord increased (most common for 1990s)
  4. Mechanism of injury not readily apparent in majority of cases despite extensive review (except SCI)
  5. 3:1 Male predominance in ulnar injury
  6. Delayed onset of symptoms in ulnar neuropathy (median 3 days)

ASA Closed Claims Project (Cont.)

- Conclusions (cont.)
  7. Ulnar neuropathy absent in pediatric population
  8. Most common mechanism of spinal cord injury:
     - Epidural hematoma
     - Chemical injury
     - Anterior spinal artery syndrome
     - Meningitis
     - Major factors in spinal cord injury:
       - Blocks for pain management
       - Systemic anticoagulation with neuraxial block

Etiology

- Compression
- Surgical Injury
- Traction/Stretch Injury
- Ischemia of Vasa Nervorum
  Most common final endpoint
Types of Nerve Injury

Neurapraxia
- Diminution or loss of function
- No anatomic injury
- Most common with positioning injury
- Recovery usually within 6 weeks
- No treatment necessary
- Complete recovery expected

Neurotmesis
- Axon, sheath, and connective tissue disruption
- Axon degenerates distal to injury; regeneration usually does not occur
- Neurosurgical reconstruction may be needed (recovery usually incomplete)
- Rehabilitation services needed
- Pain clinic services usually consulted for chronic pain control

Predisposing Factors
- Use of Tourniquet
- Hypotension
- Hypothermia
- Pre-existing Disease
- Use of Muscle Relaxants
- Positioning
- Regional Anesthesia
- Congenital
- Occupational

Predisposing Factors – Tourniquet Injury
- Causes damage by ischemia or mechanical deformation
- Ischemia alone tolerated for up to 6 hours
  - No permanent structural change
  - Function returns in 6 hrs if ischemia < 2 hrs
- Distortion of nerve under cuff likely mechanism
  - Maximal distortion under proximal edge
  - May be irreversible after 2 - 4 hrs
- Minimize injury: Wide cuff
  - Inflate just > arterial occlusion
  - Keep inflation brief

Axonotmesis
- Anatomic disruption of axon
- Preserved nerve sheath and connective tissue
  - (Epineurium and perineurium)
- Axon regenerates at rate of 1 mm/day
- Function may take a year or more to recover and may be incomplete
  - (Occurs by axon regeneration or sprouting of surviving neighboring axons)
- Physical therapy prevents joint and muscle degeneration

Fig. 4-6. Nerve injury from tourniquet represented diagrammatically, showing maximal deformation of the margins of a tourniquet. A pressure gradient is created (arrow), causing ischemia of the tissues included in the segment proximal to tourniquet. (From Okuda Y, Journal of Neurosurgical Anesthesiology 1992; 4:48-51.)
Predisposing Factors – Tourniquet Injury

- Large (A) fibers most susceptible to ischemia and mechanical damage
- Tourniquet injury manifested as:
  - Motor loss ($A_{\alpha}, B$)
  - Diminished touch, vibration, position ($A_{\alpha}, B, \delta$)
  - Preserved heat, cold, pain ($A_{\delta}, C$)
  - Absence of spontaneous paresthesias

Predisposing Factors – Preexisting Disease

- Acromegaly
- Alcohol Abuse (Liver disease)
- Amyloidosis
- Carcinoid
- Cryoglobulinemia
- COPD
- Diabetes mellitus
- Hereditary predisposition
- Hypoglycemia
- Hypothyroidism

Predisposing Factors – Preexisting Disease

- Hepatic failure
- Lymphoma
- Macroglobulinemia
- Malabsorption syndromes/Vitamin deficiency
- Monoclonal gammopathy
- Morbid obesity
- Multiple myeloma
- Polycythemia vera
- Porphyrias
- Uremia

ASA Closed Claims Database – Regional Anesthesia

- 1005 Regional anesthesia claims from 1980-1999
- 821 related to neuraxial block (368 OB + 453 non)

ASA Closed Claims Database – Regional Anesthesia – Neuraxial

- OB patients more likely to have temporary injury, unintentional IV injection, infections
- Non-obstetric patients more likely to have death/brain damage, hematoma, permanent injury

ASA Closed Claims Database – Regional Anesthesia – Neuraxial

- Hematoma, anterior spinal artery syndrome, and spinal cord infarct have high incidence of permanent damage
Janik, Daniel, MD  Perioperative Nerve Damage: Diagnosis, Prognosis, and Prevention

ASA Closed Claims Database – Regional Anesthesia – Neuraxial
Lee LA et al, Anesthesiology 2004; 101: 143-52

Table 6. Associated factors for epidural/spinal nerve damage in
Regional Anesthesiology 2004; 101: 143-52

<table>
<thead>
<tr>
<th>Factor</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65</td>
<td>67%</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>34%</td>
</tr>
<tr>
<td>Trauma in spine</td>
<td>30%</td>
</tr>
<tr>
<td>Spine deformity</td>
<td>26%</td>
</tr>
<tr>
<td>Intermittent placement of catheter</td>
<td>18%</td>
</tr>
<tr>
<td>Duration of procedure</td>
<td>18%</td>
</tr>
</tbody>
</table>

• Most hematomas are associated with a coagulopathy, usually iatrogenic (only 2/3 had intrinsic defect, one of those was pre-eclampsia)

• Increased motor block out of proportion to local anesthetic is primary presenting symptom (83%) followed by increased sensory block (53%), not back pain (25%)

• Critical factor in favorable outcome is time to treatment

ASA Closed Claims Database – Regional Anesthesia – Peripheral Blocks
Lee LA et al, Anesthesiology 2004; 101: 143-52

• Account for 13% of regional anesthesia claims

• Axillary 44%, IVRA 21%, interscalene 19%, supraclavicular 7%

• Death or brain damage associated with 11%

• Permanent nerve damage in 29% of claims
  14% Brachial plexus
  10% Median nerve
  4% Ulnar nerve
  1% Radial nerve
  1% Femoral/Sciatic nerves

• Temporary injury in 58% of claims (30% nerve damage)

Regional Anesthesia
Horlocker TT et al.  Anesthesia & Analgesia 2003; 96: 1547-52
Ben-David B et al.  Pain Practice 2006; 6: 119-23
Benumof JL.  Anesthesiology 2000; 93: 6: 1541-44

• Axillary Block:
  Single-shot:  0.2 – 19%  Continuous:  0.5%

• OK to place block while under GA?
  4298 lumbar epidurals placed under GA: no complications (no local used while asleepe)
  530 lumbar CSF drains placed under GA: no complications (no local used while asleepe)
  336 axillary blocks under sedation or GA in adults: new post-operative nerve injury in 2.6% of sedated and 4.1% of GA

• 4 cases of permanent cervical spinal cord injury following interscalene block performed under GA

Regional Anesthesia
Nerve Damage

• Needle Trauma

• Intraneural Injection

• Local Anesthetic Toxicity

• Local Anesthetic Additives
  Sodium bisulfite
  Epinephrine
  Chlorocresol

Regional Anesthesia
Nerve Damage

• Needle Trauma

  Interruption of perineural tissues breaches the blood-brain barrier, produces edema, herniation of neural contents

  Fascicle injury more likely with sharp bevel needles

  Penetration more likely with fine-gauge needles

  Penetration alone does not cause dysfunction

  Paresthesias: may (Selander 1977) or may not (Winchell 1985) be associated with more frequent nerve injury

Regional Anesthesia
Nerve Damage

• Local Anesthetic Toxicity
  -Factors: Duration of exposure
  -Concentration of local anesthetic
  -Small fibers (Aδ, B, C) more sensitive to chemical damage
  -Manifestations:
    Spontaneous paresthesia
    Deficits in pain and temperature sensation (Aδ, C)
    Preserved motor, touch, proprioception
Regional Anesthesia Nerve Damage

- Local Anesthetic Additives
  - Sodium Bisulfite
    - Antioxidant added to Chloroprocaine and epinephrine-containing solutions
    - In combination with low pH has pronounced neurotoxicity after intrathecal administration
    - Peripheral nerves more tolerant
  - Epinephrine
    - Increases toxicity of bisulfite solutions
    - Increased axon degeneration after intrafascicular bupivacaine injection

Predisposing Factors - Positioning

 Warner MA, Mayo Clinic Proceedings 1998; 73: 567-574

- Brachial Plexus
  - Dorsal extension and lateral flexion of head to opposite side stretches plexus
  - Abduction of arm>90° stretches plexus (>60°?)
  - Body weight on dependent axilla
  - Steep Trendelenburg against brace of shoulder can stretch plexus
  - Prone patient can pinch plexus between clavicle and first rib if rest is too medial; too lateral can displace head of humerus against plexus and stretch it
  - Also associated with median sternotomy

Warner MA, Anesthesiology 2000; 93(4): 938-42
Warner MA, Mayo Clinic Proceedings 1998; 73: 567-574

- Radial Nerve: compression against ether screen and humerus; trauma during insertion of arterial line or cutdown; trauma from drug injection
- Lower Extremity Neuropathies: Often associated with lithotomy position (15/991, 1.5% and 55/198461, 0.03%)
  - Risk factors identified: Prolonged duration (> 2-4 hours), current smoker, increasing age, diabetes/vascular disease, and thin body habitus (BMI<20)
  - Nerves commonly affected: common peroneal (81%), sciatic (15%), and femoral (4%)


186
Predisposing Factors


Electrophysiologic Testing: Electromyography
Aminoff MJ, Anesthesiology 2004; 100: 1298-303

- Recording electrical activity of muscle from a needle electrode inserted within it
- Presence and nature of abnormalities depend on affected component of motor unit
- Distribution of abnormalities indicates likely site

Electrophysiologic Testing: Electromyography
Aminoff MJ, Anesthesiology 2004; 100: 1298-303

- Findings suggestive of denervation:
  - Abnormal spontaneous activity (fibrillation potentials; positive sharp waves) – take 1-4 weeks to develop, disappears with reinnervation
  - Abnormalities of motor unit recruitment
    - Varies with degree of weakness
  - Therefore, EMG helpful in determining if weakness has neurogenic basis and extent of injury
    - Possible to distinguish radiculopathy, plexopathy, neuropathy, number of nerves involved

Specific etiologic diagnosis cannot be made
- Configuration of motor unit potentials help determine duration of injury and if reinnervation is occurring
- May provide guide to time of onset and chronicity

Electrophysiologic Testing: Nerve Conduction Studies
Aminoff MJ, Anesthesiology 2004; 100: 1298-303

- Permit assessment of function in motor and sensory nerves:
  - Conduction velocity
  - Size of muscle response estimates number of axons and muscle fibers activated
- Evaluates functional integrity of peripheral nerves:
  - Localize focal lesion
  - May reveal presence of subclinical neuropathy making nerves more susceptible to injury
  - May suggest underlying pathologic process (axon loss vs. demyelination) with implication for clinical course and prognosis
Electrophysiologic Testing

- Nerve Conduction Studies combined with Electromyography can:
  - help determine whether lesion is complete vs. incomplete
  - determine basis of clinical deficit
  - localize lesion
  - define severity and age of lesion
  - guide prognosis and course of recovery
  - help distinguish various possibilities of etiologies inferred on clinical grounds

Electrophysiologic Testing: Timing of Examination

Aminoff MJ, Anesthesiology 2004; 100: 1298-303

- First 2-3 days following report of weakness:
  - Reduced recruitment—nerve lesion present
  - Presence of some units under voluntary control implies incomplete lesion—more favorable prognosis
  - If presence of abnormal spontaneous activity (fibrillation potentials, positive sharp waves) as well as small muscle response to distal stimulation

  Conclusion: either pre-existing lesion is responsible for findings, or perioperative injury was superimposed on a pre-existing lesion which made nerve more susceptible to injury

Evolution of EMG/NCS Changes

Aminoff MJ, Anesthesiology 2004; 100: 1298-303

- 4 Weeks after injury:
  - More information gathered such as site of lesion, severity of lesion, and nature of lesion
  - Serial studies:
    - Not needed — recovery can be followed clinically
    - If surgical reconstruction is considered for a clinically complete lesion which is not improving, then exam every 3 months since EMG may show voluntary motor unit activity (evidence of recovery prior to clinical signs)

My Patient Reports Post-operative Nerve Dysfunction – What Should I Do? (Diagnosis)

- A Complete History is Essential First Step
  - Context of a complete differential diagnosis
    - Predisposition
    - Anatomic variants
    - Occupational/Recreational hazard
    - Toxic exposure
    - Pre-existing disorder
    - Surgical injury
    - Anesthesia injury
  - Presentation may be obvious or subtle

Diagnosis (Cont.)

- Descriptions should be as objective as possible (no implication or innuendo)
  - Especially important is the timing of when the patient first noted symptoms!
  - Site of nerve trauma is often unclear; may never be precisely defined
  - Patient may question cause of pain; may be no simple explanation of cause, management, or course (Why?)
Diagnosis (Cont.)
Loeser’s 4 mechanisms of pain generation:
Peripheral terminal sensitization
Pathophysiology of primary afferents
Crosstalk between fibers
Dorsal horn physiologic changes

• Detailed Physical Exam
• Consult With Neurologist For Objective Documentation (Consult Early; Consult Often)

Recommendations
• Close attention to positioning and padding
  Would you be comfortable in the patient’s position?
• Close attention to pressures applied to surgical wound
  Check retracts periodically; Don’t lean on patient
• Careful regional anesthesia
  Use larger gauge, short bevel needles
  Avoid paresthesias?
  Use minimally effective concentration of preservative-free local anesthetic
  Do not place block (and inject local) while under GA

Diagnosis (Cont.)
• Electromyography
  - Early (can help determine if pre-existing condition is present)
  - Degeneration potentials appear ~ 3 weeks after injury
• Nerve Conduction Studies to Map Site of Injury Along Nerve Path (inching)
• Sensory Evoked Potentials
• CT/MRI if Neuraxial Hematoma Suspected

Recommendations (Cont.)
• Assess effect of current medication regimen (vincristine, vinblastine ?)
• Assess athletes for pre-existing injury
• Minimize tourniquet time
• Be aware of potential ischemic effects of pre-existing diseases
• Selective use of muscle relaxants and careful positioning in their presence

Recommendations (Cont.)
• Avoid hypothermia
• Avoid hypotension
  Limit periods of induced hypotension to that which is absolutely necessary to accomplish surgical procedure
• Consider risk/benefit analysis of neuraxial blockade in anticoagulated patients (and vice versa)
• Generous use of padding
  No evidence that any amount of padding will help
**Recommendations (Cont.)**

- If patient complains of nerve dysfunction post-operatively:
  - Note onset time/date of symptoms
  - Obtain Neurology consult immediately, asking for EMG/NCS work-up
  - Counsel patient that dysfunction is most likely to be temporary with good prognosis for recovery
  - Follow-up with repeat neurophysiologic studies about 2 weeks later

---

**POSTOPERATIVE VISUAL LOSS**

**Post-operative Visual Loss**
Roth S et al, Anesthesiology 1996; 85:1020-7

- 60,965 anesthetics from 1988-1992
- Non-ocular surgery
- 34 Patients (0.056%) with eye injury, 2 patients (0.003%) with visual loss
- Only 21% of all cases had discernable cause

---

**Equipment**

- Properly functioning automated blood pressure cuffs on the upper arms do not affect the risk of upper extremity neuropathies
- Shoulder braces in steep head-down positions may increase the risk of brachial plexus neuropathies

**Postoperative assessment**

- A simple postoperative assessment of extremity nerve function may lead to early recognition of peripheral neuropathies

**Documentation**

- Charting specific positioning actions during the care of patients may result in improvements of care by (1) helping practitioners focus attention on relevant aspects of patient positioning; and (2) providing information that continuous improvement processes can use to lead to refinements in patient care
Post-operative Visual Loss
Warner ME, Anesthesia & Analgesia 2001; 93: 1417-21

- 501,342 anesthetics from 1986-1998
- 405 cases of visual loss
- 216 regained full vision within 30 days
- 189 lost vision > 30 days

185 underwent ophthalmologic/neurosurgical procedure with tissue damage or loss
4 without tissue damage/loss = 0.0008%

Post-operative Visual Loss
Warner ME, Anesthesia & Analgesia 2001; 93: 1417-21

- None of 26,212 neuraxial blockade patients had visual loss
- None of 11,942 spinal surgery patients had loss > 30 days (8 had loss < 30 days)
- Data contrasts with 0.06% loss after cardiac surgery (Nuttall, 2001)

Post-operative Visual Loss
Warner ME, Anesthesia & Analgesia 2001; 93: 1417-21

- Possible factors:
  - Anemia
  - Hypotension
  - Surgical Duration
  - Combination

ASA POVL Registry

- Established by ASA in June 1999
- Goal is to obtain sufficient cases (100 or more) so associations can be made and investigated
- Presently have 131 cases reported as of June 2005
- 93 Cases (71%) were spine surgery

Most Common Procedures

- Spine surgery (67%)
- Cardiac surgery (10%)
- Liver transplant
- Thoraco- and abdominal aneurysms
- Head and Neck surgery
- Thoracotomy
- Others

Most Common Causes

- Ischemic Optic Neuropathy (ION)
  - Anterior – transient nonperfusion or hypoperfusion of nutrient vessels of optic nerve at the lamina cribrosa and scleral foramen
  - Posterior – compromised perfusion to optic nerve between optic foramen and entry of central retinal artery
- Central Retinal Artery Occlusion (CRAO)
  - Often caused by emboli; also associated with extraocular pressure with obstruction to flow
- Cortical Blindness
  - Damage to occipital cortex or optic radiation
Most patients are middle-aged (median=49)
- Long duration (median=8 hours)
- Blood pressure decreases (median=37% drop; deliberate hypotension used in 40% of cases)
- Large blood loss (median=2.3L)
- Anemia (median hematocrit=25%)
- Intraoperative course may be completely unremarkable
- 18% of patients were in Mayfield holder (ION can occur without pressure on eye)
Post-operative Visual Loss

Lee LA et al, Anesthesiology 2006; 105(4): 652-659

Table 6. ASAI-POVL Registry: Lowest Blood Pressure in Spine Cases with IOH (n = 83)

<table>
<thead>
<tr>
<th>Lowest SBP, minning</th>
<th>n (% of 83 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-11</td>
<td>1 (1)</td>
</tr>
<tr>
<td>12-13</td>
<td>7 (9)</td>
</tr>
<tr>
<td>14-15</td>
<td>17 (20)</td>
</tr>
<tr>
<td>&gt;16</td>
<td>36 (43)</td>
</tr>
<tr>
<td>&gt;17</td>
<td>12 (14)</td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (6)</td>
</tr>
</tbody>
</table>

Lowest MAP or SBP as % below baseline, minning
- < 20% | 6 (7) |
- 20-39% | 47 (57) |
- 40-49% | 21 (25) |
- 50% | 7 (8) |
- Unknown | 5 (6) |

Defined hypotension

ASA = American Society of Anesthesiologists; IOH = ischemic optic neuropathy; POVL = Perioperative Visual Loss; SBP = systolic blood pressure.

Post-operative Visual Loss

Lee LA et al, Anesthesiology 2006; 105(4): 652-659

Table 4. ASAI-POVL Registry: Type of Surgical Frames, Tables, and Headrests in Spine Cases with IOH (n = 83)

<table>
<thead>
<tr>
<th>Type of surgical frame or table</th>
<th>n (% of 83 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jackson spool table</td>
<td>25 (30)</td>
</tr>
<tr>
<td>Soft-crest rolls</td>
<td>17 (20)</td>
</tr>
<tr>
<td>Kneep-crest tables</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Other/unknown tables</td>
<td>12 (14)</td>
</tr>
</tbody>
</table>

Type of headrest
- Foam pad | 47 (57) |
- Mayfield pins | 16 (19) |
- Demetrius pad | 7 (9) |
- Other/unknown | 13 (16) |

ASA = American Society of Anesthesiologists; IOH = ischemic optic neuropathy; POVL = Perioperative Visual Loss.

Post-operative Visual Loss

Lee LA et al, Anesthesiology 2006; 105(4): 652-659

Table 3. Comparison of IOH and OULC Cases from the ASAI-POVL Registry (n = 83)

<table>
<thead>
<tr>
<th>IOH (n = 83)</th>
<th>OULC (n = 11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), yrs</td>
<td>59 (16)</td>
<td>46 (15)</td>
</tr>
<tr>
<td>ASA I or II</td>
<td>53 (64)</td>
<td>53 (64)</td>
</tr>
<tr>
<td>ASA III</td>
<td>24 (29)</td>
<td>24 (29)</td>
</tr>
<tr>
<td>ASA IV</td>
<td>3 (4)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Emergency</td>
<td>3 (4)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>34 (41)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Diabetic</td>
<td>5 (6)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>39 (47)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>3 (4)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Increased intracranial pressure</td>
<td>6 (7)</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Obesity</td>
<td>44 (52)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>&gt;1 Comorbidities</td>
<td>68 (82)</td>
<td>6 (5)</td>
</tr>
</tbody>
</table>

American Society of Anesthesiologists; OULC = optical nerve ulnar clonus; IOH = ischemic optic neuropathy; POVL = Perioperative Visual Loss.

Post-operative Visual Loss

Suggested Etiologies

- Blood supply to optic nerve is vulnerable
- Known variability in blood supply
- Atypical anatomic patterns
- Poor watershed perfusion zones
- Abnormal autoregulation
- Optimal range of hematocrit and blood pressure for adequate O₂ delivery to optic nerve unknown (particularly in presence of venous congestion in prone position)

Post-operative Visual Loss

Lee LA et al, Anesthesiology 2006; 104: 1319-28

Table 1. Summary of the Advisory

- There is a subset of patients who undergo spine procedures while they are positioned prone and receiving general anesthesia that has an increased risk for development of perioperative visual loss. This subset includes patients who are anticipated preoperatively to undergo procedures that are prolonged, have substantial blood loss, or both (high-risk patients).
- Consider informing high-risk patients that there is a small, unpredictable risk of perioperative visual loss.
- The use of deliberate hypotensive techniques during spine surgery has not been shown to be associated with the development of perioperative visual loss.

ASA Practice Advisory for Perioperative Visual Loss Associated with Spine Surgery

Anesthesiology 2006; 104: 1319-28
Colloids should be used along with crystalloids to maintain intravascular volume in patients who have substantial blood loss.

At this time, there is no apparent transfusion threshold that would eliminate the risk of perioperative visual loss related to anemia.

High-risk patients should be positioned so that their heads are level with or higher than the heart when possible. In addition, their heads should be maintained in a neutral forward position (e.g., without significant neck flexion, extension, lateral flexion, or rotation) when possible.

Consideration should be given to the use of staged spine procedures in high-risk patients.

References

- Warner MA et al. Ulnar neuropathy in surgical patients. Anesthesiology 90:54-9, 1999
- Hoflocker TT et al. Small risk of serious neurologic complications related to lumbar epidural catheter placement in anesthetized patients. Anesthesia & Analgesia 2003; 96: 1547-1552
- Aminoff MJ. Electrophysiologic testing for the diagnosis of peripheral nerve injuries. Anesthesiology 2004; 100: 1298-1303
- Auroy Y et al. Serious complications related to regional anesthesia: results of a prospective study in France. Anesthesiology 1997; 87: 479-486
Cardiac Anesthesia Update

Glenn P. Gravlee, M.D.
Department of Anesthesiology
University of Colorado Denver
and Health Sciences Center

CHF Rise in USA
new cases per year

- 550,000 new cases per year
- mortality
  - 5 yr = 50%
  - 10 yr = 75%
- transplants 1998
  - 2,348

Growth Area: Operations for CHF
- Transplant? Limited resources, but what about
- LV remodeling
- LV restriction devices
- Mitral valve repairs
- CABG or Transmyocardial Laser
- Destination Ventricular Assist Devices
- Artificial hearts

Indications for Ventricular Assist Device
- Irreversible ventricular dysfunction occurring after cardiac surgery
- Bridge to heart transplantation
- Destination therapy for nontransplant candidates

LVADs in Evolution
- REMATCH Trial (Rose E, NEJM 2001;345:1435)
- 129 NHYA Class IV Pts ineligible for transplant randomized to medical Rx or LVAD

<table>
<thead>
<tr>
<th>Survival</th>
<th>1 yr</th>
<th>2 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAD</td>
<td>52%</td>
<td>23%</td>
</tr>
<tr>
<td>Med Rx</td>
<td>25%</td>
<td>8%</td>
</tr>
</tbody>
</table>

HeartMate XVE LVAS (Electric)

<table>
<thead>
<tr>
<th>Left Bypass</th>
<th>HeartMate XVE LVAS</th>
<th>Right Bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Line</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannula</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XVE System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVAD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
LVAD Outcomes after REMATCH


- Prospective observational trial
- 309 Pts: NYHA IV, LVEF <25%, Peak VO₂ < 12 ml/kg/min or inability to wean from inotropes, ineligible for transplant
- 66 centers, 288 Pts consented

<table>
<thead>
<tr>
<th>Survival</th>
<th>1 year</th>
<th>2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVAD</td>
<td>56%</td>
<td>33%</td>
</tr>
<tr>
<td>(REMATCH)</td>
<td>52%</td>
<td>23%</td>
</tr>
</tbody>
</table>

Destination LVAD Pt Selection


Ideal Current Patient
- NYHA Class IV, LVEF ≤ 25%
- Who LACKS
  - RV failure
  - Evidence of liver dysfunction (albumin, AST, ALT, INR)
  - Evidence of renal dysfunction (BUN, Creat)

Post-LVAD Risk-stratified Survival


LVADs: Ongoing controversies

- Evolving medical therapy (but survival well below VADs)
- Improved but still high mortality; 30 day mortality INCREASES
- Expense
- Device selection and evolution
- Complications: 2 year device replacement or fatal failure rate: 73%! (Lietz K, Circulation 2007;116:497)

Axial Flow Pumps

Advantages:
- Fully implantable
- Small
- Silent
- No valves required
- Less complex

Disadvantages: Nonpulsatile, afterload sensitive

Axial Flow Pumps

HeartMate II
Jarvik 2000
Open LVADs: Anesthesia

• Fast-tracking isn’t helpful
• So, why not high-dose fentanyl (30+ µg/kg) – smooth low-maintenance technique?
• Want another excuse? HD fentanyl (50) showed lower incidence of cognitive dysfunction @ 7 d than LD fent (10) [but ND @ 3 or 12 mos]
  – Silbert BS, Anesthesiology 2006;104:1137

TEE and LVAD: Pre-implant

• Patent foramen ovale (beware of false neg)
• Atrial or ventricular thrombi
• Valvular function: aortic insufficiency, tricuspid regurgitation
• RV function
• Aortic outflow site disease

CPB separation problem: Right Ventricular Failure

Diagnosis:
• Elevated CVP
• Distended RV + Small LV
Contributors:
• Elevated PVR
• Pre-existing “masked” RV compromise
• Intracoronary air emboli
Result:
• Low LVAD flow

Management of RV Failure

• Maintain systemic blood pressure (MAP>60)
• Optimize RV preload
• Reducing RV afterload
  ♦ FiO₂ = 1.0
  ♦ Reduce PACO₂: 30ish
  ♦ BUT ALSO: avoid high peak & plateau pressures: Lower VT, higher rate, pressure controlled mode
  ♦ Avoid / treat metabolic acidosis: pH > 7.35
• Support RV function
  ♦ Dobut/epi, PDE-III inhibitors, PGE₁, NO
• Bail-out: RV assist device

Vasodilatory Shock
(adequate volume loading, adequate LVAD output, but inadequate BP)

Factors potentially contributing:
• ACE inhibitors
• Amiodarone
• Milrinone or dobutamine
• Arginine vasopressin deficiency
• (Sepsis)

Treatment
• Vasopressin (1-4 U/h)
• Norepinephrine (2-20 µg/min)
• [Epinephrine (2-20 µg/min)]

TEE and LVAD: Post-implant

• VAD inflow site: alignment, thrombosis, obstruction, valve function
• VAD outflow site: ditto
  – R/O dissection
• De-airing efficacy
• Ensure continous AV closure: R/O AI
• New R-L shunts (PFO mainly)
• Left ventricular filling and function
• Right ventricular filling and function
LVAD Summary

- (slow) Growth area
- Important anesthetic implications
- Post-VAD RV failure = BIG problem
- TEE is critical

Near Infrared Spectroscopy

“Cerebral Oximeter”

Chosen because
- Some new data
- Commercial “push”

NIRS Technology

The human skull and tissues are easily penetrated by near-infrared light

NIRS Mechanism:

Reflectance Spectrometer Optode (sensor)

Spatial resolution reduces extra-cerebral contamination

How is brain signal “isolated?”

- Oxygen Sampling Density plotted as a function of depth from surface
- 3 cm light-source to detector distance (blue)
- 4 cm light-source to detector distance (green)
- Subtracting the 3 cm distance from the 4 cm distance reveals rSO2 sampling (red)
- Approx 85% brain sampling

NIRS: Like a Pulse Ox except

- Reflection rather than transmission photometry
- Corrected for tissue penetrance rather than pulsatility
- Arteriovenous sampling mix assumed @ 25/75
**Gravlee, Glenn, MD**

### Cardiac Anesthesia Update

#### NIRS Cerebral Oximetry

**Advantages**
- Noninvasive
- Bilateral
- ACA/MCA watershed location
- Good Sensitivity (few false negatives) in vivo
- Fast response time

**Disadvantages**
- Variable Skin/muscle influence
- Undefined normal range
- Limited “depth” of info
- Variable arterial vs venous mix: fixed calc
- Specificity (common false positives)

---

**Meta-analysis**


- 48 reports, only 1 RCT (pre-Murkin 2007)
- No study reached Level I evidence, 75% were classified as Level V
- “NIRS validity has not been clearly established”

---

**rSO₂ and CABG Results**

Murkin JM, Anesth Analg 2007;104:51-8

- No difference in overall incidence of complications
- Control group: Significant difference in overall major organ complications (death, ventilation >48 hrs, stroke, MI, re-exploration)
- Study underpowered to assess any of these outcomes individually

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**NIRS Cerebral Oximetry**

Prospective Studies in Cardiac Surgery

Cardiac Surgery: Murkin JM, Anesth Analg 2007;104:51-8

- 200 Elective CABG Pts
- Intervention group: maintain rSO₂ > 75% of baseline: ck head position, PaCO₂ increase to ~40 (α-stat on CPB), MAP to >60 mmHg, CPP > 50 mmHg, CI to 2.5 L/M²/min, Hct to >20. If rSO₂ still low, Inc. FiO₂, give propofol, consider pulsatile flow

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**rSO₂ Reactions to Common Intra-Op Events**


---

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**Figure 1. Incidence of 30-day major organ morbidity and mortality. CVA is cerebrovascular accident; >48 Ventilation is patients ventilated postoperatively for >48 h. Overall incidence: P = 0.048**
Murkin Study Musings

- What if some of his interventions had been routine?
  - Maintain MAP > 60 mmHg
  - Maintain Hct > 20%
  - Use α-stat, but keep PaCO2 @ 37-43
- Maybe: Keep global CPB mixed SVO2 > 70 % via manipulations of flow, Hct, PaO2, and anesthetic depth/muscle relaxation
- Would findings be more impressive in higher risk Pts?

rSO2 Potential CPB Problems

- Large Hct shifts may influence readings
- Hypothermia and pH management impact P50 & O2:hemoglobin dissociation
- Hemoglobin O2 sat, even if accurate, may not reflect tissue O2 sat during CPB
- If PaCO2, does rSO2 reflect neuronal happiness or just “arterialization?”

Troubling Study

Schwartz G, J Neurosurg Anesthesiol 1996;8:189-93

- 18 cadavers (1-73 hours): mean rSO2 53±26% (range 1-73%)
- 15 healthy young adults: mean rSO2 68±5% (range 60-76%)
- 6 cadavers had rSO2 >60%

Explanation: “It is important to appreciate that tissue oxygen saturation may be near normal in dead or nonmetabolizing brain…” Edmunds HL, Sem Cardiothor Vasc Anes 2004;8:147

NIRS conclusions (so far)

- It may improve outcomes
- Important questions remain unanswered
- NOT standard of care
- Sensitivity > specificity
- [Costs approx $325 per case]
- Most promising use may be circulatory arrest and “low flow” selective CNS perfusion

Aprotinin Under Fire

- Mangano DT et al. – Observational study of 4374 Patients, NEJM 2006;354:353
- Propensity analysis – multivariate technique attempts to correct for lack of randomization
- Aprotinin: doubles risk of renal failure in complex CABG, 55% increase in risk of MI or CHF, 81% increase in risk of stroke/encephalopathy
- EACA and TxA: No increase in risks

Aprotinin under fire

Mangano study - cont

- Q: Were the patients receiving lysine analogues and aprotinin comparable?
- A: No, but propensity analysis did correct for 97 covariates (potential risk factors)
- Q: Why did MI/CHF/stroke pop up as risk factors?
- A: Unknown, and inconsistent with previous literature
Aprotinin: fanning the flames

- Karkouti K, Transfusion 2006;46:327
- Again, propensity analysis of 440 aprotinin patients vs 10,870 TxA patients
- Transfusion rates similar (consistent)
- Adverse events comparable, EXCEPT – renal dysfunction (creat increase >50% or new dialysis) in 24% of aprotinin and 17% of TxA patients (P<0.01)

Autumn 2006 Chronology

- Two studies referred to FDA
- FDA convenes advisory panel 9/21/06
- Bayer announces “coast is clear” approx 9/22 (FDA announces nothing)
- 9/27: Bayer informs FDA about internal safety data indicating that aprotinin may increase the chance for death, serious kidney damage, CHF, and strokes.

FDA Public Health Advisory Sept 29, 2006

- New study was done for Bayer by a contract organization
- 30,000 aprotinin, 37,000 alternate products
- “Using complex epidemiological and statistical methods, the report suggested that patients receiving Trasylol were at increased risk for death, kidney failure, congestive heart failure and stroke”
- www.fda.gov – search for aprotinin or advisories

Autumn 2006 Chronology -cont

- 9/29: FDA advisory says “Physicians should consider limiting Trasylol use to those situations where the clinical benefit of reduced blood loss is essential to medical management of the patient and outweighs the potential risks.”

Autumn chronology –cont.
NY Times

- 9/30: NY Times "Bayer… failed to reveal to federal drug officials the results of a large study suggesting that a widely-used heart-surgery medicine might increase the risks of death and stroke…"
- Reports Bayer said "it mistakenly did not inform FDA" because “it was preliminary in nature.”
- Advisory committee member (UCSF professor) calls Bayer’s failure to disclose even that this study was under way “appalling.”

FDA Product Labeling Revision
Around December, 2006

- Aprotinin administration increases the risk for renal dysfunction and the need for dialysis
- Re-administration of aprotinin within 12 months is contraindicated
- Now indicated only for patients undergoing CABG with CPB who are at “increased risk for blood loss and transfusion”
Controversy precipitates Pro-Con in January ’07 A&A

Major points for Pro:

- Only aprotinin has been associated with decreased stroke incidence, as much as 47%
- Coadministration of aprotinin and a lysine analogue may have occurred in Mangano study ("rescue" aprotinin?)
- ACE inhibitor presence may increase risk with aprotinin: higher risk Pts, more ACEs, more aprotinin, ACE inhibitors not included as co-var.


January A&A Pro arguments (cont)

- Previous studies did not assoc. renal failure with aprotinin (debatable)
- Propensity matching should at best be “hypothesis generating”
- Liberal definition of MI (Mangano) and of renal dysfunction (Karkouti)


Jan ’07 A&A Con


Major Arguments

- Aprotinin cost $> lysine analogue cost X4
- Blood conserving superiority of aprotinin over lysine analogues has not been demonstrated
- Aprotinin, with documented allergic reactions and potential for renal failure, may have an inferior safety profile

Jan ’07 A&A Con –cont


- Recent meta-anal.: 13 head-to-head studies (+ 4 added by authors) – ND in RBC transfusion (vs TxA)
- CVA, renal failure, and MI associated with xs blood loss/tfsn, so the absence of a reduction in those outcomes with 30% decrease in blood loss suggests toxicity, hence dec. stroke rate is expected
- RCTs are "gold std," but unrealistic for long-term outcomes follow-up (expense, inconvenience)
- Renal dysfunction with aprotinin has been shown even in RCTs, and is assoc w/ inc. mortal even without dialysis

As January snows melt and thoughts turn to spring…

- Mangano DT, JAMA 2007;297:471-9 (Feb 7 issue)
- Continuation of previous study: All cause death over 5 years. Same Pt population and statistical techniques
- Covariate-adjusted hazard ratios for death at 5 years
  - Aprotinin 1.48 (CI 1.19-1.85)*
  - EACA 1.08 (CI 0.8-1.33) (NS)
  - TxA 1.07 (CI 0.8-1.45) (NS)

FDA Independent Analysis of Mangano and Karkouti studies

- September, 2007

- Confirms renal effects
- Confirms mortality effects
- Does NOT confirm MI, CHF, and stroke effects

www.FDA.gov
www.Trasylol.com
Sept 12, 2007

- Report on the "missing" Bayer study
- Database study: 78K US CABG Pts 2003-6, aprotinin (43%) vs EACA (57%), risk-adjusted
- Risk Ratios (RR) are HD Aprotinin to "medium dose" EACA (10-20 gm total)
- Renal failure: RR = 1.6 (1.4-1.8)
- Death: RR = 1.74 (1.55-1.96)

www.Trasylol.com
Sept 12, 2007

"The results support the hypothesis that there is an elevated risk of death and acute renal failure in aprotinin recipients by comparison to similar recipients of aminocaproic acid. The findings are not readily ascribable to chance or to distortions arising from confounding factors."

So where does this leave us with aprotinin vs lysine analogues?
- Multiple studies strongly suggest hemostatic equivalency
- Aprotinin increases the chance of renal failure
- Aprotinin may increase mortality
- Lysine analogues: less studied, so toxicity profiles are less well-defined, but are very likely OK

So, why not use lysine analogues predominantly or exclusively?
Many people are

And for now, you must
- Aprotinin withdrawn from market at FDA request
- Rationale: Preliminary results of the large Canadian trial support Mangano's work to a substantial degree
- Will aprotinin come back?
  - Don't bet on it!
Case Study

It's now 3 pm and you get the dreaded call there is an emergency case for an exploratory lap that needs to go now!

Case Study

58 y.o. male with firm, distended abdomen and severe metabolic acidosis (lactate- 5.0) coming to OR for exploratory laparotomy

Vent Settings: Pressure Control - 34 Peep- 12 R-24, FiO2= 100%, PIP- 46

ABG: 7.20 / pCO2 - 50 / pO2 - 65

CXR- reveals 3 quadrant infiltrates

HR 110, BP 75/40, C.I. - 4.0 SVR- 458

Drips: vasopressin and insulin

U/O - 5 cc last hour

SV02 - 45%
What can we do to save this patient today... that perhaps we could not have a few years ago??

But first... is he "critically ill"?

What makes for a "critically ill" patient?

What is Sepsis... and is SIRS the same thing?

Infection
Parasite
Sepsis
SIRS
Infection
Trauma
Sepsis
SIRS
Parasite
Virus
Fungus
Bacteria
Severe Sepsis
BURNS
Severe SIRS
Shock

Adapted from SCCM/ACCP Consensus Guidelines

SEPSIS TIME COURSE

Unspecific Response to an aggression, determined by the presence of at least 2 of the following:
Temp $\geq$ 38°C or $\leq$ 36°C
HR $\geq$ 90 bpm
RR $\geq$ 20/min
Leuco $\geq$ 12,000/mm$^3$ or $\leq$ 4,000/mm$^3$ or >10% immature

Sepsis with at least 1 organ failure
Cardiovascular
Renal
Respiratory
Hepatic
Hematologic
CNS
Unexplained metabolic acidosis

SIRS + Infection
SIRS Sepsis Severe Sepsis

Severe Sepsis with refractory hypotension

SEPTIC SHOCK

Sepsis with at least 1 organ failure
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Cardiovascular
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Lewis Thomas - 1972

Germs, New England Journal Of Medicine

Our arsenals for fighting off bacteria are so powerful, and involve so many different defense mechanisms, that we are more in danger from them than from the invaders.

“We live in the midst of explosive devices; we are mined!”

Lewis Thomas - 1972

Germs, New England Journal Of Medicine

600 Patients with Severe Sepsis Die Each Day in the United States
“Except on few occasions, the patient appears to die from the body’s response to infection rather than from it.”

Sir William Osler – 1904
The Evolution of Modern Medicine

Burden of Severe Sepsis

- Annual incidence: ~750,000 cases in US
- Case fatality rate: 28% to 50%
- Direct costs – National costs: ~$16.7 billion
- Incidence on the rise:
  - Aging population
  - Incidence projected to rise to 1.0 million cases annually in US during the next decade


Reference Diseases

- Incidence in US (cases per 100,000)
  - AIDS
  - Colon and rectal cancer
  - Breast cancer
  - Congestive heart failure
  - Severe sepsis

- Number of deaths in US each year
  - Acute myocardial infarction
  - Severe sepsis

5 National Center for Health Statistics. 2001.

Severe Sepsis is deadly

Severe Sepsis is Common
Severe Sepsis is increasing in incidence

Severe Sepsis cases vs. US Population

Question: Why do Septic Patients Die?

Answer: Organ Failure

Severe Sepsis-Associated Mortality Increases With the Number of Dysfunctional Organs

Organ Failure and Mortality

PATHOPHYSIOLOGY

- The (abnormal?) host response to insult
- Prolonged shock state
  - Can be from any form of shock (hypovolemic, cardiogenic, distributive/vasodilatory, or obstructive)
- Cellular level: mitochondrial dysfunction and “cytopathic hypoxia”
- or METABOLIC FAILURE!
- Caused by too much Inflammatory

PATHOPHYSIOLOGY

- “2nd hit” phenomenon
  - The initial insult “primes” inflammatory system, and a second insult amplifies the response
- “Gut” hypothesis
  - GI tract is the “undrained abscess” causing MODS. The gut leaks bacteria/products
  - GI tract is largest immune organ (GALT)
Who believes bacteria translocate from the gut to blood and cause infection?

- Yes
- No

Bacteria DO NOT translocate from the gut to the blood!
The data are relatively clear for this... but gut failure is VITAL to prevent!

WHY ???

Gut Barrier Impaired by Malnutrition
Activation of Gut Immune System
Lung and Other Organs (kidneys) Injured by Inflammatory Mediators/Toxins Translated by Lymph

Animals Undergoing Trauma
- If lymph duct is not ligated all animals get ARDS and die
- If lymph duct is ligated, no ARDS, all animals live!
- Lymph from traumatized animals is toxic to cells

Deitch E et al.

CLINICAL MANIFESTATIONS of MOFS
- Patients appear to stabilize after resuscitation to a “hypermetabolic” state
- Lungs usually the first (ALI/ARDS) to injure
- Sequence of other organs influenced by co-morbidities
- Renal dysfunction usually follows second
TREATMENT

• THERE IS VERY LITTLE
  THAT CAN BE DONE,
  EXCEPT SUPPORTIVE
  CARE!!!!!

PREVENTION

• Best defined by literature that shows
  improved outcomes or survival in
  patients typically at risk for MODS
• Prospective, randomized, placebo
  controlled trials (PRCT’s)

Evidence-based Medicine
is only meaningful when...

WE EXAMINE ENDPOINTS
THAT MATTER!

Once we have a critically ill patient… What does the latest
literature say?

1) Does Not Work

2) May Work

3) Does Work
What Doesn’t Work

Colloid vs Crystalloid Controversy


Use of Dopamine in ARF:
Meta-analysis of 17 Randomized Trials

What Might Work

Surviving Sepsis
A global program to:
Reduce mortality rates in severe sepsis

Intent: to reduce mortality rates in severe sepsis by 25% in 5 years.
Initial Resuscitation

Goals during first 6 hours:

- Central venous pressure: 8–12 mm Hg
- Mean arterial pressure ≥ 65 mm Hg
- Urine output ≥ 0.5 mL kg⁻¹ hr⁻¹

Grade B

Conventional Physiologic Variables are Insensitive for Hypoperfusion

“Cryptic Shock”
- Scalea, Crit Care Med, 1990
- Dries, Crit Care Med, 1991
- Wo, Crit Care Med, 1993
- Schwartzberg, J Ped Surg, 1988
- Blow, J Trauma, 1999
- Rivers, NEJM, 2001

Hemodynamic Variables Related to Outcome in Septic Shock

Varpula et al; ICU 2005; 3:1066-1071

- Identify optimal threshold values of hemodynamics related to outcome
- Retrospective cohort
  - 6 and 48 hours analyzed separately
- Mortality rate 33%
- Univariate and logistic regression
- MAP of 65 mmHg, \( \text{SvO}_2 \) 70%:
  - Highest AUC

Mixed venous Oxygen Saturation > 70%

- \( \text{SvO}_2 \) is one of the most important number in critical care!
- It measures oxygen delivery to tissues better than any other number we have presently
- Is effected primarily by cardiac output, hemoglobin, oxygen saturation
- Should be > 70%
- YOU SHOULD LEARN TO FOLLOW THIS
Case Study

MOST IMPORTANT POINT OF LECTURE

• 50 yo AA male presents to ER with apparent cholangitis
• BP 140/70, HR 105, Sat 95% on 2 L NC O2
• He is talking to you and complains of RUQ pain

What is his mixed venous sat?

A. 29%
B. 45%
C. 60%
D. 74%

Case Study

MOST IMPORTANT POINT OF LECTURE

• What is his mixed venous sat?
  A. 29%

Case Study

MOST IMPORTANT POINT OF LECTURE

• So the next time you are in the OR and...
• You have a large abdominal case you have given 5 L of crystalloid to and your urine is marginal...
• How can you tell if your patient is resuscitated?
• Get a mixed venous gas from your triple lumen!

Case Study

MOST IMPORTANT POINT OF LECTURE

• Patient receives 3 L lactated ringers and 5 ug/kg/min of dobutamine...
• BP 140/70, HR 105, Sat 95% on 2 L NC O2
• He is talking to you and complains of RUQ pain

What is his mixed venous sat?

• 74%

Case Study

MOST IMPORTANT POINT OF LECTURE

• How do we measure:
  1) Draw venous gas from distal port of central venous catheter
  2) Use SVO2 central venous catheter to continuously monitor
  3) Use Swan-Ganz catheter
Why Does the MVO₂ Go Up in Severe Sepsis?

Microvascular Blood Flow Is Impaired in Severe Sepsis

Early Goal-directed Therapy for Septic Shock

- RCT, n = 263
- Septic shock unresp to 20 ml/kg crystalloid or lactate > 4
- Rx (all patients receive CVP and SvO₂ monitor)
  - Traditional: CVP 8-12, Vasopressor for SBP < 90 mm Hg, keep UOP > 0.5 ml/kg/hr
  - Investigation: As above + RBCs for hct < 30 AND SvO₂ < 70, if fails add dobutamine to dose 20 ug/kg/min

EGDT in Septic Shock:
Treatments actually received (0-6 hrs)

<table>
<thead>
<tr>
<th></th>
<th>Traditional</th>
<th>EGDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluids (mL)</td>
<td>3500</td>
<td>5000</td>
</tr>
<tr>
<td>RBCs (% patients)</td>
<td>19</td>
<td>64</td>
</tr>
<tr>
<td>Vasopressor (% pts)</td>
<td>30</td>
<td>27</td>
</tr>
<tr>
<td>Dobutamine (% pts)</td>
<td>1</td>
<td>14</td>
</tr>
</tbody>
</table>

Early Goal-Directed Therapy

EGDT - Outcome

*Key difference was in sudden cv collapse not MSOF

Rivers et al NEJM 345:1368 2001
An Outcome Survey of Sepsis Initiatives with EGDT Legend

Patients, No. (Mortality %)

<table>
<thead>
<tr>
<th>Program</th>
<th>Tot Pt No.</th>
<th>Pre-implementation</th>
<th>Post-implementation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loma Linda University (6-h bundle)</td>
<td>330</td>
<td>253 (39.5)</td>
<td>77 (20.8)</td>
<td>Shapiro et al</td>
</tr>
<tr>
<td>Birmingham Heartlands</td>
<td>101</td>
<td>52 (49)</td>
<td>49 (23)</td>
<td>Gao et al</td>
</tr>
<tr>
<td>Friedrich-Schiller (BOP)</td>
<td>60</td>
<td>30 (53)</td>
<td>30 (27)</td>
<td>Kortgen et al</td>
</tr>
<tr>
<td>Redding Medical Center (shock team)</td>
<td>85</td>
<td>36 (50)</td>
<td>49 (33)</td>
<td>Sebat et al</td>
</tr>
<tr>
<td>Beth Israel Deconness (sepsis team)</td>
<td>167</td>
<td>51 (29.3)</td>
<td>116 (20.3)</td>
<td>Shapiro et al</td>
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Summary of all centers: 1,298 patients, 675 (44.8%) ± 7.8, 627 (24.5) ± 5.5.

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<td>78</td>
<td>12 (32.5)</td>
<td>66 (21.7)</td>
<td>Rogove</td>
</tr>
<tr>
<td>St. Paul's Hospital, Vancouver</td>
<td>96</td>
<td>51 (46.7)</td>
<td>45 (23.2)</td>
<td>Steinstrom et al</td>
</tr>
</tbody>
</table>

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Concerns

APACHE II Score Correlates with 28-day Mortality in Sepsis Studies

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<thead>
<tr>
<th>Study</th>
<th>APACHE II</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drotrecogina Millipore 1995</td>
<td>26.0</td>
<td>30.8</td>
</tr>
<tr>
<td>LPS Lipopolysaccharide (Endotoxin)</td>
<td>25.0</td>
<td>31.9</td>
</tr>
<tr>
<td>Anti-IL-6 mAb (Loma Linda 1998)</td>
<td>21.8</td>
<td>35.0</td>
</tr>
<tr>
<td>PAF Acetohydrolase (Crit Care Med 2004; 32:332-4)</td>
<td>24.0</td>
<td>33.9</td>
</tr>
<tr>
<td>TFPI (JAMA 2005; 32:332-4)</td>
<td>25.0</td>
<td>33.9</td>
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<tr>
<td>G-CSF (Crit Care Med 2003; 31:367-73)</td>
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<td>25.5</td>
</tr>
<tr>
<td>Anti-IL-6 mAb (Loma Linda 1998)</td>
<td>28.8</td>
<td>42.8</td>
</tr>
</tbody>
</table>

R^2 = 0.95
Other Concerns

- The Rivers et al protocol calls for maintaining blood [Hgb] >10 g/dL.
- As a result, 2/3 of the patients in the protocolized arm received PRBC transfusions within the first 6 h, a three-fold increase over the control arm.
- To adopt such a practice nationwide would place large, new demands on the nation’s blood supply and hospital transfusion services.
- Furthermore, transfusion of PRBC is associated with a small but real risk of short and long-term side effects. Aged PRBC, which are deficient in 2,3-diphosphoglycerate and are relatively noncompliant, can decrease the delivery of O₂ to tissues.
- Additionally, in a large study of critically ill patients, Hebert et al. found no benefit to transfusion beyond a threshold [Hgb] of 7 g/dL.
**VASST trial**

- Large (≈ 800 patients) randomized, controlled trial
- Septic patients requiring norepinephrine (stratified for < 15 ug/min or > 15 ug/min)
- Patients randomized within 24 h to:
  - Vasopressin up to 0.03 units/min (OR)
  - Norepinephrine (control)

**VASST trial: Important Findings**

- In pts on < 15 ug/min of Norepi:
  - Vasopressin led to large statistically significant effect on improving mortality

**Bottom line:**
- If you are on high dose levophed nothing will help you
- On low dose levophed- addition of vasopressin improves survival

**Vasopressors**

- Not a replacement for norepinephrine as a first-line agent
- Consider in refractory shock despite high-dose conventional vasopressors
- If used, administer at 0.01-0.04 units/minute in adults

Grade E- (will change when VASST is published)

**Vasopressors**

- Either norepinephrine or dopamine administered through a central catheter is the initial vasopressor of choice.
  - Failure of fluid resuscitation
  - During fluid resuscitation

Grade D
Intensive Insulin Therapy in Perioperative and Critically Ill Patients

The New England Journal of Medicine


Intensive insulin therapy in critically ill patients

HYPERGLYCEMIA AND MORTALITY

Umpierrez et al J Clin Endocrinol Metab 2002;87;978

2030 consecutive admissions

Hyperglycemia (fasting > 126 mg/dl or > 200 mg/dl on two samples) : 38%

HEART

"Admission glycemia is an independent pronostic factor" : mortality and ventricular dysfunction (180 mg/dl)

Ishihara – Am. Heart J. 2003

Admission glycemia 144mg/dl = 3.9 more deaths.

Bolk – Int J Cardiol 2001

BRAIN

Admission hyperglycemia is associated with a 2- or 3-fold increase in mortality following focal or global brain ischemia

After brain trauma, a blood glucose > 200 mg/dl is an independent prognostic factor for poor outcome.

Rovlias – Neurosurgery 2000

INFECTIOUS RISK

Hyperglycemia is an independent predictive factor of severe postoperative infection

Furnary – Ann Thorac Surg 1999

Surgical ICU 2001 (N=1548)
Mortality S-ICU study: Kaplan-Meier plots


Mortality-benefit in S-ICU as function of duration of therapy

Vanhecke I et al. Chest 2007, in press

Long-term (up to 4 y) outcome cardiac surgery pat. in ICU ≥3d


Results: mortality MICU study


Compare medical with surgical ICU study

P-values obtained by Proportional Hazard Regression & Chi square

Medical ICU?
Mixed M-ICU / S-ICU population (N=2748)

Mortality-benefit in S-ICU & M-ICU for duration of therapy

Patients with history of diabetes (N=407)?

Concerns With The Leuven Studies ?!

CALORIC INTAKE: To Much TPN!

<table>
<thead>
<tr>
<th>ITT</th>
<th>CIT</th>
<th>IIT</th>
<th>&gt;3d</th>
<th>&gt;3d</th>
<th>&lt;3d</th>
<th>&lt;3d</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIT</td>
<td>15/6</td>
<td>15/8</td>
<td>20/6</td>
<td>19/7</td>
<td>10/5</td>
<td>10/5</td>
</tr>
<tr>
<td>CIT</td>
<td>160/66</td>
<td>161/64</td>
<td>179/85</td>
<td>179/84</td>
<td>141/62</td>
<td>143/60</td>
</tr>
<tr>
<td>PN</td>
<td>85</td>
<td>87</td>
<td>75</td>
<td>77</td>
<td>96</td>
<td>97</td>
</tr>
<tr>
<td>EN</td>
<td>40</td>
<td>38</td>
<td>67</td>
<td>64</td>
<td>13</td>
<td>10</td>
</tr>
</tbody>
</table>
RISKS OF HYPOGLYCEMIA

RATE OF HYPOGLYCEMIA

<table>
<thead>
<tr>
<th></th>
<th>Leuven 1</th>
<th>Leuven 2</th>
<th>VISEP</th>
<th>Glucontrol</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIT</td>
<td>5.0%</td>
<td>18.7%*</td>
<td>12.0%</td>
<td>8.6%</td>
</tr>
<tr>
<td>CIT</td>
<td>0.7%</td>
<td>3.1%</td>
<td>2.1%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

* Independent predictor of mortality

VISEP STUDY
488 patients in 17 centres

GLUCONTROL

488 patients in 17 centres

GLUCONTROL

Multivariable analysis: hypoglycemia < 60 mg/dl

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted OR</td>
<td>7.05</td>
<td>4.72 - 10.53</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>95 % CI</td>
<td>4.72 - 10.53</td>
<td>1.38 - 3.48</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

Multivariable analysis: hypoglycemia < 40 mg/dl

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted OR</td>
<td>4.29</td>
<td>2.10 - 8.76</td>
<td>0.0001</td>
</tr>
<tr>
<td>95 % CI</td>
<td>2.10 - 8.76</td>
<td>1.15 - 2.26</td>
<td>0.0077</td>
</tr>
</tbody>
</table>

Median (IQR)
Bottom Line

Insulin Should Be Started When Your Sick Patient GLUCOSE hits:
140-150 mg/dl

Bottom Line

Goal Glucose Levels in Sick Patients:
110-150 mg/dl

Steroids in Septic Shock: Poison or Panacea??

Survey on European ICUs in 2003
GLUCONTROL Study. Ph. Devos ESICM 2005

Glucose Threshold | IC Units
---|---
110 mg/dL | 3
120 mg/dL | 5
150 mg/dL | 19

Survey on European ICUs in 2003
GLUCONTROL STUDY. Ph. Devos 2005
Concerns With Steroids? Unpublished Data and Etomidate

"Physicians should be aware that etomidate inhibits adrenal steroidogenesis, and they should consider treating selected patients with corticosteroids if etomidate is used."

Wagner, RL et al. NEJM 1984 310:1415

What do we know now?

- The best treatment for septic shock is stress dose steroids in a select population of non-responders to ACTH who have also received etomidate (a medical adrenalectomy).
The CORTICUS Trial

Entry criteria similar to Annane – pressor-requiring septic shock (etomidate use discouraged)

Corticus: Low Dose Steroid Treatment in Septic Shock: 28 Day Mortality (Non-responders vs. Responders)

Patients with Relative Adrenal Insufficiency (ACTH Test Non-responders) (~51%)

- 100%
- 80%
- 60%
- 40%
- 20%
- 0%

28-day Mortality

- 38%
- 35%

Patients Without Relative Adrenal Insufficiency (ACTH Test Responders) (~47%)

- 100%
- 80%
- 60%
- 40%
- 20%
- 0%

- Low-dose Steroids
- Placebo

Sprung, ESICM September 2006

Balancing Ventilation Priorities

Inadequate Tidal Volume or PEEP

Consequences:
- Atelectasis
- Hypoxemia
- Hypercapnia

Excessive Tidal Volume or excessive PEEP

Consequences:
- V/Q mismatch
- Alveolar-capillary injury
- Inflammation
- Pulmonary hypertension
- “Barotrauma”

What Works

Excessive Tidal Volume or excessive PEEP

Consequences:
- Atelectasis
- Hypoxemia
- Hypercapnia

Inadequate Tidal Volume or PEEP

Consequences:
- V/Q mismatch
- Alveolar-capillary injury
- Inflammation
- Pulmonary hypertension
- “Barotrauma”

Ventilator Management

- Assist control mode
- Reduce TV to 6 mL/kg predicted body weight
- Keep plateau airway pressure <30 cm H₂O
- Maintain SaO₂ / SpO₂ 88%-95% using this scale:
  - FiO₂ .3 .4 .4 .5 .5 .6 .7 .7 .8 .8 .9 .9 1.0
  - PEEP 5 5 8 8 10 10 10 12 14 14 16 18 20-24

Ventilator Management

- Accept mild respiratory acidosis
  - If pH <7.30 increase rate (max 35)
  - If acidosis persists and rate = 35, consider NaHCO₃
The PROWESS Trial: Drotrecogin Alfa (Activated) in Patients with Severe Sepsis

- **Anticoagulant**
  - Inactivates coagulation factors Va, VIIIa
  - Inhibits formation of thrombin
- **Pro-fibrinolytic**
  - Allows activity of tissue plasminogen activator (endogenous TPA)
- **Antiinflammatory**
  - Reduces IL-6 and proinflammatory cytokines

Drotrecogin Alfa (Activated) in Severe Sepsis: Phase III Study

- Randomized 1:1
- Blinded
- Large N=1690
- Placebo-controlled
  - 164 centers
  - 11 countries
  - Severe sepsis

Infection + 3 SIRS criteria and acute (<24 hr) organ failure

Treatment in <48 hours

Day 28 Outcome

Routine Care

28-Day Survival All-cause Mortality

Mortality

<table>
<thead>
<tr>
<th>Percent Survivors</th>
<th>Days from Start of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Placebo (N=840)</td>
<td>100</td>
</tr>
<tr>
<td>Drotrecogin Alfa (activated) (N=850)</td>
<td>100</td>
</tr>
</tbody>
</table>

P=0.006 (stratified log-rank test)

% Survival:
- Placebo = 25.0%
- Drotrecogin Alfa (activated) = 30.5%

Mortality by Site of Infection

<table>
<thead>
<tr>
<th>Site</th>
<th>Placebo</th>
<th>Drotrecogin Alfa (activated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>25.0%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Lung</td>
<td>27.7%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Intra-Abdominal</td>
<td>22.3%</td>
<td>28.5%</td>
</tr>
<tr>
<td>Urinary Tract</td>
<td>21.2%</td>
<td>20.9%</td>
</tr>
</tbody>
</table>

Placement of patients at baseline:
- 906 in placebo
- 906 in Drotrecogin Alfa (activated)

Homeostasis Is Unbalanced in Severe Sepsis


Coagulopathy in Sepsis: A Driving Force in Organ Failure and Death


Impaired in Severe Sepsis: Role of Antithrombotics/Profibrinolytic

Xigris™ Indication

- FDA approved 11/19/2001
- Indicated for the reduction of mortality in adult patients with severe sepsis associated with acute organ dysfunction (patients with high risk of death eg, as determined by APACHE II). See Clinical Studies

High-risk vs Low-risk
Clear vs Unclear

Sepsis is like pornography. It’s hard to define but you know it when you see it.

ICU Scoring Systems
Is it Possible That Heparin Could be Useful in Sepsis/Infection??

- How do we monitor APC??
  - Clinically
    - Signs of bleeding
  - Laboratory
    - PT, INR, PTT, Platelets, HCT, Hgb, D-dimer
    - ? Protein C, APC, Fibrinogen
    - Factor VIII and Factor V
    - Factors II, VII, IX, X, XI, and XII

Problems with Xigris

- Very Expensive ($7000-9000) per treatment
- (Heparin is about $1 a day)
- Impossible to regulate coagulation
- Takes a long time to go away if patient needs surgery
- Indications??

Survival at 28 Days among Patients with Sepsis Who Received Low-Dose (or Low-Molecular-Weight) Heparin as Compared with Those Who Did Not

<table>
<thead>
<tr>
<th>Trait and Treatment Group</th>
<th>Survival at 28 Days</th>
<th>Days Alive on or After 30 Days</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>APC Total</td>
<td>354</td>
<td>548</td>
<td>0.09</td>
</tr>
<tr>
<td>APC group</td>
<td>218</td>
<td>234</td>
<td>0.20</td>
</tr>
<tr>
<td>No APC group</td>
<td>148</td>
<td>310</td>
<td>0.03</td>
</tr>
<tr>
<td>Sample size</td>
<td>576</td>
<td>576</td>
<td>1.00</td>
</tr>
<tr>
<td>APC subgroup</td>
<td>576</td>
<td>576</td>
<td>1.00</td>
</tr>
<tr>
<td>No APC subgroup</td>
<td>576</td>
<td>576</td>
<td>1.00</td>
</tr>
<tr>
<td>All patients</td>
<td>1152</td>
<td>1098</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*95% confidence interval, APC anti-thrombin complex, and ATIII antithrombin III.


Wischmeyer, Paul, MD

Critical Care Review
Other Important New Data You Should Be Aware Of!!

**“Appropriate” antibiotics**

Kollef, Chest 1999

- Inadequate antimicrobial treatment of infection
- Defined as microbiologic documentation of infection (ie, positive culture result) not being effectively treated at time of identification
- Absence of antimicrobial agents directed at specific class of microorganisms (absence of tx for fungemia due to Candida) and administration of agent to which microorganism responsible for infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Mortality in patient group</th>
<th>Mortality in matching group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trexus</td>
<td>15/1,000 (15.0%)</td>
<td>18/1,000 (18.0%)</td>
</tr>
<tr>
<td>ELEMENT</td>
<td>16/1,000 (16.0%)</td>
<td>27/1,000 (27.0%)</td>
</tr>
</tbody>
</table>

Mortality rate in this group was 52.1%

12.2% mortality in appropriately treated group versus 52.1% (NNT = 2.5)

**Invasive strategy for VAP diagnosis**

Fagon, Ann Int Med 2000

- Examined diagnosis of ventilator associated pneumonia via bronchoscopic BAL samples and their quantitative cultures
- Versus noninvasive isolation of microorganisms by nonquantitative analysis of endotracheal aspirates, and clinical practice guidelines.

Patients who recv’d invasive diagnosis had:

- Reduced mortality at day 14 (16.2% vs. 25.8%; p < 0.02)
- Decreased Sepsis-related Organ Failure Assessment scores at day 3 and day 7
- Decreased antibiotic use (mean number of antibiotic-free days, 5.0+/-5.1 and 2.2+/-3.5; P < 0.001).
Intensivist led multidisciplinary ICU team

Young, Effective Clinical Practice 2000

- Concept of closed ICU service led by ICU physician
- Up to 60% reduction in mortality

Optimal Hemoglobin in the Critically Ill Patient?!?

- Clearly higher Hgb achieved via transfusion is not helpful and may be harmful
- Is there a lower threshold?

Transfusion Requirements in Critical Care

- Multicenter, RCT
- Subjects
  - Acutely ill in ICU, Hgb < 9.0
  - Excluded if: chronic anemia, ongoing bleeding, admission after CABG

Transfusion Requirements in Critical Care

- Randomized to 2 strategies
  - Liberal strategy:
    - Maintain Hgb between 10-12
  - Restrictive strategy:
    - Maintain Hgb between 7-9
- Endpoints
  - All cause mortality, MODS
  - Predefined subgroups: age > 55, CAD, APACHE II > 20

Hebert et al. NEJM 1999; 340:409-17
Transfusion Requirements in Critical Care

**Conclusions**

- Lower transfusion threshold was as effective as higher trigger
- Lower threshold superior in some subgroups
- Mechanism of worse outcomes with liberal strategy unclear (? promotes cytokine cascade, increased risk of ARDS)

**MORE ICU-FREE DAYS**

\[ p < 0.0001 \]
**28-Days All Cause Mortality**

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>Z Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pontes-Arruda et al., 2006</td>
<td>0.448</td>
<td>0.201-0.995</td>
<td>-1.973</td>
<td>0.049</td>
</tr>
<tr>
<td>Singer et al., 2006</td>
<td>0.295</td>
<td>0.126-0.695</td>
<td>-2.793</td>
<td>0.005</td>
</tr>
<tr>
<td>Gadek et al., 1999</td>
<td>0.563</td>
<td>0.184-1.725</td>
<td>-1.006</td>
<td>0.315</td>
</tr>
<tr>
<td>Pontes-Arruda et al., 2006</td>
<td>0.404</td>
<td>0.241-0.678</td>
<td>-3.434</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Summary**

**NEW THERAPIES (cont)**

- **Intensivist led multidisciplinary ICU team**
  - Young, Effective Clinical Practice 2000
  - Up to 60% reduction in mortality

- **“Appropriate” antibiotics**
  - Kollef, Chest 1999
  - 12.2% mortality versus 52.1% (NNT = 2.5)

- **“Invasive” strategy for VAP diagnosis**
  - Fagon, Ann Int Med 2000
  - 16.8% mortality versus 25.0% (NNT = 10)

**LESS PROVEN THERAPIES (no good placebo controls)**

- Transfusion practices
- Pulmonary artery catheters
  - Have not been shown to improve outcome
- Veno-Venous ECMO for ARDS

A clinician, armed with the sepsis bundles, attacks the three heads of severe sepsis: hypotension, hypoperfusion and organ dysfunction. Crit Care Med 2004; 320(Suppl):S595-S597
FIBEROPTIC AIRWAY MANAGEMENT

Geoffrey Lane, MB, FRCA
The Children’s Hospital
Denver

TOPICS

1. Selection and care of equipment
   - Choice of fiberoptic endoscope
   - Video systems
   - Avoiding damage
   - Cleaning and sterilization

2. Navigation skills
   - Introduction
   - Rotation
   - Flexion (control lever)
   - Anatomic deflection and direction

3. Decisions
   - Awake vs. asleep
   - Oral vs. nasal
   - Nasal: tube first or scope first?

4. Problem solving
   - The tongue is in the way!
   - The larynx is hidden because the epiglottis is stuck to the back of the pharynx!
   - Laryngeal impaction and the S bend!
   - The scope is always misting up!
   - The view seems all wrong (upside down?)

5. Advanced applications
   - Pediatric intubations
   - Single lung ventilation – double lumen tubes and blockers.
   - Intubation through the LMA.
   - Intra-operative diagnosis of ventilation problems

(Revised January 2008d)
Section 1: Selection and care of equipment

Choice of fiberoptic bronchoscopes.

Most anesthesia departments have some access to fiberoptic intubating bronchoscopes, but selecting and maintaining a set of appropriate endoscopes is an ongoing responsibility.

Desirable features include:

- Insertion tube length 50 – 60 cm
- Appropriate diameter -for ETT’s likely to be used (including double lumen tubes)
- Flexible tip (cannot maneuver without it)
- Suction channel – useful but not essential - for local anesthetics, guide wires etc.
- Ease of cleaning and sterilization
- Compatibility with light sources and video equipment.
- Digital bronchoscopes have much better resolution, and should be less easily damaged
- Durability, Durability Durability!!!
- Price

The scopes that are designed for intubation are usually cheaper (approximately $1000) than corresponding diagnostic bronchoscopes, and have a thickened sheath covering the insertion tube to protect them from abuse by anesthesiologists (other than you, of course!) They lack some of the electronic photography exposure features of diagnostic scopes, but can still be used with a video camera, and are generally the best choice for anesthesiologists.

The basic “intubation” scopes represent a compromise in regard to diameter. As the diameter is reduced, the bronchoscope can be introduced through smaller endotracheal tubes and thus extended to pediatric use, and for examining placement of double lumen tubes. The disadvantage with smaller scopes is that when passed through large adult sized endotracheal tubes, there is a greater tendency for the tube to become caught on the laryngeal inlet. This can be very frustrating, but there are several methods to avoid or manage this problem (see page 9.)

Ultra thin pediatric scopes are available and can be used inside 3.0 mm tubes. They are soft, flimsy and more difficult to use. Though valuable for pediatric use, they are not suitable for routine intubations with endotracheal tubes larger than 4.0 mm. Ultra thin scopes may be required when examining the placement of small double lumen tubes and endobronchial blockers.

Price is obviously a major consideration, but repairs are so expensive that durability is even more important. We have found that the Olympus scopes withstand
punishment well, and have used a 20-year-old LF1 that had only been repaired twice despite frequent use and abuse by all-comers.

Olympus has digital bronchoscopes which use a video chip mounted on the distal end of the bronchoscope; the image is then transmitted electronically instead of using glass fibers to transmit an analogue picture. This improves the resolution dramatically, and the scopes should be less prone to damage because the image is transmitted electrically rather than by fragile glass fibers.

Storz has new scopes with good optical resolution. They have an integral camera head mounted on the scope, the video output produces a large, clear image compared with older systems. The Storz video systems can also be used with their videolaryngoscopes.

**Video Systems**

The purchase of a camera and video system significantly enhances a fiberoptic intubation system. (When did you last see your friendly orthopod doing an arthroscopy without an expensive video tower?)

When learning or teaching, technical maneuvers can be observed on the screen and corrected easily, whereas the novice using the eyepiece can only be guided by clinical evidence of success or failure. The video system is also valuable in difficult airways, when an assistant is needed to retract the tongue and soft tissues, or to help thread a guide wire through the scope. When the assistant can see the results of his efforts on the screen, the assistance is more effective.

Video use also has psychological advantages by involving the OR team. When the surgeons and OR nurses can share your fiberoptic exploits on the screen, they are much more likely to offer support and encouragement than when your endeavors are seen only as an irritating delay before they can have their fun!

**Avoiding damage**

Success in fiberoptic intubation requires continued access to a satisfactory fiberoptic system. There are several easy but expensive ways to damage the scope and render it unusable. We teach our staff and residents this mnemonic:

“**Please Don’t Damage This Thin Scope!**”

**etroleum** based lubricants such as Vaseline and lacrilube can penetrate the cover of the scope and cause separation of the fibers; use aqueous lubricants such as KY jelly or silicone.
rawe Don't leave the scope in the drawer of the endoscopy cart while connected to the light source; shutting the drawer will crush the glass fibers.

don't Don't leave the scope plugged into the light source when removing the endoscopy cart from the room - the light cable can easily be smashed on the door frame!

eath A good bite can crush the scope - if the patient is awake, protect the scope with a bite block or airway.

ube Advancing the tube down over the scope while bending the tip may damage the vulnerable, flexible tip section - always remove pressure from the control lever and keep the tip straight while advancing the tube.

- Bend The scope can be forced into an S-bend when the tube tries to continue passing down the esophagus while the scope remains in the trachea. If you encounter resistance when advancing the scope through the larynx, DO NOT FORCE IT! Try rotating the tube 90 or 180 degrees, or use an introducer. (See pages 9-10)

Cleaning and sterilization

There are several reports of disease transmission attributable to faulty preparation of endoscopes, including episodes of hepatitis, tuberculosis and more recently, pseudomonas. Ease of cleaning and sterilization is therefore essential.

Most modern scopes may be immersed in cleaning fluids or be subjected to gas sterilization. With increasing environmental concerns regarding use of ethylene oxide, we have found the use of automated fluid sterilization machines (e.g. the Steris system) to be efficient and easy to use. We have seen damage when hot plasma sterilization systems were used.

Section 2: Navigation Skills

Introduction

The simplest approach to intubation with a fiberscope is to point the scope so that the target (larynx) is in view, and then try to advance the scope towards the target or through it. This "point and shoot" approach works in many adult patients, and is the method most people use initially. The skilful operator develops more advanced navigation skills with experience, intuition and manual dexterity. These skills will be
demonstrated in the workshops, but understanding the basic principles can enable the student to advance more quickly.

Though the distal tip of the bronchoscope can be manipulated by the control lever, most of the insertion tube is deflected passively by the airway tissues. Learning how to pass the bronchoscope skillfully through the mouth or nose to the larynx requires recognition of how to use this deflection by the anatomic structures to one’s advantage.

There are three different types of maneuvers that can be used to control the scope; the expert is able to advance and navigate the scope smoothly through the airway by combining these controls effortlessly – just like a teenager operating a video game!

(1) Rotation
The bronchoscope can be rotated around its long axis by turning both hands together. The effects on the image are different when using observed through the eyepiece of an analogue bronchoscope compared with use a camera or a digital system.

The image transmission pathway in the insertion tube of an analogue bronchoscope is constructed of bundles of parallel glass fibers. The 12 o’clock position is marked by an indent or black triangle to assist in orientation. Rotating the scope through 90 degrees will cause the 12 o’clock marker to rotate correspondingly, but so long as the observer is viewing the target through the eyepiece, the target will not change position. (The image will be carried through different fibers, but the spatial relations between target and observer are the same.)

When using a digital bronchoscope, or when a camera is placed on the eyepiece, the image displayed on the screen will rotate as the insertion tube is rotated.

When using rotation to control the scope, it is easier for novices to keep the scope relatively straight by keeping both hands as far apart as possible, otherwise a big loop may develop, and the tip may flex in unexpected directions.

(2) Flexion (control lever)

The distal tip section of the scope bends up or down with light pressure on the control lever. The flexible (or bending) part of the scope is short, and flexing it does not necessarily control the remainder of the insertion tube. It is also the most fragile part of the scope, since it has to be covered with a thin, flexible covering, and can be damaged by excessive force and by sliding the endotracheal tube down and into the flexed tip.
Since intubation scopes are only flexible in one plane, it may be necessary to combine flexion and rotation when navigating difficult or ‘tortuous’ airways.

(3) Anatomic deflection and direction

The greater part of the length of the insertion tube is not controlled directly by the control lever, but responds indirectly to pressure against anatomic features as the scope is advanced. The operator can aim the scope as it enters the mouth or nose, and by directing it against structures (e.g. the palate), can encourage the scope to assume an optimum trajectory. This type of control is demonstrated more easily than it can be described, but should be mastered if the operator is to exploit the full potentials of fiberoptic intubation.

The chances of success improve when the endoscopist has good manual control of the scope and can keep the scope in the mid-line all the way to the trachea. Recognition of the mid-line landmarks facilitates navigation, for oral intubation they include:

**Posterior:**
- Raphe (fine white line) in palate, that leads to the -
- Uvula

**Anterior**
- Furrow, or groove, down mid-line of tongue, leading to the -
- Epiglottis

Failure to understand this principle of navigation is the reason for the scope passing into the esophagus even though the operator may have visualized the larynx clearly. The problem occurs during oral intubation when the scope is introduced directly backwards (see below, A) and the tip is flexed acutely upwards to see the cords. As the scope is pushed down the airway, the tip may still lie behind the arytenoids so that the scope enters the esophagus rather than the larynx (B.) This problem is more likely to occur in small patients; adults tend to be more forgiving because the larger distances involved allow the scope to bend more towards the intended direction.

A  B
Section 3: Decisions

Awake vs. Asleep

In adults, the difficult airway can usually be managed safely and more easily in the awake patient, using good topical anesthesia, with judicious sedation.

Children do not always cooperate well under topical anesthesia, and sedation for difficult pediatric airways can quickly lead to obstruction and hypoxia. I generally recommend an inhalation anesthetic for children between 12 months and 10 years, but the ability to maintain an adequate airway using a chin thrust maneuver is essential, and relaxants should usually be avoided.

There are many ways to achieve good topical anesthesia. I prefer to use viscous lidocaine first, and will then inject lidocaine through the suction channel of the scope into the larynx. Inhaling a nebulized solution of lidocaine is also effective if administered until the airway is anesthetized. It is easy to exceed therapeutic doses of local anesthetics and cause toxicity especially in smaller patients; the safe dose should be estimated before use.

Oral vs. Nasal

Nasal intubation is technically easier than oral intubation because the intranasal structures support the scope and facilitate a smooth advance. The convexity of the cervical spine helps to direct the scope forwards and away from the posterior pharyngeal wall towards the laryngeal inlet.
There are situations where oral intubation may be preferred for surgical access, e.g. for palate surgery. There is also a risk of bleeding with nasal intubation despite the use of vasoconstrictors, and can be a sufficient concern in the most precarious airways that oral intubation may be the first choice.

Oral intubation requires more dexterity and skill in keeping the scope towards the mid-line, and in small patients it may even be necessary to press the scope against the palate to achieve enough curvature to enter the larynx.

**Nasal: tube first or scope first?**

Passing the endotracheal tube through the nose before advancing the scope may appear easier than threading the scope through the nose first, but can cause bleeding that may jeopardize the intubation. The ETT is stiff enough to penetrate the posterior wall of the pharynx, causing a false passage, or it may perform a partial adenoidectomy.

With a little practice, the scope can be directed through the nose without tearing the mucosa and adenoids, and it will make the turn at the back of the nose more easily.

**Section 4: Problem Solving**

**The tongue is in the way!**

The tongue often presents a major visual obstruction when intubating difficult airways, especially when the patient is unconscious.

Maneuvers to pull it forwards include (1) the use of a chin thrust, (2) pulling the tongue out of the mouth with a dry sponge, and (3) mechanical devices/forceps. Of these, I find that a narrow, malleable surgical retractor can be shaped and used successfully in some of the most difficult pediatric airways. Using a regular laryngoscope to lift the tongue forwards is seldom helpful as the tip of the blade usually covers the glottis; a videolaryngoscope may be more helpful.

**The larynx is hidden, because the epiglottis is touching the back of the pharynx!**

This is what difficult airways are all about! In the awake patient, a deep breath will often lift the tip of the epiglottis off the posterior wall of the pharynx enough to allow the scope to be advanced.
The anesthetized patient is more of a challenge. A chin thrust by an assistant may help, but in extreme airways, it may be necessary to pull the tongue and soft tissues forwards using a dry sponge, or by using a malleable ribbon retractor bent to an appropriate shape.

### Laryngeal impaction and the S-Bend – or- ‘the tube won’t go down the larynx!’

Very frustrating! This happens when the ETT is much wider than the scope, and the tip of the ETT impacts on the ary-epiglottic folds or on the arytenoids. Once this has occurred, the situation can often be resolved by (1) pulling the ETT back over the scope a short distance and then (2) rotating it 90 or 180 degrees. The tube is then advanced again, this time with the tip of the ETT above the scope so that enters the glottis between the anterior commissure and the scope without impacting the ary-epiglottic folds. The problem may be anticipated and avoided by several strategies:

1. Selecting a fiberscope whose diameter is as close to that of the endotracheal tube as possible will usually prevent the problem.

2. The new endotracheal tubes manufactured by Parker Medical Systems have a special tip that bends inwards to reduce trauma to the mucosa as the tube is advanced. The tip will remain in touch with a fiberscope passing through the laryngeal inlet and should avoid the “S-bend problem.”

3. An introducer can be placed between the fiberscope and the endotracheal tube just as we use a dilator or introducer between the guide wire and catheter/sheath during central venous cannulation. Suitable devices include a straight chest tube, a small uncuffed endotracheal tube, or an Aintree Intubation Catheter (Cook Catheters.) The chest tube and Aintree have the advantage of being longer; an uncuffed endotracheal tube is so short that the larger ETT may have to be shortened by 4 to 6 cms.

The appropriate sizes when using an Olympus LF2 scope are:

<table>
<thead>
<tr>
<th>Outer ETT (mm, ID)</th>
<th>Introducer: A: Chest Tube</th>
<th>Introducer: B: Uncuffed ETT (Length)</th>
<th>(Ext diam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5 mm</td>
<td>-</td>
<td>5.0 mm</td>
<td>24.5 cm</td>
</tr>
<tr>
<td>8.0 mm</td>
<td>-</td>
<td>5.5 mm</td>
<td>27.5 cm</td>
</tr>
<tr>
<td>8.5 mm</td>
<td>24 FG</td>
<td>6.0 mm</td>
<td>28.5 cm</td>
</tr>
<tr>
<td>9.0 mm</td>
<td>24 FG</td>
<td>6.0 mm</td>
<td>28.5 cm</td>
</tr>
<tr>
<td>9.5 mm</td>
<td>28 FG</td>
<td>6.5 mm</td>
<td>29 cm</td>
</tr>
</tbody>
</table>

The scope is always misting up!
This problem is usually caused by allowing the tip of the scope to touch the mucosa. Careful navigation, keeping to the lumen of the airway, will eliminate this problem, but if it does occur, clean the end with an alcohol wipe. When using a video camera, a 'white out' is a warning that you are almost touching the mucosa - retreat and find the lumen before advancing!

Section 5: Advanced Applications

Pediatric intubations

1. **Guide wire method**: a regular intubation scope can be used to intubate infants (when an ultra thin scope is not available,) by threading a long (125 cms) guide wire through the suction channel into the trachea. Suitable J wires can be ordered (or "appropriated" from the cath. lab in an emergency), a 0.032" to 0.036" diameter wire is usually appropriate. The scope is then withdrawn over the wire, and an appropriate ETT advanced, using a small suction catheter inside the ETT to facilitate the advance.

2. **Ultra thin fiberscopes**: Pediatric fiberscopes such as the Olympus LFP, with a 2.8 mm diameter that fits inside 3.0 mm ETT's have extended routine fiberoptic intubation abilities to neonates. These scopes are much softer and are more difficult to control, but can be life saving.

Single lung ventilation - double lumen tubes and blockers

Fiberoptic scopes may be used to place and verify correct positioning of double lumen tubes. Confusion regarding which lumen to use is simplified if you remember that the scope may be used for two distinct purposes.

First, the scope can be inserted through the **distal, bronchial** lumen to direct the tube from the lower trachea into the selected mainstem bronchus.

Second, it can be used to confirm and adjust the position of the bronchial cuff, to ensure that the endobronchial cuff is just inside the bronchus, and that when inflated, the cuff does not extend beyond the carina to obstruct the trachea. The practical sequence is therefore:

1. Place the tube into the trachea by conventional direct laryngoscopy.
2. Advance the tube into the main stem bronchus, either directly - by simply pushing and turning it in the traditional manner, or endoscopically - by inserting the scope through the bronchial lumen and then into the selected main bronchus.

3. The position of the bronchial cuff in relation to the carina is inspected by inserting the scope through the tracheal lumen. The scope should emerge just above the carina, and the bronchial cuff should be entirely within the bronchus - to avoid obstruction of the trachea. Correct inflation of the cuff can be observed directly to avoid hyperinflation.

Bronchial blockers can be used in smaller patients. A 5FG Fogarty embolectomy catheter has been used for pediatric patients. The catheter should be placed in the trachea prior to intubation, (a 45° bend facilitates directing it to the desired bronchus.) The scope is then passed through the ETT and positioned just above the carina to observe and adjust the position of the balloon, which is then carefully inflated with saline until the bronchus is occluded, using the minimum volume necessary. There are reports of bronchial rupture from over-inflation.

**Intubation via the LMA**

A fiberscope can be placed through an LMA (or other supraglottic airway) to facilitate intubation in patients who cannot be intubated directly for anatomical or neurologic reasons.

The Fastrach LMA can serve as a conduit for intubation without using a fiberscope, but is not available for small children.

When using a fiberscope through the LMA, the ETT can be passed over the scope and into the trachea, but the ETT is usually too short to allow the LMA to be removed. If this is necessary, then a second smaller ETT can be wedged inside the proximal end of the first ETT until the LMA is removed. Alternatively, a long guide wire can be placed through the suction channel of the fiberscope. The LMA is then withdrawn, and an appropriate size ETT is then advanced over the wire, using a suction catheter inside the ETT to support the wire and facilitate passage through the glottis.

**Intra-operative diagnosis of ventilation problems.**

The fiberoptic scope can be an asset in the diagnosis and management of a variety of intra-operative ventilation problems, for example:

1. The surgeon claims the left lung is not moving as you come off by-pass. You can try pulling the tube back - but risk extubating the patient. Passing the scope...
down the tube allows you to confirm the position (or improve it) and turns your attention to shifting the mucous plug obstructing the left bronchus.

2. Difficult ventilation in the neurosurgical patient in the sphinx or prone position: the tube may be kinked, blocked or positioned incorrectly - use of the scope may facilitate resolution of the problem.

3. Reintubation. The scope may be used to reintubate either electively, or sometimes in emergency situations (e.g. the infant accidentally extubated coming off by-pass, when direct laryngoscopy interferes with the aortic cannula)

**Suggested Reading**

2. Ovassapian, A: Fiberoptic Endoscopy and the Difficult Airway (2nd Edn); 1996, Lippincott Williams & Wilkins.
The Patient with a Known Difficult Intubation for Facelift

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Patient O.T.

- Healthcare worker, desires facelift at freestanding ASC. Cancelled 2 months previously because of URI.
- Known difficult intubation from only other surgery where with routine induction, failed laryngoscopy led to fiberoptic intubation (anterior larynx by report).
- Request case by attending plastic surgeon.

Preop continued

- Discussed sedation technique with spontaneous ventilation and no intubation.
- Discussed that if this was not possible, then might need LMA.
- Might need fiberoptic intubation while asleep, or might even require waking up with awake fiberoptic intubation.
- Patient understood and agreed.

Intraop

- Placed on OR table and given 1 mg Versed.
- Good effect from the Versed.
- Started Propofol/Alfentanil drip at 60 cc/hr. Sedated with 7 cc.
- Lost CO2 tracing, returned with chin lift. No drop in saturation.
- Placed nasal trumpet with xylocaine jelly.
- CO2 tracing returns, but patient opens eyes to verbal stimulus.

Intraop

- Sedation continues with loss of CO2 tracing, placement of oral airway.
- CO2 tracing returns, but patient continues to open eyes to verbal stimulus.
- Discussion with surgeon about using LMA.
- Search for “flexible” LMA, none found.
- Placed #3 "rigid" LMA on 2nd try.
- Good CO2 tracing, patient unresponsive to verbal stimulus. Ready for surgery.

Intraop

- Good saturation, 35 minutes into the case.
- Positioning of circuit off head of OR table.
- Decrement in CO2 tracing, returns with circuit positioned to foot.
- Patient starts to cough, bolus propofol.
- Laryngospasm!!!
- Remove LMA, attempt to ventilate by mask with tight bag.
### Intraop
- Push 120 mg Succinylcholine.
- Unable to ventilate.
- Laryngoscopy with MAC 4, no visualization tube into esophagus.
- Saturation 60%, Atropine for HR = 35.
- Laryngoscopy with straight blade, no visualization, tube into esophagus.
- Emergency trach, immediate CO2 obtained.

### Intraop
- Trach revised, propofol drip, spontaneous ventilation returns, transported to SICU.
- Responds to commands in SICU.
- Sedated for several hours, but within 24 hours is completely awake, alert, with no deficits.

### Near Follow Up
- Seen by me daily.
- Completed a "medic alert" bracelet for her stating "Difficult intubation. Needs fiberoptic awake intubation. Irritable airway with laryngospasm when sedated.”
- Repeated detailed explanations of "what happened?"

### Additional information
- Patient has history of “choking easily”.
- Has required esophageal dilations on several occasions. Always with no sedation.
- Relatives give history of patient having a “very soft voice”. “I really have to read her lips to understand her. It has been that way all her life”

### Why didn’t Succinylcholine work?
- Data from pharmacy relative to Quelicin:
  - Stable for three months at temps up to 25 °C (77 °F).
  - Loss of potency at room temp is 1% per week
  - At 40 °C (104 °F) loss is 3.2% per week (takes 22 weeks to reach 50%).
- However, use within 24 hours of preparation is recommended by manufacturer along with discarding any unused solution.

### Follow Up
- Trach downsized and removed on POD 12.
- Patient discharged without complaints on POD 13.
- Scheduled for return to plastics and consideration for facelift. Patient has been told that will need awake fiberoptic intubation.
## Discussion

- Should all known difficult intubations receive fiberoptic GA and not sedation technique?
- Is the above dependent on the proposed procedure (surgical field avoidance)?
- Should all intended fiberoptic intubations be done in hospital OR’s vs free standing ASC’s?
- Should we use LMA’s for GA on patients with a history of need for fiberoptic intubations?
- Is the above also dependent on the proposed procedure (surgical field avoidance)?
Practical TEE for Anesthesiologists

February 25, 2008

Part I

1. Important Principles of Ultrasound for clinical application of the TEE
   Tamas Seres

2. Two and 3 Dimensional Images
   Nathaen Weitzel

3. Clinical application of 3D TEE
   Tamas Seres- Nathaen Weitzel

4. Evaluation of Left Ventricular Systolic Function
   Tamas Seres

February 26, 2008

Part II

1. Evaluation of Left Ventricular Diastolic Function
   Tamas Seres

2. The Anatomy and Function of the Normal Mitral Valve
   Fadi Nasrallah

2. Evaluation of Mitral Stenosis
   Tamas Seres

3. Evaluation of Mitral Regurgitation
   Fadi Nasrallah

February 27, 2008

Part III

1. The Anatomy and Function of the Normal Aortic Valve
   Fadi Nasrallah

2. Evaluation of Aortic Stenosis
   Ferenc Puskas

3. Evaluation of Aortic Regurgitation
   Ferenc Puskas
**Continuity Equation**

The continuity equation based on assuming a constant flow of fluid through a conduit. If there is a stenosis in the conduit, the velocity of fluid will increase at the site of stenosis to keep the continuity of flow. Flow (cm$^3$/sec) in a conduit is the product of cross-sectional area (CSA) of the conduit (cm$^2$) and the velocity of the fluid (cm/sec). Continuity of flow is an important principle to evaluate areas with unknown size such as areas of AS, MS or regurgitant areas of AI or MR. The figure below represents the flow in the left ventricular outflow track (LVOT) and at the level of aortic stenosis (AS).

Flow through LVOT = Flow through AS

$CSA_{LVOT} \times V_{LVOT} = CSA_{AS} \times V_{AS}$

**LVOT**: Left Ventricular Outflow Track  
**AS**: Aortic Stenosis  
**CSA**: cross-sectional area  
**V**: velocity
Cross-sectional area (CSA) of LVOT:

CSA can be calculated from the diameter of the studied part of the conduit. For example, the diameter (d) of the LVOT can be measured using the LV long axis view:

$$CSA_{LVOT} = d^2 \times 0.785$$

Area = \((d/2)^2 \times \pi\)

Area = \(d^2 \times \pi/4\)

\(\pi/4 = 0.785\)

Area = \(d^2 \times 0.785\)

d = diameter of LVOT

Measurement of \(V_{LVOT}\):

The velocity of the flow at the level of the measurement of \(CSA_{LVOT}\) is determined by using PWD in the LV deep transgastric or transgastric long axis view.

Measurement of \(V_{AS}\):

The velocity of the flow through the stenotic aortic valve is measured by using CWD. In this way, the maximum velocity is measured through the smallest area in the direction of the measurement. The deep transgastric view and the transgastric long axis view can be used to perform the measurement.
Measurement of CSA_{AS}:

From the measurement of CSA_{LVOT}, V_{LVOT} and V_{AS} the stenotic area of the aortic valve (CSA_{AS}) can be calculated by using the flow continuity equation.

**Flow Continuity:**

\[
\text{Flow} = \text{area} \times \text{velocity (ml/s)}
\]

\[
\text{CSA}_{LVOT} \times V_{LVOT} = \text{CSA}_{AS} \times V_{AS}
\]

\[
\text{CSA}_{AS} = \frac{\text{CSA}_{LVOT} \times V_{LVOT}}{V_{AS}}
\]

The alternative way to calculate the CSA_{AS} is based on the fact that the volume during a certain cardiac circle is also constant at different cross-sectional areas. For example during the systole the stroke volume (SV) is a product of CSA (cm\(^2\)) and velocity time integral (VTI) (cm).

**Velocity Time Integral:** The blood flow and velocity are phasic in the circulation because of the change throughout the cardiac cycle. A Doppler spectrum of the velocity of blood through a valve will yield a curve that has velocity (cm/s) on the \(y\) axis and time (s) on the \(x\) axis. When this curve is integrated, it yields a velocity-time integral (VTI) in units of centimeter (cm/sec \(x\) sec = cm). It indicates the distance the blood travels during a certain cardiac circle. The product of VTI (cm) and CSA (cm\(^2\)) will yield volume (cm\(^3\)).

The SV through the LVOT area equals the SV through the AS area. The VTI_{LVOT} and the VTI_{AS} can be determined using the Doppler spectrum of the velocity of blood through the LVOT and the AS area based on PWD or CWD measurement, respectively.

**Volume Continuity:**

\[
\text{Volume} = \text{area} \times \text{VTI (ml)}
\]

\[
\text{CSA}_{LVOT} \times \text{VTI}_{LVOT} = \text{CSA}_{AS} \times \text{VTI}_{AS}
\]

\[
\text{CSA}_{AS} = \frac{\text{CSA}_{LVOT} \times \text{VTI}_{LVOT}}{\text{VTI}_{AS}}
\]
Summary for Clinical Practice:

$V_{LVOT}$ and $VTI_{LVOT}$ are measured by PWD at the level of the measurement of $d_{LVOT}$.
$V_{AS}$ and $VTI_{AS}$ are determined at the site of the stenosis by CWD.
A known area, $CSA_{LVOT}$, is used to calculate an unknown area $CSA_{AS}$ by the continuity equation.
Proximal Isovelocity Surface Area

(PISA)

In a case in which the molecules move within a large cavity toward a small orifice the velocity increases and the velocity profile is hemispherical with the cavity of the hemisphere facing the orifice. The velocity over the surface of the hemisphere is the same (isovelocity), and because the hemisphere is proximal to the orifice, the surface area is known as proximal isovelocity surface area (PISA). The flow toward a small orifice can be studied by color Doppler with the scale set. When the accelerated velocity exceeds the Nyquist limit, aliasing will take place and a semicircular shell of contrasting colors will cap the orifice. The semicircular shell is a hemisphere in three dimensions and its surface area can be calculated.

PISA surface area (hemisphere) = 2 x r² x π

r: the distance from the orifice to PISA is the PISA radius.

The velocity of the flow at PISA is the maximum velocity on the velocity scale of the color Doppler spectrum or the aliasing velocity (V_al). The flow at PISA:

Flow at the PISA = PISA x V_al

Flow at the orifice = CSA_orifice x V_orifice

V_orifice: The flow velocity through the orifice can be measured by CWD. Continuous wave Doppler measures the maximum velocity at the smallest area in the direction of the measurement.

Flow continuity:

Flow at the PISA = Flow at the orifice

PISA x V_al = CSA_orifice x V_orifice

CSA_orifice = PISA x V_al / V_orifice
Summary for Clinical Pracrice:

Using color flow Doppler and continuous wave Doppler a narrow area at MR or MS can be measured. Color Doppler is used to measure the flow at the PISA where the flow velocity is the aliasing velocity which is the maximum velocity on the color Doppler scale. The velocity at the orifice can be determined by continuous wave Doppler. The orifice area can be calculated by the continuity equation.

Example:

Calculation of EROA in MR:

The orifice area of mitral regurgitation is the effective regurgitant orifice area (EROA). The EROA is a volume independent parameter of the severity of MR. Calculation of EROA of the MR with PISA based on the continuity equation.

PISA radius = 0.96 cm  Velocity at PISA (V_{al}) = 49 cm/s
PISA flow:

The figure shows a color Doppler study of mitral regurgitation. The transition line between blue and red represents the proximal isovelocity area (PISA) where the velocity is known exactly as the maximum velocity of the color scale (49 cm/s). The flow can be calculated through the PISA area:

Flow = PISA x V_{al}

\[ PISA = 2 \times \pi \times r^2 \]

r = 0.96 cm

\[ PISA = 5.78 \text{ cm}^2 \]

\[ V_{al} = 49 \text{ cm/s} \]

Flow at PISA = 49 cm/s x 5.78 cm² = 283 cm³/s

Velocity through the MR orifice:

The maximum velocity (V_{MR}) through the MR orifice can be measured by CWD.
V_{MR} (Maximum velocity at the EROA) = 405 cm/s
VTI_{MR} (Velocity time integral of the MR) = 131.5 cm

**Calculation of EROA:**

Using the flow continuity equation:

Flow at PISA = Flow at EROA

PISA \times V_{al} = V_{MR} \times EROA

EROA = \text{Flow at PISA}/V_{MR}

Flow at PISA = 283 cm$^3$/s

EROA = 283 cm$^3$/s/405 cm/s = 0.69 cm$^2$

Severe MR: EROA \geq 0.4 cm$^2$

**Calculation of Regurgitant Volume (RV):**

Knowing the EROA and the VTI_{MR} the regurgitant volume (RV) can be calculated:

RV = EROA \times VTI_{MR}

EROA = 0.69 cm$^2$

VTI_{MR} = 131.5 cm

RV = 0.69 \times 131.5 = 90 cm$^3$

Severe MR: RV \geq 60 cm$^3$

**Calculation of Regurgitant Fraction (RF):**
RF = RV / SV + RV

SV = CSA_{AV} \times VTI_{AV}

RV = \text{regurgitant volume}
SV: \text{stroke volume}
CSA_{AV}: \text{cross-sectional area of the aortic valve}

CSA_{AV} = d^2 \times 0.785

d = 1.72 cm

CSA_{AV} = 1.72^2 \times 0.785 = 2.3 \text{ cm}^2

VTI_{AV} \text{ can be measured as the area under the velocity curve of the aortic flow using either PWD or CWD:}
VTI_{AV} = 13 \text{ cm} \text{ (from 2 measurements)}

SV = 2.3 \text{ cm}^2 \times 13 \text{ cm} = 30 \text{ cm}^3

**Regurgitant Fraction (RF):**

RF = \frac{RV}{(RV + SV)} \times 100

RF (\%) = \frac{90}{(90 + 30)} \times 100 = 75 \%

Severe MR: RF \geq 50 \%
Clinical Application of Real Time 3D TEE

Tamas Seres, MD and Nathaen Weitzel, MD
UCHSC

Real Time 2D TEE

- Transesophageal Echocardiography is part of heart surgery and cardiac anesthesia.
- It is an effective tool for fast evaluation of LV function, valve problems and atherosclerosis of the aorta.
- It is important in evaluating the results of cardiac surgery.

Real Time 2D TEE

- It needs advanced skills to use 2D images for describing 3D structures.
- Volume measurements are based on geometrical assumptions with significant errors.
- Exact localization of valve or other anatomical defects is difficult.

3D TEE

- There were attempts to reconstruct 3D structures from 2D images.
- These 3D TEE systems are sensitive for changes in ECG or ventilation and the image processing was time consuming.

Real-time Imaging

- The ideal way of three-dimensional echocardiography is on-line acquisition of a three-dimensional dataset of the heart without the need for ECG and respiratory gating avoiding spatial motion artifacts.

Real-time Imaging

- The system has a sparse matrix phased array transducer of 512 elements to scan a $60^\circ \times 60^\circ$ pyramidal tissue volume using parallel processing technology.
• The piezoelectric material in an ultrasound transducer is a fundamental determinant of system image quality.
• The same piezoelectric material – PZT (lead-zirconatetitanate) ceramics or PZT-composites – has been used for medical imaging for more than 40 years.

A new PureWave crystal technology, a transducer technology using piezocrystals that exhibit improved electromechanical coupling.
• Compared to PZT ceramics, PureWave crystals are purer, more uniform, and are able to transfer energy with greater precision and efficiency.
Real Time 3D TEE Transducer

Real Time 3D Echo
- Live 3D Echo provides quick and easy visualization of complex cardiac anatomy previously concealed during routine echo exams and has the potential for:
  - Better visualization of complex anatomic features
  - Better assessment of valvular function

Real Time 3D Echo
- Better visualization of catheters in 3D space
- Better assessment of global/regional function
- Better productivity due to decreased exam times

Real Time 3D Echo
- Modalities:
  - Parallel imaging
  - Live 3D
  - 3D Zoom
  - Full volume
    - Analyzing structures
    - Volume measurement
    - Color full volume images

Parallel Imaging
- View of the same structure in 90° rotation
- View of the same structure in rotation of variable angles

Live 3D Images
- Switch from 2D to 3D real time images
  - Real time image optimization
  - Real time rotation
3D Zoom Images

- Localize anatomical structures with parallel imaging
- Switch to zoomed real time 3D image
  - Rotation

Full Volume

- Analyzing Structures
  - Parallel imaging for optimizing the anatomical structures
  - ECG gated image collection
  - Analysis of 3D images
    - Rotation
    - Cropping for inspection inside structures

Full Volume

- Volume measurement
  - Parallel imaging for optimization
  - ECG gated image collection
  - Segment analysis
  - Parametric Imaging

Full Volume

- Color Full Volume Imaging
  - Color Doppler image of flow at valves or other structures
  - Parallel imaging for optimization
  - ECG gated image collection
  - Analysis of the color flow in 3D
  - Relating the flow to anatomical structures
Diastolic Function

- As many as 30 to 50 percent of patients with symptomatic HF exhibit diastolic rather than systolic dysfunction.
- Diastolic dysfunction is more common in women and the elderly, and in the latter it may be the dominant form of HF.
- Additional risk factors for diastolic dysfunction include a history of hypertension and diabetes mellitus.

Systolic heart failure (SHF), is characterized by progressive chamber dilation, eccentric remodeling, and abnormalities in systolic function.

Diastolic heart failure (DHF), is characterized by normal LV volume, concentric remodeling, normal LV systolic properties, and abnormalities in diastolic properties.

SHF and DHF are distinct syndromes, not a continuous spectrum of disorders.


Patients with SHF may have evidence of diastolic dysfunction, particularly during periods of symptomatic decompensation.

However, such patients have predominant abnormalities in systolic properties, with secondary abnormalities in diastolic function.

Similarly, patients with DHF may have subtle abnormalities in systolic function, but they have predominant abnormalities in diastolic properties and concentric remodeling.

• Diastolic dysfunction indicates a functional abnormality of diastolic relaxation, filling, or distensibility of the left ventricle, regardless of whether the EF is normal or abnormal and whether the patient is asymptomatic or has symptoms and signs of HF.

• DHF denotes the signs and symptoms of clinical HF in a patient with a normal EF and LV diastolic dysfunction.

Evaluation of LV Diastolic Function

• Mitral Valve PW Doppler Tracing
• Pulmonary Venous Inflow PW Doppler Tracing
• Tissue Doppler
• Velocity Propagation

Evaluation of Diastolic Dysfunction with TEE

Normal

S/D Ratio: 0.86 ± 0.28
Reversal: 0.17 ± 0.03 m/s

Pulmonary vein

E: 0.7-1.2 m/s
A: 0.42-0.7 m/s
E/A ratio: 1-2.0
Deceleration time: 150-200 s
IVRT: 50-100 ms

Mitral inflow

Impaired Relaxation

S/D Ratio: 1.63 ± 0.41
Reversal: 0.21 ± 0.03 m/s

E: < 0.7 m/s
A: > 0.7 m/s
E/A ratio: < 1
Deceleration time: > 200 s
IVRT: > 100 ms
**Restrictive Pattern**

- S/D Ratio: 0.40 ± 0.18
- Reversal: > 0.35 m/s
- E: > 1.2 m/s
- A: < 0.42 m/s
- E/A ratio: > 2.0
- Deceleration time: < 150 s
- IVRT: < 50 ms

**Pseudonormal**

- S/D Ratio: <1
- Reversal: > 0.35 m/s
- E: 0.7-1.2 m/s
- A: 0.42-0.7 m/s
- E/A ratio: 1-2.0
- Deceleration time: 150-200 s
- IVRT: 50-100 ms

**Tissue Doppler Patterns**

- Normal
- Impaired Relaxation
- Pseudonormal
- Restrictive

**Flow Propagation Velocity**

- Normal
- Impaired Relaxation
- Restrictive
Evaluation of Left Ventricular Systolic Function using TEE

Tamas Seres, M.D.
UCHSC

Myocardial Remodeling

• Cardiac remodeling is thought to be an important aspect of disease progression in HF regardless of cause.
• It is manifested clinically by changes in cardiac size, shape, and function in response to cardiac injury or increased load.

Myocardial Remodeling

• Remodeling can be a physiologic or pathologic condition:
  – Physiologic remodeling is a compensatory change in the proportions and function of the heart; this type of remodeling is seen in athletes.

  – Pathologic remodeling may occur:
    • After myocardial infarction
    • With pressure overload (eg, aortic stenosis, hypertension)
    • Inflammatory myocardial disease (myocarditis)
    • With idiopathic dilated cardiomyopathy
    • With volume overload (eg, valvular regurgitation)

Myocardial Remodeling

• Altered loading conditions (eg, increased preload) stretch cell membranes and increase wall stress, which may play a role in inducing the expression of hypertrophy associated genes.
• In cardiac myocytes, this may lead to the synthesis of new contractile proteins and the assembly of new sarcomeres.
Systolic heart failure (SHF), is characterized by progressive chamber dilation, eccentric remodeling, and abnormalities in systolic function.

Diastolic heart failure (DHF), is characterized by normal LV volume, concentric remodeling, normal LV systolic properties, and abnormalities in diastolic properties.
Evaluation of the LV Systolic Function

- Fractional Shortening: 28-41%
- Fractional Area Change: 36 - 64%
- Ejection Fraction: 45 - 75%
- Stroke Volume: 36-76 ml/m²
- Cardiac Output: 5 l/min

Teicholz Method

\[ V = \frac{7.0}{(2.4 + D)} D^3 \]

- \( V \): LV volume
- \( D \): LV internal dimension

Preload

- Evaluation of end-diastolic volume

The Effect of Increasing Preload

Afterload

- LV wall stress: \( \sigma = 1.33 P \left( \frac{A_c}{A_m} \right) \) (dynes/cm²)
- \( \sigma \): end systolic wall stress
- \( P \): cuff systolic BP
- \( A_c \): LV end systolic cavity area
- \( A_m \): myocardial area (end-systolic epicardial area – end-systolic endocardial area)

LV wall stress measurement

\[ \sigma = 1.33 P \left( \frac{A_c}{A_m} \right) \times 10^3 \text{ dynes/cm}^2 \]

Normal values: 60-100 dynes/cm²
Comparison of vascular resistance and end-systolic wall stress in evaluation of afterload

Contractility

• Maximal rate of LV pressure rise measured from mitral regurgitant jet

The Effect of Increasing Contractility

Isovolumetric Phase Index of LV Systolic Performance (dP/dt)

Normal: < 27 msec or > 1200 mmHg/s  Abnormal: > 32 msec or < 1000 mmHg/s
### Geometry

- Wall motion abnormalities

<table>
<thead>
<tr>
<th>Wall motion</th>
<th>Endocardial movement</th>
<th>Myocardial thickening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>normal</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>Mild hypokinesis</td>
<td>decreased</td>
<td>10-30 %</td>
</tr>
<tr>
<td>Severe hypokinesis</td>
<td>slight</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Akinesis</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>Dyskinesis</td>
<td>outward movement</td>
<td>thinning</td>
</tr>
</tbody>
</table>

### Tissue Velocity Imaging

- Measuring the velocity of the myocardium during systole and diastole.
- The systolic maximal velocity characterizes the longitudinal contraction.
- The diastolic velocity pattern characterizes the diastolic function.

### Tissue Tracking

- Measures distance of the movement of the myocardium.
- Velocity time integral of the tissue velocity curve.

### Strain Imaging

- Measures deformation of the myocardium between two points.
- The percent of longitudinal deformation of the myocardium (%).
Important TEE Parameters in Clinical Practice

Normal Intracardiac Dimensions(cm):

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA (left atrium)</td>
<td>3.0-4.5</td>
<td>2.7-4.0</td>
</tr>
<tr>
<td>LVIDd (LV internal diameter in diastole)</td>
<td>4.3-5.9</td>
<td>4.0-5.2</td>
</tr>
<tr>
<td>LVIDs (LV internal diameter in systole)</td>
<td>2.6-4.0</td>
<td>2.3-3.5</td>
</tr>
<tr>
<td>IVSd (Interventricular septum)</td>
<td>&lt;1.1</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>PWd (Posterior wall)</td>
<td>&lt;1.2</td>
<td>&lt;1.1</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>79-170</td>
<td>70-130</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>14-76</td>
<td>13-60</td>
</tr>
<tr>
<td>SV (ml)</td>
<td></td>
<td>70-120</td>
</tr>
<tr>
<td>LVOT (LV outflow track diameter)</td>
<td>2.0 ± 0.1</td>
<td>1.9 ± 0.1</td>
</tr>
<tr>
<td>VTI (Velocity time integral) LVOT</td>
<td></td>
<td>18-22</td>
</tr>
<tr>
<td>IVRT (Isovolumic relaxation time)(ms)</td>
<td></td>
<td>76 ± 13</td>
</tr>
</tbody>
</table>

Aortic Diameters (cm):

<table>
<thead>
<tr>
<th>Aortic Diameter</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Annulus</td>
<td>1.4-2.6</td>
<td></td>
</tr>
<tr>
<td>Sinus of Valsalva</td>
<td>2.1-3.5</td>
<td></td>
</tr>
<tr>
<td>Sinotubular Junction</td>
<td>1.7-3.4</td>
<td></td>
</tr>
<tr>
<td>Ascending Aorta</td>
<td>2.1-3.4</td>
<td></td>
</tr>
</tbody>
</table>

LV Systolic Function:

| Fractional Shortening (%)              | (LVIDd – LVIDs)/ LVIDd x 100 | Normal: 28-41 % |
| FAC (%)                                | (EDA - ESA)/EDA x 100         | Normal: 36-64 % |
| EF (%)                                 | (EDV – ESV)/EDV x 100         | Normal: 45-75 % |
| dP/dt (mmHg/s)                         | Normal: > 800                |

Wall motion: Endocardial movement Myocardial thickening

| Normal: normal                        | normal | >30%   |
| Mild hypokinesis: decreased           | slight | 10-30 %|
| Severe hypokinesis: slight            | none   | <10%   |
| Akinesis: none                        | none   | none   |
| Dyskinesis: outward movement          | thinning|        |
**Normal Doppler Velocities:**

Transmitral Inflow:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>E (Early diastolic filling)</td>
<td>0.7-1.2</td>
</tr>
<tr>
<td>A (Atrial kick)</td>
<td>0.4-0.7</td>
</tr>
<tr>
<td>E/A</td>
<td>1.0-2.0</td>
</tr>
<tr>
<td>DT (Deceleration time of E)</td>
<td>150-200</td>
</tr>
<tr>
<td>IVRT</td>
<td>50-100</td>
</tr>
</tbody>
</table>

Pulmonary Vein Flow:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>S (Systolic wave)</td>
<td>0.4-0.7</td>
</tr>
<tr>
<td>D (Diastolic wave)</td>
<td>0.4-0.6</td>
</tr>
<tr>
<td>S/D</td>
<td>0.7-1.5</td>
</tr>
<tr>
<td>A (Reversal flow during atrial kick)</td>
<td>0.15-0.33</td>
</tr>
</tbody>
</table>

Tissue Doppler Values:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Em (Mitral annulus early diastolic movement)</td>
<td>≥ 12 ± 2.8 cm/sec</td>
</tr>
<tr>
<td>Am (Mitral annulus movement during atrial kick)</td>
<td>≥ 8.4 ± 2.4 cm/sec</td>
</tr>
<tr>
<td>Sm (Mitral annulus movement during systole)</td>
<td>≥ 10 ± 1.5 cm/sec</td>
</tr>
<tr>
<td>Em/Am</td>
<td>1-2</td>
</tr>
</tbody>
</table>

Color M-mode:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vp (flow propagation velocity)</td>
<td>&gt; 45 cm/s</td>
</tr>
</tbody>
</table>

**LV Diastolic Function:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased relaxation:</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Increased LV-EDP:</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Compliance:</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E/A ratio:</td>
<td>1-2</td>
<td>&lt;1</td>
<td>1-2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Em/Am ratio:</td>
<td>1-2</td>
<td>&lt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Em (cm/s):</td>
<td>&gt;10</td>
<td>&lt;8</td>
<td>&lt;8</td>
<td>&lt;8</td>
</tr>
<tr>
<td>IVRT (msec):</td>
<td>50-100</td>
<td>&gt;100</td>
<td>50-100</td>
<td>&lt;50</td>
</tr>
<tr>
<td>DT (msec):</td>
<td>150-200</td>
<td>&gt;200</td>
<td>150-200</td>
<td>&lt;150</td>
</tr>
<tr>
<td>PV_s/PV_d :</td>
<td>≥1</td>
<td>&gt;1</td>
<td>&lt;1</td>
<td>&lt;&lt;1</td>
</tr>
<tr>
<td>PV_d (m/s):</td>
<td>&lt;0.35</td>
<td>&lt;0.35</td>
<td>≥0.35</td>
<td>≥0.35</td>
</tr>
<tr>
<td>PV_dA_dur/PV_d (msec):</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Vp (cm/s):</td>
<td>&gt;45</td>
<td>&lt;45</td>
<td>&lt;45</td>
<td>&lt;45</td>
</tr>
</tbody>
</table>
Evaluation of Valve Abnormalities:

### Grading Mitral Stenosis (ASE Guidelines):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Gradient (mmHg)</td>
<td>&lt;5</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Valve Area (cm²)</td>
<td>&gt;1.5</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Pressure half time (msec)</td>
<td>&lt;150</td>
<td>≥ 220</td>
</tr>
</tbody>
</table>

### Grading Tricuspid Stenosis:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Pressure Gradient (mmHg)</td>
<td>&lt;2</td>
<td>&gt;6</td>
</tr>
<tr>
<td>Tricuspid Valve Area (cm²)</td>
<td>&lt;2</td>
<td></td>
</tr>
</tbody>
</table>

### Grading Mitral Regurgitation (ASE Guidelines):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet area (cm²)</td>
<td>&lt;4</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Percentage of LA area (%)</td>
<td>&lt;20%</td>
<td>&gt;40%</td>
</tr>
<tr>
<td>Vena Contracta (cm)</td>
<td>&lt;0.3</td>
<td>≥ 0.5</td>
</tr>
<tr>
<td>Regurgitant Volume (ml)</td>
<td>&lt;20</td>
<td>≥60</td>
</tr>
<tr>
<td>Regurgitant Fraction (%)</td>
<td>&lt;20</td>
<td>≥60</td>
</tr>
<tr>
<td>Regurgitant orifice area (PISA)(cm²)</td>
<td>&lt;0.1</td>
<td>≥0.35</td>
</tr>
</tbody>
</table>

### Grading Tricuspid Regurgitation:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitant Volume (ml)</td>
<td>&lt;20</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Regurgitant Fraction (%)</td>
<td>&lt;20</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Regurgitant Jet Area/RA Area (%)</td>
<td>&lt;20</td>
<td>&gt;34</td>
</tr>
</tbody>
</table>

### Grading Aortic Stenosis (ASE Guidelines):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet Velocity (m/s)</td>
<td>&lt;3.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>Peak Pressure Gradient (mmHg)</td>
<td>&lt;36</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Mean Pressure Gradient (mmHg)</td>
<td>&lt;30</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Valve Area (cm²)</td>
<td>&gt;1.5</td>
<td>&lt;0.7</td>
</tr>
</tbody>
</table>

### Grading Pulmonic Stenosis:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Pressure Gradient (mmHg)</td>
<td>&lt;30</td>
<td>&gt;64</td>
</tr>
</tbody>
</table>
Grading Aortic Regurgitation (ASE guidelines):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild:</th>
<th>Severe:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet Height (cm)</td>
<td>&lt;0.4</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>Jet Height/LVOT (%)</td>
<td>&lt;25</td>
<td>≥65</td>
</tr>
<tr>
<td>Jet Area/LVOT Area (%)</td>
<td>&lt;40</td>
<td>≥65</td>
</tr>
<tr>
<td>Vena Contracta (cm)</td>
<td>&lt;0.3</td>
<td>&gt;0.6</td>
</tr>
<tr>
<td>Pressure Half Time (ms)</td>
<td>&gt;500</td>
<td>&lt;200</td>
</tr>
<tr>
<td>Regurgitant Volume (ml/beat)</td>
<td>&lt;20</td>
<td>≥55</td>
</tr>
<tr>
<td>Regurgitant Fraction (%)</td>
<td>&lt;20</td>
<td>≥55</td>
</tr>
<tr>
<td>Regurgitant orifice area (PISA)(cm²)</td>
<td>&lt;0.10</td>
<td>≥0.35</td>
</tr>
</tbody>
</table>

Grading Pulmonary Regurgitation:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild:</th>
<th>Severe:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet length (cm)</td>
<td>1-2</td>
<td>&gt;2</td>
</tr>
</tbody>
</table>

Prosthetic Heart Valves:

Mitral Valve Position:

Abnormal:

- Peak Velocity (m/s): >1.8
- Mean Pressure Gradient (mmHg): >10
- Pressure Half-Time (msec): >180
- Mitral Valve Area (cm²): <1.8
- Mitral regurgitation: > mild or periprosthetic leak

Aortic Valve Position:

Abnormal:

- Peak Pressure Gradient (mmHg): >45
- Mean Pressure Gradient (mmHg): >25
- Aortic Valve Area (cm²): <1.0
- Velocity Ratio: <0.35
- Aortic Regurgitation: >mild or periprosthetic leak
Tricuspid Valve Position:

Abnormal:
- Pressure Half-Time (msec): >160
- Tricuspid Regurgitation: > mild or periprosthetic leak

Pulmonic Valve Position:

Abnormal:
- Peak Velocity (m/s): >2.5
- Pulmonic Regurgitation: > mild or periprosthetic leak
Understanding LV Diastolic Function

**Systole**
- LUPV: left upper pulmonary vein
- LV: left ventricle
- LA: left atrium
- S wave
- Pulmonary vein
- Mitral inflow

**Early diastole**
- LUPV: left upper pulmonary vein
- LV: left ventricle
- LA: left atrium
- S wave
- D wave
- Pulmonary vein
- Mitral inflow
Atrial systole

LUPV: left upper pulmonary vein
LV: left ventricle
LA: left atrium

Pulmonary vein

Mitral inflow

A wave
Patterns of Pulmonary Vein and Mitral Inflow

Normal

- S/D Ratio: $0.86 \pm 0.28$
- Reversal: $0.17 \pm 0.03$
- E: $0.7$-$1.2$ m/s
- A: $0.42$-$0.7$ m/s
- E/A ratio: 1-2.0
- Deceleration time: 150-200 s
- IVRT: 50-100 ms

Impaired Relaxation

- S/D Ratio: $1.63 \pm 0.41$
- Reversal: $0.21 \pm 0.03$ m/s
- E: $< 0.7$ m/s
- A: $> 0.7$ m/s
- E/A ratio: $< 1$
- Deceleration time: $> 200$ s
- IVRT: $> 100$ ms
**Restrictive Pattern**

- S/D Ratio: 0.40 ± 0.18
- Reversal: > 0.35 m/s
- E: > 1.2 m/s
- A: < 0.42 m/s
- E/A ratio: > 2.0
- Deceleration time: < 150 s
- IVRT: < 50 ms

**Pseudonormal**

- S/D Ratio: <1
- Reversal: > 0.35 m/s
- E: 0.7-1.2 m/s
- A: 0.42-0.7 m/s
- E/A ratio: 1-2.0
- Deceleration time: 150-200 s
- IVRT: 50-100 ms
Etiology

- Mitral stenosis almost always is secondary to rheumatic heart disease, which leads to scarring and fibrosis of the free edges of the mitral valve leaflets.
- Fusion of the valvular commissures, progressive scarring of the leaflets, and contraction of the chordae tendineae lead to the development of a funnel-shaped mitral apparatus that can become secondarily calcified.
- Women are affected twice as frequently as men.

Symptoms

- Patients are normally asymptomatic for 20 years or more after an acute episode of rheumatic fever.
- As stenosis develops, symptoms appear, associated at first with exercise or high cardiac output states.
- Twenty percent of patients in whom the diagnosis of symptomatic mitral stenosis is made die within 1 year, and 50% die within 10 years after diagnosis, without surgical intervention.

Symptoms

- The natural history is a slow progressive downhill course with repeated episodes of:
  - Pulmonary edema
  - Dyspnea
  - Paroxysmal nocturnal dyspnea
  - Fatigue
  - Chest pain
  - Palpitations
  - Hemoptysis
  - Hoarseness due to compression of the left recurrent laryngeal nerve by a distended left atrium and enlarged pulmonary artery.

Symptoms

- Symptoms often become apparent with the onset of atrial fibrillation, and patients in atrial fibrillation are at increased risk for formation of left atrial thrombi and subsequent cerebral or systemic emboli.

Stage 1

- Mild mitral stenosis—asymptomatic with physiologic compensation.
- The normal mitral valve area is 4 to 6 cm². The patient can remain essentially symptom-free during the 20- to 30-year period of slow progression of stenosis until a valve area of 1.5 to 2.5 cm².
- At this point, moderate exercise may induce dyspnea.
- Further progression of mitral stenosis leads to increases in left atrial pressure and volume that are reflected back into the pulmonary circuit.
Stage 2

- Moderate mitral stenosis—symptomatic impairment.
- Valve area is between 1.0 - 1.5 cm², increasing symptomatology appears with only mild-to-moderate exertion.
- Severe congestive failure can be induced either by the onset of atrial fibrillation or by a variety of disease processes leading to high cardiac output states, such as thyrotoxicosis, pregnancy, anemia, or fever.
- In these conditions, the left atrial and pulmonary artery pressures suddenly rise as a result of the increased cardiac demand.

Stage 3

- Critical mitral stenosis—terminal failure.
- With a valve area less than 1.0 cm², a patient is considered to have critical mitral stenosis, and symptoms are present even at rest.
- Not only are left atrial pressures on the border of producing congestive failure, but cardiac output may be reduced. Chronic pulmonary hypertension eventually leads to RV dilation.

Example

- CO: 5000 ml/min
- HR: 60/ min
- Diastolic flow time: 0.4 sec/beat which is 24 sec/min
- Flow rate: 5000 ml/min/ 24 sec = 208 ml/sec
### Mitral Valve

- Mitral annulus size: 3-3.5 cm
- Mitral VTI: 10-13 cm
- Area: 4-6 cm²
- Mean pressure gradient: < 2 mmHg

### Mean Pressure Gradients (mmHg) in MS

- 2-5 mild MS
- 5-12 moderate MS
- > 12 severe MS

### Mitral Valve Area (MVA) in MS

- >1.5 cm² mild MS
- 1-1.5 cm² moderate MS
- < 1 cm² severe MS

### Clinical Symptoms and MVA

- Symptoms at moderate to strenuous exercise 1.5-2 cm²
- Symptoms at moderate exercise 1-1.5 cm²
- Symptoms at rest or mild exercise <1 cm²

### Pressure Half Time (PHT) in ms

- 100-150 mild MS
- 150-220 moderate MS
- >220 severe MS

### What is PHT?

- The time between $P_{\text{Max}}$ and $P_{\text{Max}}/2$ on a Doppler velocity curve
- $P_{\text{Max}} = 4 \times V_{\text{Max}}^2$
- $P_{\text{Max}}/2 = 4 \times (V_{\text{Max}}/\sqrt{2})^2 = 4 \times V_{\text{Max}}^2/2$
- PHT is the time between $V_{\text{Max}}$ and $V_{\text{Max}}/\sqrt{2}$
Rheumatic Mitral Valve

- Four features of mitral valve anatomy have been identified that correlate with the success of balloon valvotomy.
- These include valve pliability, thickening, calcification, and subvalvular involvement.
- Each of these can be quantified on a score of 0 to 4 and a total score tabulated.

### Echo Score Index for Rheumatic Mitral Stenosis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mobility</th>
<th>Leaflet Thickening</th>
<th>Subvalvular Thickening</th>
<th>Calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Highly mobile valve, only tethering present</td>
<td>Normal thickness (&lt;3 mm)</td>
<td>Minimal thickening just below leaflets</td>
<td>Single area of increased echo brightness</td>
</tr>
<tr>
<td>2</td>
<td>Valve is fixed to interventricular septum</td>
<td>Mild leaflet thickening</td>
<td>Thinning of chordae thomatis extending up to one-third of chordal length</td>
<td>Scattered area of subvalvular calcification</td>
</tr>
<tr>
<td>3</td>
<td>Valve is fixed to mitral annulus</td>
<td>Entire leaflet is thickened (&lt;4 mm)</td>
<td>Thinning of chordal structures to the distal third</td>
<td>Brightness in site of thickened leaflet</td>
</tr>
<tr>
<td>4</td>
<td>Valve is fixed to mitral annulus</td>
<td>All leaflet tissue has thickened</td>
<td>Entirely thickened and tethering of all chordal structures down to the papillary muscles</td>
<td>Extensive brightness through fusion of leaflet tissue</td>
</tr>
</tbody>
</table>


Rheumatic Mitral Valve

- Scores above 8 represent valves less likely to be successfully treated with a percutaneous approach.
- More recent studies have suggested a disproportionate impact of calcification and subvalvular involvement on the likelihood of successful balloon valvotomy.
The Association of OSA with Chronic Medical Disorders and the effects of CPAP

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Overview
• What Happens during OSA
• Hypertension
• Pulmonary Hypertension
• Stroke
• Heart Disease and Sudden Death
• Gastroesophageal Reflux Disease – GERD
• Diabetes

What Really Happens During Obstructive Sleep Apnea
• Repetitive Upper Airway Obstruction for 30 – 60 seconds
• SpO2 drops and CO2 rises
• Initially BP drops then drifts upward
• Sympathetic surge and “awakening” with resumption of breathing
• Acute rise in BP (up to 80 mm systolic)

Continued
• Polysomnographic sleep study
• Apnea-Hypopnea index = # episodes/hour
• NL = up to 5 – 10
• Not unusual to have 50/ hour
• Fragmented sleep leads to daytime somnolence.
• Long term = Sympathetic activation, endothelial dysfunction, vascular oxidative stress, inflammation, increased coagulation, metabolic dysregulation.

Systemic Hypertension
• 70% of OSA patients are hypertensive
• Animal studies show cause and effect
• Normally HR & BP “dips” during sleep
• Association of OSA with “nondippers”
• Association of stroke and end-organ damage with nondippers

Wisconsin Sleep Cohort
• Linear relation between apnea-hypopnea index and hypertension
• Even after adjustment for BMI, gender, waist and neck circumference, ETOH, and smoking
• Index > 15 meant three times greater risk of HTN.
AG Logan et al

- 41 Patients with refractory hypertension and no existing dx of OSA
- Already on 3 anti-hypertensives
- Excluded secondary HTN or poor compliance with medication regimen
- Performed sleep studies
- 83% OSA,
- 95% of the males, 65% of the females

CPAP, OSA, and HTN

- Becker et al – Decrease of 10 mm in MAP (about the same as “one” antihypertensive)
- Logan et al = Refractory HTN and A-H index > 45
- Systolic down by 10, Diastolic down by 6

Pulmonary Hypertension

- Due to Hypoxic Pulmonary Vasoconstriction
- Directly proportional to duration and degree of desaturation through the night
- Studies show PHTN prevalence of 15%-53%
- Mild increase of 25 – 30 mm HG
- If greater degrees of PHTN present, look for something else.

CPAP, OSA and PHTN

- CPAP does lower PAP in OSA
- Arias et al – randomized crossover trial
- Mean decrease from 29 to 24 with biggest decrease in patients with PHTN or LV diastolic dysfunction
Stroke

- Very strong association, perhaps as strong as association of stroke with smoking
- Sleep Heart Health Study – Direct relation between stroke and A-H index
- Mechanism? – SpO2 + CO2 lead to cerebral vasodilation and CBF. Also endothelial dysfunction, vascular oxidative stress, elevated fibrinogen and platelet activation

Stroke

- Improved outcome is not demonstrated
- Studies are small and tend to focus on "depressive symptoms"
- BP is definitely improved

Heart Disease and Sudden Death

- One study 40-50% prevalence of OSA in patients with acute coronary syndrome
- Observed nocturnal ST changes with A-P episodes
- One study 37% of CHF patients have OSA
- Gami et al – 112 patients with sudden death + sleep studies
  - 46% with OSA died 12MN – 6 AM
  - Only 21% for those without OSA

Heart Disease and Sudden Death

Cardiac sudden death as function of time of day.
Diagnosis of OSA shifts time period to 12MN – 6 AM.

CPAP, OSA and Heart Disease

- Kaneko et al – 24 CHF patients (EF<45%)
- A-H index 37 to 45 (severe OSA)
- Randomized for one month of CPAP
- CPAP group EF increase from 25% to 34%
- No change in non-CPAP group
- Systolic BP dropped 10 mm in CPAP group
- Significant reduction in LVESD.

CPAP, OSA, Stroke

Significant reduction in LVESD (not LVEDD) with 1 month of CPAP
GERD and CPAP

- 50 – 75% of OSA patients have GERD
- Even when BMI is factored out!
- ? Negative intrathoracic pressure during A-H episodes pull contents from stomach
- CPAP in increasing pressure levels has been shown to decrease GERD.
- ? Does positive pressure on pharynx cause the esophagus to close

Diabetes

- Two studies = A-H index and low SpO2 independently correlate with insulin resistance and glucose intolerance, independent of BMI.
- A-H index > 5 yields twice the risk of glucose intolerance
- A-H index > 15, diabetes > 15%
- A-H index < 5, diabetes < 3%

Mechanism for OSA and Diabetes

- Association of sleep deprivation and diabetes thru appetite dysregulation and insulin resistance
- Intermittent hypoxemia stimulates release of catecholamines and cortisol resulting in glucose intolerance and insulin resistance
- CPAP – 6 of 13 studies showed beneficial effect, especially in low BMI patients (perhaps less weight dependent diabetes)
Bibliography

11. Ip MS, Lam B, Ng NM, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med 2002; 165:670-676.
Below are listed some topics that we thought might be controversial and stir up interesting discussion. Please look these over before the workshop and let us know if there some things you would like to talk about more than others. If you don't like any of our topics, choose your own. We'll talk about anything,

- Cutoff age for young pediatric patients in freestanding outpatient facilities?
  - Absolute age?
  - Co-existing Medical Conditions?
  - Type of surgery?
- Medications for Rapid Sequence Induction
  - What the heck is wrong with Succinylcholine?
  - I never use sux,
  - I never use muscle relaxants
  - Have you tried Remifentanil?
- Pain medication for tympanotomy and tube placement? Is it overkill or entirely appropriate?
  - Do they hurt?
  - Should we be concerned about emergence?
  - Should we be concerned about side effects?
- NSAIDs for tonsils and or adenoidectomies?
  - No they will increase bleeding
  - Yes they help minimize the amount of opioid necessary and decrease the risk of respiratory depression
  - Yes, except for ketorolac
- Tricks with Propofol
  - Can it replace mivacurium?
  - Better than narcotics at end of procedure?
  - Best bet for emergence agitation?
Deep sedation and non-anesthesiologists in different kinds of facilities?
- Just part of the practice of medicine (nursing?)
- Everyone is just 5 minutes away from permanent neurological damage

Anesthesia for muscle biopsy
- They’re all MH susceptible
- What if they have the metabolic disorder that causes cell breakdown if you use propofol?
- Just do regional

Pre-op sedation for all?
- Every 2-5 year old?
- No-one?
- We can’t wait for the pre-op
- It delays emergence
- Patient with obstructive sleep apnea?

What to do with the colleague that doesn't follow the NPO rules?
Ex-preemie for a minor outpatient procedure—are we any closer to really knowing when it is safe to send them home?

Airway management for endoscopy?
- Spontaneous respiration with supplemental oxygen?
- Intubate them all!

Child presents for surgery. History significant for "snoring"
- Treat them all as if they have OSA
- Depends on type of surgery
- When should a child with OSA be done as an outpatient

Anesthesia for CT scans/other types or imaging

Neurodegeneration in immature animals/humans after exposure to common anesthetics
- Research results are not ready for prime time
- This will be the next great challenge in pediatric anesthesia

Routine BIS monitoring?
- Nah-it doesn't work anyway
- Of course it helps speed up emergence and decreases costs
- It helps me realize how excessively I overanesthetize patients

Cuffed endotracheal tubes in young children—great idea or asking for increased airway problems?

Parental presence for anesthesia induction
- Yes, yes yes and 1000 times yes for all
- No, never, that’s what midazolam is for
- Yes for some
The Anatomy and Function of the Normal Aortic Valve

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Division of Cardiothoracic Anesthesia
Department of Anesthesiology
University of Colorado at Denver and Health Sciences Center

Learning objectives

1. How does normal anatomy translates into echo views?
2. What surgeon needs to know?
3. Doppler interrogation of Aortic Valve (AoV)
4. Significance of Bicuspid AoV
5. Prosthetic alternatives
6. How much leak is too much?

Classification Used

ACC/AHA Practice Guidelines

ACC/AHA 2006 Guidelines for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease)
Barbara F. Fairbanks, MD, FACC, Chair
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Teresa A. Shaw, MD, FACC
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Barbara F. Fairbanks, MD, FACC

297
Goals of Aortic Valve (AoV) TEE exam

- Anatomy of valve, aortic root and left ventricle outflow tract (LVOT)
- Valvular and sub-valvular motion
- Relevant pathology
  - Chamber size
  - Wall thickness
  - LV function

Purpose of Intraoperative AoV TEE exam

- To refine and confirm preoperative diagnosis
- Etiology and severity of AoV disease
- Sizing of Aortic Annulus
- Surgical Success – small annulus, surgeon can be prepared for other alternatives (root enlargement, or stentless valve implantation)

20 cross-sectional views composing the recommended comprehensive TEE examination
5-Chamber view with color

ME LAX

ME LAX with color
Papillary fibroelastomas

- Aortic Valve Cusps (44.5%)
- Either side of AoV (more commonly aortic side)
- Short pedicle, multiple
- Lambl's excrescences:
  - Degenerative in origin
  - Edge of AoV along the coaptation point
- They may cause angina, infarction or embolism

AoV Endocarditis

Epiaortic views

- Midesophageal aortic valve short-axis equivalent view

Epiaortic views

- Aortic Root View

AoV short axis with color

Aortic Valve Doppler Imaging

- Continuous wave Doppler (CWD): Transvalvular velocities with modified Bernoulli equation are converted to peak and mean pressure gradients
- Pulsed wave Doppler (PWD): LVOT gradient
- Deep TG LAX view, 0-120 degrees
Aortic Valve Doppler Imaging

- Modified Bernoulli equation
  \[ \Delta P = 4V^2 \]
  - Ignored
    - Convective acceleration
    - Flow acceleration
    - Viscous force
- Peak gradient (\(\Delta P_{\text{max}}\)) is an instantaneous peak pressure gradient
- Cath Lab measures ‘peak to peak’ gradient that from physiological standpoint does not exists, it is always lower than the echocardiographic peak instantaneous gradient

Aortic velocity and gradient

<table>
<thead>
<tr>
<th>Severity of AS</th>
<th>Jet velocity m/s</th>
<th>Mean Gradient mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>&lt; 3.0</td>
<td>&lt; 25</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.0 – 4.0</td>
<td>25 – 40</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 4.0</td>
<td>&gt; 40</td>
</tr>
</tbody>
</table>

Estimation of Aortic Valve Area Using the Continuity Equation

- Assumption: Orifice is circular
  \[ \text{Area}_{\text{LVOT}} = 0.785 \times \text{diameter}^2 \]
- Rearranged Continuity equation
  \[ \text{AVA} = \frac{\text{Area}_{\text{LVOT}} \times \text{TVI}_{\text{LVOT}}}{\text{TVI}_{\text{AoV}}} \]
  \[ \text{All cm/s!} \]
Bernoulli and Continuity Equation Pitfalls

- LVOT diameter measurement error (squared)
- Subaortic obstruction (obscures LVOT VTI)
- Non-sinus rhythm
- Incorrect peak AoV velocity (MR)
- Incorrect angle: Doppler equation, importance of echo beam in relation to blood flow

Doppler equation, % error from angle of incidence

\[ \Delta f = \frac{2Ft \times v \times \cos \theta}{c} \]

<table>
<thead>
<tr>
<th>Angle °</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>45</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Error</td>
<td>0</td>
<td>2</td>
<td>7</td>
<td>14</td>
<td>30</td>
<td>50</td>
</tr>
</tbody>
</table>

Bicuspid Aortic Valve

- Bicuspid aortic valve (BAV) occurs in approximately 1% to 2% of the population
- Most BAV have 3 aortic sinuses and the larger one of the two cusps has a raphe instead of a commissure
- The right coronary artery is usually non-dominant and small
Bicuspid Aortic Valve

- Aortic Stenosis
  - 5th and 6th decade
- Aortic regurgitation
  - Isolated
  - Associated with
    - With root dilatation/aneurysm
    - Endocarditis

Bicuspid Aortic Valve and Ascending Aorta Dilatation

- 44% in normally functioning BAV
- 50-64% with various degrees of valve diseases
- Aortic Dissection - 5%
- Aortic wall medial abnormalities
  - Genetic weakness resembling cystic medial necrosis (it co-exist (co-inherited) with BAV)

Choosing Type of Valve Operation

- Surgeon’s experience and preference
- Repairable? Repair
- Contraindication to Coumadin?
- Patient factors
  - Age
  - Likely life span
  - Heart rhythm
  - Other valves?
  - Future Pregnancy?
  - Patient preference
  - Size of annulus
Prosthetic Valves

• Mechanical Valves
  • Single Tilting disk
    • Medtronic-Hall – Medtronic© (central regurgitant jet)
    • Bjork-Shiley (no longer available)
  • Double Tilting Disk
    • St. Jude – St. Jude Medical© (most widely used)
    • Carbomedics – Sulzer Carbomedics©
Prosthetic Valves

- Tissue Valves
  - Stented Bioprostheses
    - Hancock – Medtronic ©
    - Carpentier-Edwards – Baxter Healthcare®

Images of a porcine bioprosthetic valve xenograft (A), bovine pericardial valve (B), and a human aortic valve allograft (C), also called a homograft.


Tissue Valve
Stentless Aortic Bioprostheses

- St. Jude Medical Toronto SPV (porcine aortic root) – only subcoronary implant
- Medtronic Freestyle (porcine aortic root)
- Edwards Lifesciences Prima Plus
- CryoLife O’Brien, AorTech Freesewn Porcine Elan, Shelhigh No-React, Biocor PSB/SJM, Sorin Pericarbon

Medtronic Aortic Root ‘Freestyle’ bioprosthesis

- Absence of a stent a sewing ring leaves more room for blood flow
- In many cases a Freestyle valve that is one or two size larger can be implanted

Full root technique

- Sinus of Valsalva and diseased aorta excised
Root inclusion technique

- After performing an aortotomy and removing diseased aortic leaflets, the bioprosthesis is placed inside the native aorta
Complete subcoronary technique

- After performing aortotomy and removing the aortic valve leaflets, the scalloped valve is placed inside the native aorta. Clearance for the coronary ostia is allowed by scalloping all three sinuses of the bioprosthesis.

Freestyle AV LAX

Aortic Paraprosthetic Leak

- 85 patients after AVR followed for 5 years
- Paraprosthetic Leaks were detected in 47% of the patients, 90% were small and remained unchanged
- New sudden severe paravalvular regurgitation (3 patients) was associated with endocarditis (2) and prosthetic valvular failure (1)

Intraoperative Aortic Regurgitation with Stentless Valves

- 96 patients with Freestyle bioprosthesis
- Post-pump minimal to mild regurgitation was present in 52% of the patients
- One year no patient had more than mild regurgitation
- Aortic regurgitation completely resolved in 62% with post-pump regurgitation
- Conclusion: Minimal to mild regurgitation is common and does not predict clinically significant progression


The Anatomy and Function of the Normal Aortic Valve

Thank you!
Evaluation of Aortic Stenosis

Ferenc Puskas, MD, PhD
Assistant Professor
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University of Colorado at Denver and Health Sciences Center

Learning Objectives

• Pathophysiology of Aortic Stenosis, with Aortic Sclerosis as an early lesion
• Surrogate finding with AS, effecting surgical decision making
• Bicuspid Aortic Valve
• Doppler interrogation of the Aortic Valve
• What about the MR?
• How much leak is too much?

Aortic Stenosis

• Prevalence of 2% to 4% of adults over 65 years
• In the US over 50000 AVR per year
• Standard evaluation is echocardiography
• Symptom onset does not correspond to a single value in all patients
• Symptoms warrant AVR or
• Patient with moderate AS needs a cardiac surgery
Aortic Sclerosis

- Irregular valve thickening without LV outflow obstruction
- 25% of adults over 65 yrs, 48% over 84 years
- Associated with a 50% increased risk for MI or cardiac death (without CAD)
- Antegrade Velocity < 2.5 m/s
- Maybe a surrogate marker for systemic inflammatory condition

Effect of AoV Calcification

A. Patients with severe AS (jet velocity >4.0 m/s)
B. Patients with mild to moderate AS (jet velocity 2.5 to 4.0 m/s)
✓ Extent of valvular calcification significantly affected event free survival, with events defined as either death of valve replacement necessitated by symptom onset

Freeman, R. V. et al. Circulation 2005;111:3316-3326
Aortic Stenosis
(Etiology)

• Acquired
  – Rheumatic
  – Degenerative (calcium)
  – Prosthetic
  – Infective endocarditis
• Congenital

Aortic Stenosis – Most Common Cause

• Calcification of normal trileaflet
• Calcification of congenital bicuspid valve

  – From the base of the cusp to the leaflet
  – Reduction of leaflet motion and effective valve area
  – Without commissural fusion

Stenotic BAV
Rheumatic AS – less common

- Fusion of commissures
- Scarring
- Eventual calcification
- Usually accompanied by Mitral valve disease

AS Associated Pathology

- Left Ventricular hypertrophy (LVH)
- Diastolic Dysfunction
- Mitral Regurgitation
- Aortic Root/Ascending Aortic Dilatation
- Aortic Atherosclerosis
- Other Valvular Calcification
- Coronary Artery Disease

Goals of the Echo Study

- Etiology of AS
- Level of obstruction
- Valve calcification
- Leaflet motion
- Aortic root anatomy
- LV response to pressure overload
TEE assessment of severity

1. Aortic valve area (AoV)
   a. Planimetry
   b. Continuity equation
   c. Index
2. AoV gradient
   a. Mean
   b. Peak
3. Dimensionless index
4. LV function (LV Hypertrophy)

Severity of Aortic Stenosis

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet velocity (m/sec)</td>
<td>&lt; 3</td>
<td>3.0 – 4.0</td>
<td>&gt; 4.0</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&lt; 25</td>
<td>25 – 40</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>&gt; 1.5</td>
<td>1.0 – 1.5</td>
<td>&lt; 1.0</td>
</tr>
<tr>
<td>Valve area index (cm²/m²)</td>
<td></td>
<td>&lt; 0.6</td>
<td></td>
</tr>
</tbody>
</table>

Bonow et al. Circulation 2006;114;84-231

Planimetry

- Maximal Aortic Cusp Separation (MACS)
- Position leaflet tips at the center of two dimensional sector in the AV long axis view
- Rotate to AV short axis view, to ensure smallest orifice of aortic valve at leaflet tips
Planimetry Pitfalls

- Elusive measurement in AS
- Valve calcification causes
  - Reverberations
  - Shadowing
- Difficult to locate leaflet tips
Shadowing and Reverberations

Scatter-plot with linear regression fit and 95% confidence intervals for AVA\textsubscript{CT} (16 detector row CT) and AVA\textsubscript{TEE} planimetry in 40 patients

Continuity Equation

Velocity of a moving column of fluid increases through areas of narrowing

\[ Q = A_1 V_1 = A_2 V_2 \]

\[ \frac{A_1}{A_2} = \frac{V_2}{V_1} \]

\[ Q = \frac{A_1 V_1}{A_2} = \frac{4}{3} \]

\[ V = \frac{Q}{A} \]

\[ P = \frac{V}{T} \]

\[ Zoghby et al. Circulation. 73,3:452-1986 \]
**Continuity Equation**

- Measure LVOT diameter just proximal to aortic leaflet attachment
- Measure LVOT flow (TVI) where diameter was measured

\[ \text{AVA} = \text{CSA}_{\text{LVOT}} \times \frac{\text{pkv}_{\text{LVOT}}}{\text{pkv}_{\text{AoV}}} \]

- CSA = 0.785 x diameter\(^2\)
- pkv = peak velocity
- All cm/s!

**AoV Gradient**

- Change in cross sectional flow leads to convective acceleration
- This velocity can be converted into pressure gradient using the modified Bernoulli equation:
  \[ \text{Gradient} = 4v^2 \]
  - Gradient: mmHg
  - v: velocity, m/s
- Locate maximal velocity
- Most clearly defined spectral velocity envelope

**PWD LVOT**
CWD AoV

Has been validated in several studies

Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: a simultaneous Doppler-catheter correlative study in 100 adult patients


Circulation. 71;6:1162-1169. 1985

Pressure recovery

- Increase of pressure downstream from a stenosis due to re-conversion of kinetic into potential energy
- Most important variable is the size of the aorta (clinically relevant in small size aorta < 3 cm)
- Marked overestimation of catheter gradients by Doppler
  - Bileaflet prosthetic valves
  - Coarctation of Aorta
  - HOCM
  - Fixed tunnel obstruction

Baumgartner et al. JACC 33;6, 1999.
Remember the Pitfalls

- Doppler equation (beam – blood flow angle < 20°)
- High quality, complete spectral envelope does not guarantees that the angle of incidence is negligible
- Use multiple transducer positions
- Do not confuse with MR jet!

Doppler Imaging of AS

- Dimensionless index
  \[ \frac{\text{Area}_{LVOT} \times (\text{TVI}_{LVOT} / \text{TVI}_{AOV})}{\text{Area}_{AOV}} = \frac{\text{TVI}_{LVOT}}{\text{TVI}_{AOV}} < 0.3 = \text{Severe AS} \]

Left Ventricular Hypertrophy

<table>
<thead>
<tr>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nml</td>
<td>Nml</td>
</tr>
<tr>
<td>0.8-0.9</td>
<td>0.8-1.2</td>
</tr>
<tr>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td>1.3-1.5</td>
<td>1.1-1.3</td>
</tr>
<tr>
<td>Sev</td>
<td>Sev</td>
</tr>
<tr>
<td>0.16</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Evaluation of Left Ventricular Hypertrophy (LVH)

LVH transgastric short axis
Mitral Regurgitation (MR) and AS

- Frequently associated
- Abnormal loading conditions
- Surgical treatment of MR during AVR is controversial
- MR can potentially regress after AVR

Mitral Regurgitation (MR) and AS

- 30 patients with normal LV function for AVR pre and post TTE and TEE (comparatively and prospectively)
- Moderate MR regresses early after AVR (only the regurgitant jet area, not jet width)
- Predictors for improvement: Left ventricular mass
- Predictive factors of fixed MR: Mitral calcification and/or left atrial dilation
Additional risk factors are:
- Left atrial diameter <5 cm
- Peak aortic gradient <60 mm Hg
- Mean aortic gradient <40 mm Hg
- Atrial fibrillation

Severity of MR following AVR – impact on survival
- 196 patients with isolated AVR and MR was followed for average of 2 years
- MR improved 1-2 grades in 48% of patients
- 2+ MR: 43% improved, 36% unchanged and 21% worsened
  - Survival: 98%
- 3+ MR: 38% unchanged
  - Survival: 78%
- Conclusion: Repair moderate to severe MR during AVR

What to tell the Surgeon?
- Identify 3+ to 4+ MR during AVR
- Look for surrogate findings:
  - Mitral leaflet pathology
  - Calcified Mitral Annulus
  - LV dysfunction/Hypertrophy
  - LA size
  - Assess Aortic gradients (low gradient predictor of LV dysfunction)
Evaluation of Aortic Stenosis

Thank you!
Evaluation of Aortic Regurgitation

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Learning objectives

• What causes AR?
• When to replace?
• Assessment of severity with pitfalls
• What is the most accurate measurement?

Causes of AR in Patients Having Isolated AVR at Baylor University Medical Center (1993–2005)

Aortic Root Disease

Dilated LV in AR
Puskas, Ferenc  
Evaluation of Aortic Regurgitation

![Survival of patients with chronic severe AR by symptoms (NYHA class) and LV diameter](image1)

![Survival in patients after aortic valve replacement as a function of preoperative LVEF](image2)

**Indications with pure, chronic AR for AVR**

- Severe AR $\implies$ AVR (irrespective of LV function)
- Mild AR – not candidates, if LV dysfunction, other causes have to be considered (CAD)
- Moderate AR – during CABG or surgery on Ascending Aorta $\implies$ AVR
Additional Consideration for Surgery
• Symptomatic patient with LV dysfunction (EF 0.25 to 0.5) \(\rightarrow\) AVR
• Asymptomatic patient with LV dysfunction (EF 0.25 to 0.5) \(\rightarrow\) AVR
• Asymptomatic patient with normal LV function, but end diastolic dimension > 75 mm, or end-systolic dimension > 50 mm is an indication for AVR

TEE assessment of AR severity
• Color jet area
• Vena contracta
• AR pressure half-time (PHT)
• Aortic flow reversal
• Quantitative Doppler Flow measurements

Severity of Aortic Regurgitation (Qualitative)

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic grade</td>
<td>1 +</td>
<td>2 +</td>
<td>3 – 4 +</td>
</tr>
<tr>
<td>Color Doppler width</td>
<td>Central jet, width &lt; 25% of LVOT</td>
<td>Greater than mild but no sign of severe</td>
<td>Central jet, width &gt; 65% of LVOT</td>
</tr>
<tr>
<td>Doppler vena contracta width (cm)</td>
<td>&lt; 0.3</td>
<td>0.3 – 0.6</td>
<td>&gt; 0.6</td>
</tr>
</tbody>
</table>
**Severity of Aortic Regurgitation (Quantitative)**

<table>
<thead>
<tr>
<th></th>
<th>Mid</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitant volume (ml/beat)</td>
<td>&lt; 30</td>
<td>30 – 59</td>
<td>≥ 60</td>
</tr>
<tr>
<td>Regurgitant fraction (%)</td>
<td>&lt; 30</td>
<td>30 – 49</td>
<td>≥ 50</td>
</tr>
<tr>
<td>Regurgitant orifice area (cm²)</td>
<td>&lt; 1.0</td>
<td>0.1 – 0.29</td>
<td>≥ 30</td>
</tr>
<tr>
<td>Additional criteria: LV size</td>
<td>Increased</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Color jet area**

- Jet width/LVOT width
- Fast, easy, helps assessing mechanism
- Impacted by blood pressure (BP) – high-pressure jets appear larger than a low-pressure jet
- Eccentric (wall) jets only 50% the size of central jets (Coanda effect)
- Effect of instrumentation (next slide)

**LVOT width**
Effect of Color Doppler Instrumentation on Color Doppler Jet Size

- Increased Jet size:
  - ↑ Gain and output power
  - ↑ PRF (encoding lower velocities) – lowest velocity visible is 1/16 of the maximal velocity (determined by PRF)
  - ↑ Transducer frequency – Frequency effect (encoding lower velocities) – dominates TEE
  - ↓ Transducer frequency – Attenuation effect (higher frequency is attenuated more) – dominates TEE
  - ↓ Wall filter
**Color Jet width**

**AR by Vena contracta**

- Vena contracta is the narrowest portion of the jet located at or just distal to its orifice
- It is slightly smaller than the anatomic orifice due to contraction of the flow stream by viscous friction and boundary layer effects
- Afterload independent
- \( EROA = \pi \times (\text{VC width} / 2)^2 \)


**Linear regression plots showing a comparison of vena contracta width in the long-axis view to regurgitant fraction (left) and regurgitant volume (right) assessed by intraoperative aortic flow probe**

Linear regression plots showing a comparison of vena contracta area in the short-axis view to regurgitant fraction (left) and regurgitant volume (right).

\[ R^2 = 0.65 \]
\[ R^2 = 0.71 \]

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**Short Axis VC**

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**VC Limitations**

- Jet width depends on valve morphology

 Underestimates  Overestimates
VC Limitations

- Color Doppler instrumentation changes may affect jet size
  - Increased Jet size:
    - $\uparrow$ Gain and power
    - $\uparrow$ Transducer frequency
    - $\downarrow$ PRF
    - $\downarrow$ Transducer frequency
    - $\downarrow$ Wall filter

Pressure half time (PHT)

- Quantitative parameter of the pressure equilibration between aorta and left ventricle
- With increasing severity of AR the aortic regurgitant velocity slope gets steeper, and PHT shortens
**Pressure half time (PHT)**

- Mild AR: Slow > 500 ms, incomplete/faint spectral density
- Moderate AR: Medium 500 – 200 ms, dense
- Severe AR: Steep < 200ms, dense

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**Color Jet Area**

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**Pressure Half Time**

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Limitation of PHT

- Pressure equilibration is not only influenced by regurgitant orifice area **BUT**
- By the systemic vascular resistance: Increasing SVR increases regurgitation and increases PHT (contradiction!)
- By left ventricle compliance: Decreased compliance increases PHT

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Limitation of PHT

- In the presence of impaired left ventricular relaxation the pressure or velocity decay of aortic regurgitation is not related to its severity
- PHT assessment of aortic regurgitation should only be used in patients with pure AR, normal EF and normal LV mass

Marchi et al. Heart. 1999;82:607

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Aortic Flow Reversal

- PWD sample obtained in the descending aorta just beyond the aortic arch at a multiplane angle around 90°
Aortic Flow Reversal

- Diastolic flow reversal in descending aorta with Pulsed Wave Doppler (PWD)
  - Mild: brief, early
  - Moderate: Intermediate
  - Severe: Holodiastolic reversal

➢ Most Reliable!

Regurgitant Volume (RV) in AR

1. ERO (effective orifice area) x AR flow (VTI)
2. Difference between total SV and forward SV (no intracardiac shunt)
   1. RV = Total SV – Forward SV
      • Total SV = (CSA_{LVOT} x VTILVOT)
      • Forward SV = (CSA_{PA} x VTIPA)

Regurgitant Volume (RV) in AR

- Mild: < 30 ml/beat
- Mild to Moderate: 30 – 44 ml/beat
- Moderate to Severe: 45 – 59 ml/beat
- Severe: ≥ 60 ml/beat
How Do We Measure AR?

Evaluation of Aortic Regurgitation

Thank you!