Optimizing Immunoglobulin Therapy in the Treatment of Primary Immunodeficiency Disease

By Jordan Orange, M.D., Ph.D.

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This continuing education article is intended for pharmacists, nurses, and other alternate-site infusion professionals.

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Continuing Education Objectives
1. Describe changes in the landscape of immunoglobulin G (IgG) products in recent years
2. List emerging treatment options with IgG therapy
3. Explain the impact of current research in optimization of IgG therapy for patients with primary immune deficiencies
4. Describe ongoing research and future implications for IgG therapy

DISCLOSURES: Dr. Jordan Orange is a paid consultant to Talecris Biotherapeutics, Baxter Healthcare, CSL Behring and is on the Research Grants Committee of Octapharma USA, all manufacturers of immunoglobulin therapy. He is also on the speakers bureau of Baxter Healthcare and is on the Scientific Advisory Board of IBT Reference Laboratories (a commercial entity that offers diagnostic testing for immunological disorders). Clinical trials and off-label uses will be discussed but in a fair and unbiased manner.

Continuing education credit is free to NHIA members, and available to non-members for a nominal processing fee. To apply for nursing or pharmacy continuing education, go to www.nhia.org/CE_Infusion and follow the online instructions.
The field of immunoglobulin therapy is changing—what we knew just a few years ago is already outdated. As our understanding of the human immune system continues to evolve, so, too, does research into treatment options that will be most efficacious for a wide variety of immune-related disorders. Home infusion clinicians on the front line of patient care, and consequently in the best position to observe patient response to treatment, can take what they learn in this educational program and apply it directly to their clinical practice. Armed with new knowledge about the impact of serum immunoglobulin G (IgG) trough levels on rates of pneumonia in primary immunodeficiency disease (PIDD), clinicians can collaborate with prescribing physicians and payers to ensure each patient is receiving the drug, dose and administration method that results in his/her best clinical outcome.

Therapeutic Polyclonal IgG—Mechanism of Action and Indications for Use

Therapeutic polyclonal IgG is a highly purified human IgG, a major antibody in human blood produced by type B lymphocytes. The IgG molecule contains billions of specificities, giving it an important and virtually limitless role in the immune system. This antibody specifically binds to harmful substances such as bacteria, viruses, and toxins, neutralizing the substance while it interfaces with immune cells to protect against disease. Receptor-specific components on the IgG molecule bind to receptors on immune cells, accessing and regulating immune function. The IgG molecule is a bridge between the functioning cells of the immune system and foreign invaders that enter the body. Without it, common bacteria and viruses can become life threatening.

IgG products are made from tens of thousands of pooled plasma donors to ensure broad specificity of antigen exposure. The U.S. Food and Drug Administration (FDA) requires that a single batch of fractionated blood product be produced from a pool of 15,000 to 60,000 donors, and that all IgG products sold in the U.S. be manufactured from donated plasma. Plasma donations account for the vast majority of IgG products, and represent selfless donors who receive no monetary reward for their time spent in plasma collection centers. From this pooled plasma, IgG is manufactured into several preparations, including IVIG (intravenous), IMIG (intramuscular), SCIG (subcutaneous), and hyperimmune immunoglobulins which have guaranteed specificity against a certain organism, such as tetanus or Hepatitis B.

IgG products are available in different forms (liquid, lyophilized), employ different stabilizers (sucrose, glucose), contain different levels of sodium, different levels of IgA and have different osmolarity. Because of these numerous differences, IgG products are not considered clinically interchangeable. Product selection requires knowledge of factors that are pertinent to each patient’s specific disease states and conditions, as well as the patient’s tolerability. Changing a product that a patient is tolerating well is not ideal, and should be avoided whenever possible. Considerations when selecting an IgG product for a specific patient are listed in Table 1 below.

To date, only seven indications have received FDA approval for immune globulin therapy (see Box, p. 2). In addition to these ap-

<table>
<thead>
<tr>
<th>CONSIDERATION</th>
<th>PRODUCT(S)</th>
<th>AVOID IN</th>
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<tbody>
<tr>
<td>Sucrose used as a stabilizer</td>
<td>Carimmune®</td>
<td>• Patients at risk for renal complications</td>
</tr>
<tr>
<td>Glucose used as a stabilizer</td>
<td>Gammagard SD®</td>
<td>• Patients with diabetes</td>
</tr>
<tr>
<td>Sodium content</td>
<td>Gammagard SD®-0.85% Garamune®</td>
<td>• Infants</td>
</tr>
<tr>
<td>High Osmolality</td>
<td>Gammagard SD®</td>
<td>• Infants</td>
</tr>
<tr>
<td>Fluid load</td>
<td>5% preparations including Flebogamma® and Octagam®</td>
<td>• Patients with fluid restriction</td>
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<tr>
<td>Amino acids as stabilizers</td>
<td>Gammunex®, Gammagard Liquid®- contains Glycine Privigen®- contains Proline</td>
<td>• Patients with a history of reactivity</td>
</tr>
<tr>
<td>IgA levels</td>
<td>All products except Gammagard SD®</td>
<td>• Patients with a history of reaction</td>
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proved indications, there are approximately 200 conditions documented for off-label use of the product, ranging from the cosmetic (and not medically necessary), to the emerging treatment of extremely serious disorders such as Alzheimer’s disease.\(^1\) Any product that is manufactured from donated human plasma is inherently in limited supply, therefore clinicians must be aware of the most effective use of IgG for the most serious disorders, and prioritize drug supply accordingly.

Fortunately, resources are available to assist clinicians in navigating these complex decision-making processes. In 2006, the American Academy of Allergy, Asthma and Immunology (AAAAI) convened a committee of primary immunodeficiency experts to address this IVIG prioritization challenge. They classified the level of benefit demonstrated in the many IVIG studies conducted for more than 80 PIDD disorders.\(^2\)

This reference remains a valuable resource for clinicians in the development and consistent application of an IVIG prioritization algorithm for use in their own practice settings. As new indications are approved for the use of IgG, clinicians must be advocates for patients with indications where the product is an essential, life-saving therapy.\(^2\)

**Primary Immunodeficiency**

Primary immunodeficiency is the inherent inability of the immune system to function as the result of an inborn defect. There are more than 150 individual primary immunodeficiency disorders (PIDD), ranging from mild to severe. Therapeutic options involve treating and avoiding infection, as well as attempts at correcting the deficiency, and include: adjunct therapies, antibiotic prophylaxis, immunoglobulin therapy, hematopoietic stem cell transplantation, and gene therapy. Advances in medical treatment are even bringing about cures in some severe and life-shortening PIDDs, such as the treatment of Severe Combined Immunodeficiency Syndrome (SCIDS) with hematopoietic stem cell transplantation, and gene therapy. Advances in medical treatment are even bringing about cures in some severe and life-shortening PIDDs, such as the treatment of Severe Combined Immunodeficiency Syndrome (SCIDS) with hematopoietic stem cell transplantation. Many states have adopted SCID neonatal screening programs in order to identify and treat these medically fragile infants as early as possible, before life-threatening infections set in.

In addition to administering the most appropriate treatment for the patient’s PIDD, it is also important to manage comorbid conditions. Clinicians in the home have a unique opportunity to identify and address potential environmental factors that could be having an impact on their patient’s health, such as the presence of mold or mildew, or second-hand cigarette smoke. It is a fragile balance, being in the patient’s home and suggesting changes that could improve their health without causing insult. Home assessment tools can provide an objective method for documenting and discussing these environmental opportunities with patients and family members. We also know that vaccines, stress-reducing therapies, nutrition, probiotics, and hygiene-related issues may all impact the patient’s overall health, although little research exists beyond anecdotal experience at this time.

Before any steps can be taken to manage a primary immune deficiency disorder, the patient must first be identified and diagnosed. The Jeffrey Model Foundation hosts a public service announcement to educate parents about the potential for PIDD, using the phrase “He’s a kid is NOT a diagnosis.” In other words, frequent infections in very young children should be examined for an underlying cause rather than being attributed to childhood.

Consider this case study as an example: an infant receives his first diagnosis of ear infection at six months of age. In the ensuing months, he experiences four more ear infections in addition to other frequent infections, and is described as “always getting sick.” Lab results revealed the following: below-normal levels of IgG (72 mg/dL), IgM (12 mg/dL), and IgA (<10 mg/dL). Further diagnostic study revealed his agammaglobulinemia was the result of a genetic defect in the Bruton’s Tyrosine Kinase (BTK) gene, leading to a deficiency of BTK protein that is essential for the development and maturation of B cells. Since mature B cells are needed to produce antibodies or immunoglobulins, their absence creates a medical crisis for this young patient. In his case, IgG replacement therapy will be life-saving, and lifelong.

Immunoglobulin therapy has been widely used as treatment for PIDD, beginning in the 1970s as an intramuscular injection due to

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**FDA-Approved Indications for Immunoglobulin Therapy**

1. Treatment of primary immunodeficiencies
2. Prevention of bacterial infection for patients with hypogammaglobulinemia due to B cell chronic lymphocytic leukemia
3. Prevention of coronary artery aneurysms in Kawasaki disease
4. Prevention of infections and graft-versus-host disease after bone marrow transplantation
5. Reduction of serious bacterial infection in HIV-infected children
6. Increasing platelet count in Idiopathic Thrombocytopenic Purpura (ITP) to prevent bleeding
7. To improve neuromuscular disability in Chronic Inflammatory Demyelinating Polyneuropathy
impurities that made intravenous (IV) infusion a high-risk and severe reaction-prone procedure. By 1979, the advent of purified IVIG preparations revolutionized the management of virtually all immunodeficiency syndromes characterized by failure of antibody responses, greatly improving survival rates. Twenty years of data show that infection frequency in PIDD is reduced by IgG replacement—almost to levels experienced in the general population.4,5

A proposed simplified scheme for categorizing the complex listing of antibody deficiency includes three categories: B cells (present or absent), IgG quantity (absent, low, normal), and IgG quality (absent, low, normal).2 These categories provide a foundation for further understanding the relative effectiveness of IVIG with different combinations of factors, and are the basis for new recommendations for IVIG therapy in PIDD patients.6 Table 2 presents a matrix of deficiency categories and treatment recommendations.

### Table 2
Conceptual Classification of the Primary Antibody Immunodeficiencies

<table>
<thead>
<tr>
<th>Category</th>
<th>B Cells</th>
<th>IgG Quantity</th>
<th>IgG Quality (antigen-specific antibody)</th>
<th>Diagnostic Examples</th>
<th>Ig Replacement Therapy</th>
<th>Cessation of Therapy for Re-evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Agammaglobulinemia SCID</td>
<td>Absolute indication, provide immediately</td>
<td>Inappropriate</td>
</tr>
<tr>
<td>II</td>
<td>Present</td>
<td>Low</td>
<td>Low</td>
<td>Hyper IgM CVID NEMO deficiency (subset)</td>
<td>Absolute indication, provide after firm diagnosis</td>
<td>Inappropriate if molecularly defined, otherwise a single lifetime trial of cessation is appropriate</td>
</tr>
<tr>
<td>II</td>
<td>Present</td>
<td>Normal</td>
<td>Low</td>
<td>Specific antibody deficiency NEMO deficiency (subset) Subclass deficiency with specific antibody defect</td>
<td>Provide if diagnosis is firm or infections persist</td>
<td>Single trial appropriate if diagnosis is not related to specific genetic defect</td>
</tr>
<tr>
<td>IV</td>
<td>Present</td>
<td>Low</td>
<td>Normal</td>
<td>Transplant Hypogammaglobulinemia of infancy Primary hypogammaglobulinemia</td>
<td>Provide when clinically indicated</td>
<td>Reassess if indicated with a single trial</td>
</tr>
<tr>
<td>V</td>
<td>Present</td>
<td>Normal, but IgG subclass deficient</td>
<td>Normal</td>
<td>IgG1, IgG2, or IgG3 subclass deficiency</td>
<td>Provide when clinically indicated</td>
<td>Reassess if indicated with a single trial</td>
</tr>
<tr>
<td>VI</td>
<td>Present</td>
<td>Normal</td>
<td>Normal</td>
<td>Recurrent infections</td>
<td>Provide as adjunct therapy as indicated</td>
<td>As appropriate</td>
</tr>
</tbody>
</table>

asking regarding each patient include: How is the patient feeling between doses? How many illnesses have they experienced, and when do they occur in their IgG cycle? Do they report good health and a generally high level of well-being throughout their cycle, or are they feeling increasingly “tired” as they approach their next dose, with more frequent reports of upper respiratory or other infection symptoms? A patient’s IgG trough level may be in the range mandated by their payer for insurance coverage; however, their physical symptoms and patterns of infection can tell another story about the adequacy of their current IgG dose. What, if any, adverse reactions does the patient experience following their IgG dose? As previously stated, IgG products are not equivalent, and patient tolerance of individual products can vary widely, sometimes necessitating a product change to achieve an acceptable and therapeutic response.

In spite of provider and physician collaboration and best efforts, optimal use of IgG in treating PIDD is often hampered by a payer’s lack of understanding about how this therapy works best, and the chronic nature of both the underlying PIDD condition as well as the need for lifelong treatment. In general, payers have an under-appreciation for the antibody quality of IgG as an indication for therapy. Other common misunderstandings include guidelines that may require any or all of the following: excessive trough level monitoring; dosage reductions to achieve “target” troughs (in the absence of any data to support this approach); dosing only after a particular IgG threshold is crossed (again, in the absence of any data to support this approach); and documented infections before approving therapy. Payers may also make excessive requests for cessation of therapy, particularly when the patient appears to be “better,” with few to no reported infections between treatments—which, ironically, is the goal of therapy and only achievable with adequate and uninterrupted treatment.

To be effective and prevent adverse outcomes, therapy needs to be delivered in optimal doses at optimal intervals, and for an indefinite period of time in many primary immune deficiency diseases. PIDD, in general, is not a condition that children “outgrow” or adults “overcome.” It’s important for clinicians and physicians, as a team, to advocate for the patient in achieving coverage of optimal therapy dosing, frequency and duration. This advocacy extends to ensuring that reimbursement issues do not interfere with the health of their patients.

When challenged by payers, physicians report altering their treatment plans, changing sites of care, reducing infusion frequency, and reducing dosage. Physicians also report that their patients experience health problems as a result of payer-man-

dated dose/schedule challenges. Few patients are able to self-pay for IgG therapy, therefore payer approval of the treatment plan is essential. This information indicates that the patient may not be getting the “best” dose or regimen for their specific situation. How do we rectify this? Clearly, optimizing costly IgG therapy is in everyone’s best interest—the patients as well as the payers.

While decisions on dosing, troughs, frequency or waiting for presence of infection should not be made arbitrarily by a payer, data is the tool needed to support the arguments made by prescribers and infusion providers for coverage of patient-specific IgG regimens. These are hard to obtain in such rare diseases. In the past few years, however, trough levels have been increasingly watched as a means of optimizing therapeutic effectiveness, with prescribing physicians generally targeting trough levels of 500-600 mg/dL. Immunologists who devote their practice to PIDD patients, however, are trending toward higher doses based on their personal experience observing patient outcomes. While a number of studies in the past decade have inferred connections between higher trough levels and improved patient outcomes, the actual trough levels required to minimize infection have not been previously established.

In an attempt to determine the nature of the relationship between IgG dose, trough level, and the incidence of infections, we conducted the first-ever meta-analysis in immunoglobulin therapy, which was published in 2010. Of the 16 studies meeting criteria for inclusion, the primary end point consistently measured was the incidence of pneumonia. The mean number of patients per study was 34, of which 49% had a diagnosis of Common Variable Immune Deficiency (CVID) and 37% had a diagnosis of x-Linked Agammaglobulinemia (XLA). Pneumonia was diagnosed in these studies by chest radiograph and hospitalization in one study, unspecified in 10 studies, or specifically identified as “bacterial pneumonia” in six studies.

The findings demonstrated a connection between IgG dose, trough level, and the incidence of pneumonia. Trough IgG was found to increase 121mg/dL for every 100mg/kg increase in dose, up to a trough of 1000mg/dL with a dose of 600mg/kg. This is not a maximum threshold, but simply where the data ends in the meta-analysis. Of clinical significance, particularly for those patients who continue to experience pneumonia despite current treatment with IVIG, was this finding: in general, for every 100mg/kg dose increase, and resultant 121 mg/dL trough increase, a 27% decrease was observed in the incidence of pneumonia up to a dose of 600mg/kg (the maximum studied). See Figures 1 and 2 for a visual representation of the linear increase
Figure 1
Relation of IgG Dose to Trough Level


Trough IgG increases 121mg/dl for every 100mg/kg dose increase

Figure 2
Relation of IgG trough Level to Pneumonia Incidence


Every 100mg/kg trough level increase decreases pneumonia incidence by 27%
in IVIG trough observed with incremental increases in dose, as well as the clinical outcome of reduced incidence of pneumonia.

This study demonstrates that previous recommendations for therapy based on a specific trough, such as 500 mg/dL, may not be in the patient’s best interest, and has the potential for higher risk of pneumonia. According to the relevant trends at the meta-level, patients have fewer infections with higher doses and therefore higher trough levels. These results can be utilized by the care team to advocate for payer coverage of higher doses for their patients.

Although it has not yet been studied, these findings may also be applicable to other types of serious infections. In fact, the researchers noted that their challenge in identifying consistent endpoints across the many studies they reviewed underscores the need to better define and coordinate research efforts in PIDD patients. They assert that clinicians in the field need to reach a standardized definition for infection, and consistently apply and report endpoints relevant to therapy.11

Another study released at nearly the same time, demonstrated similar findings.12 These researchers compared IVIG doses and IgG troughs to determine levels required for the patient to be considered “infection-free” and identified dose-related outcomes. This further supports that optimization of therapy is possible, and that home infusion providers play an integral role in communicating how their patients are responding to therapy so that adjustments in dose can be made by the prescriber.12

Risks of Immunoglobulin Therapy
IgG replacement therapy does present certain risks to patients, including anaphylaxis, transmitted infection, aseptic meningitis, renal failure, neurodegeneration and thrombosis/stroke. In addition, patients can experience mild events, such as chills, fever, headaches, vomiting and anxiety.13 Many reactions are rate- and/or product-specific and can be managed via rate reductions or trying a new product.

In a 2002 survey of PIDD patients, 61 percent reported infusion rate-related adverse events and 44 percent reported “serious” adverse events.14 If this data is an accurate representation of patient experience, then rates of adverse events are actually higher than those reported in product licensing studies.

A complete and accurate patient history—and collaboration among providers—is critical in evaluating the Ig therapy to minimize adverse events and optimize clinical results. It is important for home infusion providers to report back to the prescriber any issues as well as response to therapy.

**Subcutaneous Immunoglobulin Therapy**

For some patients, subcutaneous Ig (SCIG) therapy may be the best choice. This delivery method is therapeutically equivalent to intravenous administration for PI patients, but offers numerous advantages, including fewer systemic adverse events. Side effects tend to be localized to the administration site, making this a therapy suitable for self-administration. In addition, SCIG patients typically demonstrate greater stability in their serum Ig levels, compared to the peak and gradually diminishing trough experienced by IVIG patients over the course of several weeks between treatments.15,16 While SCIG therapy requires more frequent infusions (usually weekly as compared to monthly IVIG infusions), the reduced side effects and independence that come with self administration may offer improved quality of life.17

Candidates for SCIG are patients who have experienced adverse events with IVIG therapy, have IV access problems, have difficulty accessing nursing care or medical facilities, or have some other reason to seek independence from IV infusion.18 SCIG is a particularly beneficial option for patients who have experienced anaphylaxis with a previous IVIG dose.

The initial recommended weekly dose of SCIG is 100-200mg/kg body weight. Individual patient dose is determined by first multiplying the previous IVIG dose by 1.37 (when administering a 16 or 10 percent SCIG solution) or by 1.53 (when administering a 20 percent SCIG solution), then dividing the sum into weekly doses based on the previous treatment interval. Slight adjustments can be made to the final weekly dose to match vial size—no drug should be wasted in making the conversion from IVIG to SCIG. IVIG patients should begin SCIG one week following their regularly scheduled IVIG treatment.

A number of factors must be considered when choosing subcutaneous administration sites, including patient tolerance and lifestyle given that a typical infusion lasts from one to three hours. The total infusion time can be shortened by infusing into multiple sites at the same time. The FDA recommends no more than 15 mL per site, but many patients tolerate more than this volume. In reality, when a single infusion pump or device is used to administer therapy into multiple sites, it is not possible (today) to control the volume of drug that any one site receives. Ideally, each site would receive the same calculated total, however we know from experience that some sites are more amenable to expansion during the infusion and allow more drug to be deposited than others. Sites should continually be evaluated over time for any signs of tissue damage, avoiding such areas in the future. Rotating sites is an important aspect of patient and caregiver education, including documentation of site
placement so a rotation pattern can be established. Interestingly, better site tolerance has been found with 20% SCIG compared to the 16-percent solution.

SCIG is administered via a syringe driver or infusion pump, through specialized subcutaneous needle devices that have been specifically designed for this type of infusion. Future innovation may bring packaged systems or autoinfusers, but today patients and caregivers follow a multi-step process of drug and pump preparation, needle set and supply preparation, infusion site selection and skin antisepsis, needle insertion and blood return check and infusion initiation. With practice, this process becomes very routine, which is why sound principles of asepsis in handling drug and supply items is an essential component of initial patient education.

Although very few systemic side effects are reported with SCIG infusions, local side effects are common, including pain and erythema at the site. Because a “depot” of drug solution is being instilled into the subcutaneous tissue, a swelling or “lump” is expected that may persist for hours to days.

Recent studies have examined the use of SCIG preceded by a subcutaneous hyaluronidase injection, an enzyme that acts to increase tissue permeability, with the expectation that more SCIG may be infused per site in a monthly subcutaneous infusion. Initial results suggest single-site infusions of more than 600 mL with once or twice a month dosing may be possible. Infusion rates of 300 mL/hr led to mostly mild local reactions. Longer-term safety data are needed, and clinical trials are currently in progress. It is possible that patients who have experienced IV-associated adverse events may better tolerate IgG therapy via this enhanced subcutaneous delivery method. Questions remain about a patient and/or caregivers ability to perform self-administration with this therapy regimen, in addition to other specific management considerations.

**Best Practice for Immunoglobulin Therapy in PIDD Patients**

The American Academy of Allergy and Immunology Primary Immunodeficiency Committee has developed an “IVIG toolkit” to educate payers and regulators who are responsible for coverage determinations, and to aid physicians in the safe, effective and appropriate use of IVIG for patients with primary immunodeficiency diseases (available for download from the AAAAI website at www.aaaai.org/members/resources/initiatives/ivig.stm). In addition to work group findings and guidelines, the toolkit includes eight guiding principles for safe, effective and appropriate use of IVIG (see Table 3).

**Table 3**

Eight Guiding Principles for Safe, Effective and Appropriate Use of IVIG

1. **Indication.** Ig therapy is indicated as replacement therapy for patients with primary immunodeficiency diseases characterized by absent or deficient antibody production.
2. **Diagnoses.** There are a large number of primary immunodeficiency diagnoses for which IVIG is indicated and recommended.
3. **Frequency of Ig Treatment.** IVIG is indicated as continuous replacement therapy for primary immunodeficiency.
4. **Dose.** IVIG is indicated for patients with primary immunodeficiency at a starting dose of 400-600mg/kg every 3-4 weeks (100-200mg/kg/wk for SCIG).
5. **IgG Trough Levels.** IgG trough levels can be useful in some diagnoses to guide care but are NOT useful in many and should not be a consideration in access to Ig therapy.
6. **Site of Care.** The decision to infuse IVIG in a hospital, hospital outpatient, community office or home-based setting must be based upon clinical characteristics.
7. **Route.** Route of immunoglobulin administration must be based upon patient characteristics.
8. **Product.** IVIG products are not interchangeable.

In particular, the guiding principle for “site of care” is further delineated in the tool kit with criteria supporting each care setting. The decision of where to administer a patient’s IgG therapy should be made based upon patient experience and circumstance in order to minimize risk to the patient. Any changes of IGIV product brand should be provided under physician supervision in a facility equipped to handle the most severe acute medical complications whenever feasible. In addition, the AAAI PIDD Committee notes that certain patients will require higher levels of monitoring and intervention during IGIV infusions. Conversely, patients who have tolerated IGIV therapy without a history of adverse events may be considered for lower levels of supervision during infusion. Bottom line: there is no one “ideal” site of care for all patients, but rather an ideal site of care for each specific patient.

**Conclusion**

Ig therapy represents life-saving or life-altering treatment for many patient diagnoses, however because it is a blood product
inherently in limited supply, prioritizing its use is a responsibility shared by all prescribers. Optimization of Ig replacement regimens is best accomplished through a collaborative effort among the patient’s care team, and can be enhanced with new trough level data. Treatment decisions are complex and multi-factorial, and should always be made with the patient’s health and well-being at the forefront. How the IgG therapy is administered is yet one more decision to be made, and research has demonstrated that there may be an advantage to SCIG administration for the right patients. Optimal use needs to be tailored to the patient, and requires communication between providers about patient issues and response to therapy as well as a thorough understanding of relevant history and patient conditions.

Our knowledge regarding the optimal use of immunoglobulin therapy has changed rapidly over the last 10 years. As research continues to yield new insights into future uses and administration methods, home infusion providers will need to stay informed and prepared for new approaches in the home setting.

References


About the Author

Dr. Jordan S. Orange is an Associate Professor in the Department of Pediatrics at the University of Pennsylvania School of Medicine and an attending physician in the Divisions of Immunology, Allergy, and Rheumatology in the Children’s Hospital of Philadelphia. He received his MD and a PhD in immunology Brown University and served as a resident in pediatrics at The Children’s Hospital of Philadelphia. He received subspecialty training in Allergy Immunology and Rheumatology at Boston Children’s Hospital. He is currently the holder of the Jeffrey Modell Endowed Chair in Immunology at The Children’s Hospital of Philadelphia.

Dr. Orange is actively involved in basic and clinical research. From a clinical standpoint he has focused entirely on Primary Immunodeficiency diseases and has focused on defects of innate immunity. He has received funding from the National Institutes of Allergy and Immunology and the US Immunodeficiency Network to support his laboratory work. Dr. Orange has also participated in several relevant clinical scholarship projects. These include the 2005 Practice Parameter for the Diagnosis and Management of Primary Immunodeficiency Diseases published in the *Annals of Asthma Allergy and Immunology*, and is the lead author on the 2006 supplement to the *Journal of Allergy and Clinical Immunology* entitled “Use of IVIG in Human Disease”. In 2010, Dr. Orange and colleagues published the first meta-analysis examining the correlation of IVIG trough level to incidence of pneumonia.

In addition to his work in immunodeficiency research, Dr. Orange participates in advocacy efforts on behalf of patients affected by primary immunodeficiency diseases and is the recipient of the Immune Deficiency Foundation 2007 Advocacy Award.

Dr. Orange is a Fellow of the American Academy of Allergy Asthma and Immunology and is currently serving as chair of the Basic and Clinical Immunology interest section. He also serves as a member of the US Immunodeficiency Network’s Education and Advisory Committees and has participated on several projects with the Clinical Immunology Society including the Summer School for Primary Immunodeficiency and the Primary Immunodeficiency Diseases Consortium. Dr. Orange is also a member of the Medical Advisory Council of the Immune Deficiency Foundation and is Director of the Jeffrey Modell Diagnostic Center at The Children’s Hospital of Philadelphia.