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Pediatric and Neonatal Transfusion Medicine: A Roadmap for Research

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Pediatric transfusion medicine (PTM) has been evolving as a subspecialty over the past 30 years. Those individuals knowledgeable about PTM recognize the significant physiological adaptation intrinsic to the transition from fetus to neonate to childhood and adolescence. They also recognize the effect of congenital abnormalities, unique disease states, and unusual presentations of common disorders. Considerations include the maternal-fetal unit; ever-changing body weight; blood and plasma volumes; developing hepatic, renal, hematologic, and immune systems; and the effect of environmental and drug-related toxicants on the developmentally evolving system.

Pediatric transfusion medicine as a discipline, therefore, can be seen as ensuring the collection, processing, testing, and availability of blood components and derivatives optimally suited to the variable needs of patients undergoing multiorgan growth and development and/or suffering from the effects of congenital or acquired disorders [1]. In addition, methods to ensure the appropriate delivery of those components for intrauterine and extrauterine transfusion to pediatric patients are a focus. Specialized procedures and technologies including extracorporeal membrane oxygenation, apheresis, and intraoperative

cell salvage are integral to the treatment of vulnerable patients and inseparably linked to PTM [1]. Furthermore, PTM extends to the appropriate manufacture and use of plasma derivatives, recombinant coagulation factors and anticoagulants, hematopoietic progenitor cells, and other regenerative technologies [1]. Hence, the wide breadth of areas that comprise PTM demands that resources, both clinical and research-focused, be allocated to this heretofore undersupported area of transfusion medicine.

In the 1970s and 1980s, a few pathologists and even fewer pediatric hematology-oncology-trained physicians and neonatologists dedicated their clinical and research careers to investigating and defining evidence-based transfusion practices for infants and children. A dedicated group of individuals that includes Ronald Strauss, Naomi Luban, Heather Hume, Catherine Manno, Maureen Andrews, Patricia Pisciotto, Dan Ambruso, Edward Bell, John Widness, Susan Roseff, Jay Herman, and Christopher Hillyer paved a path, built a foundation, and trained future generations of physician-scientists and clinicians who are at the cusp of transforming PTM into a formal discipline worldwide. The US National Institutes of Health have catalyzed and propelled the PTM discipline through their support. The adoption of a policy which required that National Institutes of Health investigators include pediatric subjects in their research endeavors or give explicit justification for their exclusion-afforded researchers the opportunity to study children in a clinical research setting and not just extrapolate results from adult studies [2].

At the heart of PTM is the drive of investigators to ensure that evidence-based practices are informed by clinical, translational, and basic science research specific to pediatric patients. The need for pediatric studies has been echoed throughout the transfusion medicine community and reflected in the outputs of the 3 National Heart, Lung, and Blood Institute-sponsored State of the Science meetings convened in 2009, 2015, and 2016 [3,4]. All participants at the 2009 and 2015 meetings felt that the National Institutes of Health had to support clinical, translational, and basic science studies over the next 5 to 10 years. The impact of the recommendations from the physician-scientist 2015 meeting resulted in a separate meeting in 2016 focused exclusively on developing a research agenda specific to PTM. Six key areas were targeted: neonatology and perinatology, oncology and transplant, chronic transfusion, devices, and surgery, intensive care and trauma, and teenage blood donation. Several cross-cutting areas of need were identified: (1) the need for better baseline data and databases to support retrospective and longitudinal studies in neonates to young adults receiving blood products, (2) the need for novel in vitro and in vivo models to examine the impact of transfusion in specific diseases/conditions, and (3) the need for randomized clinical trials directed toward assessing outcomes in pediatric patients receiving transfusion therapies.

Pediatric transfusion medicine as a discipline is now at a crossroad. There is clear-cut momentum, an invigorated generation of junior PTM physician-scientists with experienced mentors and the recognition that collaboration with neonatologists, pediatric critical care physicians, pediatric anesthesiologists, immunologists, pediatric surgeons, pediatric nurses, pediatric hematologists/oncologists, and internists is required to ensure timely and effective research results [5]. A roadmap for research has been created with this Special Edition of *Transfusion Medicine Reviews*. We provide background and relevance and present areas

where there are insufficiently answered critical PTM questions. We provide background and relevance and present areas where there are insufficiently answered critical PTM questions. Authors were asked to address specific focused areas. For neonates, these include modifications, indications, and adverse consequences of red blood cell (RBC), platelet, and plasma transfusion; hemolytic disease of the fetus and newborn; cardiopulmonary bypass and extracorporeal membrane oxygenation; and the use of recombinant and plasma-derived coagulation and anticoagulation products. For children, these include indications and adverse consequences of RBC and platelet transfusions, and massive transfusion; complex transfusion issues in stem cell transplant; RBC genotyping for sickle cell disease and thalassemia; apheresis therapy; and patient blood management.

We hope that this issue will detail research needs in PTM and inspire young investigators to dedicate themselves to basic, translational, and clinical research that will improve outcomes for neonates, children, and adolescents who require transfusions.

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