**AGE OF BLOOD IN CHILDREN (ABC PICU)**

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ABC PICU enrollment has begun at Sainte-Justine Hospital and Washington University in St. Louis. The remaining five vanguard sites, Children’s Healthcare of Atlanta, University of Minnesota, Nationwide Children’s, Seattle Children’s Hospital, Children’s National Medical Center beginning in the next month along with some Canadian sites. An additional 33 US sites will be added over the next six months including the following sites:

**CANADIAN SITES**
- British Columbia’s Children’s Hospital, Vancouver, British Columbia
- Centre Mère-Enfant du CHUQ, Quebec, Quebec
- Children’s Hospital of Eastern Ontario, Ottawa, Ontario
- Hamilton Health Science/McMaster University Medical Center, Hamilton, Ontario
- The Hospital for Sick Children, Toronto, Ontario
- London Health Sciences Centre/Children’s Hospital, London, Ontario
- Stollery Children’s Hospital, Edmonton, Alberta

**US SITES**
- Children’s Hospital and Health System, Milwaukee, WI
- Children’s Hospital of Los Angeles, Los Angeles, CA
- The Children’s Hospital and Network of Care, Aurora, CO
- Children’s Hospital of Orange County / UC Irvine School of Medicine, Orange, CA
- The Children’s Hospital of Philadelphia, Philadelphia, PA
- The Children’s Hospital of San Antonio, San Antonio, TX
- Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
- Columbia University Medical Center, New York, NY
- Diamond Children’s Medical Center, Tucson, AZ
- Duke Children’s Hospital, Durham, NC
- Golisano Children’s Hospital at Strong, Rochester, NY
- John’s Hopkins University, Baltimore, MD
- Maria Fareri Children’s Hospital, Valhalla, NY
- Medical College of Virginia, Richmond, VA
- The Medical University of South Carolina, Charleston, SC
- Phoenix Children’s Hospital, Phoenix, AZ
- Riley Children’s Hospital, Indianapolis, IN
- Texas Children’s Hospital/ Baylor College of Medicine, Houston, TX
- University of Alabama, Birmingham, Birmingham, AL
- University of California - San Francisco, San Francisco, CA
- University of Michigan – CS Mott Children’s Hospital, Ann Arbor, MI
- University of Virginia Children’s Hospital, Charlottesville, VA
- UT Southwestern – Children’s Medical Center, Dallas, TX
- Weill Cornell Medical College – New York Presbyterian Hospital, New York, NY
- Woman and Children’s Hospital of Buffalo, Buffalo, NY

**For more information about ABC PICU, visit abcpicu.wustl.edu**
BLOODNET PILOT STUDY

Prospective, Randomized Study of Prophylactic Fresh Frozen Plasma Administration during Neonatal-Pediatric Extracorporeal Membrane Oxygenation

PI: Caroline P. Ozment, MD
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A pilot study at Duke University is currently underway researching the effect of scheduled fresh frozen plasma (FFP) on ECMO circuit life.

BACKGROUND: Exposure of patient blood to the ECMO circuit creates a massive inflammatory and clotting response during which clotting factors are activated and consumed and clots are formed on the foreign surfaces. Anticoagulation is thus necessary to prevent thrombosis within the circuit but with it comes the increased risk of patient bleeding. Despite significant advancements in ECMO, circuit clotting and patient bleeding continue to be the most common and potentially life-threatening complications on ECMO. In fact, mechanical failure due to circuit clotting occurs in 2-18% of all pediatric ECMO cases. Changing out an ECMO circuit can have significant effects including a large inflammatory response in the patient, cardiac arrest, and exposure to more blood products with the priming of the new circuit. In addition, circuit changes cost thousands of dollars in equipment and require assistance of multiple personnel. An analysis of circuit changes in the Duke pediatric intensive care units from 2009-2012 showed that 80% of circuit changes were associated with coagulation derangements. FFP contains both anti and pro-coagulant factors. This study hypothesizes that scheduled administration of FFP will lengthen circuit life and decrease hospital cost and overall patient transfusions by maintaining more physiologic levels of coagulation factors.

METHODS OVERVIEW: As part of the pilot study, forty pediatric ECMO patients up to age 18 years old will be enrolled in this prospective randomized study. The treatment group will receive 15ml/kg of FFP every 48 hours as well as when clinically indicated by the treating physician. The control group will receive FFP per current Duke protocol which includes FFP transfusion after three red blood cell transfusions in 24 hours or as clinically indicated.

OUTCOMES: The primary outcome will be circuit life measured in hours. Additional outcomes to be analyzed include hemorrhagic complications including intracranial hemorrhage and pleural and pericardial hemorrhage. Hematologic and coagulation markers (including plasma free hemoglobin, activated partial thromboplastin time, heparin level, antithrombin III levels, TEG scans) and circuit life will be also be collected and analyzed for associations. Number of transfusions for each patient including red blood cells, platelets, FFP, cryoprecipitate, and thrombate and their association with circuit life and patient complications will also be examined for statistical significance. This will be the first study to evaluate the effect of FFP on circuit life.

MULTI-SITE INVOLVEMENT: This preliminary data will assist in the design and development of a larger, multicenter randomized study with a formal power calculation to more thoroughly address correlations between anticoagulation monitoring labs as well as on bleeding/clotting complications between the FFP and control group. While it is very early in the process, they will begin to analyze their current accumulated data and develop a multi-site plan.

FUNDING: At this point, funding for this pilot study has been requested locally via a Children's Miracle Grant.

BLOODNET STUDY UPDATE

Pediatric Cardiac Surgery Post-Operative Transfusion Management: A global epidemiologic inception study.

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The inception study of transfusion practices in children with congenital heart disease was presented at New Orleans in October 2013. It was well received at that meeting by those present during the PALISI session, with interest in participation expressed. The study is a multicenter inception (observational) study looking at transfusion practices in children undergoing by-pass surgery for congenital heart disease (CHD) for birth to 16 years of age. The primary outcome is the pre-transfusion hemoglobin concentration and the secondary outcomes are transfusion strategies of other blood products (platelets, FFP, cryoprecipitate); incidence of organ dysfunction in post-operative by-pass CHD patients; all cause mortality at 28 and 90 days. A maximum of 15 centers, from Australia, New Zealand, Canada and North America, will be involved in providing data on 50 patients per center. These fifty patients will be divided into 10 CHD by-pass patients that did not receive blood products in ICU, 20 corrective CHD by-pass cases that received a blood transfusion in ICU and 20 palliative CHD by-pass cases that received a blood transfusion in ICU. Data from 750 patients will be assessed and this will form the basis of the design of a potential RCT study assessing liberal vs restrictive ICU transfusion strategies in children that have undergone palliative by-pass CHD surgery.

A grant submission to the Intensive Care Foundation (AUS$50,000) was not successful this time, but the feedback given by the reviewers has been evaluated and the issues have been addressed. One of the main areas that received significant attention was that of feasibility due to the large amount of data for each patient and the large number of centers. To overcome this challenge the team in Sydney, Australia are in the process of creating a collaboration with the George Institute, a research group that has a strong track record for producing excellent multicenter research such as SAFE, CHEST, ADRENAL, SAFE-EPIC and many others. Submission to other grants bodies will occur over the next couple of months in an attempt to fund the initial phase of the study question.
Registry of ECMO Anticoagulation in Pediatrics (REAP)

PI: Laura L. Loftis, MD
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The current national extracorporeal support database has provided a wealth of information for this most complex and risky intervention however it only provides dichotomous outcomes. This has proven to be inadequate to truly inform our understanding of the risks of this intervention. In addition, almost no systematic effort has striven to collect information on methods on anticoagulation monitoring as well as the effects of anticoagulation and component blood product administration on outcomes. The Registry of ECMO Anticoagulation in Pediatrics (REAP - acronym courtesy of Phil) is a web-based data platform aimed at consistent data collection which will hopefully inform future clinical trials and improve the practice of anticoagulation during extracorporeal support. Each center may use their own data set to inform quality assurance appraisals and supporting investigators may use the larger data set (de-identified) to inform future research questions. This has been collaborative effort between Phil Spinella (Washington University), Sheila Hanson (Medical College of Wisconsin), Heather Chandler (Emory University), Melania Bembea (John’s Hopkins University) and I (Laura Loftis, Baylor College of Medicine), along with the generous support of my section chief, Dr. Lara Shekerdemian, and the guidance of our Research Resources Office Bioinformatics team led by Dr. Uma Ramamurthy. Our research assistant Michelle Goldsworthy has been instrumental in creating the case report form, the data dictionary and numerous other component parts of the larger project.

The first module is primarily of a neonatal and pediatric respiratory focus and Heather has been spearheading the future cardiac module. The data to be collected consists of in-depth anticoagulation testing, records of hemostatic agents and blood product usage, along with more clinical outcomes than are currently being followed in the ELSO registry. As a first “test” of the system we will be piloting a newly created daily bleeding score (loosely based off of the International Society of Thrombosis and Hemostasis DIC score). The goal of such a score would be to better capture an evolving clinical picture prior to a catastrophic bleed and possibly correlate this with changing patterns of laboratory measures. We actively encourage other investigators to use the larger data set to inform quality assurance appraisals and supporting investigators to use the larger data set to inform future research questions. This has been collaborative effort between Phil Spinella (Washington University), Sheila Hanson (Medical College of Wisconsin), Heather Chandler (Emory University), Melania Bembea (John’s Hopkins University) and I (Laura Loftis, Baylor College of Medicine), along with the generous support of my section chief, Dr. Lara Shekerdemian, and the guidance of our Research Resources Office Bioinformatics team led by Dr. Uma Ramamurthy. Our research assistant Michelle Goldsworthy has been instrumental in creating the case report form, the data dictionary and numerous other component parts of the larger project.

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We expect the database to ready to open in March. We will initially open this registry up to the 5 centers listed above and after screening for any systems issues will open up to any who wish to participate.

PROphylaxis against ThRombosis prACTice Study (PROTRACT)

PI: E. Vincent Faustino, MD
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The PROphylaxis against ThRombosis prACTice Study (PROTRACT) study is a BloodNET-sponsored point prevalence study. The aims of the study are to determine the frequency of thromboprophylaxis in critically ill children, and to identify characteristics of the patient, physician and the pediatric intensive care unit that are associated with thromboprophylaxis. We wanted to understand the process of care variables surrounding the provision of thromboprophylaxis in critically ill children.

PROTRACT was completed in early 2013 and was electronically published in Critical Care Medicine in December 2013. We enrolled 2,484 children <18 years old from 59 pediatric intensive care units in Australia, Canada, New Zealand, Portugal, Singapore, Spain and the United States over 4 study days. Of these children, 2,159 (86.9%) had at least 1 risk factor for thrombosis. Only 308 (12.4%) of all children in the study were receiving pharmacologic thromboprophylaxis. Thromboprophylaxis included aspirin, low-molecular weight heparin or unfractionated heparin. Of 430 children indicated to receive pharmacologic thromboprophylaxis based on consensus recommendations from the American College of Chest Physicians, only 149 (34.7%) were receiving it. Mechanical thromboprophylaxis was used in 156 of 655 (23.8%) children 8 years and older. The presence of cyanotic congenital heart disease and spinal cord injury had the strongest independent associations with the use of pharmacologic and mechanical thromboprophylaxis, respectively. Units with more than 20 beds were more likely to use pharmacologic thromboprophylaxis, while units in North America were less likely to use it. No physician characteristics were independently associated with thromboprophylaxis. We concluded that thromboprophylaxis was infrequently used in critically ill children. These findings will allow us to pursue randomized controlled trials on thromboprophylaxis in critically ill children.

Secondary analysis of the dataset is ongoing. We are investigating the association between hemoglobin, patient demographics and organ dysfunction. We are describing the practice of thromboprophylaxis in Spain and Portugal. We are also describing the use of heparin in critically ill children with central venous catheters.

The dataset is open for anyone who has clinically important questions that may be answered with the dataset. Please contact Vince Faustino (vince.faustino@yale.edu) for details.
1:00 - 1:30 Introduction and brainstorming for new study ideas and network involvement

1:30 - 2:00 REAP Update
Laura L. Loftis, MD
Medical Director, Pediatric ECMO Service
Texas Children's Hospital
Associate Professor of Medical Ethics
Center for Medical Ethics and Health Policy
Baylor College of Medicine

2:00 - 2:30 ABC PICU Update
Marisa Tucci, MD
Clinical Associate Professor
Department of Pediatrics
University of Montreal and CHU Sainte-Justine

2:30 - 2:45 MTP Survey / Registry Update

2:45 - 3:00 Cardiac Surgery RBC Transfusion Trial Update
Philip C. Spinella, MD
Associate Professor of Pediatrics
Director, Translational Research Program
Division of Pediatric Critical Care
Washington University in St. Louis

3:00 - 3:30 Break

3:30 - 4:00 Plasma PPS
Marisa Tucci, MD
Clinical Associate Professor
Department of Pediatrics
University of Montreal and CHU Sainte-Justine

4:00 - 4:30 Identification of critically ill children at increased risk of catheter-related thrombosis
E. Vincent S. Faustino, MD
Assistant Professor
Yale University School of Medicine

4:30 - 5:00 TEG-A / TEG-S / CRIT Updates
Philip C. Spinella, MD