Exercise as Medicine
Prescribing the Right Amount

How to Diagnose Infants with PIDD

Understanding & Treating CVID

Defending Kids Against Bullying

Diagnosing Specific Antibody Deficiency
GAMUNEX®-C
Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use GAMUNEX®-C safely and effectively. See full prescribing information for GAMUNEX-C.

GAMUNEX-C, [Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified]
Initial U.S. Approval: 2003

WARNING: ACUTE RENAL DYSFUNCTION and FAILURE
See full prescribing information for complete boxed warning.

- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients.
- Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMUNEX-C does not contain sucrose.
- For patients at risk of renal dysfunction or failure, administer GAMUNEX-C at the minimum concentration available and the minimum infusion rate practicable.

INDICATIONS AND USAGE
GAMUNEX-C is an immune globulin injection (human) 10% liquid indicated for treatment of:

- Primary Humoral Immunodeficiency (PI)
- Idiopathic Thrombocytopenic Purpura (ITP)
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

CONTRAINDICATIONS

- Anaphylactic or severe systemic reactions to human immunoglobulin
- IgA deficient patients with antibodies against IgA and a history of hypersensitivity

WARNINGS AND PRECAUTIONS

- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available immediately to treat any acute severe hypersensitivity reactions.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of developing acute renal failure.
- GAMUNEX-C is not approved for subcutaneous use in ITP patients. Due to a potential risk of hematoma formation, do not administer GAMUNEX-C subcutaneously in patients with ITP.
- Hyperproteinemia, with resultant changes in serum viscosity and electrolyte imbalances may occur in patients receiving IGIV therapy.

ADVERSE REACTIONS

- PI – The most common adverse reactions (≥5%) with intravenous use of GAMUNEX-C were headache, cough, injection site reaction, nausea, pharyngitis and urticaria. The most common adverse reactions (≥5%) with subcutaneous use of GAMUNEX-C were infusion site reactions, headache, fatigue, arthralgia and pyrexia.
- ITP – The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, vomiting, fever, nausea, back pain and rash.
- CIDP – The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, fever, chills, hypertension, rash, nausea and asthenia.

DRUG INTERACTIONS

- The passive transfer of antibodies may transiently interfere with the response to live viral vaccines, such as measles, mumps and rubella. Passive transfer of antibodies may confound serologic testing.

USE IN SPECIFIC POPULATIONS

- Pregnancy: no human or animal data. Use only if clearly needed.
- Geriatric: In patients over 65 years of age do not exceed the recommended dose, and infuse GAMUNEX-C at the minimum infusion rate practicable.

Talecris Biotherapeutics

Talecris Biotherapeutics, Inc.
Research Triangle Park, NC 27709 USA
U.S. License No. 1716
08939771/08939782-BS
Revised: October 2010
Important Safety Information for GAMUNEX-C

Gamunex-C, Immune Globulin Injection (Human), 10% Caprylate/Chromatography Purified, is indicated for the treatment of primary humoral immunodeficiency disease (PI), idiopathic thrombocytopenic purpura (ITP), and chronic inflammatory demyelinating polyneuropathy (CIDP).

Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Gamunex-C does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gamunex-C at the minimum concentration available and the minimum infusion rate practicable.

Gamunex-C is contraindicated in individuals with acute severe hypersensitivity reactions to Immune Globulin (Human). It is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity.

Gamunex-C is not approved for subcutaneous use in patients with ITP or CIDP. Due to the potential risk of hematoma formation, Gamunex-C should not be administered subcutaneously in patients with ITP.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy.

Thrombotic events have been reported in association with IGIV. Patients at risk for thrombotic events may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization and/or known or suspected hyperviscosity.

There have been reports of noncardiogenic pulmonary edema [Transfusion-Related Lung Injury (TRALI)], hemolytic anemia, and aseptic meningitis in patients administered with IGIV.

The high dose regimen (1g/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.

Gamunex-C is made from human plasma. Because this product is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient’s blood may yield positive serological testing results, with the potential for misleading interpretation.

In clinical studies, the most common adverse reactions with Gamunex-C were headache, fever, chills, hypertension, rash, nausea, and asthenia (in CIDP); headache, cough, injection site reaction, nausea, pharyngitis, and urticaria with intravenous use (in PI) and infusion site reactions, headache, fatigue, arthralgia and pyrexia with subcutaneous use (in PI); and headache, vomiting, fever, nausea, back pain, and rash (in ITP).

The most serious adverse reactions in clinical studies were pulmonary embolism (PE) in one subject with a history of PE (in CIDP), an exacerbation of autoimmune pure red cell aplasia in one subject (in PI), and myocarditis in one subject that occurred 50 days post-study drug infusion and was not considered drug related (in ITP).

*CIDP=Chronic inflammatory demyelinating polyneuropathy; PI=Primary immunodeficiency; ITP=Idiopathic thrombocytopenic purpura.


You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see adjacent page for brief summary of GAMUNEX-C full Prescribing Information.
About IG Living
IG Living is the only magazine dedicated to bringing comprehensive healthcare information, immune globulin information, community and reimbursement news, and resources for successful living directly to immune globulin consumers and their healthcare providers.

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All manuscripts should be submitted in MS Word, in Arial font. Manuscripts should be between 650 and 1,300 words in length, with unjustified margins and without any other formatting. Submission guidelines are available for download from the Contact Us page on www.IGLiving.com. Email manuscripts to editor@IGLiving.com. IG Living retains the right to edit submissions. The contents of each submission and their accuracy are the responsibility of the author(s) and must be original work that has not been, nor will be, published elsewhere, without the written permission of IG Living. A copyright agreement attesting to this and transferring copyright to FFF Enterprises will be required. Acceptance of advertising for products and services in IG Living is in no way constitutes endorsement by FFF Enterprises. ©2012 FFF Enterprises Inc.

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IG Living Magazine is read by 30,000 subscribers who are patients who depend upon immune globulin products and their healthcare providers. For information about advertising in IG Living, download a media kit at www.igliving.com/Advertise.aspx. Or contact Cheryl Brooks at (800) 843-7477 x1177 or cbrooks@ff ENTERPRISES.com.
Diagnosing PIDD in Infants
"With modern diagnostic testing, a definitive diagnosis can be made in most cases of PIDD, and the precise molecular defect often can be identified."

MARK T. HAGGARD
High School Teacher, Football Coach
and Parent of PIDD Children

Defending Kids Against Bullying
"Kids who show outward signs of illness make them a target of opportunity."

TERRY O. HARVILLE, MD, PHD
Medical Director, Special Immunology Laboratory, University of Arkansas for Medical Sciences

Diagnosing Specific Antibody Deficiency: Interpreting Pre-/Post-Immunization Pneumococcal Vaccine Responses
"Whether a patient makes specific antibodies can be determined by performing pre-/post-immunization antibody titer analyses to pneumococcal vaccine."

KRIS MCFALLS
Patient Advocate, IG Living magazine

Medicare and IG
“Both intravenous IG (IVIG) and subcutaneous IG (SCIG) therapy are covered under Medicare Part B.”

Simple But Effective Home Exercise Equipment
“While there may not be a cure for most chronic illnesses, regular exercise has been proved to decrease pain, increase stamina and improve overall health.”

MATTHEW HANSEN, DPT, MPT, BSPTS
Physical Therapist
How Much Exercise Is Too Much or Too Little?
“The easiest formula for finding the right amount of exercise is for a patient to take note of how they feel afterward.”

Connect with Other IG Living Readers through Monthly Teleforums!
IGL’s Readers Group Teleforums allow readers to connect with others to share their experiences living with chronic diseases. Here’s how you can participate:

- Email IG Living to be added to our email invitation list for the teleforums.
- IG Living will send you invitations to let you know when the two-per-month, hosted, toll-free teleforums will be held, as well as what topic relevant to the IG community will be discussed.
- The moderated, hour-long calls will be filled on a first-come, first-served basis and will be limited to 15 readers.

In addition to connecting with others, IG Living’s patient advocate can help you determine if there’s a patient organization support group in your area. Or, she can help you to start an IGL Readers Group of your own. To join a group or start one in your area, visit www.IGLiving.com and click on IGL Readers Groups.

Sign up for the Teleforums now by emailing rrhodes@IGLiving.com or calling (800) 843-7477, ext. 1362.
It’s Tough Being a Kid with a Chronic Illness

Being a kid is tough. Being a kid with a chronic illness is tougher. Just ask those kids, their parents, the doctors and the advocates on their behalf who diagnose, treat and support them. In this issue of IG Living, we look at the topic of chronic illness in children from all perspectives.

In our feature article, Diagnosing PIDD in Infants, Dr. Melvin Berger, a specialist in pediatric immunology, shares his vast knowledge about the various forms of primary immunodeficiency diseases, their symptoms, the stages of diagnostic evaluation and the urgent need for greater awareness about these diseases. Dr. Berger is one of the few physicians in this specialized area who can answer the often-asked questions: “Why does it take so long to diagnose an immune deficiency in children?” “What are the telltale signs and tests to recognize and confirm an immune deficiency in kids?” And, “What needs to be done to increase awareness among medical professionals about immune deficiencies to help children get diagnosed sooner and allow them to lead healthy, productive lives?”

Diagnosis is key to helping kids with chronic illness, but there are other concerns. Oftentimes, having a chronic illness can exacerbate issues that all kids may face such as bullying, a problem that affects some 2.7 million students nationwide. As Mark Haggard, a father of two children with common variable immune deficiency, explains in his article, Defending Kids Against Bullying, chronically ill children often show outward signs of illness, which makes them “a target of opportunity” for bullies. Mark discusses why kids bully, and he provides some guidance for kids and their parents about how to respond.

With all the added challenges of chronic illness, it takes courage and mental toughness to grow up as a sick kid. Those attributes aptly describe 20-year-old Sarah Eames, who was diagnosed at age 15 with myasthenia gravis. Our interview with Sarah in our Let’s Talk column reveals that for her the most difficult part of being a teen with a chronic illness was coming to terms with it herself and not letting it define her. Now, her experience has led to her desire to work with kids, and her advice to other children who are chronically ill is to “keep going forward even when the going gets tough.”

Thankfully, there is a lot of support for children with chronic illness and their parents to make life a little less tough. Due to efforts by physicians like Dr. Berger, organizations that devote effort to raising the awareness of immune deficiency diseases, and advances in diagnostic testing, these diseases are becoming more recognizable, and many more children are getting the IG treatment they so desperately need.

Support for kids such as Sarah and their parents also comes from patient advocates. IG Living is proud to offer patients everywhere access to a patient advocate, and we have been very blessed to have had Kris Mc Falls on our team for the past seven years providing advice and guidance that has helped so many of our readers. As Kris explains on the adjoining page, she has accepted a new challenge. It is with heartfelt gratitude for her work with us and for all she has done and continues to do for the patient community that we wish Kris all the best, and we support her in her new endeavors.

Ronale Tucker Rhodes, MS, Editor
Celebrating New Opportunities

It has been nearly seven years since I began my position with IG Living’s founder and publisher, FFF Enterprises. And, I remember feeling then what I still feel now: It was a wonderful opportunity full of challenge and promise. Not only have I had the chance to work for a company like FFF Enterprises, which has integrity and a patient-first philosophy I have long admired, I have had the chance to connect with all of you — patients within the immune globulin (IG) community — through IG Living magazine. It has been an honor and a privilege to serve as a writer for IG Living, as well as a patient advocate for many of you. I take pride in the amazing work that has been done to serve the IG community. That is why it is with mixed emotions that I am announcing I have once again been blessed with a wonderful new opportunity. I have accepted the position of manager of reimbursement with CSL Behring, and this will be my last issue as a member of the IG Living staff.

The funny thing about opportunities is that sometimes when you least expect them, they find you. And I assure all of you that is the case for me. My colleagues here at IG Living celebrate with me as I embark on this new journey, and while I won’t be as visible, I will still be very much involved with this community. I can tell you, without a doubt, that the work is far from done, and I will always be a part of it in some way.

Winston Churchill was quoted as saying: “There is nothing wrong with change, if it is in the right direction.” I believe at IG Living we have made positive changes in the right direction, always with an eye toward our mission to support the IG community through education, communication and advocacy. For instance, our social media outreach has allowed readers from all over the globe to connect with one another. Many of our articles are now being written by experts in the fields of immunology, rheumatology and neurology. And, in 2011, we launched the first of what we plan to be an annual writing contest through which several of our readers shared the intimate details of their personal battles with chronic illness.

I have enjoyed reading your letters, emails, Facebook comments, as well as comments submitted with your subscription requests. And I can promise you that I have personally read every single one of them, as have many others on our IG Living staff. We take the responsibility to be good stewards of the rare disease community very seriously. Therefore, positive, forward change will continue to happen at IG Living, and you can be part of it. I encourage all of you to keep telling your story, continue to comment on the articles, and continue to make suggestions for new articles. Your needs can only be met if you let them be known!

I would like to thank my sons, Konner and Keegan, for allowing me to make their lives so public. It is only through sharing our trials that others can understand them. And I am grateful they allowed me to share some of our experiences with you. Additionally, I would like to thank the IG Living staff for their wonderful support and for making me look like a bona fide writer. Many on our staff go unrecognized and unnoticed, but I can promise you, they all care as much as I do. I must give a special thanks to Patrick Schmidt, FFF’s CEO, who has had the vision, caring and determination to invest in this community and to back a publication that is patient-focused. Thanks also go out to the IG Living advertisers who continue to believe in and support this publication and our community. Without this support, IG Living would not be able to continue. Last, I would like to thank all of you, our readers, for allowing me the honor of being a small part of your lives. I encourage you to celebrate your opportunities, rise to your challenges and embrace them all with passion. Know that, as I step into my new professional role, my personal role as part of this wonderful community and as a Facebook fan and avid IG Living reader will continue.

Kris McFalls, IG Living’s Patient Advocate

My colleagues here at IG Living celebrate with me as I embark on this new journey, and while I won’t be as visible, I will still be very much involved with this community.
**Immunology 101: Diagnosing Specific Antibody Deficiency: Interpreting Pre- and Post-Immunization Pneumococcal Vaccine Responses**

By Terry O. Harville, MD, PhD

As we discussed in previous columns, an antibody deficiency disorder can be diagnosed in two ways: 1) deficient serum IgG levels, usually accompanied by deficient IgA and/or IgM levels, in a patient who also fails to make appropriate specific antibodies (such as in X-linked agammaglobulinemia) or 2) normal IgG, IgA and IgM serum levels in a patient who fails to make specific antibodies.

Whether a patient makes specific antibodies can be determined by performing pre- and post-immunization antibody titer analyses to pneumococcal vaccine. For instance, a poor response to pneumococcal vaccination, whether a patient has low IgG (and/or IgA and IgM) levels or normal serum IgG, IgA and IgM levels, can be a determinant of a specific antibody deficiency (SAD). However, many medical and insurance personnel may be confused by a SAD diagnosis for patients with normal serum IgG, IgA and IgM levels, even though these patients respond poorly to pneumococcal vaccination. It’s a common misconception that if the IgG serum levels are normal, then the humoral immune system must be normal. That is wrong! The humoral immune system (antibodies and complement proteins) may be within normal parameters only when appropriate specific antibody levels are made and maintained after pneumococcal vaccination.

Currently, 23 different strains of pneumococcal bacteria are used to make up the pneumococcal vaccine. Since each strain will result in the production of a "unique" antibody, the term "serotype" is used to denote each strain and the antibody directed against it. Therefore, 23 pneumococcal serotypes can be identified in the vaccine, and they are composed of 23 unique antibodies and the "strength" of each antibody response, which is called the "titer." Thus, 23 serotype titers can be determined from the pneumococcal vaccine.

To perform a pneumococcal assay, first a blood sample is taken from a patient (pre-immunization serum), and then the pneumococcal vaccine is given. In approximately four weeks, another blood sample is obtained for the post-immunization serum. Both sera are then assayed to obtain specific titer values.

The number of serotype titers analyzed has changed over the years. Initially, as few as four serotypes were analyzed. This grew to seven, 10, 12, 14, 15 and, now, to the full 23 serotypes. Many studies comparing the assay regarding the potential for diagnosing an antibody deficiency have looked at the responses of 10 to 15 serotypes. Based on these studies, a consensus has developed concerning the interpretation of the results. In general, a titer value exceeding 1.3 mcg/mL is defined as protection against the specific pneumococcal serotype tested, whereas values less than 1.3 mcg/mL are defined as not protective. Previously, the titer value was considered a meaningful immune response if there was a fourfold increase between the pre- and post-immunization titers (example: if pre = 4 mcg/mL, then post >16 mcg/mL would be considered normal). Now, if the pre-immunization titer is greater than 1.3 mcg/mL, then a twofold increase may be accepted as normal (example: if pre = 4 mcg/mL, then post >8 mcg/mL is considered normal). For nonprotective pre-immunization titers, the post-immunization titer values should increase into the protective range, with a threefold increase expected. For very low pre-immunization titers, a fourfold increase into the protective post-immunization range is expected.

The next issue considered is the "number" of appropriately protective post-immunization serotype titers. For children between 2 and 6 years of age, "normal" is defined by having more than 50 percent of the post-immunization titers well into the protective range, with titer increases of twofold to fourfold, depending on how low the pre-immunization titers were. For adults, it is 75 percent.

TERRY HARVILLE, MD, PhD, is medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, and a consultant for immunodeficiencies, autoimmunities and transplantation.

**Editor’s Note:** This Immunology 101 column, introduced in the April-May 2010 issue of IG Living, is intended to be a basic course in immunology.
WARNING: ACUTE RENAL DYSFUNCTION AND ACUTE RENAL FAILURE

- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs.

- Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. [1] GAMMAKED does not contain sucrose.

- For patients at risk of renal dysfunction or failure, administer GAMMAKED at the minimum concentration available and the minimum infusion rate practicable. (see Warnings and Precautions)

Please see the GAMMAKED Brief Summary of Prescribing Information on the following page for additional prescribing details.
GAMMAKED consists of immune globulin injection (human) 10% liquid that is used:

**Indications**

- **Use:** GAMMAKED is indicated for the treatment of acute hypogammaglobulinemia due to primary immunoglobulin deficiencies (PI) and for the treatment of hypogammaglobulinemia due to secondary causes such as infections, cancer, or immune dysfunction.

**Contraindications**

- GAMMAKED is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin.
- GAMMAKED is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity.

**Warnings and Precautions**

- Severe hypersensitivity reactions may occur with IGIV products, including GAMMAKED. In this case, discontinue GAMMAKED infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reaction.
- Assure that patients are not volume depleted prior to the initiation of the infusion of GAMMAKED. Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk for developing acute renal failure. Assess renal function, including measurement of blood urea nitrogen (BUN)/serum creatinine, prior to the initial infusion of GAMMAKED and at appropriate intervals. If renal function deteriorates, consider discontinuation of GAMMAKED. For patients judged to be at risk for developing renal dysfunction (e.g., any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs) administer GAMMAKED at the minimum infusion rate practicable.

- Do not administer GAMMAKED subcutaneously in patients with ITP because of the risk of hematoma formation.

**Adverse Reactions**

**Clinical Trials**

- **PI:** The most common adverse reactions (≥5%) with intravenous use of GAMMAKED were headache, cough, injection site reaction, nausea, and hives. Vomiting was reported more frequently in pediatric patients. The most common adverse reactions (≥5%) with subcutaneous use of GAMMAKED were infusion site reactions, headache, fatigue, joint pain, and fever.
- **ITP:** The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, vomiting, fever, nausea, back pain, and rash.
- **CIDP:** The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, fever, chills, hypertension, rash, nausea, and weakness.

**Postmarketing Experience**

- **Hemolytic anemia and aseptic meningo-**

- **Drug Interactions**

- **Respiratory:** Apnea, Acute Respiratory Distress Syndrome (ARDS), TRALI, cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm
- **Cardiovascular:** Cardiac arrest, thromboembolism, vascular collapse, hypotension
- **Neurological:** Coma, loss of consciousness, seizures/convulsions, tremor
- **Integumentary:** Stevens-Johnson syndrome, epidermolysis, erythema multiforme, bullous dermatitis
- **Hematologic:** Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coomb's) test
- **General/Body as a Whole:** Pyrexia, rashes
- **Musculoskeletal:** Back pain
- **Gastrointestinal:** Hepatic dysfunction, abdominal pain

**Use in Specific Populations**

- **Pregnancy Category C.** There is no human or animal data. It should only be given to a pregnant woman if clearly needed.
- **Geriatric:** In patients over 65 years of age, do not exceed the recommended dose, and administer GAMMAKED at the minimum infusion rate practicable.

**Rx Only**

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Research Triangle Park, NC 27709

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Fort Lee, NJ 07024

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Contest
Enter IG Living’s Second Annual Essay Contest!

IG Living is hosting its second annual essay contest open to IG patients and their caregivers ages 18 and older. Similar to last year’s contest, we are asking entrants to start their essay with an identical phrase. This year, we have chosen the topic of risk-taking.

When have you taken a risk, no matter how small? Have you tried an exotic food to ease GI issues, learned a new language to take your mind off your illness, or flirted with a complete stranger to feel a little more “normal”? How did things turn out? What did you learn? To participate in the contest, begin your essay by completing this sentence: The last time I did something for the first time, I...

Guidelines for essay submittal are as follows:

- Write no more than 600 words, and be sure the essay is typed and double-spaced.
- Include a title for your essay, and make sure it includes the author's name, complete address, email, phone number and word count.
- Submit your entry electronically as a Microsoft Word attachment to editor@IGLiving.com, or submit it by mail to: IG Living Essay Contest, 41093 County Center Drive, Temecula, CA 92591, Attention: Carla Schick.
- Mail your entry by June 1, 2012 (must be postmarked by that date).

IG Living's judges will rate the entries on a scale of one to 10 on five criteria:
- Organization (the writing flows logically with clear structure)
- Mechanics (spelling, capitalization and punctuation are correct)
- Content (subject is discussed clearly, and the reader is left with a finished feeling)
- Creativity (content is compellingly interesting for our audience)
- Effectiveness (the whole entry is effective in its purpose for our audience)

Winners will be announced on July 1st. The first-place winner will be awarded a new Kindle eReader, and their essay will be published in IG Living magazine. Second- and third-place winners will be awarded a $50 gift card, and their essays will be published in an IG Living blog.

This is your opportunity to get published in IG Living! For additional entry rules, refer to the IG Living blog contest page at www.IGLiving.com.

Research
Autoimmune Disease Linked to Non-Healing Wounds

A study by a Georgetown rheumatologist found that patients who had open wounds that were very slow to heal also had underlying autoimmune diseases. The study reviewed charts of 340 patients treated at a high-volume wound clinic at Georgetown University Hospital in Washington, D.C., for mostly leg ulcers during a three-month period in 2009. Forty-nine percent of those patients had diabetes, which is a typical rate, yet 23 percent also had underlying autoimmune diseases. Of those 78 patients who had autoimmune diseases, most had rheumatoid arthritis, lupus or livedoid vasculopathy, a type of vascular disease. According to the researchers, the connection between these relatively rare disorders and wounds that don’t heal is unrecognized. The findings also showed that autoimmune disease-associated wounds were significantly larger at the patient's first visit, and that skin grafts were more likely to fail in these patients.
**Research**

**Combined IVIG Treatment Effective to Treat Kawasaki Disease**

Researchers from Kitasato University School of Medicine in Japan found that combining intravenous methylprednisolone pulse and intravenous immunoglobulin (IVIG) to treat patients with Kawasaki disease appears safe and effective. The researchers looked at data on 122 patients with Kawasaki disease who were randomly assigned to either the combined treatment or IVIG alone. Fever abated more quickly in 19 of 22 patients in the combined group compared with six of 26 patients in the IVIG group. In addition, coronary artery dimension z scores of 2.5 or more at one month were higher in the IVIG group than in the combined treatment group. Adverse events of the combination therapy included hypothermia, bradycardia and hypertension in some patients; however, these events were transient and not serious in either group. “Approximately 15 percent to 20 percent of patients with [Kawasaki disease] are not responsive to initial IVIG treatment, and these patients are at a higher risk for coronary artery lesions,” the researchers wrote. “It is important to identify these patients because they might benefit from more aggressive initial treatment.”

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I imagine caring for your child with hemophilia with no factor, refrigerator, running water, electricity, or transportation to a clinic. This is the reality for thousands of families in developing countries. For just $20 a month, you can help an impoverished child with hemophilia. Become a sponsor today!

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Caring for people with hemophilia around the world—one at a time.
Research
Two in Five Adults with RA Are Inactive

A new study finds that two in five adults (42 percent) with rheumatoid arthritis (RA) are inactive. The study, which was funded by a grant from the National Institutes for Arthritis and Musculoskeletal and Skin Diseases, analyzed data on 176 RA patients 18 years of age and older enrolled in a randomized controlled trial to assess the effectiveness of an intervention promoting physical activity. Researchers evaluated pre-intervention data for inactivity, which was defined as no sustained 10-minute periods of moderate to vigorous physical activity during a week. They also assessed the relationships between inactivity and modifiable risk factors such as motivation for physical activity, obesity and pain. In addition to the inactivity findings, researchers found that 53 percent of study participants lacked strong motivation for physical activity, and 49 percent lacked strong beliefs in the benefits of physical activity.

Until the early 1980s, medical experts recommended medication and rest for those with RA. However, current medical evidence suggests that regular moderate physical activity benefits arthritis sufferers by maintaining joint flexibility, improving balance, strengthening muscles and reducing pain. Therefore, taking measures to motivate RA patients to increase their physical activity will improve public health. “While there is much evidence of the benefits of physical activity, RA patients are generally not physically active, and physicians often do not encourage regular physical activity in this patient population,” explains Dr. Jungwha Lee, an assistant professor in the Department of Preventive Medicine at Northwestern University Feinberg School of Medicine in Chicago, Ill., and the study’s lead researcher. “Our study aims to expand understanding of the risk factors associated with inactivity among adults with RA and encourage clinical interventions that promote participation in physical activity.”

SCiG infusion problems? ... it could be the needles.

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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Octagam, Immune Globulin Intravenous (Human), safely and effectively. See full prescribing information for Octagam.

Octagam® [Immune Globulin Intravenous (Human)]
5% Liquid Preparation
Initial US Approval: 2004

WARNING: ACUTE RENAL DYSFUNCTION and RENAL FAILURE
See full prescribing information for complete boxed warning.

- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may be associated with Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients.
- Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Octagam 5% liquid does not contain sucrose.
- Administer IGIV products at the minimum concentration available and the minimum infusion rate practicable.

Recent Major Changes

Warnings and Precautions – Hyperproteinemia 8/2008

Indications and Usage

- Octagam is an immune globulin intravenous (human), 5% liquid, indicated for treatment of primary humoral immunodeficiency (PI).

Dosage and Administration

Intravenous use only.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Initial Infusion rate</th>
<th>Maintenance infusion rate (if tolerated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>300-600mg/kg</td>
<td>0.5mg/kg/min</td>
<td>3.33mg/kg/min Every 3-4 weeks</td>
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</tbody>
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- Ensure that patients with pre-existing renal insufficiency are not volume depleted; discontinue Octagam 5% liquid if renal function deteriorates.
- For patients at risk of renal dysfunction or thrombotic events, administer Octagam 5% liquid at the minimum infusion rate practicable.

Dosage Forms and Strengths

Octagam 5% liquid is supplied in 1.0g, 2.5g, 5g, 10g, or 25g single use bottles.

Contraindications

- Anaphylactic or severe systemic reactions to human immunoglobulin.
- Immunoglobulin A (IgA) deficient patients with antibodies against IgA and a history of hypersensitivity.
- Patients with acute hypersensitivity reaction to corn.

Warnings and Precautions

- Hyperproteinemia, increased serum viscosity and hyponatremia occur in patients receiving IGIV therapy.
- Thrombotic events have occurred in patients receiving IGIV therapy. Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity.
- Aseptic Meningitis Syndrome has been reported with Octagam 5% liquid and other IGIV treatments, especially with high doses or rapid infusion.
- Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration.
- IGIV recipients should be monitored for pulmonary adverse reactions (TRALI).
- The product is made from human plasma and may contain infection agents, e.g. viruses, and theoretically, the Creutzfeldt-Jakob disease agent.

Adverse Reactions

Most common adverse reactions with an incidence of >5% during a clinical trial were headache and nausea. To report SUSPECTED ADVERSE REACTIONS, contact Octapharma at 1-866-766-4860 or FDA at 1-800-FDA-1008 or www.fda.gov/medwatch.

Drug Interactions

- The passive transfer of antibodies may confound the results of serological testing.
- The passive transfer of antibodies may interfere with the response to live viral vaccines.

Use in Specific Populations

- Pregnancy: no human or animal data. Use only if clearly needed.
- In patients over age 65 or in any person at risk of developing renal insufficiency, do not exceed the recommended dose, and infuse Octagam 5% liquid at the minimum infusion rate practicable.

How Supplied

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www.octapharma.com/usa

Revised: September 2009
IMPORTANT SAFETY INFORMATION

Octagam® is contraindicated in individuals with intolerance to immunoglobulins, especially in immunoglobulin A (IgA) deficiency, when the patient has IgE mediated antibodies to IgA. Immune Globulin Intravenous (Human) (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Other possible side effects with Octagam include: aseptic meningitis, hemolysis, transfusion-related acute lung disease (TRALI) and thrombotic events.

Immune Globulin Intravenous (Human) products have been reported to be associated with various minor reactions, such as headache, chills, backache, chest pain, fever, allergic reactions, arthralgia, dizziness, and changes in blood pressure, cutaneous reactions and/or nausea and vomiting. Cases of reversible aseptic meningitis and migraine and isolated cases of reversibly hemolytic anemia and reversible increases in liver function tests have been observed with Octagam. Immediate anaphylactic and hypersensitivity reactions are a remote possibility.

As with all medicine made from human plasma, the risk of spreading infections agents, including viruses, cannot be completely eliminated.

Some types of blood glucose testing systems falsely interpret the maltose contained in Octagam as glucose. This has resulted in falsely elevated glucose readings and, consequently, in the inappropriate administration of insulin, resulting in life-threatening hypoglycemia.

References
1. Octagam®, Immune Globulin Intravenous (Human) 5% Liquid Preparation, complete Prescribing Information. 2009.

For more information, please contact us:

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Proven clinical efficacy in patients with primary immunodeficiency (PI)1,2
Updated manufacturing process to enhance thromboembolic safety3
Validated pathogen safety

Immune Globulin Intravenous (Human) 5%
Liquid Preparation

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REFINED
REASSURED

Please see Highlights of Prescribing Information

For the safe and optimal use of human proteins
How Much Exercise Is Too Much or Too Little?

By Matthew D. Hansen, DPT, MPT, BSPTS

For chronically ill patients, the amount of exercise needed depends upon what is right for each individual, but inactivity is not an option.
As human beings, we often struggle with knowing how much is too much and how much is too little in many aspects of our lives. For instance, we wonder about how much sleep, food, drink, attention, work, entertainment, relaxation, fiber, etc., we really need. But, for those patients who live with a chronic illness, few questions have consequences that are more far-reaching than: “How much exercise/activity is too much, and how much is too little?”

The easiest formula for finding the right amount of exercise is for patients to take note of how they feel afterward.

One day of really overdoing exercise may put someone with a chronic illness out of the game for the rest of the week; worse yet, with some diagnoses, it may actually exacerbate the condition! Consequently, many patients find it easier to simply justify not exercising at all. “After all,” they think, “why risk getting worse when I barely have the energy to get started anyhow?” Unfortunately, this is a fallacy in thought that is all too common, and it’s not just found with patients who experience a chronic illness.

Risks of Inactivity

Scientific research has long established many of the risks of not exercising, including high blood pressure and/or heart disease, obesity and associated type 2 diabetes, possible increased risk of certain cancers, osteoporosis, increased risk of muscular and soft tissue injuries, anxiety and depression. Living with a chronic illness can present enough anxiety. Why add any more?

A meta-analysis published in the February 2010 issue of Archives of Internal Medicine reviewed 40 studies on the effects of exercise in nearly 3,000 participants living with a chronic illness. In 90 percent of the studies analyzed, those who exercised regularly reported an approximately 20 percent reduction in anxiety symptoms compared with those who did not exercise. Co-author Rod Dishman, PhD, explained that “because not all study participants completed every exercise session, the effect of exercise on anxiety reported in our study may be underestimated.”

Overactivity certainly can lead to greater exhaustion. However, somewhat ironically, inactivity deconditions the body and may not only lead to exhaustion, but it can actually make symptoms of the condition even worse. So, what’s the answer to this seeming “catch-22”? If the solution isn’t inactivity, and it’s not just grinning and bearing it, it must be — as is often the case in life — somewhere in between. The easiest formula for finding the right amount of exercise is for patients to take note of how they feel afterward. All people may experience some tiredness and muscle soreness after exercising (especially when they are just getting started); however, those feelings should not be debilitating, and after patients have had a chance to rest, they should usually feel better than they did previous to exercising. If any pain or exhaustion persists to the point that it is interfering with patients’ normal daily routine the next day, they have likely overdone it (gotten too much exercise). If they don’t have any discomfort or exhaustion after exercising, but aren’t experiencing any of the apparent benefits either, they can probably afford to increase at least one component of their routine (intensity, frequency and/or duration).

Seems simple enough, right? It may seem simple, but finding the proper balance can be a confusing and sometimes frustrating process. In order to assist in the
task, I have found two tools to be invaluable: the exercise log and visual charts used to monitor pain and exhaustion.

Exercise Log

An exercise log is basically a journal that records patients’ activities for the day and their physical response to those activities (see Figure 1). It also can be used to set goals, measure progress and serve as a visual motivator. If patients have ever kept an infusion or diet log, they’re already familiar with the concept of keeping these types of records. However, I highly recommend that they personalize their log to meet individual needs and style. Here are several components for consideration and an example of a log that patients may use:

- Date and time
- How patient felt before exercise
- Type of exercise(s) performed
- Length of time of each exercise
- Intensity level (one to five) experienced while performing exercise(s)
- How patient felt immediately after exercising
- How patient felt four hours after exercising
- How patient felt the day after exercising
- Goals for the next exercise session

Again, there’s no standard format. Patients can use narratives, check boxes, graphs or whatever they like to track these or other factors of their own. The key to using an exercise log is for patients to find or develop a system that works for them and to use it! This means not only recording in their exercise log daily, but also reviewing past entries to discover patterns, such as what exercises made them feel better, what exercises made them feel worse, how far they can walk on a flat surface without becoming exhausted, and how many repetitions of a given exercise they can perform before it causes pain.

Visual Chart

A regular element of each of the exercise logs that I helped to develop is a visual chart to monitor exhaustion and pain. I prefer to keep it simple and use a graduated five-point scale (five- and 10-point scales seem to be the norm, though there isn’t anything that says that a seven-point scale can’t be used if it’s someone’s favorite number). Patients may also choose to use a color scale and/or figures to represent their energy and/or pain status. (See Figure 2.)
How to Avoid Doing Too Much

It’s almost always better for patients to ease into activity versus overdoing it and getting discouraged as a result. However, as a rule of thumb, I like to recommend that patients use their current activity level as their baseline and increase activity (intensity and/or duration) by no more than 10 percent to 20 percent per week until they experience any hint that they may be starting to overdo it. At that point, it’s important to slightly scale back until the initiation of symptoms disappears. Despite my rules (and my thumbs), patients with a chronic illness should always visit with their doctor prior to beginning a new exercise program or significantly increasing an established one.

What might the 10 percent rule look like? Patients who may be able to walk five minutes without stopping to rest, for example, may attempt to begin by increasing their routine to walking five and a half minutes without stopping. Maybe they are able to walk 100 feet, arm curl 5 pounds, or perform 10 knee bends. The point is to increase this amount by just 10 percent to 20 percent per week. As you can imagine, by increasing activity level in small intervals, it may take chronically ill patients a number of weeks (even months) to establish their maximum symptom-free exercise routine. However, consistency is important, because deconditioning may occur even more quickly if no exercise is performed over an extended period of time.

Exercise tolerance can vary daily in the chronically ill patient population. It’s all right to avoid exercise during a symptom flare-up, scale back to a prior level, or substitute for an exercise with an easier activity or light stretching. Pacing techniques also are important. Oftentimes, it’s safer and just as effective for chronically ill patients, depending on the purpose of the program, to exercise several times a day for shorter intervals than to lump it all together into one longer session. If a planned activity becomes too much, it’s better to stop than to push through the exercise and pay for it later.

Meditation techniques also can be used as a warm-up to aerobic or strengthening exercises, and will oftentimes help patients to direct their session. Moreover, meditation is a fantastic stress-reducing activity that can be utilized in just about any situation. It can be performed through the use of yoga, tai chi, stretching or simply sitting still and listening.

By learning to listen to their own body, and using tools such as exercise logs and visual charts to assist, patients will soon discover how to tell how much exercise is too much and how much is too little. The rest is a walk in the park, or at least it could be — that’s up to the patient!

MATTHEW DAVID HANSEN, DPT, MPT, BSPTS, is a practicing physical therapist in Utah, and president of a healthcare consulting and fitness product company, SOMA Health, LLC. The company’s latest product, the Freedom2Move exercise program and video series, was inspired by an IG Living Readers Teleconference. Matt completed his formal education at the University of Utah in Salt Lake City.

Reference
1. Herring, MP, and O’Connor, PJ. The Effect of Exercise Training on Anxiety Symptoms Among Patients, Archives of Internal Medicine, (reprinted) February 2010.
Primary immune deficiency diseases (PIDDs) are caused by genetic abnormalities that increase patients’ susceptibility to infection. Since the immune system cannot readily be seen when we look at a baby or child, most forms of PIDD are diagnosed only after the patient has suffered unusual, severe or recurrent infections. Recognizing those patterns of infection that suggest PIDD requires awareness and astute observation by primary care physicians. The National Institutes of Health, the Immune Deficiency Foundation (IDF) and the Jeffrey Modell Foundation (JMF) devote considerable effort to raising the awareness of PIDD among physicians and the general public, and they have developed guidelines for the recognition, diagnosis and management of these diseases.1,2,3
Diagnosing SCID

The most serious form of PIDD is called severe combined immune deficiency (SCID). The incidence of SCID is about one in 50,000 to one in 100,000 live births. In the 1970s, a patient with SCID whose story has been widely recounted was kept free from infection only by having him live inside a sterile plastic chamber to completely isolate him from all infectious agents. This led to the adoption of the term “bubble boy disease” for SCID. Today, many forms of SCID can now be corrected by stem cell transplantation, gene therapy or enzyme therapy.

SCID is caused by mutations in genes that control the development and most basic functions of the immune system, which makes these patients nearly defenseless. Surprisingly, in most cases, there is no outward sign that a newborn baby has SCID. As a consequence, that child may experience devastating infections that result from exposure to germs that are everywhere in the environment — germs that are harmless to people with normal immune systems. Once a serious or life-threatening infection sets in, expensive and complicated intensive care may be needed, and damage to organs such as the lungs or liver may make subsequent definitive corrective therapy difficult.

There are some conditions that can mimic SCID, but they are not nearly as serious. Therefore, a correct and early diagnosis is extremely important. Fortunately, there are now tests for SCID that can be performed on the dried blood spots obtained from all babies in the U.S., allowing physicians to detect SCID before infection occurs. Essentially all forms of SCID result in very low levels of T cells, and SCID babies have extremely low levels of a unique kind of DNA fragment called T cell receptor excision circles (TRECs), which are formed when T lymphocytes are made. Tests for TRECs performed on the dried blood spots have been adopted in several states to screen newborns for SCID. Once diagnosed with SCID, these babies can receive stem cell transplants that provide them with a new immune system. When stem cell transplants are performed in the first few months of life, the long-term survival rate is greater than 95 percent, and many of these babies can be considered cured.

Unfortunately, only a few states offer newborn screening for SCID. Where screening is not available, awareness by the primary care physician and/or principal caregiver is key. The family history can provide important clues, particularly if male relatives on the mother’s side died or had serious infections in infancy.

Diagnosing Other Serious PIDDs

Several of the most common PIDDs, including an important form of antibody deficiency known as Bruton’s type of agammaglobulinemia (antibody deficiency), as well as Wiskott-Aldrich syndrome, are called “X-linked” because the mutation that causes the disease is carried on the X-chromosome. Females have two X chromosomes, so even if one has a PIDD-causing mutation, they are usually healthy carriers. On the other hand, males have only one X chromosome, so if that has a mutation, the male will have the disease.
Some serious immune deficiencies such as DiGeorge’s syndrome, Wiskott-Aldrich syndrome, hyper-IgE syndrome and others are associated with other abnormalities that may be more readily apparent. Unusual cases of pneumonia, severe or prolonged diarrhea with failure to thrive, and certain skin rashes all can be indicative of serious immune deficiencies.

Evaluation of suspected immune deficiencies in infants should include a careful physical exam with documentation of the presence or absence of tonsils and lymph nodes, as well as a search for other abnormalities that might suggest immune deficiency. Laboratory evaluation by the primary care physician should include a chest X-ray for assessment of the presence or absence of the thymus and a complete blood count with differential. The latter test may reveal low numbers of lymphocytes, suggesting a deficiency of T cells or of neutrophils, which are needed for engulfing and killing bacteria and other invaders. It is important to compare blood count results against age-adjusted normal values, since babies should have higher numbers of lymphocytes than older children and adults. If these tests suggest a serious PIDD, consultation by an experienced immunologist should be sought without delay.

**The second stage of the diagnostic evaluation includes tests for specific antibodies to immunizations patients should have received as part of the regular childhood immunization schedule.**

The Immune Deficiency Foundation offers several publications, including Diagnostic and Clinical Guidelines for PIDD and the Patient and Family Handbook for Primary Immunodeficiency.

The second stage of the diagnostic evaluation includes tests for specific antibodies to immunizations patients should have received as part of the regular childhood immunization schedule.

Diagnosing More Common PIDDs

Full-term infants are born with the same levels of IgG as normal adults, even though they cannot make much antibody on their own, and they have very low levels of IgA and IgM. This is because IgG is transferred from the mother across the placenta during the last three months of pregnancy. This IgG gives some protection to the newborn, so PIDDs that mainly affect antibody production (more than half of all known types of PIDD) are often not detected in early infancy. However, by the time the baby is 4 to 6 months old, the IgG from the mother is metabolized (used up), and babies with antibody deficiencies or PIDDs other than SCID usually will start to have an increased severity and/or frequency of infections after that age. The frequency and severity of infections, though, are highly variable because of differences in exposure to infectious agents. For example, a first-born baby living at home with his or her mother is much less likely to be exposed to germs that cause ear infections and pneumonia than a baby who starts in daycare or preschool at an early age, or a baby who has multiple school-aged siblings. School-aged children (and adults with a high degree of exposure to children and/or each other) are much more likely to be ill with frequent viral and bacterial infections.

As with older children and adults, awareness by the primary care physician is the most important element in appropriate diagnosis and management of these PIDDs. Unfortunately, the diagnosis is often delayed — by as much as 10 years in many cases. The JMF publishes a poster titled “10 Warning Signs of Primary Immunodeficiency”. These warning signs have been formulated and periodically updated by expert immunologists. The poster is available in both text and cartoon formats, in versions applicable to adults and children, and in many languages.

If multiple and/or particularly severe infections occur in babies and children who also have histories of diarrhea,
poor weight gain and/or failure to thrive, or in adults who are losing weight and/or having unexplained fevers or cough and other lung symptoms, a careful physical exam may reveal additional signs of PIDD, such as the absence of tonsils and lymph nodes (in Bruton’s disease), enlargement of the spleen and/or liver, atypical rashes, and/or chronic changes due to infection. Parents or patients themselves who are concerned about the possibility of PIDD may find helpful information on the websites listed in the Sources section of IG Living, and may be interested in downloading or requesting a free hard copy of the Patient and Family Handbook for Primary Immunodeficiency Diseases from the IDF. That publication is now in its fourth English edition, and it is also available in Spanish and French versions. The JMF also publishes a poster explaining the four stages in the diagnostic evaluation of patients suspected of having PIDD.

As noted above, the initial screening steps such as a complete blood count with differential, a chest X-ray and a test for immunoglobulin levels can be obtained in virtually any practice or community hospital in the U.S. These tests alone usually can distinguish between those patients who can be reassured that they are unlikely to have a PIDD and that their infections are within the range expected for their degree of exposure, those who should be watched more closely, and those who should be referred to an immunologist. Caution must be used, however, to be sure the results are compared with age-adjusted normal values, since the absolute lymphocyte count (obtained from the CBC and differential) and immunoglobulin (IgA, IgG and IgM) levels vary during a child’s development into adulthood.

If any physician does not know to whom to refer a suspected PIDD patient, the IDF, the Clinical Immunology Society and the JMF maintain directories of immunologists with expertise in PIDD. The IDF also publishes a booklet titled Diagnostic and Clinical Guidelines for PIDD, which is very useful and represents a consensus among experts in PIDD.

The second stage of the diagnostic evaluation includes tests for specific antibodies to immunizations patients should have received as part of the regular childhood immunization schedule. These tests may also involve looking at the specific antibody response before and after certain vaccines like Pneumovax. Blood samples for these tests are frequently sent to large national reference laboratories, but they can be ordered by any doctor. These tests help to distinguish between patients who have low or borderline IgG levels but whose antibody production is really normal, and those who have PIDDs such as common variable immune deficiency (CVID) and other defects in antibody production.

The third tier of testing involves determination of the numbers of each different type or “subset” of lymphocytes in the blood using a technology called “flow cytometry.” This test is usually performed at regional referral centers and often leads directly to a definitive diagnosis of the specific type of PIDD the patient has. This level of testing also includes tests of the lymphocytes’ ability to respond to stimulation in the laboratory and/or of the ability of certain white blood cells to generate active oxygen molecules that kill bacteria.

Finally, specific tests and mutation analyses performed in specialized research laboratories can identify the exact molecular defect responsible for many, but not yet all, specific types of PIDD. This information is very useful for genetic testing and for developing a specific treatment plan for each type of PIDD. When developing a treatment plan, the IDF Patient and Family Handbook for Primary Immunodeficiency can be an invaluable aid to understanding what the doctors are talking about when they slip into their medical jargon, as well as a guide to knowing what treatment options are available. In addition, the IDF makes
available a guide for teachers and other school personnel, which can be helpful in ensuring that appropriate provisions are taken when a child with PIDD is in the classroom.

PIDDs and Childhood Vaccinations
Although most of the early childhood vaccines can be given safely to babies with SCID and other PIDDs, a few of these vaccines contain live viruses and should be avoided. The only live vaccines currently recommended for routine childhood immunization in the U.S. are those against rotavirus, measles, mumps and rubella (MMR), chicken pox (varicella/zoster) and the nasal influenza vaccine. Routine diphtheria, tetanus and pertussis (DTaP), injectable influenza, inactivated (Salk) polio vaccine, hepatitis A and B vaccines, and hemophilus and pneumococcal vaccines may or may not be effective in patients with PIDD, but they do not pose special risks for them. If there is any question about the safety of vaccines for any child, a CBC and differential count to rule out lymphopenia (low lymphocyte counts) should be conducted, and inquiries should be directed to an expert immunologist.

Advances and Education Are Key to Diagnosing PIDD
With modern diagnostic testing, a definitive diagnosis can be made in most cases of PIDD, and the precise molecular defect often can be identified.
Imagine having to choose between FEEDING YOUR FAMILY and getting a lifesaving MEDICATION.

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It could be said that Jenny Gardner is the face of common variable immune deficiency (CVID). Not because she is alone in suffering from the disease. Hardly. It’s because she has become one of the many strong vocal advocates for patients with CVID and other immune deficiency diseases. Jenny’s story is a glaring example of what many individuals endure in their lifelong struggle with this disease. It is a story of suffering through years of illness before finally being diagnosed, fighting a losing battle with insurance companies to be reimbursed for the expensive treatment, and continuing to battle the effects of the illness despite treatment.

What Is CVID?

People with CVID have deficient numbers of serum immunoglobulins (IGs), which are antibodies that fight off infection. Why people develop CVID is unknown, but the disease is the most common of the immune deficiency diseases, hence the name “common,” and the degree and type of IG deficiency varies, hence the name “variable.” Some patients treated with immune globulin (IG) have a deficiency in both IgG and IgA antibodies, while others may be deficient in all three types of antibodies: IgG, IgA and IgM.¹

CVID affects approximately one person in 50,000 worldwide and occurs in males and females equally and in all races. It can occur in infants, young children, adolescents or even those ages 20 years to 40 years and older. And, while peaks of onset occur in children ages 1 to 5 years and in young adults ages 16 to 20 years, more than two-thirds of patients are 21 years or older when diagnosed,² and in the majority of patients, diagnosis is not made until the third or fourth decade of life.³

That is the case with Jenny, who was sick all of her life but who wasn’t diagnosed until age 45. This was after being told many times that her illness was psychological and that she was a hypochondriac. “I was so frustrated,” explains Jenny. “I told one doctor that he needed to get more creative, as I’d been told that before. But something was wrong with me, and I wanted answers.”

Symptoms of CVID

Symptoms of CVID can occur in the first few years of life, as with Jenny, or they may not develop until the second or third decade, or even later.¹

Symptoms include recurring infections of the respiratory tract, such as sinus infections, otitis, bronchitis and pneumonia, which is caused by bacteria, including streptococ-
cus pneumonia, hemophilus or moraxella. If severe lung infections repeatedly occur, it’s possible that permanent damage to the bronchial tree may result and a chronic condition of the bronchi can develop, causing widening and scarring of the breathing tubes (known as bronchiectasis).

Patients also frequently experience diarrhea and chronic lambliasis (an intestinal infection). Occasionally, infections of the skin, urinary tract and herpes zoster (shingles) may occur. And, rarely, patients will experience cytomegalovirus infection, viral meningitis and tuberculosis. Approximately 20 percent of patients also develop autoimmune complications, such as rheumatoid arthritis (in the knees, ankles, elbows and wrists), vitiligo (a skin condition), hemolytic anemia, thrombocytopenia and neutropenia. And, CVID patients have an increased risk of cancer, especially cancer of the lymphoid system, skin and gastrointestinal tract.

Fortunately, unless complications have developed, CVID patients do not experience physical abnormalities. However, some patients may have an enlarged spleen and lymph nodes. And, if chronic lung disease has developed, patients may not be able to exercise due to decreased lung capacity. In some cases, gastrointestinal disorders may cause decreased growth in children or weight loss in adults.

Jenny’s symptoms ran the gamut. “If any bug was going around, I got it and was sick the longest. Strep throat was a constant problem,” says Jenny. When she was 8, she had rheumatic fever, which kept her out of school for three months, and she was sick so much throughout junior high and high school that the school district sent someone to her home to investigate her parents. “I might have been the first home-school patient,” says Jenny. As an adult, in addition to repeatedly becoming ill, including a bout with German measles, she went through three sinus surgeries.

CVID affects approximately one person in 50,000 worldwide and occurs in males and females equally and in all races.

Causes of CVID
Despite 40 years of research, what actually causes CVID is unknown. It’s possible that genetic factors may be involved. For instance, in approximately 20 percent of CVID patients, a first-degree family member has a selective IgA deficiency. When more than one family member is affected with CVID, approximately 5 percent of patients have a concurrent IgA deficiency. However, no clear pattern of inheritance has been observed.

Jenny has no family members who also have been diagnosed with CVID. However, she has tried to make a genetic connection, since her physician told her it is not uncommon for this disease to skip a generation or two, and it’s possible that someone in her family may have had the disease but not known it. Her brother “seems to get everything that comes around,” says Jenny, but he is able to fight off the infections with the help of antibiotics.

Research also has shown the involvement of a small group of genes in some patients. Patients with CVID appear to have normal numbers of B lymphocytes, but those fail to mature into plasma cells capable of making the different types of IgGs. Other CVID patients lack T lymphocyte function, which is necessary for a normal antibody response. And, yet other CVID patients have excessive numbers of cytotoxic T lymphocytes, whose role in the disease is unclear.

Diagnosing CVID
To diagnose CVID, the patient’s history is examined to look for types of infections and their severity and frequency, and the family history is explored to determine whether there have been relatives diagnosed with primary immunodeficiency or those who have an unusual susceptibility to infections. This is followed by a physical exam to rule out other possible reasons for a high rate of infections, which could include the suppression of normal immune responses due to malnutrition, injuries such as burns, drugs such as corticosteroids, diseases such as leukemia and infections such as mononucleosis, measles, chicken pox and AIDS. In children, the physical examination should show whether the child is growing well and is well-nourished. A severely immunodeficient child is likely to look sickly and pale.

If an infection is present, samples of mucus, sputum and stool will be cultured to determine the type of germs involved. Common bacteria typically elicit antibodies. Therefore, sinus and respiratory infections, which often are due to bacteria, suggest an antibody deficiency. On the other hand, viruses and fungi stimulate T cells. Therefore,
infections caused by viruses and fungi point to a T cell defect. Recurrent infections involving the skin or soft tissues often can be traced to problems with phagocytes, and blood-borne infections caused by encapsulated bacteria, including meningitis, may be linked to complement deficiencies.

If CVID is suspected, lab tests are necessary. These include a complete blood count to measure the levels of red and white blood cells, as well as platelets; a quantitative immunoglobulin test that measures IgG, IgM and IgA antibody levels in the blood; a blood test to show if the blood contains antibodies to the usual childhood immunizations (i.e., tetanus, measles, pertussis and diphtheria); a complement test using a sample of the blood to indicate how effectively the complement system is working; and skin tests that are similar to tuberculosis tests to show how well T cells are functioning.5

Jenny suffered from infections and illness for years before she finally got lucky and was diagnosed. This happened when she was required to change insurance carriers and was able to pick from a new list of doctors. “I called a friend who is a nurse, and I asked her to tell me who was the best at allergy and immunology,” says Jenny. Her friend referred her to a doctor who, after unsuccessfully treating her for allergies, tested her IG numbers and diagnosed her with CVID.

Treatment for CVID

While there are a number of treatment options for CVID, the most common is IG therapy to provide the patient with protective antibodies. IG almost always brings improvement of symptoms. Generally, intravenous IG (IVIG) is dosed at 400 mg/kg every three to four weeks. Subcutaneous administration of immunoglobulin (SCIG) also can now be performed with a variety of dosing schedules to suit the preference of the patient, with the overall goal of administering a total of 400 mg/kg every three to four weeks.

Prophylactic antibiotics may help patients with chronic sinusitis or chronic lung disease. Antibiotics also may help control small bowel bacterial overgrowth. For those with bronchiectasis, physical therapy and postural drainage will remove the secretions from the lungs and bronchi.1,5

Jenny was started with gamma globulin injections, and when that didn’t work, she was treated with IVIG. She was first administered 5 grams, and that was increased to 10, and then 15, 20, 30 and 40. However, she continued to get sick, although not quite as often, and she suffered from terrible IVIG side effects, including migraines and nausea, and she would often need to recuperate in bed for two or three days afterward. Because of the side effects, Jenny was sent to another doctor for a second opinion: He ran extensive tests and told her that her dosage was too low. After being prescribed 50 grams, her insurance carrier cut it back to 40 and she again was frequently ill. Jenny is also frequently treated with antibiotics.

While many people never have a problem with reimbursement for their IG treatments, unfortunately many others do. Jenny just happens to be one of those. In addition to not getting the number of grams of IG she needed, Jenny also began experiencing another problem. Her insurance carrier was forcing her doctor to buy the least expensive IG brand, so every month, Jenny was infused with a different IG product. Then, in 2006, her insurance company canceled her policy, and after her COBRA plan expired, she was unable to convert that plan into a private individual plan. And, while she qualified for disability in the state of Florida, where she resides, she is ineligible for a Medigap/supplemental insurance plan until age 66, leaving her responsible for paying for 20 percent of the cost of her IVIG treatments. She appealed, but she was told that “it was cheaper to let me die than to treat me,” says Jenny. “That really got to me.” Age 66 is still five years away for Jenny, and she still has no insurance. Today, she relies on both clinical trials and patient assistant programs to receive her IVIG. “Every day, I am fearful that I will not have either of these available to me, and it really worries me,” explains Jenny.

Managing Day to Day

Even with treatment, CVID patients may still experience infections and their consequences. For Jenny, who was a vice president of a national bank in Florida, chronic illness caused her to leave that job and work as an administrator at her church, where her pastor insisted that her illness and doctor appointments would not be a problem. However, that pastor moved on to another church and his replacement was not so sympathetic. Jenny quit that job as well, and since January 2000, she has been on disability.

While patients can’t prevent infections from occurring,
Enhancing life’s defenses

Gammaplex
Immune Globulin Intravenous (Human), 5% Liquid

Positive efficacy outcomes
For PI patients receiving Gammaplex there were:

> No reports of Acute Serious Bacterial Infection
> Just 0.75 days per year of subjects hospitalized
> Only 8.73 days per subject year out of work/school/day care

Low IgA levels
> The content of IgA is <10 µg/mL

Convenient infusion schedule
> Infusion rate can be increased every 15 minutes to a maximum rate of 0.08 mL/kg/min

Robust 3-step virus reduction
> An extremely low risk of viral transmission

Room temperature storage
> Gammaplex can be stored between 2°C and 25°C (36°F to 77°F) unopened for 2 years

Effective January 1, 2012, the permanent HCPGS “J” code for Gammaplex is J1557
For more information visit www.gammaplex.com

IMPORTANT SAFETY INFORMATION
Gammaplex is indicated for the replacement therapy of primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome and severe combined immunodeficiencies.

WARNING: Renal dysfunction, acute renal failure, osmotic nephropathy and death may be associated with the administration of Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Gammaplex does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gammaplex at the minimum infusion rate practicable. See full prescribing information for complete boxed warning.

Gammaplex is contraindicated in patients who have had a history of anaphylactic or severe systemic reactions to human immune globulin and in patients with selective IgA deficiency and in patients with a history of hypersensitivity.

In patients at risk of developing renal failure, monitor urine output and renal function including blood urea nitrogen (BUN) and serum creatinine. Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy. Thrombotic events may occur following treatment with Gammaplex and other IGIV products. Monitor patients with risk factors for thrombotic events, including a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization and/or known/suspected hyperviscosity. Aseptic meningitis syndrome (AMS) may occur infrequently with IGIV treatment. AMS usually begins within several hours to 2 days following IGIV treatment. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae. AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IGIV. Hemolysis and hemolytic anemia can develop subsequent to IGIV treatments. Noncardiogenic pulmonary edema may occur in patients following IGIV treatment (i.e. transfusion-related acute lung injury (TRALI)). Monitor patients for pulmonary adverse reactions (TRALI). Test product and patient’s serum for anti-neutrophil antibodies.

Gammaplex is derived from human plasma. The risk of transmission of infectious agents, including viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

In clinical studies, the most common adverse reactions with Gammaplex were headache, fatigue, nausea, pyrexia, hypertension, myalgia, pain and vomiting.

Please see the Brief Summary of Prescribing Information, including boxed warning, on the reverse.

Report adverse reactions to adr@bpl.co.uk

REFERENCES

For product information and inquiries, please call (866) 398-0825
or email BPLinfo@LashGroup.com
**Gammaglobulin Intravenous (Human), 5% Liquid**

**BRIEF SUMMARY**

**CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION PRIOR TO USE**

**INDICATIONS AND USAGE**

Gammaglobulin®, Immune Gammaglobulin Intravenous (Human), 5% Liquid, is indicated for the replacement therapy of primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome and severe combined immunodeficiencies.

**CONTRAINDICATIONS**

Gammaglobulin, Immune Gammaglobulin Intravenous (Human), 5% Liquid, is contraindicated in patients who have had an anaphylactic or severe systemic reaction to human gammaglobulin and in IgA-deficient patients with antibodies to IgA.

**WARNINGS**

Use of Immune Gammaglobulin Intravenous (IGV) products, particularly those containing sucrose, have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephropathy and death. Patients at risk of acute renal failure include those with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age (above 65 years of age), volume depletion, sepsis, paraproteinemia, chronic kidney disease who are overweight or are receiving known nephrotoxic drugs. Gammaglobulin does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gammaglobulin at the minimum infusion rate practicable.

See WARNINGS AND PRECAUTIONS and DOSAGE AND ADMINISTRATION sections in the Package Insert for important information intended to reduce the risk of acute renal failure.

Because this product is made from human plasma, it may contain infectious agents, e.g. viruses and, theoretically, the Creutzfeldt-Jakob (CJD) agent that can cause disease. The risk has been reduced by screening plasma donors for prior exposure, testing donated plasma and inactivating or removing viruses during manufacturing. Despite these measures, Gammaglobulin carries an extremely remote risk of transmission of viral diseases. The physician should discuss the risks and benefits of this product with the patient, before prescribing it to the patient.

All infections suspected by a physician possibly to have been transmitted by this product should be reported to (866) 398-0825 or email BPLInfo@LastGroup.com on behalf of Bio Products Laboratory Ltd.

Gammaglobulin, Immune Gammaglobulin Intravenous (Human), 5% Liquid, should only be administered intravenously.

**PRECAUTIONS**

**General**

The product should be used promptly after piercing the cap. Any partially used or unused product should be discarded. Visually inspect each bottle before use. Do not use if the solution is cloudy or turbid. Solution that has been frozen should not be used.

**Hypersensitivity**

Severe hypersensitivity reactions may occur. In case of hypersensitivity, discontinue Gammaglobulin infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions.

**Renal dysfunction/failure**

Ensure that patients with pre-existing renal deficiency are not volume depleted before infusion of IGV. Periodic monitoring of renal function and urine output is particularly important in patients considered to be at increased risk of developing acute renal failure. Renal function, including blood urea nitrogen (BUN) and serum creatinine, should be assessed before administering Gammaglobulin and at appropriate intervals thereafter. If renal function deteriorates, consider discontinuing Gammaglobulin.

**Information for patients:** Patients should be instructed to report the following signs and symptoms to their healthcare professional: decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath (which may suggest kidney damage).

**Hyperproteinemia, increased serum viscosity, and hyponatremia**

Hyperproteinemia, increased serum viscosity and hyponatremia may occur in patients receiving IGV therapy. Consider baseline assessment of blood viscosity at risk of hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triglycerolds (triglycerides), or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Gammaglobulin at the minimum rate of infusion practicable.

**Thrombotic events**

Thrombotic events may occur following treatment with IGV products. Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known suspected hyponatremia. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triglycerolds, hyponatremia or monoclonal gammopathies (See WARNINGS AND PRECAUTIONS: Monitoring; Laboratory Tests). For patients judged to be at risk of developing thrombotic events, administer Gammaglobulin at the minimum rate of infusion possible.

**Aseptic meningitis syndrome (AMS)**

Aseptic meningitis syndrome (AMS) may occur infrequently with Immune Gammaglobulin Intravenous (IGV) treatment, usually beginning within several hours to days after IGV. AMS may occur more frequently with high doses (2 g/kg) and/or rapid infusion of IGV. Discontinuation of IGV treatment has resulted in remission of AMS within several days without sequela.

**Hemolysis**

IGV products can contain blood group antibodies (hemolysins) that coat red blood cells (RBCs) in vivo with immune globulin, resulting in a positive direct antiglobulin test (DAT). Acute hemolysis has been reported with IGV. Delayed hemolytic anemia can develop due to RBC sequestration. IGV recipients should be monitored for clinical signs and symptoms of hemolysis (See WARNINGS AND PRECAUTIONS: Monitoring; Laboratory Tests).

**Transfusion-related Acute Lung Injury (TRALI)**

Noncardiogenic pulmonary edema (Transfusion-related Acute Lung Injury (TRALI)) may occur in patients following IGV treatment. Symptoms (fever, severe respiratory distress, pulmonary edema, hypoxemia but normal left ventricular function) typically appear within 1 to 6 hours following infusion. If TRALI is suspected, test for anti-neutrophil antibodies in both the product and the patient’s serum (See WARNINGS AND PRECAUTIONS: Monitoring; Laboratory Tests). Management includes oxygen and appropriate ventilatory support.

**Laboratory Tests**

For appropriate monitoring, see previous sections on Renal, Hyperproteinemia, Hemolysis and TRALI.

**Drug Interactions:** Passive transfer of antibodies may transiently interfere with the immune response to live virus vaccines such as measles, mumps, rubella and varicella (SEE PATIENT COUNSELING INFORMATION IN PACKAGE INSERT).

**Pregnancy Category C:** Animal reproduction studies have not been conducted with Gammaglobulin. It is not known whether Gammaglobulin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Gammaglobulin should be given to a pregnant woman only if clearly needed.

**ADVERSE REACTIONS**

**General**

Gammaglobulin, Immune Gammaglobulin Intravenous (Human), 5% Liquid, contains no reducing carbohydrate stabilizers (e.g. sucrose, maltose) and no preservative.

**Postmarketing Experience**

The following adverse reactions have been identified during post-approval use of IGV products.

**Intusion reactions:** hypersensitivity (e.g., anaphylaxis), headache, chills, dizziness, fever, malaise, nausea, vomiting, rigors, back pain, myalgia, arthralgia and chills.

**Renal:** Acute renal dysfunction/failure, osmotic nephropathy.

**Respiratory:** Apnea, Acute Respiratory Distress Syndrome (ARDS), Transfusion-related acute lung injury, hypoxemia, pulmonary edema, dyspnea, bronchospasm.

**Cardiovascular:** Cardiac arrest, thromboembolism, vascular collapse, hypotension.

**Neurological:** Coma, loss of consciousness, seizures, tremor, aspetic meningitis syndrome.

**Integument:** Stevens-Johnson syndrome, epidermolysis, erythema multiforme, dermatis (e.g., bullous dermatitis).

**Hematologic:** Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs) test.

**Gastrointestinal:** Hepatic dysfunction, abdominal pain.

**Primary Humoral Immunodeficiencies (PI)**

In a multicenter, open-label, non-randomized clinical study, 50 subjects with primary humoral immunodeficiency received 703 infusions with Gammaglobulin. Doses ranged from 279 to 799 mg/kg every 21 days (mean dose 465 mg/kg) or 28 days (mean dose 458 mg/kg), for up to 12 months. At some time during the study, all 50 subjects had an adverse event (AE) and in twenty-four subjects (48.0%) it was considered product-related.

The temporally associated AEs that occurred in more than 5% of subjects during a Gammaglobulin infusion or within 72 hours after the end of an infusion, irrespective of causality are given in the table below:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
<th>Infusions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>18 (30%)</td>
<td>53 (75%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>8 (16%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7 (14%)</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Pain</td>
<td>6 (12%)</td>
<td>7 (10%)</td>
</tr>
<tr>
<td>Chills</td>
<td>5 (10%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6%)</td>
<td>9 (1.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (6%)</td>
<td>4 (0.6%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
</tbody>
</table>

Five subjects (10%) experienced seven serious AEs. Two of these serious AEs were considered related to Gammaglobulin treatment (thrombosis and chest pain). Three other subjects withdrew from the study due to the following AEs: pnerepsis, bronchospasm and pregnancy.

During this study, no subjects tested positive for infection due to human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), or Parvovirus B19.

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**Bio Products Laboratory**

A commitment for life

December 2011 US/Gv/1211/0001
there are some things they can do to help to manage their disease. For instance, they should eat a normal, balanced diet with sufficient vitamins and fiber. Those with chronic gastritis or diarrhea should make sure to peel fruit, wash salads well and cook vegetables, and they should keep away from raw eggs, mussels and whipped ice cream. While immune stimulants have not been proved in any clinical trials to help, they do in some cases. However, patients should take caution if immunosuppressive substances have been prescribed. Light fitness training is recommended, but high-performance sports training is not advised.

Patients should be sure to get annual checkups and regular blood checks. Should patients be exposed to someone who is ill, they should keep their distance as best as possible. If patients become ill, they should be examined by a physician to determine the causal bacteria type and to be prescribed the appropriate antibiotics. It should be noted that blood screening tests for bacterial antibodies in CVID patients usually result in false negative readings. A serious infection may be present with or without a fever.

Another precaution: Live virus vaccines such as polio, measles and yellow fever should not be administered to CVID patients.

Last, women with CVID who are pregnant may require an increase in the frequency of IgG infusions. And, for the safety of the child, the choice of antibiotics may be an issue. These patients also should discuss the risk of inheritance with their doctor.³

**Future Outlook**

Fortunately, IG therapy combined with antibiotic therapy has greatly improved the outlook of CVID patients, helping them to decrease the number of infections and, in many cases, prevent the development of chronic lung disease. However, the future for patients depends on how much damage occurred prior to diagnosis and treatment, as well as their ability to get treatment. This is why advocacy efforts to spread the awareness of CVID and its symptoms for more timely diagnoses for patients, as well as to enact legislation that will provide adequate reimbursement for the expensive IG therapy, is crucial.

Jenny, who advocates at both the local and national level, advises that others who advocate for patients need to make sure that work is done at home before going to the national level. Her first advocacy trip was to her state Capitol in Tallahassee, Fla. She was then asked by the Immune Deficiency Foundation to accompany the organization on a lobbying trip to Washington, D.C. Since then, to talk to other patients and hear their stories to realize that I needed to do this for the patients. I am especially concerned for the children with this disease. It's not about me anymore; it's about the entire patient community. Sometimes, I think we are just spinning our wheels, and then I look back and see what has been accomplished, and I realize that baby steps turn into victories.”

**While there are a number of treatment options for CVID, the most common is immune globulin (IG) therapy to provide the patient with protective antibodies.**

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.

**References**

If given the opportunity, few of us would choose to be 15 again; the teen years are challenging by anyone’s standards, even under the best of circumstances. That’s why we were so inspired by Sarah Eames’s story. Sarah is a strong and optimistic young woman who was diagnosed with life-altering myasthenia gravis shortly after her 15th birthday. Five years later, the 20-year-old has resolved not to let the disease define her or limit her choices in life. An active college student, Sarah draws strength from her family and her faith, is dedicated to enjoying life to the fullest, and hopes to inspire other young people living with chronic disease to do the same.

**Sarah:** I have a very tough, seldom life-threatening, autoimmune neuromuscular disease called myasthenia gravis (MG). Right now, the disease is stable. I am on very low-dose steroids, an immune booster called Naltrexone. I have potassium every day and high-dose intravenous immune globulin (IVIG) treatments.

**Trudie:** Tell me about your diagnosis.

**Sarah:** I had MG as a baby. I had failure to thrive at 2 weeks old and was given only a 20 to 50 percent chance of survival. When I turned 2 years old, it simply went away. The disease came back strong when I was 12 years old, and I started losing a ton of weight and was catching pneumonia and viral illnesses. When I was in seventh grade, the disease almost took my life, and I ended up in Children’s Hospital in the intensive care unit (ICU). I had severe pneumonia, which is thought to be caused by MG. I believe God saved my life. A year later, I ended up in ICU again with a severe case of the flu, followed by pneumonia. My neurologist ordered a blood test and it was positive for MG. At that time, I was started on Mestinon.

**Trudie:** Tell me about the time following your diagnosis.

**Sarah:** A few months after my diagnosis, I had my first MG flare. I couldn’t walk, stand, sit up or grip anything with my hands. I had to have physical therapy, speech therapy and occupational therapy. I was started on IVIG infusion and it helped me out a lot. After a week in the hospital, I was back to my old self. I was

**When I was first diagnosed,**

**I was 15, although it is thought that I had MG as a baby.**
started on IVIG infusions a month later. My doctor then took a scan of the thymus and found that I had a condition called thymic hyperplasia: my thymus was larger than it should have been. I was started on high doses of prednisone for over a year to keep me out of the ICU and also had a thymectomy, which is like open heart surgery. The disease was then put into partial remission, and I had restoration of the swallowing muscles that used to be paralyzed, as well as restoration of vision, which I had partially lost because of weakness of the eye muscles. I was also able to get off the high dose of steroids.

I am learning to accept this disease and not to let MG define who I am.

Trudie: As a young person, what has been the most difficult thing about living with chronic illness?
Sarah: The most difficult thing for me about living with a chronic illness has been accepting it and fighting off infections. I am learning to accept this disease and not to let MG define who I am. I try to stay positive when the going gets tough. When I do have a flare, I start back on prednisone, which brings me right out of the flare. The IVIG infusions really help me, as I am not prone to catching pneumonia anymore and I don’t end up in ICU that much anymore.

Trudie: Where do you get your infusions and how often?
Sarah: I have monthly IVIG infusions at Overlake Hospital as an inpatient in Bellevue, Wash.

Trudie: How has having a chronic illness affected your friendships and relationships?
Sarah: Having a chronic illness has not really affected my social life much except for when I am sick or when I am in the hospital. I’m fortunate because my friends are very understanding.

Trudie: Tell us about your hobbies.
Sarah: I love swimming, hiking, walking, jogging, going to the club, going out to movies, going out to eat, going out for ice cream, going to sleepovers, going to youth group and hanging out with friends.

Trudie: What helps you maintain a positive outlook?
Sarah: I stay positive by praying, going to church and by exercising.

Trudie: What are your plans/goals for the future?
Sarah: I am working toward a general education college degree and pursuing the early childhood education program and also the certified nursing assistant program at Bellevue College. I would love to work in a preschool environment or a daycare center. I also love taking music classes at Bellevue. In my spare time, I design Christmas cards for Seattle Children’s Hospital and try and take art classes whenever I can.

Trudie: What advice would you give to younger IVIG patients?
Sarah: My advice to younger IVIG patients is to keep going forward even when the going gets tough and not let their disease define who they are.

Sarah Eames was diagnosed with myasthenia gravis at age 15, despite having symptoms when she was as young as 2 weeks old. Today, IVIG helps her to live a normal life, and she is pursuing a college degree.

TRUDIE MITSCANG is a staff writer for IG Living magazine.

If your life depends on immune globulin and you have a unique experience to share, we want to feature you in this column! Email us at editor@IGLiving.com.
Patient: My new insurance policy states that subcutaneous immune globulin (SCIG) medication must be purchased through a pharmacy benefits manager (PBM). As a result, the specialty pharmacy that I must use is charging me double the copay that my insurance policy dictates. In addition, because my dose requires two different vial sizes, the PBM insists I now have to pay two copays even though it is one prescription. The specialty pharmacy told me these kinds of things are becoming a real problem for SCIG patients using a PBM. What are my options?

Kris: The double copay issue should not be hard to resolve. Simply provide a copy of your policy to both your specialty pharmacy provider and your PBM and ask them to read it. If you continue to have a problem, inform your employer’s human resources (HR) department. Chances are it is simply a misunderstanding between the PBM and the specialty pharmacy that also may be affecting your co-workers, and your HR department should be able to fix it for everyone.

While I have not encountered the issue concerning copays for different vial sizes, I did speak with a CSL Behring representative who says they have recently received similar reports from patients using SCIG therapy. Although this practice is not yet prevalent for IG products, it is quite common for oral medications in retail pharmacies. When medications fall under the pharmacy benefit, patients can be charged multiple copays if filling their prescription requires the use of different doses. When possible, retail pharmacists can work with the patient and doctor to find a solution that will result in one copay. For instance, consider a prescription that directs the patient to take 12.5 milligrams of drug XYZ. If drug XYZ comes in only 5 or 10 milligram doses, the retail pharmacist may suggest the prescription be filled with 5 milligram tablets. The patient would then split one of the tablets and take two and one-half tablets daily. That way, the patient has only one copay but still receives the needed amount of medication.

Unfortunately, this is a little more difficult to do with IG products because of the limited number of vial size options, but it can be done. You could speak with your doctor and pharmacist about dosing that will allow you to be treated with one vial size. This solution may require the use of several smaller vial sizes or one larger one.

Before you do that, however, a better option would be to contact your PBM and ask for a supervisor or case manager. Explain that your physician is happy to change their prescription to accommodate their copay policy, but you would prefer to keep costs down and not waste medication or use up more ancillary supplies that will be needed when using multiple smaller vial sizes. While they may not change their policy, they may, at least in your case, see your logic and grant you an exception.

Last, I would suggest contacting the manufacturer of your medication. Speak with someone in the company’s reimbursement department about your experience to make sure they are aware of the problem. Chances are, they have already heard from other patients, and they may have some other suggestions.

Kris McFalls has two adult sons with chronic diseases treated with IG. She is formerly a physical therapist assistant, and currently is IG Living’s full-time patient advocate.

Have a question?

Email us at editor@IGLiving.com. Your information will remain confidential unless permission is given.
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“PHEW! We r almost there, Honi!” I texted my husband, Mark.

A few moments later, my cell phone chirped, signaling Mark’s response: “Yup! ‘nother 6 grd yr on the books! Way 2 go momma!”

Pride swelled in my heart knowing that Mark and I got another one of our three primary immune deficient disease (PIDD) kids through a year of middle school — and survived.

Sixth grade seemed to be this mother’s Achilles’ heel, as this was the year Galileo Middle School learned, ahem, about the birds and bees (read: ugh!). I could have used my upbringing as comfort and guidance, but my parents got out of “it” scotch-free, or should I call it scotch-free.

Flashback to the very late 1970s. It had to be a Wednesday afternoon because I and the rest of Girl Scout Troop 782 were excited about our meeting after school: We were touring a landmark bakery in my hometown. The mystery of a sudden assembly had us well-scheduled 10- to 11-year-old female-types completely freaked out. Even more puzzling was the fact that our parents were exiting the café-gym-atorium just as we were being escorted in. They closed the door behind Troop 782 and the rest of the sixth-grade girls from Eagle Elementary, waving and blowing comforting kisses.

Soon after, a public health nurse explained why our near future included various belts, sanitary napkins and — gasp! — tampons. I sat in shock while my best friend fell into my lap sobbing. Some girls begged for their mommies, while others needed straitjackets. Two days later, a fifth-grade informant snitched on our parents: While we were being tortured by a public health nurse, our moms and dads passed the proverbial buck while sucking down adult beverages.

So, when our eldest son, Calvin, interrupted laundry duties with “Mom, can we have ‘the talk’?” what he really asked me to do was confuse and frustrate him. Period.

Panicking, I grabbed a washcloth, placed it over my head so I didn’t have to look my firstborn in the eye, and instructed: “Calvin, this is a woman’s uterus.” Calvin stood in quiet and mortified submission as
younger sister Molly's rolled-up training bra became ovaries, and a pair of "tighty whities" traveled ever so softly down the fallopian tubes. A knock on my washcloth interrupted my health lesson.

“What in the world are you doing, Cheryl?” Mark demanded. Calvin stood silent; his furrowed brow told me he was either in shock, confusion or both. Needless to say, it has taken Mark two years of constant "conception" therapy to straighten out my boy. To this day, I can’t get either of them to do the whites!

For us parents of PIDD kids, we get a double whammy. You see, not only do we field the nightmarish "Where do babies come from?" question, but we also must answer excruciatingly painful inquiries about our PIDD kids’ immune disease. I don’t think it’s fair! I don’t mean to be an infantile whiner, but do “normal” parents of prepubescent children know how lucky and blessed they really are?

Since humiliating myself with the Calvin fiasco, I’ve spent much time mulling over being an “abnormal” parent. When I walked the halls of my PIDD kids’ junior high school, I didn’t know who felt more awkward: me or the hormonal middle schoolers who brushed by the bulletin board I worked on. It felt as if a large talk bubble loomed over my head that read: “Mrs. Haggard doesn’t know how her children got here.”

I carried my burden throughout the school year, and then word got out among the PTA about how I misguided my child — of all things — using a load of whites. That was all I needed. I was banished to the Isle of Misfit Mothers and was expected to do the mundane and routine only — and never without supervision. Never mind that I know which antibiotic is good for a sinus infection or that I’m quite capable of infusing my daughter’s intravenous immune globulin. None of this mattered to the Normal Mothers of America and, like the kids, I was counting down to the last day of school before summer vacation so I didn’t have to face them any longer.

The last day of school finally arrived, and I decided to go to the traditional schoolwide picnic with my then-third-grader, Molly. As I panned the vast field of normalcy trying to spy my Molly, the smell of the everyday cliché PB&Js wafted in the soft breeze. This place even reeks of normal, I griped.

Out of the corner of my eye, I saw Molly sharing a blanket with a good friend, Wintyr, her little brother and — gasp! — her mother.

“Will you come join us?” asked Alexis, Wintyr’s mom, welcomingly making space for me on their blanket.

Only if you want a freak show to interrupt your normalcy, I thought, as I nodded and smiled, accepting Alexis’ offer.

Alexis and I shared small talk as the girls ate. Alexis’ son played with a truck, creating a road with his tortilla chips.

I began to ease into our picnic, letting my guard down just a smidge as I noshed on smoked turkey on wheat.

“So, do you have plans for this summer, Cheryl?” Alexis asked.

“Yeah, we’re going to do a little camping. Nothing too exciting,” I shared. “And you? Do you have anything exciting in store for your family?” Alexis responded with how her family enjoys visiting grandparents and how they go to the lake and watch fireworks for the Fourth of July. The word “normal” entered my thoughts as I listened to Alexis describe their summer plans, dousing any hope of our friendship going past the fringe of her blanket.

I looked at Alexis’ son and asked: “So, are you going to see the ‘boom booms’ go off at the lake for the Fourth of July?”

He cocked his head with a puzzled look on his face. Turning to his mom, he reached out both hands and did the unthinkable, unimaginable and the completely abnormal: the 4-year-old tot placed one chubby, jelly-stained hand on each of Alexis’ well-endowed, uh, “boom booms” and began groping his mother. Mortified, Alexis swatted away her son’s befuddled limbs and explained: “Uh, my sister and I decided to have a secret code for our privates. So when we were complaining about female ‘stuff’ the kids wouldn’t have a clue. They figured it out anyway. I’m so embarrassed.”

“Alexis, I feel so close to you,” I cried. And as I shared my story of washcloths and tube socks, the “abnormal” title I had given myself faded away with every laugh we shared.

On the Fourth of July, I got a text from Alexis that read: “@ the lake. Herez hopin’ ur boom booms r flying high, exciting & perky!”

CHERYL L. HAGGARD is a stay-at-home mom and has three children, two of whom have CVID. She and her husband, Mark, also operate Under the Hood Ministries at www.underthehoodministries.org.
I HAVE REACHED a milestone. After six years of infusing immune globulin intravenously (IVIG), I have switched to infusing subcutaneously (SCIG). It wasn’t a difficult decision to make. I suddenly started having severe reactions to my every-two-week IVIG infusions, so my doctor and I concluded that the subcutaneous route would be safer.

The idea of switching to SCIG was intriguing. I wouldn’t have to leave the house! I would no longer have to drive 30 minutes or arrange for someone to pick me up on infusion day. And, I wouldn’t have the limited 12 channels on an archaic, squeaky accordion television! I could stream Netflix if I wanted to. I could order a pizza to be delivered, and I could pin and pin and pin on Pinterest.com — all while I was infusing at home. This was going to be great, I thought! So much freedom!

But, when I first switched, I was a little sad. I actually missed my four-hour Benadryl-induced naps; they were an excuse to lie down and not answer my phone for an extended period of time. Also, before the scary IVIG side effects began, I looked forward to my infusion days; they were an escape from the demands of life — a day when I could just worry about myself and nothing more.

I was also nervous. The idea of sticking six needles into myself was less than appealing. After all, who wants to voluntarily inflict pain on themselves? But, when it came time to do the deed, it wasn’t so bad. My favorite nurse, Lois, in my immunologist’s office trained me. She explained that I would be infusing in the office three times, and if I passed the test and did everything right by the third time, I would give myself my fourth infusion at home. Lois also taught me a trick. She taught me to hold the needle in one hand and to pinch my skin tightly where the needle would go with my other hand. Then, as I poked in the needle, I was to blow out my breath and, what do you know, I didn’t feel a thing! On the day of my third SCIG infusion, I did everything by myself with Lois’ supervision and I passed with flying colors. I made a cake to celebrate!

A week went by, and it was time to fly solo. I was so anxious. I looked around my little apartment, and I realized that this was my new infusion center. I cleaned my kitchen table twice and laid out all of my supplies in the order I needed to use them. It took me about an hour to get completely set up, filling the syringes, priming the tubing and finding the perfect places to poke the needles. As I clicked my Freedom 60 pump to the “on” position, I felt accomplished, but also a little sad. There was medical equipment all over my house; I had overlapped my two worlds. I felt I had made a mistake. Wasn’t my home supposed to stay my medical-free zone — with the exception of a bag of pill bottles? With IVIG, the medical procedures stayed in the sterile hospital, and I was able to go home to my cozy personal space.

Changing routines was more difficult than I had anticipated. I had to step back and gain some perspective. The whole reason I switched to SCIG was because it was better for my health. This was going to be the solution to all of the scary side effects I was experiencing with IVIG. And, I was going to be comfortable at home. I decided the best way to cope was to think positively and set up an infusion day game plan. When I am not infusing, everything goes back into the designated “Infusion Day Box” in the closet. This way, my apartment is clear of any medical reminders and more of a home. But, when infusion day rolls around, I allow myself to go all out: nothing but me, trash TV and a Zebra Snuggie!

EVER FECSKE was diagnosed with CVID and interstitial lung disease in 2004. She is a fashion design student, loves spending time with her fiancé, family and bulldog, Dunkin, and can’t get enough of writing, cake decorating and anything that sparkles!
Transitions

By Carla Schick

Crossing the Pond for Better Health

Change is often a challenge. Now and then change is necessary, but oftentimes it is a decision patients make to improve their well-being. For instance, they may decide to change their physician if they feel that he or she is not providing them with adequate care. Or, they might switch their intravenous immune globulin (IVIG) brand to lessen the occurrence of side effects. But, occasionally, they might have to make the decision to change those elements, and more, nearly simultaneously. Raye Churchill made that choice when she and her husband, John, were determined to pick up stakes and move from the Arizona desert to the United Kingdom. For Raye and John, crossing the pond to improve her health has made all the difference.

Coming to Terms

When Raye was 49 years old, she had two open-heart surgeries. After her second surgery, Raye was “overwhelmed with health issues and seeing specialists to try to get a proper diagnosis as to why I wasn’t getting better.” After numerous tests, Raye was diagnosed in 1992, at age 51, with common variable immunodeficiency (CVID), allergic rhinitis and pulmonary coccidioidomycosis. For the next 16 years, Raye and John did their best to cope with her declining health and increasing medical bills. But with advancing age and the stress of his wife’s illness, John, a native of Great Britain, began to “develop migraines and syncope events.” He made the decision to stop working. By this time, both Raye and John were receiving Social Security, so they began looking for a place to enjoy their retirement years.

A Blessing in Disguise

In 2008, the couple “took a trip to England to look around and make sure John didn’t want to return to his homeland.” To their surprise, Raye says, they “found it quite refreshing and to our liking, since the desert was causing allergies to begin to
appear in both our health patterns.” During their visit, Raye experienced a blessing in disguise when she developed an ear infection and had to go for medical help. While being treated, Raye and John “found the U.K. healthcare [system] was more to our [taste] as seniors.” Raye remembers thinking: “If healthcare in the U.K. could fill the bill on medical, it could be the answer to remove a great deal of stress, and we would be in John’s country of birth.”

As soon as they returned home from England, Raye began to research the possibility of moving to another country, with a new healthcare system and different infusion therapy options. She contacted IG Living’s patient advocate, Kris McFalls, who told her about the Primary Immunodeficiency Association (PIA). Through the PIA website, Raye eventually began emailing a gentleman in the U.K. who was being treated with IVIG and who told her that SCIG is the preferred method of delivery by most primary immunodeficiency disease (PIDD) patients in the U.K. With Raye’s permission, her information was forwarded to a specialist nurse in hopes that he would know more about the Vivaglobin supply in the U.K. The nurse informed her that Vivaglobin was the most widely used SCIG product in England and most of Europe.

While she waited for her visa to be approved, Raye decided to make the switch to SCIG to “see if I could tolerate the SCIG with all my allergies and issues … since I had been on IVIG for 16 years.” It was important to Raye that the switch to SCIG be a success because she didn’t want to get to England and need an infusion with a new doctor in an unfamiliar place. “I needed to be free to settle in and not need an infusion ASAP,” explains Raye.

Through her involvement in IG Living reader teleconference calls to learn how patients were dealing with SCIG at home, as well as her acquaintance with a nurse at the infusion center who had previously been involved with SCIG home treatment, Raye successfully made the switch from IVIG therapy to SCIG at-home treatments.

Making the Move
Just months after Raye’s visa was approved, Raye and John moved to England in January 2010. “The healthcare system is very different from the U.S.,” says Raye. “Seniors are highly respected and well taken care of. Medical insurance is set up so that citizens are given a National Health Insurance [NI] number, which they acquire from their local ‘surgery,’ a facility that staffs several doctors.” From there, patients can make an appointment to see a general practitioner (GP) whose office is close to their residence. Raye’s GP reviews her health on her birthday, and all necessary tests are scheduled at that visit. If she needs treatment and she’s too ill to travel to her GP’s office, the doctor will visit her home 24 hours a day. When her symptoms are beyond her GP’s field of knowledge, she is automatically referred to a specialist, and according to Raye, if she “has someone in mind … a referral letter is sent by the GP to that specialist. At that point, the specialist then does the necessary treatment and reports back to the GP’s office.”

Raye did have one setback, however. It took a little time to find an immunologist with whom she was happy. Initially, her GP referred her to “an immunologist closer to where we lived, but we did not like the system in that area, so we asked for a second referral to the Royal London Hospital [RLH] where I had originally contacted Dr. Hilary Longhurst while...
When Raye arrived at the RLH, “it was very refreshing and totally different from the one closer to our residence,” she says. “Blood work, extensive exams and review of all my immunology information from the U.S. [were] sent in advance. The doctors have been very helpful, friendly and eager to take care of us.” And the best part is that everything is “covered under the National Health Service [NHS], including prescriptions, blood tests, X-rays and scans.”

An added advantage of the NHS is that there is no paperwork for IG reimbursement once patients are registered with an NI number. Raye says that “everything is computerized. If you need to move from one part of the U.K. to another, your medical records are programmed to follow you.”

Overall, their move to the U.K. has allowed Raye and John to enjoy their retirement years and their improved health. “I have had fewer infections and my health has allowed me to be active…. My breathing is far better — deeper than it’s been in years — and I believe the fresh air has been good for me. In speaking with my GP and the immunologist, they see an improvement.” While they were living in the U.S., they were paying $20,000 per year for medical expenses. Now, everything is covered. Comfortably settled in a suburb of London, Raye still stays in contact with her old friends in the U.S. She also is a member of the PIA and plans to get involved with other support groups.

“Life is less stressful, and we have time to relax!” exclaims Raye.

CARLA SCHICK is a staff writer for IG Living magazine.

If you have a life-transitioning story brought about with the help of IG, we want to share it with our readers. Email us at editor@IGLiving.com.
MY 20 YEARS as an educator have given me keen insight into the adolescent community. Much of it is quite inspiring; some of it is not. I have broken up a number of fights on high school campuses. Unfortunately, 90 percent of those fights are instigated by 10 percent of the kids. In the past few years, schools and law enforcement agencies have started making a more concerted effort to target these instigators who bully their way across our children’s campuses. And as a parent of kids with an immune deficiency disease, this is a welcome sight.

Nationwide, the statistics attributed to bullying are astounding. About 2.7 million students between kindergarten and 12th grade are bullied every year, while about 2.1 million students engage in bullying. More than half of students say they have witnessed incidents of bullying at school, while one student in seven is a victim of bullying.

What Is Bullying?

Dan Olweus, Norwegian psychologist and the creator of the Olweus Bullying
Prevention Program, states that “a person is bullied when he or she is exposed, repeatedly and over time, to negative actions on the part of one or more other persons, and he or she has difficulty defending himself or herself.” Bullying may take the form of threats or name-calling, stealing or destroying personal property, being excluded by others, or physical abuse such as hitting, kicking, shoving or spitting. A study by the National Institutes of Health reports that boys are more likely to bully their classmates physically, while girls are more likely to bully by spreading rumors, making sexual comments and by snubbing.

A newer form of bullying is “cyberbullying,” which occurs when hurtful messages are sent via the Internet, text messages or social networking sites. It is different from traditional face-to-face bullying because messages and images can be sent any time. Types of cyberbullying include sending mean messages to a person, spreading rumors or lies about a person online, threatening or harassing another person online, taking pictures of a person and posting them online, or hacking into someone’s account and using it to send hurtful messages to a third person. Forty-five percent of teens report viewing back-and-forth rude or mean behavior on a social networking site.

**Why Do Bullies Pick on Sick Kids?**

Why do bullies threaten and engage in physical violence? According to Olweus, many kids bully because they have a strong need for power and dominance. Some find satisfaction from causing injury to another person, or they receive some material and psychological reward for their actions. Other researchers suggest that many bullies are abused at home and it is a learned behavior. Bullies want to feel that they are in control — that they are stronger, smarter or better than others. Some see others bullying and copy the behavior as a way to fit in with the crowd. Some see bullying as a preemptive strike: It is better to be the bully than to be bullied.

Kids who show outward signs of illness often become a target of opportunity. This is because their recurring illnesses often cause them to be less physically adept than their bullying classmates, who are generally bigger than those they bully. In addition, numerous absences due to illness may make it harder for sick kids to make friends. Unfortunately, in trying to look out for the best interests of their children, parents often insist their kids go to school even when they are sick and physically weakened, sometimes unaware that they are a target for bullies.

**How to Respond to Bullying**

Ultimately, despite their illness, kids are simply kids, subject to the same social forces as everyone else on campus. And, parents have an important role to play in protecting their kids against bullying. The most important defense against bullying is to help kids maintain a strong sense of self-esteem. Students who carry themselves well on campus are not often targets of bullies. Self-confident students are more likely to assert themselves in the face of a bully and firmly tell the bully to leave them alone. In contrast, kids with low self-esteem are not likely to assert themselves, making them a direct target of bullies. Confident kids also have a solid group of friends that acts as support against bullies. This is why children should become involved in one of the many activities offered at the school — be it sports, band or one of the other campus clubs — where they will find immediate support.

For kids who don’t have strong self-esteem, the easiest answer is for them to avoid the parts of the campus where the bullies hang out. However, that isn’t always possible, so kids should be taught to stand firm in the face of bullies and to tell them to leave them alone. This may require practice at home. But, bullies are usually insecure themselves, and they will likely back down when confronted.

If a child becomes the victim of a bullying incident, it must be reported to school or law enforcement officials. Principals are possessive of their campuses, and they do not want their schools to gain a reputation as a haven for bullies. When my own son was bullied in fifth grade, we brought the behavior to the attention of the principal of the school. The next fall, the bully was no longer enrolled.

Although a child may complain that reporting the incident seems like “tattling” or that the bully has threatened further harm, telling the authorities that kids who show outward signs of illness often become a target of opportunity.
puts the bully on notice that the consequences of his or her next act might be a juvenile detention facility.

**Responding to Cyberbullying**

As children begin their lives “online,” it is important they understand that cyberbullying, like any other form of bullying, is wrong, no matter who started it. Children should be completely insulated while working on their computers. They should have passwords that are difficult to decipher, and they should never share their passwords, except with their parents. Furthermore, they should never open anything from someone they do not know. Nor should children ever share personal information online, since anything they post stays in cyber-space forever.

The most important defense against bullying is to help kids maintain a strong sense of self-esteem.

Parents can become more deeply involved in their kids’ online activities by keeping their computer in a high-traffic area of the house. In addition, kids should be required to “friend” their parents on their social networking sites so the parents can see messages their kids receive. This is not spying on them; it is for their protection. Kids also should be encouraged to speak up if they feel they are being bullied online. Many teens will not tell their parents about cyberbullying out of fear that the parents will take their computer privileges away — a fate they believe is worse than bullying.

If a child becomes a victim of cyberbullying, the authorities may need to become involved if it does not stop. Most importantly, children must be told not to retaliate. Retaliation gives the bully a sense of gratification and leads to further nasty messages and continued retaliation. This back-and-forth behavior online is referred to as “flaming,” and it is attractive to those who are likely to join in on the unwanted behavior. Rather than retaliate, kids should either ignore bullies or respond with short, unemotional responses like: “Knock it off.” Parents also can block the email address of the bully. However, if unwanted communication continues, parents should keep messages as evidence in building a case against the bully. The parents of the bully are legally responsible for their children’s actions, and if they do not do anything to make it stop, they may face legal consequences.

If a cyberbully is sending messages anonymously or with a fake name, the Internet Service Provider can track the sender. If the messages are threatening or damaging, parents can go to the police. Many email providers or social networking sites will shut down an account if they are provided evidence that it is being used for cyberbullying. Parents can notify social networking sites about this behavior by going to the “contact” page and sending copies of the unwanted messages. Unfortunately, if these actions do not work at deter-ring a cyberbully, the last option may be to change the child’s email address.

**An Arsenal Against Bullying**

Although children with an illness may be attractive targets for bullies, there are defense mechanisms in place to protect them. The first and most important line of defense is instilling in them a strong sense of self-worth. If a bully continues his or her unwanted behavior, school administrators and law enforcement are bound by the law to intervene on parents’ behalf. And parents are responsible for the behavior of their children; even the “hardest” parents can be mollified when threatened with jail time. Especially online, where cyberbullying has become prevalent, parents are not alone in seeking help. They have a powerful arsenal to defend their children from those who wish to threaten and abuse.

MARK T. HAGGARD is a high school teacher and football coach, and has three children, two of whom have CVI. He and his wife, Cheryl, also operate Under the Hood Ministries at www.underthehoodministries.org.

**Sources**


Almost half of all Americans have a chronic health condition, and by the year 2030, half of the United States population will have a chronic illness. People with chronic conditions are the most frequent users of healthcare in the United States, accounting for 81 percent of hospital admissions, 91 percent of prescriptions filled and 76 percent of all physician visits. From March 2008 to March 2009, more than 1,500 patients with chronic illnesses completed a detailed survey reporting on their experiences as a patient and, in particular, the obstacles they face and the strategies they use to try to surmount these obstacles. The rich trove of data that resulted suggests important directives for advocates. In this paper, that data is summarized and evaluated to reveal what these advocates believe are important points to be considered when seeking to improve the experience, both within and outside of the healthcare system, of individuals with chronic illnesses.

Strong at the Broken Places
Author: Richard Cohen

Strong at the Broken Places was written out of the desires by many who suffer from chronic illness to share their stories in the hope that the sick and those who love them will see that they are not alone. New York Times bestselling author Richard A. Cohen spent three years chronicling the lives of five diverse “citizens of sickness”: Denise, who suffers from ALS; Buzz, whose Christian faith helps him deal with his non-Hodgkin’s lymphoma; Sarah, a determined young woman with Crohn’s disease; Ben, a college student with muscular dystrophy; and Larry, whose bipolar disorder is hidden within. The five are different in age and gender, race and economic status, but they are determined to live life on their own terms. Though each individual’s illness wreaks havoc in a different way, Cohen shows how their experiences are strikingly similar and offers lessons for all — on self-determination, on courage in the face of adversity and public ignorance, on keeping hope alive, and on finding strength and peace under the most difficult of circumstances.

Diabetes Weight Loss — Week by Week: A Safe, Effective Method for Losing Weight and Improving Your Health
Author: Jill Weisenberger, MS, RD, CDE
Publisher: American Diabetes Association

This book is a no-fad, no-trick method to lose weight and keep it off for a lifetime. Written by a registered dietitian and a diabetes educator with more than 20 years’ experience helping people meet their weight and health goals, it is a one-year journey to weight control while managing diabetes. Each week, readers learn new skills that build on previous lessons, including how to set reasonable, achievable goals, recover from dietary setbacks, avoid low blood sugar while losing weight and exercising, snack with a purpose, and ask for the support they need. The book will be available in July.
For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.

**General Resources**

These organizations provide information about various disease states, which can be found by conducting a search of the disease state name.

- **Advocacy for Patients with Chronic Illness**: www.advocacyforpatients.org
- **The Alliance for Biotherapeutics (fair access to plasma therapies)**: www.bioalliance.org
- **American Autoimmune Related Diseases Association (AARDA)**: www.aarda.org
- **American Chronic Pain Association (ACPA)**: www.theacpa.org
- **Band-Aides and Blackboards**: www.lehman.cuny.edu/faculty/jfleitas/bandaides
- **eMedicine from WebMD**: emedicine.medscape.com
- **FamilyDoctor.org**: www.familydoctor.org
- **Johns Hopkins Medicine**: www.hopkinsmedicine.org
- **KeepKidsHealthy.com (pediatrician’s guide to children health and safety)**: www.keepkidshealthy.com
- **Kids Health (medical and emotional impact of caring for an ill child)**: www.kidshealth.org/parent/system/ill/seriously_ill.html
- **Mayo Clinic**: www.mayoclinic.com
- **National Committee for Quality Assurance (detailed report cards on health plans, clinical performance, member satisfaction and access to care)**: www.ncqa.org
- **National Infusion Center Association**: www.infusioncenter.net
- **National Institute of Neurological Disorders and Stroke (NINDS)**: www.ninds.nih.gov/disorders/disorder_index.htm
- **National Institutes of Health**: http://www.niams.nih.gov/Health_Info
- **National Organization for Rare Disorders (disease-specific support groups and virtual communities for patients and caregivers)**: www.rarediseases.org
- **Office of Rare Diseases Research**: rarediseases.info.nih.gov
- **Patient Advocate Foundation (patient access to care, maintenance of employment and financial stability)**: www.patientadvocate.org
- **WebMD (medical reference)**: www.webmd.com

**Disease-State Resources**

### Ataxia Telangiectasia (A-T)

**Websites**

- **A-T Children’s Project**: www.atcp.org

### Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

**Websites**

- **GBS/CIDP Foundation International**: www.gbs-cidp.org
- **The Neuropathy Association**: www.neuropathy.org

### Evans Syndrome

**Online Peer Support**

- **Evans Syndrome Research and Support Group**: www.evanssyndrome.org

### Guillain-Barré Syndrome (GBS)

**Websites**

- **GBS/CIDP Foundation International**: www.gbs-cidp.org
- **The Neuropathy Association**: www.neuropathy.org

**Online Peer Support**

- **GBS Support Group**: www.gbs.org.uk
- **GBS/CIDP Foundation International Discussion Forums**: www.gbs-cidp.org/forums

### Idiopathic Thrombocytopenic Purpura (ITP)

**Websites**

- **ITP Support Association – UK**: www.itpsupport.org.uk
- **Platelet Disorder Support Association**: www.pdsa.org

### Kawasaki Disease

**Websites**

- **American Heart Association**: www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#T1T2bPWE0
- **American Academy of Family Physicians**: www.aafp.org/afp/2006/1001/p1141.html
- **Kawasaki Disease Foundation**: www.kdfoundation.org
- **KidsHealth**: http://kidshealth.org/parent/medical/heart/kawasaki.html
Mitochondrial Disease
Websites
• United Mitochondrial Disease Foundation: www.umdf.org
• MitoAction: www.mitoaction.org

Multifocal Motor Neuropathy (MMN)
Websites
• The Neuromuscular Center at Washington University: http://neuromuscular.wustl.edu
• The Neuropathy Association: www.neuropathy.org

Multiple Sclerosis (MS)
Websites
• All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
• Multiple Sclerosis Association of America: www.msaaa.com
• Multiple Sclerosis Foundation: www.msfocus.org/learn-about-multiple-sclerosis.aspx
• National Multiple Sclerosis Society: www.nationalmssociety.org

Online Peer Support
• Friends with MS: www.friendswithms.com
• Msworld’s Chat and Message Board: www.msworld.org

Myasthenia Gravis (MG)
Websites and Chat Rooms
• Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org

Online Peer Support
• Genetic Alliance: www.geneticalliance.org

Myositis
Websites
• International Myositis Assessment and Clinical Studies Group: http://www.niehs.nih.gov/research/resources/collab/imacs/main.cfm
• The Cure JM Foundation: www.curejm.com (760) 487-1079
• The Myositis Association: www.myositis.org

Online Peer Support
• Juvenile Myositis Family Support Network: www.curejm.com/family_support/index.htm
• Myositis Association Community Forum: www.myositis.org

• Myositis Support Group: www.myositissupportgroup.org
• Myositis Support Group – UK: www.myositis.uk

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)
Websites
• P.A.N.D.A.S. Network: pandasnetwork.org
• Behavioural Neurotherapy Clinic – Australia: www.adhd.com.au/PANDAS.htm

Pemphigus and Pemphigoid
Websites
• The International Pemphigus and Pemphigoid Foundation: www.pemphigus.org

Peripheral Neuropathy (PN)
Websites
• The Neuropathy Association, www.neuropathy.org, is devoted exclusively to all types of neuropathy, which affects upwards of 20 million Americans. The Association’s mission is to increase public awareness of the nature and extent of PN, facilitate information exchanges about the disease, advocate the need for early intervention and support research into the causes and treatment of neuropathies. (212) 692-0662

• Neuropathy Action Foundation: www.neuropathyaaction.org
• Calgary Neuropathy Association: www.calgaryneuropathy.com

Primary Immune Deficiency Disease (PIDD)
Websites
• The Immune Deficiency Foundation (IDF), www.primaryimmune.org, is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research. (800) 296-4433

• The Jeffrey Modell Foundation, www.info4pi.org, is dedicated to early and precise diagnosis, meaningful treatments and, ultimately, cures for primary immunodeficiency. (212) 819-0200

• The National Institute of Child Health and Human Development (NICHD), www.nichd.nih.gov, is part of the National Institutes of Health. Go to the “Health Information and Media” tab on the website and do a search under

• American Academy of Allergy, Asthma & Immunology: www.aaaai.org
• International Patient Organization for Primary Immunodeficiencies (IPOPI): www.ipopi.org
• Michigan Immunodeficiency Foundation: www.facebook.com/groups/108048062584350
Sources

- National Institute of Child Health and Human Development (NICHD) (Click on "Health Information" then "A to Z health & human development topics” and select “P” for "Primary Immunodeficiency"): www.nichd.nih.gov
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.uhospitals.org/tabid/132/Default.aspx
- Team Hope (for families and patients in New England): www.teamhope.info

Online Peer Support
- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: http://idffriends.org/forum
- IDF Friends: http://idffriends.org
- Jeffrey Modell Foundation Message Board: www.info4pi.org
- Rhode Island peer group: http://health.groups.yahoo.com/group/RhodeIslandPIDD

Scleroderma

Websites
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Scleroderma Center: http://www.hopkinsmedicine.org/rheumatology/clinics/scleroderma_center.html

Online Peer Support
- Scleroderma Support Forum: curezone.com/forums/a-to-z.html
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Stiff-Person Syndrome (SPS)

Websites
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- Living with Stiff Person Syndrome (personal account): www.livingwithsp.com
- Stiff Person Syndrome: www.stiffpersonsyndrome.net

Other Resources

Education and Disability Resources
  Provides protection for people with disabilities from certain types of discrimination, and requires employers to provide some accommodations of the disability.
  U.S. Federal government’s disability-related information and resources.
- Individuals with Disabilities Education Improvement Act of 2004: http://idea.ed.gov/explore/home
- National Disability Rights Network: www.ndrn.org. This website offers a search tool to find resources in your state to assist with school rights and advocacy.
- Social Security: www.ssa.gov/disability
- U.S. Department of Education Website: www.ed.gov. This federal government website offers a parents section titled “My Child’s Special Needs.”

  Spells out your rights under Section 504 of the Rehabilitation Act.

Medical Research Studies
- ClinicalTrials.com: www.clinicaltrials.com
  This site has a registration form to request that you be notified about recruitment for future studies.
- ClinicalTrials.gov: www.clinicaltrials.gov
  A registry of federally and privately supported clinical trials conducted in the United States and around the world.

Food Allergies
- Allergic Disorders: Promoting Best Practice: www.aaaai.org
- American Partnership for Eosinophilic Disorders: www.apfed.org
- Food Allergy and Anaphylaxis Network: www.foodallergy.org
- World Allergy Organization: www.worldallergy.org

Product Information
- Influenza and the influenza vaccine: www.cdc.gov/flu or call (800) CDC-INFO: (800) 232-4636
- IVIG Fiebogamma 5% DIF and 10% DIF: www.grifols.com/portal/en/US/bioscience?div=8883
- IVIG/SCIG Gammagard Liquid: www.gammagardliquid.com
- IVIG Gammagard S/D: www.baxter.com/patients_and_caregivers/products/gammagard_sd_5.html
- IVIG/SCIG Gammaked: www.gammaked.com
- IVIG Gammalex: www.gammalex.com
- IVIG Privigen: www.privigen.com
- SCIG Hizentra: www.hizentra.com

Pump and Infusion Sets Websites
- EMED Corporation: www.safetymedicalproducts.com
- Graseby Marcal Medical: www.marcalmedical.com
- Intra Pump Infusion Systems: www.intrapump.com
- Micrel Medical Devices: www.micrelmed.com
- Norfolk Medical: www.norfolkmedical.com
- Repro Med Systems, Inc: www.rmsmedicalproducts.com
- Smith Medical: www.smiths-medical.com/brands/cadd

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.
Hizentra®
Immune Globulin Subcutaneous (Human), 20% Liquid

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

1 INDICATIONS AND USAGE

Hizentra is an Immune Globulin Subcutaneous (Human) (IGSC), 20% Liquid indicated as replacement therapy for primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

4 CONTRAINDICATIONS

Hizentra is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin or to components of Hizentra, such as polysorbate 80.

Hizentra is contraindicated in patients with hyperprolinemia because it contains the stabilizer L-proline (see Description [11]).

Hizentra is contraindicated in A/G-deficient patients with antibodies against IgA and a history of hypersensitivity (see Description [11]).

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Severe hypersensitivity reactions may occur to human immune globulin or components of Hizentra, such as polysorbate 80. In case of hypersensitivity, discontinue the Hizentra infusion immediately and institute appropriate treatment.

Individuals with IgA deficiency can develop anti-IgA antibodies and anaphylactic reactions (including anaphylaxis and shock) after administration of blood components containing IgA. Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions with administration of Hizentra. Hizentra contains ≤50 mcg/mL IgA (see Description [11]).

5.2 Aseptic Meningitis Syndrome (AMS)

AMS has been reported with use of IGIV or IGSC. The syndrome usually begins within several hours to 2 days following immune globulin treatment. AMS is characterized by the following signs and symptoms: severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea, and vomiting. Cerebrospinal fluid (CSF) studies frequently show pleocytosis up to several thousand cells per cubic millimeter, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dL. AMS may occur more frequently in association with high doses (>2 g/kg) and/or rapid infusion of immune globulin product.

Patients exhibiting such signs and symptoms should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. Discontinuation of immune globulin treatment has resulted in remission of AMS within several days without sequelae.

5.3 Reactions Reported to Occur With IGIV Treatment

The following reactions have been reported to occur with IGIV treatment and may occur with IGSC treatment.

Renal Dysfunction/Failure

Renal dysfunction/failure, osmotic nephropathy, and death may occur with use of human immune globulin products. Ensure that patients are not volume depleted and assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, before the initial infusion of Hizentra and at appropriate intervals thereafter.

Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk of developing acute renal failure. If renal function deteriorates, consider discontinuing Hizentra. For patients judged to be at risk of developing renal dysfunction because of pre-existing renal insufficiency or predisposition to acute renal failure (such as those with diabetes mellitus or hypovolemia, those who are overweight or use concomitant nephrotoxic medicinal products, or those who are over 65 years of age), administer Hizentra at the minimum rate practicable.

Thrombotic Events

Thrombotic events may occur with use of human immune globulin products[9]. Patients at increased risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and/or known or suspected hyperviscosity. Because of the potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Hizentra at the minimum rate practicable.

Hemolysis

Hizentra can contain blood group antibodies that may act as hemolytins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin (Coombs’) test result and hemolysis.4a Delayed hemolytic anemia can develop subsequent to immune globulin therapy due to enhanced RBC sequestration, and acute hemolysis, consistent with intravascular hemolysis, has been reported.4b

Monitor recipients of Hizentra for clinical signs and symptoms of hemolysis. If these are present after a Hizentra infusion, perform appropriate confirmatory laboratory testing. If transfusion is indicated for patients who develop hemolysis with clinically compromising anemia after receiving Hizentra, perform adequate cross-matching to avoid exacerbating on-going hemolysis.

Transfusion-Related Acute Lung Injury (TRALI)

Noncardiogenic pulmonary edema may occur in patients administered human immune globulin products.10 TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Typically, it occurs within 1 to 6 hours following transfusion. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support.

Monitor Hizentra recipients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient’s serum.

5.4 Transmissible Infectious Agents

Because Hizentra is made from human plasma, it may carry a risk of transmitting infectious agents (e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease [CJD] agent). The risk of infectious agent transmission has been reduced by screening plasma donors for prior exposure to certain viruses, testing for the presence of certain current virus infections, and including virus inactivation/ removal steps in the manufacturing process for Hizentra.

Report all infections thought to be possibly transmitted by Hizentra to CSL Behring Pharmacovigilance at 1-866-915-6958.

5.5 Laboratory Tests

Various passively transferred antibodies in immunoglobulin preparations may lead to misinterpretation of the results of serological testing.

6 ADVERSE REACTIONS

The most common adverse reactions (ARs), observed in ≤5% of study subjects receiving Hizentra, were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, vomiting, pain, and fatigue.

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, AR rates observed in clinical studies of a product cannot be directly compared to rates in the clinical studies of another product and may not reflect the rates observed in clinical practice.

The safety of Hizentra was evaluated in a clinical study for 15 months in subjects with PI who had been treated previously with IGIV every 3 or 4 weeks. The safety analyses included 49 subjects in the intention-to-treat (ITT) population. The ITT population consisted of all subjects who received at least one dose of Hizentra (see Clinical Studies [14]).

Subjects were treated with Hizentra at weekly doses ranging from 66 to 331 mg/kg body weight during the wash-in/wash-out period and from 72 to 379 mg/kg during the efficacy period. The 49 subjects received a total of 2264 weekly infusions of Hizentra.

No deaths or serious ARs occurred during the study. Two subjects withdrew from the study due to ARs. One subject experienced a severe injection-site reaction one day after the third weekly infusion, and the other subject experienced moderate myositis. Both reactions were judged to be “at least possibly related” to the administration of Hizentra.

Table 2 summarizes the most frequent adverse events (AEs) (experienced by at least 4 subjects), irrespective of causality. Included are all AEs and those considered temporally associated with the Hizentra infusion, i.e., occurring during or within 72 hours after the end of an infusion. Local reactions were the most frequent AEs observed, with injection-site reactions (i.e., swelling, redness, heat, pain, and itching at the site of injection) comprising 98% of local reactions.
### Table 2: Incidence of Subjects With Adverse Events (AEs)* (Experienced by 4 or More Subjects) and Rate per Infusion, Irrespective of Causality (ITT Population)

<table>
<thead>
<tr>
<th>AE (&gt;4 Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%) of Subjects: (n=49)</td>
<td>Number (Rate)† of AEs (n=2264 Infusions)</td>
</tr>
<tr>
<td>Local reactions*</td>
<td>49 (100)</td>
<td>1340 (0.592)</td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>13 (26.5)</td>
<td>40 (0.18)</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (16.3)</td>
<td>9 (0.04)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 (14.3)</td>
<td>8 (0.04)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6 (12.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Back pain</td>
<td>5 (10.2)</td>
<td>11 (0.05)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (10.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>5 (10.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (10.2)</td>
<td>7 (0.03)</td>
</tr>
<tr>
<td>Local heat</td>
<td>4 (8.2)</td>
<td>7 (0.03)</td>
</tr>
<tr>
<td>Migraine</td>
<td>4 (8.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (8.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>4 (8.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>4 (8.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (8.2)</td>
<td>5 (0.02)</td>
</tr>
</tbody>
</table>

* Excluding infections.
† Rate of AEs per infusion.
‡ Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.

The ratio of infusions with temporarily associated AEs, including local reactions, to all infusions was 1338 to 2264 (59.1%; upper 95% confidence limit of 62.4%). Excluding local reactions, the corresponding ratio was 173 to 2264 (7.6%; upper 95% confidence limit of 8.9%).

Table 3 summarizes the most frequent ARs (i.e., those AEs considered by the investigators to be "at least possibly related" to Hizentra administration) experienced by at least 2 subjects.

### Table 3: Incidence of Subjects With Adverse Reactions (Experienced by 2 or More Subjects) to Hizentra and Rate per Infusion (ITT Population)

<table>
<thead>
<tr>
<th>Adverse Reaction (≥2 Subjects)</th>
<th>Number (%) of Subjects: (n=49)</th>
<th>Number (Rate)† of Adverse Reactions (n=2264 Infusions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions§</td>
<td>49 (100)</td>
<td>1338 (0.591)</td>
</tr>
<tr>
<td>Other ARs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12 (24.5)</td>
<td>36 (0.016)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Pain</td>
<td>3 (6.1)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Confusion</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Migraine</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
</tbody>
</table>

§ Rate of AEs per infusion.
§ Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.

Table 4 summarizes injection-site reactions based on investigator assessments 15 to 45 minutes after the end of the 683 infusions administered during regularly scheduled visits (every 4 weeks).

### Table 4: Investigator Assessments* of Injection-Site Reactions by Infusion

<table>
<thead>
<tr>
<th>Injection-Site Reaction</th>
<th>Number† of Reactions (n=683 Infusions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema/induration</td>
<td>467 (0.68)</td>
</tr>
<tr>
<td>Erythema</td>
<td>346 (0.50)</td>
</tr>
<tr>
<td>Local heat</td>
<td>108 (0.16)</td>
</tr>
<tr>
<td>Local pain</td>
<td>88 (0.13)</td>
</tr>
<tr>
<td>Itching</td>
<td>64 (0.09)</td>
</tr>
</tbody>
</table>

† 15 to 45 minutes after the end of infusions administered at regularly scheduled visits (every 4 weeks).
‡ For multiple injection sites, every site was judged, but only the site with the strongest reaction was recorded.
§ Rate of injection-site reactions per infusion.
¶ Number of infusions administered during regularly scheduled visits.

Most local reactions were either mild (93.4%) or moderate (6.3%) in intensity.

### 6.2 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions or establish a causal relationship to product exposure.

The following adverse reactions have been identified and reported during the postmarketing use of IGIV products:

- **Infusion reactions:** Hypersensitivity (e.g., anaphylaxis), headache, dizziness, nausea, vomiting, rigors, back pain, myalgia, arthralgia, and changes in blood pressure
- **Renal:** Acute renal dysfunction/failure, osmotic nephropathy
- **Respiratory:** Apnea, Acute Respiratory Distress Syndrome (ARDS), TRALI, cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm
- **Cardiovascular:** Cardiac arrest, thromboembolism, vascular collapse, hypotension
- **Neurological:** Coma, loss of consciousness, seizures, tremor, aseptic meningitis syndrome
- **Integumentary:** Stevens-Johnson syndrome, erythema multiforme, dermatitis (e.g., bullous dermatitis)
- **Hematologic:** Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs') test
- **Gastrointestinal:** Hepatic dysfunction, abdominal pain
- **General/Body as a Whole:** Pyrexia, rigors

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6938 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

### 7 DRUG INTERACTIONS

#### 7.1 Live Virus Vaccines

The passive transfer of antibodies with immunoglobulin administration may interfere with the response to live virus vaccines such as measles, mumps, rubella, and varicella (see Patient Counseling Information [17]).

#### 7.2 Serological Testing

Various passively transferred antibodies in immunoglobulin preparations may lead to misinterpretation of the results of serological testing.

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Hizentra. It is not known whether Hizentra can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Hizentra should be given to pregnant women only if clearly needed.

#### 8.3 Nursing Mothers

Hizentra has not been evaluated in nursing mothers.

#### 8.4 Pediatric Use

The safety and effectiveness of Hizentra have been established in the pediatric age groups 2 to 16, as supported by evidence from adequate and well-controlled studies. Hizentra was evaluated in 10 pediatric subjects with PI (3 children and 7 adolescents) in a study conducted in the US (see Clinical Studies [14]) and in 23 pediatric subjects with PI (18 children and 5 adolescents) in Europe. There were no differences in the safety and efficacy profiles as compared with adult subjects. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels.

Safety and effectiveness of Hizentra in pediatric patients below the age of 2 have not been established.

#### 8.5 Geriatric Use

Of the 49 subjects evaluated in the clinical study of Hizentra, 6 subjects were 65 years of age or older. No overall differences in safety or efficacy were observed between these subjects and younger subjects.
If you live with primary immunodeficiency disease (PIDD)…

Make the leap to Hizentra

The Sub-Q Ig therapy that fits your life

Hizentra is a subcutaneous immune globulin (Sub-Q Ig) therapy that was deliberately designed to give you freedom and flexibility with your Ig treatment.

- The 20% concentration delivers an Ig dose in half the volume of 10% solutions
- Convenient room temperature storage for up to 30 months
- Always ready for immediate use

*Based on an equivalent dose in grams.

To learn about the benefits of Hizentra, visit www.LearnAboutHizentra.com

Ask your doctor about Hizentra today.

Important Safety Information

Hizentra is indicated for the treatment of various forms of primary immunodeficiency (PI).

If you have a history of anaphylactic or severe systemic response to immune globulin preparations or selective immunoglobulin A deficiency, check with your physician, as Hizentra should not be used.

Hizentra is to be infused under your skin only; do not inject into a blood vessel.

Hypersensitivity reactions may occur with Hizentra. If your physician suspects you are having a negative reaction or are going into shock, treatment will be discontinued. Because Hizentra contains proline, you cannot be treated with Hizentra if you have hyperprolinemia (a high level of proline in your blood).

Hizentra is derived from human plasma. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

The most common drug-related adverse reactions (seen in 5% or more of subjects in the clinical trial) were local reactions (swelling, redness, heat, pain, and itching at the injection site), headache, vomiting, pain, and fatigue.

Your physician will monitor for potentially serious reactions associated with intravenous immunoglobulin treatment that might also occur with Hizentra, including renal dysfunction/failure, osmotic nephropathy, thrombotic events, aseptic meningitis syndrome (AMS), hemolysis, and transfusion-related acute lung injury (TRALI).

Ig administration may impair the effect of virus vaccines, such as measles, mumps and rubella. Before getting any vaccination, inform your doctor that you are using Hizentra.

Please see brief summary of full prescribing information for Hizentra on previous pages.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
The **Products** you need when you need them.

- Flu Vaccine
- Immune Globulins
- Coagulation Products
- Hyperimmunes
- Albumin
- Other Vaccines and Specialty Biologicals