Co-PI: Philip C. Spinella  
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In a joint venture led by Philip Spinella and Marisa Tucci, Washington University School of Medicine in St. Louis and CHU Sainte-Justine have received a $7.8 million grant to determine whether the length of time red blood cells (RBCs) are stored affects organ failure in critically ill children who receive RBC transfusions.  

The five-year grant, from the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH), Canadian Institutes of Health Research (CIHR) and the Ministère de la Santé et des Services Sociaux (MSSS) will fund a trial involving more than 1,500 critically ill children who require RBC transfusions at St. Louis Children’s Hospital, CHU Sainte-Justine and some 30 other medical centers in the United States and Canada.  

The trial will be one of the largest studies ever performed in pediatric critical care and will compare the risk of new or progressive multiple organ failure in two groups of critically ill children ages 3 days to 16 years randomly assigned to receive RBC transfusions as a course of treatment. One group will receive RBCs stored for a week or less, and the other will receive RBCs stored an estimated average of 21 days. (The average length of time that RBCs are stored before being used is 17 days, but this study will exclude young patients who, for specific reasons, always receive fresh RBCs. Their exclusion from the study raises the average storage time to an estimated 21 days.)  

Generally, patients who require RBC transfusions receive cells stored anywhere from three to 42 days. The standard approach to allocating RBCs is to use those stored the longest first.  

RBCs are stored for up to 42 days in the United States and Canada, based largely on survival and recovery studies of RBCs. However, no clinical studies have been performed to show whether RBCs stored for 42 days are effective at delivering oxygen or are as safe as RBCs stored for shorter durations.  

If the new trial finds that fresher RBCs reduce such risks, it could lead to significant changes in how blood is stored and allocated to patients, particularly critically ill children.
TITLE: Point-Prevalence Study of Plasma Transfusion Exposure
Hypothesis: In pediatric critical care, more than a third of plasma transfusions are given to non-bleeding patients in whom there are no planned invasive procedures and plasma transfusions fail to correct mildly abnormal coagulation tests (INR < 2, TP ratio < 2, aPTT ratio < 2).
P: Oliver Karam, MD

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TITLE: Inception Study On Transfusion Practice In Children With Congenital Heart Disease
Aims: To determine the haemoglobin (Hb) level at which children with CHD receive transfusions in the post-operative period and to review if the Hb trigger level is different for post-operative corrective surgery compared to palliative surgery. Also to understand why clinicians transfuse PRBC in this group of children and assess if there are differences between the two surgical pathways. Finally, we will document the incidence of, NPMODS, morbidity and mortality using an international cohort.
P: Elena Cavazzoni, MD

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TITLE: Outcomes Associated with Damage Control Resuscitation Principles and Massive Transfusion Protocol Activations in Children
Hypothesis: 1) It is feasible to develop a multicenter registry of MTP activations and it is feasible to develop clinical trials in this population; 2) MTP will be activated more commonly (>50%) for non-trauma indications in children and that hemostatic resuscitation (> 1:2 ratio of FFP:RBCs) is not applied early (within 4 hours of activation) for the majority of cases; 3) Transfusion of a high ratio of FFP:RBCs is associated with increased survival in children requiring massive transfusion and this association varies by MTP indication.
P: Philip C. Spinella, MD

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TITLE: An open-label, multicenter, Post-Marketing Requirement (PMR) study to investigate the safety, tolerability and efficacy of octaplasLG in the management of pediatric patients who require replacement of multiple coagulation factors.
P: Philip C. Spinella, MD

Overview: An open-label, multicenter, Post-Marketing Requirement (PMR) study to investigate the safety, tolerability and efficacy of octaplasLG in the management of pediatric patients who require replacement of multiple coagulation factors.

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**Thrombosis & Hemostasis**

PI: Sheila Hanson, MD
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The Thrombosis and Hemostasis subgroup of Blood Net is an active collaboration of investigators from over 15 children’s hospitals organized to advance the care of critically ill children through clinical research in the area of clotting and bleeding. A major focus of this group has been the prevention of blood clots in this vulnerable population. The investigators have successfully facilitated development of multi-site protocols including the PREVENT Study (Prevalence in Thromboprophylactic Practice), the COAST (Coagulation Function in Sepsis Trial), as well as multiple single site studies. The Multi-National Study of Thromboprophylaxis Practice in Critically Ill Children, a prospective multi-national cross-sectional study over 4 study dates across 59 pediatric intensive care units in 7 countries, has recently been completed through the successful collaboration of this group.

Another important target for this subgroup is safer and more effective anticoagulation monitoring. A data registry and platform, including a common data set for anticoagulation during pediatric extracorporeal life support is currently being developed to glean the most effective practices for monitoring anticoagulation in this under-researched area. Other ongoing clinical studies developed under the auspices of the Thrombosis and Hemostasis subgroup are attempting to overcome the limitations with current anticoagulation monitoring by comparing the results with an evolving technology, whole blood thromboelastography.

The Thrombosis and Hemostasis subgroup of Blood Net has a track record of successful communication, development and administration of clinical research and is well poised for ongoing successful collaboration in the critical areas of blood clots and anticoagulation in critically ill children.

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**Clinical Decision Support Reducing Inappropriate Transfusions (CRIT)**

PI: Eloa Adams, MD
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Clinical decision support (CDS) has been associated with improvements in efficiency and patient safety and was recently endorsed by the IOM as a means of accelerating the best clinical knowledge into care decisions. The application of different CDS tools aimed at improving red blood cell transfusion (RBCT) utilization have proven to be effective in isolated adult hospitals. In 2010 the clinical resource management team at Lucille Packard Children’s Hospital at Stanford demonstrated that the application of a “smart” CDS tool was able to accelerate the adoption of evidence based RBCT practices in a single, large free-standing academic pediatric hospital. This particular tool was unique in...
CRIT continued

its ability to interrogate the medical record determining when a RBCT was ordered outside of evidence-based guidelines. The logic supporting the CDS tool was extracted from a seminal randomized controlled trial demonstrating the safety of a restrictive transfusion strategy in stable yet critically ill pediatric patients. When an RBCT order was written outside of evidence-based recommendations, a pop-up alert informed the clinician of the evidence and provided a web link to the article should they wish to educate themselves. The tool did not constrain the clinician’s ability to proceed with the RBCT order but rather provided real-time critical information. This intervention proved successful and resulted in a decreased number of inappropriate transfusions with over 400 fewer RBCT’s and direct cost savings of over $160,000 in one year.

After witnessing the effectiveness of this tool, the Clinical Decision Support Reducing Inappropriate Transfusions (CRIT) collaborative was formed in an effort to disseminate and advance the use of CDS tools and improve transfusion utilization across multiple institutions. CRIT currently consists of multiple affiliated hospitals and institutions across the United States. The goals of the CRIT collaborative are threefold: First, we exist to provide a venue for multiple institutions to share experiences and projects surrounding blood utilization. Second, we are working to study the impact of decision support tools and their ability to advance the adoption of evidence based practice in our institutions. Our third goal is to provide the framework for future collaborations using effective decision support tools. Over the past two years we have been successful in working toward these goals.

At our bimonthly meetings we have disseminated data and experience from institutions across the country. Several institutions have installed or are in the process of installing the RBCT CDS tool that inspired this collaborative. We plan to analyze the data generated from these institutions to learn more about the effectiveness of this tool across varied institutions. In April we submitted a Patient Centered Outcomes Research Institute (PCORI) grant that if funded will support a 60 center study investigating the effects of our CDS tool across both pediatric and adult institutions. CRIT has become closely aligned with blood management and research collaboratives such as Blood Net and the Society for the Advancement of Blood Management (SABM). Coupling with these large transfusion science collaboratives has created the unique opportunity for a direct conduit from publication to practice. Finally membership and participation with CRIT is open to any person or institution that is interested in learning more about how CDS tools can advance the adoption of evidence based transfusion practices. For more information regarding the CRIT collaborative please visit CRIT.stanford.edu.

STUDIES NEEDING ADDITIONAL SITES FOR RECRUITMENT

<table>
<thead>
<tr>
<th>TITLE</th>
<th>Impact of a decision support rule on appropriate transfusion of red blood cells – CPOE Reducing Inappropriate Transfusions (CRIT)</th>
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<tr>
<td>HYPOTHESIS</td>
<td>Implementation of an automated decision-support “rule” will significantly decrease the number of unnecessary red cell transfusions.</td>
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<tr>
<td>PI</td>
<td>Eloa Adams, MD <a href="mailto:eloa.s.adams@kp.org">eloa.s.adams@kp.org</a></td>
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<th>Clot Strength in Critically Ill Children with Sepsis (TEG-Sepsis)</th>
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<td>HYPOTHESIS</td>
<td>Thromboelastography (TEG) 1. will demonstrate abnormalities in hemostatic mechanisms (hypo and hypercoagulability) in patients with severe sepsis who then later progress to multiple organ dysfunction, 2. these abnormalities will correlate with measures of inflammation and endothelial injury.</td>
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<tr>
<td>Co-PI</td>
<td>John Lin, MD <a href="mailto:lin_j@kids.wustl.edu">lin_j@kids.wustl.edu</a></td>
</tr>
<tr>
<td>Co-PI</td>
<td>Philip C. Spinella, MD <a href="mailto:spinella_p@kids.wustl.edu">spinella_p@kids.wustl.edu</a></td>
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<th>TITLE</th>
<th>Clot Strength in Patients Receiving Anti-Coagulants (TEG-Anticoagulation)</th>
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<tr>
<td>HYPOTHESIS</td>
<td>Xa and PTT directed dose titration of anticoagulation does not adequately reduce clot strength consistently in critically ill children and Xa and PTT directed does titration of anticoagulation does not adequately reduce clot strength consistently in critically ill children.</td>
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<td>PI</td>
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BLOODNET SUBGROUP UPDATE

Blood Conservation

Co-PI: Jennifer York, MD
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Co-PI: Stacey Valentine, MD, MPH
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Phlebotomy induced blood loss in critically ill pediatric patients is a well documented problem. In 2008 Bateman et al, published a multicenter prospective observational study evaluating anemia and transfusion practices in the PICU which showed that phlebotomy accounted for 73% of blood loss, and was associated with increased odds of transfusion. In 2010 Hassan et al. demonstrated a reduction in phlebotomy volumes, hemoglobin drops and transfusions with the implementation of blood conservation guidelines. Valentine and Bateman showed in 2012 that blood draws taken from an indwelling catheter result in significantly greater blood draw volumes, that blood draw volumes may be avoidable and that reducing phlebotomy blood loss may reduce anemia. York, Doctor and Spinella have an ongoing blood conservation project that has shown overdraw in 87% of PICU blood samples. The volume
Blood Conservation continued

of blood removed was greater in patients that required a PRBC transfusion and in those patients the hemoglobin decreased 4.2 g/dl from admission to PRBC transfusion. The Blood Conservation subgroup was formed to stimulate interest and production of blood conservation projects and our current members are Stacey Valentine, Jennifer York, Nabil Hassan, Eloa Adams, Sheila Hanson and Phil Spinella. We are developing an anonymous, electronic survey to evaluate the use of blood conservation techniques in the pediatric and adult intensive care populations to inform development and implementation of blood conservation protocols to reduce blood loss and subsequent anemia. Our primary hypothesis is that blood conservation techniques vary across pediatric and adult intensive care units. Our secondary hypothesis is that understanding baseline blood conservation techniques across institutions through the blood conservation survey will help guide implementation of blood conservation protocols to decrease blood loss and subsequent anemia in critically ill patients.

The target data to be collected includes the use of blood conservation practices (the presence or absence of a formal blood conservation program, published guidelines, decision support tools, and electronic medical records), the use of bleeding reduction methods (TPA, erythropoietin, and TEG) and the use of phlebotomy conservation techniques (closed loop blood draw systems, micro-containers, waste return, grouping blood draws, phlebotomy rounding tools). Our goal response rate is greater than 50% with a goal of 40 different sites.

Blood Conservation continued

68 Members • 37 Sites • 4 Countries

FUNDING OPPORTUNITIES

- NHLBI PAR-10-034: Selected Topics in Transfusion Medicine (R01)
- NHLBI PAR-10-033: Selected Topics in Transfusion Medicine (R21)
- PAR-10-005: NHLBI Clinical Trial Pilot Studies (R34)
- The Clinical Trials Development Resource for Hematologic Disorders (U24)
- NHLBI Ancillary Studies in Clinical Trials (R01) – RFA-HL-13-003
- NHLBI PAR (R21) for secondary dataset analyses
- PAR-10-096: NHLBI Investigator-Initiated Multisite Clinical Trials (Collaborative R01)
- PAR-10-234: Bioengineering Research Partnerships (BRP)[R01]
- PA-10-009: Bioengineering Research Grants (BRG)[R01]
- PA-10-010: Exploratory/Developmental Bioengineering Research Grants (EBRG) [R21]
- BARDA CBRN BAA-12-100-SOL-00011: Advanced Research and Development of Chemical, Biological, Radiological, and Nuclear Medicine Countermeasures

FUTURE BLOOD NET MEETINGS

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<tr>
<td>Oct 2, 2013</td>
<td>New Orleans, LA</td>
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<tr>
<td>March 11, 2014</td>
<td>Park City, UT</td>
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www.BloodNetResearch.org