The role of intravenous immunoglobulin (IVIG) has evolved over the past 50 years from its initial use as replacement therapy in primary immunodeficiency diseases (PIDDs) to a more expanded role as an immunomodulatory and anti-inflammatory agent. There are only six US Food and Drug Administration-approved indications for the use of IVIG, but there are far more diseases for which it is used “off-label.” I am grateful for the opportunity, as guest editor of this issue of Pediatric Annals, to present articles authored by several outstanding clinicians detailing the use of IVIG in their respective fields. Authorities in the fields of immunology, hematology/oncology, rheumatology, and infectious disease will discuss the role of IVIG in their respective subspecialties. IVIG is also used in neurology to treat immune-mediated conditions, such as Guillain-Barré syndrome and chronic idiopathic demyelinating polyneuropathy, as well as in dermatology to treat conditions such as autoimmune bullous diseases and toxic epidermal necrolysis.

IVIG is a blood product, containing the pooled immunoglobulin (Ig) of thousands of donors. It is predominantly composed of IgG (>95%), but has trace amounts of IgM and IgA. It was initially administered intramuscularly but is now given either intravenously or subcutaneously. The dose varies depending upon the indication, and the mechanism of action is dose-dependent. Replacement therapy, as is used in PIDDs, is low dose (400-600 mg/kg) and given monthly. IVIG at higher doses (2 g/kg) functions in an immune-modulatory manner through various mechanisms that have been described in the literature and is discussed in this issue. These include Fc- and Fab-mediated mechanisms, complement activation, neutralization of anti-idiotype antibodies, and modulation of various inflammatory mediators, such as immune cells and cytokines. IVIG is generally considered a safe therapy in children, and most of the side effects are mild and may be ameliorated with slower rates of infusion, premedication, and hydration.1,2

The first article, “Intravenous Immunoglobulin in the Treatment of Primary Immunodeficiency Diseases,” by Dr. Nana Sarkoah Fenny and myself focuses on the use of IVIG in PIDDs, as this is the field in which it was first used. Agammaglobulinemia, which is an absence of gamma globulin in the blood, was first described by Ogden Bruton in the early 1950s after administration of IVIG therapy in a young boy prone to recurrent episodes of bacterial sepsis led to resolution of these episodes. The gene for this condition was later discovered in 1993 and named Bruton’s tyrosine kinase. This disease is now known as X-linked Agammaglobulinemia, which is an absence of gamma globulin in the blood, and subsequent increased vulnerability to bacterial infections. Lifelong IVIG replacement therapy is the standard of care for this condition as well as many other primary humoral deficiencies that are discussed in this issue.

The second article, “Intravenous Immunoglobulin in the Treatment of Hematologic Disorders in Pediatrics,” by Drs. Gabriela Villanueva, Jill L. O. de Jong, and Jennifer L. McNeer shifts the focus to the use of IVIG in hematology/oncology. The authors expertly describe its use as a first-line agent to increase platelet counts in immune-mediated thrombocytopenia. It has been used in this capacity since 1981, when a landmark study3 detailed the effectiveness of high-dose IVIG in this condition. It is also used to treat autoimmune cytopenias in other conditions, such as autoimmune lymphoproliferative syndrome. Other diseases that are discussed in the context of IVIG therapy include acquired red blood cell aplasia and Rh incompatibility.

The next article, “Intravenous Immunoglobulin in Pediatric Rheumatology: When to Use It and What Is the Evidence” by Drs. Martha M. Rodriguez and Linda Wagner-Weiner, discusses the various uses of IVIG in rheumatology, the majority of which are “off-label.” IVIG has been shown to be effective in juvenile dermatomyositis and is often used as first-line therapy in those children with more severe dis-
ease. The authors also describe the use of IVIG in other pediatric rheumatic diseases, including systemic lupus erythematosus, juvenile idiopathic arthritis, and vasculitis.

In our final article, “Intravenous Immunoglobulin for the Treatment of Kawasaki Disease,” Dr. Stanford T. Shulman delivers an insightful review of Kawasaki disease and the benefits associated with early administration of IVIG. Dr. Shulman has written many of the seminal articles detailing the diagnostic criteria and management strategies for this disease, which have been widely published.\textsuperscript{4,5} We are honored to have his participation in this issue, as his research has had a major impact on how we treat children with Kawasaki disease.

In conclusion, IVIG has a broad range of applications, from replacement therapy in PIDDs to anti-inflammatory/immunomodulatory therapy in many autoimmune conditions. Our understanding of its mechanisms of action continues to expand. We hope that readers gain insight not only into how this drug works, but also the conditions for which it is beneficial.

**REFERENCES**


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**About the Guest Editor**

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