PANDAS
Understanding the Rare & Controversial Disease

Parenting: Diagnosing Immune Deficiency in Childhood

Effects of Age-Related Immune Disorders

PIDD Diagnoses: Understanding the Long-Term Risks

Alternative Therapies for Pain Relief
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
- 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 (AMS) has been reported with GAMUNEX-C and other IGIV treatments, especially with high doses or rapid infusion.
- Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration. Monitor patients for hemolysis and hemolytic anemia.
- Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
- Volume overload
- GAMUNEX-C is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease agent.
- Passive transfer of antibodies may confound serologic testing.

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.

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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).


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.

The PROOF is everywhere you look

GAMUNEX-C has proven efficacy and patient outcomes in CIDP, PI, and ITP*1

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

Evidence based. Patient proven.
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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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Long-Term Effects of PIDDs
“Most long-term effects occur due to two reasons: frequent infections and/or the presence of autoimmune complications.”

Diagnosing Specific Antibody Deficiency: Summary of Discussions, Part 1
“Regardless of the serum levels of immunoglobulins, the key to making a diagnosis of an antibody deficiency is demonstrating that there is an inability to produce appropriate, specific antibodies when immunized with a specific vaccine.”

Pain Relief: Alternative Therapies
“Because pain is subjective to the person experiencing it, caregivers, family and friends must be careful to not discount a patient’s complaints.”

“There will come that eventual day when I will need to tell whomever I’m out with that I’m sick.”

Be a Part of IG Living’s Blog and Facebook Discussions!

IG Living isn’t just a magazine; it’s an interactive community of people with interesting stories. And, we want you to be a part of it!

Our blog, which has a new entry posted each Friday, provides interesting perspectives on topics such as living with IG, people to be admired, support and encouragement, current news of interest and things you just need to know. We encourage you to comment with your opinions and stories. And, better yet, if you have a blog you’d like to post, send it our way!

IG Living’s Facebook page has hundreds of fans who respond to our questions that are posted each Monday through Friday. Together, these fans share their life stories and thoughts. What’s more, they are making a connection with one another that otherwise wouldn’t be possible.

So, be a part of it now at www.igliving.com/blogengine and www.Facebook.com/IGLivingMagazine.

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 monthly, 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 akazemi@IGLiving.com or calling (800) 843-7477, ext. 1366.
A “Rare” Diagnosis

The Office of Rare Diseases Research lists 7,000 rare (or orphan) diseases on its website. Rare diseases are generally considered to have a prevalence of fewer than 200,000 affected individuals in the United States. Immune deficiency and autoimmune diseases are classified as rare diseases. Yet, while they are not as rare as they used to be, diagnosis can often still be difficult and lengthy.

There are many reasons why a rare disease is difficult to diagnose, but the top reasons are that 1) individuals often have to see a number of doctors before finding one who knows something about what they have, 2) symptoms of a rare disease are “nonspecific,” meaning they are not signs of a specific disease but can be the results of many different diseases, 3) symptoms often are unusual and 4) it can be difficult to get in to see a specialist who may know something about the disease.

In this issue, we explore all of these aspects of getting a diagnosis and more. One autoimmune disease that is especially difficult to diagnose is pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS). With so much unknown about PANDAS and no conclusive proof that strep is the cause of the disease, some medical professionals refuse to believe in its existence and, thus, children whom it affects are unable to get the treatment they need. For example, Kap Smith, diagnosed with PANDAS in 2010, struggled to find treatment that helped. His story is a revealing example of the lengths to which parents sometimes have to go to get the often-needed immune globulin therapy to treat their children’s debilitating symptoms.

In his parenting column, Mark Haggard, father of three immunodeficient children, describes getting a diagnosis for primary immunodeficiency disease (PIDD) as “nailing Jell-O to the wall.” It’s not that doctors aren’t trying to diagnose a child’s recurrent infections, he explains, but often they are struggling to find a diagnosis for many reasons, including ruling “in” the right disease. For instance, a child’s symptoms might be similar to those associated with many different illnesses, and often non-specialists don’t recognize the hallmark symptoms of PIDD. Or, as in the case of common variable immunodeficiency, symptoms often don’t present until much later in life.

Of course, the problems with delayed diagnosis or failure to get a diagnosis are many. Without a correct diagnosis, patients are often unable to get the treatment they need. If they are treated, they may be unable to get reimbursed. And, with no treatment, they may end up with long-term permanent damage to their bodies.

As our patient advocate Annaben Kazemi explains in her article Long-Term Effects of PIDDs, delayed or misdiagnosis can result in organ damage, disability and, sometimes, death. In addition, PIDD patients often also present with autoimmune diseases, which can cause long-term complications. Therefore, receiving an early diagnosis is crucial. And, as Dr. Marc Riedl explains, that can only happen with a good team of doctors.
**Immunology 101:**

**Diagnosing Specific Antibody Deficiency: Summary of Discussions, Part 1**

By Terry O. Harville, MD, PhD

**IN THE PAST** several columns, I have discussed the issue of how an antibody deficiency diagnosis is made. In this and the next issue’s columns, I will summarize these, as we will be soon delving into new issues.

A patient presents with clinical symptoms and features that suggest a primary immunodeficiency disease (PIDD). The hallmark symptoms are recurrent/chronic infections of the respiratory tract, commonly called sinopulmonary infections. And these are suggestive of a possible deficiency in the humoral immune system, which consists of 1) complement proteins, 2) mannann binding lectin (MBL) and 3) immunoglobulin. Complement deficiencies are relatively much rarer than other immunodeficiencies, but a test known as the “CH50” may be assayed to verify no problem with the complement system. The MBL serum level also may be measured to verify that it is in the normal range. The focus is on determining whether there are any deficiencies within the immunoglobulins.

Typically, serum levels of IgG, IgM, IgA and IgE are measured. Deficiencies or elevations of specific components may be found in patients with PIDD. In X-linked agammaglobulinemia, all are typically low. In hyper-IgM syndrome, the IgM level is elevated, but the rest are typically very low. In hyper-IgE syndrome, serum IgE is quite elevated, whereas the remainder are typically very low. IgA deficiency is complicated, because approximately one in 500 people have to absent serum IgA levels but do not appear to have any associated disease, whereas perhaps one in 10,000 people have low to absent IgA and do have recurrent infections or other problems. Another major condition is common variable immunodeficiency (CVID), which, as the name implies, has variability in the features and laboratory studies. In general, though, most believe that patients with CVID will have low serum levels of IgG, IgA and, at some point, also IgM. The patients most difficult to diagnosis are those with apparent normal or near-normal serum levels of IgG, IgA and IgM but with recurrent sinopulmonary infections and absence of deficiencies of complement or MBL.

Regardless of the serum levels of immunoglobulins, the key to making a diagnosis of an antibody deficiency is demonstrating that there is an inability to produce appropriate, specific antibodies when immunized with a specific vaccine. Testing for an antibody deficiency is performed by 1) obtaining serum (for pre-immunization testing), 2) giving the vaccine and 3) in approximately four weeks, obtaining serum for the post-immunization testing. The pre- and post-immunization antibody levels are compared, and a judgment is rendered as to whether the response is normal or abnormal.

Diphtheria and tetanus toxoid vaccines are typically used to determine whether appropriate antibody responses can be made to “protein” antigens. (Antigen is the name given to a substance against which the immune system is expected to respond.) The post-immunization response is expected to be in the normal protective range, with some significant increase over the pre-immunization response (usually considered to be two to four times higher).

The pneumococcal vaccine is used to test for the response to polysaccharide antigens (which are found on the surfaces of most bacteria and other pathogens that cause infections). There are now two commonly used pneumococcal vaccines: 1) conjugated (Prevnar 13) and 2) nonconjugated. The conjugated vaccine is typically given to children, and utilizes the inherent ability of the immune system to respond reasonably well to the diphtheria toxoid antigen in order to “trick” the immune system into also responding to the 13 attached different polysaccharide antigens, each from a different strain of the pneumococcal bacteria. The nonconjugated pneumococcal vaccine consists of 23 different strains of pneumococci (13 of which are the same as in the conjugated vaccine). Therefore, there are typically 10 nonconjugated pneumococcal strains for assessing how well antibodies are being made in response to the polysaccharide antigens within the pneumococcal vaccine.

We will continue this discussion in the next issue.

**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.**
**Immunosenescence: Slowing the Effects of Age-Related Immune Disorders**

There are many theories concerning age-related immune disorders that might help improve the quality and extend the length of seniors’ health.

By Mark T. Haggard

**THE LIFE EXPECTANCY** of the average American is 76 years. Studies show that once a person turns 60, his or her chances of dying double every eight years. For instance, a person who is 68 is twice as likely to die within the next year than the person who is 60. Much of this trend can be attributed to poor immune health.

As people age, their immune cells age. Federico Licastro of the Universita di Bologna, Italy, laments: “Age-related diseases are the price we pay for an active immune system that defends us in youth, but may harm us later on. The process of life for the individual is the struggle to preserve its biological and immunological integrity. However, the preservation of the integrity of the organism comes with a price of responsiveness to systemic inflammation, which must be finely tuned, otherwise dysregulation becomes a damaging accompaniment.” In essence, where periodic inflammation is necessary for the destruction of pathogens in a young body, extended periods of chronic inflammation become destructive to the older body. Adds Licastro: “A long period of [immune cell] activation may lead to chronic inflammation, which inexorably damages several or all organs and is the phenotype linked to both aging and chronic disease.”

So, is there hope for people older than 60? Certainly. Life expectancy can be extended by improving immune health.

**Causes of Age-Related Immune Disorders**

Immunosenescence is the gradual deterioration of the immune system brought on by the aging process. The result of this age-related immune deficiency may be something as simple as a general feeling of lethargy or malaise, or may progress into severe infections, autoimmune issues, increased incidences of cancer and chronic inflammatory disorders such as Alzheimer’s disease, atherosclerosis and type 2 diabetes.

Hard evidence about the causes of immunosenescence are hard to come by, and the theories that have been posited are many and varied. According to Calogero Caruso of the University of Palermo, Italy: “It is often difficult to determine whether changes in particular cell type are intrinsic to that cell, or caused by environmental changes, or both.” Studies on the causes of immunosenescence focus on three areas: the ability of immune cells to proliferate, changes made in the structure of immune cells, and the introduction of “rogue” cells in the body.

One theory suggests that normal cells go through a finite and predictable number of divisions in tissue culture before reaching an irreversible state of growth arrest; once that number of divisions is met, the tissues and the body begin to decline. In a younger person, cells reproduce quickly to replace the dying cells. But, as the body ages, the ability of B cells and T cells to undergo rapid cell division is slowed to the point where they cannot keep up with the cell division of bacteria and viruses, and immune cells are eventually overrun by pathogens.

A similar theory holds that immunosenescence is the result of the inability of leukocytes — which differentiate into lymphocytes and phagocytes — to self-renew. The result is a decline in the number of phagocytes, a decline in the cytotoxicity of natural killer (NK) cells, and a decline in the population of B cells with smaller immunoglobulin diversity and affinity.

Studies of the thymus gland, which controls immune response, show that
thymic influence on the production and maturation of B cells and T cells is reduced with age. Proliferation of T lymphocytes is essential for rapid, clonal expansion of immune cells, but thymic involution causes T cell proliferation to decline with age.

A second theory has resulted in studies at the University of Utah, which have focused on the telomeres of DNA. Telomeres, located on the end of chromosomes, keep DNA from becoming damaged. Each time a cell divides, the telomeres become shorter, sacrificing a little bit of themselves to protect the genetic code of DNA, and become progressively shorter with each division until the cell dies. In the absence of telomeres, the ends of chromosomes fuse together, degrading the cell's genetic blueprint and causing it to malfunction, die or become cancerous.

One more theory of reduced immune response in older age is damage to leukocytes — white blood cells that function as phagocytes of fungi, bacteria and viruses, and detoxifiers of toxic proteins. As rogue molecules bind to receptor sites on immune cells, they inhibit the cells' ability to communicate with other cells. This may be the result of oxidative damage to the body's DNA by oxygenated ions (free radicals), much like oxygen causes the browning of a slice of apple or the rusting of metal. It may be the result of glycation, which is the binding of glucose or fructose molecules to cells and the creation of rogue molecules termed “advanced glycation endproducts” (AGEs). Or, it may be the result of both. The changes made to cells by oxidation or glycation are believed to initiate an autoimmune response when the immune system cannot recognize its own cells.

### Preventing Age-Related Immune Disorders

Knowing the theories behind age-related immune disorders could improve the quality and length of an individual's life. Studies in England showed that thymic atrophy could be reversed by surgical or chemical castration, which improved immune response in aged subjects. Another study reversed thymic atrophy with therapeutic intervention with interleuken-7 and its derivatives.

But, there are other less-intrusive ways to improve immune system health in older individuals than surgical or chemical castration. Annual flu vaccinations aid in the proliferation of immune cells, because introducing hundreds of memory cells into the body can immediately counter an invasion of any pathogen. Those who smoke can quit to slow the onset of age-related disease. Not only are cigarettes associated with various pathologies such as cardiovascular disease and respiratory disease, they also are a source of free radicals, and recent studies show that smoking shortens the length of telomeres in circulating lymphocytes, worsening immunosenescence.

Studies conducted by the World Health Organization suggest that good oral health has a profound impact on overall health. The increased antigen burden associated with oral disease in aging increases the risk of atherosclerosis and Alzheimer's disease.

Malnutrition in seniors aggravates immune deficiency. Beta-carotene supplementation has been shown to improve NK cell activity, and vitamin E supplementation has shown to increase lymphocyte proliferation. Free radicals can be eliminated from the body by eating colorful fruits and vegetables and foods rich in beta carotene, vitamin C and vitamin E, either raw or lightly cooked. Limiting caloric intake slows down the “glycation” of cells and improves immune health. Because AGEs have such a deleterious impact on health, it is important to avoid the things that promote their creation such as cooking food at a high temperature.

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**What is ingested has a significant impact on how an individual lives in his or her golden years.**

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### Additional Information:

- University of Utah study on telomeres: [learn.genetics.utah.edu/content/begin/traits/telomeres](learn.genetics.utah.edu/content/begin/traits/telomeres)
- Wayne State University School of Medicine study on zinc deficiency: [www.translationalres.com/article/S1931-5244(06)00338-0/abstract](www.translationalres.com/article/S1931-5244(06)00338-0/abstract)
- Professional articles on immnosenesence: [www.immunityageing.com](www.immunityageing.com)
Instead, foods should be cooked at a low temperature — by boiling, poaching or stewing — rather than frying or grilling. Processed carbohydrates also are high in AGE content. It was previously believed that AGES simply accumulated in the body, but a 2009 study revealed that AGES actually can be reduced with a low-calorie diet.

Many studies have revealed the importance of zinc for immune health. One showed that the effects of zinc deficiency are complex and impact hundreds of genes, playing a key role in cell DNA replication, cell division and proliferation. Zinc deficiency impairs the function of immune cells such as neutrophils and NK cells, and compromises B lymphocyte development and the production of IgG. It also may adversely affect the operations of the macrophage and, therefore, phagocytosis, cytokine production and intracellular killing. A study at the Wayne State University School of Medicine showed that zinc deficiencies in the elderly may impair zinc-dependent signaling and, therefore, immune function. Suppressed production of interleukin-2 proved quickly corrected with zinc supplements. And, a study by the National Institute of Health in Italy discovered a significant increase in the number of cytotoxic T cells and helper T cells in residents of a retirement home who had been supplemented with 25 mL of zinc per day.

Healthy in the Golden Years

As a person grows older, the tendency is for cells, including immune cells, to break down. There is no consensus among doctors as to what causes immunosenescence, but a decline in immune health can be slowed by the proper care and maintenance of bodies. What is ingested has a significant impact on how an individual lives in his or her golden years. Following good dietary habits is not likely to bring back the glory days, but it has the potential to significantly increase the number of golden years to be lived.

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

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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Research

Study Shows Rozrolimupab Effective for Treating ITP

Results from the final Phase II clinical trial of Symphogen’s rozrolimupab shows it is safe and effective in inducing a rapid increase in platelet counts in patients with primary immune thrombocytopenia purpura (ITP). Rozrolimupab is a novel human recombinant mixture of 25 antibodies that are all manufactured simultaneously.

The Phase II open-label, multicenter clinical trial evaluated the efficacy, safety and tolerability of rozrolimupab (SYM001) in adult, RhD positive, non-splenectomized ITP patients. A total of 61 patients were treated with single doses from 75 µg/kg to 300 µg/kg as single intravenous infusions of 15 to 20 minutes’ duration. The trial demonstrated that at 300 µg/kg, eight of 13 (62 percent) patients responded at day seven. Within five to eight hours after rozrolimupab administration, 23 percent of patients achieved platelet responses (≥ 30x10^9/L and increase in platelet count by > 20x10^9/L from baseline). Median time to response was 59 hours (approximately 2.5 days), and the median duration of response was 14 days. The most common adverse events observed were headache, mostly mild or moderate (20 percent), pyrexia (13 percent), chills (10 percent) and fatigue (8 percent). Four serious adverse events considered related to the drug were reported: decreased hemoglobin, extravascular hemolysis/dizziness and two cases of transient rise in D-dimer values without clinical symptoms.

According to Tadeusz Robak, MD, professor at the University of Lodz, Poland: “These results suggest an efficacy and safety profile similar to that seen with plasma-derived immunoglobulin products. It seems promising that rozrolimupab rapidly yields platelet responses. This unique recombinant human monoclonal antibody mixture, rozrolimupab, can be produced indefinitely and may represent a novel and convenient replacement for blood-derived immunoglobulins with more limited supply.”

The study was published in the August 22 edition of Blood.

Survey

UAE Pediatricians Deficient in PIDD Knowledge

A recent study exploring physicians’ knowledge and experience about primary immunodeficiency (PIDD) found a noteworthy deficiency in PIDD workup. The self-administered questionnaire was conducted among 263 pediatricians of wide education backgrounds practicing in the United Arab Emirates (UAE) working in the 27 government hospitals in all regions of the UAE. It included questions on PIDD signs and symptoms, syndromes associated with immunodeficiency, screening tests, interpreting laboratory tests and case management.

Of the 50 questions, 20 percent of pediatricians answered fewer than 60 percent of the questions correctly, 76 percent answered 60 percent to 79 percent of the questions correctly, and 4 percent answered fewer than 80 percent of the questions correctly. Seventeen of the 19 PIDD signs and symptoms were identified by 55 percent to 97 percent of pediatricians. Four of five syndromes associated with immunodeficiency were identified by 50 percent to 90 percent of pediatricians. Appropriate screening tests were chosen by 64 percent to 96 percent of pediatricians. And, attention to the laboratory reference range values as a function of patient age was notably limited. The overall performance of the pediatricians did not differ based on their age, gender, origin of certification, rank or years of experience.

PIDD is a cluster of serious disorders that require special alertness on the part of the medical staff for prompt diagnosis and management of the patient. The conclusion of the study was to implement effective educational strategies to improve the competency of pediatricians to diagnose and manage PIDD disorders.
Disease Awareness

Scleroderma Foundation Launches Video Campaign

The Scleroderma Foundation has launched the “Walk for Cure” video awareness campaign to support its signature fundraising and awareness event, “Stepping Out to Cure Scleroderma.” Supporters are asked to upload an original video on WalkForCure.org, a video-sharing website, that describes why they walk. The goal is to increase scleroderma awareness and provide hope and inspiration to the entire scleroderma community. WalkForCure.org was open for video submissions until 11:59 p.m. (Pacific), Monday, Oct. 15, 2012. In November, all uploaded videos were edited together, burned onto DVDs and sent to members of Congress and the president of the United States.

Resource

IDF Publishes New IG Therapy Guide for Nurses

The Immune Deficiency Foundation (IDF) has released the IDF Guide for Nurses Immunoglobulin Therapy for Primary Immunodeficiency Diseases — 3rd Edition.” Developed by the IDF Nurse Advisory Committee, the pocket-size guide includes topics on general information about primary immunodeficiency diseases, delivery of immunoglobulin replacement therapy, product selection and characteristics, troubleshooting subcutaneous immunoglobulin therapy and more. It can be ordered by contacting the IDF at (800) 296-4433 or idf@primaryimmune.org, or a PDF of the guide can be downloaded at primaryimmune.org/about-primary-immunodeficiency-diseases/idf-publications.

People and Places

NexDx Inc., a science-driven molecular diagnostics company providing next-generation products and services for personalized medicine in rheumatoid arthritis and other autoimmune diseases, announced today the appointment of internationally renowned physician and scientist Mary K. Crow, MD, to its scientific advisory board.

The Scripps Research Institute has been awarded a new $22.5 million, five-year grant from the National Institutes of Health to study the immune system. The ongoing research examines innovative technologies that may provide data for treating a wide range of human diseases that include viral and bacterial infections and inherited immune disorders.

Legislation

Florida Will Test Newborns for SCID

The Florida Department of Health has added severe combined immune deficiency disease (SCID), known as bubble boy disease, to the list of conditions that all newborns in the state are screened for at birth beginning October 1, 2012. SCID is a primary immunodeficiency disease where affected infants lack T lymphocytes or white blood cells that help fight infections from a wide array of viruses, bacteria and fungi, leaving the infants susceptible to serious, life-threatening infections. Babies with SCID appear healthy at birth, but without early treatment, most often by bone marrow transplant, these infants cannot survive.

In the time since the federal recommendation that all states screen for SCID, dozens of babies have been born with this condition and have gone undetected until serious infection made it known. Three babies born in Florida suffered from this fate; one passed away at the age of five months last year, while the other two babies spent months in the hospital for treatment. Both remain in delicate circumstances awaiting recovery. In June 2011, Florida Governor Rick Scott vetoed a program that would add a test for SCID to the list of genetic diseases newborns are tested for in the state.
Did You Know?

IG Living magazine is now inviting teens to submit their stories to be published in a new Teen Talk column. The column will debut in the February-March 2013 issue. If you are a teen living with a primary immune or autoimmune disease that is treated with immune globulin, we encourage you to submit your story of what it is like to live with a chronic illness. Submit your 600- or fewer-word story to Editor@IGLiving.com.

Research

Refined Gene Therapy May Restore Immune Systems in Kids with SCID

Researchers have demonstrated that a refined gene therapy approach safely restores the immune systems of some children with severe combined immunodeficiency (SCID). SCID is a rare condition that blocks the normal development of a newborn’s immune system, causing chronic infections and a lifespan of two years if their immunity cannot be restored.

The 11-year study tested a combination of techniques for gene therapy in 10 patients with ADA-deficient SCID. The researchers used two slightly different DNA insertion vehicles, called retroviral vectors, to deliver the healthy ADA gene into the bone marrow cells of the patients. Retroviruses have the specialized ability to become a permanent part of host cells. Four of the patients remained on enzyme-replacement therapy throughout the procedure. The other six patients stopped enzyme-replacement therapy beforehand and were treated with a low dose of a chemotherapy that depletes stem cells in the bone marrow, making space for the gene-corrected stem cells that had been given the new gene in the laboratory and then returned to the patient’s body. That step proved to be important. The procedure has produced normal levels of immune function for three of those six patients for up to five years and has eliminated the need for enzyme-replacement injections. The researchers suggest that enzyme-replacement therapy during the procedure may dilute the numbers of corrected lymphocytes in the patients’ immune systems, diminishing the treatment’s effect.

An additional eight children, most of whom are 1 year old or younger, have been added to a second phase of the study. And, according to the researchers, the younger patients are showing even more favorable response rates to the therapy.

Resource

IDF Introduces New Patient Insurance Center

The Immune Deficiency Foundation has introduced a Patient Insurance Center on its website that provides information regarding insurance issues, as well as other possible sources of assistance, for patients and their families. The center includes a patient advocate corner that provides individualized assistance for patients who face insurance problems, including denials for therapy, procedures related to primary immunodeficiency diseases, reimbursement complications, help getting insurance, as well as the ability to locate a specialist, connect with peer support, request educational materials and more. Also offered is a FAQs page where patients can read answers to frequently asked questions, the American Academy of Allergy, Asthma & Immunology (AAAAI) IVIG Toolkit that outlines patients’ rights in terms of treatment and standards of care, a guide for how to appeal a health insurance denial, a list of manufacturers’ patient assistance programs, a list of insurance and treatment resources, an explanation of how healthcare reform affects patients, and a list of questions and answers submitted by patients over the years. The center can be accessed at primaryimmune.org/patients-and-families/patient-insurance-center.
**Clinical Trial**

**First Human Clinical Trial for Autoimmune Drug ShK-186**

Kineta Inc. has received regulatory approval in the Netherlands to initiate a first-in-human clinical trial of ShK-186, an autoimmune drug candidate that specifically inhibits the Kv1.3 potassium ion channel. ShK-186 is the first Kv1.3-specific inhibitor to advance to the clinic in hopes of developing an immune-sparing therapy for autoimmune diseases such as multiple sclerosis (MS), rheumatoid arthritis (RA) and lupus (SLE).

Kv1.3 instigates activation of effector memory T cells that are major mediators of autoimmune disease. Kineta scientific adviser and University of California, Irvine, professor K. George Chandy, MD, PhD, and his collaborators discovered the Kv1.3 channel and invented ShK-186 by modifying natural sea anemone-derived peptide inhibitors of Kv1.3. They found that by blocking the Kv1.3 channel, ShK-186 can reduce disease symptoms and pathology in animal models of MS, RA and SLE without broadly suppressing the immune system.

According to Dr. Tim Coetzee, chief research officer for the National Multiple Sclerosis Society and an early supporter of Dr. Chandy’s research, “There is a clear, unmet medical need for new therapies to treat MS that have novel mechanisms of action and may offer freedom from the side effects that accompany broad suppression of the immune system.”

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**Research**

**Trial to Evaluate Therapeutic Vaccine for Celiac Disease**

ImmusanT has initiated clinical trials in New Zealand, Australia and the U.S. to evaluate Nexvax2, a therapeutic vaccine for patients with celiac disease. Nexvax2 is designed to re-establish patients’ tolerance to the toxic effects of gluten, a protein in wheat, barley and rye, and allow them to return to a normal diet. There are currently no approved medicines available for people with celiac disease, who must manage their condition by eliminating gluten-containing foods from their diet.

Advancing the earlier Nexvax2 clinical trial, the new trial in Australia and New Zealand is a randomized, double-blind, placebo-controlled Phase 1b study evaluating multiple ascending doses of Nexvax2 for the induction of gluten tolerance in patients on a gluten-free diet. ImmusanT expects to enroll 84 subjects at approximately four study sites in the two countries in order to evaluate the safety, tolerability and pharmacokinetics, and to select doses for investigation in subsequent studies.

The second study, a randomized, double-blind, placebo-controlled Phase I trial being conducted in the U.S., will determine the safety, tolerability and pharmacokinetic profile of Nexvax2 in patients with celiac disease well controlled by a gluten-free diet. ImmusanT plans to enroll 30 adult subjects at approximately four trial sites.

“We are kicking off a robust clinical program that we hope demonstrates Nexvax2 dramatically reduces the body’s immune response to dietary gluten so patients can resume a normal diet and return to good health,” said Patrick H. Griffin, MD, chief medical officer of ImmusanT. “Our clinical development program will allow us to further examine the role of antigen-specific T cells in celiac disease activation and in the re-establishment of tolerance to gluten.”
Despite a growing body of research, little is understood about this childhood disorder, and controversy flourishes about whether PANDAS, and now PANS, is real and how prevalent it is.

By Ronale Tucker Rhodes, MS

The stories are all too similar: Parents describe their once-active and normally behaving children who overnight became obsessive-compulsive and moody with tics, deteriorating motor skills and severe separation anxiety. It is a terrifying phenomenon for both parents and the children who don’t understand what is happening. But, it is happening all too often.
The problem is that the true prevalence of PANDAS (pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections), and now PANS (pediatric acute-onset neuropsychiatric syndrome), is not known. Even worse, despite the growing body of research behind the disease, there is still too much that is unknown, and some medical professionals refuse to believe it exists.

**What Is PANDAS?**

The term PANDAS is used to describe a subset of children and adolescents who have obsessive compulsive disorder (OCD) and/or tic disorders whose symptoms worsen following strep infections such as strep throat and scarlet fever.\(^1\) It is listed as a rare disease by the Office of Rare Diseases of the National Institutes of Health, meaning PANDAS affects less than 200,000 people in the U.S.\(^2\) According to the PANDAS Network, a conservative estimate of the number of PANDAS cases in the U.S. is 162,000. However, the true prevalence is unknown. It is known that the ratio of boys to girls over 8 years old who have PANDAS is 2.6 to 1, and under 8 years old, it is 4.7 to 1. Based on a survey of 700 family self-reports to PANDAS Network.org, the onset of PANDAS occurred between ages 1 to 3 in 11 percent of those families, ages 4 to 9 in 69 percent, ages 10 to 13 in 19 percent and ages 14 and older in 1 percent. The primary symptoms described by the families were OCD (37 percent), tics (14 percent) and both (49 percent). And, the infections reported by the families were strep (81 percent) or others, such as mycoplasma, lyme disease, etc. (19 percent).\(^3\)

PANDAS was first observed in the 1980s when researchers at the National Institute of Mental Health (NIMH) were studying childhood-onset OCD. The researchers, who included Drs. Susan Swedo, Henrietta Leonard and Judith Rapoport, observed that some of the children had an unusually abrupt onset of symptoms unlike typical cases of OCD. Rather than symptoms beginning gradually and, in many instances, hidden by the child for weeks or months because of their embarrassment, the symptoms of the children in the PANDAS subgroup occurred very suddenly (overnight or out of the blue) and with dramatic onset (within 24 to 48 hours). In addition to the OCD and tic symptoms, these PANDAS children experienced a variety of other neuropsychiatric symptoms, including separation anxiety, anxiety attacks, irritability, extreme mood swings, temper tantrums, immature behaviors (like baby talking), hyperactivity, problems with attention and concentration, handwriting changes and problems with math, reading and other school subjects. The NIMH researchers discovered that all of the symptoms usually occurred following a strong stimulant to the immune system such as a viral infection or bacterial infection. These first cases were given the name PITANDS (pediatric infection triggered autoimmune neuropsychiatric disorders), but when it was discovered they followed infections with influenza, varicella (chicken pox) and streptococcal bacteria (strep throat and scarlet fever), the researchers later decided to focus on OCD symptoms that occurred after streptococcal infections because of the connection between OCD and Sydenham chorea, the neurological form of rheumatic fever. Hence, the disease was renamed PANDAS.\(^1\)

Despite the growing body of research behind PANDAS, there is still too much that is unknown, and some medical professionals refuse to believe it exists.

Because it is often difficult to demonstrate the relationship between strep infections and OCD/tic symptoms, which can result in delayed diagnosis and treatment of affected children, clinicians and researchers met in 2010 at the National Institutes of Health to discuss changing the diagnostic criteria. As a result, the PANDAS criteria were modified to describe PANS, which encompasses the larger class of acute-onset OCD cases. PANS and PANDAS are comparable to cancer and leukemia (respectively), as PANS is the large class of disorders and PANDAS is one specific type.\(^1\)

**A Controversial Diagnosis**

One of the reasons a PANDAS diagnosis is so controversial is because some physicians say there isn’t enough evidence to prove that strep or a similar infection can lead to OCD. The PANDAS hypothesis was based on observations in
clinical case studies at the NIH and in subsequent clinical trials where children appeared to have dramatic and sudden OCD exacerbations and tic disorders following infections. Yet, while there is supportive evidence for the link between strep and onset in some cases of OCD and tics, proof of causality has remained elusive. 4

At present, determining whether a child has PANDAS can be based only on a clinical diagnosis, meaning the diagnosis is made on the basis of knowledge obtained by medical history and physical examination alone, without benefit of laboratory tests. Clinicians use five diagnostic criteria for the diagnosis of PANDAS: 1) presence of OCD and/or a tic disorder, 2) pediatric onset of symptoms (ages 3 years to puberty), 3) episodic course of symptom severity, 4) association with group A beta-hemolytic streptococcal infection (a positive throat culture for strep or history of scarlet fever) and 5) association with neurological abnormalities (motoric hyperactivity or adventitious movements such as choreiform movements). 5

Children with PANDAS also seem to have dramatic ups and downs in their OCD and/or tic severity. Whereas children with OCD may have good days and bad days or even good weeks and bad weeks, children with PANDAS have a very sudden onset or worsening of their symptoms.

In January 2011, 10-year-old Kap Smith started coughing nonstop. It started not long after his sister contracted a strep infection and Kap complained of a sore throat. Assuming Kap also had strep, his pediatrician prescribed antibiotics, but they didn’t heal his sore throat; instead, Kap also was lethargic and, then, out of the blue, his cough developed.

For three months, Kap’s doctor tried to figure out what was wrong with him. He was treated for allergies; he was sent to a therapist for depression; he was hypnotized — but nothing worked. “He was exhausted,” said Kap’s mom, Kristi. “He looked wiped out, and he didn’t sleep at night.” As a last resort, Kap was sent to National Jewish Health in Denver, Colo., a 30-minute drive from his home in Boulder. National Jewish is considered the No. 1 respiratory hospital in the nation. A doctor there diagnosed Kap with PANDAS. “I was just blown away when she wrote it down as PANDAS,” said Kristi. “I felt like we were starting all over again.”

Kap was sent to Children’s Hospital for treatment. But, they didn’t believe the diagnosis. “They said the jury is still out on PANDAS,” explained Kristi. “And they put him on meds that made him crazy. He would hide in closets. He was out of school for about four months. At that point, I told a friend about it, and she knew another gal whose kid had PANDAS, and he couldn’t leave his home or mom.” That friend’s child was treated for PANDAS by a physician in Chicago.

Kristi called the doctor in Chicago. “That’s when we learned about IVIG [intravenous immune globulin] and off-label uses,” said Kristi. “We had a lot of phone conversations with him, and he did a bunch of tests to ensure it was PANDAS and not something else.” In fact, Kap had been tested for strep a number of times previously, but the tests always came up negative. But, those doctors, said Kristi, were only testing for the most common types of strep. The doctor in Chicago had him tested for a specific strain of strep that showed unusually high b titers, which indicated PANDAS.

In July, Kap and his parents flew to Chicago for IVIG therapy. His IVIG infusion lasted two days. The bad news: As is often the case for treatments that are prescribed off-label, the insurance company refused to reimburse the family for IVIG treatment. The good news: Kap is now symptom-free. “He didn’t wake up the next day and stop coughing,” said Kristi. “It happened over time; it was like the pages turning backward.” And, according to his doctor, there is no reason to believe Kap will relapse. However, as a precautionary measure, he was given antibiotics after his IVIG therapy.

Kap is now 13. This past year, the energetic young teen won the national tennis championships match in Las Vegas, Nev., as an unseeded player in both singles and doubles. Asked whether his bout with PANDAS may have had anything to do with his success, Kristi said: “I think it’s made him a lot more driven. He was always really good in sports. But he feels like he’s missed a year, and he’s going to make up for it.”

As for Kristi, she gives this advice to other parents facing the same situation: “Don’t be afraid to find the real root of the problem. Be persistent. You know your own kid. So, just search for the answer until you get what you want.”

Kap’s Story

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If you are a Hizentra patient or caregiver

Get connected through

Voice2Voice℠

Voice2Voice is a peer-to-peer support program from CSL Behring, the maker of Hizentra. Voice2Voice connects Hizentra patients and caregivers with advocates who have direct experience with Hizentra and know what it’s like to live with primary immunodeficiency disease (PIDD).

Find out what a Voice2Voice advocate can do for you.

A Voice2Voice advocate is someone you can share your story with. They can help answer your non-medical questions* and connect you to helpful resources. In addition, Voice2Voice advocates can share their own real-life treatment stories and offer encouragement as only someone who’s “been there” can do.

*Voice2Voice advocates are not healthcare professionals or medical experts. For medical questions, please contact your physician. Individuals appearing in the Voice2Voice videos are compensated by CSL Behring LLC for their time and/or expenses.

Important Safety Information

Hizentra treats various forms of primary immunodeficiency (PI) in patients age 2 and over.

Hizentra should not be used if you have had serious negative reactions to immune globulin (Ig) preparations or a deficiency of an Ig known as IgA. Because Hizentra contains the amino acid proline as stabilizer, patients with hyperprolinemia (too much proline in the blood) should not take Hizentra.

Infuse Hizentra under your skin only; do not inject into a blood vessel.

Allergic reactions can occur with Hizentra. If your doctor suspects you are having a bad allergic reaction or are going into shock, treatment will be discontinued. Immediately tell your doctor or go to the emergency room if you have signs of such a reaction, including hives, trouble breathing, wheezing, dizziness, or fainting.

Please see additional Important Safety Information on next page. Please see brief summary of full prescribing information for Hizentra on adjacent pages.
For people with PIDD

Hizentra is the Ig therapy that’s deliberately designed for SubQ use

Voice2Voice™

Sign up for Voice2Voice.
Log on to Hizentra.com/V2V to get connected with an experienced Voice2Voice advocate for helpful peer-to-peer support.

Backed by the expertise of CSL Behring, Hizentra 20% is currently being used by more than 10,000 patients and providers,¹ a number that’s growing every day

• Hizentra helps keep IgG levels stable with low-volume self-infusions
  —The first and only 20% Ig concentration delivers a consistent level of protection against infection
  —Individualized dosing means you can have confidence that you are getting the dose that’s right for you

Important Safety Information (continued)

Tell your doctor about any side effects that concern you. Your doctor will monitor for potentially serious reactions that have been seen with Ig treatment, including thrombotic events (blood clotting); aseptic meningitis syndrome (brain swelling); osmotic nephropathy (a kidney condition); hemolysis (a blood problem) and transfusion-related acute lung injury.

The most common drug-related adverse reactions in the clinical trial for Hizentra were injection-site reactions (swelling, pain, redness, heat or itching); headache; back pain; diarrhea; tiredness; cough; rash; itching; nausea and vomiting.

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

Vaccines (such as measles, mumps and rubella) might not work as well if you are using Hizentra. Before receiving a vaccination, tell the healthcare professional that you are being treated with Hizentra. Also tell your doctor if you are pregnant or nursing, or if you plan to become pregnant.

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

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

Hizentra®,
Immune Globulin Subcutaneous (Human), 20% Liquid

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references to refer 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) in adults and pediatric patients 2 years of age and older. 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 IgA-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 Thrombotic Events

Thrombotic events have been reported with the use of immune globulin products1-3, including Hizentra. 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, Factor V Leiden, known or suspected hyperviscosity, and/or those who use estrogen-containing products. 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.

5.3 Aseptic Meningitis Syndrome (AMS)

AMS has been reported with use of IGIV4 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.

5.4 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.

Hemolysis

Hizentra can contain blood group antibodies that may act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin (Coombs') test result and hemolysis.4-6 Delayed hemolytic anemia can develop subsequent to the administration of globulin therapy due to enhanced RBC sequestration, and acute hemolysis, consistent with intravascular hemolysis, has been reported.9 Monitor Hizentra recipients 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.

5.5 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.

5.6 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 (e.g., swelling, redness, heat, pain, and itching at the injection site), headache, diaphoresis, fatigue, back pain, nausea, pain in extremity, cough, rash, pruritus, vomiting, abdominal pain (upper), migraine, and pain.

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.

US Study

The safety of Hizentra was evaluated in a clinical study in the US for 15 months (3-month wash-in/wash-out period followed by a 12-month efficacy period) 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 median doses ranging from 66 to 331 mg/kg body weight (mean: 181.4 mg/kg) during the wash-in/wash-out period and from 72 to 379 mg/kg (mean: 213.2 mg/kg) during the efficacy period. The 49 subjects received a total of 2264 weekly infusions of Hizentra.
The proportion of subjects reporting local reactions decreased over time from approximately 20% following the first infusion to <5% by the end of the study. Three subjects withdrew from the study due to ARs of mild to moderate intensity. One subject experienced injection-site pain and injection-site pruritus; the second subject experienced injection-site reaction and hypersensitivity. All reactions were judged by the investigator to be “at least possibly related” to the administration of Hizentra.

### 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.

### Hizentra

The following adverse reactions have been identified during postmarketing use of Hizentra. This list does not include reactions already reported in clinical studies with Hizentra (see Adverse Reactions [6.1]):

- **Infusion reactions:** Allergic-anaphylactic reactions (including swollen face or tongue and pharyngeal edema), pyrexia, chills, dizziness, hypertension/changes in blood pressure, malaise.
- **Cardiovascular:** Thromboembolic events, chest discomfort (including chest pain)
- **Respiratory:** Dyspnea

### General

The following adverse reactions have been reported during postmarketing use of immune globulin products:

- **Infusion reactions:** Hypersensitivity (e.g., anaphylaxis), headache, diarrhea, tachycardia, fever, fatigue, dizziness, malaise, chills, flushing, urticaria or other skin reactions, wheezing or other chest discomfort, 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, epidermolysis, 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 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

### Table 2: Incidence of Subjects With Adverse Reactions (ARs)* (Experienced by 2 or More Subjects) and Rate per Infusion (ITT Population), US Study

<table>
<thead>
<tr>
<th>AR (≥2 Subjects)</th>
<th>Number (%) of Subjects</th>
<th>Number (Rate †) of ARs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions‡</td>
<td>49 (100)</td>
<td>1322 (0.584)</td>
</tr>
<tr>
<td>Headache</td>
<td>12 (24.5)</td>
<td>32 (0.014)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (10.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (8.2)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Back pain</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (8.2)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>4 (8.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Cough</td>
<td>4 (8.2)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Migraine</td>
<td>3 (6.1)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Pain</td>
<td>3 (6.1)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Contusion</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>2 (4.1)</td>
<td>2 (&lt; 0.001)</td>
</tr>
</tbody>
</table>

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

### Table 4: Incidence of Subjects With Adverse Reactions (ARs)* (Experienced by 2 or More Subjects) and Rate per Infusion, European Study

<table>
<thead>
<tr>
<th>AR (≥2 Subjects)</th>
<th>Number (%) of Subjects</th>
<th>Number (Rate †) of ARs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions†</td>
<td>24 (47.1)</td>
<td>105 (0.057)</td>
</tr>
<tr>
<td>Other ARs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>9 (17.6)</td>
<td>20 (0.011)</td>
</tr>
<tr>
<td>Rash</td>
<td>4 (7.8)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>4 (7.8)</td>
<td>13 (0.007)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (5.9)</td>
<td>5 (0.003)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>2 (3.9)</td>
<td>3 (0.002)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (3.9)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Erythema</td>
<td>2 (3.9)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>2 (3.9)</td>
<td>3 (0.002)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (3.9)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>2 (3.9)</td>
<td>3 (0.002)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>2 (3.9)</td>
<td>4 (0.002)</td>
</tr>
</tbody>
</table>

† Rate of ARs per infusion.
‡ Includes infusion-related reaction: infusion-site mass; infusion-site erythema, hematomata, induration, inflammation, edema, pain, pruritus, rash, reaction, swelling; injection-site extravasation, nodule; puncture-site reaction.

### Table 3: Investigator Assessments* of Injection-Site Reactions by Infusion, US Study

<table>
<thead>
<tr>
<th>Injection-Site Reaction</th>
<th>Number (Rate †) 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 (0.51)</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>

† Rate of injection-site reactions per infusion.
† Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.
followed by a slow, gradual improvement. And, if they get another strep infection, their symptoms suddenly worsen again with the severity persisting for at least several weeks but sometimes months or longer. Then, the tics or OCD gradually fade away, and they often enjoy a few weeks or several months without problems.⁶

At present, determining whether a child has PANDAS can be based only on a clinical diagnosis.

He looked for the presence of OCD and tic disorders in families involved in the current rheumatic fever resurgence in his region. His goal was to see if Tourette disorder (TD) or OCD was associated with the Sydenham chorea criteria for rheumatic fever. In a pilot survey of 100 families, he found almost four times as many Sydenham chorea probands (22%) had relatives with TD/tics or OCD than non-Sydenham chorea rheumatic fever patients (6%). He feels this supports an as-yet unidentified “common genetic risk factor.”⁷

A PANS diagnosis also is made entirely on the basis of its history and physical examination. The three criteria developed for a diagnosis of PANS includes: 1) abrupt, dramatic onset of OCD (including severely restricted food intake), 2) concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least two of seven categories: anxiety (particularly, separation anxiety); emotional lability (extreme mood swings) and/or depression; irritability, aggression and/or severely oppositional behaviors; behavioral (developmental) regression (such as baby talk, throwing temper tantrums, etc.); deterioration in school performance; sensory or motor abnormalities; somatic signs and symptoms, including sleep disturbances, bedwetting or urinary frequency.

It’s important to note that there does appear to be a genetic susceptibility to PANDAS. Dr. William McMahon, child psychiatrist and geneticist at the University of Utah, studied the broader area of general familial genetic risk.

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### Diagnostic Criteria for PANDAS and PANS

The National Institute of Mental Health has developed a set of criteria for both PANDAS and PANS, the latter of which encompasses the larger class of acute-onset OCD cases.

#### Criteria for the Diagnosis of PANDAS

1. Presence of OCD and/or a tic disorder
2. Pediatric onset of symptoms (ages 3 years to puberty)
3. Episodic course of symptom severity
4. Association with group A beta-hemolytic streptococcal infection (a positive throat culture for strep or history of scarlet fever)
5. Association with neurological abnormalities (motoric hyperactivity or adventitious movements such as choreiform movements)

#### Criteria for the Diagnosis of PANS

1. Abrupt, dramatic onset of OCD (including severely restricted food intake)
2. Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least two of seven categories:
   - anxiety (particularly, separation anxiety)
   - emotional lability (extreme mood swings) and/or depression
   - irritability, aggression and/or severely oppositional behaviors
   - behavioral (developmental) regression (such as baby talk, throwing temper tantrums, etc.)
   - deterioration in school performance
   - sensory or motor abnormalities
   - somatic signs and symptoms, including sleep disturbances, bedwetting or urinary frequency
3. Symptoms are not better explained by a known neurologic or medical disorder such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder or others
and somatic signs and symptoms, including sleep disturbances, bedwetting or urinary frequency and 3) symptoms are not better explained by a known neurologic or medical disorder such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder or others.¹

Successful Treatments

The best treatment for acute episodes of PANDAS is to get rid of the strep infection causing the symptoms (if it is still present). This is accomplished with a throat culture to detect the presence of strep bacteria in the throat. If the throat culture is negative, the child should be tested for an occult strep infection, such as a sinus infection or strep bacteria infecting the anus, vagina or urethral opening of the penis. While these latter infections are rare, they have been shown to trigger PANDAS symptoms in some patients. A single course of antibiotics such as amoxicillin, penicillin, azithromycin and cephalosporins will usually get rid of the strep infection.¹

The best treatment for acute episodes of PANDAS is to get rid of the strep infection causing the symptoms.

While conventional treatments for PANDAS are generally not universally agreed upon, the main treatments include off-label use of common medications used in general practice, including antibiotics, corticosteroids, selective serotonin reuptake inhibitors (SSRIs) and immunomodulatory therapies. When these therapies fail to work, more novel therapies have been used, including intravenous immunoglobulin (IVIG) and plasmapheresis. However, these treatments are not an option for all because of their expense and lack of availability.⁸

Several studies have proved the benefit of these different therapies. In one study, 23 subjects with PANDAS were enrolled in a double-blind, randomized controlled trial and administered antibiotic prophylaxis with penicillin or azithromycin for 12 months. Rates of streptococcal infections and neuropsychiatric symptom exacerbations were compared between the study year and the baseline year prior to entry. Results showed significant decreases in streptococcal infections during the study year compared with the baseline year, as well as significant decreases in neuropsychiatric exacerbations during the study year compared with the baseline year.⁹

In another study, researchers investigated whether plasma exchange or IVIG would be better than a placebo in reducing the severity of neuropsychiatric symptoms. Of the 29 children in the study, 10 received plasma exchange (five single-volume exchanges over two weeks), nine received IVIG (1 g/kg daily on two consecutive days) and 10 received a placebo (saline solution given in the same manner as IVIG). Symptom severity was rated at baseline and at one month and 12 months after treatment. At one month, the IVIG and plasma-exchange groups showed striking improvements in OCD symptoms, and tic symptoms also were significantly improved with plasma exchange. Treatment gains were maintained at one year, with 14 (82 percent) of 17 children much or very much improved over baseline (seven of eight for plasma exchange, and seven of nine for IVIG).¹⁰

Cognitive behavior therapy (CBT) also has been shown to be safe and minimally invasive. In one study, seven children with OCD of the PANDAS subtype (range 9 to 13 years) were treated in a three-week intensive CBT program conducted at a university clinic. Six of seven children were taking SSRI medication(s) upon presentation. Assessments were conducted at four time points: baseline, pretreatment approximately four weeks later, posttreatment, and three-month follow-up. Six of seven participants were classified as treatment responders (much or very much improved) at posttreatment, and three of six remained responders at follow-up. However, self-reported general anxiety and depression symptoms were not significantly reduced.¹¹

There are cautions concerning SSRIs. Because children with PANDAS appear to be unusually sensitive to the side effects of SSRIs and other medications, it is recommended that treatment be prescribed at very small starting doses of the medication and increased slowly enough that the child experiences as few side effects as possible. If symptoms worsen, the dosage should be decreased promptly. However, abruptly stopping SSRIs and other medications may also cause difficulties.¹

While not a conventional treatment, a literature review of several case studies showed that treatment with tetrabenazine and, subsequently, tonsillectomy, prevented reinfection of strep infections. In one case, an 11-year-old boy who developed PANDAS with severe choreic movements...
was initially treated with tetrabenazine 12.5 mg twice daily with remission of the neurological symptoms. Subsequently, the patient underwent tonsillectomy and has been asymptomatic since, with antistreptolysin O titer levels in range.12

Preventing Relapses
In many cases, recurrent episodes can occur when there is a resistant strain of the strep infection, when the child contracts another strep infection or even when exposed to strep such as through a family member.

Most children outgrow PANDAS at puberty (ages 12 to 15).

To avoid recurrent episodes, antibiotics are sometimes used as prophylaxis against strep infections. In the antibiotic prophylactic study mentioned previously, the results were successful. However, the use of prophylactic antibiotics is controversial. According to the PANDAS Network, in many of the acute cases profiled on its website, the typical course of antibiotics has not been helpful; the children continue to suffer for months, and symptoms often increase in severity. It is not clear if the acute cases are the exception or the rule.13

Most children outgrow PANDAS at puberty (ages 12 to 15). While it's not clear entirely why this occurs, it is known that strep infections are not usually prevalent in children after they have reached puberty. It is suggested that after exposure to multiple strains throughout childhood, a natural immunity to strep infections builds. Families in the PANDAS Network know of many girls who, at the onset of menses, have suddenly stopped having any PANDAS symptoms. And, there are reports of several boys, at age 13 or so, who have stopped having PANDAS symptoms as well.13

The Need for Additional Research
Many researchers across the nation have developed hypotheses about the cause of, contributing factors for and treatment of PANDAS. But because PANDAS has been recognized as a rare disease for less than half a decade, it is still unknown just how many children have been stricken with the disorder, possibly putting them at risk of not receiving the treatment they need. Therefore, a great deal of research is yet needed to definitively determine its cause, to find more effective treatments and to put to rest the controversy over whether the disorder is in fact real. ■

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

References
Long-Term Effects of PIDDs

By Annaben Kazemi

Many primary immune deficiency disease (PIDD) patients express concern about whether they may experience long-term complications from their disease. And while it’s reassuring to know that the majority of patients do not suffer long-term effects, it’s important to be knowledgeable about what the effects are, as well as the risk factors involved.

Most long-term effects occur due to two reasons: frequent infections and/or the presence of autoimmune
complications. PIDD patients have an increased susceptibility to infections both before diagnosis and during follow-up, some of which can lead to permanent organ damage, disability and possibly even death if left untreated. The most common infections include pneumonia, acute diarrhea, acute sinusitis and otitis media. These patients also are susceptible to respiratory infections of the lungs and bronchial tubes, which can cause permanent damage to organs, as well as acute and recurrent infections, particularly those that involve the gastrointestinal system. In fact, respiratory, acute and recurrent infections are a common thread that binds a large cross section of common variable immune deficiency (CVID) patients.

PIDD patients often also develop autoimmune diseases, which can cause long-term complications. The presence of autoimmune complications is recognized in up to two-thirds of CVID patients. Among the autoimmune manifestations reported, cytopenias are the most common, including thrombocytopenia, anemia and neutropenia.

**Risks of Organ Damage**

“Timely diagnoses and proper treatment, such as immunoglobulin replacement therapy, are the most effective ways to reduce the risk of organ damage in immune-deficient patients,” says Dr. Marc Riedl, section head of clinical immunology and allergy in the Department of Medicine and the director of clinical trials for the UCLA Food and Drug Allergy Care Center at UCLA Medical Center. But, as Dr. Riedl explains, diagnostic delay remains common due to the limited awareness of the presenting features of PIDD. While immunologists are trained specifically to diagnose and treat PIDD, patients often are initially referred to other specialists. And, since immunology is a very complex area of medicine, diagnosis of PIDDs by other specialists has been difficult and protracted.

Particular types of PIDDs pose greater risks for permanent organ damage; therefore, it’s important to recognize those conditions and be proactive in seeking treatment from a specialist. According to Dr. Riedl, “Certain immune deficiencies such as CVID and XLA [X-linked agammaglobulinemia] can result in permanent organ damage because of the risks of recurrent infection due to antibody deficiency.” CVID and XLA are multisystem disorders and, thus, present to physicians in diverse specialties. As a result, diagnosis is often delayed until the second or third decade of life, which results in irreversible organ damage.

In a 2009 study of 62 newly diagnosed PIDD patients in immunology departments across the United Kingdom, 79 percent of patients had suffered repeated upper- and lower-respiratory infections before diagnosis, and of those patients, 27 percent who waited more than seven years for a diagnosis had suffered permanent lung damage. In the two years before diagnosis, 85 percent of patients had been referred to other specialists before being referred to an immunologist. More than half of this group had been admitted as hospital in-patients prior to diagnosis. The most common diagnosis (56 percent of patients) was CVID, followed by specific antibody deficiency (10 percent). The most common symptoms experienced by patients included chest infections/pneumonias (79 percent), lower-respiratory tract infections (40 percent), chronic diarrhea (13 percent), eye infection (9 percent), abscesses/boils (9 percent), failure to thrive (in pediatric patients) (7 percent), urinary infection (7 percent) and sepsis (7 percent). Thirty-four percent of patients also had suffered other serious infections.

**Most long-term effects occur due to two reasons: frequent infections and/or the presence of autoimmune complications.**

**Risks of Physical Disability and Death**

While the risk of physical disability and/or even death is increased with late diagnoses, there is good news. Replacement therapy with immunoglobulins (IGs) is proved to increase life expectancy and reduce the frequency, as well as the severity, of infections. Whether IG is administered intravenously or subcutaneously, the results demonstrate a lower risk of severe infections that could result in morbidity or even death. Replacement therapy is not only effective, but safe. According to Michael A. Friedman, MD, formerly with the U.S. Food and Drug Administration (FDA): “A five-layer system of overlapping safeguards forms the core of the blood safety system established by FDA. This system starts at the blood collection center and extends to manufacturers and distributors of blood products…. In addition to these layers of protections, many plasma derivative products also are processed to inactivate viruses that may be present.”

Problematically, PIDD patients generally have a lower level of daily activity as a result of their condition.
Disability resulting from total loss of hearing, gastrointestinal problems, pulmonary dysfunction, as well as a multitude of other issues can severely limit daily and life activities. In addition, PIDD patients have a higher mortality rate as a result of multiple and reoccurring infections and organ damage as a result of nontreatment. Death is associated with major organ failure and/or wide systemic infections that are diagnosed too late.

**PIDD patients generally have a lower level of daily activity as a result of their condition.**

In a study at Mount Sinai Medical Center, 473 patients in New York with CVID were followed over four decades. Ninety-four percent of patients had a history of infections, and 68 percent also had noninfectious complications, which included hematologic or organ-specific autoimmunity, 28.6 percent; chronic lung disease, 28.5 percent; bronchiectasis, liver damage, 15.4 percent; lymphoma, 8.2 percent; other cancers, 7 percent. Reduced survival was associated with age at diagnosis, lower baseline IgG, higher IgM and fewer peripheral B cells. The risk of death was 11 times higher for patients with noninfectious complications. And, 19.6 percent of patients died, which was a significantly shorter survival than age- and sex-matched population controls. The study’s authors concluded that mortality was associated with lymphoma, any form of hepatitis, functional or structural lung impairment and gastrointestinal disease, but not with bronchiectasis, autoimmunity, other cancers, granulomatous disease or previous splenectomy.

**Preventing Permanent Organ Damage and Physical Disability**

The importance of receiving early preventive care to limit negative effects of the disease can’t be overemphasized. While there is no guarantee that patients won’t suffer long-term effects, awareness and early diagnoses are the most effective ways of preventing adverse conditions. “The longer a patient goes untreated, the higher the risk,” says Dr. Riedl. “In order to navigate treatment, the patient needs a good team.” Periodic follow-up with a specialist and developing a team of doctors who can work together to treat the patient are crucial to maintaining optimal health.

Both intravenous IG (IVIG) and subcutaneous IG (SCIG) treatments appear to be safe, with comparable efficacy. A starting dose of 300 to 400 mg/kg/month for IVIG and 100 mg/week for SCIG is recommended. The goal is to achieve IgG trough levels greater than 5 g/L for patients with agammaglobulinemia and 3 g/L greater than the initial IgG level for patients with CVID; however, clinical response should be foremost in choosing the dose and trough level. With either infusion method, adverse reactions are generally mild owing to improved manufacturing processes of the IG products.

In addition to IG replacement therapy, other medications such as antibiotics, anti-inflammatories or other immunomodulatory medication may be necessary depending on the associated conditions in individuals with PIDD.

It is important to note that parents can play a key role in early diagnosis and, as such, reduce the risk of organ damage. There is some evidence of genetic susceptibility, with 20 percent of patients having a dominantly inherited disorder with variable expression of symptoms. Therefore, knowing the family history and sharing it with an individual’s pediatrician or doctor can help with early diagnosis. Preventive care and regular doctor visits are key in diagnosis.

**Long-Term Risks of Medical Therapies**

While the most common long-term risks of medical therapies are overuse of antibiotics and the negative effects of steroid treatment, the effects of long-term IG replacement therapy are still generally unknown.

Patients with chronic sinusitis or chronic lung disease may require long-term treatment with broad-spectrum antibiotics in addition to IG therapy. Due to the nature of their reduced immunity, these patients need higher doses and longer courses of antibiotics than other adults. If mycoplasma or chlamydia infections are suspected, antibiotics specific for those organisms may be indicated. Prophylactic antibiotics can be used in PIDD patients, but the concern is that too much use of an antibiotic can cause bacteria to become increasingly antibiotic resistant, and that the resistant bacteria will not respond to the antibiotic in the future when this therapy may truly be needed. Diarrhea also can be a common side effect of antibiotic therapy.
Prednisone is a corticosteroid commonly used to treat PIDD patients with inflammatory conditions because of its anti-inflammatory effects. Corticosteroids have a rapid onset of action and profoundly affect many parts of the immune system, as well as most other body systems. Prednisone is not without side effects, most commonly weight gain, hypertension, bone thinning, easy bruising and glucose intolerance. However, not all side effects occur in every patient. Many of the side effects of steroids are predictable and related to the amount of steroid a patient takes in his/her daily dose and the length of time the patient remains on the medication. Despite the numerous potential side effects of steroids, when used properly, these drugs save lives and avert threats to the function of important organs.¹⁰

IG replacement therapy is a growing field of study. While new therapies are being tried and multiple disciplines are experiencing a raised level of awareness of PIDD, there are few long-term studies that show its effects. However, IG replacement therapy is proved to increase life expectancy and reduce the frequency and severity of infections. Both IVIG and SCIG are safe when dosed appropriately and monitored.⁵

**Both intravenous IG and subcutaneous IG treatments appear to be safe, with comparable efficacy.**

A five-year multicenter prospective study looked at 201 patients with CVID and 101 patients with XLA to identify the effects of long-term IG treatment and the IgG trough level to be maintained over time required to minimize infection risk.¹¹ Overall, 21 percent of the patients with CVID and 24 percent of patients with XLA remained infection-free during the study. However, the effect of IG therapy at replacement dosage for noninfectious co-morbidities (autoimmunity, lymphocytic hyperplasia and enteropathy) remains to be established.

**An Encouraging Prognosis**

While the prognosis is encouraging for PIDD patients who are treated with IG replacement therapy, the best outcome is produced through the formation of partnerships between medical professionals and PIDD patients. Early detection and treatment are the primary keys to reducing long-term organ damage and avoiding disability and death.

The medical community across multiple disciplines needs to have a heightened awareness of PIDD and evaluate patients for an immune deficiency if suspicion is raised. The nature of the disease and the fact that it is multisymptomatic and multidiscipline lends itself to widespread information-sharing across the medical community, as well as between patients and the medical community.

Patient outreach programs can play a key role in mitigating the effects of organ damage by raising awareness in the general population, thus helping in early detection and diagnosis of PIDDs.

**ANNABEN KAZEMI is the patient advocate for IG Living magazine.**

**References**

Pain is the most common motive for a patient to seek out their physician. It is a universal ailment. In fact, everyone experiences pain to some degree, from birth to the grave. But, pain shouldn’t be mistaken for a runny nose, cough, gastrointestinal symptoms or other physical ailment. Instead, it is something that has the potential to harm the body.

The International Association for the Study of Pain describes the concept of pain as: “An unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life. It is unquestionably a sensation in a part of the body, but is also unpleasant, and therefore also an emotional experience. Many people report pain in the absence of tissue damage or likely pathophysiological cause; usually this happens for psychological reason. There is no way to distinguish their experience from that due to tissue damage, if we take this subjective report.”

When the body’s pain mechanism is functioning correctly, it serves the very useful purpose of alarming the individual that something is, has or could harm their body. Without pain, there is extreme potential for extensive damage. For instance, what would result if one couldn’t feel anything after casually leaning up against a hot stove and staying

For patients who would prefer to forgo or who don’t respond to traditional pain medications, there are alternative options that can provide relief.

By Matthew D. Hansen, DPT, MPT, BSPTS
there to finish a conversation, or breaking a leg while walking down the front steps and then taking a jog because they didn’t feel anything was wrong? Fortunately for most, the worse the damage, the worse the pain. So if something is being done that increases damage to the body (e.g., continuing to run on a broken leg), the body is going to try to stop the damage by making the pain increasingly intolerable.

Because pain is subjective to the person experiencing it, caregivers, family and friends must be careful to not discount a patient’s complaints.

Some patients don’t tolerate or don’t respond well to traditional pain medications. Others would rather avoid prescribed medication altogether, if possible. Therefore, alternative pain therapies can be tried. But, first, in order for a patient and their caregivers to better comprehend how to combat pain, it’s important to understand the basics of what causes it and how the pain signal can be interrupted. The body’s pain mechanism is actually a quite fascinating and complicated physiological process; however, for the purposes of this article, the following should provide a helpful — if oversimplified — overview.

The Pain Cycle

Every tissue in the body is innervated with nociceptors (special nerve receptors designed to detect painful stimuli). When the nociceptor is activated, the nerve fires a signal that travels back to the spinal cord and then up to the brain, where it passes through a region called the thalamus and then to different areas of the cortex (the largest and outer layer of the brain). The brain interprets the pain signal differently depending on what area(s) of the brain is/are activated.

With chronic pain, which lasts longer from the time of a specific injury than would be expected (generally defined as more than three months) or which comes back for an unknown reason, the normal link between tissue damage and pain is disrupted. Due to repeated or prolonged activation of the nociceptor pathway, less of a signal is required to result in an interpretation of pain. Actual changes also may occur to the structure of the brain itself,
increasing the size and sensitivity of the area(s) interpreting the pain.

Neuropathic pain (as opposed to nociceptive pain) is caused by the misfiring of the pain pathway and the experience of pain without tissue damage. The pain is often severe (commonly described as tingling, burning or electric) and can be triggered by something as seemingly innocent as a bed sheet on the patient's legs or a light touch.

People commonly speak of having a high or low tolerance for pain, and many refer to people who are “unable to take it [the pain]” as weak, crybabies or attention-seekers. However, because of the many factors involved in pain interpretation (e.g., strength, speed and duration of the nociceptor signal; region of the brain being activated; and psychological influences), it is impossible for an outside observer to truly know what a patient is feeling. Instead of criticizing or discounting a patient's complaints — a mistake made too often even by medical caregivers — continued efforts should be made to help find a way to break or at least interrupt the pain cycle.

**The body has mechanisms (a.k.a. gates) built in along the highways to affect the way pain is perceived.**

**Gate Control Theory**

The gate control theory describes how the body regulates pain. To understand gate control, think of pain signals as traffic traveling along highways (i.e., nerve fibers) back to the brain. The body has mechanisms (a.k.a. gates) built in along the highways to affect the way pain is perceived. The first gate region, located in the spinal cord, utilizes (non pain) sensory fibers to suppress the pain nerve fibers by closing the gate. For instance, if someone misses a nail with a hammer and smashes their thumb, their immediate (nonverbal) reaction would probably be to grab and squeeze their thumb, rub it, shake it in the air, maybe even suck it or squeeze it between their teeth. Why? Even subconsciously, their brain knows that activating the nonpain fibers in the thumb can inhibit or at least dampen the pain by closing the gate in the spinal cord. The body's second gate region of pain regulation is in the brain, where special chemicals called neurotransmitters (e.g., endorphins and serotonin) can help to suppress the feeling of pain. These neurotransmitters' release can be influenced by a number of factors, and strongly influence a general sense of well-being.

**Alternative Therapies for Pain**

There are a number of alternative therapies for pain. Some are supported by sound scientific research for their use, while many others are not. Nevertheless, as was discussed, psychological factors can have a significant impact on pain perception, either amplifying the pain as an impact of anxiety or depression, or reducing the pain as a consequence of happiness, peace and confidence. So, even if a given treatment has no other evidence for its use other than its effect as a placebo, clinicians should remember that placebos have repeatedly been shown to have a positive pain-reducing effect on patients. The point is that if a treatment is effective in reducing a patient's pain and doesn’t otherwise hurt them (physically, psychologically or financially), why not stick with it?

**Exercise.** Exercise is one alternative therapy that has the most scientific support for pain control. Physical activity increases the production of endorphins in the pituitary gland and their release into the spinal cord and brain. These chemicals interact with the body's pain receptors to decrease the perception of pain, relax the body and increase feelings of contentment. Early studies also suggest that exercise helps to decrease the presence of inflammation-promoting substances called cytokines, helping to reduce, but not necessarily eliminate, neuropathic and chronic pain.

These are only a few of the many benefits of exercise that can be experienced by just about anyone. Regardless of a patient's athletic ability or current physical condition, appropriate exercise exists for their unique situation.

**Mind-body therapies.** As we all know, pain can exert a profound influence on emotions, but often the impact that emotions can have on pain is overlooked. Relaxation techniques can help to relax muscle tension, control heart rate, increase endorphin and serotonin production and release, and otherwise override pain signals in the brain. These methods include abdominal breathing, guided imagery (imagining a relaxing experience or calming place), meditation, self-hypnosis and biofeedback (use of equipment to monitor the body's processes [e.g., respiratory or pulse rate] in an attempt to control them). It should be noted that some patients actually deal with pain better when they are distracted or in a noisier environment.
versus focusing on their own thoughts. They may find that watching television, engaging in conversation or taking part in some other form of recreation are effective means of dealing with their pain.

**Exercise is one alternative therapy that has the most scientific support for pain control.**

*Movement therapy.* Movement therapy is the connection between exercise and mind-body therapies. It promotes a central focus of achieving balance between body and mind. These therapies, which include yoga, Qigong and tai chi, can be particularly effective at releasing endorphins.

*Massage.* Therapeutic massage techniques help to alleviate trigger points (hyperirritable muscle knots), enhance blood flow in a region and reduce stress and tension through the release of endorphins. Massage also may help to decrease cytokines in an area and close the pain gates through non-painful stimuli.

*Acupuncture.* Acupuncture has been used for thousands of years. Traditional Chinese medicine asserts that the practice regulates the flow of qi (vital energy) through the body along pathways known as meridians. Though conventional science has not yet determined how acupuncture works, there are a number of theories, and the technique has been utilized effectively for a number of pain complaints.

*Electrical stimulation (e-stim).* E-stim is a treatment performed by placing a set of two or four electrodes on the surface of the patient’s skin near a location of — typically neuromuscular — pain. The other ends of the electrical leads are attached to a unit that allows for the adjustment of a current delivered to the body. The current works to relieve pain by delivering a nonpainful (though distinct) sensation through the nervous system that interferes with the pain signal by closing the gate.

*Herbal therapy.* Herbal remedies for pain predate recorded history. Despite this fact, scientific studies into the efficacy of many of these herbs are still in their infancy. It should also be remembered that just because they’re natural doesn’t mean that the use of herbs can’t present undesired side effects or that a patient won’t be allergic to them. When in doubt, or when planning to try a new herbal regimen, it is still best for a patient to conduct their own research and consult with their physician regarding the appropriate dose, means of administration and interaction with other medications.

Presented below are several of the more common herbal remedies and their uses (herbs are taken orally in pill form or as an infusion unless otherwise specified):

- **Arnica:** applied as an ointment/liniment for muscular and other soft tissue injuries, or taken orally for post-surgical pain or as an anti-inflammatory
- **Capsaicin:** prepared as a topical cream for arthritis and neuropathy
- **Devil’s claw:** taken for back pain and osteoarthritis
- **Fish oil:** taken for joint pain related to arthritis and autoimmune disorders
- **Turmeric:** taken for arthritic pain and inflammation
- **St. John’s wort:** long used as a natural remedy for depression; also used for neuropathic pain and arthritis
- **Valerian root:** taken as a muscle relaxant, sedative and/or pain aid
- **Boswellia:** taken for inflammatory conditions, including rheumatoid arthritis
- **Willow bark:** taken for rheumatoid and osteoarthritis, gout, muscle soreness, headache and general pain (acts similarly to aspirin)

**Do No Harm**

The pain-relieving techniques presented in this article are by no means exhaustive. However, they do represent many of the best-supported and/or most widely used alternative therapies. In attempting them, clinicians and caregivers should remember to not discount the patient’s complaints and to “do no harm” with treatment. Everyone experiences pain to some degree, but they also can experience relief.

**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**

Let’s Talk!

By Trudie Mitschang

Ian: I was always active as a child. Upon leaving the hospital, it was my goal to return to playing the games that I loved and to play at a high level. I am blessed to have had some of the best doctors in the world who have encouraged me to be active and a family that has been with me every step of the way. At times, life got discouraging as I endured the pains and setbacks that come with Crohn’s disease, but by having great people around, I was able to persevere at a young age and continue to grow athletically.

Trudie: How do you respond when people say you don’t look sick?

Ian: I often get this question. When I talk about my experiences with Crohn’s disease, people often look at me and think that it is nothing serious. Crohn’s disease is definitely something that I remain apprehensive about. I am fortunate to be in control now, but in the back of my mind, my previous experiences of excruciating pain remain, and I know they are capable of returning. Although I may not appear sick, an invisible illness is very real that affects my everyday life.

Trudie: Tell us about your basketball career and why you gave it up for bodybuilding.

Ian: I loved basketball because it is a high-paced athletic contest that tests athletic ability, work ethic and conditioning. I was not always the most naturally gifted athlete, but no one outworked me on the court or in the off-season. Upon entering college, my eyesight was starting to deteriorate, severely impacting my game. As I concluded my freshman year of college, I decided to pursue bodybuilding. Then, as I saw myself gaining more weight and muscle, which had been a trouble for me in the past, I knew that this was going to be my new passion.

Trudie: What are your top-three bodybuilding secrets?

Ian: First, change your routines periodically so your muscles do not become used to the same exercises. Second, time the use of protein shakes. Take a shake before and after your workout with water so it digests faster. Then have a shake before you go to bed with milk because milk has casein protein, which takes longer for your body to digest.
to break down. Third, stick with it. It will be difficult, especially when you hit a plateau, get sick or experience an injury, but don’t quit!

**Trudie:** You recently suffered a health setback with your eyesight. Tell us about that.

**Ian:** In December of 2011, I was diagnosed with a rare degenerative eye disease of the cornea called keratoconus, and I was told that I was going progressively blind. When I learned the surgery capable of correcting keratoconus was not approved by the FDA and therefore not covered by insurance, I was devastated. In an amazing turn of events, I received a phone call from the producer of the CBS Emmy-nominated TV show “The Doctors.” They wanted me on the show, and we had 12 hours to fly out to Beverly Hills to have the procedure done on camera. Immediately, my mother and I flew to Los Angeles, where Dr. Brian Boxer Wachler and his staff saved my sight. It was an amazing experience; I went from being an apprehensive adult going progressively blind to a new man who gained a truly new perspective on life.

**Trudie:** How do you stay positive?

**Ian:** When I feel like quitting, I reflect upon what I have already been through. I think about where I came from and where I am now. When I am upset or angry, I go to the gym and hit the weights; it helps me think clearly. I also think about the people I have thus far already impacted at a young age, and I think how many more lives I can touch by continuing to work hard every day.

**Trudie:** What is your mission in life?

**Ian:** I am still young, so I have time to see what God’s calling for me is, but I am in a great position and would be satisfied wherever life leads me. I only know for now that I will continue to work hard in bodybuilding and my studies to best prepare myself for my future.

**Trudie:** What advice do you offer others living with chronic illness?

**Ian:** For me, the biggest hurdle is managing stress; my biggest stress reliever is working out. I believe that it is imperative to have a support group around you to provide encouragement through difficult times. Lastly, becoming an advocate has positively impacted me. I no longer have to fear how others perceive me. I am confident in who I am as a person, and I believe that in continuing to spread my story, I will be able to help more people who have endured pain like I have.

**TRUDIE MITSCHANG** is a staff writer for IG Living magazine.
**Reader:** My husband has been receiving weekly intravenous immune globulin (IVIG) infusions for one-and-a-half years. Because he has a port, he is able to get home health care. Normally, the home health nurse stays during the treatment, which typically takes three hours. Yesterday, the nurse got a call from the home office that said the nurse no longer has to stay with IVIG patients, and she was told to leave to go to another patient. Since then, the nurse just comes to get the IVIG started, and then she leaves. So, not only is my husband alone, but he has to spike the second bottle to get it started, flush his port and remove the needle. Is this normal? Shouldn’t the nurse watch to make sure he is able to do this on his own before leaving? Our nurse is wonderful, and she didn’t want to leave him, but she was told to.

**Michelle:** This situation has become more routine in the IVIG world lately. Unfortunately, the driving force is most likely insurance reimbursement. The cost of IVIG is rising, and the reimbursement for the drug and for the cost of infusion has been declining. Not having the nurse with the patient for the entire infusion cuts the costs of the overall infusion.

This situation is likely OK if your husband has no reactions, knows how to manage the remainder of the infusion, and knows what to do in the event of a reaction. I would recommend the following:

1. First and foremost, make sure your husband’s physician is OK with him being left alone. At the end of the day, the physician is the one ordering this therapy, and it is his or her decision to make concerning whether being left alone is appropriate. If it isn’t, the provider should be told that his physician does not approve of this practice and the nurse will have to stay, or your husband will have to be switched to a provider that allows the nurse to remain onsite during the infusion.

2. Make sure your husband is not alone for any portion of the infusion after the nurse leaves. Can you or someone else stay with him in case there is a problem?

3. It is best if the nurse leaves only after the IVIG reaches the maximum infusion rate. Most reactions occur during the titration phase of the infusion.

4. Make sure that your husband understands all of the potential side effects and reactions that can occur with IVIG, and what to do in case they arise. Your provider should be able to give you this information and training.

5. Ensure there is an anaphylaxis kit in the home, and that you and/or your husband know when and how to use it.

6. Be aware of the brand of IG your husband is prescribed, and check the vials prior to each infusion to ensure the brand of IG hasn’t changed. If it has, the nurse needs to stay for the entire infusion. Each brand of IG is different, so if the brand is not the same as usual, the infusion needs to be treated as though it were his first.

Your husband will likely be fine, but you and your husband should definitely follow these instructions just in case. And, again, your husband’s physician must be made aware this is taking place.

**Reader:** Is idiopathic thrombocytopenic purpura (ITP) considered a primary immune deficiency disease (PIDD)?

**Michelle:** ITP is not a PIDD. Patients with ITP develop antibodies that attack and destroy their platelets. It is a primary or secondary autoimmune disorder that occurs in relation to another disorder of the immune system. People with primary and secondary immune deficiencies can develop ITP. It’s estimated that 20 percent of people with common variable immune deficiency (CVID), which is a type of PIDD, develop an autoimmune disorder, and about 10 percent of the time, that autoimmune disorder is ITP. Most people are diagnosed with ITP before the CVID diagnosis is made, but it also can be diagnosed simultaneously and even after immune globulin (IG) therapy is initiated. The reason ITP occurs is not known, but it likely has something to do with a defect somewhere in the production of B cells. Since treatment of ITP frequently involves steroids, and long-term steroid use can make someone more susceptible to fungal infections, the primary treatment for ITP in people with CVID is intravenous IG.

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“HOW LONG DO you think you can go without telling someone?” my best friend, Joe, asks me. When I consider the question, I feel I only have a month. Mostly because within that month’s time, I will either have far too many doctor appointments to go out, have gone to the ER or have been hospitalized. Last year, if I add up all the days, I spent about a month and a half in the hospital. I even had to cancel a date with a medical student because I was an inpatient at the hospital where he studies.

My situation is not normal. I’m always confronted by how soon I should let someone know about the multiple chronic health conditions I’ve dealt with my entire life. It was easier as a child, but it’s not the same now that I’m older. I may look relatively healthy and strong, but my health can be as fragile as Laura Wingfield’s little glass unicorn.

I go to great lengths to look as healthy and normal as possible. For a while, I experimented with different self-tanners to try to accomplish that “healthy glow.” I also have used gloss treatments in my hair to give it that shiny glow that vitamin deficiencies have taken away from me. I was utterly surprised by how many family members and friends commented on how fantastic I looked; oh, how looks can be deceiving.

Even when I get to a point of a normal appearance, there are so many things that get in the way for me. I have to take pills with every meal — at the beginning, middle and end — so I can absorb my food. Eating feels like a pill buffet, and I approach dinner dates with utter dread; it’s a top-secret covert mission to make sure I get my medications taken. I also still live at home because it is probably a horrible idea for me to live by myself. This has created a situation in which I spend a fair amount of time making out in a car because there is nowhere else to go. Once, I was horrified to find out the next day that the blood thinners I take to prevent life-threatening blood clots caused serious bruising. I looked like I was abused after a make-out session. And, I’m surprised how many guys talk about kids. I will never be able to have kids, something I’ve known since I was young. It’s just one more thing that separates me from the rest. How am I supposed to explain all of this?

There will come that eventual day when I will need to tell whomever I’m out with that I’m sick. That may come about because I’m so Google-able. I am involved with health organizations, I was a poster child for the hospital I went to, and I was a Wish kid. Or, it may come about because the answer to “What did you do today?” will be “I laid in bed with a migraine that wouldn’t respond to medication, but I hauled my butt out to eat a meal I’m too nauseous to eat because, gosh darn it, I like you!”

It’s not that I’m ashamed or embarrassed about my health issues, it’s just that they provide such a layer of complication. I don’t want to be rejected for my glaring imperfections that have shadowed me since I was a small child. I need encouragement. I need verification. I need security. I want to connect. It feels like a weight that sits on me until I will collapse.

When I do tell that person, I know I will fidget. I’ll try to look away, knowing that I need to explain what that “family emergency” was last weekend. Hopefully, he’ll tell me it all doesn’t matter. But even if he says that, my walls will stay up. When he talks about the future, I won’t. It’s my safeguard; if I don’t plan, I won’t get hurt. If he doesn’t stick around, there will eventually be one more person I will have to tell all of my secrets to.

This is the painful shock that makes me wonder if I can manage dating. It makes me wonder if someone can love me despite everything. I hope I find the fool who does, because I will never let him go.

SAMI JANKINS has an autoimmune clotting disorder and runs a small non-profit that provides access to the arts for chronically ill children. She is the co-chair of the National Youth Leadership Institute for the National Hemophilia Foundation, and has served on the teen council for the Immune Deficiency Foundation.
I AM HAPPY to report that I am now married, and it has been a long journey to get here with so much to look forward to. As they say, first comes love, then comes marriage, then comes...

Jim, my new husband, and I began dating about six months before I was diagnosed with common variable immune deficiency (CVID). When I look back on that time, I feel so lucky that we made it. For a while, we didn’t know if I was going to make it, but I did know that Jim and I would. I have never met a stronger, more loyal man who could easily have run away from a really difficult situation. And, I wouldn’t have held it against him if he had wanted to leave. There were more than a few times that I gave him his “out” when the days got really dark. But, he stayed — through ambulance rides, hospital stays, weight gain and experimental drugs.

Jim and I were married in June, and it would be an understatement to say that I had the time of my life at my wedding! It truly was more than I could have hoped for. We started the day with early-morning hair appointments with my sister and “new sisters” who flew into Los Angeles from Massachusetts for the big day. My mom drove the bridal party in a 12-passenger van to Hollywood, where we got ready in a bridal suite. We had our makeup done by a professional makeup artist, and during the makeover, we danced to Michael Jackson and the Spice Girls! The ceremony was breathtaking, and the best part was that everyone I love so much was there to share not only our love but the eight-year journey Jim and I have taken to get here. And what a journey it has been. What could possibly be next?

Living with a chronic illness is unpredictable. Sometimes I am fearful that my current “relative” health won’t last. And looking back on the last eight years, I have never worked so hard in my life. I made “life” my full-time job because I was and I am still convinced that there is so much to live for. Maybe my health won’t last, but I am a firm believer in living in the moment. In this moment, I see so many opportunities, and one of them is becoming a mother.

Since I was a little girl, I always wanted to be a mom. As I got older and learned about my body and how it doesn’t always work as it should, my hopes of having my own baby were in question. I didn’t know if it would ever be possible, or if I would be capable and healthy enough to carry a pregnancy to term. I wondered whether the baby would be healthy or if the pregnancy would affect my health. And while I still have so many fears, questions and concerns, I am happy to announce that I am pregnant! Jim and I are taking it day by day, but overall, I feel great. I have a wonderful obstetrician who is taking nothing for granted. I see her every two weeks, and she is as committed as we are to helping us have a healthy baby.

Jim and I know that there are still a lot of questions to be answered, but right now we are truly enjoying the idea of becoming parents very soon. I am finishing my second trimester; the baby has a strong heartbeat and is full of energy wiggling and flipping around. I will be sure to update all of you as to how I am doing. And remember, anything is possible.

EVER FECESKE MAZZA was diagnosed with CVID and interstitial lung disease in 2004. She is a fashion design student, loves spending time with her husband, family and bulldog, Dunkin, and can’t get enough of writing, cake decorating and anything that sparkles!
WARNING! READING the following may cause heaviness in and around the eyelids, the urge to fight off slumber, yawning, head bobbing, body weaving, snoring, snoozing, an elbow to the seventh rib, drooling and dreaming.

I’m anything but boring — or so I thought. I am proud to be sanguine with a terrific sense of humor. I also have been known to walk into a room with my mouth wide open, wit on my left and comedy on my right. I’m a cool cat fully loaded with hysterical hip shots who likes to entertain and make ‘em laugh! So what’s gotten me so defensive, frustrated and all around “ticked off”? Read on (no pillow required).

Soon after our children were diagnosed with a primary immune deficiency disease, I went on a warpath, desperately seeking someone who would study our family and find the cure for our disease. Easier said than done. Because my family’s diagnosis was too weird and complicated at the time, no one really wanted to touch us with a 10-foot pole (good thing, too, as the Haggard clan is a green snot-wielding, cryptosporidium-excreting, influenza A-Z-infecting, sneezing and wheezing human germ bomb).

Fifteen years later, with 18 ear tubes placed, 10 tonsils obliterated, 10 adenoids laser lifted, five sinuses plumbed, countless gallons of antibiotics and immune globulin infused, not to mention a PICC line or two, we finally found someone who thought we were scientifically valuable in the hopes of solving the mystery of what causes common variable immune deficiency (CVID), why it tends to run in families and, especially, why if one is diagnosed with CVID, they also have the potential of becoming ill with non-Hodgkins lymphoma (I lost my father to complications of CVID with non-Hodgkins lymphoma in 2008).

The six-hour drive to the teaching hospital where the study was being conducted flew by, despite having to infuse Molly while keeping Caleb from constantly sticking his head out the window pretending to be our black Labrador retriever and Calvin from thrusting his arms out the other side to see how many bugs he could snatch at 77 miles per hour.

Electric excitement was everywhere as I unbuckled my seatbelt and placed my weary feet onto the parking garage floor. I just knew that every step I took toward the immunology clinic was one step closer to a cure for my family. A hallway or two later, we found ourselves in the waiting room of the good folks who would find a cure to this awful immune disease.

Despite my sheer joy, I was kind of nervous. Even though we had been to umpteen billion physicians’ offices over the years for the various illnesses CVID causes, I began to feel a bit intimidated. I started to imagine the scenario I was moments away from: a cold room with very little space for the 15 whitecoats peppering me with questions. They are studying me. Every little move I make they scrutinize, and every once in a while, the super scientists scribble something illegible, biological, chemical or immunological in their notepads. They all stand like human
question marks towering over me.

“Haggard?” A triage nurse called, saving me from my overactive imagination.

“I guess that’s us!” I called, trying to get the young man’s attention.

“I think we only want to talk to Mom for now.”

Mark’s countenance went from exasperated from a six-hour drive to lily white. “Just wanting to talk to Mom for now” translates to: Mark has the honor of amusing his three children for who knows how long and with very little to keep them from scaling the walls. Our kids have learned how to quell extended waiting room boredom by consuming gallons of sugar water shots from the complimentary coffee cart and making masks of celebrities from the jacket pages of fan magazines. Ten minutes later, my talented teens were performing an impromptu soap opera as if they were modern-day Marilyn and Bob on a goodwill tour for the troops (the other “wait-ees” in the room).

The exam room was outdated with cool green paint, chocolate chip ice cream floor tiles and three Thomas Kinkade knockoffs dotting the walls. The blinds streamed inviting, fresh sunlight that allowed me to study a brochure on plaque psoriasis. Dr. Tillher (chief immunologist, seriously sweet and unexpectedly overwhelmingly seasoned) and an intern (no name, but he had so many bags under his eyes one might suspect he suffered from Louis Vuitton syndrome) entered the room so quietly, they must have thought I was a napping newborn.

Our eyes met, then came the friendly handshake and then: “I’m Dr. Tillher and it is very nice to meet you. This is Dr. Jack Sonso-as…ehm,” and that’s when I could no longer hear a word Dr. Tillher was saying.

“I’m sorry, I didn’t hear you, Dr. Tillher,” I apologized.

“Yes, this is Dr. Jack Sonsoas…m…eh…er, my lab intern, and…” something something quieter and quieter until I saw was Dr. Tillher’s lips moving. I finally resolved that Dr. Jack Sonsoas…m…eh…er was a resident at Dr. Tillher’s lab studying immunology.

Dr. Tillher’s special way of communicating — his long-windedness — could generate enough air pressure to travel around the world in 80 days (well, maybe 180 days).

At 10 o’clock, Dr. Tillher began with: “Let’s start at the beginning when your firstborn, Calvin....” At least that’s what I think he said. At noon, we were just starting Caleb’s second sinus surgery at 18 months and barely touching on 3-month-old Molly’s oral infections. My kids are currently 15, 13 and 11, so we had a ways to go. Mark, I was sure, had melted like Frosty on the first day of spring, while the kids had scarred the entire immunology staff for life. And the end was not even close as our diagnoses are crammed with details, a multitude of intricate procedures, tests and chemistry that would confuse the president of Mensa.

Even I was losing it; we had about a third of our history, exams and blood work left to go, and I still had no clue where Dr. Tillher’s lab was! While Dr.Tillher continued, I looked at the door handle, and contemplated my moment to run for it, when I glanced at Dr. John Sonsoas…m…eh…er something-or-other, who began to close his eyes. Is this really happening? Is the lab intern, who is supposed to be paying attention, actually falling asleep? I was hurt! My family has been called a lot of things, but boring to the point of slumber is certainly not one of them. Besides, doesn’t this guy get tested on this later?

Then, I had a change of heart. Dr. John S., became my focus for how to get through the rest of my own family’s medical history. Watching this poor sap do what every other resident out there is avoiding like the plague was tear-inducing hysterical! It went a little something like this: First, the eyelids began to close halfway as his shoulders slumped. Next came the head tilt to the right, along with full eyelid closure. Finally, for Dr. John Whatever, full REM sleep had been achieved, and as for me, I was fighting back a full-blown “bahahahaha!”

Then, the piece de resistance: Dr. John slumped over into Dr. Tillher.

I couldn’t hold it back any longer. I started with a small giggle that grew into full-blown laughter. Even with apologies all around, we all enjoyed a good belly laugh. And when we finally reunited and explained the hysteria, Mark said, “Well, I’m happy for you,” as he was scraping our kids off the ceiling.

The happy ending is that Dr. John Sonsoas…m…eh…er must have found Dr. Tillher’s lab, because the good folks studying CVID are getting closer to a cure. As for you, gentle IG Living reader, wake up! ■
GETTING TO THE root of my children’s immune deficiencies has been the greatest battle of my career as a parent. Each of my children has some degree of immune deficiency. My 15-year-old, Calvin, has a low IgG value, but does not require immune globulin (IG) replacement. My 13-year-old, Caleb, has a low neutrophil count and requires intravenous IG (IVIG) once every four weeks. My 11-year-old daughter, Molly, has low IgG and IgA levels and requires subcutaneous IG (SCIG) twice a week. My children faced unique challenges: The most important was getting the correct diagnosis. Everything else fell into place afterward.

I remember the continual tests and trials to discover why Caleb kept getting repeated infections. Scratching his back open and exposing him to different allergens revealed nothing. After blowing out three ear tubes before the age of 3, my boy required Rocephin via a PICC line to clear a particularly nasty infection. The phone call I received at work from my wife announcing the possibility of cystic fibrosis ruined what had been a generally good day. A sweat chloride test, delivering an electrical current through my 3-year-old’s arm for 10 minutes, returned negative, and doctors ruled out that particular disease.

The trouble is ruling “in” the right disease. Our doctor at Central California Children’s Hospital ordered a number of tests that proved inconclusive. He finally instructed Caleb to chew a piece of gauze for five minutes, then drained the saliva into a test tube. Tests on the saliva returned negative for IgA. Caleb, at long last, was diagnosed with selective secretory IgA deficiency and prescribed infusions of IVIG every four weeks. Caleb’s earlier diagnosis later helped doctors also diagnose Molly with selective secretory IgA deficiency. Later, when we moved to Idaho, our new doctors rejected the diagnosis of selective secretory IgA deficiency, but when their infections continued, our children were referred to the University of Washington, where they were diagnosed with an “unspecified” immunodeficiency and prescribed IVIG.

When we submitted claims to our insurance company, they chose not to cover the cost of IVIG. They determined that for an “unspecified” immunodeficiency, the treatment was “not medically necessary” and “experimental.” After another two years of testing and battling our insurance company, we finally received a diagnosis of common variable immune deficiency (CVID) for both Caleb and Molly. When we claimed this specific diagnosis with its corresponding ICD-9 code, our insurance company started to pay for IVIG.

Many families go through similar battles. Like our immunologists, yours may be struggling to find a diagnosis for your children. With all the twists and turns of growing children’s bodies, diagnosing them is something like nailing Jell-O to the wall. Let’s face it, we need to understand that our doctors face many challenges in getting a correct diagnosis for our children.

The Maturation of the Immune System

Like children themselves their immune systems must go through a process of
In reality, all babies are born immune deficient.

growing and maturation. By 14 weeks in utero “naive” T lymphocytes begin to develop. Each can become mature when they come into specific contact with an antigen that they can recognize, after which they become “memory” T cells, and they are able to initiate a secondary immune response when they come into contact with each specific antigen. This process generally begins after birth and may take several years until a more mature immune repertoire is in place. During this time, children will tend to have apparently numerous or frequent infections. B lymphocytes develop independently from T cells, producing the immune system’s IgM, the immune system’s first responder. If those cells do not come into contact with an antigen, they will die; if they contact a pathogen, they also become activated and produce memory B cells.

In reality, all babies are born immune deficient. They are dependent on maternal antibodies until about the age of 3 months. IgA and IgM cannot cross the placenta; therefore, none is present at birth. IgG can cross the placenta, and babies are born with IgG, but their levels drop for the first 3 to 6 months of life. Generally, IgG, IgA and IgM do not reach adult levels until the age of 6 years.

After birth, out from under the protection of maternal antibodies, children’s immune systems enter a cesspool of infections. Their bodies become sick as new pathogens make their way into their bodies. With each new exposure, naive T lymphocytes are maturing into memory cells, prepared to spark an immune response for the next invasion. The number of infections decreases over time as the children’s bodies change and their immune systems develop. When children reach school age, their rate of infection is generally the same as an adult. Studies show that children in day care get more infections early in life, but the rate of infection decreases over time, with the norm being one per month. Children raised in the home get fewer infections early, then get more infections as they interact with more children over time, with the numbers of infections peaking at the beginning of the first year of school. Children with siblings have a rather constant rate of infection because they share germs with their brothers and sisters.

“In a perfect world,” says Terry Harville, MD, medical director in the special immunology laboratory at the University of Arkansas for Medical Sciences, “this would all occur in the first month after birth.” In this manner, infants would become exposed to the pathogen and develop their immune response to it while still being somewhat protected by the presence of the maternal antibodies. Dr. Harville asserts that Edward Jenner’s system of immunization is “the most important medical advance in the history of mankind.” Introducing children’s immune systems to common pathogens converted more of those naive cells into memory cells. For example, haemophilus influenzae type-B (HIB) infections once took many lives before the introduction of the HIB vaccine. Subsequently, the so-called conjugated streptococcal vaccine, Prevnar7, greatly reduced the infections, morbidity and deaths associated with pneumococcal bacteria. Both these types of organisms tended to cause infections in children under 3 years of age, and in some instances, under 1 year of age, while their immune systems were still gaining maturity. Further, measurement of the antibody responses to immunizations are, in general, required for doctors to diagnose an antibody immunodeficiency.

Diagnosing Specific Immune Deficiencies

The number and severity of childhood infections are concerns for immunologists. Parents should suspect an immune deficiency if infections are persistent. Among the Jeffrey Modell Foundation’s “Ten Warning Signs of Primary Immunodeficiency” are four or more ear infections within one year, two or more serious sinus infections within one year, two or more months on antibiotics with little effect, two or more pneumonias within one year, two or more deep-seated infections, or the need for intravenous antibiotics to clear infections. Any of these signs or a combination of them should cause parents to consider testing their child for a primary immune deficiency disease (PIDD).

Dr. Harville has had a number of patients with frequent infections referred to him under the suspicion of being immune deficient. But pediatri-
cians, with only a few minutes to garner information about a patient, may miss some environmental factors contributing to frequent infections such as time in day care or smoking in the home. Frequent infections are only part of the immune deficiency puzzle.

One “hallmark of a more severe immune abnormality is a child’s failure to thrive,” says Dr. Harville. But, some patients are undersized for reasons other than immune deficiency. For instance, one patient experienced recurrent pneumonia and tested low in IgA and IgG, but the cause was not PIDD. Instead, it was childhood acid reflux that caused malnutrition in the patient. Proper medication corrected the acid reflux disease and restored the child’s immune system. In another case, a child suffered from frequent vomiting and failure to thrive. The culprit was not an immune deficiency, but rather pyloric stenosis, a blockage between the stomach and intestines. The child was malnourished, not immune deficient. After surgical correction of the problem, the immune responses became normal. In another patient, allergies to milk protein led to bleeding in the lungs and frequent pneumonias; what was thought to be an immune deficiency was hypersensitivity to cow’s milk.

It is difficult to judge the health of the immune system strictly by number of infections. Dr. Harville adds a caveat to the Ten Warning Signs of Immunodeficiency: The types, seriousness and opportunism of the infection also must be considered. “It’s a matter of quality rather than quantity,” he explains. Rashes, unusual infections, chronic diarrhea and failure to thrive also must be considered. A family history of PIDD is another good indicator of PIDD in a patient.

Dr. Harville also listens to the parent’s gut when it’s telling them “something is just not right.” It’s said that when most doctors hear “hoofbeats,” they think of “horses.” In fact, most doctors do not have the time or the resources to do an in-depth check of a child’s immune system; instead, they “play the odds” and consider the most likely problem. “When I hear hoofbeats,” says Dr. Harville, “I always consider the possibility of zebras and unicorns.”

Early diagnosis and treatment of PIDD are necessary to prevent infections from causing permanent damage to the body. Many severe immune deficiencies are caught at the age of 9 months due to the severity of the problems, but in most cases, the problems actually had begun by 3 months of age. Therefore, even in those with more severe PIDD, diagnosis may be delayed by six months from the onset of symptoms. For example, in severe combined immunodeficiency (SCID), in which there is a complete absence of T cells, and X-linked agammaglobulinemia (XLA), in which there is an absence of B lymphocyte function, infections may begin as the maternal antibodies wane, usually by 3 months of age, but the diagnosis is not made until approximately 9 months of age. In those with combined immunodeficiency (the presence of some T and B lymphocyte function), diagnosis may not occur until 2 or 3 years of age since it is not clear that the infections occurring are outside the norm expected for that age. Yet, by 3 years of age or so, it may become more obvious that too many or too severe infections continue, when they should have lessened as the immune system became more experienced in fighting infections. Other immune deficiencies such as hyper-IgM syndrome may not be diagnosed until later when the pattern of recurrent infections becomes more obvious. Many antibody deficiencies often are not diagnosed until adulthood.

CVID is particularly difficult to diagnose for immunologists because the symptoms present themselves later in life, or it may take many years of evolution until the full features of the disease are more obvious. My father-in-law was in his late 60s when he was diagnosed. On the other hand, my children were part of the mere 20 percent who are diagnosed before the age of 16. Early in the lives of CVID patients, IgA levels may be low, but IgG and IgM may be normal. Over time, it is thought that patients lose more of the serum IgG and B lymphocyte function. During this time, serum IgM levels may become elevated, perhaps trying to compensate for the loss of IgG antibodies. Eventually, all levels of functional...
antibodies are low, and the diagnosis tends to be easier to make. The Epstein-Barr virus, the cause of mononucleosis, in some cases is thought to be the catalyst for the onset of CVID because the virus attacks the patient’s B cells, which may be lost and not recovered.

Insurance and the “Unspecified” Immunodeficiency

One thing I learned firsthand is that an absolutely correct specific diagnosis is critical when submitting an insurance claim. After all, insurance claim-processing personnel are simply looking at a code on a billing statement, not at the patient. In my family’s case, our frustration with our insurance company was based upon its rejection of a treatment billed as an “unspecified immunodeficiency.” For most patients, it is not until there is a diagnosis of a specific immunodeficiency — with its proper corresponding code — that the claim will be paid. To be fair, there’s a slippery slope in approving payment for such an immunodeficiency: Could not everyone who was ever sick claim an “unspecified immunodeficiency” and reap the benefits of an important but costly therapy? If insurance were to cover IVIG for all, what would that do to our premiums?

No doubt, the difficulty of getting a proper diagnosis of a specific immunodeficiency is well documented. It may be that your experience is similar to my own. Dr. Harville explained his own challenges in arriving at correct diagnoses when treating young children with ever-changing and maturing immune systems. However, overcoming these frustrating obstacles to reach the correct diagnosis is necessary, not only for proper medical care, but for proper financial care from insurance companies.

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

For more information on diagnosing PIDD, see the Jeffrey Modell Foundation website at www.info4pi.org.
FEW PEOPLE REALIZE just what it takes for a nonprofit organization to operate until they make a special connection with one. That special connection may happen for a variety of reasons, one of which is being diagnosed with a serious illness. For instance, many people who know someone diagnosed with cancer were inspired to get involved with a cancer fundraiser. But, while charities such as the American Cancer Society are well-known, others like the Jeffrey Modell Foundation and The Myositis Association don’t receive such widespread attention and, as such, have a greater challenge getting the support they need to fulfill their missions.

Compassion is what fuels charities. But it takes more than just the founders of the organizations to meet their fundraising goals. It requires the help of everyone who is connected. And, while it’s not easy to ask for donations, sometimes that’s all it takes. Just ask Marianne Moyer. Marianne, who has polymyositis and is a member of three charitable boards, recently admitted that the hardest question anyone can ask is: “Would you please give me some money?”

Giving Is In

Despite the economy and hard times faced by many, giving is in. In 2011, donations to charitable organizations totaled $298.42 billion, an increase of 4 percent from 2010. And, as in previous years, the majority (73 percent) of those donations came from individuals. Health charities benefited by an increase in donations of 2.7 percent in 2011.1

Marianne is one of the reasons for this increase. She has served as chair of The Myositis Association (TMA) board for the past two years, and as she explains, it has taught her more about the fundraising challenges facing an organization that represents a rare disease. Participating in special events, and holding raffles and silent auctions, she learned, were not enough to fund research. “Myositis patients want to see a cure for our disease, and a cure is not going to magically appear,” says Marianne.

The Right Way to Ask

Typically, donations are made upon request. People respond to people, and the secret to a successful “ask” is the right prospect asked by the right person in the right way at the right time for the right request in the right amount.2 For Marianne, all those “rights” came about with the death of a friend who also had polymyositis. Knowing that her friend had left generous bequests to her church and family, Marianne decided to “ask” but not without being torn. “Do I intrude on [her husband’s] grief by asking him to give some of his inheritance to TMA, or do I stay quiet?” explains Marianne. “I decided to take the risk — to offer him the opportunity to give a donation in his wife’s name and to help fund future research into myositis. His [donation] was one of the more meaningful — to me, to him and his family, and to TMA.”

All for a Worthwhile Cause

The following list of charitable organizations is not exhaustive, but it does represent some of the larger organizations in the immune globulin community. A more extensive list of organizations can be found on the IG Living website at www.igliving.com/IGTreatedDisorders.aspx. If you have compassion for one or more of them, perhaps you will do your part and ask for a donation.

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

References
Cure JM Foundation
Cure JM was founded in 2003 by Harriet Bollar, Shari Hume and Lisa Felix, grandmother and mothers (respectively) of children diagnosed with juvenile myositis (JM). The nonprofit organization was created specifically to find a cure while also providing support and information for families suffering with JM. All fundraising and donations go toward supporting Cure JM’s focus of raising awareness and funding research in hopes of curing juvenile dermatomyositis and juvenile polymyositis.
www.curejm.com, (760) 487-1079, info@curejm.com

GBS-CIDP Foundation International
The GBS-CIDP Foundation was founded in 1980 by Estelle and Robert Benson after Robert was diagnosed with Guillain-Barré syndrome (GBS). It started with eight people and has grown to tens of thousands of members throughout several countries. Its mission is to improve the quality of life for individuals and families worldwide affected by GBS and chronic inflammatory demyelinating polyneuropathy (CIDP) by providing a network for all patients. The foundation provides public and professional educational programs designed to heighten awareness and improve the understanding and treatment of GBS and CIDP. Donations are used to expand the foundation’s role in sponsoring research and engaging in patient advocacy.
www.gbs-cidp.org, (866) 224-3301, info@gbs-cidp.org

Immune Deficiency Foundation (IDF)
Marcia Boyle founded IDF after her son was born with a primary immune deficiency disease (PIDD). It is a national patient organization, hosting both national and regional patient meetings throughout the U.S. Since 1980, IDF has provided information and created educational resources and programs for the nearly quarter-million Americans who have been diagnosed with PIDDs. The foundation uses donations, service sponsorships and core contributions to support its mission of improving the diagnosis, treatment and quality of life of persons with PIDDs through advocacy, education and research.
www.primaryimmune.org, (800) 296-4433, idf@primaryimmune.org

Jeffrey Modell Foundation (JMF)
JMF was established by Vicki and Fred Modell in memory of their son Jeffrey, who died at the age of 15 due to an underlying primary immunodeficiency disease (PIDD). The foundation is dedicated to early and precise diagnosis, meaningful treatments and finding cures for PIDDs. JMF’s focus is to affirm its absolute commitment to clinical and basic research in order to better understand and treat PIDDs. One hundred percent of its revenue is from donors — the public, corporations, foundations and government — which go toward programs to fulfill its mission.
www.jmfworld.org, (866) 463-6474, info@jmfworld.org

Neuropathy Association
The Neuropathy Association was started in 1995 by people suffering from disorders that affect the peripheral nerves. Today, the membership reaches more than 50,000 people with more than 120 support groups spread throughout the United States and 15 centers of excellence. The association relies on donations to support its mission to help and heal people with peripheral neuropathy through awareness, education, support, advocacy and research.
www.neuropathy.org, (212) 692-0662, info@neuropathy.org

The Myositis Association (TMA)
TMA was originally organized by Betty Curry, an inclusion body myositis patient. Its goal is to provide support to myositis patients and their families, provide connections between the medical advisory board and the general medical and patient communities, and increase funding to support myositis research. TMA brings information, support, advocacy and research for all forms of myositis. Local support groups known as KIT (Keep In Touch) can be found in several locations throughout the U.S. TMA hosts an annual national patient meeting that is usually held in September. The Myositis Association depends on generous support to continue its mission.
www.myositis.org, (800) 821-7356, TMA@myositis.org
The **Products** you need when **you need** them.

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

Use your smart phone app to view our complete product catalog and place your order today!

(800) 843-7477  
www.FFFenterprises.com
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
- 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 Heart, Lung and Blood Institute: www.nhlbi.nih.gov/health/health-topics/by-alpha
- National Institutes of Health: health.nih.gov/see-all-topics.aspx
- 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

**IG MANUFACTURER WEBSITES**
- Baxter: www.baxter.com
- Bio Products Laboratory: www.gammalex.com
- CSL Behring: www.cslbehring.com
- Grifols: www.grifolsusa.com
- Kedrion: www.kedrionsusa.com
- Octapharma: www.octapharma.com

For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.

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**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

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### 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

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### Idiopathic Thrombocytopenic Purpura (ITP)

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

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### Kawasaki Disease

**WEBSITES**
- American Heart Association: www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#.T1t2boePWEO
- Kawasaki Disease Foundation: www.kdfoundation.org

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### Mitochondrial Disease

**WEBSITES**
- United Mitochondrial Disease Foundation: www.umdf.org
- MitoAction: www.mitoaction.org
Multifocal Motor Neuropathy (MMN)

**WEBSITES**
- Neuromuscular Disease Center at Washington University: 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.msaa.com
- 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**
- The Myositis Association, www.myositis.org, is devoted exclusively to all types of myopathy, 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, and advocate the need for early intervention and support research into the causes and treatment of myopathies. (202) 887-0088
- International Myositis Assessment and Clinical Studies Group: www.niehs.nih.gov/research/resources/collab/imacs/main.cfm

Peripheral Neuropathy (PN)

**WEBSITES**
- Neuropathy Action Foundation: www.neuropathyaction.org
- Calgary Neuropathy Association: www.calgaryneuropathy.com
- Texas Chapter of the Neuropathy Association: www.handsfeetheart.org

Primary Immune Deficiency Disease (PIDD)

**WEBSITES**
- The National Institute of Child Health and Human Development (NICHD): www.nichd.nih.gov/health/topics/Primary_Immunodeficiency.cfm
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organisation for Primary Immunodeficiencies (IPOPI) — UK: www.ipopi.org
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.uhospitals.org/rainbow/services/allergy-immunology
- Team Hope (for families and patients in New England): www.teamhope.info

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

**WEBSITES**
- P.A.N.D.A.S. Network: pandasnetwork.org

Pemphigus and Pemphigoid

**WEBSITES**
- The International Pemphigus and Pemphigoid Foundation: www.pemphigus.org

Primary Immune Deficiency Disease (PIDD)

**WEBSITES**
- 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 Myositis Association, www.myositis.org, is to find a cure for inflammatory and other related myopathies, while serving those affected by these diseases. (202) 887-0088

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, and advocate the need for early intervention and support research into the causes and treatment of neuropathies. (212) 692-0662
**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
- Michigan Immunodeficiency Foundation: www.facebook.com/groups/108048062584350
- Rhode Island peer group: health.groups.yahoo.com/group/RhodelsiandPIDD

**Scleroderma**

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

**ONLINE PEER SUPPORT**
- 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.livingwithspss.com
- Stiff Person Syndrome: www.stiffpersons syndrome.net

**Education and Disability Resources**
- Americans with Disabilities Act of 1990: www.ada.gov Provides protection for people with disabilities from certain types of discrimination, and requires employers to provide some accommodations of the disability.
- Individuals with Disabilities Education Improvement Act of 2004: 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: www2.ed.gov/parents/landing.jhtml?exp=4 This federal government website offers a parents section titled “My Child’s Special Needs.”

**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 Flebogamma 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 Gammaphlex: www.gammaphlex.com
- IVIG Privigen: www.privigen.com
- SCIG Hizentra: www.hizentra.com

**Source**
- sugars.com — Provides information on sugar content in various foods and beverages.

**Other Resources**
- EMED Corporation: www.safetymedicalproducts.com
- Marcal Medical Inc.: www.marcalmedical.com
- Intra Pump Infusion Systems: www.intrapump.com
- Micrel Medical Devices: www.micrelmed.com
- Norfolk Medical: www.norfolkmedical.com
- RMS Medical Products: 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.
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.

**INDICATIONS AND USAGE**

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

**DOSEAGE AND ADMINISTRATION**

**Intravenous use only.**

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<th>Maintenance infusion rate (if tolerated)</th>
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<td>PI</td>
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<td>3.33mg/kg/min Every 3-4 weeks</td>
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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.

**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**
- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions.
- Epinephrine should be available immediately to treat any acute severe hypersensitivity reactions.
- Monitor renal function, including blood urea nitrogen and serum creatinine, and urine output in patients at risk of developing acute renal failure.
- Falsely elevated blood glucose readings may occur during and after the infusion of Octagam 5% liquid with some glucometer and test strip systems.

**ADVERSE REACTIONS**
The most serious adverse reactions observed with Octagam® 5% liquid treatment have been immediate anaphylactic reactions, aseptic meningitis, and hemolytic anemia.

**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 vacances.

**HOW SUPPLIED**

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**MANUFACTURED BY:**
OCTAPHARMA Pharmazeutika
Produktionsges.m.b.H.
Oberlaaer Strasse 235
A-1100 Vienna, Austria

**DISTRIBUTED BY:**
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www.octapharma.com/usa

Revised: September 2009
CONTRAINDICATIONS

octagam® 5% liquid is contraindicated in patients who have acute severe hypersensitivity reactions to human immunoglobulin. octagam® 5% liquid contains trace amounts of IgA (not more than 0.2 mg/ml in a 5% solution). It is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity. octagam® 5% liquid is contraindicated in patients with acute hypersensitivity reaction to corn. octagam® 5% liquid contains maltose, a disaccharide sugar which is derived from corn. Patients known to have corn allergies should avoid using octagam® 5% liquid.

WARNINGS AND PRECAUTIONS

IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. Epinephrine should be available immediately to treat any acute severe hypersensitivity reactions. Monitor renal function, including blood urea nitrogen and serum creatinine, and urine output in patients at risk of developing acute renal failure. Falsely elevated blood glucose readings may occur during and after the infusion of octagam® 5% liquid with some glucometer and test strip systems. 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 infectious agents, e.g. viruses and, theoretically, the Creutzfeldt-Jakob disease agent.

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

Please see Highlights of Prescribing Information on adjacent page.
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