

CONFERENCE PROCEEDINGS

Volume 3, May 2007

The Proceedings of the
Third International Conference on
**PEDIATRIC MECHANICAL
CIRCULATORY SUPPORT SYSTEMS
& PEDIATRIC
CARDIOPULMONARY PERFUSION**



• May 17–19, 2007 •

The Hotel Hershey
Hershey, Pennsylvania, USA

Editor: Akif Ündar, PhD

HONORARY CHAIRS

William S. Pierce, MD • John A. Waldhausen, MD

PROGRAM CO-CHAIRS

Brian W. Duncan, MD • Pedro J. del Nido, MD • John L. Myers, MD • Gerson Rosenberg, PhD
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Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

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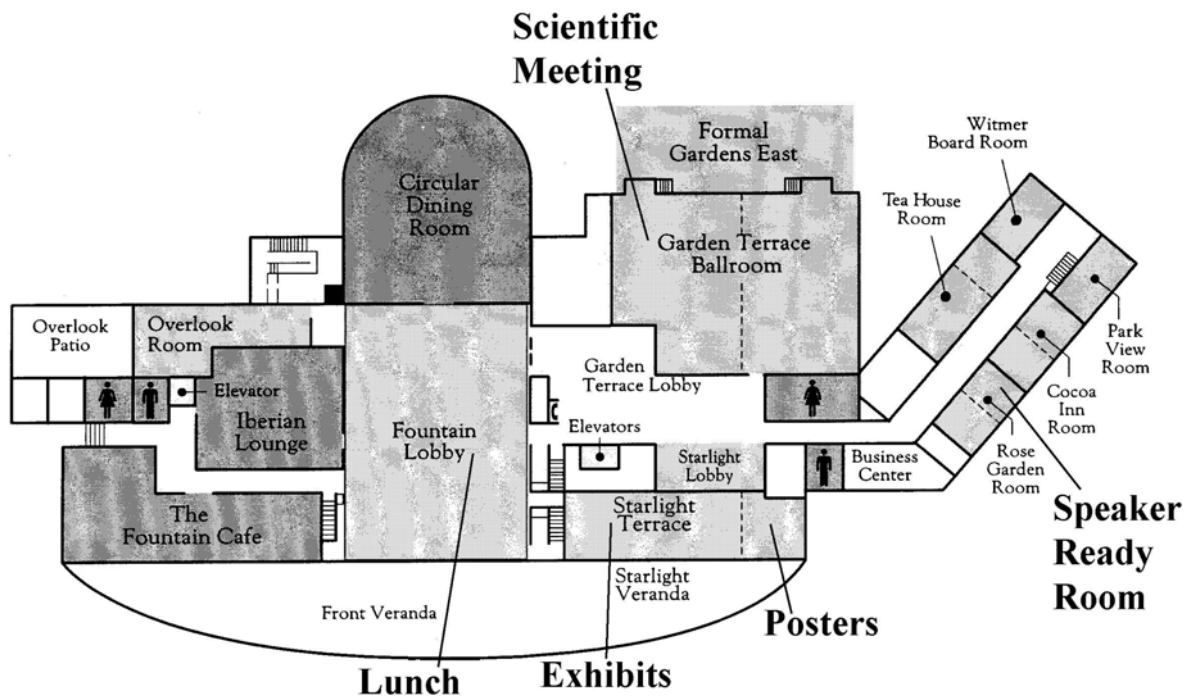
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The Hotel Hershey





Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Welcome to the Third Annual Event

Akif Ündar, PhD, Conference Founder
Departments of Pediatrics, Surgery, and Bioengineering,
Penn State College of Medicine, Penn State Children's Hospital, Hershey, Pennsylvania, USA

On the behalf of the organizers of the **Third International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion** at the Hotel Hershey, Hershey, Pennsylvania, May 17-19, 2007, I welcome you and extend our sincere appreciation for your interest and support.

With the **Third Annual Event**, we continue to focus on the objective of our previous two conferences, that is, to *explicitly describe the problems with current pediatric mechanical circulatory support systems, methods, and techniques during acute and chronic support*. Over three dozen well-known invited speakers from around the world, including pediatric heart surgeons, engineers, basic scientists, pediatric cardiologists, intensive care specialists, and pediatric perfusionists, will participate at the **Third Event**.

This international event was uniquely designed to bring *all* major players, not just clinicians or engineers or basic scientists, into the same arena to discuss problems with current devices and techniques. The organizers of these continuing events believe that bringing together respected international scholars from 20 different countries (more than 500 attendees) has already made a significant impact on the treatment of pediatric cardiac patients. To date, participants from many countries, including Austria, Belgium, Canada, China, Finland, France, Germany, Greece, Italy, Japan, New Zealand, South Korea, Taiwan, Turkey, the United Kingdom, and the United States, have registered for the 2007 event.

This conference is designed to be a truly academic event. The *American Society for*

Artificial Internal Organs (ASAIO) is again endorsing the conference and will dedicate the November-December issue of the *ASAIO Journal* to the manuscripts submitted during this conference.

This event could not be possible without the generous financial support year after year from the Penn State Children's Hospital, and the Penn State College of Medicine. This year we have received the financial support from a record number of exhibitors including *ATS Medical, Berlin Heart, Levitronix, Luna Innovations, MedImmune, Medos, Miromed Cardiovascular, Mosby/Saunders/Elsevier, Somanetics, Sorin Group Italia, and St. Jude Medical*. In addition, we have also received educational support from the following companies: *Circulite, Ino Therapeutics, Maquet/Jostra, Medtronic Cardiac Surgery, and Terumo Cardiovascular Systems*.

I am honored to welcome each of you to this unique international event. *If the course of just one child's life is improved as a result of this event, we have reached our goal.*

References:

1. Ündar A. Outcomes of the First International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion [Invited Editorial]. *ASAIO Journal* 52: 1-3, 2006.
2. Ündar A. Outcomes of the Second International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion [Invited Editorial]. *ASAIO Journal* 53: 1-3, 2007.



Third International Conference on **Pediatric Mechanical
Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Scientific Committee

Honorary Chairs

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Evan Pugh Professor of Surgery
Penn State College of Medicine
Hershey, PA, USA

John A. Waldhausen, MD
Professor Emeritus
Founding Chairman of Surgery
Penn State College of Medicine
Hershey, PA, USA

Program Co-chairs

Brian W. Duncan, MD
Department of Cardiac Surgery
Children's Hospital
Cleveland Clinic Foundation
Cleveland, OH, USA

Gerson Rosenberg, PhD
Departments of Surgery and Bioengineering
Penn State College of Medicine
Hershey, PA, USA

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Penn State College of Medicine
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Bioengineering
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Hershey, PA, USA

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Boston, MA, USA

Ross M. Ungerleider, MD
Oregon Health and Sciences University
Doernbecher Children's Hospital
Portland, OR, USA

Brigitte Stiller, MD, PhD
Deutsches Herzzentrum Berlin
Berlin, Germany



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Endorsements

American Society for Artificial Internal Organs

Conference Supporters

CircuLite, Inc.

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Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Final Scientific Program

Wednesday, May 16, 2007

5–10 pm Registration/Speaker Ready Room Open

Thursday, May 17, 2007

7:00 am Registration/Breakfast/Speaker Ready Room Open

8:00 Welcome
John L. Myers, MD; A. Craig Hillemeier, MD; Akif Ündar, PhD, Hershey, PA, USA

8:15 **PLENARY SESSION #1**
Pediatric Mechanical Circulatory Support and ECMO: Current Practices and Devices
Co-chairs: John A. Waldhausen, MD, and William S. Pierce, MD, Hershey, PA, USA

INVITED LECTURES

Pediatric Mechanical Circulatory Support Systems: An Overview
Brian W. Duncan, MD, Cleveland, OH, USA

Interagency Registry for Mechanical Circulatory Support: A First Look at Registry Data Potential
Elizabeth D. Blume, MD, Boston, MA, USA

The Berlin Heart EXCOR: The Risks and Chances in the Pediatric Use
Brigitte Stiller, MD, PhD, Berlin, Germany

ECMO in Children: What's New?
Heidi Dalton, MD, Washington, DC, USA

10:00 Break/Exhibits/Posters

10:45 **INVITED LECTURE**
Hemostasis during Congenital Heart Surgery: Is BioGlue an Option?
Scott A. LeMaire, MD, Houston, TX, USA
Moderator: Ross M. Ungerleider, MD, Portland, OR, USA

11:10 **KEY NOTE LECTURE #1**
What Can the Plasma Proteome Tell Us about CPB?
Kent E. Vrana, PhD, Hershey, PA, USA
Introduction: Akif Ündar, PhD, Hershey, PA, USA

12:00 noon **Lunch**



Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

1:00 pm

PLENARY SESSION #2

Advances in Pediatric CPB to Improve the Outcome

Co-chairs: Brian W. Duncan, MD, Cleveland, OH, USA and Carmelo Mignosa, MD, Taormina, Italy

INVITED LECTURES

The Effect of Advances in Perfusion on Outcomes for HLHS

Ross M. Ungerleider, MD, Portland, OR, USA

Neuromonitoring during Pediatric Cardiopulmonary Bypass

Erle H. Austin III, MD, Louisville, KY, USA

Myocardial Protection

Bradley S. Allen, MD, Houston, TX, USA

Evolution of CPB Techniques for Single Ventricle Circulations: A Single Centre Experience

Timothy J. Jones, MD, FRCS, Birmingham, United Kingdom

Bridge to Neonatal Fontan Repair of Single Ventricle

Mark Rodefeld, MD, Indianapolis, IN, USA

3:00

Break/Exhibits/Posters

3:45

REGULAR SLIDE PRESENTATIONS #1

ECMO/Cardiopulmonary Bypass

Co-chairs: Francis Fynn-Thompson, MD, Boston, MA, USA and Pirooz Eghtesady, MD, PhD, Cincinnati, OH, USA

S.1. Rescue Extracorporeal Membrane Oxygenation in Children with Refractory Cardiac Arrest

Eva Maria Delmo Walter, MD, Berlin, Germany

S.2. Usefulness of Low Prime Perfusion Pediatric Circuit in Decreasing Blood Transfusion

Yves Durandy, MD, Massy, France

S.3. A Simple Solution is "Prime" for Fetal Cardiopulmonary Bypass

Scott Baker, BS, Cincinnati, OH, USA

S.4. Efficacy of a Miniature Centrifugal Rotary Pump for Transfusion-Free Cardiopulmonary Bypass in Neonatal Piglets

Shinya Ugaki, MD, Okayama-shi, Japan

S.5. Benefits of Pulsatile Perfusion on Vital Organ Recovery during and after Pediatric Open-Heart Surgery

Tijen Alkan, MD, Istanbul, Turkey

S.6. Comparison of Single-, Double-, and Diagonal Pumps for Pulsatile Perfusion in Pediatric Cardiac Surgery

Jörg Optenhöfel, Hanover, Germany



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- S.7. Application of Modified Perfusion Technique on One-Stage Repair of Interrupted Aortic Arch in Infants—A Case Series**
Jinping Liu, MD, Beijing, China
- 5:30 Program Slide Presentation Adjournment
- 6:00-7:00 pm **MODERATED POSTER PRESENTATION SESSION #1**
- ECMO/Cardiopulmonary Bypass**
Co-chairs: Tijen Alkan, MD, Istanbul, Turkey, J. Brian Clark, MD, Boston, MA, USA and Long Cun, MD, Beijing, China
Moderator: J. Brian Clark, MD
- P.1. Using Plasma Proteomics in the Identification of Pathology-Related Markers in Pediatric Patients Undergoing Cardiopulmonary Bypass**
Melinda E. Lull, BA, Hershey, PA, USA
- P.2. Low Prime Pediatric Cardiopulmonary Bypass Using the Dideco Kids D100™ Oxygenator**
Christopher D. Derby, MD, Wilmington, DE, USA
- P.3. Impact of Miniaturization of Cardiopulmonary Bypass Circuit on Neonatal Open-Heart Surgery**
Yasuhiro Kotani, MD, Okayama, Japan
- P.4. PMEA-Coated Bypass Circuits Reduce Activation of Coagulation System and Inflammatory Response in Congenital Cardiac Surgery**
Yasuyuki Suzuki, MD, Hirosaki, Japan
- P.5. Postoperative Prophylactic Peritoneal Dialysis in Neonates and Infants after Complex Congenital Cardiac Surgery**
Tijen Alkan, MD, Istanbul, Turkey
Moderator: Long Cun, MD
- P.6. Effect of Modified Ultrafiltration on Neonates Undergoing Arterial Switch Operation**
Yasuhiro Kotani, MD, Okayama, Japan
- P.7. Variability of Pediatric Blood Viscosity**
George M. Pantalos, PhD, Louisville, KY, USA
- P.8. Technique for the Norwood Procedure Using Normothermic Selective Cerebral Perfusion**
Richard N. Gates, MD, Orange, CA, USA
- P.9. Safety Mechanism of Low Prime ECMO System with Dual Servo-Regulation Mode for Lower Body Perfusion during Coarctation Repair**
Takeshi Saito, MD, Niigata, Japan
- P.10. Absence of Rapid Deployment ECMO Team Does Not Preclude Resuscitation ECMO in Pediatric Cardiac Patients with Good Results**
Olivier Ghez, MD, Marseille, France



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Moderator: Tijen Alkan, MD

- P.11. Extracorporeal Membrane Oxygenation for Pediatric Severe Respiratory Failure—
Report from a Single Institute**
Jih-Hsin Huang, MD, Taipei, Taiwan
- P.12. Selective Na⁺/H⁺ Exchanger Inhibitor H0E642 Preconditioning Reducing Calcium
Overload and Exhibiting Markedly Protective Effect on Immature Rabbit Hearts**
Long Cun, MD, Beijing, China
- P.13. Comparison of Four Different Pediatric 10 Fr Aortic Cannulae during Pulsatile
Versus Non-pulsatile Perfusion in a Simulated Neonatal Model of CPB**
Alan R. Rider, Hershey, PA, USA
- P.14. Does Pulsatile Flow Increase Arterial Line Gaseous Microemboli during
Cardiopulmonary Bypass?**
Bingyang Ji, MD, Hershey, PA, USA

UNMODERATED POSTER PRESENTATIONS

- P.15. Congenitally Isolated Defect on the Anterior Mitral Valve and Surgical Repair: Two
Rare Cases**
Tijen Alkan, MD, Istanbul, Turkey
- P.16. Congenital Heart Surgery Cases Accompanied with Genetic Syndromes**
Tijen Alkan, MD, Istanbul, Turkey
- P.17. Surgical Repair of Congenital Supravalvular Aortic Stenosis in Adult**
Tolga Coskun, MD, Bad Oeynhausen, Germany

7:30-10:00 pm **GALA DINNER**

INVITED LECTURE

Managing the Demands of Professional Life
Ross M. Ungerleider, MD, Portland, OR, USA
Moderator: John L. Myers, MD

AWARDS RECOGNITION

Moderators: John L. Myers, MD, Hershey, PA, USA and Gerson Rosenberg, PhD,
Hershey, PA, USA

Friday, May 18, 2007

7:00 am **Registration/Continental Breakfast**

8:00 **PLENARY SESSION #3**

Pediatric Heart Pumps under Development

Co-chairs: Tim Baldwin, PhD, NHLBI, Bethesda, MD, USA and William S. Pierce, MD,
Hershey, PA, USA



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INVITED LECTURES

Development of the PediaFlow™ Ventricular Assist Device for Infants and Small Children

Harvey Borovetz, PhD, Pittsburgh, PA, USA

Development of the Penn State Pulsatile Pediatric VAD

William Weiss, PhD, Hershey, PA, USA

Progress of the Pediatric Jarvik 2000 Hearts

Bartley P. Griffith, MD, Baltimore, MD, USA

The Ension pCAS System

Mark Gartner, PhD, MBA, Pittsburgh, PA, USA

The PediPump: A Versatile, Implantable, Pediatric Ventricular Assist Device

T. Stephan Weber, Dipl.-Ing., Cleveland, OH, USA

FDA's Perspectives on Pediatric Cardiac Assist Devices

Eric A. Chen, MS, FDA, Rockville, MD, USA

10:00 Break/Exhibits/Posters

10:45 INVITED LECTURE

Hemorheology of Mechanical Blood Damage

Marina V. Kameneva, PhD, Pittsburgh, PA, USA

Moderator: Harvey Borovetz, PhD, Pittsburgh, PA, USA

11:10 MINI-SYMPOSIUM #1

Pediatric Heart Transplantation

Co-chairs: Elizabeth D. Blume, MD, Boston, MA, USA and Brigitte Stiller, MD, PhD, Berlin, Germany

INVITED LECTURES

Heart Transplantation for the Patient with Single Ventricle Anatomy

James S. Tweddell, MD, Milwaukee, WI, USA

Cardiac Retransplantation in Children

Francis Fynn-Thompson, MD, Boston, MA, USA

Special Aspects of Cardiac Transplantation in Fontan Patients

Sabine H. Däbritz, MD, Munich, Germany

12:15 pm Lunch

1:15 KEY NOTE LECTURE #2

Pediatric Cardiac Bioengineering: Who, What, Where, and How?

Pedro J. del Nido, MD, Boston, USA

Introduction: Erle H. Austin III, MD, Louisville, KY, USA



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2:00

MINI-SYMPOSIUM #2

Pediatric Perfusion: Novel Approaches

Co-chairs: Mark Rodefeld, MD, Indianapolis, IN, USA and Larry D. Baer, CCP, Hershey, PA, USA

INVITED LECTURES

Approaches toward Continuous Monitoring of Pediatric Cardiopulmonary Bypass Procedures Using Cytometric Bead Processing within a Microfluidic Device

Jeffrey D. Zahn, PhD, Piscataway, NJ, USA

Peri-operative Use of Near-Infrared Spectroscopy to Monitor Regional Perfusion

George M. Hoffman, MD, Milwaukee, WI, USA

Survey: The Use of Aprotinin in Pediatric Cardiopulmonary Bypass

Eileen L. Heller, CCP, Portland, OR, USA

Pediatric Cardiopulmonary Bypass: Evidence Based or Performance Art?

Robert C. Groom, CCP, Portland, ME, USA

3:00

Break/Exhibits/Posters

3:45

REGULAR SLIDE PRESENTATIONS #2

Pediatric Cardiac Assist Devices/ECMO/Pediatric Heart Transplantation

Co-chairs: Kurt A. Dasse, PhD, Waltham, MA, USA, and James S. Tweddell, MD, Milwaukee, WI, USA

- S.8. The Pediatric Mechanical Circulatory Support Program in Innsbruck, Austria and Impact on Lack of Donor Hearts in Europe**
Ulrich Schweigmann, MD, Innsbruck, Austria
- S.9. Bridge to Recovery with Pulsatile Pump Support in Children under Three Years of Age**
Richard G. Smith, MSEE, Tucson, AZ, USA
- S.10. Thromboelastography to Monitor the Balance of Hemostasis in Infants and Children with Ventricular Assist Devices**
Holger Buchholz, MD, Edmonton, Alberta, Canada
- S.11. Use of Mechanical Circulatory Support in Pediatric Patients with Acute Cardiac Graft Rejection**
David L.S. Morales, MD, Houston, TX, USA
- S.12. Extra Corporeal Life Support in Congenital Heart Diseases**
Tolga Coskun, MD, Bad Oeynhausen, Germany
- S.13. A Novel External Aortic Counterpulsation Device for Pediatric Cardiac Support**
Minoo N. Kavarana, MD, London, KY, USA
- S.14. Non-blood Contacting Mechanical Support of the Failing Rabbit Heart**
Curtis J. Wozniak, MD, Dayton, OH, USA



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- S.15. Mechanical Lung Assist with a Miniature Centrifugal Pump Improves Forward Blood Flow Following a Primary Bidirectional Cavopulmonary Shunt in Pigs**
Osami Honjo, MD, PhD, Toronto, Ontario, Canada

5:30-7:30 pm **WINE AND CHEESE**

MODERATED POSTER PRESENTATION SESSION #2

Co-chairs: Choon Hak Lim, MD, Seoul, Korea, William Weiss, PhD, Hershey, PA, USA, and Amy L. Throckmorton, PhD, Indianapolis, IN, USA

Moderator: William Weiss, PhD

- P.18. Lessons Learned from Implantation of a Berlin Heart Biventricular Assist Device in a Failing Single Ventricle**
Meena Nathan, MD, Boston, MA, USA
- P.19. Successful Implantation of a Berlin Heart Excor Pediatric Ventricular Assist Device for 174 Days as a Bridge to Transplant in a Three-Year-Old Child with a Single Ventricle**
Holger Buchholz, MD, Edmonton, Alberta, Canada
- P.20. Implantation of a Berlin Heart as Left Ventricle By-Pass on Fontan Circulation in Single Ventricle Failure**
Davide Calvaruso, MD, Palermo, Italy
- P.21. Abiomed BIVAD as a Bridge to Transplantation in a 14-Year-Old with Cardiomyopathy from Ventricular Non-compaction**
Meena Nathan, MD, Newark, NJ, USA
- P.22. A Pediatric Extra-Aortic Counterpulsation Device Provides Augmentation in a Piglet Model of Heart Failure**
Michael E. Mitchell, MD, Milwaukee, WI, USA
Moderator: Amy Throckmorton, PhD
- P.23. Feasibility of a TinyPump System for Pediatric CPB, ECMO and Circulatory Assistance**
Setsuo Takatani, PhD, DMed, Tokyo, Japan
- P.24. In Vitro Performance Evaluation of the Pediatric Cardiopulmonary Assist System (pCAS)**
George M. Pantalos, PhD, Louisville, KY, USA
- P.25. A Study on Weaning Using Particle Image Velocimetry in the 12cc Penn State Pediatric Ventricular Assist Device**
Breigh N. Roszelle, BS, State College, PA, USA
- P.26. Computational Fluid Dynamics-Based Analysis of a Pump-Oxygenator System**
Mark Gartner, PhD, MBA, Pittsburgh, PA, USA
- P.27. Heparin-Loaded Nanogels for Minimizing Thrombogenicity of Polyurethane Urea Biomaterials**
Gauri P. Misra, PhD, Hershey, PA, USA

Moderator: Choon Hak Lim, MD



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- P.28. Differential Plasma Protein Abundances in Hepatic and Pulmonary Compartments**
Willard M. Freeman, PhD, Hershey, PA, USA
- P.29. Cardiac Surgery of Prematures and Low-Birth-Weight Newborns: Is It Possible to Change Fate?**
Tijen Alkan, MD, Istanbul, Turkey
- P.30. The Effect of Using Processed Red Cell with Continuous Auto Transfusion System (CATS) on Neonates during Cardiopulmonary Bypass: A Preliminary Evaluation Study**
Jinping Liu, MD, Beijing, China
- P.31. Biogenic Amine and Iron Metabolism during Pediatric Cardiopulmonary Bypass Procedure: A Pilot Clinical Study**
Nurgul Carkaci-Salli, PhD, Hershey, PA, USA
- P.32. A Diffraction-Grating Doppler Ultrasound Transducer Based Micro-emboli Detection System for Pediatric Cardiopulmonary Bypass**
Sowmya Ballakur, BS, Hershey, PA, USA

UNMODERATED POSTER PRESENTATIONS

- P.33. A Rare Case with Holt-Oram Syndrome and “Swiss cheese” VSD: Surgical Treatment and Follow-Up**
Tijen Alkan, MD, Istanbul, Turkey
- P.34. Surgical Correction of Iatrogenic Severe Aortic Insufficiency and LAD Dissection in a Case with Congenital Coronary Artery Fistula during Coil Embolization**
Tijen Alkan, MD, Istanbul, Turkey
- P.35. Heart Transplantation after Fontan Procedure in Adult**
Tolga Coskun, MD, Bad Oeynhausen, Germany

Saturday, May 19, 2007

7:00 am Continental Breakfast

8:00 **PLENARY SESSION #4**

Device Manufacturers: New Products and Novel Designs

Co-chairs: Harvey Borovetz, PhD, Pittsburgh, PA, USA and Walter E. Pae Jr., MD, Hershey, USA

INVITED LECTURES

Abiomed’s Approach to Pediatric Heart Support with a Catheter-Based Pulsatile 12F Rotary Blood Pump

Thorsten Siess, PhD, Aachen, Germany

Critical Considerations Contributing to the Successful Design and Clinical Utility of a Pediatric Centrifugal Pump for Pediatric Cardiac or Cardiopulmonary Support

Kurt A. Dasse, PhD, Waltham, MA, USA



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Berlin Heart Excor: Results to Date and Lessons Learned in the U.S. and Canadian Pediatric Patient Population

Johannes Müller, MD, Berlin, Germany

New Vision in Pediatric Cardiopulmonary Bypass

Andrea Mengoli, Mirandola, Italy

Circulite: Ultra-small Blood Pump for Long-Term Cardiac Assist

Wolfgang Kerkhoffs, Aachen, Germany

Clinical Experience with Thoratec Ventricular Assist Devices in Children and Adolescents

David Farrar, PhD, Pleasanton, CA, USA

Improvements to the HDE-Approved MicroMed DeBakey VAD[®] Child

Lee Hudson, PhD, Houston, TX, USA

Quantitative Gaseous Microemboli Monitoring in a CPB Circuit with the EDAC[™] QUANTIFIER

Ted Lynch, PhD, Roanoke, VA, USA

10:00 Breaks/Exhibits/Posters

10:45 **INVITED LECTURE**

Pulsatile versus Non-Pulsatile Flow in Neonates and Infants during Acute and Chronic Support

Akif Ündar, PhD, Hershey, USA

11:10 **KEY NOTE LECTURE #3**

Designing Pediatric Circulatory Support Devices: What We Know, What We Think We Know, and What We Don't Know

Gerson Rosenberg, PhD, Hershey, PA, USA

Introduction: William S. Pierce, MD, Hershey, PA, USA

12:00 noon Lunch

1:00 pm **REGULAR SLIDE PRESENTATIONS #3**

Pediatric Cardiac Assist Devices/Bioengineering Aspects/Computational Fluid Dynamics/Pulsatile Perfusion

Co-chairs: Salvatore Agati, MD, Taormina, Italy and Thorsten Siess, PhD, Aachen, Germany

S.16. The Creation and Use of Anatomic Models in Virtual Fitting Studies

Angela Noecker, BS, Cleveland, OH, USA

S.17. Anatomic Fit Assessment for the Penn State Pediatric Ventricular Assist Device (PVAD)

John M. Connell, MD, MPH, Hershey, PA, USA

S.18. In Vitro Evaluation of the TandemTot Pediatric Centrifugal Pump

Robert G. Svitek, PhD, Pittsburgh, PA, USA



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Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

- S.19. Mechanical Cavopulmonary Assist for the Univentricular Fontan Circulation Using a Novel Folding Propeller Blood Pump**
Amy Throckmorton, PhD, Indianapolis, IN, USA
- S.20. Neonatal Aortic Arch Hemodynamics and Perfusion during Cardiopulmonary Bypass**
Kerem Pekkan, PhD, Pittsburgh, PA, USA
- S.21. The Effects of Dopamine, Ephinephrine and Esmolol on Hemodynamic Energy in Terms of Energy Equivalent Pressure**
Choon Hak Lim, MD, Seoul, Korea
- S.22. Pulsatile Versus Non-pulsatile Flow to Maintain the Equivalent Coronary Blood Flow in the Fibrillating Heart**
Jae Seung Jung, MD, Seoul, Korea
- S.23. In Vitro Cavitation and Hemolysis Study of the Pulsatile Pneumatic PVAD**
Branka Lukic, MS, Hershey, PA, USA

3:30–6:30 **TOUR OF THE PENN STATE MILTON S. HERSHEY MEDICAL CENTER**



Third International Conference on **Pediatric Mechanical
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International Scientific Committee

Salvatore Agati, MD, Italy
Atif Akcevin, MD, Turkey
Tijen Alkan, MD, Turkey
Bradley S. Allen, MD, USA
Christopher Almond, MD, MPH, USA
Erle H. Austin III, MD, USA
Aydin Aytaç, MD, Turkey
Larry D. Baer, CCP, USA
Scott Baker, BS, USA
Tim Baldwin, PhD, USA
Sowmya Ballakur, BS, USA
Joyce Bigley, CCP, USA
Ute Blanz, MD, Germany
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Harvey Borovetz, PhD, USA
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Tolga Coskun, MD, Germany
Long Cun, MD, China
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Sabine H. Däbritz, MD, Germany
Heidi Dalton, MD, USA
Edward Darling, MS, CCP, USA
Kurt A. Dasse, PhD, USA
Eva Maria Delmo Walter, MD, Germany
Christopher D. Derby, MD, USA
Pedro J. del Nido, MD, USA
Steven Deutsch, PhD, USA
Peter W. Dillon, MD, USA
Wen-Xiang Ding, MD, China

Thorsten Drews, MD, Germany
Brian W. Duncan, MD, USA
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Pirooz Eghtesady, MD, USA
Martin Elliott, MD, UK
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Willard M. Freeman, PhD, USA
Francis Fynn-Thompson, MD, USA
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George M. Hoffman, MD, USA
Osami Honjo, MD, PhD, Canada
Jih-Hsin Huang, MD, Taiwan
Shu-Chien Huang, MD, Taiwan
Lee Hudson, PhD, USA
Nathan Ibbott, CCP, New Zealand
Kou Imachi, PhD, Japan
Bingyang Ji, MD, USA
Greg A. Johnson, PhD, USA
Timothy J. Jones, MD, FRCS, UK
Jae Seung Jung, MD, Korea
Marina V. Kameneva, PhD, USA
Kirk R. Kanter, MD, USA
Minoo N. Kavarana, MD, USA
Wolfgang Kerkhoffs, Germany
Stephen Kimatian, MD, USA
Reiner Koerfer, MD, Germany
Yasuhiro Kotani, MD, Japan
Roman Kustos, MD, Poland
Scott A. LeMaire, MD, USA



Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Adolfo A. Leirner, MD, PhD, Brazil
Choon Hak Lim, MD, Korea
Herbert H. Lipowsky, PhD, USA
Betty Littleton, USA
Jinfen Liu, MD, China
Jinping Liu, MD, China
Matthias Loebe, MD, PhD, USA
Branka Lukic, MS, USA
Melinda E. Lull, USA
Ted Lynch, PhD, USA
Andrea Mengoli, Italy
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Pediatric Mechanical Circulatory Support Systems: An Overview

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Purpose

The present discussion will 1) summarize the characteristics of the devices available for pediatric circulatory support 2) describe a decision matrix that to guide the selection of these devices in a given clinical setting and 3) describe devices that may be available in the future.

Currently Available Devices

ECMO and the Bio-Pump have established records in the management of children with advanced cardiorespiratory failure. However, each of these modalities possesses a number of limitations; importantly, their use is restricted to short-term applications while their extracorporeal design precludes ambulation and effective physical rehabilitation during support. A number of devices designed for adults, including the Thoratec and Heartmate VADs, the BVS 5000 and the NovaCor LVAS have been used successfully to support older children and adolescents. The MicroMed DeBakey VAD *Child* was granted Humanitarian Device Exemption (HDE) status by the Food and Drug Administration and became available for use in 2004. Under the current HDE the VAD *Child* is to be used as a bridge to cardiac transplantation for children from 5-16 years of age. Finally, the Berlin Heart VAD is a pulsatile, paracorporeal system with the smallest pump sizes suitable for infant support. The Berlin Heart VAD has been used successfully in pediatric patients for more than a decade in Europe and increasingly in North America.

A Clinical Setting Decision Matrix for Device Selection for Heart Failure in Children

In an attempt to aid in the selection of the most appropriate device in any given case, a decision matrix has been developed which attempts to define the relevant clinical setting of pediatric heart failure according to 1) patient size and 2) the anticipated duration of support (Figure 1). On this “Clinical Setting Decision Matrix”, patient age is a surrogate

for patient size and is plotted on the Y-axis while the anticipated duration of support is plotted on the X-axis. The clinical setting may then be considered to belong to one of four quadrants: young patients requiring short-term support, young patients requiring long-term support, older children and adolescents requiring short-term support and older children requiring long-term support. This two-dimensional graph defining the clinical setting in terms of patient size and anticipated duration of support may be used to match the most appropriate device to a given clinical setting after consideration of each device’s characteristics.

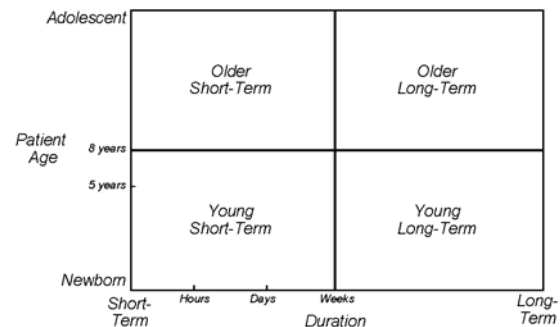


Figure 1) Clinical Setting Decision Matrix for pediatric MCS.

Possible Future Devices

In the spring of 2004, five contracts were awarded by the NHLBI under its Pediatric Circulatory Support Program to support preclinical development of a variety of pediatric VADs and similar circulatory support systems. The goal of the program is to have these devices ready to begin human trials at the completion of the funding period in 2008.



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Interagency Registry for Mechanical Circulatory Support: A First Look at Registry Data Potential

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The Intermacs NIH contract was awarded in June 2005. The first 15 months consisted of database construction, clinical and adverse events definitions, and site recruitment. Pediatric specific data fields, adverse events, and clinical outcome measures were created. Enrollment of patients and recruitment of pediatric sites continues. This talk will be the Intermacs update as it pertains to the pediatric MCS registry and the impact on pediatric MCS trials.

The Berlin Heart EXCOR: The Risks and Chances in the Pediatric Use

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Children with advanced heart failure and profound cardiogenic shock who would otherwise die immediately may be kept alive using ventricular assist devices and may either completely recover or qualify for heart transplantation. Widely used devices such as ECMO or centrifugal pumps may sustain the circulation for several days or weeks. The Berlin Heart EXCOR (Berlin Heart GmbH, Germany) is a miniaturized extracorporeal pneumatically driven VAD for small children and infants and has been demonstrated to qualify for long-term application and full patient mobilization at any age.

The advantages of this long-term mechanical circulatory assistance are less anticoagulation, enteral nutrition and full mobilization of the patient, combined with low complication rates. However, all mechanical circulatory assist systems are associated with a wide range of possible **risks and complications**, of which bleeding and thrombo-embolic complications are the most frequent and most serious. Infections, hemolysis, pulmonary edema and multi-organ failure have also been reported. The choice of the pulsatile Berlin Heart EXCOR systems instead of ECMO seems to significantly lessen these complications, especially if the duration of circulatory assistance exceeds 1-2 weeks. The use of the Berlin Heart in children with immunodeficiency, hemophilia or acute infections has to be carefully considered. Also, the HLA status and the number of panel reactive antibodies (often elevated after blood transfusions or previous homograft implantation) have to be measured before the implantation of a long-term device, to gain information about the chances for later transplantation.

Berlin results: At our institution 80 infants and children were treated with the Berlin Heart for periods of between several days and 14 months (mean 36 days). Long-term survival in myocarditis and cardiomyopathy patients was initially 70% and has been raised to 90% during the past 6 years. Berlin Heart Excor enables prolonged circulatory support; it offers time to restore organ function, allows

extubation, mobilization and neurological examination and increases the chances for transplantation.

Following these satisfactory results, about 4 years ago an enormous number of centers established the EXCOR.

- *Infrastructure of a VAD center:* The following requirements are essential to obtain satisfactory results in the application of pediatric EXCOR systems: an advanced surgical infrastructure including a well-equipped neonatal and pediatric intensive care unit (level III), a cardiothoracic surgery department with comprehensive experience and the personnel and technical equipment necessary to treat children of all ages, a highly experienced pump technician team, and a laboratory permanently available to monitor coagulation status.

- *Decision-making in cardiomyopathy:* Children in whom all intensive pharmacological treatment fails should be supported with the EXCOR, since heart transplantation is the primary goal. The waiting time in Europe is unpredictable and many children die while on the waiting list. There is, however, in children as in adults, the infrequent possibility of complete cardiac recovery through VAD support allowing pump explantation with the prospect of long-term clinical stability.

- *Decision-making in fulminant myocarditis:* The children with acute viral myocarditis are the most promising group. These patients were healthy until the onset of fulminant myocarditis, and prolonged circulatory support is an effective method for bridging until cardiac recovery. If there is no improvement in myocardial function on the EXCOR, there is still the possibility of transplantation.

- *Patient selection and time of implantation:* remains a major factor influencing outcome and survival. In our early experience, BerlinHeart devices were mostly implanted as a last resort in extremely ill patients who had required resuscitation and whose prognosis was dismal. With the system proving to be technically safe and reliable, earlier implantation has

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been considered justified and in several cases this has contributed to improvement in outcome. But how early is too early? Or how late is too late? Due to the daily severe risks of bleeding and clotting, the medical team and especially the parents have to be virtually certain that there is absolutely no other

chance for the child to survive with an acceptable quality of life. This implies that earnest and all-embracing talks with the parents are essential before the decision for VAD implantation. Only if religious, cultural and family aspects have been adequately addressed in the decision process, can the family later accept the inevitable.



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ECMO in Children: What's New?

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 Chair, Extracorporeal Life Support Organization

This session will give an overview of the ELSO registry over time, with particular emphasis placed on the use of ECMO in the cardiac patient population. Data from the ELSO registry as of January 2007 are shown below:

	<i>Total Patients</i>	<i>Survived ECLS</i>		<i>Survived to DC or Transfer</i>	
Neonatal					
Respiratory	20,993	17,889	85%	16,005	76%
Cardiac	2,898	1,684	58%	1,095	38%
ECPR	274	176	64%	109	40%
Pediatric					
Respiratory	3,390	2,173	64%	1,895	56%
Cardiac	3,658	2,199	60%	1,624	44%
ECPR	523	263	50%	200	38%
Adult					
Respiratory	1,255	740	59%	646	51%
Cardiac	671	300	45%	216	32%
ECPR	189	80	42%	59	31%
Total	33,851	25,504	75%	21,849	65%

ECMO remains the primary support mechanism for children with cardiac and respiratory disease. Over 8,000 infants and children have received ECMO for cardiac support. Over 400 patients have been bridged to transplant with ECMO and further details on this means of support will be discussed.

The use of ECMO as a resuscitative tool has increased dramatically over the past few years.

Details of such use will be provided. Changes in the extracorporeal life support arena in terms of patient population, equipment and management techniques will also be outlined. By the end of the session, the attendee will have a better understanding of the current patient populations and ECLS techniques currently in use.



Hemostasis during Congenital Heart Surgery

Is BioGlue an Option?

Scott A. LeMaire, MD

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The Challenge of Surgical Hemostasis

The repair of congenital heart defects in neonates and infants carries a particularly high risk of perioperative hemorrhage due to several factors, including hemodilution, the inflammatory response to cardiopulmonary bypass, and multiple suture lines involving fragile tissues. Inadequate hemostasis can result in prolonged cardiopulmonary bypass times and increased transfusion requirements, and secondarily lead to coagulopathy, organ failure, and other complications. Surgical adhesives and sealants have been used to improve hemostasis during congenital heart operations and reduce the complications associated with bleeding. Although the potential to reduce perioperative bleeding in children is attractive, surgical adhesives and sealants can cause early and long-term complications. Thus, the balance between maximizing benefit and minimizing risk should be evaluated for each individual patient; this analysis requires a thorough understanding of each product's potential benefits and associated risks.

Early Enthusiasm for BioGlue

BioGlue surgical adhesive is a two-component, aldehyde-based glue that has become widely available. BioGlue is composed of 45% purified bovine serum albumin and 10% glutaraldehyde, which mix within the delivery tip during application. The adhesive reaches maximum bonding strength in 2 to 3 minutes. Compared with other agents, such as fibrin sealant, BioGlue demonstrates excellent tensile and shear strengths. Based on these properties, there was early enthusiasm about BioGlue's potential value in congenital heart surgery.

BioGlue has yielded subjective benefits when used for cardiovascular repairs in adults. The adhesive appears to improve hemostasis, strengthen weak tissues, provide anastomotic support, and enhance the durability of repair; these benefits are especially

pronounced in patients with marked tissue fragility. Whether BioGlue provides long-term benefits, such as a decreased incidence of late reoperation, remains unclear.

Uncovering the Risks

Although BioGlue can facilitate surgical hemostasis, this agent has been associated with several risks that warrant consideration. The glutaraldehyde component has been reported to be directly toxic to nerves; thus, when using this agent, surgeons need to take extra care to protect the phrenic and recurrent laryngeal nerves that lie nearby common cardiovascular anastomoses. The concerns about nerve toxicity also apply to cardiac conduction tissue. Reports have also raised concerns about BioGlue leaking into the aortic lumen, resulting in valve dysfunction or systemic embolization. Several reports have suggested that BioGlue may injure vascular tissue – particularly if used improperly – and potentially lead to necrosis, fibrosis, and pseudoaneurysm formation. Most importantly in the context of congenital heart surgery, BioGlue has been associated with the development of vascular strictures and impaired aortic growth; therefore, this agent is not recommended for use during cardiovascular reconstructions in pediatric patients.

Conclusions

In the setting of congenital heart surgery, the risks of using BioGlue are likely to outweigh potential benefits in most cases. When a hemostatic adjunct is needed, alternative agents – such as fibrin sealant – are more appropriate in pediatric patients. There remains a need for new biocompatible adhesives that can rapidly seal fragile suture lines in children.

What Can the Plasma Proteome Tell Us About Pediatric Cardiopulmonary Bypass (CPB)?

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Purpose

This presentation will review recent efforts to use broad scale discovery proteomics to examine plasma of pediatric patients undergoing CPB. Specifically, efforts have been made to identify serum biomarkers of perioperative complications that might provide guidance in the care and management of these fragile patients.

Methods

Heparinized blood was collected at five time points before, during and after cardiopulmonary bypass. Following centrifugation, the resulting plasma was depleted of the most abundant proteins, increasing the sensitivity for detecting rarer proteomic species. These samples were then subjected to discovery proteomics analysis using the 2-DIGE (two-dimensional in-gel fluorescence electrophoresis) approach. Specifically, samples were differentially labeled with cyanine dyes and subjected to two-dimensional gel electrophoretic resolution. Following quantification, differentially-regulated proteins were identified by in-gel trypsin digestion and MALDI-ToF/ToF mass spectroscopy. As noted in the results, promising leads were followed-up with quantitative immunoblot analysis or ELISA characterization of relevant small molecules.

Results

We have used discovery proteomics to investigate the plasma proteome from 11 different pediatric patients undergoing cardiopulmonary bypass. The surgical interventions ranged from the repair of mitral valve through a Fontan and repair of a Tetralogy of Fallot. Details of the experimental results are presented in three separate poster presentations (Carkaci-Salli et al.; Freeman et al.; and Lull et al.), but are presented in overview here. Discovery plasma proteomics is a non-invasive window on pathology. That is, plasma proteins represent surrogate markers for

physiological response of tissues and organs to the CPB intervention. In the present context, a preliminary proteomic screen of samples from a patient undergoing placement of a Glenn Shunt and the takedown of a Blalock-Taussig shunt indicated that there was an extensive remodeling of the plasma proteome with significant changes in oxidative stress markers (ceruloplasmin, hemopexin, and inter-alpha inhibitor H4). These findings led us then to investigate detailed changes in levels of small molecule indicators of stress status (catecholamines, serotonin, iron, and copper). Specifically, in ten pediatric patients, iron and serotonin were significantly decreased 24 hours after surgery. The sympathetic marker norepinephrine was significantly elevated following surgery. Interestingly, while both epinephrine and copper levels changed during the surgery, they had normalized 24 hours afterwards. Finally, in a fascinating study of plasma samples from distinct hepatic and pulmonary compartments of *the same patient* (undergoing a completion Fontan), quite significant proteomic differences were observed. Such organ-specific plasma compartments may hold promise to aid in identification of biomarkers of organ damage.

Conclusions

Plasma proteomics provides an important way to assess pathophysiological changes in pediatric patients undergoing CPB. Experimentally, the technique provides a unique opportunity for repeated non-invasive sampling of the same patient and may permit discrimination of individual organ compartments and responses. The technology is already providing important insights into pathophysiological responses in these young patients.



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The Effect of Advances in Perfusion on Outcomes for HLHS

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Over the past decade, substantial improvements have occurred in the outcomes for infants born with Hypoplastic Left Heart Syndrome (HLHS). Hospital survival has approached (and even exceeded) 90% in many programs. Furthermore, it appears that the survivors are transitioning to Glenn and Fontan in a fairly reliable way. Compared with the early 1990's, families are now being offered hope for their children born with HLHS.

The purpose of this review is to identify the role that improvements in cardiopulmonary perfusion strategies has played in these outcomes. The major issues surrounding outcome for HLHS are 1) Stage I survival and 2) Neurologic outcome following Stage I survival with relevance to neurologic performance at the time of Glenn.

Babies with HLHS come to the operating room with a variety of pre-existing risks for which we can do little other than be aware of their importance. These include white matter abnormalities, low birth weight and anatomic variations that contribute risk, such as intact atrial septum. Regardless of the presence of these, or other risk factors, surgical teams are commonly asked to create a successful staged procedure that will lead to Fontan. One option has been to avoid cardiopulmonary bypass entirely by banding the pulmonary arteries and stenting the ductus (the *hybrid procedure*) and a few groups are gathering experience with this approach.

For the most part, at this time, the standard approach to Stage I has been to perform an arch reconstruction and to provide a reliable source of pulmonary blood flow.

This talk will describe the important contributions that have evolved from perfusion that have led to improved outcomes. In particular, the current capabilities to provide asanguinous surgery using a miniaturized circuit, the decreased inflammation that can result from the use of more moderate vs. profound levels of hypothermia and some perfusion strategies that decrease brain injury will all be discussed.

The talk will also describe the advantages of cardiac output support following surgery to provide adequate cerebral oxygen delivery. Following exposure to CPB, regardless of whether the repair is performed under continuous perfusion or utilizing brief periods of circulatory arrest, the hypoxic brain is vulnerable to decreased cardiac output (much more so than the non-hypoxic brain). This vulnerability may last as long as 24-48 hours, which coincides with the time of increased systemic vascular resistance and characterizes the period where systemic flow may be impaired. This problem may be overcome with the use of afterload reduction (e.g. phenoxybenzamine) or with mechanical augmentation of systemic cardiac output (e.g. ventricular assist). The data suggests that this may be the more important period of time (as opposed to what happens in the operating room) to which neurologic outcome is related.

Finally, the talk will emphasize the importance of teamwork in achieving excellent results for HLHS.

Neuromonitoring during Pediatric Cardiopulmonary Bypass

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Background

As survival rates for pediatric cardiac surgery have improved, there has been an increased focus on the quality of life of the survivors. Neurologic outcome, of course, is of paramount importance. Neurologic sequelae of pediatric cardiac surgery have been reported in up to 25% of patients. Longer term effects on cognitive and motor function are suspected but less well known. Although ultimate neurologic outcome may reflect a preexisting condition or other events during the child's hospitalization, the period of cardiopulmonary bypass (with or without circulatory arrest) represents a critical period during which the brain is in great jeopardy. Our group has opined that monitoring the brain during pediatric heart surgery provides important information regarding blood and oxygen delivery and permits timely and appropriate alteration in bypass management to prevent or minimize neurologic injury.

Methods

Since 1995 our group has routinely monitored all pediatric cardiac surgery patients using three concomitant neuromonitoring modalities: 4 channel electroencephalography (EEG), transcranial Doppler, and transcranial near-infrared spectroscopy (NIRS). Multimodality neuromonitoring improves the sensitivity and specificity of each single modality and permits development of an algorithm for intervention. Changes detected with these three modalities include: abnormalities in cerebral perfusion (including the presence of gas emboli), cerebral venous oxygen desaturation, insufficient anesthetic depth, and insufficient cooling. Interventions applied when abnormalities are detected include: adjustment of

pump flow, cannula repositioning, additional deairing maneuvers, transfusion of red blood cells, additional anesthesia, and additional cooling.

Results

A retrospective analysis of our first 250 patients demonstrated significant changes in 176 (70%) with cerebral venous oxygen desaturation in 99, abnormal cerebral perfusion in 68, insufficient anesthesia in 8, and insufficient cooling in 1. Initially neuromonitoring was only observational and no interventions were applied. Among 42 patients with notable changes but no intervention, neurologic complications were noted in 12 (28%). After deciding to intervene when significant changes were detected, neurologic complications decreased to 5% (7/134) ($p < .003$). Based on this initial experience we have continued to apply multimodality neuromonitoring to essentially all patients undergoing cardiac surgery (open and closed) except for PDAs. As a result we have averted several potentially devastating neurologic injuries from air embolism and cannula misplacement. More subtle neurologic injury may have been prevented by adjusting bypass flows, systemic vascular resistance, and oxygen carrying capacity based on feedback from neuromonitoring.

Conclusions

Multimodality neuromonitoring during pediatric cardiopulmonary bypass provides a window into the brain permitting early detection of potentially damaging hypoperfusion or hypoxia. This continuous feedback allows timely interventions that can optimize neurologic outcome.

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Myocardial Protection

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Significant advances have been made in the technical performance of operations for infants and neonates with congenital heart disease. However, postoperative organ dysfunction is a frequent problem, particularly in hypoxic (cyanotic) infants and neonates. The infant heart is at high risk of damage from poor protection as a result of preoperative hypertrophy, cyanosis, and ischemia. Contrary to popular belief, these factors may make the immature (pediatric) heart more sensitive to cardioplegic arrest compared with the mature (adult) heart. We will describe the experimental infrastructure and subsequent successful clinical application of a comprehensive cardioplegic strategy that limits intraoperative injury and improves postoperative outcome in pediatric patients. The preoperative

factors of cyanosis and pressure volume overload will be discussed followed by the strategies of warm cardioplegia with substrate enhancements, multi-dose cardioplegia, and a modified intergraded approach to allow ischemia only when visualization is needed in pediatric surgeries. The importance of using a blood cardioplegia solution specifically formulated for this use, as well the importance of monitoring the cardioplegia infusion pressure will also be discussed. A practical clinical frame work based on these experimentally proven principles will then be presented to allow the surgeon to apply these strategies clinically. Application of these concepts should improve the safety of myocardial protection of the infant heart and reduce postoperative morbidity and mortality.

Evolution of CPB Techniques for Single Ventricle Circulations: A Single Centre Experience

Timothy J Jones MD FRCS(CTh)
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Hypoplastic left heart syndrome (HLHS) accounts for 2% of all congenital cardiac conditions and 25% of cardiac deaths. Without intervention the condition is universally fatal with most patients dying in the first month of life. The development of staged surgical reconstruction for HLHS and other univentricular circulations has resulted in a previously inoperable condition now being associated with a 70% 5 year survival.

The successful development of HLHS surgery mirrors the advances made in all aspects of congenital cardiac surgery with a current overall operative mortality rate of less than 5%. Successful outcome can no longer be judged on survival alone and there is an increasing need to focus on reducing post operative morbidity particularly perioperative brain injury. The precise effects of hypothermia, altered perfusion, haemodilution, acid-base management, embolisation and the systemic inflammatory response remain unclear.

Cardiopulmonary bypass (CPB) remains a non physiological therapy. Deep hypothermia, reduced perfusion and profound haemodilution are of historic importance and continue to be valuable therapeutic tools. However in our attempts to reduce post operative morbidity we are moving towards a more physiological intraoperative environment performing surgery at warmer temperatures and higher flow rates whilst developing techniques to avoid the use of deep hypothermic circulatory arrest. Intuitively this appears to be correct but the evidence to support current practices is at best confusing and at worst

absent. This partly reflects the diverse and heterogeneous nature of our patient population associated with relatively small numbers of patients with individual conditions. It also reflects the difficulty in choosing appropriate outcome measures when each patient's outcome is influenced by many dependent and independent variables.

The 3 stages of surgical reconstruction for HLHS present specific and different challenges to the surgeon, perfusionist and anesthetist. By looking at the evolution of practice over time at a single institution we can evaluate the evidence supporting current practices and hopefully identify areas requiring further study.

Conclusions

Paediatric CPB is generally a well tolerated procedure. Significant advances in understanding and technique have enabled complex neonatal cardiac surgery such as the Norwood procedure to be routinely undertaken. The diverse cardiac pathologies and surgical techniques make trials to discover optimum CPB strategies difficult to design. Much of our current practice is based on animal data and shared experiences. It is vital that human randomised prospective clinical trials are attempted in order to give this complex area a more evidence based approach with the aim of reducing post operative morbidity such as neurodevelopment impairment even further.



Bridge to Neonatal Fontan Repair of Single Ventricle

Mark Rodefeld, MD
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Mechanical augmentation of cavopulmonary blood flow in a univentricular Fontan circulation would reduce systemic venous pressure, increase preload to the single ventricle, and temporarily produce stable physiology similar to that of a biventricular circulation. This unique means of support can be applied to across the spectrum of single ventricle physiology from neonates undergoing staged Fontan palliation to adults with failing Fontan physiology as a bridge-to-recovery or -transplant. Cavopulmonary assist introduces new anatomic and physiologic challenges which are very different from those of traditional circulatory support devices. Principal amongst these are the need to provide low-pressure flow through the pulmonary vascular bed while minimizing obstruction of systemic venous pathways. A blood pump specifically designed to provide cavopulmonary assist has never been developed. In our laboratory, we are investigating a folding propeller pump and protective cage design as an optimal means of providing cavopulmonary assist.

The hydraulic performance of a 2-bladed propeller prototype was characterized in an experimental flow loop. Ideal design characteristics included the ability to produce a pressure rise of 5-20 mmHg and to be minimally obstructive to cavopulmonary blood flow in the systemic venous pathway. Physiologic flow rates for the cavopulmonary circulation were measured over a range of operating speeds. We have evaluated 5 distinctive, but successive, pump models and estimated their hydraulic performance using computational fluid dynamics (CFD).

The prototype performed well over the design range of 0.5-4.5 LPM, producing physiologic pressure rises of 5-40 mmHg. The CFD analysis of the models predicted a physiologic pressure range of 5-40 mmHg over a flow range of 0.5-4.5 LPM for rotational speeds of 4,000-15,000 RPM.

These prototypes met hydraulic performance expectations. Optimization of these configurations will further reduce fluid stress levels, minimize regions of recirculation, and improve hydraulic performance of the folding propeller. Cavopulmonary assist with a percutaneous folding propeller device may be the optimal therapeutic tool for patients with univentricular Fontan physiology as a bridge-to-neonatal repair, -recovery, or -transplant.

Rescue Extracorporeal Membrane Oxygenation in Children with Refractory Cardiac Arrest

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Objectives:

We describe our experience with extracorporeal cardiopulmonary resuscitation using extracorporeal membrane oxygenation in children with refractory cardiac arrest, and determine predictors for favorable outcome.

Methods:

Fifty-five children, mean age 3.2 years (1 day-17 years), required veno-arterial ECPR (1992-2006). Patients were post-cardiotomy (n=35) or had uncorrected congenital heart diseases (n=4), cardiomyopathy (n=8), respiratory failure (n=5), or myocarditis (n=3). The cannulation site was chest in all. Multivariate regression analysis determined factors associated with favorable outcome and time-related survival.

Results:

ECMO was successfully discontinued in 29 patients (weaned, n=18; heart transplantation, n=11). Nineteen (34%) survived to discharge. Causes of mortality were ischemic brain injury (n=5), consumption coagulopathy (n=3) and myocardial infarction (n=2). Sixteen (29%) patients had favourable outcome. Mean pre-

ECMO CPR duration for patients with favorable against unfavourable outcome was 43 minutes (range:14-93) versus 41 minutes (range 19-102). Using logistic regression model, none of the following factors: age, weight, sex, etiology (cardiac vs. non-cardiac), CPR duration, blocked aorto-pulmonary shunts nor timing of ECMO institution was a significant predictor of favorable outcome.

Time-related survival at 1 and 3 years was 29% (CI:19-39%), and 27% (CI:17-37%). Risk factors for time-related mortality were male sex (OR:1-4, CI:1.2-4.8), and non-cardiac etiology (OR:3.4, CI:3-9.5).

Conclusions:

Rescue extracorporeal cardiopulmonary resuscitation in children with prolonged cardiac arrest up to 93 minutes can achieve acceptable survival and neurological outcomes. Heart transplantation is often needed for a successful ECMO exit strategy. Lack of predictors of poor outcome support aggressive attempts to initiate CPR in all patients followed by subsequent assessment of organ salvage.

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Usefulness of Low Prime Perfusion Pediatric Circuit in Decreasing Blood Transfusion

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ICPS, Institut Hospitalier Jacques Cartier - Massy France

Small prime volume is a major factor in decreasing homologous blood transfusion.

In 2006, 259 patients weighing less than 15Kg underwent surgery:

Group 1: 134 neonates and infants with prime (140 ml) composed of blood (fresh frozen plasma and packed red cell)

Group 2: 125 infants and children with prime (170 ml) composed of blood or of lactated Ringer solution (50%) and hydroxyethyl Starch (50%).

We never use hemofiltration or cell salvage. At the end of CPB, the circuit blood and the unused blood bank products are collected to be transfused later, if necessary.

In this study, transfusion indicate the total amount of blood used for one patient within the intra and postoperative period.

None of the 259 patients had platelets infusion.

The cut-off point for transfusion is 8 kg:

- Only 5 patients (out of 41) under 8 Kg had a bloodless surgery (12%)
- The 84 patients weighing 8Kg or more had a nonhaemic prime, 85 % of whom had a bloodless surgery.

In the 76 “bloodless patients” haemoglobin level varies from 11.5 ± 1.8 g/dl before cardiopulmonary bypass to 9.4 ± 1.7 during and 10.5 ± 1.8 after. The lowest level was 7.2 g/dl during bypass.

The overall incidence of re-operation for bleeding was 0.8%.

Small prime volume is a valid alternative to more complex and expensive techniques in decreasing blood consumption. In our experience, haemoglobin is kept within safe level and no adverse effect are encountered.

	Group 1	Group 2
Number of Patients	134	125
Weight Kg : Range	2,1- 5,9	6 – 15
Mean \pm sd	4.0 ± 0.9	9.5 ± 2.7
Prime volume ml	140	170
Transfusion < 1 FFP + 1RPC	134	49
Transfusion > 1 RPC	5	3
Bloodless surgery	0	76 (61 %)

A Simple Solution is “Prime” for Fetal Cardiopulmonary Bypass

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Purpose:

Optimal prime constituents for fetal cardiopulmonary bypass have yet to be defined. Calcium and sodium bicarbonate are frequently added to the prime solution for adjustments towards physiologic values. We examined whether similar manipulations are warranted with fetal bypass and their potential effects on placental gas exchange.

Methods:

Ovine fetuses (n=10) 104-110 days gestation were placed on bypass for 30 minutes. The pump system was normothermic and non-pulsatile (200-250 mL/min/kg), consisting of a roller pump with vacuum assisted drainage, heat exchanger, primed with maternal donor blood. Calcium chloride and sodium bicarbonate were added to adjust the prime ionized calcium and pH toward “normal” fetal values. Fetal arterial blood gases were collected immediately before (pre-bypass), and at 15 and 30 min on bypass. Correlations and R^2 values were determined using best-fit method.

Results:

A total of 7.9 ± 1.8 mEq sodium bicarbonate (median 8.5, range 5-10) and 179 ± 96 mg calcium chloride (median 175, range 0-300) were added to the prime to achieve near physiologic values (pH was 7.30 ± 0.08 (Mean \pm SD) and iCa 0.85 ± 0.41 , (median 0.79, range

0.39 - 1.51). Added prime calcium did affect fetal iCa levels on bypass (Pre-bypass 1.53 ± 0.15 ; on bypass 1.34 ± 0.14 , $p=0.01$). However, added bicarbonate did not affect fetal pH with initiation of bypass (pre-bypass 7.26 ± 0.06 ; on bypass 7.24 ± 0.04). A negative linear correlation existed between calcium added to the prime and fetal pH at 15 and 30 minutes on bypass ($R^2 \geq 0.63$). A similar, but weaker negative correlation existed for bicarbonate added to the prime ($R^2 \geq 0.34$).

Conclusions:

Fetal gas exchange is adversely affected with addition of calcium to the prime, likely through worsening of placental vascular resistance. A similar adverse relationship may exist with bicarbonate supplementation that should be addressed with additional studies.

Efficacy of a Miniature Centrifugal Rotary Pump for Transfusion-Free Cardiopulmonary Bypass in Neonatal Piglets

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Background:

Toward transfusion-free pediatric open heart surgery, we developed a low priming cardiopulmonary bypass (CPB) circuit incorporating a miniature centrifugal rotary pump (Tiny-pump, volume=5 ml). In the present study, we performed CPB in neonatal piglets without transfusion by using this circuit or another larger circuit with a Bio-pump (BP-50), and compared the data on hemolysis, hemodilution and inflammatory response.

Methods:

Twelve 1-week-old piglets weighing 3.4 ± 0.2 kg were used. The circuit comprised a centrifugal pump, a membrane oxygenator (Terumo Capiox RX 05) and a cardiomy reservoir, with a priming volume of 68 ml for Tiny-pump group (n=6) and of 111 ml for Bio-pump group (n=6). CPB was established by aortic and right atrial cannulation, and was maintained for 3 hours with mild hypothermia (30-32 C) at a flow rate of 150 ml/kg/min.

Results:

All animals were weaned from CPB without inotropic support. Cardiac index did not change after CPB and did not differ between the groups.

Tiny-pump was driven at a higher rate than Bio-pump (3508 ± 166 vs. 2005 ± 55 bpm), but plasma free hemoglobin levels at 3 hours on CPB were not different between the groups. After cessation of CPB, Tiny-pump group had higher hematocrit (27 ± 3 vs. $22 \pm 2\%$), lower platelet reduction rates (1.09 ± 0.29 vs. 1.62 ± 0.38), lower thrombin-antithrombin complex (29.9 ± 8.7 vs. 41.2 ± 3.5 ng/ml) and lower IL-6 (2097 ± 386 vs. over 5000 pg/ml) than Bio-pump group. Although slight myocardial edema occurred in both groups, better lung compliance with less water content was observed in Tiny-pump group.

Conclusions:

The Tiny-pump well controlled CPB at low flow rate and employment of this pump reduced hemodilution as well as inflammatory response in neonatal piglets. Thus, the miniaturized CPB circuit may make transfusion-free open heart surgery feasible in neonates and would help to prevent post-operative organ dysfunction.

Benefits of Pulsatile Perfusion on Vital Organ Recovery during and after Pediatric Open-Heart Surgery

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Introduction: There is controversy concerning the utilization of pulsatile flow during cardiopulmonary bypass (CPB) with regard to improved patient outcomes. The aim of the present study was to evaluate pulsatile perfusion in pediatric patients undergoing CPB in a clinical setting.

Methods: 215 consecutive pediatric patients undergoing open heart surgery for repair of congenital heart disease were prospectively entered into the study and were randomly assigned to either the pulsatile perfusion group (Group P, n = 151) or the nonpulsatile perfusion group (Group NP, n = 64). All patients received identical surgical, perfusional, and postoperative care. Study parameters included intubation time, duration of ICU and hospital stay, the need for inotropic support, pre- and postoperative enzymes (ALT, AST), creatinin, CRP, lactate, albumine, blood count (leukocytes, hematocrit, platelets), mean urine output (ml/day) and total drainage (ml). Major complications and clinical outcome were documented.

Results: There were no statistically significant differences seen in either preoperative or operative parameters between the two groups (age, BSA, weight, X-Clamp and CPB time, base flow, flow rates and hemofiltration).

The Group P, compared to Group NP, had significantly less inotropic support (number of agents 1.4 ± 0.07 vs 2 ± 0.12 , $p = 0.0012$; dopamine 7.14 ± 0.28 vs 9.04 ± 0.42 $\mu\text{g}/\text{kg}/\text{min}$, $p = 0.00025$; dobutamine 4.12 ± 0.3 vs 5.3 ± 0.6 $\mu\text{g}/\text{kg}/\text{min}$, $p = 0.036$, adrenalin 0.026 ± 0.005 vs 0.046 ± 0.005 $\mu\text{g}/\text{kg}/\text{min}$, $p = 0.021$), less intubation period (10.26 ± 1.04 vs 18.64 ± 1.99 hours, $p = 0.021$), less duration of ICU (1.53 ± 0.07 vs 2.75 ± 1.19 days, $p = 0.012$) and hospital stay (6.71 ± 0.19 vs 11.16 ± 0.58 days, $p = 0.002$).

Although there were no significant differences in either creatinin, enzyme levels and drainage amounts between two groups, lower lactate levels 16.27 ± 2.02 vs 24.66 ± 3.05 mg/dL, $p = 0.00034$, higher albumine levels 3.15 ± 0.03 vs 2.95 ± 0.06 $\mu\text{g}/\text{kg}/\text{min}$, $p = 0.046$) and higher urine output (602.82 ± 21.5 vs 505.55 ± 34.2 ml/day, $p = 0.016$) during ICU period was observed in Group P.

Conclusions: We found statistically meaningful results regarding outcomes (shorter ICU and hospital stay period) for CPB in pediatric patients compared to pulsatile and nonpulsatile type perfusion systems. We conclude that the use of pulsatile flow resulted in improved patient outcome in preserving cardiac function and maintaining better renal and pulmonic function (shorter intubation period) in the early post-bypass period.

Comparison of Single-, Double- and Diagonal Pumps for Pulsatile Perfusion in Pediatric Cardiac Surgery

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Purpose:

Pulsatile perfusion is usually achieved by two occlusive roller pumps: the first for continuous flow through the oxygenator, the second with pulsatile flow behind the oxygenator. Low resistance oxygenators permit pulsatile flow with one pump. DeltaStream® (Medos AG, Germany) is a non occlusive pump with diagonal blood stream that combines hemocompatibility with the option for pulsatile perfusion. We examined the impact of pump type (roller single/double vs. diagonal) on Energy Equivalent Pressure (EEP) during pulsatile perfusion in a pediatric cardiac surgery model.

0.6-1.0l/min at 60-90 bpm. The pulse width of the roller pumps varied from 30 to 70%, the ground flow from 0 to 60%. The diagonal pump speed difference ranged between 3000 and 5000 rpm.

Pressure and flow were continuously measured. Minimum/maximum and mean flow/pressure, EEP and EEP/MAP were determined ten times and averaged.

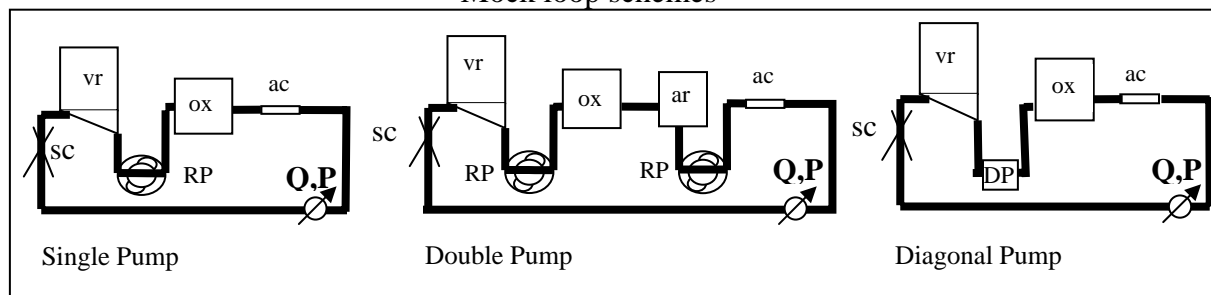
Material and Methods:

Three mock loops with double-, single- and diagonal pump systems were filled with 280ml saline suspension of packed erythrocytes and perfused with

Results:

The double pump is most effective for reaching highest EEP-Levels (17-50%) over a wide range of settings for flow, pulse width, ground flow and pulse rate. The efficiency of the single pump is a little restricted (8-35%). The diagonal pump still reaches sufficient EEP-Level (8-22%) in most settings.

Mock loop schemes



- sc : screw clamp resistance
- vr : venous reservoir (Hilite 2800)
- RP : Roller Pump (Stoekert S III)
- ox : oxygenator (Hilite 2800)
- ac : arterial cannula (Medos, Ø3mm)

- Continuous Flow => 60 mmHg
- ar : arterial reservoir bag
- DP : Diagonal Pump (Medos, DeltaStream)
- Q,P : Measurement of flow and pressure

Conclusion:

All pumps can be used for an effective pulsation. Primarily selection of the diagonal pump is useful for high risk patients for eventual postoperative ventricular support.

Application of Modified Perfusion Technique on One Stage Repair of Interrupted Aortic Arch in Infants—A Case Series

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Purpose:

One stage repair of interrupted aortic arch (IAA) associated cardiac anomalies in neonates and infants is a big challenge for whole surgical team. Deep hypothermic circulatory arrest prolongs myocardial ischemia and might induce cerebral and major organ's dysfunction. We reviewed the perfusion experiences of 13 cases with a modified technique of regional cerebral perfusion under deep hypothermic circulatory arrest (DHCA) during one stage repair of IAA in infants.

Methods:

From May 2004 to May 2006, 13 infants with IAA underwent one stage repair by median sternotomy under deep hypothermia circulation arrest (DHCA) and continuous regional cerebral perfusion. HTK solution (40-45ml/kg) was perfused into the aortic root for myocardial protection. The age ranged from 2-27 months, and the body weight ranged from 3.8-11.5 kg (mean 5.58 ± 2.15 kg). The temperature in nasopharynx was decreased to 18-20°C; the

temperature in rectum was controlled to 19-22°C.

The regional cerebral perfusion flow rate was maintained with 20-25ml/kg during DHCA. The mean artery pressure (MAP) measuring from right radial artery was 32.5 ± 5.8 mmHg, and the MAP from femoral artery was 11.2 ± 3.5 mmHg.

Results:

All patients were survived, and no cases experienced complications of the central nervous system. CPB time was 112~207 min (141.6 ± 21.7 min). Clamp time was 48~79 min (mean 52.3 ± 10.9 min). The duration of regional cerebral perfusion was 28-45 min (mean 31.5 ± 12.4 min). The intubations time in ICU was 32-96 hr (mean 54.7 ± 12.6 hr); the ICU stay was 45-122 hrs (mean 67.9 ± 28.4 hrs).

Conclusion:

One-stage total arch IAA repair under DHCA using continuous regional perfusion technique is an excellent method that may minimize neurologic complications without mortality.

Using Plasma Proteomics in the Identification of Pathology-Related Markers in Pediatric Patients Undergoing Cardiopulmonary Bypass

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Purpose:

The objective of this study was to screen the plasma proteome of pediatric patients undergoing cardiopulmonary bypass (CPB) procedures to identify potential clinical biomarkers related to tissue damage, inflammation, or other pathologies.

Methods:

Heparinized blood was collected from patients undergoing cardiopulmonary bypass at five time points: before surgery (1), 5 minutes on bypass (2), at the conclusion of the surgery (3), 1 hour post-weaning from bypass (4), and 24 hours post-weaning (5). Blood was collected in EDTA vacutainers and cells were spun down at 1000g for 15 minutes at 4°C. Resulting plasma was depleted of six high-abundance proteins to improve sensitivity to low abundance proteins. Depleted plasma samples from a single patient at timepoints 2 and 4 were labeled with Cy3 and Cy5 dyes, respectively, and separated using isoelectric focusing followed by a second dimension gel separation by molecular weight. Gels were imaged and analyzed for changes in levels of individual protein species. Changes of 50% or more were chosen for identification using MALDI-ToF/ToF mass spectrometry. Confirmation of

changes in 10 patients across all 5 timepoints was done using western blot analysis. One-way ANOVA analysis followed by Student-Neuman-Keuls multiple comparison tests were used to determine significant changes in immunoblot analyses.

Results:

Analysis of a single patient showed 79 differentially regulated spots out of 1379 total spots (5.7%) with changes ranging from 50-330%. Of these changes, 13 unique proteins have been identified, including ceruloplasmin (60% decrease), hemopexin (60% increase) and inter-alpha inhibitor H4 (ITI-H4, 53% decrease). The change in ceruloplasmin has been confirmed in 10 patients, and levels at all 5 timepoints were observed. Other changes in protein expression will be confirmed in a similar manner.

Conclusions:

Changes in the levels of plasma proteins are associated with CPB procedures. Several putative markers of pathology have been identified among these changes and may indicate the need for preventative measures and/or treatments during and following CPB procedures in pediatric patients.

Low Prime Pediatric Cardiopulmonary Bypass Using the Dideco Kids D100TM Oxygenator

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Purpose:

The systemic inflammatory response associated with cardiopulmonary bypass (CPB) in neonates and infants is implicated as a major cause of post-CPB organ dysfunction. This has spurred significant efforts to miniaturize components in order to reduce priming volume, limit exposure to foreign surfaces and reduce the need for blood product transfusion. The Sorin Group has recently introduced the Dideco Kids D100 neonatal oxygenator to the North American market. The D100, a hollow fiber, phosphorylcholine-coated oxygenator with integrated heat exchanger and hard-shell venous reservoir, currently offers the lowest available priming volume of 31cc. This study describes our use of the D100 in a series of six patients under 6 months of age.

Methods:

For each patient, the extracorporeal circuit consisted of a D100 oxygenator and 3/16-inch tubing throughout. Four circuits included a Dideco D736 arterial filter, while two circuits contained no arterial filter, reducing priming volume by an additional 40cc. Tubing lengths were minimized by employing vacuum-assisted venous drainage with a Cobe SIII

heart-lung machine and mast-mounted arterial and suction rollers. Patients underwent repair using deep hypothermic low-flow and/or circulatory arrest keeping hematocrit $\geq 30\%$.

Results:

Priming volume for all cases was 125 +/- 21cc. Bloodless prime was used in 2 patients. Mean patient weight was 4.4 +/- 1.3kg. Median patient age was 68 days (10-143). Bypass times and crossclamp times were 108 +/- 32.5 and 52 +/- 18 minutes, respectively. Flows ranged from 150 to 1000cc/min. There were no deaths and no complications attributed to CPB.

Conclusions:

The D100 performed well across a wide range of pump flows. The use of a miniaturized circuit has potential to modulate the inflammatory response to CPB and limit requirement for blood product transfusion. Further study may show this translates into improved outcomes following neonatal and infant CPB.

Impact of Miniaturization of Cardiopulmonary Bypass Circuit on Neonatal Open-Heart Surgery

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Purpose:

Cardiopulmonary bypass (CPB) circuit for neonatal open-heart surgery inevitably requires blood prime because of the patient’s body size/circuit volume mismatch. The aim of this study was to determine the impacts of miniaturization of CPB circuit on amount of blood use and hemodynamics in neonatal open-heart surgery.

Methods:

This retrospective study includes 102 neonates undergoing open-heart surgery between June 2002 and December 2006. We divided the entire cohort into 3 groups: Group 1 (n=28), Dideco 902 Oxygenator + 5/16” line; Group 2 (n=29), Dideco 901 oxygenator + 5/16” line; Group3 (n=45), Dideco

901 Oxygenator + 3/16” line. Amount of priming volume, blood transfusion, and bicarbonate use during CPB and hemodynamics were compared.

Results:

Priming volume in the group 2 and 3 was significantly reduced compared to the group 1 (Table). Blood transfusion during CPB in the group 2 and 3 was significantly smaller compared to the group 1. Bicarbonate use to adjust pH during CPB in the group 2 and 3 were significantly decreased compared to the group 1 (Group1: 54±11, Group2: 27±7, Group3: 30±5ml, p<0.05). Hemodynamics during CPB was comparable. There were no differences between the group 2 and 3 in any of parameters.

	Priming of CPB circuit		Blood Transfusion Volume (ml)			Hematocrit (%)		
	Volume (ml)	Hematocrit (%)	Prime	During CPB	Total Use	Pre-CPB	Lowest during CPB	Post-CPB
Group 1	705±37	33±2	520±0	0±0	520±0	40±8	31±3	48±4
Group 2	458±12*	26±2*	262±9*	72±42*	334±40*	44±6	30±3	50±4*
Group 3	456±5¶	28±1¶§	258±16¶	62±42¶	320±45¶	42±5	29±2¶§	48±4

*p<0.05 vs. Group1, ¶ p<0.05 vs. Group 1, §p<0.05 vs. Group 2

Conclusions:

Miniaturization of CPB circuit resulted in decrease in priming volume and subsequent reduction in blood and bicarbonate use. Downsizing the line size has minimal impact on any of parameters, and further efforts should be made to achieve neonatal open-heart surgery without blood transfusion.

PMEA-Coated Bypass Circuits Reduce Activation of Coagulation System and Inflammatory Response in Congenital Cardiac Surgery

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Surface coated cardiopulmonary bypass (CPB) has been shown excellent biocompatibility during the cardiac surgery in adults. But there have been few reports demonstrating the efficacy of these coating for congenital cardiac surgery. Blood artificial surface interaction during CPB is stronger in children than in adults, because children have higher ratio of CPB circuit internal surface area to patient blood volume than adults. We tested the efficacy of poly-2-methoxyethylacrylate (PMEA) –coating for CPB circuit compared with no coated circuits in the congenital cardiac surgery.

Eleven operative cases of the ventricular septal defect were studied: control group (no coating, n=5), P group (PMEA coating, n=6). After anesthetic induction, all patients received a bolus of heparin (400 U/kg) and underwent the ventricular septal defect closure with patch using CPB as usual manner. Platelet count, β -thromboglobulin (β TG), fibrinogen (FBG), a thrombin antithrombin complex (TAT), neutrophil elastase were measured before heparin; 5 minutes after CPB; at end of CPB; at end of operation and at the next morning.

Postoperative chest tube drainage was analyzed and the surface of the artificial lung was observed with an electron microscope.

Elevation of the TAT was suppressed in P group (<0.05 ; ANOVA), and the neutrophil elastase was significantly low at the end of CPB ($P < 0.05$). Observation with the electron microscope of the artificial lung surface revealed clearly less platelet, red blood cell and white blood cell which stuck to the surface in P group than control group. The FBG and the postoperative bleeding showed relatively low in P group, but there were no significant differences between groups. Platelet count, β TG was same in the both groups.

We conclude that the PMEA-coating circuit reduces activation of the coagulation system and the inflammatory reaction in pediatric cardiac surgery.

Postoperative Prophylactic Peritoneal Dialysis in Neonates and Infants after Complex Congenital Cardiac Surgery

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Introduction: Peritoneal dialysis (PD) after complex congenital cardiac surgery was introduced to a group of neonates and infants (n = 912, age: 0-1 years) between May 1993 and December 2006. Indications of peritoneal dialysis were determined as well as methods, prolonged dialysis and its outcomes.

Material and method: Demographic characteristics, preoperative risk factors, intraoperative variables and postoperative complications were compared in 912 cases with ages below one year. All cases underwent conventional ultrafiltration during perioperative stage. 216 cases (23.7 % of total) required peritoneal dialysis (in addition to perioperative ultrafiltration). The cardiac pathology was TGA in 154 cases, TOF in 42, IAA-APW in 5, and TAPVR in 8 and other complex pathology in 7 cases. Those patients who required perioperative ventilation, cases that had long bypass and TCA (total circulatory arrest) durations due to their complex pathologic conditions and those experiencing pulmonary hypertensive (PH) crisis were defined as “high risk group”. Prolonged peritoneal dialysis

was usually required in infants with low-weight, with episodes of PH crisis ($p < 0.05$), and with preoperative renal dysfunction. No major complication (peritonitis or hemodynamic instability) was observed related to the peritoneal dialysis catheter (during the use or following the withdrawal).

Results: 31 of 216 patients (14.4 %) had acute renal failure (ARF) and 11 of them died (1.2% of all patients underwent operation, 35.5% of those with ARF). It has been demonstrated that the combination of peritoneal dialysis with perioperative ultrafiltration application was effective in providing the required postoperative negative fluid balance in especially complex congenital pathologic cases affected the survival positively.

Conclusions: Protection of the renal functions and its maintenance therapy, which is an important factor in postoperative morbidity and mortality, can be safely and effectively done by prophylactic perioperatively initiated peritoneal dialysis in complex cardiac pathologies in neonatal period.

Age (day)	12 (2-72)
Weight (kg)	3.4 (1.8-5.2)
PD timing (postop.hour)	4,2 (4-20)
Total fluid intake (cc/kg/day)	108 (50-180)
Total fluid output (cc/kg/day)	228 (130-560)
- Diuresis	96 (35-180)
- PD UF	121 (40-300)
Negative fluid balance (cc/kg/day)	120 (80-380)

Table 1. Features of patients

	Pre-PD	Post-PD	p value
Serum creatinine level (mg/dl)	0.36	0.41	NS
Mean urine output (cc/kg/h)	2.1	3.9	< 0.01
Mean number of inotropics agents	2.12	1.61	< 0.05

Table 2. Parameters of pre- and post PD period

Effect of Modified Ultrafiltration on Neonates Undergoing Arterial Switch Operation

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Purpose:

Modified ultrafiltration (MUF) has been shown to improve clinical outcomes in pediatric patients, but the impacts of MUF on neonates with transposition of the great arteries (d-TGA) undergoing arterial switch operation has not been assessed.

Methods:

This retrospective study includes 36 consecutive neonates undergoing arterial switch operation for d-TGA between April 1998 and September 2006. Mean age and weight at surgery was 14±10 days and 3.2±0.6 kg, respectively. Conventional cardiopulmonary bypass (CPB) without MUF was employed in the former 21 patients (Control), and arteriovenous MUF was performed after CPB for 10 to 15 minutes in the latter 15 patients (MUF group). Parameters included hematocrit, hemodynamics,

respiratory function, drain loss, and length of intubation and ICU stay.

Results:

There was no MUF-related morbidity. The hematocrit increased from 34±2% to 47±4% in the MUF group, whereas the hematocrit remained unchanged in the control group. Blood pressure in the MUF group was significantly increased without any change of central venous or left atrial pressure (Table). Post-operative oxygenation in the MUF group was greater than that of control group (P/F ratio: 258±92 vs. 170±100mmHg, p<0.05), which did not contribute to decrease in intubation time (54±33 vs. 52±29 hours, p=NS). Post-operative chest drain loss was comparable. The length of ICU stay in the MUF group was significantly shorter than that in controls (101±34 vs. 139±42 hours, p<0.05).

	Systolic Blood Pressure		Diastolic Blood Pressure		Mean Blood Pressure		Central Venous Pressure		Left Atrial Pressure	
	pre-MUF	post-MUF	pre-MUF	post-MUF	pre-MUF	post-MUF	pre-MUF	post-MUF	pre-MUF	post-MUF
Control	63±8	64±7	41±7	41±7	50±7	50±7	6.4±2.2	6.4±2.2	4.3±1.7	5.0±1.8
MUF	52±7*	66±5 ¶	46±5*	46±4*	41±5*	55±4 ¶	7.5±3.0	6.4±2.9	4.8±1.4	4.0±1.5

* p<0.05 vs Control, ¶ p<0.05 vs pre-MUF

(mmHg)

Conclusions:

MUF brought improvement in blood pressure and gas exchange capacity and subsequent shorter ICU stay, while improved gas exchange capacity did not directly shorten ventilatory support. This safe and effective technique would be an essential perfusion strategy to minimize cardiopulmonary bypass-related adverse effects in neonates undergoing arterial switch operation.

Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Variability of Pediatric Blood Viscosity

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 University of Louisville Cardiovascular Innovation Institute and Department of Mechanical Engineering, Louisville, Kentucky, and Ension, Inc., Pittsburgh, Pennsylvania

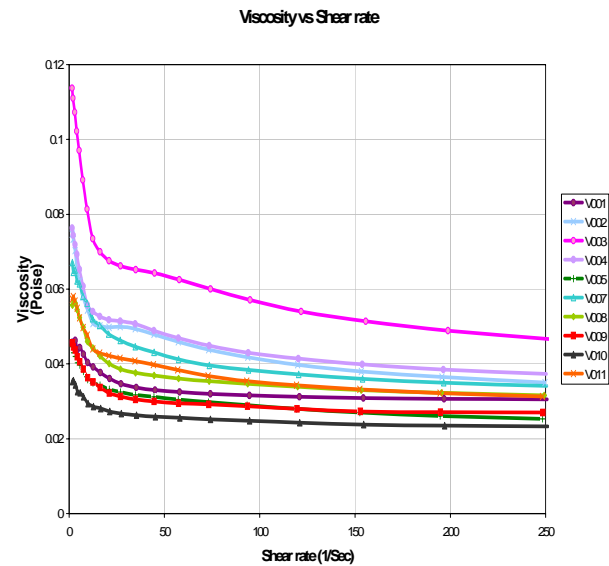
Purpose: The performance of blood pump systems being developed to provide circulatory support for infants and small children may be dependent on the viscosity (μ) of the blood. To determine the range in μ of pediatric blood to be considered for test performance evaluation, blood samples were obtained from pediatric patients and analyzed with a viscoelastometer to produce shearing rate profiles.

Methods: Pediatric patients scheduled for cardiac surgical procedures at the Kosair Children’s Hospital were enrolled into the investigation during July and August, 2006. Consistent with the specifications of the NHLBI Pediatric Assist Device Program, only patients weighing less than 25 Kg were included in this evaluation. The age, weight, most recent hospital hematology data, and surgical procedure to be performed were recorded at the same time a blood sample was obtained. The sample was immediately put into an EDTA anticoagulant tube and iced until analyzed by a Vilastic-3 viscoelasticity analyzer (Vilastic, Inc.) within 2 hours to produce a shearing rate profile.

Results: Ten patients with an average weight of 10.5 ± 6.9 Kg [1.7 to 20.2 Kg] and average age of 2.0 ± 2.1 yrs [0.03 to 6.3 yrs] were enrolled. The surgical procedures to be performed on these 10 patients were VSD closure (1), ASD closure (2), Norwood procedure (1), Fontan procedure (2), bi-directional Glenn procedure (2), aortic coarctation repair (1), and bi-lateral pulmonary artery banding (1). The average hospital spun hematocrit was $42.1 \pm 7.3\%$ [33.7 to 55.4%] and the average laboratory spun hematocrit was $39.5 \pm 7.7\%$ [30 to 51%]. The hospital hematocrit was larger (usually by a few percent) in 8 of the 10 patients. The blood density was $1.0523 \pm$

0.0052 gm/ml [1.0459 to 1.0599 gm/ml]. An acceptable shearing rate profile was obtained for each sample [figure below]. The asymptotic μ (shearing rate @ 250 sec^{-1}) was 3.2 ± 0.7 cP [2.3 to 4.7 cP]. The variation in asymptotic μ correlated moderately well ($r = 0.85$) with the corresponding hematocrit. Higher values of μ were often found in samples from patients with cyanotic heart disease requiring the Norwood, Glenn, or Fontan procedures.

Conclusions: A two-fold range of asymptotic viscosity was found in pediatric blood and needs to be considered when testing the performance of viscosity-dependent, pediatric blood pump systems.



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Technique for the Norwood Procedure Using Normothermic Selective Cerebral Perfusion

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Purpose:

The Norwood procedure is commonly performed utilizing either circulatory arrest or deep hypothermia with low flow CPB. We describe our technique using selective cerebral perfusion with normothermia (NSCP).

Methods:

A right radial artery catheter is placed and cerebral NIRS applied. The ascending aorta and all arch vessels are dissected distally and the descending aorta well beyond the ductal insertion. A C-clamp placed upon the innominate artery and a 3.5 Gorex shunt placed. The SVC and IVC are cannulated, cardiopulmonary bypass is established through the shunt and the ductus is snared. The duct is now divided and the main PA transected. The distal PA is augmented with an autologous pericardial patch. A 7.0 purse-string is placed at the beginning of the arch and a cross-clamp applied and cold cardioplegia given by hand. The septum is removed and a 5.0 purse-string placed about the coronary sinus. A 2mm coronary perfusion cannula is inserted into the sinus and intermittent retrograde cold all-blood cardioplegia is delivered using the Quest MPS pediatric unit.

The left carotid and subclavian are snared and a C-clamp placed on the distal descending aorta. The cross-clamp is now repositioned across the base of the innominate and pump flow is reduced to about 40%. This results in arch isolation with a bloodless field for either standard Norwood reconstruction or the Mee modification. The arch is de-aired and the arch snares and clamps removed. A purse-string is placed in the neo-aorta and perfusion transferred to a neo-aortic cannula. The central shunt is then completed.

Results:

A good result may be achieved with a CPB time of about 60 minutes and cardiac arrest time of about 20 minutes.

Conclusion:

The Norwood procedure can be successfully performed with NSCP thereby offering the theoretical benefit of avoiding deep hypothermia with or without circulatory arrest.

Safety Mechanism of Low Prime ECMO System with Dual Servo-Regulation Mode for Lower Body Perfusion During Coarctation Repair

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Extracorporeal circulatory assistance (ECCA) can be widely used to protect the spinal cord and splanchnic organs during surgical treatment for coarctation of the aorta (CoA). Paraplegia is a rare, but serious complication of CoA repair. In the neonatal CoA repair using an ECCA, venous drainage from the pulmonary artery, requiring a pump oxygenator, is more stable than that from the left atrium. We have recently developed a safer ECMO system for reducing the risk of cannulation problems, excessive hemodilution, and the internal surface area of the system (reducing contact responsiveness to a foreign body). This ECMO system has a 2-stage pressure regulation (*slow mode* or *stop mode*) roller pump with the prime volume including a heat exchanger of only 88 ml. The key safety mechanism includes the first regulation (changes to a *slow mode* by a slight negative/positive circuit pressure) and the second regulation (changes to a *stop mode* by a further negative/positive circuit pressure), with an auto

regulation system to normal perfusion when returning to a safe pressure range.

In our hospital, two neonatal patients with CoA complex underwent CoA repair using our ECMO system. The pump flow rate to the descending aorta during the aortic cross-clamping was approximately 1.2 to 1.5 ml/kg/m²; arterial pressure of the lower body was 35 to 40 mmHg. The 2-stage safety mechanism worked effectively without sudden circulatory arrest. The CRP value was below 1mg/dl on the 4th postoperative day in both patients. There was no postoperative death, neurological dysfunction, or ECMO-related complications.

In conclusion, a low prime ECMO system with a dual servo-regulation mode may contribute to risk reduction in circulatory support during the CoA repair.

Absence of Rapid Deployment ECMO Team Does Not Preclude Resuscitation ECMO In Pediatric Cardiac Patients with Good Results

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Purpose:

To evaluate our results with ECMO used as resuscitation for cardiac patients undergoing CPR, in our setting where no perfusionist or surgeon are always on-site, and no circuit ready.

Methods:

Between 2003 and 2006, we used ECMO for all cardiac patients who underwent cardiac arrest in the PICU or Cath Lab. We reviewed retrospectively 14 consecutive files (15 episodes). Eleven patients were in PICU after cardiac surgery and 2 for severe cardiomyopathy. Two patients were cannulated in the Cath Lab after an interventional procedure. One already had a post-operative resuscitation ECMO during a previous hospitalization. Pathologies are detailed in the table. The circuit was mounted and

primed while CPR occurred and while the surgical team got ready for cannulation.

Results:

Mean CPR time before ECMO institution was 44 minutes (10 to 110 minutes). The surgeons, perfusionist and scrub nurse, not on site for 3 of these patients, had to be called in simultaneously with institution of CPR. Two of them died on ECMO, the third one was successfully transplanted after 5 days. Globally, 10 patients could be weaned (66%). Eight patients (57%) survived to hospital discharge, 7 without obvious neurological damage. One patient was bridged to an LVAD and was eventually successfully transplanted. He had an ischemic brain lesion which good recuperation and no sequel.

Pathology	n=15	Weaned (n=10)	Survived to discharge (n=8)
Cardiomyopathy	2	2	2
Acute graft rejection	1	1	1
Pulmonary atresia, VSD,	5	3	2
Small left ventricle or HLHS	3	0	0
Double outlet right ventricle	1	1	1
Tetralogy of Fallot	1	1	0
Cor triatriatum	1	1	1
Truncus arteriosus	1	1	1

Conclusions:

Even without an institutional rapid deployment ECMO set-up, it is possible to obtain good results with resuscitation ECMO. These encouraging results justify such an institutional development.

Extracorporeal Membrane Oxygenation for Pediatric Severe Respiratory Failure—Report from a Single Institute

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Purpose:

Extracorporeal membrane oxygenation (ECMO) is a proven modality for the treatment of severe respiratory failure in the neonates, but its efficacy in larger children is not well established. The objective of this investigation was to review the experience of ECMO in pediatric patients and find suitable timing for ECMO initiation in this group.

Methods:

The pediatric patients (age between 3 months and 16 years old) with severe respiratory failure and received ECMO in our center were reviewed. The ECMO configuration was venous-venous (VVECMO) or venous-arterial (VVECMO) if hemodynamic instability. The ECMO circuit consisted of a centrifugal pump and a hollow fiber oxygenator. The demographic data, pre-ECMO ventilator days, ventilator setting, blood gas data, and hemodynamic data, inotropic agent score, and outcomes were reviewed. Factors associated with survival were examined.

Results:

There were 13 patients included in this study. The etiology included bacterial pneumonia (n=8) and viral pneumonia (n=5). The median ventilator days before ECMO were 5 days (range 1-24 days). Before initiation of ECMO, the mean PaO₂/FiO₂ was 62.7, and the mean airway pressure was 26 cmH₂O and 7 patients once received high frequency oscillatory ventilator (HFOV). The mean ECMO duration was 240 hours. Comparing the survivors (n=4) and the non-survivors (n=9), the non-survivors had lower pH, higher inotropic agents, oligouria, and use of HFOV.

Conclusions:

Although ECMO could successfully rescue patients with advanced respiratory failure, pre-ECMO use of inotropic agents, acidosis and oligouria were associated with poor outcome. The ECMO should be initiated before the hemodynamic compromise and renal dysfunction developed.

Selective Na⁺/H⁺ Exchanger Inhibitor HOE642 Preconditioning Reducing Calcium Overload and Exhibiting Markedly Protective Effect on Immature Rabbit Hearts

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Objective:

To investigate the protective effect of HOE642 preconditioning against ischemia-reperfusion injury on immature myocardium and its mechanisms.

Methods:

The Langendorff perfused isolated working immature rabbit heart model was established. After perfused by Krebs-Henseleit buffer bubbled with 95% O₂-5% CO₂ gas mixture at 70cmH₂O for 20min, 20 isolated hearts of New Zealand healthy white immature rabbits (3-4 weeks old, weighing 300-350g) were randomly divided into 2 groups: the group I: the control group (n=10); group II: HOE642 preconditioning group (n=10). In group I, the hearts were perfused for 15min by Krebs-Henseleit buffer; in group II, HOE642 (5μmol/L) was added to Krebs-Henseleit buffer and the hearts were perfused for 15min. Then St. Thomas solution was used, and all hearts were subjected to 45min global ischemia and 60min reperfusion. Perfusate temperature and the ischemic heart temperature were both maintained at 37. Myocardial calcium content was examined. Hemodynamics variables (LVDP, ±dp/dt), myocardial water content (WC), coronary artery flow (CAF), leakage of myocardial enzyme (CK, CK-MB, LDH) were also calculated. Myocardial and endothelial structure was observed under election microscope.

Results:

1. Myocardial function: LVDP, ±dp/dt, CAF recovery was markedly higher in group II than that in group I (p<0.01 or p<0.05).
2. Myocardial calcium content was markedly lower in group II (p<0.01).
3. Myocardial enzyme is significantly lower in group II than group I (p<0.05).
4. Myocardial water content (WC) was markedly lower in group II (p<0.01).
5. Myocardial structure: the optimal group was group II, which had better protective effect on myocardial structure and endothelium of coronary artery.

Conclusion:

HOE642 Preconditioning provide a significant protection against ischemia-reperfusion injury on immature myocardium mostly through reducing myocardial calcium overload.

Key words:

Na⁺/H⁺ exchanger; Preconditioning; immature myocardium; Ischemia-reperfusion injury; Calcium overload

Comparison of Four Different Pediatric 10 Fr Aortic Cannulae during Pulsatile vs. Non-pulsatile Perfusion in a Simulated Neonatal Model of CPB

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Purpose:

The purpose of this investigation is to compare four different pediatric aortic cannulae with different geometry during pulsatile vs. non-pulsatile perfusion in terms of *surplus hemodynamic energy* (SHE) level in a vitro neonatal model of CPB.

Methods:

The mock loop in this simulated pediatric model is composed of two parts. One part is the extracorporeal circuit, which consists of a Jostra HL-20 heart-lung machine (for both pulsatile and non-pulsatile modes of perfusion), a Jostra-30 heat-cooler system, a Capiiox Baby RX hollow-fiber membrane oxygenator, a Capiiox pediatric arterial filter, 5 feet of arterial tubing, and 6 feet of venous tubing with a ¼ inch diameter. The other part is the simulated Penn State neonatal patient, which includes a chamber, and a Penn State neonatal LVAD. One of four arterial cannulae is placed at the distal end of the arterial line to the chamber, while the insertion tip of the cannula

is fixed to inlet of the simulated Penn State neonatal patient. The pseudo patient is set to a pump flow rate of 600 ml/min and the mean arterial pressure is set at a constant 40 mmHg via Hoffman clamp. A 20 second segment of the pressure and flow waveforms with non-pulsatile flow are then recorded at the pre-cannula and post-cannula sites. The perfusion mode is then switched to pulsatile flow. The following formula is used to calculate the SHE levels.

$$SHE \text{ (ergs/cm}^3\text{)} = 1332 [((\int p dt) / (\int f dt)) - \text{Mean Arterial Pressure}] \text{ (} f = \text{flow, } p = \text{pressure)}$$

Results:

The following table represents the Surplus Hemodynamic Energy (SHE) level results of four different pediatric arterial cannulae (Mean ± SD) at the pre-cannula and post-cannula sites with a pump flow rate of 600ml/min.

Table 1. Surplus Hemodynamic Energy results

Type of Cannula	SHE (Pre-Cannula) (ergs/cm ³)		SHE (Post-Cannula) (ergs/cm ³)	
	NP	P	NP	P
DLP (Short tip)	2,924±24	*20,449±266	93±19	*718±145
DLP (Long tip)	2,961±79	*19,339±1,613	88±34	*623±188
RMI (Long tip)	2,759±158	*20,250±791	111±58	*872±368
Surgimedics (Short tip)	2,796±46	*17,143±625	35±8	*218± 44

**p* <0.001, when compare pulsatile vs. non-pulsatile

NP = Non-pulsatile flow

P = Pulsatile flow

SHE = Surplus Hemodynamic Energy

Conclusions:

The results suggest that pulsatile perfusion generates more “extra” hemodynamic energy compared to the non-pulsatile perfusion mode with all 4 cannulae used in this particular study. Furthermore, the geometry of the cannula has a great impact on the amount of SHE delivered to the pseudo patient.



Does Pulsatile Flow Increase Arterial Line Gaseous Microemboli during Cardiopulmonary Bypass Procedure?

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Purpose:

Gaseous and particle microemboli is a major cause for neuropsychological dysfunction after cardiopulmonary bypass (CPB) procedure in pediatric and adult cardiac patients. The purpose of this study was to compare the effect of perfusion modes on microemboli delivery in a simulated neonatal CPB model using bovine blood.

Methods:

An extracorporeal circuit consisted of the following: a Jostra HL-20 heart-lung machine (for both pulsatile and non-pulsatile modes of perfusion), a Jostra-30 heat-cooler system, a Capiiox Baby RX hollow-fiber membrane oxygenator, a Capiiox pediatric arterial filter, 5 feet of arterial tubing, and 6 feet of venous tubing with a ¼ inch diameter. The circuit was primed with fresh heparinized bovine blood, and the temperature was maintained continuously at 35°C during CPB. The purge line of the arterial filter was closed in all experiments.

The mock loop was subjected to five different pump flow rates of equal 100 ml/min intervals, ranging from 400 to 800 ml/min. At each pump flow rate, the pump pressure was set at a constant 100 mmHg via Hoffman clamp. When the target pump flow rate was achieved, 5 cc air was injected into the venous line and gaseous microemboli counts were obtained by three transducers at post-pump, post-oxygenator and post-filter sites using the Emboli Detection and Classification (EDACTM) QUANTIFIER at five-minute intervals. This system can classify microemboli with diameters from 10 microns to the size of any connector diameter.

Results:

The following table represents the total microemboli count results of five different flow rates at post-pump, post-oxygenator, and post-filter sites with non-pulsatile vs. pulsatile perfusion.

Flow rates (ml/min)	Total microemboli count Post-pump		Total microemboli count Post-oxygenator		Total microemboli count Post-filter	
	NP	P	NP	P	NP	P
400	195.7±59.6	*262.2±79.6	0.3±0.5	0.2±0.4	0.0±0.0	0.0±0.0
500	259.6±24.8	*299.0±100.9	1.6±1.7	0.8±1.0	0.0±0.0	0.0±0.0
600	457.3±168.7	*705.5±318.6	3.7±3.3	5.2±6.9	0.2±0.4	0.3±0.5
700	601.8±370.2	*790.5±245.7	6.0±4.0	8.3±7.4	0.3±0.5	0.8±0.8
800	872.3±353.3	*1070.8±321.0	15.3±10.2	**21.0±14.7	1.0±0.6	1.5±0.8

* p < 0.001 P vs.NP; **p = 0.01 Pvs NP; NP = Non-pulsatile flow P = Pulsatile flow

Conclusions: Our results suggest that regardless of perfusion mode, when increasing the pump flow rate, more microemboli are generated at post-pump site. Compared with non-pulsatile flow, pulsatile flow did generate significantly more microemboli at post-pump site, but there was no difference between the two groups in terms of microemboli counts at post-oxygenator and post-arterial filter sites. The Capiiox baby RX hollow-fiber membrane oxygenator significantly reduced the microemboli counts in both groups at all five pump flow rates.

Congenitally Isolated Defect on the Anterior Mitral Valve and Surgical Repair: Two Rare Cases

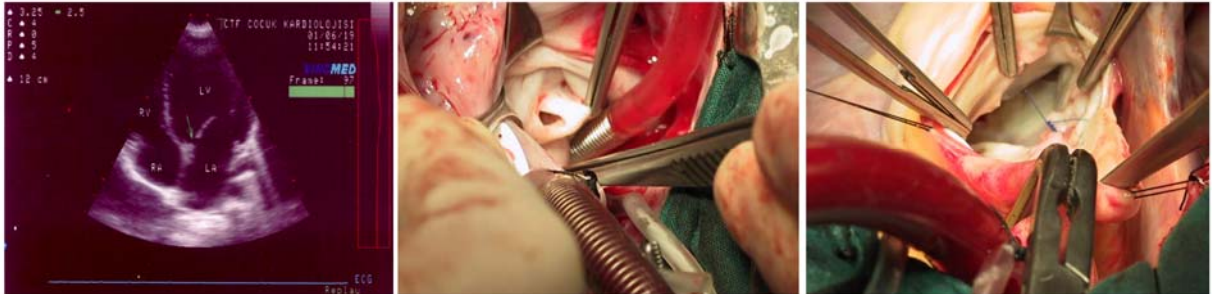
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Congenitally isolated mitral cleft and related mitral insufficiency is a rare cardiac defect.

Cases: In our clinic, 2 patients who were 1 and 4 years old underwent surgery with this pathology and the cleft primary was closed. Both of the cases were female patients; the 1 year old was admitted due to rapid exhaustion while eating, the other while exercising. In physical examination both had grade 3/6 systolic murmur and left axial transmission. Neither patient had any history of

infection (acute rheumatic fever, endocarditis) or trauma and nor had any stigmas for connective tissue or storage disease. ECG and laboratory tests (acute phase reactants and ASO) were normal in both. Echocardiography showed isolated perforation with regular margins (0.5-0.7 mm) on the anterior leaflet of mitral valve and normal cordal anatomy and papillary muscle arrangement. Postoperative echocardiographies showed no mitral leak in either case and patients were followed up with echocardiography.



Congenital Heart Surgery Cases Accompanied with Genetic Syndromes

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Introduction:

Genetic syndromes concomitant with the congenital heart defects in the patients who will undergo surgery is diagnosed early through genetic research and evaluation modalities and while the cardiac pathology of the patient is treated, at the same time genetic consultancy is provided to the patient and his/her family to make it possible to take the necessary measures. It is still not clear whether concomitant genetic syndromes have any effect on the development of the cardiac defects.

Material-method:

During our retrospective screening, we found genetic syndromes (in 68 cases) which accompanied with the congenital cardiac surgery cases (total: 1750 cases) who were operated in our clinic during the period of May 1993-December 2006. The results were confirmed with the genetic research laboratory. Syndromes concomitant with the Fallot's Tetralogy (total : 302 cases) : 22q11.2 microdeletion (Shprintzen syndrome) in 5 cases, Trisomy 21 in 5 cases , Trisomy 18 in 1 case, VACTERL syndrome in 1 case (vertebral, anal, cardiac, tracheoesophageal, renal and extremite anomalies). Syndrome concomitant with atrioventricular channel defects (total : 90 cases) : Trisomy 21 was present in 36 cases. Holt-Oram syndrome accompanied Swiss-cheese VSDs in one case. Anomalies accompanying Isolated Ventricular septal defect (total : 408 case) : joint

congenital glaucoma and Trisomy 21 in 2 cases and Trisomy 18 in one case. Marfan Syndrome was present in 8 cases and surgical approach was applied on aorta and arc in these cases. William syndrome was present in 2 cases with supravalvular aorta stenosis. In one case, Noonan syndrome accompanied pulmonary stenosis (valvular and infundibular), ASD, and persistent left SVC. 5 of the cases with aorta coarctation suffered from Turner syndrome (45XO). Average follow-up period was: 49 ± 5 months and all patients were given family screening and genetic consultancy along with the clinical controls.

Discussion:

Although the 22q11 microdeletion and Trisomy 21 found in Fallot's Tetralogy cases which are described as conotruncal anomalies and are accompanied with genetic syndromes in particular does not affect the clinical course significantly, it is of great importance to diagnose the syndrome, orientate the mental development, and provide psychological and genetic consultancy to bringing these children back into the society. During the screening works, 22q11 microdeletion is diagnosed in around%20 of the TOF cases. Final diagnosis can be reached through the FISH test. Furthermore, works are under way regarding the effectiveness of this deletion on the cardiac pathology.

Surgical Repair of Congenital Supravalvular Aortic Stenosis in Adult

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Introduction:

Supravalvular aortic stenosis is a rare congenital cardiac anomaly occurring mainly as a part of Williams-Beuren Syndrome. Aortic narrowing above the level of the aortic valve causes obstruction of the left ventricular outflow tract and a pressure gradient between the left ventricle and the aorta causes left ventricle hypertrophy. Beneath Sudden death progression in peripheral pulmonary stenosis is common in untreated patients. Indications for surgery are clinical deterioration, gradient between left ventricle and ascending aorta greater than 50mmHg and coronary obstructions or ectasies.

Case:

We report here a case of a 22-year-old male who underwent extended patch aortoplasty recommended by Doty et al. because of supravalvular aortic stenosis accompanying Williams-Beuren syndrome. He was in New York Heart Association (NYHA) functional class III

with localized hourglass type supravalvular aortic stenosis. Related to Arterial hypertension he was in a cardiac decompensation. Mean pressure gradient was 73mmHg and maximum gradient 104 mmHg. Electrocardiography indicated left ventricle hypertrophy which was also seen in X-ray as heart enlargement. We successfully treated this patient with extended patch aortoplasty and immediate postoperative echocardiographies showed reduction of gradient.

Conclusion:

Good surgical outcome of congenital supravalvular aortic stenosis in adult can be achieved with this treatment. This technique provides symmetric reconstruction of the aorta with good post operative results and no gradient across aortic valve and aortic valve insufficiency remains, providing excellent long term relief of localized supravalvular gradients and preservation of aortic valve competence.

Development of the PediaFlow™ Ventricular Assist Device for Infants and Small Children

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Purpose: Our consortium is developing a mixed-flow turbodynamic ventricular assist device utilizing a magnetically levitated (mag-lev) impeller capable of producing 0.3-1.5 liters per minute (LPM) of blood flow for infants and small children weighing 3-15 kg with minimal anticoagulation requirement and optimal biocompatibility.

Methods: Over 20 design variations were initially considered, with three pump topologies selected for further design refinement and evaluation. The three designs, two centrifugal and one mixed-flow pumps, were judged based on a multi-component objective function based on several criteria including anatomic fit, hydrodynamic performance, estimated biocompatibility, heat generation and transfer, mag-lev suspension robustness, and manufacturability. This evaluation led to selection of the mixed-flow topology.

The design then underwent further optimization to improve the geometry of the predicted blood flow path to maximize hydrodynamic performance and minimize blood damage. The housing was modified to improve surgical fixation. Other ongoing efforts are focused on controller development, materials selection, biocompatible coating application, cannula design, anatomic fit simulation, driveline infection resistance, and overall assessment of hemodynamic performance and basic biocompatibility.

Results: The finalized pump design, shown in Figure 1, is 51 mm in length and 28 mm in diameter with 5 mm diameter inlet and outlet conduits. The mass is approximately 100 grams. In bench top testing a prototype pump generated 0.5 LPM against an 80

mm Hg pressure rise at 9,000 RPM, which was within predicted performance targets. The current configuration would allow either a paracorporeal or intracorporeal pump placement.

Conclusion: A mag-lev, mixed-flow, turbodynamic pediatric ventricular assist device has been developed through a robust design refinement and optimization procedure. Prototype pumps are undergoing *in vitro* verification and will soon begin testing in juvenile ovines. Overall, we believe the application of modern design principles, including intensive computational modeling and component simulation, will produce a safe pediatric ventricular assist device with optimal biocompatibility.

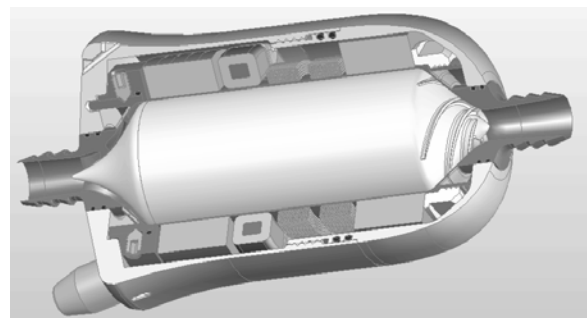


Figure 1. The Generation 1 PediaFlow pump.



Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Development of the Penn State Pulsatile Pediatric VAD

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The Penn State Pediatric Ventricular Assist Device (PVAD) is a pneumatically-actuated positive displacement pump similar in design to the adult VAD developed at Penn State and commercialized by Thoratec Corp (Pleasanton, CA). The infant PVAD has a dynamic stroke volume of 12-15 ml, resulting in an output of 0.5 to 1.5 liters/min. A 25-30 ml stroke volume child-sized PVAD is being developed in parallel.

During the past year, the 12 ml PVAD was implanted in 4 lambs weighing 14-19 kg. Anticoagulation was by intravenous heparin to maintain the PTT at 2 times normal. The PVAD rate was adjusted manually to approximately 80 beats per min (1 liter per min).

The intended study duration was 30 days. However, the studies were terminated at 21, 15, 6, and 1 days. In the first study there was significant thromboembolism and occlusion of the outlet cannula due to a defective mandrel coating process, which was corrected for the subsequent studies. The second and third studies were encouraging in that the pump and cannulae surfaces were relatively free of thrombus. However, pleural effusions, hemothorax, and respiratory failure, typically after 2-4 days post-op, have resulted in early terminations in the last three studies.

Particle image velocimetry studies have focused on the effect of valve type on the fluid flow patterns in the pump chamber. We are evaluating the Björk-Shiley Monostrut 17 mm valve and the Carbomedics 16 mm bi-leaflet valve. *In vitro* measurements of cavitation during inlet valve closure and hemolysis are continuing.

Two candidate polymers were tested to compare the effect of surface modifying additive and heat forming on the mechanical and structural properties. During this year we have made substantial improvements in the quality and consistency of the polymeric components.

Manufacturing efforts focused on completing four 12 ml pumps (version 2 design), primarily for use in implant studies; two pumps with Björk-Shiley valves and two with Carbomedics valves. Documentation of the pump subassemblies and final pump assembly processes are nearly complete.

Software was further developed to automatically detect pump filling and ejection using a differential pressure flow sensor in the driveline. This was tested during the animal study and used to adjust the pump drive parameters.



Third International Conference on **Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion**

Progress of the Pediatric Jarvik 2000 Hearts

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Purpose:

The pediatric Jarvik 2000 hearts are currently being developed for mechanical circulatory support for children and infants. They are based on intraventricular rotary axial blood pump technology utilizing an apical placement with the outflow graft connected to the aorta. The purpose of this paper is to present the design and development progress and the initial in-vivo performance of the pediatric Jarvik 2000 hearts in the pediatric setting.

Methods:

The pediatric Jarvik 2000 hearts are scaled down from the adult Jarvik heart. The bearings and blood flow path were optimized using a series of computational and experimental approaches, including bearing wear analysis, computational fluid dynamics analysis, and bench experimental measurements. Acute and chronic in-vivo performance evaluation was carried out in 9 juvenile sheep (8 for child size, 1 for infant size). The pump was placed into the left ventricle through an apical insertion. The outflow graft was anastomosed to the descending aorta. Two transonic flow probes were placed around the main pulmonary artery and the outflow graft to measure the cardiac output and the pump supported flow. Daily hemodynamic measurements of cardiac output and pump output at varying pump speeds were taken. In addition, plasma free hemoglobin (PFH), lactic acid dehydrogenase (LDH) and platelet activation from blood samples were determined at baseline, post-implantation and twice a week thereafter.

Results:

In-vitro experimental evaluation demonstrated that the optimized child size and infant size Jarvik hearts are able to deliver a blood flow up to 5 liters/min and 2 liters/min against the physiological pressure load (100 mmHg) with acceptable biocompatibility, respectively. In all 9 sheep, the pediatric Jarvik 2000 hearts fit comfortably into the thoracic cavity. All chronic animals tolerated the procedure and were subsequently recovered. The flow through the outflow graft at five speeds ranged from 1.57 to 4.0 liters/min for the child size pump and 0.5 liters/min to 1.2 liters/min for the infant size pump. Plasma free hemoglobin spiked initially and returned to normal in four chronic animals, but in the two remained somewhat elevated.

Effective anticoagulation was not achieved in these sheep. Thrombus accumulation around the bearings occurred which eventually caused the pump to stop in most animals. A version of the adult size Jarvik 2000 with modified blades to meet reduced child flow requirements remained free of significant thrombus and did not stop. Modifications of the child size design to permit it to remain free of serious thrombus like the adult size pump are underway.

Conclusions:

The progress up to date indicates that the pediatric Jarvik 2000 hearts anatomically fit within the thoracic cavity of juvenile sheep and are capable of providing partial to near complete circulatory support with acceptable adverse effects on blood components. However, the bearing thrombosis remains a challenging issue.



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The EnSION pCAS System

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EnSION, Inc. is developing an integrated cardiopulmonary assist system (pCAS) designed to support neonatal and infant patients requiring extracorporeal membrane oxygenation (ECMO). pCAS addresses shortcomings associated with current ECMO systems focusing particularly on improved biocompatibility, resistance to microporous hollow fiber plasma breakthrough, and reduced system complexity to facilitate parent-child bonding. Bleeding complications and systemic inflammatory response are typical biocompatibility challenges resulting from systemic anticoagulation and blood contact with foreign surfaces, particularly the relatively large surface area of the membrane oxygenator. EnSION is developing a heparin-based biocompatible coating intended to mitigate the body's reaction to device surfaces and reduce the need for high levels of anticoagulation.

Bioactivity of this coating is balanced with the need to simultaneously maximize mass exchange permeance and mitigate plasma breakthrough. Several prototype coatings have been tested for post-sterilization (ethylene oxide) bioactivity and permeance in vitro with acceptable results. In addition, coatings applied to microporous hollow fiber mat have been tested in human platelet rich plasma to demonstrate that, under static conditions, thrombin activation could be suppressed compared with an uncoated control. Related in vitro data indicate acceptable levels of blood damage using abattoir bovine blood. pCAS functionality evaluations have included demonstration of ability to achieve target flow rates, mass exchange specifications, and pressure rises distal to the outflow cannula.

The PediPump: A Versatile, Implantable, Pediatric Ventricular Assist Device

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Purpose:

The following describes the PediPump, which is a VAD under development at The Cleveland Clinic to be used for pediatric applications.

The PediPump: A Description of the Device

The PediPump is a passive magnetic bearing, mixed flow, rotary VAD designed to provide support for the entire range of patient sizes encountered in pediatrics. Blood enters axially at the inlet and is accelerated and turned in the impeller to exit the pump at an intermediate angle (Figure 1). The PediPump will be implanted with standard, although substantially downsized, cannulation strategies employed for currently available axial flow pumps (Figure 2).

Current Status of PediPump Development

Basic engineering concepts: Progress within the last year has focused on the assembly and testing of PediPump prototypes. The procurement process was completed for all pump parts sufficient to build a number of prototypes and the initial performance

maps based on in vitro testing were judged to be satisfactory. All in vitro testing was performed to support animal testing which began in 2006 as described below.

Anatomic fitting studies: As part of the PediPump program, 3D modeling techniques based on routine, clinically obtained CT scans have been developed. During 2006, the same techniques developed using clinically obtained CT scans were applied to CT scans obtained from the sheep model employed in animal studies to guide pre-surgical planning.

Animal studies: Animal implantation of working PediPump prototypes commenced in July, 2006; a total of four short-term (4-6 hour) implantations were performed throughout the remainder of the year. In vivo pump hemodynamic performance was satisfactory as predicted from in vitro prototype testing. Hemolysis levels were quite low, while other hematologic and biochemical parameters remained within an acceptable range during the short duration of study.

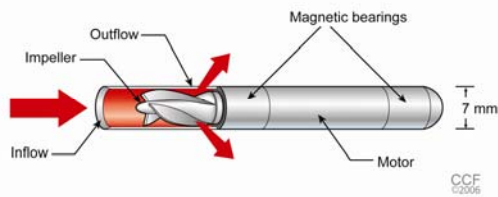


Figure 1) PediPump with direction of blood flow demonstrated by arrows.

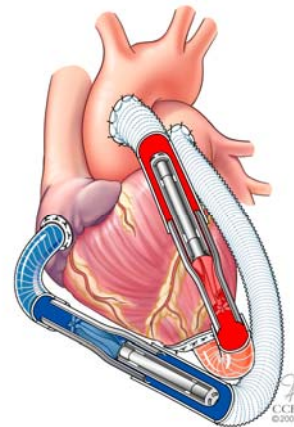


Figure 2) PediPump in BVAD configuration.



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FDA's Perspectives on Pediatric Cardiac Assist Devices

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Introduction:

The mission of the Center for Devices and Radiological Health at the Food and Drug Administration (FDA) is to promote and protect the health of the public by ensuring the safety and effectiveness of medical devices.

Methods:

FDA recognizes that designing medical devices for use in pediatric patients can be challenging. Because the need is great, FDA is committed to supporting the development and availability of safe and effective medical devices for pediatric patients. Current initiatives at the FDA to support the development of medical devices intended for pediatric patients include recruiting pediatric experts for FDA advisory panels, ensuring adequate protection of children participating in clinical trials, and collaborating with groups such as the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACs) to collect data on the use of cardiac assist devices in pediatric patients.

Results:

In the past, clinicians have used cardiac assist devices intended for adults to treat pediatric heart failure patients. However, due to the size of approved cardiac assist devices, some pediatric patients are underserved.

At present, several cardiac assist devices intended for use in pediatric patients are being developed in the United States and abroad. These devices should be eligible for consideration as humanitarian use devices because of the small number of pediatric patients; as well, no suitable alternative devices are available.

In seeking a humanitarian device exemption (HDE) application, the devices should undergo rigorous bench and animal testing to assure reasonable safety and probable benefit for the intended patient population. FDA believes that clinical data to support such safety and probable benefit may be derived from a small focused clinical trial in this target population, and developers may want to consider this approach for approval of an HDE application.

Conclusions:

Pediatric device development is challenging and early communication with FDA to develop an appropriate regulatory and scientific pathway is advised and warranted.

Hemorheology of Mechanical Blood Damage

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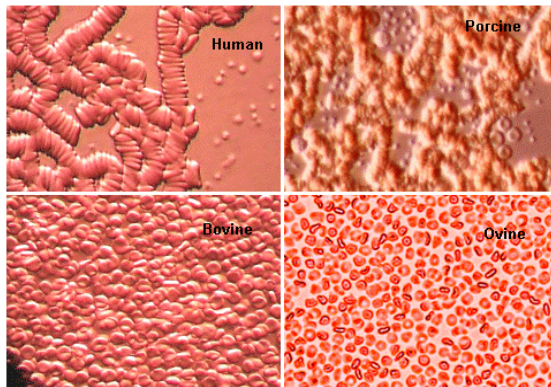
Purpose:

Mechanical blood trauma is a widely recognized challenge in development and use of blood-contacting devices. Various aspects of mechanical damage to blood have been studied for several decades by investigators worldwide. While mechanical forces responsible for this blood damage are harmful for all elements including blood cells and plasma components, the major goal of this lecture is to delineate the effects of mechanical stress on rheological properties of blood. Especially sub-lethal trauma to red blood cells (RBCs) and the associated effects on hemorheology and hemodynamics will be discussed.

Background:

Blood rheological properties are important in maintaining of normal organ and tissue perfusion. Blood exhibits a non-Newtonian (thixotropic) behavior which is largely due to two major characteristics of the RBCs: their tendency to form aggregates when at rest or at low flow, and their deformability. In other words, blood viscosity is a function of shear rate and is represented by a curve, not a number.

The high deformability of mammalian RBC is due to the absence of a nucleus, and to the elastic and viscous properties of its membrane. Rheological properties of blood vary between species (Figure 1).



A number of studies have indicated that the rheological properties of neonatal blood are different from those of the adult. RBC mechanical fragility is higher [Bohler et al., 1992] and their lifespan is significantly shorter [Oski and Naiman, 1982] in human neonates than those in adults.

It has been long time known that blood cell trauma in hear-assist devices is related to non-physiological flow conditions which may induce a variety of damage mechanisms: overstretching or fragmentation of RBCs causing free hemoglobin to be released into plasma (hemolysis), activation or dysfunction of platelets and leukocytes, and sublethal blood trauma such as alterations in rheological properties of RBCs as manifested by an increase in RBC aggregation and a decrease in their deformability. RBC deformability is responsible for their ability to enter and passing the smallest blood capillaries and to provide adequate transport of gases, etc. Reduction of RBC deformability causes a shortening of RBC life span, a decrease in density of functioning capillaries and area of contact surface of RBCs with capillary walls, and may lead to anemia, tissue hypoxia and other serious complications.

Some experience with mechanical circulatory-assist devices demonstrated a reduction in RBC deformability in blood of the implanted patients [Kormos et al., 1987; Frattini et al., 1989; Hung et al., 1991]. A number of basic *in vitro* hemorheological studies on the effects of mechanical stress on RBC deformability supported observations reported in pre-clinical and clinical tests. Decrease in RBC deformability after exposure of blood to various levels of mechanical stress *in vitro* has been demonstrated in [Dao et al., 1994; Kameneva et al., 1995; Kameneva et al., 1999; Baskurt et al., 2004; Marascalco et al., 2006; Lee et al., 2007]. Assessment of sub-lethal blood damage in preclinical animal tests and clinical evaluation of blood of patients implanted with hear-assist devices by measurements of hemorheological parameters might be useful for prevention of potential complications.

Heart Transplantation for the Patient with Single Ventricle Anatomy

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The patient with failing single ventricle anatomy who requires heart transplantation faces unique but surmountable challenges including: previous surgery, complex anatomy and pulmonary vascular changes.

Complex anatomy: Successful heart transplantation requires that patient's venous and arterial connections be made to conform to that of the donor heart. A variety of techniques have been developed to manage problems as simple as the presence of a left superior vena cava to more complex anatomic challenges such as situs inversus with dextrocardia. (1,2) In patients with heterotaxy syndrome anomalies of pulmonary venous drainage are common. Unobstructed anomalous pulmonary venous drainage seems to add little to the risk of transplantation. Pulmonary venous obstruction remains an important risk factor. (3) Techniques similar to the 'sutureless neoatrial repair' have been applied to patients with pulmonary vein stenosis undergoing heart transplantation with some success.

Pulmonary vascular changes: Accurately assessing the pulmonary vascular resistance (PVR) of patients palliated with a Fontan remains a challenge and frequently the measured preoperative PVR is importantly lower than the PVR experienced in the early postoperative period. (4) Postoperative management may require use of pulmonary vasodilators and even mechanical support. Arteriovenous malformations (AVMs), connections between the pulmonary arteries and veins that allow blood to traverse the lungs without gas exchange can occur in patients following bidirectional superior cava to pulmonary artery anastomosis (BDG) and Fontan procedures. These patients can have significant pulmonary venous

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desaturation that can result in cyanosis and complicate the post-transplant course. With time and presumably due to the restoration of 'hepatic factor' and improved flow distribution to the all segments of the pulmonary vascular bed, AVMs have been noted to regress. (5) Long standing cyanosis will result in the development of arterial collaterals to the pulmonary circulation and can result in a significant increase in pulmonary blood flow. In the postoperative transplant patient this can translate into elevated pulmonary artery pressure resulting in right ventricular failure and left sided volume overload. Large aortopulmonary collaterals may require occlusion in the catheterization laboratory.

Mechanical support: Adult patients with normal anatomy and dilated cardiomyopathy have benefited enormously from various long-term ventricular assist devices (VAD) that result in improved end-organ function and a reduction in PVR. Patients with failing single ventricle anatomy can also benefit from mechanical support, but the anatomic challenges are substantial and a device that adapts to unique native and surgical anatomy of this group of patients is essential. There is increasing experience using ECMO and other VADs such as the Thoratec, DeBakey VAD and Berlin Heart as bridge to transplant. (6)

Conclusions. Heart transplantation in patients with single ventricle anatomy is a useful and increasingly necessary therapy. Success requires recognition and management of the unique aspects of the single ventricle patient including; previous surgery, complex anatomy and alteration of the pulmonary vascular bed.



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Cardiac Replantation in Children

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Heart transplantation plays an important role in the management of end stage heart failure in children. Cardiac transplantation is performed annually in approximately 350 children. While the post transplant survival in children is superior to that for adults, graft failure ultimately occurs in a significant number of children.

Most pediatric transplant centers routinely undertake cardiac retransplantation for those recipients with graft failure. However the practice of retransplantation remains controversial given the

critical shortage of cardiac allograft donors. The most common indications for retransplantation are primary graft failure, chronic graft dysfunction, development of graft vasculopathy and intractable acute rejection.

The incidence, clinical characteristics and outcomes of pediatric cardiac retransplantation as well as risk factors for mortality will be reviewed. Data analysis from our institution, the UNOS (United Network for Organ Sharing) registry and Pediatric Heart Transplant Study (PHTS) will be presented.

Special Aspects of Cardiac Transplantation in Fontan Patients

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The Fontan circulation: The Fontan circulation has special characteristics with regard to the surgical patchway, the systemic ventricle and atrioventricular valves, the pulmonary, the systemic and the lymphatic circulation as well as the collateral circulation. The surgical pathway has suboptimal flow dynamics leading to energy loss, arrhythmias and thromboembolic complications in up to 1/3 of patients. The systemic ventricle is chronically underloaded and thus prone to diastolic dysfunction. Structural characteristics (RV or LV), progression of subaortic stenosis and AV-valve (TV or MV) regurgitation may be additionally present. The pulmonary circulation is characterized by loss of the ventriculo-arterial-coupling leading to an increase of pulmonary vascular impedance and afterload. Cardiopulmonary interactions, like maximal forward flow in inspiration, are disturbed. The splanchnic venous system has a two to three times increased pressure and the liver capillary bed interposes an additional resistance. Furthermore, the resistance interposed by the pulmonary circulation is placed in series and adds to this non-physiologic condition. The lymphatic circulation is impaired by the elevated pressure in the splanchnic territory which leads to increased production of lymph and ultimately may cause protein losing enteropathy (PLE). The elevated venous pressure also causes increased myocardial and pulmonary lymphatic stasis with increase of PVR. Fontan patients are prone to develop pulmonary collaterals and pulmonary AV-fistulae in up to 30%, both leading to chronic de-saturation and to volume overload.

Morbidity of the Fontan circulation: Due to the above reasons, causes of late morbidity and late Fontan failure are rhythm disturbances, suboptimal Fontan flow dynamics, collateral blood flow, atrioventricular (AV) valve regurgitation, subaortic obstruction, ventricular failure, elevated PVR and PLE and very rarely plastic bronchitis. Mostly, Fontan failure is multifactorial. In ventricular failure, PLE and plastic bronchitis, cardiac transplantation (HTx) is the only therapeutic option and is the solution of most Fontan problems.

Results of HTx in Fontan patients: Generally, HTx shows excellent results in all age groups. However, the 'failing' Fontan has mortality rates between 33% and 44%, particularly in grown-up patients (GUCH) with mortality rates up to 50%. This is according to our own experience with a mortality of 33%. Causes of mortality are hemorrhage and primary graft failure due to time consuming dissection caused by prior surgery and the necessity of additional procedures to reconstruct cardiac structures or to adjust to anatomical variants. Thus, HTx after Fontan has prolonged ECC and ischemic times which are risk factors for early mortality. Fontan patients additionally present with impaired organ function particularly with regard to liver and kidneys due to venous congestion; this is worst in PLE – factors which add to side effects of immunosuppression. One major risk factor is an increased pulmonary vascular resistance (PVR) with consecutive right ventricular failure. PVR is difficult to assess in Fontan patients prior to HTx due to collaterals and low cardiac output, but has been shown to be increased in late Fontan failure. Long-term outcome of HTx after Fontan seems to be comparable to other patients.

Strategies for HTx in Fontan patients: Patients with Fontan circulation need to be listed early and need to get the best organs. Organisation of the HTx has to be optimal and dissection may be started before the organ 'o.k.' is given. HTx should be performed by two surgeons with experience in cardiac transplantation and in congenital heart surgery. PVR and right ventricular function need to be observed carefully in the postop. period. Standard immunosuppression (in our institution since 1995 cyclosporine or tacrolimus combined with mycophenolat mophetil and corticosteroids) may need to be adjusted individually.

In view of the high mortality of HTx following Fontan operation, the decision to go for a Fontan in a borderline patient has to be weighed against the side effects of long-term immunosuppression.

Summary: Failing of the Fontan circulation has multiple causes. For most patients cardiac

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transplantation is the only life saving procedure, although the `failing´ Fontan carries the highest operative risk for cardiac transplantation. Special strategies need to be considered to improve outcome.

Multi-institutional studies are necessary for further analysis of this patient entity. Good long-term outcome justifies cardiac transplantation in the `failing´ Fontan.



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Pediatric Cardiac Bio-Engineering: Who, What, Where, and How

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A great number of advances have occurred in the past decade in several areas of bioengineering that have already had or will soon have a significant positive impact on health care. Children, however, have not benefited as much from many of these advances as adults. An example of the discrepancy in research and development between adults and children is the mechanical heart assist device. Although there are several assist pumps currently available for use in adult patients and there have been for over a decade, only in the past few years has such a device become clinically available for pediatric patients despite the great need.

The reasons for this lag are several, including:

- Differences in patient size, together with the need for a wide range of sizes,
- The need to design devices or materials that accommodate growth,
- Required additional longevity,
- Potential long-term adverse effects of interventions,
- The wide range of anomalies and unique structural defects seen in children.

Many of these obstacles can present new complicating factors that affect the design and development of equipment and devices. For this reason, many manufacturers and pharmaceutical companies are reluctant to embark upon potentially costly research and development projects that may have a smaller commercial application and potentially higher risk when compared to those aimed at the needs of adult patients. Nevertheless the health

care impact of pediatric diseases is great, particularly when patient longevity, duration of illness, and economic consequences of lifelong disability are considered.

Examples where special research initiatives aimed at the pediatric patient population are needed include:

- **Imaging** - Non-invasive, non-radiation based, to guide interventions.
- **Robotics** and microsurgical instrumentation to minimize tissue trauma and collateral damage to adjacent structures.
- **Tissue engineering** to use the child's own tissues to replace defective or absent structures.
- **Biomaterials** - development for drug delivery, tissue regeneration that account for the more aggressive response to foreign material seen in children.
- **Computational Methods** to analyze complex blood flow and tissue structure-function biomechanics in congenital heart defects.

To advance in these areas, a multidisciplinary group of investigators with expertise in the various medical and bioengineering subspecialties will be required together with an administrative structure to coordinate and integrate the various projects. Partnerships between academia, industry, and government will be required since no one institution can advance independently given the complexity of the problem and risks involved.

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Approaches toward Continuous Monitoring of Pediatric Cardiopulmonary Bypass Procedures using Cytometric Bead Processing within a Microfluidic Device

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Several studies have clearly shown that cardiac surgery induces systemic inflammatory responses, particularly when cardiopulmonary bypass (CPB) is used. CPB induces complex inflammatory responses characterized by complement, neutrophil, and platelet activation, and the release of pro-inflammatory cytokines. These systemic responses are attributed to several factors, including exposure of blood to nonphysiologic surfaces of the heart-lung circuit, ischemia-reperfusion of the involved tissues, surgical trauma and hypothermia. Currently, there is no effective method to prevent this systemic inflammatory response syndrome in patients undergoing CPB. The ability to clinically intervene in inflammation, or even study the inflammatory response to CPB, is limited by the lack of timely measurements of inflammatory responses (complement, neutrophil, monocyte, platelet activation, and the release of pro-inflammatory cytokines). Current technology provides measurements of the effects of cardiopulmonary bypass on activation of complements, neutrophils, platelets, and cytokines hours or days post-surgery. More immediate measurements would aid in understanding the mechanisms of cellular activation, and modify surgical and perfusion protocols for minimizing adverse effects of cardiopulmonary bypass. The objective of this project is to develop and test a microanalytical system for online monitoring of inflammatory responses during the CPB procedure.

The long-term goal of this research is to develop clinical applications for cardiopulmonary bypass procedures in the treatment and prevention of systemic inflammatory responses (not only plasma cytokine concentrations) during cardiac surgery in pediatric and adult patients. It is believed that the determination of the plasma cytokine and complement concentrations will be one of the fundamental steps in solving this particular devastating problem associated with the CPB procedures. Timely measurements of inflammatory indicators will enable a greater understanding of, and intervention in, inflammation processes for which current methods of prevention and

management are limited.

A microfluidic device designed for continuous biosensing of inflammatory markers based on analyte binding with cytometric beads is introduced. The operating principle of the continuous biosensing is based on a novel concept named "particle cross over" mechanism in microfluidic channels. By carefully designing the microfluidic network the beads are able to "cross-over" from a carrier fluid stream into a recipient fluid stream without mixing of the two streams and analyte dilution. After crossing over into the recipient stream bead processing such as analyte-bead binding may occur. The microfluidic device is composed of a bead solution inlet, an analyte solution inlet, two washing solution inlets, and a fluorescence detection window. To achieve continuous particle cross over in microfluidic channels, each microfluidic channel is precisely designed to allow the particle cross over to occur. The functionality of the device has been experimentally demonstrated using a commercially available fluorescent biotinylated fluorescein isothiocyanate (FITC) dye and streptavidin coated 8 μm -diameter beads. After, demonstrating particle cross over and biotin-streptavidin binding, the fluorescent intensity of the 8 μm -diameter beads was measured at the detection window and linearly depends on the concentration of the analyte (biotinylated FITC) at the inlet. The detection limit of the device was a concentration of 50 ng/ml of biotinylated FITC. Future studies will focus on conducting binding studies on clinically relevant complements such as the anaphylatoxins C3a, C4a and C5a with antibody bound cytometric beads.

Keywords: Immunosensing, blood separation, real time monitoring, microfluidics



Peri-operative Use of Near-Infrared Spectroscopy to Monitor Regional Perfusion

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Purpose:

The learning objectives for this talk are designed to enable participants to utilize of near-infrared spectroscopy (NIRS) to improve patient care in the perioperative period.

Methods:

We have employed the Somanetics INVOS NIRS system at CHW for the past four years for monitoring of cerebral and somatic beds in almost all perioperative cardiac patients, allowing comparison to an extensive invasive hemodynamic database.[1] The session will review data on five major topics: basic principles NIRS technology; shock physiology with emphasis on neonates and infants; limitations of conventional monitors to identify global or regional perfusion abnormalities; risk factors for cerebral and splanchnic hypoperfusion; relationship between NIRS monitoring, conventional parameters, and organ function.

Data:

NIRS is a non-invasive spectrophotometric method of assessing the oxygen saturation of hemoglobin in a field of tissue by quantifying the differential transmission of two or more wavelengths of light. The monitored field depends on the location of the sensor, and both patient- and device-specific factors.

Sympathetic nervous system activation will maintain blood pressure as cardiac output falls by redistribution of blood flow from splanchnic, mesenteric, and renal vessels to the brain and heart. In shock states, survival and freedom from organ system failure can be improved by targeting SvO₂ or other parameters indicating adequate global and regional oxygen. [2] Organ system morbidities are related to SvO₂ in the perioperative period in neonates after the stage 1 palliation of HLHS. [3,4]

The risk of cerebral and somatic hypoxia extends throughout the perioperative period. [1, 4] Two-site NIRS can approximate SvO₂ with precision that is acceptable for clinical use. [5] The distribution of somatic and cerebral saturation predicts the risk of anaerobic metabolism or biochemical shock. [6] Manipulation of ventilatory parameters alters the partitioning of cardiac output between brain and body. [7] Somatic NIRS predicts perioperative renal function and length of ICU stay following S1P. [8]

Conclusions:

Cerebral and somatic NIRS allows non-invasive continuous monitoring of regional and quasi-global systemic oxygen economy which is related to outcome.

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Survey: The Use of Aprotinin in Pediatric Cardiopulmonary Bypass

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Purpose:

Cardiopulmonary Bypass (CPB) results in the inappropriate activation of the coagulation and fibrinolytic systems. Factors such as the degree of hemodilution, the use of deep hypothermic circulatory arrest, the influence of cyanosis on hemostasis and coagulation and the immature coagulation system of the newborn will each increase the risk of problematic perioperative bleeding.

Neonates and children undergoing cardiac operations with the use of CPB are at higher risk of hemostatic disturbances. Aprotinin, a serine protease inhibitor, has the capacity to block fibrinolysis in low doses and attenuate contact activation and generation in higher concentrations. Clinical studies on the use of aprotinin in pediatric practice are difficult to interpret due to wide variations in dosing regimens, patient size and type of operation and plasma levels may be greatly affected by different perfusion techniques and circuit

coatings. The objective of this national survey was to gain insight as to the frequency of use and the dosing regimens practiced by those who employ aprotinin routinely.

Methods:

A national survey was sent out to pediatric cardiac programs. The thirty-five question survey requested information on patient selection, dosing regimens, hypersensitivity reactions and specific perfusion techniques employed in relation to the use of aprotinin during pediatric cardiopulmonary bypass. Statistical analysis of responses is provided. The techniques and dosing during the operative period are considered more determinant of aprotinin's effectiveness.

Conclusions:

The information gained in this survey will hopefully spark more in depth study and interest as to the use and effects of aprotinin in pediatric cardiac surgery.

