Contents

Preface: The Development of the Nascent Field of Pediatric Transfusion Medicine xi

Sarah R. Vossoughi and Brie A. Stotler

Transfusion in Pediatric Patients: Review of Evidence-Based Guidelines 1

Yunchuan Delores Mo and Meghan Delaney

Children require transfusion of blood components for a vast array of medical conditions, including acute hemorrhage, hematologic and nonhematologic malignancies, hemoglobinopathy, and allogeneic and autologous stem cell transplant. Evidence-based literature on pediatric transfusion practices is limited, particularly for non–red blood cell products, and many recommendations are extrapolated from studies in adult populations. Recognition of these knowledge gaps has led to increasing numbers of clinical trials focusing on children and establishment of pediatric transfusion working groups in recent years. This article reviews existing literature on pediatric transfusion therapy within the larger context of analogous data in adult populations.

Transfusion in Neonatal Patients: Review of Evidence-Based Guidelines 15

Patricia E. Zerra and Cassandra D. Josephson

Transfusion of red blood cells, platelets, and fresh frozen plasma in neonatal patients has not been well characterized in the literature, with guidelines varying greatly between institutions. However, anemia and thrombocytopenia are highly prevalent, especially in preterm neonates. When transfusing a neonatal patient, clinicians must take into consideration physiologic differences, gestational and postnatal age, congenital disorders, and maternal factors while weighing the risks and benefits of transfusion. This review of existing literature summarizes current evidence-based neonatal transfusion guidelines and highlights areas of current ongoing research and those in need of future studies.

Massive Transfusion in Pediatric Patients 35

Lucas P. Neff, Michael Aaron Beckwith, Robert T. Russell, Jeremy W. Cannon, and Philip C. Spinella

Massive transfusion in pediatric patients is infrequent but associated with much higher mortality than in adults. Blood transfusion and hematology has conceptualized ideas such as blood failure and the interplay of the blood-endothelium interface to understand coagulopathy in the context of hemorrhagic shock. Researchers are still searching for an appropriate definition of what constitutes a pediatric massive transfusion. There is no universally accepted protocol for massive transfusion and how to address the many complications that can arise. Pharmacologic adjuncts to resuscitation may prove beneficial in reducing coagulopathy during pediatric massive transfusion, but high-quality evidence has not yet emerged.

Pediatric Hemovigilance and Adverse Transfusion Reactions 51

Nataliya Sostin and Jeanne E. Hendrickson

Some types of transfusion reactions occur more frequently in the pediatric than the adult population. Allergic reactions are the most common, followed by nonhemolytic transfusion reactions; male children seem most susceptible to such reactions. Platelets are often implicated and pulmonary reactions are understudied in children. Clinical sequelae in neonates, such as bronchopulmonary dysplasia/chronic lung disease and intraventricular hemorrhage, have received increasing attention in relation to transfusion. There is a need to better understand the pathophysiology of transfusion reactions in neonatal and pediatric populations so preventive strategies can be undertaken. There is also a need for robust hemovigilance systems.

Inventory Management and Product Selection in Pediatric Blood Banking 69

Jenna T. Reece and Deborah Sesok-Pizzini

Blood banks need to understand patterns of use and ordering practices to provide the blood donor centers with the best information with which to develop daily scheduled deliveries of blood products. Blood use is a large component of this process through maximizing physician education about appropriate ordering practices and use of appropriate tools. Simple measures can help provide guidance on the number of available components and the need to order more from the blood donor center. Special product requests in pediatrics, such as fresh blood, leukoreduction, irradiation, and antigen-negative units can also drive inventory practices and use patterns.

Evaluation and Management of Coagulopathies and Thrombophilias in Pediatric Patients 83

HyoJeong Han, Lisa Hensch, Shiu-Ki Rocky Hui, and Jun Teruya

The diagnosis of coagulopathy or thrombophilia in pediatric patients can be challenging. Congenital coagulopathies often present in the pediatric period and require appropriate work-up for diagnosis and ongoing management. Acquired coagulopathies of childhood are frequently encountered in hospitalized children and warrant appropriate coagulation testing for goal-directed therapy. The incidence of thrombosis is increasing in pediatric patients. After identifying the presence of thrombus, acute management includes initiating therapeutic anticoagulation. Choice of anticoagulant depends on patient's clinical status, along with availability of the anticoagulant. Thrombophilia evaluation is performed when children present with spontaneous thrombosis. Thrombophilia tests are inaccurate during acute illness.

Transfusion and Cellular Therapy in Pediatric Sickle Cell Disease 101

Yan Zheng and Stella T. Chou

Red blood cell (RBC) transfusion is critical in managing acute and chronic complications of sickle cell disease. Alloimmunization and iron overload remain significant complications of transfusion therapy and are minimized with prophylactic Rh and K antigen RBC matching and iron chelation. Matched sibling donor hematopoietic stem cell transplant (HSCT) is a

curative therapeutic option. Autologous hematopoietic stem cell (HSC)–based gene therapy has recently shown great promise, for which obtaining sufficient HSCs is essential for success. This article discusses RBC transfusion indications and complications, transfusion support during HSCT, and HSC mobilization and collection for autologous HSCT with gene therapy.

Cellular Therapy in Pediatric Hematologic Malignancies **121**

Susan Kuldanek, Bryce Pasko, Melkon DomBourian, and Kyle Annen

Advances in cellular therapies for pediatric patients have created many opportunities for improved survival with reduced morbidity. This article reviews current cellular therapies in pediatric hematological malignancy, including the most updated practices in hematopoietic stem cell transplant and the use of chimeric antigen receptor (CAR) therapy in T cells. Hematopoietic stem cell transplant has evolved with improvements in chemotherapy regimens, immunosuppression, and donor-matching options. Novel therapies in development which will likely further improve the options for patients are reviewed including Natural Killer, Regulatory T-cells and $\alpha\beta$ depletion.

Hemolytic Disease of the Fetus and Newborn: Historical and Current State **133**

Melanie E. Jackson and Jillian M. Baker

Hemolytic disease of the fetus and newborn (HDFN) is an immune-mediated disorder affecting neonates globally, with a range of clinical presentations from severe and life threatening to mild or even asymptomatic. Historically, HDFN has been responsible for a large proportion of perinatal mortality, and, despite advances in diagnosis and management, this morbidity and mortality has not been eradicated. Blood banking techniques and blood transfusion have contributed to improved prophylaxis and management, drastically improving the outcome of newborns with HDFN over the last century.

Novel Blood Component Therapies in the Pediatric Setting **153**

Shannon C. Walker and Jennifer Andrews

There have been recent advances in safer blood component preparation and use of adjuvant blood derivatives, which have limited safety and efficacy data on use in children. This article reviews the literature on use of whole blood, solvent/detergent-treated plasma, pathogen-reduced platelets, and fibrinogen concentrate in pediatric patients. Many countries have adopted pathogen-reduced blood product technology, and hospitals in the United States are slowly adopting these products. The pediatric transfusion medicine community needs to appraise the evidence for their use and continue to advocate the inclusion of children in the most robust randomized clinical trials for novel blood components.