Congenital Cardiac Anesthesia Society

ANNUAL MEETING

AT PEDIATRIC ANESTHESIOLOGY 2010

April 15, 2010 • THE GRAND HYATT • SAN ANTONIO, TEXAS

SYLLABUS

Congenital Cardiac Anesthesia Society
2209 Dickens Road, Richmond, VA 23230-2005
Phone: 804-282-9780 • Fax: 804-282-0090
www.pedsanesthesia.org/ccas/

VERIFICATION OF PARTICIPATION

CCAS Spring Meeting 2010

April 15, 2010 • The Grand Hyatt • San Antonio, TX

Return to: SPA, 2209 Dickens Road, Richmond, VA 23230-2005 or fax to (804) 282-0090.
Forms MUST be returned no later than May 21, 2010 to receive a CME certificate for this educational offering.

The *Society for Pediatric Anesthesia (SPA)* maintains records of learner participation for six years . To enable SPA to maintain accurate records of your participation and **TO RECEIVE YOUR CME CERTIFICATE**, you must complete, sign and return this form to the SPA's headquarters office. Certificates of participation will be mailed to non-members within 4-6 weeks. **SPA members must log in to the SPA website (www.pedsanesthesia.org) to print their own certificates. Certificates will be available online 30 days after the meeting.**

SPA designates this educational activity for up to **9** *AMA PRA Category 1 Credit(s)* ™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

PLEASE PRINT CLEARLY AND COMPLETE ALL SECTIONS

Last Name: __|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__| First Name: __|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|__|

Mailing Address: _____

_____

City: _____ State: _____ Country: _____ Zip/Postal Code: _____

Email address: _____Daytime Phone # ( )_____Ext: _____

I wish to claim the following number of credits for the above-captioned CCAS meeting:	_____**CREDITS**

I certify that I am claiming the number of hours I actually spent in the educational activity.

_____ _____

Signature of Attendee Date

From the Physician's Recognition Award Information Booklet for CME Providers:

"Certificates for *AMA PRA category 1 Credit(s)*™ should only be given to physicians. Certificates should be provided after physicians complete the educational activity so they can document participation. Certificates should only be given for the actual credit claimed and earned by the physician."

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Moderator: Anshuman Sharma, MD, FFARCSI

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MEETING INFORMATION

Education Mission Statement

The annual Winter/Spring Meeting will focus on topics of interest to those who provide anesthesia, sedation, pain management, and critical care services to infants and children. The overall goals for attendees of the program are to reinforce and enhance their existing fund of knowledge, and to introduce them to new and state-of-the-art issues that affect their practice in order to improve the perioperative/critical care of pediatric patients.

Scope & Types of Activities

The program brings together experts from clinical and basic science disciplines related to pediatric medicine, anesthesia, and surgery.

General topic areas include anatomy, pathophysiology, anesthetic pharmacology, sedation, pain management, patient safety, and child advocacy issues. We will also discuss practice and career management issues. The presentation format is varied, and includes lectures and refresher courses, panel discussions, hands-on workshops and problem-based learning discussions. Additionally, an important part of the program is the presentation of new clinical and basic science research in oral and moderated poster-discussion forums. Significant attendee involvement and feedback are encouraged in all aspects of the program, and will be facilitated by the use of real time computerized audience polling as well as sessions where the audience directly participates in case discussions. Program content is, in fact, the direct result of membership input and extensive audience polling at prior meetings.

Target Audience

This program is intended for anesthesiologists and other practitioners who care for children in their practice of anesthesiology and/or critical care. It is also intended for clinical and basic science researchers whose areas of investigation relate to pediatric anesthesia.

The Society for Pediatric Anesthesia is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Society for Pediatric Anesthesia designates this educational activity for a maximum of 9 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

FACULTY & DISCLOSURES

Dean B. Andropoulos, MD, MHCM
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Houston, TX

Steve M. Auden, MD
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Louisville, KY

Kenneth M. Brady, MD
Johns Hopkins Hospital
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Anthony J. Clapcich, MD
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CCAS Board Disclosures

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DISCLOSURE KEY:

1. No Relationship with Commercial Supporters
2. Employment
3. Management Position
4. Independent Contractor (including contracted research)
5. Consulting
6. Speaking and Teaching
7. Membership on Advisory Committees or Review Panels
8. Board Membership
9. Other Activities
10. Author did not provide disclosure information prior to printing. Disclosure will occur prior to the presentation.

CCAS Faculty Disclosures

Dean B. Andropoulos, MD, MHCM .1

Steve M. Auden, MD 1

Kenneth M. Brady, MD 1

Anthony Clapcich, MD 1

Suanne M. Daves, MD 1

Duncan De Souza, MD 1

Jeffrey R. Fineman, MD..... 1

Robert H. Friesen, MD..... 1

Nina A. Guzzetta, MD 1

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Ian James, MB, ChB, FRCA..... 1

Deborah Kearney, MD 1

Naomi J. Kertesz, MD..... 1

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Wanda Miller-Hance, MD..... 1

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Chandra Ramamoorthy, MBBS, FRCA 1

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James M. Steven, MD, FAAP 1

David F. Vener, MD..... 1

CCAS Poster Presenters

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Shiu-Yi Emily Chen, MD..... 1

Erin A. Gottlieb, MD..... 1

Gregory B. Hammer, MD..... 1

Todd J. Kilbaugh, MD 1

Jyrson Guilherme Klamt, MD..... 1

David A. Rosen, MD
NICHD (Funding, Principal Investigator)..... 4
Hospira (Consulting Fee)..... 5

Aris Sophocles..... 1

Jamie McElrath Schwartz, MD..... 1

Scott G. Walker, MD..... 1

Prior to the start of the meeting all identified conflicts of interest will be resolved as per the SPA CME Resolution of Conflict of Interest (COI) Policy dated August 5, 2005.

OBJECTIVES

Session I: Storm: Recent Advances in Neurologic Monitoring and Protection

The Role of Brain MRI in Pediatric Cardiac Surgery
Learning objectives: At the conclusion of this lecture, the participant will understand the role of brain MRI in evaluating children with congenital heart disease in the perioperative period. A review of the impact of MRI on decision making and prognosis will be discussed.

Beyond an Oximeter: NIRS as a Monitor of Cerebral Autoregulation
Learning objectives: In this presentation, the audience will learn various methods to interpret the data from monitoring cerebral oxygenation. The use of near infrared spectroscopy to examine cerebral autoregulation will be discussed.

Antegrade Cerebral Perfusion: Recent Advances
Learning objectives: The speaker will review the history of antegrade cerebral perfusion use in pediatric cardiac surgery. The application and impact of ACP on neurologic outcome following pediatric cardiac operations will be examined.

Session II: Safe sweets; Glucose Management in Pediatric Cardiac Surgery

Review of Glucose Homeostasis in Pediatric Cardiac Surgery
Learning objectives: At the end of this lecture, the participant will learn the physiology of glucose metabolism in children undergoing cardiac surgery. Variables impacting glucose homeostasis in the setting of cardiac surgery will be discussed.

Pro: Strict Glycemic Control is Essential in PCS
Learning objectives: The audience will learn factors supporting the need for strict glycemic control in cardiac surgery and the risks of hyperglycemia.

Con: Hyperglycemia is Accepted and Safe in PCS
Learning objectives: The audience will review the safety of hyperglycemia in children undergoing cardiac surgery.

Session III: Pulmonary Hypertension: An Update

Pathophysiology of Cardiac Pulmonary Hypertension
Learning objectives: At the end of this discussion the participant will have a state-of-the-art review of the history, etiologies and pathophysiology of pulmonary hypertension in children with congenital heart disease. The review will also discuss recent advances in the management and outcome of patients with pulmonary hypertension.

Perioperative Management of Pulmonary Hypertension Patients
Learning objectives: Following this lecture, the audience will be familiar with the guidelines for preoperative preparation, anesthetic management and recovery options in children with pulmonary hypertension undergoing cardiac or non-cardiac procedures. Risk assessment and perioperative morbidity will also be reviewed.

Session IV: Study of a Lesion – Complete AV Canal Defects

Anatomic Review and Specimens
Learning objectives: At the conclusion of the lecture the audience will be introduced to a review of the anatomic characteristics of atrioventricular canal defects and learn the variant lesions present in this defect. Pathologic specimens will be presented and examined.

Echocardiographic Evaluation
Learning objectives: The presentation will outline the echocardiographic examination of children with atrioventricular canal defects. The audience will learn the important TEE findings to examine in the perioperative period and methods of assessment of surgical repairs.

Surgical Approaches and Decisions
Learning objectives: The purpose of this session is to present to the participants a comprehensive review of surgical options for the repair of children with complete atrioventricular canal defects. The audience will learn the factors considered in the process of surgical decision making in these children and the outcomes of the various repair strategies.

Session V: Pacemakers and Defibrillators – An Interactive Workshop

Review of Defibrillators and Pacemakers
Learning objectives: At the conclusion of this lecture the audience will learn the indications, applications and complications associated with defibrillators and pacemakers in children. The nomenclature and methods of interpretation and setting of these devices will be reviewed.

Interactive session – Audience Response
Learning objectives: This is an interactive session with the goal of examining the knowledge gained and applied regarding defibrillators and pacemakers in children.

Session VI: Cardiac Jeopardy

Learning objectives: To encourage audience participation in the evaluation of various clinical scenarios, interpretation of diagnostic studies and discussion of decision making processes in children with congenital heart disease in the perioperative period.

PROGRAM AT A GLANCE

7:00 - 7:30 am	**Registration & Continental Breakfast with Exhibitors**
7:30 - 7:45 am	**Welcome & Outline of Educational Program** Chandra Ramamoorthy, MBBS, FRCA; Anshuman Sharma MD, FFARCSI; Emad Mossad, MD

Session I: Brainstorm! Recent Advances in Neurologic Monitoring and Protection

Moderator: Duncan De Souza, MD

7:45 - 8:10 am	**The Role of MRI in Pediatric Cardiac Surgery** Dean B. Andropoulos, MD, MHCM
8:10 - 8:35 am	**Beyond an Oximeter: NIRS Monitoring of Cerebral Autoregulation** Kenneth M. Brady, MD
8:35 - 9:00 am	**ACP: Recent Advances** Jeffrey Heinle, MD
9:00 - 9:15 am	**Questions and Discussion**
9:15 - 9:30 am	**Coffee Break with Exhibitors**

Session II: Safe Sweets! Glucose Management in Pediatric Cardiac Surgery

Moderator: Nina A. Guzzetta, MD

9:30 - 9:50 am	**Review: Glucose Management in Pediatric Cardiac Surgery** Ian James, MB, ChB, FRCA
9:50 - 10:05 am	**PRO: Strict Glycemic Control is Essential in PCS** Barry David Kussman, MB, BCh
10:05 - 10:20 am	**CON: Hyperglycemia Should Be Accepted and Safe in PCS** James M. Steven, MD, FAAP
10:20 - 10:30 am	**Questions and Discussion**

Session III: Pulmonary Hypertension: An Update

Moderator: Anshuman Sharma, MD, FFARCSI

10:30 - 11:10 am	**Pathophysiology of Cardiac PHTN** Jeffrey R. Fineman, MD
11:10 - 11:30 am	**Perioperative Management of PHTN Patients** Robert H. Friesen, MD
11:30 - 11:45 am	**Questions and Discussion**
11:45 am - 1:00 pm	**Introduction to the STS Database/Lunch** David F. Vener, MD

Session IV: Study of a Lesion: CAVC

Moderator: Wanda Miller-Hance, MD

1:00 - 1:30 pm	**Anatomic Review and Specimens** Deborah Kearney, MD
1:30 - 2:00 pm	**Echocardiographic Evaluation** Isobel A. Russell, PhD, MD
2:00 - 2:30 pm	**Surgical Approaches and Decisions** Jeffrey Heinle, MD
2:30 - 2:40 pm	**Questions and Discussion**
2:40 - 3:00 pm	**Afternoon Break with Exhibitors – Anatomy Specimen Station**

>>> MORE

PROGRAM AT A GLANCE

Session V: Pacemakers and Defibrillators-An Interactive Workshop

Moderator: Steve M. Auden, MD

3:00 - 3:30 pm	**Review of Defibrillators and Pacemakers** Naomi J. Kertesz, MD
3:30 - 4:00 pm	**Interactive Workshop** (Audience Response) Suanne M. Daves, MD
4:00 - 4:15 pm	**Questions and Discussion**
4:15 - 4:30 pm	**Coffee Break with Exhibitors**

4:30-5:00 pm – Session VI: Cardiac Jeopardy

Moderator: Anthony Clapcich, MD

5:00-6:00 pm – Walk Around Poster Discussion Session/Reception

Session I: Brainstorm! Recent Advances in Neurologic Monitoring and Protection

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7:45 - 8:10 am	**The Role of MRI in Pediatric Cardiac Surgery** Dean B. Andropoulos, MD, MHCM
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9:15 - 9:30 am	**Coffee Break with Exhibitors**

JOHNS HOPKINS
CHILDREN'S CENTER

Beyond an Oximeter:

NIRS Monitoring of Cerebral Autoregulation

Ken Brady, MD
Monday, March 22, 2010

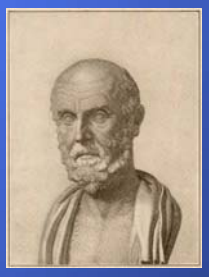
Disclosures

Under a licensing agreement with Somanetics, Dr. Brady is entitled to a share of fees and royalty received by The Johns Hopkins University on the monitoring technology described in this talk. The terms of this arrangement are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

Pediatric TBI

- A 2 year old girl chased a ladybug through her second story window. She fell two flights, into a stairwell and hit her head on the edge of a concrete step.
- She arrives seizing, without iv access, without a measurable blood pressure, and her lips are blue.

Secondary Injury

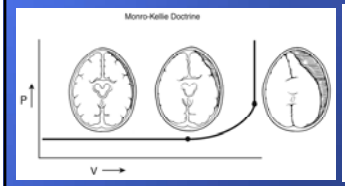


"There is no injury to the head so trivial that it can be ignored, and no injury so severe that it should invoke despair."

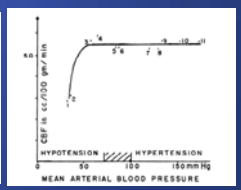
-Hippocrates

Hypoperfusion from high ICP or low ABP

•**1820's Monro-Kellie Doctrine:**

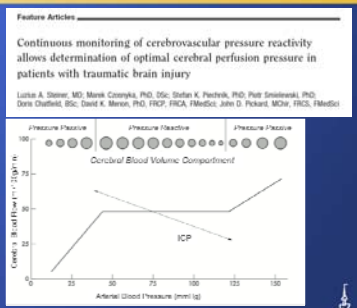


1959 Lassen's Curve



-Monroe A, Observations on the structure and function of the nervous system, 1823
-Kellie G, ...Some reflections on the pathology of the brain... 1824
-Lassen NA, *Physiological Reviews*, 1959

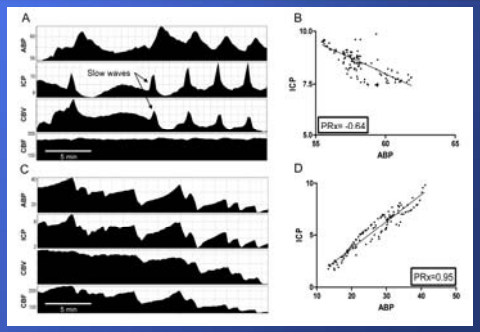
The Cambridge Hypothesis


Feature Articles

Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury

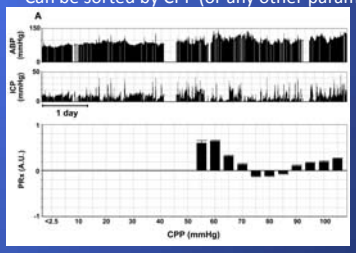
•Czosnyka M, *Stroke*, 1996
•Steiner LA, *Crit Care Med*, 2002

The Cambridge Method: Pressure Reactivity Index (PRx)

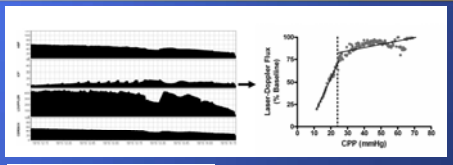


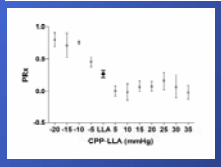
Using the PRx to find optimal CPP

- Continuous measurements
- 1,440 measurements per day
- Can be sorted by CPP (or any other parameter)



PRx validation in piglets





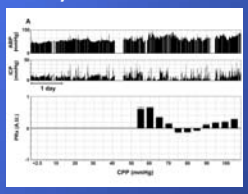
- ABP lowered to zero in piglet
- LDF vs. CPP to find lower limit of autoregulation
- PRx compared against LLA

Brady K, et al: *Stroke* 2008
Lee J, et al: *Stroke* 2009

PRx in children with TBI

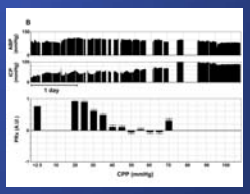
Survivor

4 year old, GCS 6 after motorcycle accident



Non-survivor

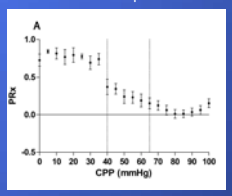
20 month old, GCS 7 after inflicted TBI

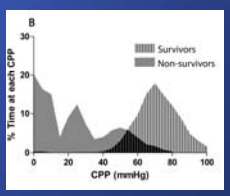


Brady K, et al: *Pediatrics* 2009

PRx in children with TBI

PRx is CPP-dependent





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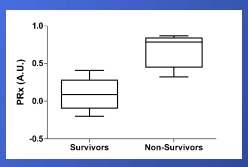
Brady K, et al: *Pediatrics* 2009

PRx in children with TBI

High PRx is associated with death



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- 21 patients
  - Single center
  - 6 nonsurvivors
  - iTBI included
  - High CPP management in survivors
  - Poor ICP control in non-survivors

Brady K, et al: *Pediatrics* 2009

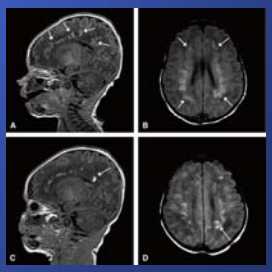
Brain Injury and CPB

- Clinical Stroke: 1-3%
- MRI Lesions: 30-75%
- Neurocognitive Dysfunction: 50%

Andropoulos D, *et al* JTCVS (2010)
Wernovsky G, *et al* Curr Opin Cardiol (2005)

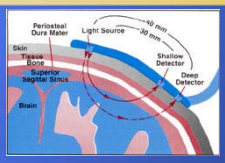
Brain Injury from CPB is multifactorial

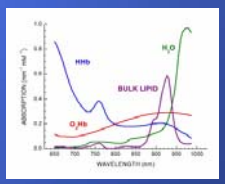
- Ischemic Vulnerability
  - Delayed maturation
- Clinical Insults
  - Hypoxia
  - DHCA
  - Emboli
  - Anemia
  - ***Hypotension***



Andropoulos D, *et al* JTCVS (2010)

NIRS can trend CBF and CBV non-invasively



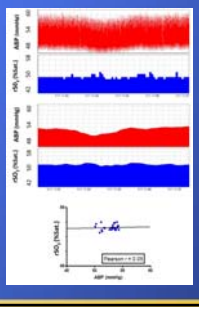


- <u>rSO_2:</u>
  - **CBF**
  - $CMRO_2$
  - HCT
  - SaO_2
- <u>BVI:</u>
  - **CBV**
  - HCT

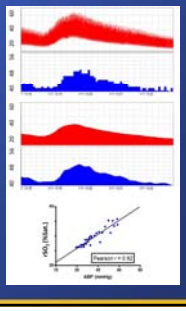
Cerebral Oximetry Index

(Substitute rSO_2 for TCD in Cambridge Equation)

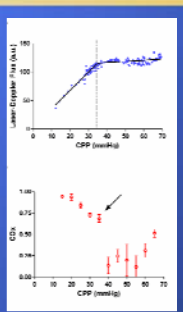
Intact Autoregulation



Impaired Autoregulation



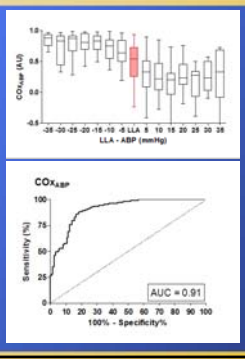
Cerebral Oximetry Index (COx)



- NIRS as a surrogate measure of CBF
- NIRS-ABP correlation is low above the LLA
- NIRS-ABP correlation is high below the LLA

Brady K, et al: *Stroke* 2007

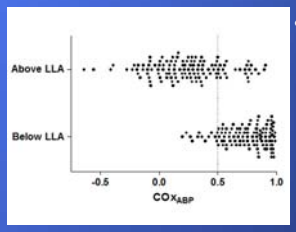
COx: Receiver Operator Characteristics



- 25 piglet experiments
- Naïve intracranial compartment
- ABP lowered to zero over 3-4 hours
- LLA determined with L-doppler
- COx curves compared against L-doppler curves

Brady K, et al: *A&A in press*

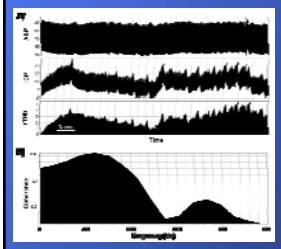
COx: Finding a Threshold Value



- COx > 0.5:
  - 89% Sensitive
  - 81% Specific for ABP below the LLA

Brady K, et al: *A&A in press*

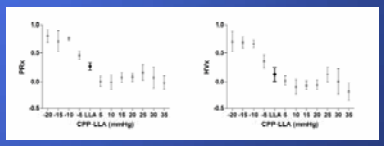
NIRS can also trend CBV



- ICP slow waves replicated with measurements of blood volume
- ICP and blood volume are coherent at "slow wave" frequency

Lee J, et al: *Stroke* 2009

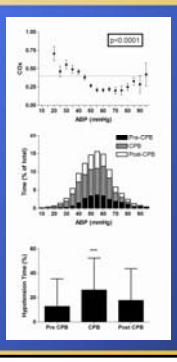
Hemoglobin Volume Index



- Substituting cerebral blood volume for ICP in the Cambridge equation re-creates the PRx

Lee J, et al: *Stroke* 2009

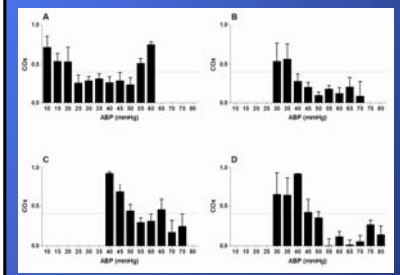
Where is the pediatric LLA during CPB?



- COx is significantly ABP-dependent
- Time below the cohort LLA is overrepresented by the recordings from CPB.

Brady K, et al: *Stroke in press*

COx: individual monitoring during CPB



A. 6-day-old: IAA (LLA 25 mmHg)

B. 7-month-old: VSD (LLA 40 mmHg)

C. 2-year-old: VSD (LLA at 50 mmHg)

D. 7-year-old: anomalous right coronary artery, (LLA at 45 mmHg)

Brady K, et al: *Stroke in press*

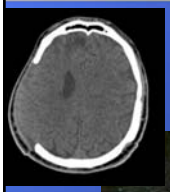
Summary

- Autoregulation monitoring can help optimize CPP for patients with head trauma
- NIRS can be used to monitor autoregulation in patients on CPB

Summary

- COx uses rSO_2 as a surrogate for CBF to detect pressure-passive flow.
- HVx uses BVI as a surrogate for CBV to detect pressure-passive vascular diameter
- Individual hemodynamic optimization

Thank You



- Blaine Easley
- Kathy Blizzard
- Jen Mytar
- Jen Lee
- Marek Czosnyka
- Peter Smielewski
- Charles Hogue
- Ray Koehler
- Hal Shaffner
- John Ulatowski
- Adam Sapirstein

Session II: Safe Sweets! Glucose Management in Pediatric Cardiac Surgery

Moderator: Nina A. Guzzetta, MD

9:30 - 9:50 am	**Review: Glucose Management in Pediatric Cardiac Surgery** Ian James, MB, ChB, FRCA
9:50 - 10:05 am	**PRO: Strict Glycemic Control is Essential in PCS** Barry David Kussman, MB, BCh
10:05 - 10:20 am	**CON: Hyperglycemia Should Be Accepted and Safe in PCS** James M. Steven, MD, FAAP
10:20 - 10:30 am	**Questions and Discussion**

Review: Glucose Management in Pediatric Cardiac Surgery

Ian James
Great Ormond Street Hospital for Children, London

Learning Objectives:

- Review of the physiology of glucose metabolism in children undergoing cardiac surgery;
- Variables impacting glucose homeostasis in the setting of cardiac surgery.

Carbohydrates are the best source of short-term fuel in animals because they are much simpler to metabolise than fats or amino acids; of these glucose is the most important and is the primary source of energy for most cells. Glucose undergoes 3 metabolic steps to release its energy; glycolysis, in which glucose is converted to pyruvate, decarboxylation of pyruvate to produce Acetyl CoA, and the entry of this into the Krebs cycle where most of the energy is released in the form of NADH and ATP. Other substrates, such as amino acids and fatty acids, also feed into the Krebs cycle in the form of Acetyl CoA; indeed, the primary energy source for myocardial cells are fatty acids.

Excess glucose is converted to glycogen, although this is not an efficient storage medium as it has a high affinity for water. Longer term energy storage is by conversion via Acetyl CoA to fatty acids, triglycerides and lipids, although humans are unable to re-synthesise glucose from lipid.

The level of glucose in the blood is very tightly regulated so that normal fasting blood sugar is 3.5 – 5.6 mmol/l, (or 60-100 mg/dl, the conversion factor being x18). There is normally only enough circulating glucose to serve the body's needs for about 30 minutes. Brain cells are almost entirely dependent upon glucose, as only astrocytes are able to store glycogen, and neurological dysfunction is an early sign of hypoglycaemia. Seizures are likely when blood glucose falls below about 2mmol/l (40mg/dl), and neuronal silence occurs at around 0.5mmol/l (10mg/dl).

Regulation of blood glucose is hormonal; the catabolic hormones glucagon, growth hormone and cortisol, and the catecholamines increase blood glucose, while insulin decreases blood sugar. Insulin induces the liver to convert glucose into glycogen, and muscle cells and fat to take up glucose. By binding to receptors on cell surfaces insulin stimulates the release from storage vesicles and movement to the cell surface of glucose transport proteins, such as GLUT 4, which facilitate the diffusion of glucose into the cell.

When blood sugar is low, the catabolic hormones stimulate glycogenolysis, in which glycogen stored in the liver and muscle is converted to glucose. The liver can release this glucose into the blood stream for transport and use elsewhere, but that from muscle is not released and is only available locally. Gluconeogenesis is also stimulated, in which liver lactate is converted back to glucose via pyruvate; most amino acids and glycerol are also used as energy substrates, but not fatty acids.

It has long been recognised that stress, whether it be trauma, burns or critical illness is associated with hyperglycaemia; this is also the case with surgery, particularly cardiac surgery involving cardiopulmonary bypass. This has multifactorial causes, mainly attributed to the stress response and the release of catabolic hormones and catecholamines, but also to insulin resistance at cellular level. Blood glucose rises pre-bypass, and during and after bypass; blunting the stress response, for example with fentanyl, can attenuate but does not abolish this rise. The hyperglycaemia that occurs with cardiac surgery may last for many hours into the postoperative period, and may exceed 20mmol/l (~400mg/dl).

Many anaesthetic and surgical factors are implicated in this peri-operative hyperglycaemia, such as:

- Anaesthetic technique; for example volatile agents may impair insulin secretion;
- Use of stored blood, which has a very high glucose content; many centres now wash their pump primes when blood is used;
- Choice of fluid for the pump prime;
- The use of pulsatile or non-pulsatile bypass;
- Fluctuation in body temperature;
- The adminstration of perioperative steroids;
- The admininistration of catecholamines

There is wide variation between institutions and between individuals within institutions as to what constitutes hyperglycaemia, and what level warrants treatment with insulin. Transient hyperglycaemia has long been thought by many to be relatively harmless, although there is evidence that prolonged hyperglycaemia is associated with adverse outcomes. The literature is full of conflicting evidence about the influence of hyperglycaemia on neurological outcome in a variety of situations such as head injury, burns and cardiac arrest. The current controversy as to the benefits or otherwise of tight glycemic control in critical illness in general and in pediatric cardiac surgery in particular is one of the more interesting topics at this time and I look forward to hearing the arguments for and against this.

Pro: Strict Glycemic Control is Essential in Pediatric Cardiac Surgery

Barry D. Kussman, MBBCh, FFA(SA)

Introduction

Elevated blood glucose (BG) levels has been identified as a modifiable risk factor for morbidity and mortality in multidisciplinary adult [1-5] and pediatric [6-12] critical care units (CCU). Stress hyperglycemia can be attributed to peripheral and hepatic insulin resistance, increased stress hormone release, drugs (catecholamines, steroids), and excessive dextrose or calorie administration.[13] Although hyperglycemia is an adaptive response to stress, over the short term it causes a negative fluid balance (glycosuria), increased inflammation (increased pro-inflammatory cytokines), impaired immune function (impaired neutrophil and monocyte chemotaxis, phagocytosis and oxidative burst, decreased complement function), endothelial dysfunction (impaired reactive endothelial nitric oxide generation), and a prothrombotic state (platelet aggregation, vasoconstriction), resulting in multi-organ system dysfunction.[4,14] Glucose is specifically toxic to the mitochondria of cells that take up glucose independent of insulin and in proportion to the circulating levels of glucose. In critical illness, overexpression of insulin independent glucose transporters leads to glucose overload in the central and peripheral nervous system, endothelium, liver, immune cells, renal tubules and gastrointestinal tract.[15-17]

The landmark study by Van den Berghe et al. from Leuven, Belgium[18] ushered in the era of intensive insulin therapy (IIT) and tight glycemic control for the critically ill. In the adult cardiac surgery population, hyperglycemia is associated with increased wound infections and mortality.[4] Although a recent meta-analysis of adult studies found that lowering blood glucose with insulin did not affect mortality in all critically ill patients, IIT was effective in lowering the risk of death among postoperative surgical patients [19,20]. Possible explanations for these findings include different patient populations, variability in what constitutes “usual care”, different definitions of tight glucose control, success in achieving target glucose levels, variability in blood glucose level (fluctuation in blood glucose may be worse than constant moderate hyperglycemia),[3,12,21] and accuracy of glucose measurements. In postoperative surgical patients, greater use of central venous and arterial lines allows for greater precision in monitoring and correcting glucose, and the shorter delay between the onset of hyperglycemia and start of glycemic control may be important if there is a time window for prevention of glucose toxicity.

Improved clinical outcomes may not be solely due to control of BG levels. Insulin lowers free fatty acids (excess of which impairs mitochondrial function), normalizes endothelial function, and has anabolic, anti-inflammatory, cardio-protective, and anti-thrombotic effects, all of which may contribute independently to improved outcomes in critical illness.[14,22] It is difficult to distinguish the effects of glycemic control from those of increased insulin levels.

Pediatric Cardiac Surgery Studies

There is mounting evidence that strict glycemic control may be beneficial for the pediatric patient undergoing cardiac surgery.

Observational (retrospective or prospective) studies in pediatric cardiac surgery (PCS) have found an association between perioperative glycemic derangement and poor early outcome, with the majority of the studies focusing on the postoperative period. In 184 infants undergoing CPB, Yates et al found that duration of hyperglycemia (glucose ≥ 126mg/dL) in the first 72 hours postoperatively was associated with increased mortality and morbidity (renal and hepatic insufficiency, infection, CNS event, need for extracorporeal membrane oxygenation (ECMO), and increased duration of mechanical ventilation, intensive care and hospital stay).[23] Although intraoperative glucose levels did not differ between survivors and nonsurvivors, peak postoperative glucose was associated with death. Falcao et al, in a cohort of 213 children, found an independent association between duration of hyperglycemia and morbidity (odds ratio [OR]1.95) and mortality (OR 1.41).[24] After the first postoperative day the durations of mild (126-160 mg/dL), moderate (161-200 mg/dL) and severe (>200 mg/dL) hyperglycemia were significantly longer in nonsurvivors. In a study by Ghafoori et al, a peak BG > 130 mg/dL during the first 24 postoperative hours was a significant multivariate predictor of mediastinitis.[25] Patients with glucose levels >175 mg/dL during CPB are three times more likely to have postoperative bacteremia.[26]

In contrast, some observational studies have not found an association between glucose metrics and outcome after PCS. Rossano et al reported that following the arterial switch operation, infants who spent > 50% of the time in the first 24 postoperative hours with glucose levels between 80-110 mg/dL were at increased risk of adverse events, while those with levels >200 mg/dL were not at increased risk for adverse events.[27] Similarly, DeCampli et al found that in infants <10 kg, postbypass and postoperative hyperglycemia were not risk factors for morbidity and mortality, although specific glucose levels used for the analysis were not clearly defined.[28] Three secondary analyses of studies in infant cardiac surgery did not find an association between hyperglycemia and late neurodevelopmental outcome. In infants with D-transposition of the great arteries undergoing an arterial switch operation (Boston Circulatory Arrest Study cohort), de Ferranti et al found no association between intraoperative hyperglycemia (categorical glucose level ≥150 mg/dL) and neurodevelopmental outcomes at 1, 4, and 8 years.[29] In infants < 6 months undergoing two-ventricle repairs,[30] or Stage I palliation,[31] hyperglycemia during the first 48 postoperative hours was not associated with adverse neurodevelopmental outcome as assessed by the Bayley scales at one year of age.[30]

Limitations of the aforementioned observational studies include small sample size, limited risk adjustment, high hospital mortality, small number of outcomes for meaningful multivariate analysis, and variability in the definition of hyperglycemia. Polito et al. attempted to overcome some of these limitations and identified associations between perioperative glycemic derangement and poor outcome after complex PCS. [32] In 378 patients (RACHS-1 category ≥3[33], metrics of glucose control (average, peak, minimum, standard deviation, duration of hyperglycemia) were determined intraoperatively and for 72 hours postoperatively. The primary outcome was days of postoperative hospitalization, and the secondary outcome was a composite morbidity-mortality variable (≥1 of the following: death, nosocomial infection, cardiac failure

requiring extracorporeal membrane oxygenation, renal failure requiring dialysis, hepatic injury, new CNS injury). Potential cofounders adjusted for were age, any genetic syndrome, at least one major noncardiac structural anomaly, prematurity, RACHS-1 category, CPB time, multiple procedures during a single operation, need for reoperation or interventional catheterization during the same admission, and inotrope score. Intraoperatively, only a minimum glucose ≤75 mg/dL was associated with greater adjusted odds of reaching the composite morbidity-mortality end point (OR, 3.1; 95% CI, 1.49-6.48); intraoperative hyperglycemia was not found to be harmful. Postoperatively, greater duration of hyperglycemia (>126 mg/dL) was associated with longer duration of hospitalization (P<0.001). An average glucose <110 mg/dL (OR, 7.3; 95% CI, 1.95-27.25) or >143 mg/dL (OR, 5.21; 95% CI, 1.37-19.89), minimum glucose ≤75 mg/dL (OR, 2.85; 95% CI, 1.38 to 5.88), and peak glucose ≥250 mg/dL (OR, 2.55; 95% CI, 1.2-5.43) were all associated with greater adjusted odds of reaching the composite morbidity-mortality end point. As optimal glucose levels in critically ill children are unknown, this study concluded that the optimal postoperative glucose range may be 110 to 126 mg/dL.

The first randomized controlled trial of IIT in pediatric critical care was published in 2009 by the Leuven group.[34] Seven hundred critically ill children were randomized to target BG concentrations of 2.8-4.4 mmol/L (1 mmol/L = 18 mg/dL) in infants (aged < 1 year) and 3.9-5.6 mmol/L in children with insulin infusion throughout CCU stay (intensive group, n=349) or insulin infusion only to prevent BG from exceeding 11.9 mmol/L (conventional group, n=351). Postoperative cardiac surgical patients (median RACHS-1 score 3) comprised 75% of the cohort. Primary endpoints were duration of CCU stay and inflammation (decrease in C-reactive protein). Mean blood glucose concentrations were lower in the intensive group than in the conventional group (infants: 4.8 [SD 1.2] mmol/L vs. 6.4 [1.2] mmol/L, p<0.0001; children: 5.3 [1.1] mmol/L vs. 8.2 [3.3] mmol/L, p<0.0001). Hypoglycemia (defined as blood glucose ≤2.2 mmol/L (40 mg/dL) occurred in 87 (25%) patients in the intensive group (p<0.0001) versus five (1%) patients in the conventional group. Duration of ICU stay was shortest in the intensively treated group (5.51 days [95% CI 4.65-6.37] vs. 6.15 days [5.25-7.05], p=0.017). The inflammatory response was attenuated at day 5, as indicated by lower C-reactive protein in the intensive group compared with baseline (-9.75 mg/L [95% CI -19.93 to 0.43] vs. 8.97 mg/L [-0.9 to 18.84], p=0.007). The number of patients with extended (>median) stay in PICU was 132 (38%) in the intensive group versus 165 (47%) in the conventional group (p=0.013). Nine (3%) patients died in the intensively treated group versus 20 (6%) in the conventional group (p=0.038). The authors concluded that targeting of blood glucose concentrations to *age-adjusted* normal fasting concentrations improved short-term outcome of patients in the pediatric ICU, and that the effect on long-term survival, morbidity, and neurocognitive development still needs to be investigated.

Gu et al performed a randomized controlled trial of insulin therapy in PCS, examining the modulating effects of insulin on inflammatory mediators during CPB.[35] Infants undergoing cardiac surgery with bypass were randomly assigned into a routine therapy group (n=30) or intensive insulin therapy group (n=30). BG levels intraoperatively were 4.4-10 mmol/L (79-180 mg/dL) in the insulin therapy group, with levels 3.1 fold higher in the routine care group by the end of CPB. After the initiation of CPB, the rise in TNF-α, IL-1β, and IL-6 (pro-inflammatory cytokines) was significantly attenuated, while IL-10 levels (anti-inflammatory cytokine) were significantly higher in

the intensive insulin therapy group. Correspondingly, the rise in Nuclear factor-κβρ65 (induces transcription of pro-inflammatory cytokines, adhesion molecules, enzymes generating reactive oxygen species) was significantly attenuated, while the expression of Iκβ (inhibitor of NF-κβ) was significantly higher. This study thus showed that insulin administration during PCS can control blood glucose levels and attenuate the systemic inflammatory response.

Two ongoing pediatric trials are the "Trial of Euglycemia in Cardiac Surgery (TECS)" being performed at Children's Hospital Boston, and the "Control of Hyperglycemia in Paediatric Intensive Care (CHiP)", a multicenter study in the UK.

Risk of Hypoglycemia

Hypoglycemia is a frequent complication in critically ill children, even in the absence of insulin therapy, and is associated with mortality and morbidity.[11,12] In children, neural dysfunction (sensory evoked potentials) occurs when the venous plasma glucose concentration decreases below 47mg/dL,[36] suggesting a physiological threshold in the range of 50-60 mg/dL. In neonates, there is no conclusive evidence or consensus in the literature that defines an absolute value or duration of 'hypoglycemia' that must occur to produce neurological injury,[37] and little is known of the vulnerability, or lack of it, of the brain of infants at different gestational ages.[38] In the critical care population, early signs of hypoglycemia may be masked by sedatives or muscle relaxants. Adequate glucose intake depends on age and clinical situation, and virtually no extensive studies regarding glucose intake in critically ill children have been performed.[14]

The incidence of hypoglycemia in adult trials of IIT ranged from 5.1-28.6% with a pooled risk ratio of 6.0 (95% CI, 0.78-1.28), and did not differ by CCU setting.[19] In PCS, as described above, a minimum glucose ≤75 mg/dL intraoperatively was associated with a greater adjusted odds of reaching a composite morbidity-mortality end point.[39] In the prospective randomized trial by the Leuven group, the incidence of hypoglycemia (defined as blood glucose ≤2.2 mmol/L (40 mg/dL) was 25% in the intensive insulin group versus 1% for the conventional group. Thus, as demonstrated in adults studies of IIT, hypoglycemia is a real risk when aiming for strict glycemic control. The risk may be reduced by maintaining higher target levels of plasma glucose concentrations and utilizing continuous rather than intermittent bedside glucose monitoring. In a study of pediatric patients during and after cardiac surgery, the Guardian RT (Medtronic Minimed, Northridge, CA) real-time subcutaneous glucose monitor provided clinically reliable measurements when compared with blood glucose concentrations with the sensor performance remaining reliable under conditions of hypothermia, inotrope use, and body-wall edema.[40] The holy grail for management would be an automated closed-loop glucose control system.

Conclusion

Studies from this decade have shown that a minimalist approach to glucose control in selected perioperative and critically ill patient populations is unwarranted, particularly in those with stress-induced hyperglycemia [41]. In the pediatric cardiac surgical population, intraoperative hypoglycemia and postoperative hyperglycemia and hypoglycemia are associated with adverse outcomes. Unresolved issues are the tightness of the glycemic control needed to improve outcome, whether all patients are at equal risk

for adverse events at a given level of dysglycemia, and whether the benefits of avoiding hyperglycemia justify accepting the known risk of treatment-induced hypoglycemia. A key question is not whether insulin therapy should be given to all critical care patients, but how cellular toxicity caused by glucose levels that are higher than the patient's premorbid levels can be avoided and what the window of opportunity is for doing so [20].

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Session III: Pulmonary Hypertension: An Update

Moderator: Anshuman Sharma, MD, FFARCSI

10:30 - 11:10 am	**Pathophysiology of Cardiac PHTN** Jeffrey R. Fineman, MD
11:10 - 11:30 am	**Perioperative Management of PHTN Patients** Robert H. Friesen, MD
11:30 - 11:45 am	**Questions and Discussion**
11:45 am - 1:00 pm	**Introduction to the STS Database/Lunch** David F. Vener, MD

Anesthetizing the Child with Pulmonary Arterial Hypertension

Robert H. Friesen, M.D.
Professor of Anesthesiology
Children's Hospital, University of Colorado Denver

Conflicts of Interest
I have no relevant financial or professional conflicts of interest to report.

Objectives
At the conclusion of this presentation the participant should be able to

1. Appreciate the increased perioperative risk associated with pulmonary hypertension..
2. Know potential perioperative triggers and the mechanism of cardiac failure associated with a pulmonary hypertensive crisis.
3. Understand the principles of perioperative care in children with pulmonary hypertension.
4. Be aware of new developments in acute pulmonary vasodilator therapy.

Introduction

Pulmonary arterial hypertension (PAH) is defined as the presence of a mean pulmonary artery pressure that exceeds 25 mmHg at rest or 30mmHg during exercise. PAH can be idiopathic (primary) or associated with a variety of underlying causes including congenital heart disease, chronic lung disease, chronic airway obstruction, and chronic liver disease. PAH is associated with significant perioperative risk for major complications. It is important that anesthesiologists be aware of this increased risk, understand the pathophysiology of PAH, form an appropriate anesthetic management plan, and be prepared to treat a pulmonary hypertensive crisis.

Cardiovascular Risks

Several mechanisms can be associated with hemodynamic deterioration in patients with PAH. Hypercarbia, hypoxia, acidosis, and noxious stimuli such as pain and airway instrumentation can trigger a rapid increase in PVR that can lead to a pulmonary hypertensive crisis and/or right heart failure. A pulmonary hypertensive crisis is characterized by a rapid increase in PVR to the point where pulmonary artery pressure (PAP) exceeds systemic blood pressure. The resulting right heart failure leads to a decrease in pulmonary blood flow, decreased cardiac output, hypoxia, coronary hypoperfusion, and biventricular failure. Right ventricular dilation is associated with leftward displacement of the interventricular septum, leading to inadequate filling of the left ventricle, decreased stroke volume, and decreased cardiac output. Systemic hypotension or a decrease in systemic vascular resistance (SVR) can cause a decrease in coronary artery blood flow, leading to biventricular ischemia. Risk of perioperative complications is greater in patients with supra-systemic PAH and in those having major surgery. Risk may be less in patients who are treated with pulmonary vasodilators preoperatively.

Treatment of Pulmonary Hypertensive Crisis

The goals of treatment are to vasodilate the pulmonary vasculature, support cardiac output, and remove stimuli associated with increases in PVR.

1. *Administer 100% oxygen*. Increasing PO_2 can decrease PVR.
2. *Hyperventilate to induce a respiratory alkalosis*. PAP was directly related to PCO_2 in mechanically ventilated children with congenital heart disease.
3. *Correct metabolic acidosis*. PVR is directly related to H^+ concentration.

4. *Administer pulmonary vasodilators*. Inhaled nitric oxide (iNO) is generally the first drug of choice; intravenous or inhaled prostacyclin analogs are effective.
5. *Support cardiac output*. Adequate preload is important. Inotropic support is often necessary. A variety of inotropic drugs can be used. Dobutamine reduces PVR, but often dopamine is preferred in order to maintain SVR and enhance coronary perfusion.
6. *Attenuate noxious stimuli* (provide analgesia). Noxious stimuli, such as pain and tracheal suctioning, can increase PVR. These responses can be attenuated by pretreatment with fentanyl.

Anesthetic Management

The goals of anesthetic management are to provide adequate anesthesia and analgesia for the surgical procedure, minimize stimuli for pulmonary vasoconstriction, minimize systemic cardiovascular depression, and maintain the ability to treat increases in PVR if they occur. Depending on the procedure, these goals can be successfully met by sedation/analgesia, regional analgesia, or general anesthesia. Although tracheal instrumentation can trigger an increase in PVR, airway management method (natural airway, laryngeal mask airway, or endotracheal tube) should be appropriate for the surgical procedure. Since the anesthesiologist must maintain the ability to immediately assist or control ventilation, the use of endotracheal tubes and laryngeal mask airways is often preferred.

No single anesthetic agent is ideal for patients with PAH. Many anesthetics exhibit mixed hemodynamic effects, such as pulmonary vasodilatation along with depression of myocardial contractility, and may be unacceptable when used in full anesthetic dosage. The pulmonary vascular effects of most anesthetic drugs have been incompletely studied, particularly in the presence of PAH. We usually employ a balanced anesthetic technique, in which subanesthetic doses of several drugs are combined to provide general anesthesia. Typically, we use oral or intravenous midazolam for premedication. Induction is cautiously achieved with midazolam, fentanyl, a small dose of propofol, and/or a low concentration of sevoflurane. Anesthesia is maintained with intermittent fentanyl and isoflurane or sevoflurane. Rocuronium or pancuronium are used for neuromuscular blockade as indicated. Perioperative use of pulmonary vasodilators is recommended in patients with significant PAH.

Pulmonary Vasodilators

Inhaled nitric oxide (iNO) provides selective pulmonary vasodilation and is often the first drug of choice for intraoperative use because of its effectiveness, rapid onset, and ease of administration. iNO bypasses the damaged pulmonary vascular endothelium present in pulmonary hypertensive disorders and diffuses into the vascular smooth muscle cell, where it activates soluble guanylate cyclase. This increases cGMP concentrations resulting in vasodilation. In children with systemic or suprasystemic PAH, we administer iNO through the breathing circuit intraoperatively beginning with anesthetic induction. Postoperatively, it is continued via mask or nasal cannulae until the patient is stable and weaned over time. Rebound pulmonary hypertension following weaning of iNO can occur, especially after a prolonged or severe pulmonary hypertensive episode. iNO is expensive, so other pulmonary vasodilators suitable for acute therapy are being investigated as alternatives.

Prostacyclin analogs cause vasodilation by increasing cAMP concentration through stimulation of adenylate cyclase and have proven to be highly effective in the treatment of PAH. They are characterized by rapid onset of action and very short half-lives. Epoprostenol, the most studied, is administered by continuous intravenous infusion; chronic therapy has improved

the five-year survival of children with idiopathic PAH. Many children with idiopathic PAH who are on epoprostenol therapy require anesthesia for central venous line placement or replacement; it is important that the epoprostenol infusion remain uninterrupted because of its extremely short half-life. The inhaled prostacyclin analog, iloprost, has been shown to be as effective as iNO in the short term reduction of PVR in children with congenital heart disease. It is also effective for long term therapy, but is associated with bronchoconstriction in some patients. Iloprost is administered as an aerosol by nebulization.

Phosphodiesterase (PDE) inhibitors block the hydrolysis of cGMP, thus increasing the concentration of cGMP in the vascular smooth muscle cell. The PDE-5 inhibitors, sildenafil and dipyridamole, are highly effective pulmonary vasodilators with rapid onset of action and the ability to attenuate rebound hypertension following withdrawal of iNO. Sildenafil is currently only approved for enteral use (if needed intraoperatively, it can be administered via a nasogastric tube); however, intravenous sildenafil is effective, and this use is expected to be approved soon. Milrinone, a PDE-3 inhibitor, is a less specific blocker of cGMP hydrolysis, but is often used perioperatively because it decreases PVR while augmenting myocardial contractility. Milrinone has been successfully administered by inhalation.

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Session IV: Study of a Lesion: CAVC

Moderator: Wanda Miller-Hance, MD

1:00 - 1:30 pm	**Anatomic Review and Specimens** Deborah Kearney, MD
1:30 - 2:00 pm	**Echocardiographic Evaluation** Isobel A. Russell, PhD, MD
2:00 - 2:30 pm	**Surgical Approaches and Decisions** Jeffrey Heinle, MD
2:30 - 2:40 pm	**Questions and Discussion**
2:40 - 3:00 pm	**Afternoon Break with Exhibitors – Anatomy Specimen Station**

Atrioventricular Septal Defects (AVSD)

Professor Isobel Russell / CCAS 2010

Anatomy and Physiology

AVSDs, or canal defects, are characterized by abnormal endocardial cushion development, resulting in deficiency of the atrioventricular septum. There is a spectrum of size of the atrial and ventricular components of the defect which may range from very small to very large and altered formation of the atrioventricular valves (1,2). In the *complete form* of this malformation there is an inferior interatrial communication or ostium primum defect, an interventricular communication at the superior aspect of the inlet or posterior muscular septum and a common atrioventricular valve. In the *partial form,* an ostium primum ASD is accompanied by a cleft or commissure in the left-sided atrioventricular valve and two functionally distinct atrioventricular valvular orifices are generally identified. The prevalence of these defects is frequent among patients with Down syndrome.

Complete AVSDs are typically associated with non- restrictive intracardiac shunting, excessive pulmonary blood flow, and excessive systemic pressures in the right ventricle and pulmonary artery. Without intervention this may result in early pulmonary vascular changes and the development of fixed pulmonary vascular obstructive disease. The severity of atrioventricular valve regurgitation also influences the clinical presentation. Partial AVSDs are less likely to be associated with pulmonary overcirculation severe enough to cause significant heart failure symptoms.

Long-Term Outcome. Most adults with the complete form of this defect have undergone complete repair in childhood. In some patients, initial palliation may have consisted of pulmonary artery banding to restrict pulmonary blood flow, followed by subsequent definite repair. Over the last several decades, the surgical approach has evolved from a two-stage intervention to a single surgical strategy of primary repair in infancy (3). The long-term outlook after repair of AVSDs is generally good. In a few patients, uncorrected defects have resulted in Eisenmenger's physiology, rendering them inoperable candidates. This is associated with significant late morbidity and early death (4,5,6). Although definitive repair is usually accomplished during childhood, various publications have documented the results of surgical intervention in adults with partial forms of defects. Patients older than 40 yr of age may undergo reparative surgery with low operative risk (7); however, they may require long-term surveillance because late mitral valve dysfunction may occur. Among 50 patients who underwent surgery for partial AVSDs (mean age, 36.6 yr; 39 of them being intervened for the first time for a substantial shunt), a low operative risk was reported and excellent long-term results were achieved (8).

Complications after repair of an AVSD include residual intracardiac shunting, left atrioventricular valve stenosis or regurgitation, and subaortic obstruction.

Transesophageal echocardiography (TEE)

In patients with AVSDs, TEE is useful in confirming the anatomy and defining the type and extension of the septal defects (9). Two- and three-dimensional TEE imaging has been shown to

be of benefit preoperatively, not only during the initial repair but also when reinterventions have been necessary (10,11). The deficiency in the atrial and ventricular septa and the large common atrioventricular valve can be readily identified in the mid esophageal four-chamber view (Fig. 1) The ventricular component of the defect is best defined during systole when the atrioventricular valves are closed. If there are dense chordal attachments to the crest the ventricular component may be delineated with color flow imaging. Charecterization of the "bridging leaflets," which span the common orifice, assists in the classification of these defects into types A, B, or C as proposed by Rastelli et al. (1) according to the anterosuperior bridging leaflet morphology. (Fig. 2). The posteroinferior leaflet almost invariably has chordal attachments to the crest of the septum. Other information of interest that is well outlined by TEE includes atrioventricular valve competency, associated ventricular outflow obstruction, and noninvasive assessment of pulmonary artery pressures. Additional muscular VSD'S can be found in 10% of the patients. Other lesions less frequently encountered include tetralogy of Fallot (3.5%), valvar pulmonar stenosis, double outlet right ventricule, truncus arteriosus and ventriculoarterial discordence.

One of the most frequent associated lesions is left ventricular outflow obstruction, including subaortic stenosis either due to chordal attachments to the crest of the septum or due to a subaortic fibrous ridge (4%), valvar stenosis and aortic subaortic coarctation. Presence of a patent ductus arteriousus is common, particularly in Down's Syndrome and can create an additional risk of Pulmnary hypertension. In the postoperative patient, TEE can assist in the determination of residual defects, status of the atrioventricular valves, and evaluation of ventricular function. Tee is also helpful in the situation of assessing ventricular size, in unbalanced AVSD's where one ventricle is smaller an alternative surgical approach is pulmonary artery banding which allows the diminutive ventricle to grow.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) IN THE EVALUATION OF AVSD

Tee Planes & Information Provided	Postsurgical Evaluation
ME 4-CH and 2-CH--morphology of AVV, bridging leaflets and their attachments in the complete form of the defect, severity of AVV regurgitation. Size/location of intracardiac defects.	Residual shunts, AVV regurgitation, LVOT obstruction, ventricular function.

AVSD : Long term outcome

Partial or intermediate forms

- □ Presentation of unrepaired partial defect (ostium primum ASD and cleft mitral valve) in adulthood not uncommon; most are symptomatic by 40 years of age
- □ in the short term, the results of surgical repair similar to those after closure of secundum ASDs
- □ mitral valve regurgitation, sub AS and atrioventricular block may develop or progress □ occasionally mitral stenosis results, with surgical revision required in 5% to 10% of patients

Complete forms

- □ most presently corrected in infancy □
- If prior palliation with pulmonary artery banding, may have resulted in inadequate protection of pulmonary vascular bed □
- uncorrected defect in the adult often associated with Eisenmenger's syndrome
- first degree atrioventricular block is common and complete atrioventricular block may occur

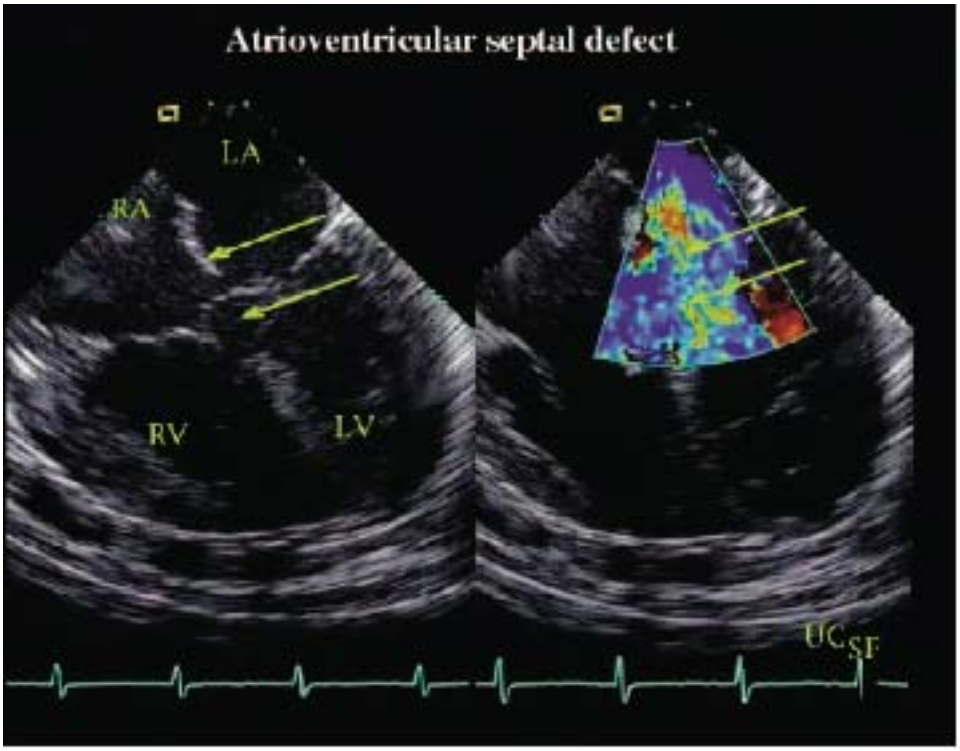

Figure 1. Complete Atrioventricular Septal Defect. Left: Mid-esophageal four-chamber view demonstrating a complete atrioventricular septal defect. The malformations characteristic of this lesion are shown, namely a primum atrial septal defect at the inferior aspect of the interatrial septum (upper arrow) and the posteriorly located, inlet-type ventricular septal defect (indicated by the lower arrow). Bridging of the common atrioventricular valve over the ventricular septum is seen. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle. Right: Color flow Doppler showing extensive left-to-right atrial and ventricular level shunting.

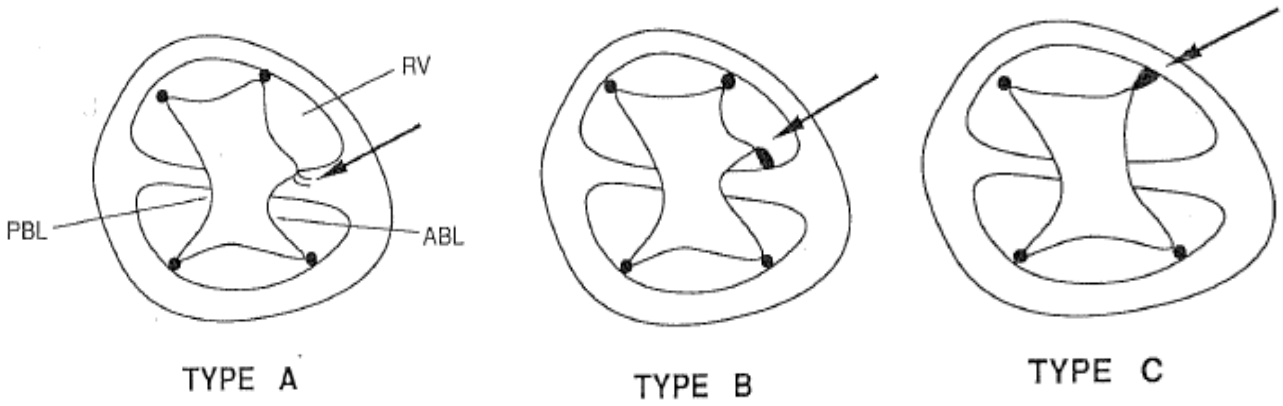

Figure 2. Schematic demonstration of the three different types of atrioventricular septal defects according to Rastelli et al. (1). **Top**. The anterior bridging leaflet (ABL) is attached to the crest of the ventricular septum (arrow), characteristic of a type A defect. **Middle**. The anterior bridging leaflet is attached to a papillary muscle on the right side of the ventricular septum (arrow), characteristic of the type B defect. **Bottom**. The anterior bridging leaflet is unattached to the septum but is attached to a large anterior papillary muscle in the right ventricle (arrow), characteristic of a type C defect. (From Higgins C, Silverman NH, Kersting Sommerhoff B, Schmidt KG, Congenital heart disease: Echocardiography and magnetic resonance imaging. New York: Raven Press, 1990)

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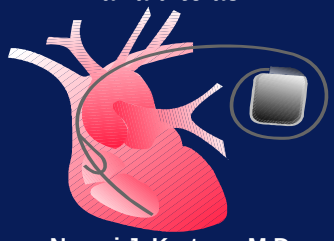
Session V: Pacemakers and Defibrillators- An Interactive Workshop

Moderator: Steve M. Auden, MD

3:00 - 3:30 pm	**Review of Defibrillators and Pacemakers** Naomi J. Kertesz, MD
3:30 - 4:00 pm	**Interactive Workshop** (Audience Response) Suanne M. Daves, MD
4:00 - 4:15 pm	**Questions and Discussion**
4:15 - 4:30 pm	**Coffee Break with Exhibitors**

Pacemakers and Defibrillators

Everything you wanted to know but were afraid to ask



Naomi J. Kertesz, M.D.
Associate Professor of Pediatrics
Associate Director Pacing and Electrophysiology

NBG Code

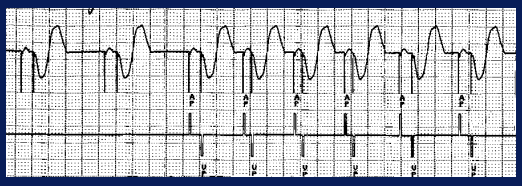
I Chamber Paced	II Chamber Sensed	III Response to Sensing	IV Programmable Functions/Rate Modulation	V Antitachy Function(s)
V: Ventricle	V: Ventricle	T: Triggered	P: Simple programmable	P: Pace
A: Atrium	A: Atrium	I: Inhibited	M: Multi-programmable	S: Shock
D: Dual (A+V)	D: Dual (A+V)	D: Dual (T+I)	C: Communicating	D: Dual (P+S)
O: None	O: None	O: None	R: Rate modulating	O: None
S: Single (A or V)	S: Single (A or V)		O: None	

Magnet Operation in Pacemakers

- Either AOO, VOO, or DOO
- No intrinsic cardiac activity is sensed
- Magnet rate many times is not lower rate limit of device and varies between pacemaker companies
  - Not appropriate for long cases
  - Can vary from 46 bpm to 98 bpm
  - Will change if the pacemaker is near end of service life
  - Magnet placement on device at end of service life can cause cessation of pacing altogether

Magnet Operation

- Magnet application causes asynchronous pacing at a designated "magnet" rate

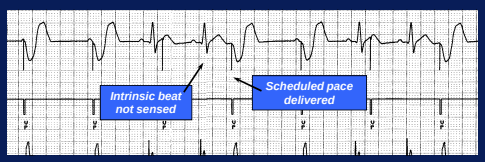


Sensing

- Sensing is the ability of the pacemaker to "see" when a natural (intrinsic) depolarization is occurring
  - Pacemakers sense cardiac depolarization by measuring changes in electrical potential of myocardial cells between the anode and cathode

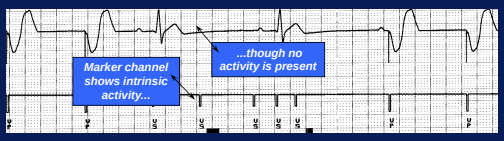
Undersensing . . .

- Pacemaker does not "see" the intrinsic beat, and therefore does not respond appropriately



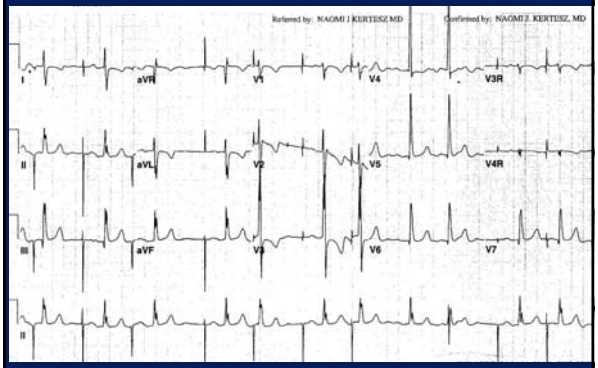
VVI / 60

Oversensing



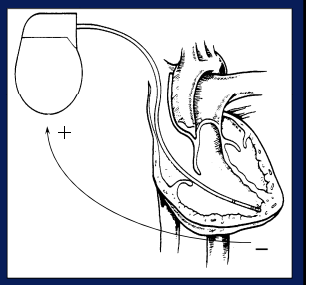
VVI / 60

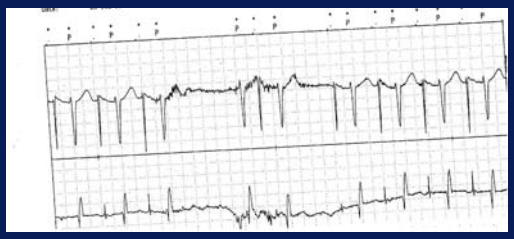
- An electrical signal other than the intended P or R wave is detected
- Seen more commonly with unipolar devices



Unipolar Sensing

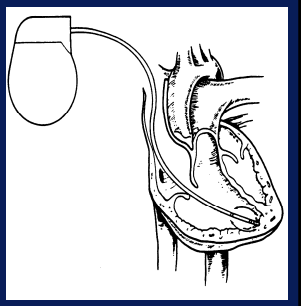
- Produces a large potential difference due to:
  - A cathode and anode that are farther apart than in a bipolar system





Bipolar Sensing

- Produces a smaller potential difference due to the short interelectrode distance
  - Electrical signals from outside the heart such as myopotentials are less likely to be sensed



Electromagnetic Interference (EMI)

- Interference is caused by electromagnetic energy with a source that is outside the body
- Electromagnetic fields that may affect pacemakers are radio-frequency waves
  - 50-60 Hz are most frequently associated with pacemaker interference
- Few sources of EMI are found in the home or office but several exist in hospitals

Sources of EMI Are Found Most Commonly in Hospital Environments

- Sources of EMI that interfere with pacemaker operation include surgical/therapeutic equipment such as:
  - Electrocautery
  - Transthoracic defibrillation
  - Extracorporeal shock-wave lithotripsy
  - Therapeutic radiation
  - RF ablation
  - TENS units
  - MRI

Electrocautery is the Most Common Hospital Source of Pacemaker EMI

- Outcomes
  - Oversensing–inhibition
  - Undersensing (noise reversion)
  - Power on Reset
  - Permanent loss of pacemaker output (if battery voltage is low)
- Precautions
  - Reprogram mode to VOO/DOO, or place a magnet over device
  - Strategically place the grounding plate
  - Limit electrocautery bursts to 1-second burst every 10 seconds
  - Use bipolar electrocautery forceps

Transthoracic Defibrillation

- Outcome
  - Inappropriate reprogramming of the pulse generator (POR)
  - Damage to pacemaker circuitry
- Precautions
  - Position defibrillation paddles apex-posterior (AP) and as far from the pacemaker and leads as possible

Defibrillators

- All defibrillators are pacemakers
- Additional ability to overdrive pace and/or defibrillation
- Oversensing due to electrocautery may cause inappropriate therapies i.e. defibrillation – therefore therapies should be turned off at the beginning of the case and turned on at the end
- Application of magnet in most devices will turn therapies off while magnet is in place

Know the Patient's Indication for Pacing

- Sinus node dysfunction
- Complete AV Block
- Underlying escape rate
  - Pacemaker dependant or no underlying rate
- Remember to reprogram patient's device back to original settings after the case is finished

Temporary Pacing

- Used for bradycardia support
  - Sinus node dysfunction – AAI or VVI
  - Complete AV block – DDD
- Promote AV synchrony
  - Accelerated junctional rhythm – AAI or DDD

Emergency Temporary Pacing

- Push the red button on the pacemaker
- Pacemaker comes on DOO at full output pacing at 80 beats per minute

Emergency Pacing

- Change the rate by turning the dial
- You must push the key at the top right of the pacemaker to unlock it
- Turn down atrial output to change into VOO or may run risk of atrial flutter or fibrillation

- Note ASYNC under sensitivity

Default Settings

- When you turn device on it comes on DDD with 10mA on the A and V leads
- Upper rate is 110 beats per minutes which is not appropriate for most children
- PVARP is 300
- AV delay 170
- Note this is menu 2

Select the Mode

- Menu M
- AAI pacing
  - Sinus bradycardia
  - Accelerated junctional rhythm
    - Promotes AV synchrony
- DDD pacing
  - AV Block

Programming the Pacemaker

- Program the device before you hook it up to the patient
- At the beginning of the case have the device set
  - VOO at 100bpm
  - 20mAmp
  - To program VOO select DOO in the mode and then turn the atrial output to zero
  - When the bovie stops being used you can switch the mode to VVI by changing the sensitivity to 2.0mA on Menu 1

Single Chamber Pacing

- Lower rate limit
  - Dependant on age and hemodynamic status
- Atrial and Ventricular output
  - Normal pacing threshold for new leads is about 2 mA
- Thresholds
  - Turn down output until lose capture. Set output at 2x lowest capture threshold. If capture at .5 and lose at .4 set at 1.0

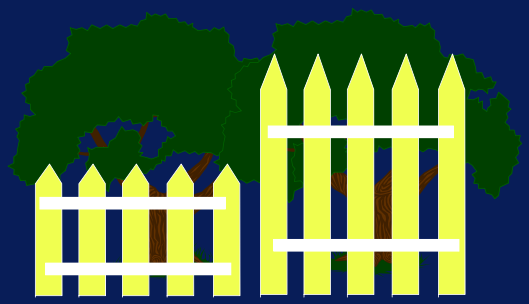
The Medtronic Temporary Pacemaker

- How to change mode
  - No AAI or AOO or VOO mode on device
  - For AAI turn ventricular output to zero after selecting DDD
  - For either VOO or AOO turn output to zero after selecting DOO
- How to change battery

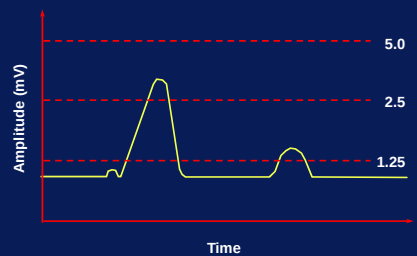
Sensing

- The lower the number the more sensitive the device
- Atrial lead can be turned lower than ventricular lead because P waves smaller than QRS
- Bipolar leads (two leads on the heart) less likely to have problems with oversensing

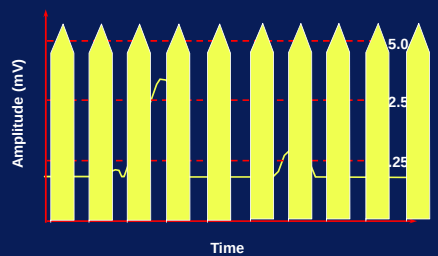
Sensitivity – The Greater the Number, the *Less* Sensitive the Device to Intracardiac Events



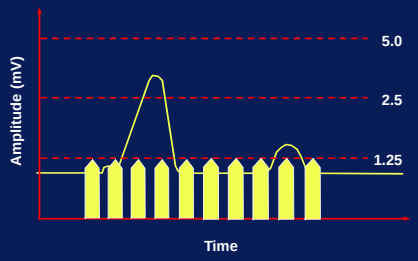
Sensitivity



Sensitivity



Sensitivity



- This message will come up when you are pacing in DOO mode.
- Push on and it will come on with some sensing but it will need to be adjusted

AAI Pacing

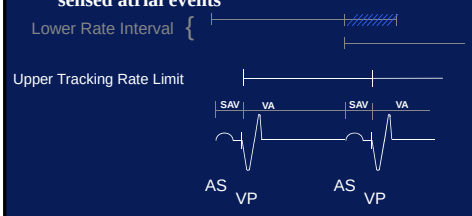
- Usually AAI is not an option in mode selection
- Select DDD
- Turn ventricular output to zero and the mode will switch to AAI

Dual Chamber Pacing

- Get another device and program it before hooking up to patient
- Lower rate limit
- Upper tracking limit – default is 110bpm
- AV delay
- PVARP

Upper Tracking Rate

- The maximum rate the ventricle can be paced in response to sensed atrial events



DDDR 60 / 100 (upper tracking rate)
Sinus rate: 100 bpm

Upper Rate Programming

- Make sure A Tracking is on –which is default
- If it is off you will pace DDI which means you will effectively be VVI

Dual Chamber Pacing

- Post Ventricular Atrial Refractory Period
  - PVARP
  - The time after the ventricular paced event that the atrial lead sensing is off
- AV delay
  - The time from the atrial spike that the pacemaker looks for a native QRS before pacing the ventricle

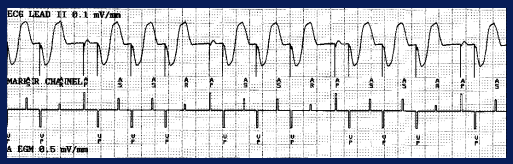
Dual Chamber Programming

- PVARP
  - Usually around 220 – 250 msec
  - May need to shorten to achieve higher tracking rates
- AV Delay (PR interval)
  - Around 150 msec
  - Do not make too short or will not allow time for atria to empty

Total Atrial Refractory Period

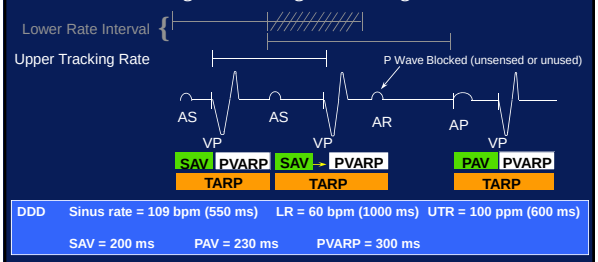
- PVARP + AV Delay = TARP
- Above this rate the device will track every other P wave
- Default is 300 + 170 = 470 or 127 bpm
- 220 + 150 = 370 or 2:1 block rate of 160 bpm
- In infants may shorten AV delay to 120 and PVARP to 200 to achieve tracking up to 185 bpm

Is This Normal Device Operation?



Wenckebach Operation

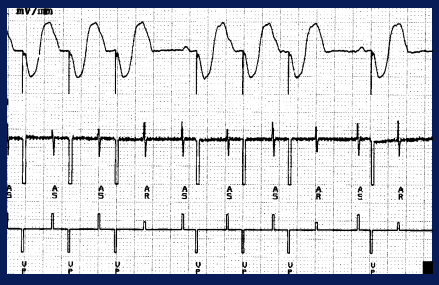
- Prolongs the SAV until upper rate limit expires
  - Produces gradual change in tracking rate ratio



DDD Sinus rate = 109 bpm (550 ms) LR = 60 bpm (1000 ms) UTR = 100 ppm (600 ms)

SAV = 200 ms PAV = 230 ms PVARP = 300 ms

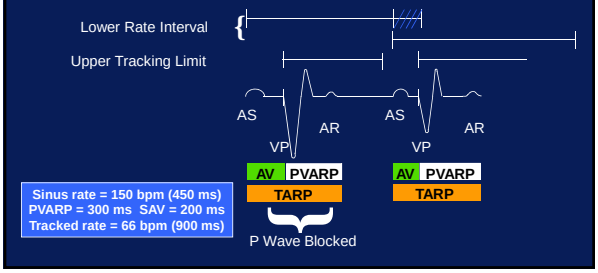
Wenckebach Operation



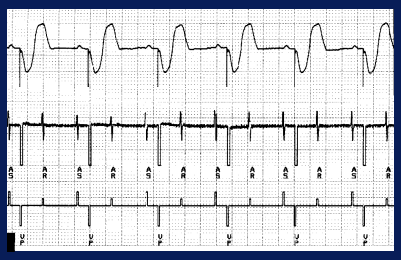
DDD / 60 / 120 / 310

2:1 Block

- Every other P wave falls into refractory and does not restart the timing interval



2:1 Block



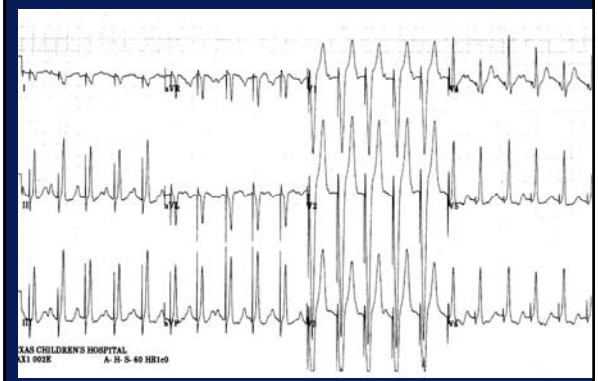
DDD / 60 / 120 / 310

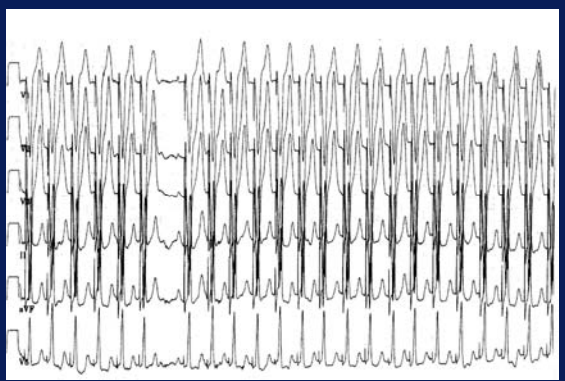
Wenckebach vs. 2:1 Block

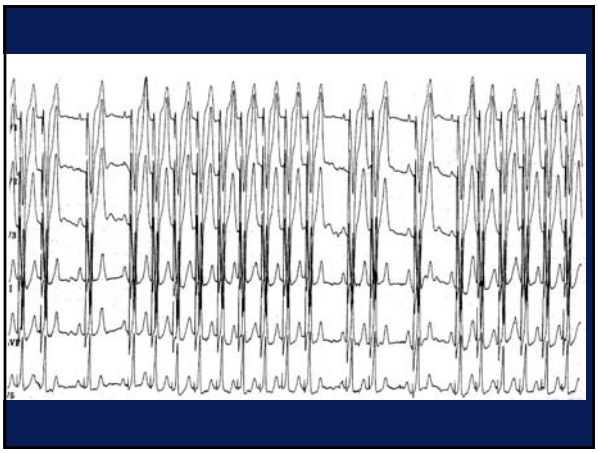
- If the upper tracking rate interval is longer than the TARP, the pacemaker will exhibit Wenckebach behavior first…
- If the TARP is longer than the upper tracking rate interval, then 2:1 block will occur

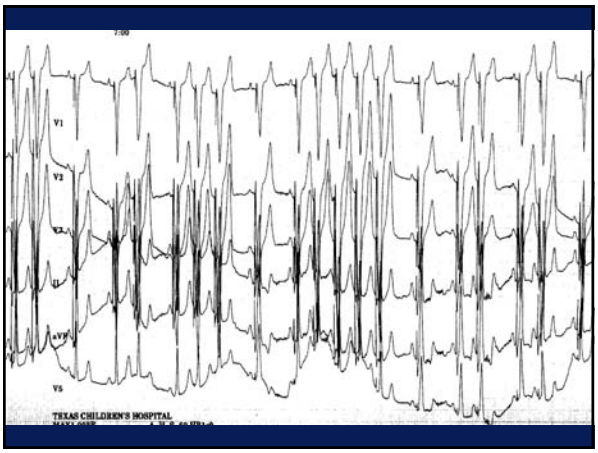
Upper Rate Behavior

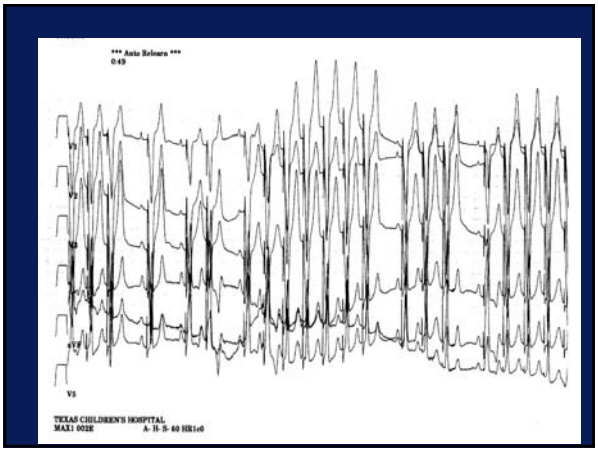
- When you program your upper rate without adjusting the AV delay and PVARP the pacemaker gives you this message

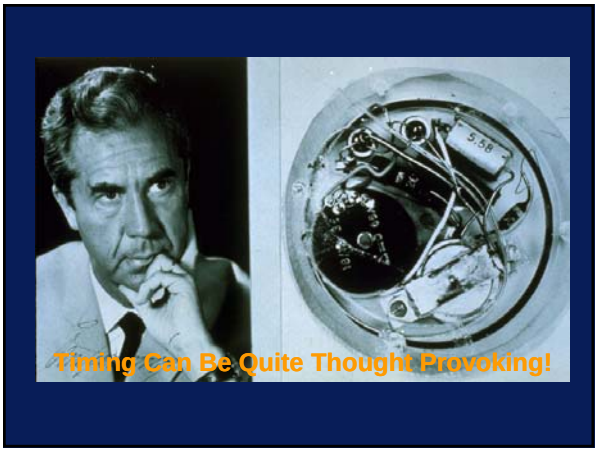


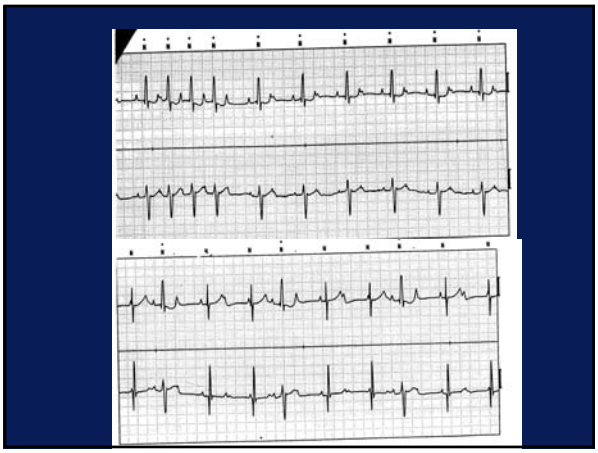












Pacing Wires

- In perfect world
  - Two atrial wires
  - Two ventricular wires
- In emergency if only one ventricular wire placed by surgeons
  - Place skin electrode and plug wire on the heart into negative port
  - If one ventricular and one atrial wire then place ventricular wire in negative port and atrial wire in positive port

Temporary Pacing

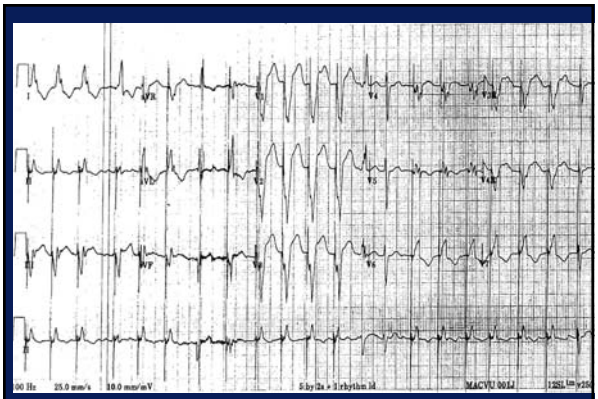
- Pacing spikes do not mean the heart is beating
  - Make sure pulse or pulse ox or arterial line is registering a pulse
- Pacing spikes on monitor do not mean the pacemaker is pacing
  - Look at lights on the box
- Know how to change the battery

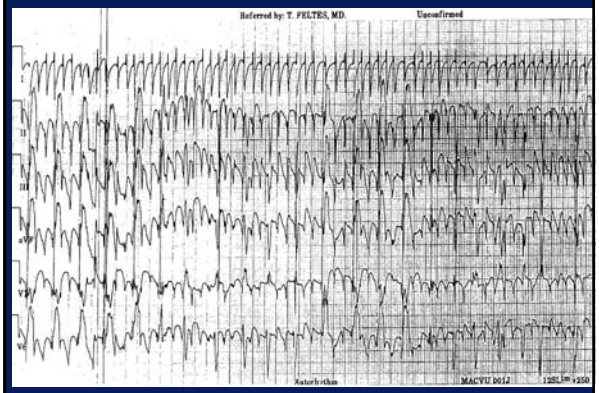
Laminate for Your Pocket

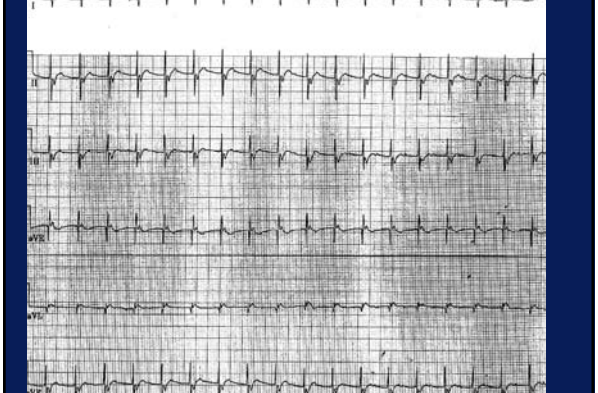
- Front of Device
  - Rate 80 to 100
  - A Output 5 mA
  - V Output 5 mA
- Menu M
  - Select DDD
- Menu 1
  - A sensing 0.5 mV
  - V sensing 2.0 mV
- Menu 2
  - Upper rate 150
  - PVARP 220-240 mS
  - AV interval 150 mS

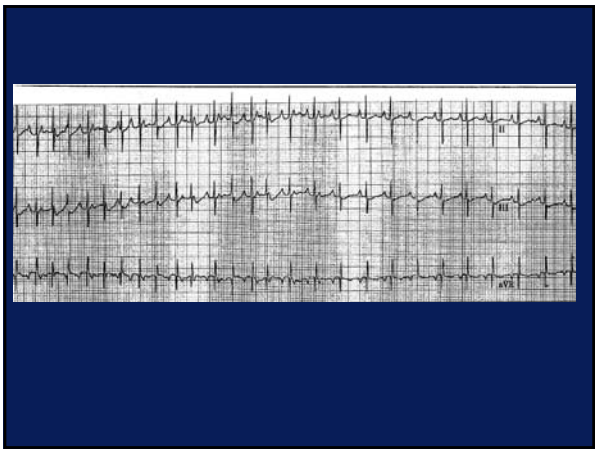
Diagnostic Utility of Pacing Wires

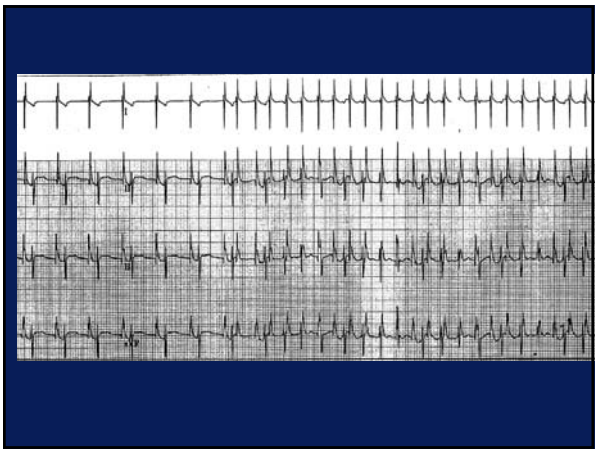
- Atrial electrograms
- Hook RA and LA ECG leads to the atrial wires if there are two – atrial activity on lead I
- Hook V1 to the atrial wire if only one – atrial activity on V1
- Also use lights on pacing box

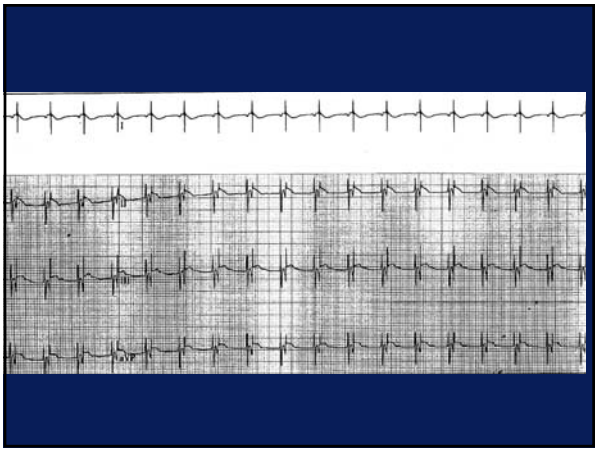


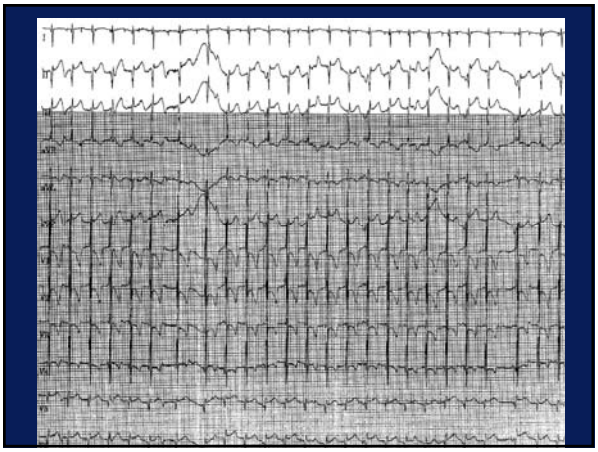


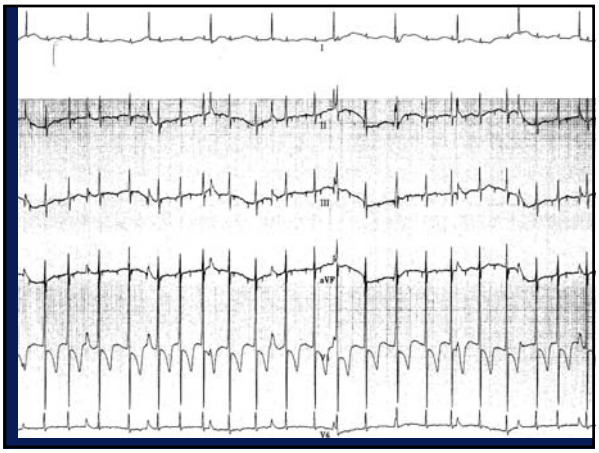


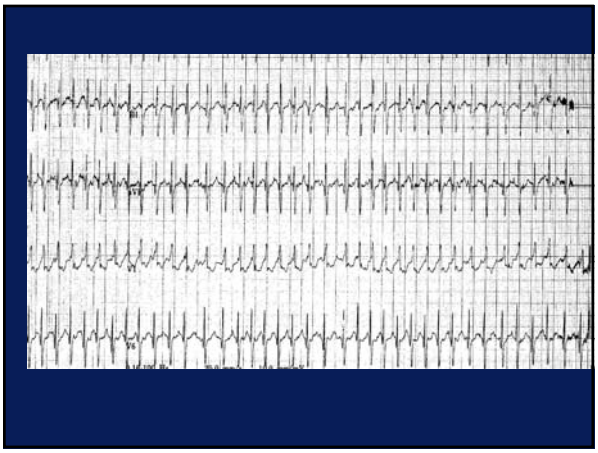


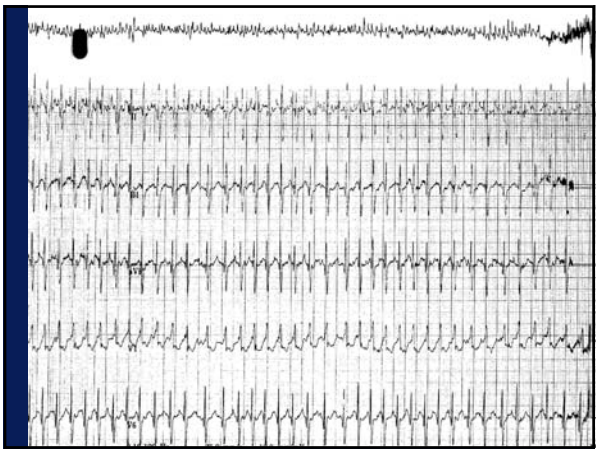


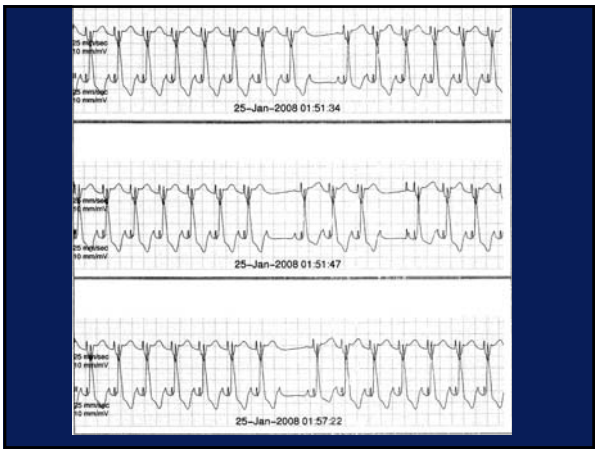








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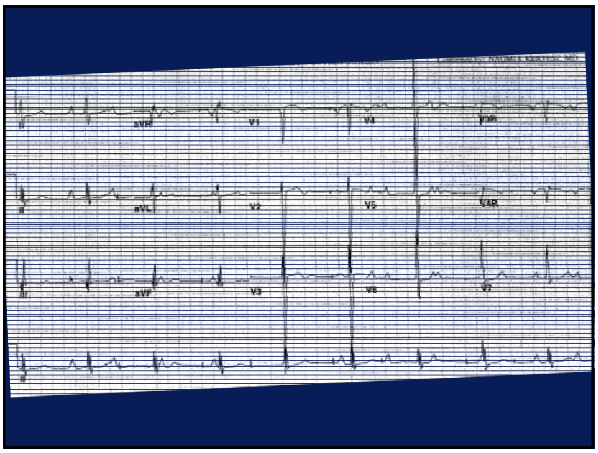
25-Jan-2008 01:51:47
25-Jan-2008 01:57:22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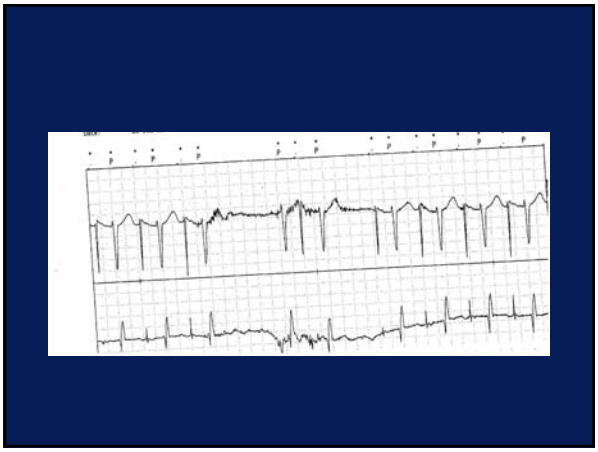
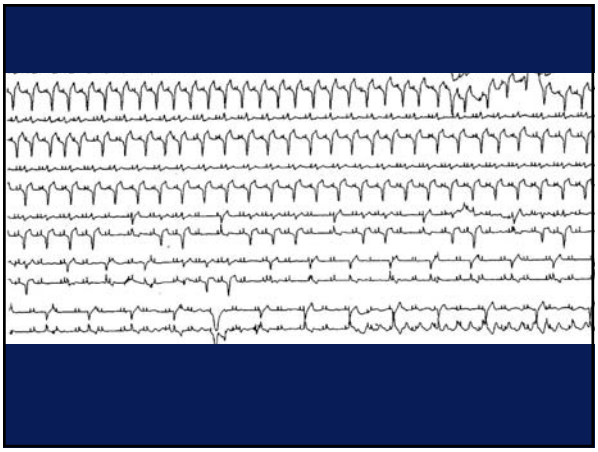
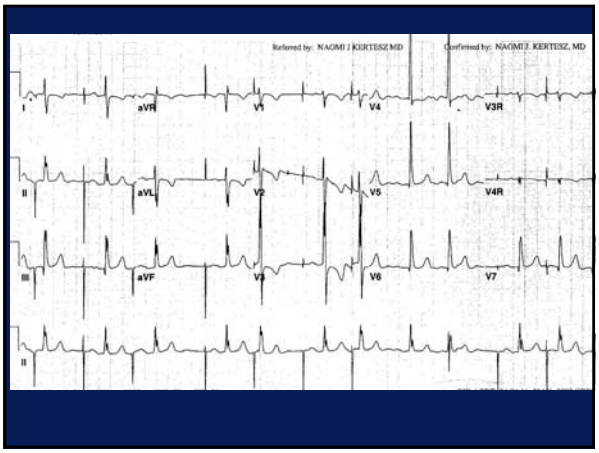
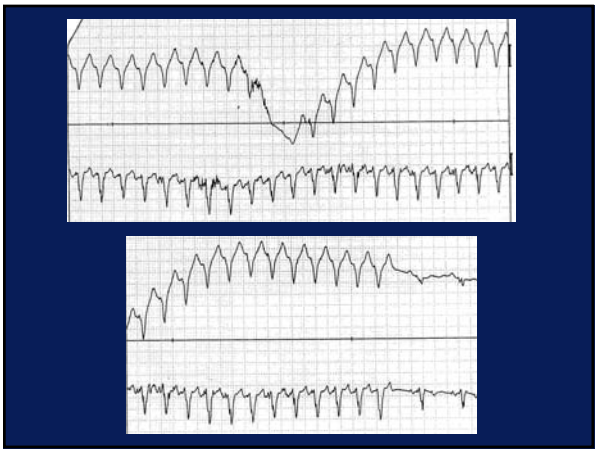
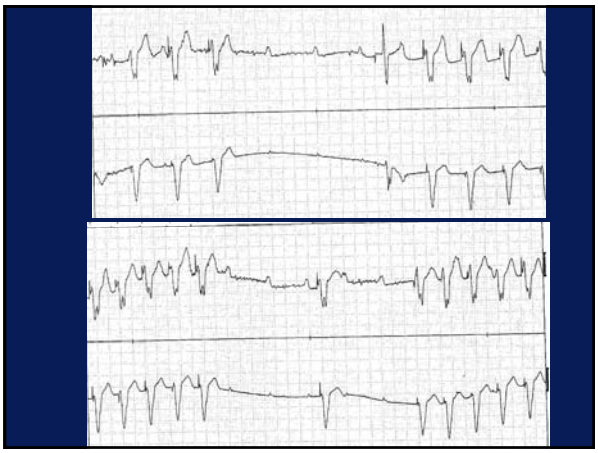
V1
V4
V3R
II
aVL
V2
V5
V4R
III
aVF
V3
V6
V7

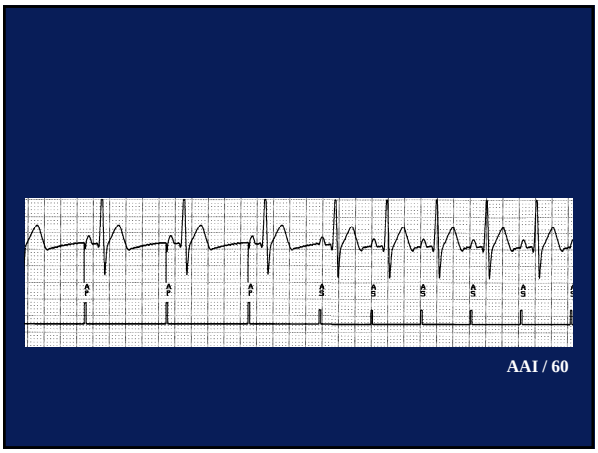


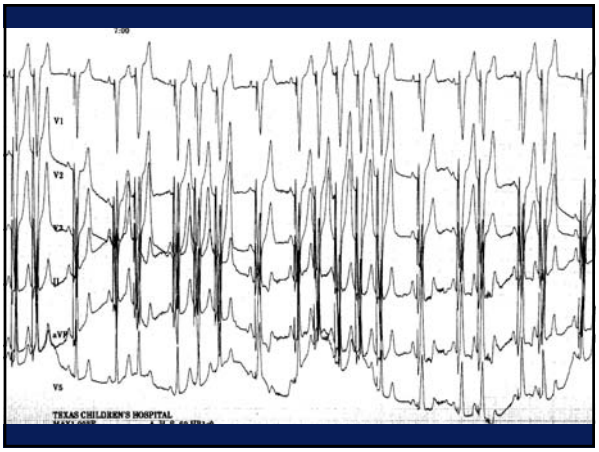


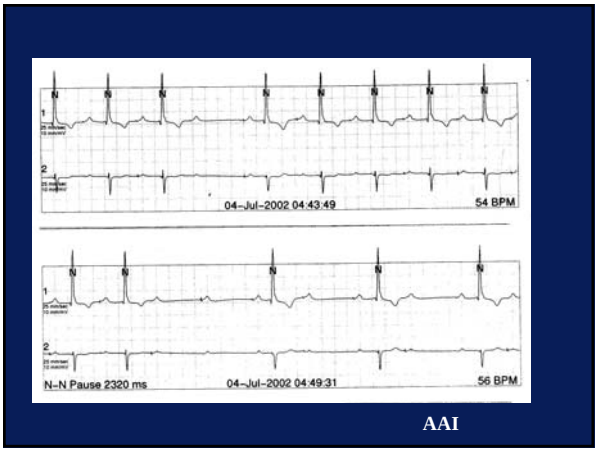

Referred by: NAOMI J KERTESZ MD
Confirmed by: NAOMI J. KERTESZ, MD
I
aVR
V1
V4
V3R
II
aVL
V2
V5
V4R
III
aVF
V3
V6
V7
II

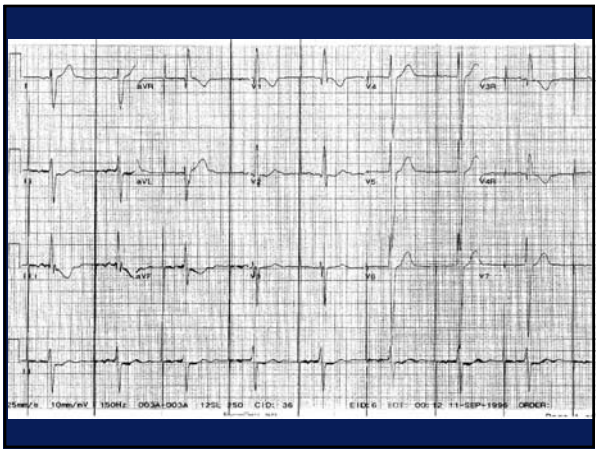


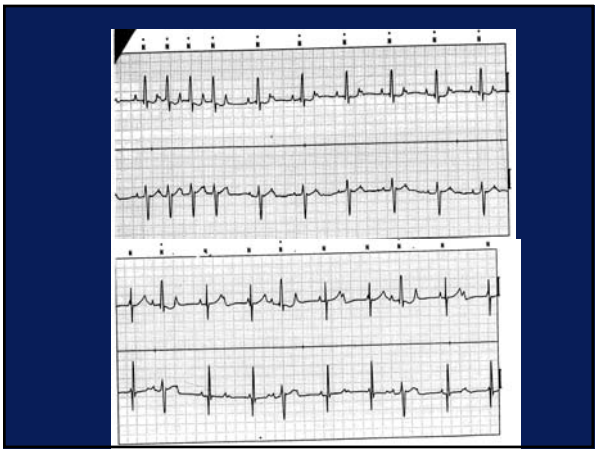



AAI / 60


V1
V2
V3
V5
TEXAS CHILDREN'S HOSPITAL


04-Jul-2002 04:43:49
54 BPM
N-N Pause 2320 ms
04-Jul-2002 04:49:31
56 BPM
AAI





Session VI: Cardiac Jeopardy

Moderator: Anthony Clapcich, MD

Walk Around Poster Discussion Session/Reception

C1 The Pharmacokinetics of Ketamine in Pediatric Cardiac Patients
C Ramamoorthy, GB Hammer, J Galinkin, DR Drover
Stanford University

C2 NSE and S100 protein levels are potential markers of neurological injury in children undergoing cardiopulmonary bypass
A Sophocles, Z Pan, R Friesen, M Twite
The Children's Hospital & University of Colorado School of Medicine, Denver CO

C3 Cefazolin Tissue Penetration in a Porcine Model of Cardiac Surgery and Cardiopulmonary Bypass Measured by In Vivo Microdialysis
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The Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA

C4 Ability of GFAP to detect neurologic injury in pediatric patients with cardiac disease on ECMO: A preliminary study.
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S.S. Sharma MD MPH, James Pierce MD, G.A. Bushman MD Sabine Von Busse MD, Mari Baldwin MD
Childrens Hospital Los Angeles, University of Southern California, USC Keck School of Medicine

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Klamt JG, Nabarro P, Vicente WVA, Garcia LV
Faculty of Medicine of Ribeirão Preto – University of São Paulo

C8 Limitations of cerebral oxygenation monitoring in children with congenital heart disease and profound polycythemia
EA Gottlieb, EB Mossad
Baylor College of Medicine, Texas Children's Hospital, Houston, Texas

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CA Knoderer, SA Saft, SG Walker, DP Healy, KM Sowinski
Indiana University School of Medicine, Butler University College of Pharmacy and Health Sciences, Purdue University College of Pharmacy, Nursing, and Health Sciences, University of Cincinnati, Winkle College of Pharmacy

C10 Cold Agglutinins in Children Undergoing Repair of Congenital Heart Defects with Cardiopulmonary Bypass
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The Pharmacokinetics of Ketamine in Pediatric Cardiac Patients

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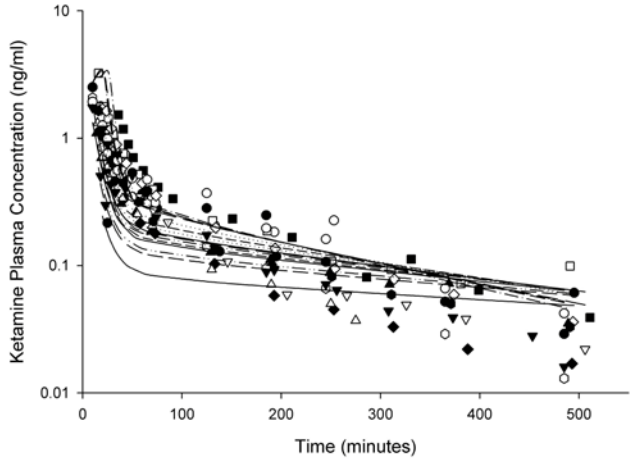
Introduction: Ketamine has been used safely in children with pre-existing heart disease (1). Limited data describing the pharmacokinetics (PK) of ketamine in children have been previously reported and there are no data for the PK in children with heart disease.

Methods: Following IRB and parental consent, children between the ages of 6 months and 18 years undergoing cardiac catheterization were enrolled in this prospective, open label study. Following the induction of anesthesia and tracheal intubation, arterial and central venous lines were placed per institutional protocol. A baseline (T0) venous blood sample was obtained following which ketamine 2mg/kg IV was administered over 5 minutes. Five minutes after the end of the bolus, timed blood samples were drawn at t= 5, 10, 15, 20, 30, 45, 60 min and t=2, 3, 4, 5, 6 and 8 hours. The blood samples were processed immediately following collection and plasma was separated and frozen for batched assay. Demographic data were collected in all subjects. PK data were analyzed using a NONMEM, population-based analysis.

Results: 15 subjects were enrolled, ages 6 months to 16 years (median: 7 yrs); weights were 5.5 to 54.7 kg (median: 18.3 kg). Twelve of the 15 (80%) were ASA 3 or 4; 11 of 15 (73%) had heart disease, 5 of whom had cyanotic heart disease. PK data best fit a 3-compartment model vs. a 2-compartment model ($p<0.001$). The fit was significantly improved with allometric scaling of mean weight (27 kg) on CL1 of the first compartment ($p<0.001$). Typical population values are: V1= 9.0L, V2=82L, V3=4.9L, CL1=0.42(weight)/27 L/min, CL2=0.65 L/min, and CL3=0.12 L/min. Plot show measured plasma concentrations and best individual fits to the data.



Discussion: The plasma concentrations of ketamine were best fit to a 3-compartment model with allometric scaling of weight to clearance. Dosing of ketamine should be based on patient weight. Although there was a significant age range in our patients, age is not a significant factor in dosing. No effect of cyanotic disease was discovered for the pharmacokinetics.

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NSE and S100 protein levels are potential markers of neurological injury in children undergoing cardiopulmonary bypass

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Introduction: The systemic inflammatory response (SIRS) to cardiopulmonary bypass (CPB) affects all organ systems including the brain. Perioperative brain injury in children with congenital heart disease (CHD) is often clinically silent and multifactoral in nature. The plasma biomarkers S100 and NSE show potential for predicting neurological injury. S100 protein is found in high concentrations in glial and Schwann cells and has a biological half-life of 2 hours. Neuron specific enolase (NSE) protein is an intracytoplasmic glycolytic enzyme found in neurons and has a half-life of a 24hrs. The three objectives of this study were to examine the relationship between S100/NSE and the:

1. SIRS as manifest by plasma levels of IL-6, IL-8 and IL-10
2. Parameters of CPB
3. Development of serious neurological injury post-surgery

Method: After IRB approval and informed parental consent, 50 children undergoing cardiac surgery with CPB had blood samples drawn from an arterial line at three time points: after induction of anesthesia; immediately post-CPB and at 24hrs in the CICU. Blood samples were analyzed at each time point for S100 and NSE protein levels as well as the inflammatory cytokines IL-6, 8 and 10. Data was collected on CPB times and neurological injury diagnosed in the postoperative period.

Results:

1. Positive correlation was found between IL-6, IL-8, IL-10 and S100 and NSE (Table 1).
2. Analysis of covariance (ANCOVA) was used to assess the association between S100/NSE and duration of CPB, duration of aortic cross clamp (XC), and if the patient underwent circulatory arrest or regional low flow cerebral perfusion (CA/RLFCP) (Table 2).
3. Three patients suffered serious neurologic insult or death. Wilcoxon rank sum test showed these patients had elevated levels of NSE (p=0.02) and S100 (p=0.09) during the post-CPB period, and S100 during the CICU period (p=0.09).

Discussion: S100 and NSE levels have been shown to correlate with CPB and XC time, and neurologic injury in adults (1,2) and children (3). Gu et al. found that the detection of both S100 and NSE is more specific than either by itself (2). The positive correlation between NSE, S100, inflammatory cytokines, and neurologic deficits suggest that the SIRS contributes to neurologic injury. Plasma proteins specific to neurologic injury when combined with imaging, such as MRI, may help in the early detection of neurological injury. This may enable future brain protective strategies to be implemented, as well as identify children who require long-term neurodevelopmental follow up.

Table 1 Spearman correlation coefficient of NSE and S100 with inflammatory markers

	NSE					S100				
	Pre-CPB	Post-CPB	CICU	Δ Pre-Post-CPB	Δ Post-CPB to CICU	Pre-CPB	Post-CPB	CICU	Δ Pre-Post-CPB	Δ Post-CPB to CICU
IL-6	-0.09	0.40*	0.22	0.41*	0.32*	-0.01	0.16	0.13	0.20	0.31*
IL-10	-0.16	0.10	0.20	0.11	0.05	0.21	0.12	0.33*	0.30*	0.10
IL-8	0.05	0.41*	0.22	0.45*	0.39*	-0.03	0.14	0.23	0.21	0.20
S100b	0.09	0.55*	0.40*	0.50*	0.42*					

*p<0.05 for testing the null hypothesis that Spearman correlation = 0

Table 2 ANCOVA results for NSE and S100

	Post-CPB NSE	CICU NSE	Post-CPB S100	CICU S100
Duration of CPB	+*	+	+*	-
Duration of XC	+	+*	+	+
CA/RLFCP	+*	+*	+	+

+/- for positive or negative correlation. *p<0.05

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Cefazolin Tissue Penetration in a Porcine Model of Cardiac Surgery and Cardiopulmonary Bypass Measured by In Vivo Microdialysis

Author(s): Kilbaugh TJ, Berkowitz D, Kubin J, Pastuszko A , Zaoutis TE, Jobes DR, Greeley WJ, Zuppa AF

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ABSTRACT BODY:

Introduction: Surgical site infections (SSI) are the second most common cause of nosocomial infection. There is limited data in pediatrics, but surgical site infection rates may range from 2 to 12% of all pediatric cardiac surgical patients, despite current standard prophylactic antibiotics [1, 2]. Unfortunately, antibiotic dosing is guided by plasma concentrations and not by actual tissue penetration. We hypothesize that currently accepted cefazolin dosing guidelines do not adequately achieve tissue concentration above the mean inhibitory concentration (MIC_{90}) for common organisms causing surgical site infections in cardiac surgery; and, that by using in vivo microdialysis in a immature porcine model of cardiac surgery and cardiopulmonary bypass, knowledge can be gained to develop informed dosing guidance that will optimize tissue penetration and ultimately reduce the incidence of SSI.

Methods: Following IACUC approval, piglets (3-5 days old, female N=4/group) underwent median sternotomy (MS) or median sternotomy + cardiopulmonary bypass (MS + CPB). In vivo microdialysis was employed to measure unbound interstitial concentrations of cefazolin in subcutaneous tissue and muscle immediately adjacent to median sternotomy incision [3]. Each piglet received an intravenous dose of cefazoin (25 mg/kg) immediately prior to incision, and MS + CPB group received an additional dose of 25mg/kg (total 50 mg/kg) during initiation of CPB via priming volume. Plasma and dialysate concentrations were collected. Pharmacokinetic parameters, including Cmax and Tmax were identified. The area under the concentration time curve (AUC) was calculated using non-compartmental analysis .

Results: Median peak concentrations of 41.5 (ug/ml) in the muscle and 49.5 (ug/ml) in the subcutaneous space occurred at 15 and 30 min, respectively during MS. Median peak concentrations resulted in of 49 (ug/ml) in muscle and 44 (ug/ml) following initiation of CPB and the second dose of cefazolin during MS + CPB. There was no significant difference between the dose normalized (AUC/dose) AUC in muscle for pigs on CPB vs. those that underwent sternotomy alone (p=0.68). However dose normalized AUC in plasma was significantly higher in the CPB group (p=0.057).

Table 1 and 2: Pharmacokinetic parameters represented as Median (range) values

Table 1. Sternotomy (MS)	Plasma	Muscle	Subcutaneous
AUC (ug*min* ml^{-1})	2691 (2056,8501)	2629 (1789, 3585)	3501 (1836,4034)
Cmax (ug/ml)	154 (75, 179)	41.5 (32, 46)	49.5 (40, 59)
Tmax (min)	5	15 (15, 30)	30 (15, 30)

Table 2. MS + CPB	Plasma	Muscle	Subcutaneous
AUC (ug*min* ml^{-1})	20791 (14194,25024)	3994 (14194, 25024)	5222(4177,6429)
Cmax 1(ug/ml)	189 (132, 280)	26 (21, 47)	38 (31, 48)
Tmax 1(min)	5	30 (15, 30)	30 (15, 30)
Cmax 2(ug/ml)	111 (76, 130)	49 (21, 86)	44 (30, 59)
Tmax 2(min)	42.5 (30, 60)	52.5 (30,60)	45 (45, 60)

Discussion: The goal of prophylactic antibiotics is to achieve tissue concentrations exceeding the MIC_{90} of common bacteria that cause surgical site infections; gram positive organisms: *S epidermidis* and *S aureus*, and gram negative organisms: *Serratia sp* and *Enterobacter*. Current dosing recommendations in our model of porcine cardiovascular surgery resulted in plasma concentrations exceeding MIC_{90} for all organisms. **However, interstitial tissue concentrations (muscle/subcutaneous) did not exceed MIC_{90} for the gram negative organisms, *Enterobacter and Serratia* prior to incision or at ANY time over a four hour period during median sternotomy or CPB.** Furthermore, pigs that underwent MS + CPB received twice the amount of drug that pigs than MS alone, yet maximal tissue concentrations were similar in both groups. Despite the significantly larger plasma dose normalized AUC in the CPB group; pigs that underwent CPB did not achieve higher dose-normalized muscle AUCs. This suggests that either tissue becomes saturated and maximal tissue concentrations are achieved despite higher plasma exposures or that hypothermia associated with CPB impacts the ability for drug to penetrate into tissue. The latter is supported by an additional observation that despite the decrease in plasma concentrations after rewarming and removal from CPB, tissue concentrations increase This warrants further investigation in pediatric patients to better understand the impact of CPB and hypothermia on antibiotic disposition, specifically tissue penetration.

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Title: Ability of GFAP to detect neurologic injury in pediatric patients with cardiac disease on ECMO: A preliminary study.

Authors: JM Schwartz, MM Bembea, W Savage, LA Vricella, RB Easley, A Everett.

Institution: Johns Hopkins School of Medicine, Baltimore, MD 21287

Introduction: Children undergoing cardiopulmonary bypass (CPB) experience neurologic injury in 30-70% of cases.[1,2] Extracorporeal membrane oxygenation (ECMO) represents a similar support modality with a risk of neurologic injury in 10-60% of cases.[3,4] We hypothesized that a brain specific protein, glial fibrillary acidic protein, (GFAP), could serve as a plasma biomarker for neurologic injury in these vulnerable patients while on ECMO.

Methods: As part of a prospective study of pediatric patients on ECMO, only those patients with history of critical cardiac disease and ECMO were included in this evaluation. Demographic information such as age, diagnosis, duration of ECMO and outcome at time of PICU discharge was recorded. Serial blood samples during the ECMO course were evaluated for GFAP using an electroluminescent assay developed at our institution.

Results: A total of 7 children with critical cardiac disease were enrolled. Median duration of ECMO support was 5.2 days (range: 1 to 12 days). The 2 children who underwent ECMO post-CPB had GFAP levels similar to other children who underwent ECMO only. One patient who experienced acute neurologic injury had plasma GFAP levels that were 100 fold greater than those without neurologic injury; the increase in plasma GFAP coincided with detection of neurologic injury by imaging. The plasma GFAP levels during the ECMO course for each patient are shown in Table 1.

Conclusions: Plasma GFAP appears to correlate with neurologic injury in this series of patients with critical heart disease on ECMO. This may aid in detection of neurologic injury in patients on ECMO and during CPB. Studies are underway to more precisely define this biomarker in patient populations at high risk for neurologic injury.

Diagnosis	pt	GFAP Measurements						CPB XC	Neuro Injury	Survival
		1	2	3	4	5	6			
Heart transplant for DCM s/p bivad, inabilty to separate from CPB	A	0.074	0.433	11.3	20.5			400 min 69 min	Stroke, ICH	No
Dilated Cardiomyopathy	B	0.052	<0.04	0.053					None	Yes
Dilated Cardiomyopathy	C	0.162	<0.04	<0.04					None	Yes
Cardiogenic shock, Critical AS,MS	D	<0.04	<0.04		0.061	0.068	0.194		None	Yes
PPHN D-TGA, POD #1 s/p BAS	E	<0.04	<0.04	0.083	0.164				None	Yes
Cardiogenic shock s/p PA stenting, h/o TOF, RV-PA conduit	F	0.068	0.09	0.054					None	Yes
POD #3 RV-PA Conduit for TA, hypoxemia	G	<0.04	<0.04					201 min 130 min	None	Yes

Abbreviations: pt-patient, XC-cross clamp, Neuro-neurologic, DCM-dilated cardiomyopathy, bivad-biventricular assist device, min- minutes, ICH-intracranial hemorrhage, AS-aortic stenosis, MS-mitral stenosis, PPHN-persistent pulmonary hypertension of the newborn, D-TGA-dextro-transposition of the great arteries , POD-post-operative day, BAS-balloon atrial septostomy, PA-pulmonary artery, TOF-tetralogy of fallot, RV-right ventricle, TA-truncus arteriosus.

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Title: Cervical epidural for diagnosis of catecholaminergic polymorphic ventricular tachycardia in a pediatric patient

Author(s): Shiu-Yi Emily Chen, Gerald Bushman, Giovanni Cucchiaro

Affiliation(s): Childrens Hospital Los Angeles, University of Southern California

Introduction: Etiologies for polymorphic ventricular tachycardia (PVT) include long QT syndrome (LQTS), ischemic cardiomyopathy, acute fulminant myocarditis, and catecholamine stimulation.[1,2,3] Therapeutic options are beta blockers (BB), amiodarone, and implantable cardioverter-defibrillators (ICD).[2] A left cardiac sympathetic denervation (LCSD) is a valid alternative in cases refractory to pharmacological interventions.[3,4] We report a case of catecholaminergic polymorphic ventricular tachycardia (CPVT) in a previously healthy 2 year old female found in cardiogenic shock after days of upper respiratory illness (URI). Increased adrenergic tone was associated with frequent PMVT. Thoracoscopic LCSD was performed after a trial of high thoracic-cervical epidural autonomic blockade.

Case Report: A 2 year old female with URI presented to the emergency room in cardiogenic shock. She was stabilized with IV adenosine, amiodarone, and fluid resuscitation; however, she continued to decompensate and was sedated, intubated and placed on vasopressor support and transferred to our institution for further medical management. Examination revealed irregular tachycardia with bibasilar crackles on auscultation. Echocardiogram showed mild tricuspid and mitral regurgitation, dyssynchronous ventricular contractility, normal intra-cardiac anatomy, and LVSF 23%. Despite high dose amiodarone (7.5mcg/kg/min) and esmolol (150mcg/kg/min) infusions to maintain sinus rhythm, she continued to have daily breakthrough PVT associated with agitation on fentanyl (5 mcg/kg/hr) and midazolam (3mcg/kg/min) drips. Episodes of PVT resolved with boluses of fentanyl (45 mcg) and midazolam (1.7mg). A differential diagnosis included cardiac hamartomas or adrenergic-induced arrhythmia. Cardiac MRI was negative for hamartoma, a potential arrhythmogenic focus. To rule out adrenergic-induced arrhythmia and to verify the potential benefit of LSCD, an autonomic blockade by high thoracic-cervical epidural was performed. With general anesthesia, a C_7-T_1 epidural catheter was placed under fluoroscopic guidance. After a negative test dose, 0.25% bupivacaine @ 3ml per hour was used to establish an autonomic blockade. Episodic PVT decreased in duration and frequency with the same anti-arrhythmic doses. Sustained PVT resolved two days after the epidural placement. Due to the success of the epidural trial, patient underwent thoracoscopic LSCD with epidural catheter removal on post-operative day (POD) 5. She was extubated three days later. There were no episodes of PVT in the post-operative period. Conversion to PO amiodarone (50mg bid) and propranolol (80mg qid) occurred 10 days after LSCD. No signs of Horner's syndrome were observed. Outpatient Holter monitoring revealed mostly sinus bradycardia.

Discussion: We have shown that a selective pharmacological autonomic blockade using a high thoracic-cervical epidural can be useful in identifying CPVT. Reid reported the first case of CPVT in 1975 in a 6 year old girl with bidirectional tachycardia induced by emotional stress and reproducible with pharmacological stimulation.[1] The documented mean age of the onset of symptoms is 7.8±2.5 years, and diagnosis at 10.6±3.5 years.[1] Initial clinical presentations include faintness, dizziness, visual disturbance, syncope, or hyper-or hypotonia with bladder and bowel incontinence. Epilepsy can be a misdiagnosis. Positive family history of syncope, sudden death, or PVT strongly suggests the presence of CPVT.[1,2] The differential diagnosis include LQTS, cardiac hamartoma, or CPVT. Radiologic examination and pharmacologic induced arrhythmia can help to differentiate the potential cause. CPVT can be confirmed if the corrected QT interval is normal and there is no structural cardiac lesion by resting 12-lead EKG and stress test.[1,2] Diagnosis depends on the induction of CPVT either by exercise or isoproterenol infusion. Holter monitoring is helpful in capturing premature ventricular ectopy with progression to CPVT but is not discretely diagnostic. Cardiac ryanodine (RyR2) and cardiac CASQ2 receptors are implicated in familial occurrence of CPVT.[2] Nadolol is used in outpatient setting for both prophylaxis and heart rate control but increasing doses of BB have significant side effects. ICD can be implanted in case of CPVT refractory to medical therapy. Potential inappropriate discharge, possible lead fracture or migration, and the need for repeated generator replacement limits its use in pediatric patient.[2] Recurrent appropriate ICD shocks despite optimized medical therapy can be an indication for LCSD.[4] LCSD is a surgical interruption of the left sympathetic chain from T_1 to T_5. Thoracoscopic LCSD is associated with excellent results and minimal complications in both LQTS and CPVT.[3,4] LCSD reduces arrhythmias and raises the threshold for ventricular fibrillation. No post-denervation supersensitivity arises from pre-ganglionic denervation. Heart rate does not change because of right sided sympathetic ganglion chain compensation.[3] Early diagnosis of CPVT is important because it responds well to BB, and the role of autonomic blockade by an epidural catheter may be useful in predicting a successful outcome of LCSD.

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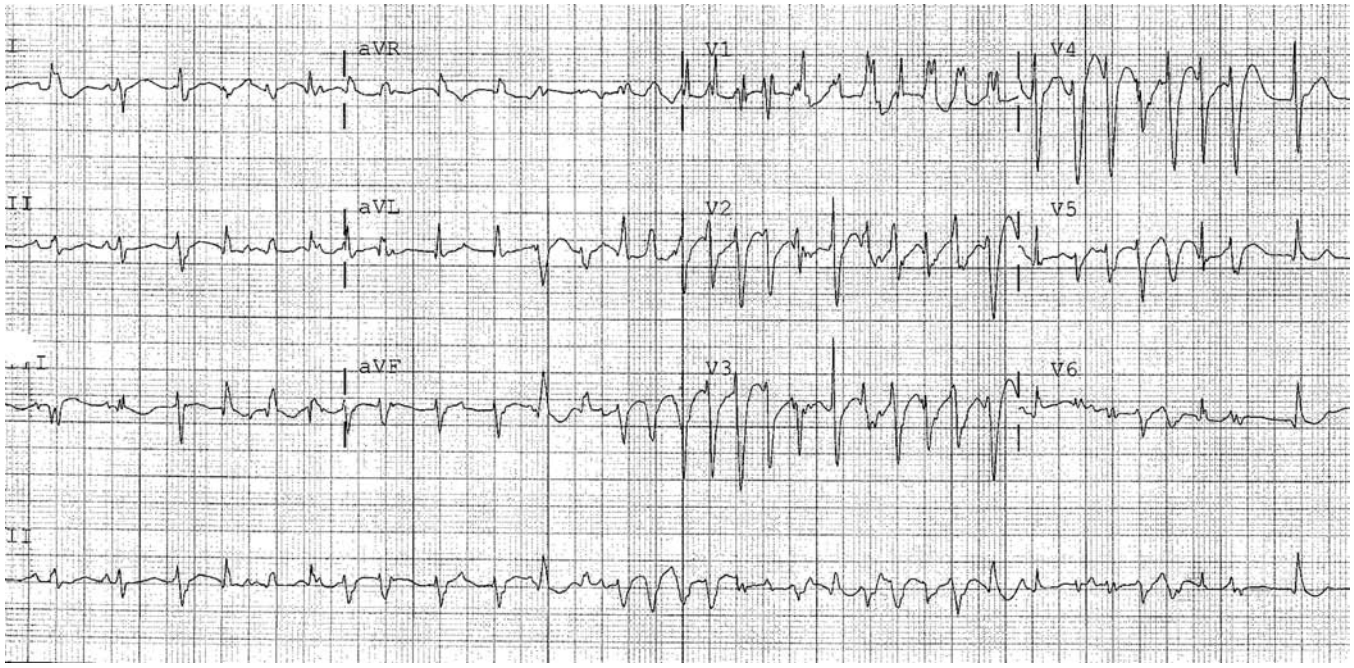
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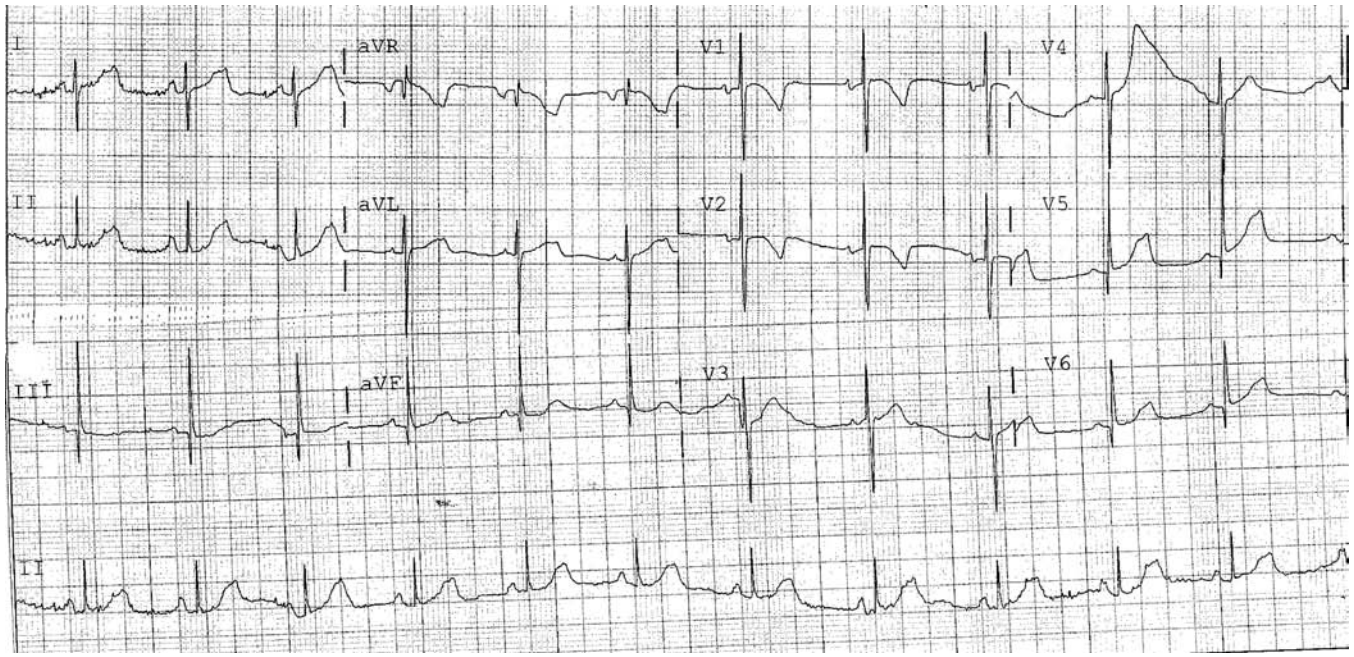
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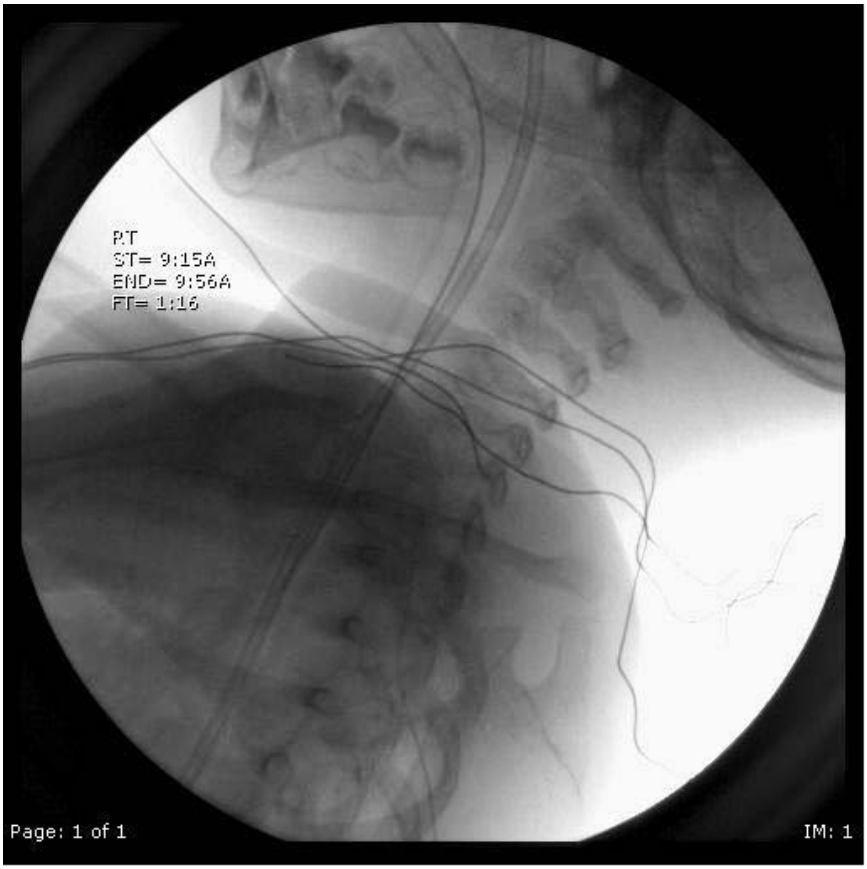
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Title: Risk Profile for Infants with Single Ventricle Physiology Undergoing Noncardiac Surgery While Palliated with a BT Shunt or Sano Conduit

Author(s): S.S. Sharma MD MPH, James Pierce MD, G.A. Bushman MD Sabine Von Busse MD, Mari Baldwin MD
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Introduction: Surgical palliation after Stage I reconstruction of hypoplastic left heart syndrome (HLHS) is associated with hospital survival of at least 70% in many experienced centers. Despite improving results, Stage I patients are physiologically fragile. The common sources of pulmonary blood flow include the modified Blalock-Taussig Shunt (BTS) and the right ventricle-to-pulmonary artery shunt (Sano conduit). Interstage mortality remains high as up to 15% of Stage 1 survivors die after hospital discharge but prior to admission for Stage 2 palliation with a venous shunt. Previous studies have characterized interstage mortality and the medical surveillance and management believed to be important in reducing risk. This study was performed in a single institution with a high volume cardiac surgical practice. We report preliminary data regarding the procedural risks associated with Stage 1 patients who require repeated anesthetics for non-cardiac surgery while palliated with a BTS or Sano conduit.

Methods: A retrospective chart review was conducted on patients with HLHS or variant who had received Norwood palliation. Specifically, this analysis focused on patients with either a BTS or Sano conduit and whom subsequently had one or more noncardiac procedures performed under anesthesia. IRB approval was obtained with informed consent waived. Hospital electronic medical records and the Compurecord automated anesthesia record system were accessed for review. Demographics, procedural (surgical and anesthetic) and postoperative events were reviewed and recorded in a database.

Results: Preliminary analysis revealed 66 single ventricle patients who underwent a total of 167 anesthetics for noncardiac procedures following Stage I surgery (Fig.1). Imaging studies or interventional radiology procedures represented the greatest numbers of anesthetics, followed by open abdominal general surgical procedures, and ENT procedures (Fig.2). Induction of anesthesia was accomplished with an inhalational agent (31%), combined IV and inhalational agent (50%), or intravenous agent alone (19%). The frequency and type of IV agent used are shown in Fig. 3. Complications of induction of anesthesia were noted in up to 3% of patients. Hypotension was noted in 1.3% and significant change in SaO2 from baseline noted in 3.3%. There were no catastrophic airway issues. Sustained hypotension was noted intraoperatively in 7.8% of patients and sustained hypoxia noted in 7.2% of patients. Unexpected inability to extubate was noted in 0.7%. Although no one required reintubation within 6 hours of emergence and extubation, 2.1% were reintubated within 6-24 hours for respiratory failure and 1.4% were reintubated after 24 hours.

Patients were admitted to the floor 37.9% of the time, but 3.4% unexpectedly were diverted from the OR for postop care in the ICU. Approximately 1.4% of patients were admitted to the floor and then decompensated requiring ICU admission. Also, 21.4% of patients required ICU admission for observation and management up to seven days, 11% spent 8 days to 1 month, and 29.7% convalesced in the ICU for more than one month after a noncardiac procedure.

Finally our analysis revealed significant postoperative complications. Sepsis following a noncardiac procedure was observed in 12.4% and pneumonia in 6.9% of patients. The overall mortality for this cohort was 13.6% with an intraoperative mortality of 1.5%.

Discussion: Non-cardiac procedural care after Stage I palliation of HLHS occurs frequently and can prove to be quite challenging. Identifiable risk factors involve planning issues; the availability of appropriate resources and personnel; patient-related problems such as abnormal convalescence, infection, and feeding problems; and procedural risks related to the conduct of the anesthetic and surgical/interventional procedure. Similar to the system complexities routinely encountered in the pediatric cardiac operating room, procedural care for these patients after Stage 1 palliation involves similar system-related risk and deserves extensive further study.

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Fig. 1

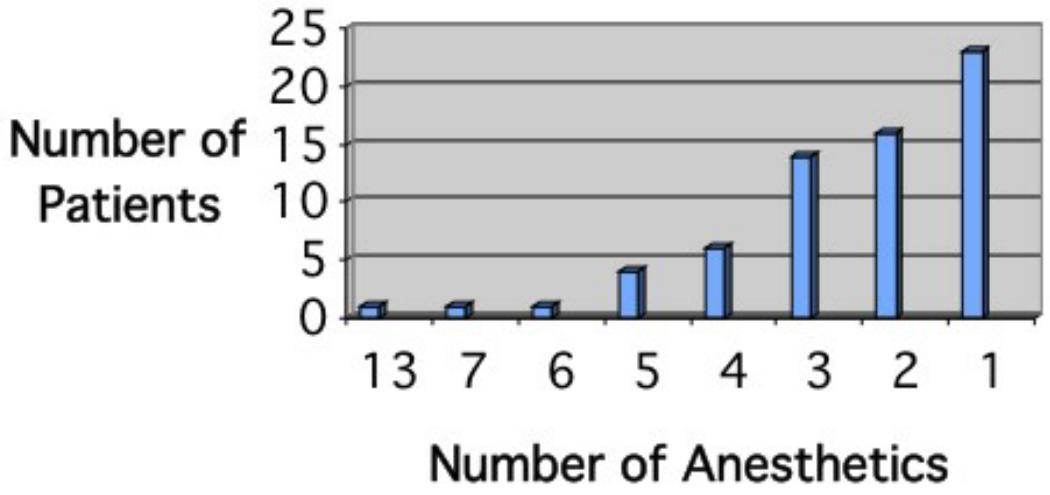

Fig. 2

Neuro Procedures	3
ENT	19
Thoracic	12
Scope Abd	7
Open Abd	29
Radiology	77
Other	5

Fig. 3

IV Agents Used With Other Agents for Induction

18.6% received Ketamine
29% received Etomidate
4.1% received Propofol
13.1% received an opioid
3.4% received midazolam

Title: SjO_2/SvO_2 correlation during pediatric cardiac surgery with cardiopulmonary bypass (CPB) under fentanyl-midazolam anesthesia

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ABSTRACT BODY:

Introduction: The jugular venous oxygen saturation (SjO_2) is an objective measurement of the cerebral oxygen delivery, quality of neuroprotection, detection of ischemia (SjO_2<50%), and adequate management (1). Poor correlation between SjO_2 and central venous oxygen saturation (SvO_2) has been shown in children (2), so that SjO_2 is required to access cerebral oxygenation. Intermittent jugular blood sampling may provide useful information for adequate management. Particularly, when NIRS or jugular cooxymetry are not available. This retrospective study compares the SjO_2 and SvO_2 at some critical time periods of the pediatric cardiac surgery.

Methods: Twelve pediatric patients aged from 3 to 120 months undergoing cardiac surgery with CPB and anesthetized with fentanyl (20 $\mu g.kg^{-1}$ followed by 5 $\mu g.kg^{-1}.h^{-1}$) and midazolam (0.2 $mg.kg^{-1}$ followed by 0.1 $mg.kg^{-1}.h^{-1}$) and supplemented with isoflurane, received a central 5F catheter placed through right internal jugular and a 22 or 20G intravenous catheter placed through the left internal jugular at the cricoid ring and advanced retrograde. Blood samples of one ml were withdrawn simultaneously from the two venous catheter and artery line every 10 minutes and when deemed necessary. SjO_2, SvO_2 and SaO_2 (arterial oxygen saturation) data were recorded for analyses at the following time periods: after venous and arterial catheter insertion (IN), before the start of bypass (BCPB), after complete cooling (C), after re-warming (RW), and after protamine administration ((PROTA). Blood gas was managed by alpha-stat strategy.

Results: Regression analyses of the pooled data showed no correlation between SjO_2 and SvO_2 (r^2=0.14, slope=0.3) but low correlation was observed after protamine administration (r^2=0.46 and slope =1). The means were similar at all time period except at PROTA, when SvO_2 (87.8 ± 8.5 %) was significantly higher than SjO_2 (68.2 ± 13.9 %) (Mann-Whitney test). SjO_2 < 50% were detected in 4 patients comparing to 1 SvO_2<50% after re-warming. After weaning from CPB, only one sample with SjO_2<50% was observed. Glucose levels increased significantly from 82.4 ± 24 (IN) to 209±34 $mg.dl^{-1}$ (PROTA) in the central venous blood and similar values were found in the jugular blood, but arterial-jugular difference were higher than arterial-central venous in all periods time. Jugular and central venous lactate increased similarly, from 1.7±1.0 (IN) to 3.6 $nmol.L^{-1}$ (PROTA) in the central venous blood.

Discussion: SvO_2 may not predict the SjO_2, and greater difference between SjO_2 and SvO_2 can occur after re-warming and after weaning from bypass.

Limitations of cerebral oxygenation monitoring in children with congenital heart disease and profound polycythemia

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Introduction: Monitoring of regional cerebral oxygen saturation index (rSO_2i) using near-infrared spectroscopy (NIRS) is employed in an effort for early detection and prevention of neurological complications in pediatric cardiac surgery[1,2]. Although NIRS is reliable in most clinical circumstances, there are reported limitations to the technology. We report a series of pediatric polycythemic patients presenting for surgical treatment of congenital heart defects in whom an rSO_2i was not measurable until hematocrit was decreased with hemodilution.

Methods: Seven cyanotic patients with congenital heart disease (CHD) and significant polycythemia (HCT>60%) were included in this report. After induction of anesthesia, bilateral pediatric Somanetics INVOS 5100 sensors (Somanetics, Inc. Troy, MI) were placed on the patient's forehead. If rSO_2i was not measureable, the probes were removed, placed on the attending anesthesiologist to prove that the probes were functioning and replaced with new probes. With every blood gas, hematocrit, hemodynamic variables, ventilatory variables, and the presence or absence of rSO2i were recorded.

Results: The series of patients had a mean age of 53 +/- 16.5 months, weight of 14.5 +/- 3.1 kg, initial HCT of 63.1 +/- 2.7 % and a baseline oxygen saturation of 85 +/- 4%. Five of seven patients were Hispanic. One patient was Caucasian, and one patient was African American. All patients had cyanotic congenital heart disease and were scheduled for palliative or reparative surgery. The first measurable rSO_2i for each patient and the hematocrit at which the rSO_2i became measureable are reported in Table I, as well as intraoperative hemodynamics at induction, prior to cardiopulmonary bypass (CPB), on CPB, and following protamine administration. The mean HCT at which rSO2i was detected was 48.3 +/- 13.3 %.

Discussion: Several limitations of NIRS monitoring have been reported in patients with increased serum bilirubin, sickle cell disease, dark skin pigmentation, and after injection of methylene blue[3,4]. The penetration, absorption and scatter of NIR light is described by the Beer-Lambert equation [log lo/l = α.c.d] and can thus be affected by the concentration of serum hemoglobin[5]. It has previously been reported that polycythemia does not affect rSO_2i[6]. However, in the current report, we found that rSO_2i was not measureable in the significantly polycythemic patients with CHD until hemodilution reduced the hemoglobin levels.

Table I: Intraoperative data:

	Pre-Incision mean(SD)	Pre-CPB mean (SD)	On-CPB mean (SD)	Post-CPB mean (SD)
HCT %	63.1 (2.7)	60.7 (2.8)	38.5 (3.1)	45.7 (6.5)
SpO_2 %	85 (4)	78 (12)	NA	92 (11)
$PaCO_2$ mmHg	51.3 (18.1)	54.6 (8.6)	44.8 (8.7)	45.7 (6.5)
$ETCO_2$ mmHg	34.1 (4.1)	31.4 (5.5)	NA	31.6 (3.1)
MAP mmHg	56.4 (7.8)	56.2 (6.3)	41.3 (1.2)	57.1 (6.9)
T ºC	35.9 (0.3)	36.3 (0.8)	36.0 (0.4)	36.3 (0.4)
NIRS detected	0 (n=7)	3 (n=7)	6 (n=6)*	6 (n=6)*
rSO_2i (average)	NM	71.7 (1.2)	73.5 (8.8)	75.1 (16.9)

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Title: Pharmacokinetics of cefuroxime are not significantly altered by cardiopulmonary bypass in children

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Introduction: Surgical site infections are a serious and frequent complication of cardiac surgery. Cardiopulmonary bypass (CPB) may alter the pharmacokinetics of prophylactic antibiotics. The pharmacokinetics of cefuroxime in children have been studied, but no data are available which have evaluated the effects of CPB on cefuroxime pharmacokinetics in pediatric patients. (1, 2) The objective of this study is to determine the pharmacokinetics of cefuroxime in pediatric subjects undergoing CPB.

Methods: Infants and children undergoing CPB were enrolled in the study. The study was approved by the IUPUI/Clarian IRB and written informed consent was obtained from the subject's parent or guardian prior to participation. Following routine practice at our institution, an initial dose of cefuroxime was administered prior to surgical incision and a second dose was administered in the CPB prime solution. Serial blood samples were obtained at strategic points before, during and after the CPB process. Blood samples were collected into heparinized blood collection tubes and the plasma was collected and stored frozen at -70deg C. Samples were shipped on dry ice to the analytical laboratory and concentrations determined by a validated HPLC method. A two-compartmental pharmacokinetic model was fitted to the data with ADAPT 5 using MAP Bayesian estimation, with weight as a covariate. Monte Carlo simulations of a single-dose (25 mg/Kg pre-CBG) approach and a two-dose (25 mg/Kg pre and 12.5 mg/Kg prime solution dose) were performed.

Results: Fifteen subjects (8M/7F) were enrolled in the study with median (range) age and weight of: 11 (3-34 months) and 9.5 (4.5-15.4 Kg), respectively. The median (range) duration of CPB was 136 (71-243 minutes). The median first dose of cefuroxime that was administered was 24.2 mg/Kg and second dose in the CPB prime solution was 12.5 mg/Kg. Median and range cefuroxime pharmacokinetic parameters were: Cmax dose 1: 344 (150-512) mg/L; Cls: 0.050 (0.041-0.058) L/hr/Kg; Vss: 0.213 (0.081-0.423) L/Kg; Vc: 0.072 (0.046-0.162) L/Kg and elimination half-life: 3.76 (1.03-6.81) hrs. Median six-hour post-dose simulated cefuroxime concentrations were 37.4 and 23.5 mg/L for the two-dose and single-dose regimens respectively.

Table I, Pharmacokinetic Parameters, n=15

	Dose 1 (mg/Kg)	Dose 1 Cmax (mg/L)	Dose 2 (mg/Kg)	Cls (L/hr/Kg)	Vss (L/Kg)	Vc (L/Kg)	t1/2 (hrs)
Median	24.2	344	12.5	0.050	0.213	0.072	3.76
Range	20.9-26.7	150-512	0-29.1	0.041-0.058	0.081-0.423	0.046-0.162	1.03-6.81

Discussion: Based upon the results of this study, the pharmacokinetics of cefuroxime are not altered by CPB. Currently recommended pediatric doses of cefuroxime (25-50 mg/Kg) can be used in infants and children undergoing CPB to maintain adequate concentrations for surgical site infection prophylaxis.

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Title: Cold Agglutinins in Children Undergoing Repair of Congenital Heart Defects with Cardiopulmonary Bypass

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ABSTRACT BODY:
Introduction: Hypothermic cardiopulmonary bypass and cold cardioplegia solutions are regularly used during repair of congenital heart defects. The result is that the blood is exposed to a cooling process. Blood may contain auto antibodies which at cold temperatures cause an agglutination process to occur. The purpose of this abstract is to report the incidence of this problem at our institution and discuss possible solutions to dealing with the problem.
Methods: Children presenting for cardiac surgery with cardiopulmonary bypass were screened for the presence of cold agglutinins. Blood samples were drawn in EDTA and patient plasma was tested for agglutinins using 3 screening red cells (Panoscreen I, II, and III, Immucor, Norcross GA). Cold agglutinin screening was performed by mixing, 1 drop of each screening cell with 2 drops patient plasma. Samples were incubated for 30 minutes at both room temperature (RT) and 4 degrees C, centrifuged, and visualized for agglutination. When the cold agglutinin screen was positive, additional studies were performed by incubating samples at 4, 12, room temperature, 30, and 37 degrees for 1 hour. All agglutination reactions were graded from 0 (no agglutination) to 4 (strong agglutination) after centrifugation.
Results: During a six month period (April to September 2009) 56 children were screened for cold agglutinins of who 11 (19.6%) were found to have positive screens requiring further study. Of these, 2/11(18%) had 3-4+ reactivity at 4C. The remainder (9/11) had weaker (1-2+) reactivity at 4C. At 12 degrees 8 of 11showed reactivity, but only 1 had stronger than a 2+ reaction. None of these samples reacted at room temperature or higher. No patients had antibodies with RBC specificity (e.g. anti-M, P1, etc.).
Discussion: Cold agglutinins react reversibly and can become clinically relevant when red cells are cooled below the thermal amplitude for agglutination. This can result in increased blood viscosity and red cell clumping, compromising organ perfusion. The etiology of cold agglutinins is often related to infections. Mycoplasma is well known to stimulate IgM autoagglutinins. The cold agglutinins develop early in the disease (7 -10 days), peak at 2-3 weeks, and can persist for 2 to 3 months. The only symptom the patient may have is a dry persistent cough. Our cold agglutinin screening strategy resulted in patients being postponed or the cardioplegia technique being modified. Prior to delivery of the cardioplegia to the patient, blood was added to the cadioplegia/heat exchanger and examined at 5-15 degrees for signs of agglutination. Two patients underwent acute normovolemic hemodilution after induction of anesthesia prior to bypass to lower the circulating agglutinins. Dilution on bypass also had an effect on decreasing the cold agglutination titer. Patients with cold agglutinins appeared to wake and became extubated slower. The literature contains regular reports of morbidity and mortality from this uncommon problem. We documented an incidence close to 20% in 2009. In 2004, Madershahianm, examined 2294 patients and documented an incidence of only 1.6%. They reported 1 death in an unscreened patient with cold agglutinins who developed intracoronary RBC clumping, myocardial ischemia, and hemolysis that underwent moderate (31 degree) hypothermia. In the rest of their 37 patients, strategies were used to minimize the effects of the cold agglutinin. Cold agglutinins are commonly detected pre-surgically in pediatric cardiac patients, and some of these react at temperatures used during bypass. The impact of these agglutinins is unclear, but may be relevant in certain patients. Strategies are needed to determine how to identify and manage patients at risk from cold agglutinins.

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