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Preface

Max J. Coppes and Russell E. Ware

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Decision Analysis in Pediatric Hematology

Sarah H. O'Brien

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Decision analysis is a simulation, model-based research technique in which investigators combine information from a variety of sources to create a mathematical model representing a clinical decision. This tool can be used to address many clinical dilemmas in pediatric hematology for which traditional clinical trials are unfeasible or impossible. This article outlines the basic steps of performing and analyzing a decision analysis tree and describes several decision analyses published in the field of pediatric hematology and how to evaluate and judge the decision analysis literature.

Venous Thromboembolism in Children

Neil A. Goldenberg and Timothy J. Bernard

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With improved pediatric survival from serious underlying illnesses, greater use of invasive vascular procedures and devices, and a growing awareness that vascular events occur among the young, venous thromboembolism (VTE) increasingly is recognized as a critical pediatric concern. This review provides background on etiology and epidemiology in this disorder, followed by an in-depth discussion of approaches to the clinical characterization, diagnostic evaluation, and management of pediatric VTE. Prognostic indicators and long-term outcomes are considered, with emphasis on available evidence underlying current knowledge and key questions for further investigation.

Timothy J. Bernard and Neil A. Goldenberg

Arterial ischemic stroke (AIS) is a rare disorder in children. Research suggests that risk factors, outcomes, and presentation are different from those of adult stroke. In particular, prothrombotic abnormalities and large vessel arteriopathies that are nonatherosclerotic seem to play a large role in the pathogenesis of childhood AIS. This review examines the epidemiology and etiologies of neonatal and childhood AIS and provides a detailed discussion of approaches to the clinical characterization, diagnostic evaluation, and management. Long-term outcomes of recurrent AIS and neuromotor, speech, cognitive, and behavioral deficits are considered. Emphasis is on evidence underlying current knowledge and key questions for further investigation.

The Role of the Hematologist/Oncologist in the Care of Patients with Vascular Anomalies**339**

Denise M. Adams and Mary Sue Wentzel

Pediatric hematologist/oncologists have a critical role in the diagnosis and management of patients who have complex vascular anomalies. They provide the clinical and medical skills needed to diagnose, treat, and manage these patients. Hematologist/oncologists also provide support for clinical trials and drug development to further treatment options for these patients.

Advances in Hemophilia: Experimental Aspects and Therapy**357**

Nidra I. Rodriguez and W. Keith Hoots

This article describes recent clinical and research advances in hemophilia therapy. Different prophylactic regimens for the management of severe hemophilia are described along with the use of adjuvant treatment options to achieve hemostasis. The safety and efficacy of radionuclide synovectomy with phosphorus 32-sulfur colloid to treat existing joint arthropathy also are described. The development of inhibitors to factor VIII or IX remains a challenge for hemophilia care and recent approaches to achieve immune tolerance induction are discussed. Finally, recent advances in hemophilia are mentioned, including the role of iron, inflammation, and angiogenesis in the pathogenesis of hemophilic arthropathy.

von Willebrand Disease**377**

Jeremy Robertson, David Lillicrap, and Paula D. James

von Willebrand disease is a common inherited bleeding disorder and many cases are diagnosed in childhood. It has a negative impact on the quality of life of affected individuals; therefore, it is

important that the condition be recognized and diagnosed. This article reviews the pathophysiology of the condition, the current classification scheme, and the available treatments, highlighting issues specific to the pediatric population.

Childhood Immune Thrombocytopenic Purpura: Diagnosis and Management

Victor Blanchette and Paula Bolton-Maggs

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Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system. ITP can be classified as childhood versus adult, acute versus chronic, and primary versus secondary. Persistence of thrombocytopenia defines the chronic form of the disorder. Secondary causes of ITP include collagen vascular disorders, immune deficiencies, and some chronic infections. This review focuses on the diagnosis and management of children who have acute and chronic ITP. Emphasis is placed on areas of controversy and new therapies.

Blood Component Therapy

Ross Fasano and Naomi L.C. Luban

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Blood component transfusion is integral in the treatment of infants and children by pediatricians, surgeons, intensivists, and hematologists/oncologists. Technologic advances in blood collection, separation, anticoagulation, and preservation have resulted in component preparation of red blood cells, platelets, white blood cells, and plasma, which are superior to whole blood used in the past. Advances in donor selection, infectious disease testing, leukoreduction filters, and gamma irradiation have made products safer. Physicians prescribing blood components should have a basic understanding of indications (and contraindications) and be cognizant of methods of preparation, proper storage conditions, and requirements for modification of blood products to prevent potential adverse effects.

Update on Thalassemia: Clinical Care and Complications

Melody J. Cunningham

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β -Thalassemia, originally named Cooley anemia, is an inherited blood disease. Various types of thalassemia are inherited anemias caused by mutations at the globin gene loci on chromosomes 16 and 11, affecting the production of α - or β -globin protein, respectively. The combination of early diagnosis, improvements in monitoring for organ complications, and advances in supportive care have enabled many patients who have severe thalassemia syndromes to live productive, active lives well into adulthood.

Oral Iron Chelators

Janet L. Kwiatkowski

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Effective chelation therapy can prevent or reverse organ toxicity related to iron overload, yet cardiac complications and premature death continue to occur, largely related to difficulties with compliance in patients who receive parenteral therapy. The use of oral chelators may be able to overcome these difficulties and improve patient outcomes. A chelator's efficacy at cardiac and liver iron removal and side-effect profile should be considered when tailoring individual chelation regimens. Broader options for chelation therapy, including possible combination therapy, should improve clinical efficacy and enhance patient care.

Hydroxyurea for Children with Sickle Cell Disease

Matthew M. Heeney and Russell E. Ware

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Hydroxyurea therapy offers promise for ameliorating the clinical course of children with sickle cell disease (SCD). Hydroxyurea is a prototypic therapeutic option; it can be administered with minimal side effects, has a relatively wide therapeutic window, and has mechanisms of action that address pathophysiologic pathways of sickling, vaso-occlusion, hemolysis, and organ damage. There are limited data regarding hydroxyurea's ability to prevent or diminish organ dysfunction, and the long-term risks of hydroxyurea therapy remain incompletely defined. Although clinical trials are underway to address long-term issues, hydroxyurea remains an effective but underutilized therapy for SCD.

Partial Splenectomy for Hereditary Spherocytosis

Elisabeth T. Tracy and Henry E. Rice

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The significant risks associated with total splenectomy have led to interest in the use of partial splenectomy as an alternative surgical therapy for children who have congenital hemolytic anemia. Partial splenectomy is designed to remove enough spleen to gain desired hematologic outcomes while preserving splenic immune function. Although preliminary data demonstrate successful laboratory and clinical outcomes after partial splenectomy in various congenital hemolytic anemias, conclusive data comparing the efficacy of partial splenectomy to total splenectomy are not reported. Based on preliminary data, a definitive clinical trial of partial splenectomy in children who have severe congenital hemolytic anemia may be warranted.

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