

The Role of **Vitamin D** in Autoimmune Disease

**PIDD Antibody and
Subclass Deficiencies**

**How and Why to Track
Healthcare Treatment**

Home School
or Private School?

The Roles of Case Manager
and Patient Advocate

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use octagam[®], Immune Globulin Intravenous (Human), safely and effectively.

OCTAGAM[®]

Immune Globulin Intravenous (Human) 5% Liquid Preparation

Initial U.S. Approval: 2004

RECENT MAJOR CHANGES

Warnings and Precautions - Hyperproteinemia 8/2008

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).

DOSAGE FORMS AND STRENGTHS

octagam[®] 5% liquid is supplied in 1.0 g, 2.5 g, 5 g, 10 g or 25 g single-use bottles

CONTRAINDICATIONS

- Anaphylactic or severe systemic reactions to human immunoglobulin
- 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.
- 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.

ADVERSE REACTIONS

Most common adverse reactions with an incidence of > 5% during a clinical trial were headache and nausea. To report SUSPECTED ADVERSE REACTIONS, contact Octapharma at 1-866-766-4860 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

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

HOW SUPPLIED

	1g	2.5g	5g	10g	25g
Size	20ml	50ml	100ml	200ml	500ml
NDC#	67467-843-01	67467-843-02	67467-843-03	67467-843-04	67467-843-05
NDC#	68209-843-01	68209-843-02	68209-843-03	68209-843-04	

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A clear solution



IMPORTANT SAFETY INFORMATION

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

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

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

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

See brief summary of PI on facing page.

¹Ochs HD, Pinciaro PJ and the octagam® Study Group. octagam® 5%, an Intravenous IgG Product, is Efficacious and Well Tolerated in Subjects with Primary Immunodeficiency Diseases. *J. Clin Immunol* 2004;24;3:309-314

octagam®

Immune globulin intravenous (human)
5% liquid preparation

If you've been looking for an IGIV solution, take a look at **octagam®**.

octagam® has earned its reputation for safety and documented clinical efficacy¹.

To ensure tolerability¹, **octagam®** is carefully produced to retain as many of the characteristics of natural plasma as possible.

With over 40 million grams of **octagam®** infused world-wide, Octapharma is committed to helping PI patients live more active and healthier lives.

Ask your health care provider today about **octagam®** and find out if it could be the right solution for you.

For clinical or technical questions, please call our Medical Affairs team at 888-429-4535.

octapharma

For the safe and optimal use of human proteins

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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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IG Living Magazine is read by 30,000 subscribers who are patients who depend upon immune globulin products and their healthcare providers. For information about advertising in *IG Living*, download a media kit at www.igliving.com/web_pages/advertising.html. Or, contact our advertising specialist: Trudie Mitschang, (800) 843-7477, ext. 1340, tmitschang@igliving.com.

Pharmacy Accreditation and Reimbursement



I enjoyed reading my first issue of *IG Living* this month. I am a quality assurance director at a large system of pharmacies and have two comments regarding Kris McFalls' article on selecting a pharmacy [How to Choose a Specialty Pharmacy and/or Homecare Company, February-March 2010, pp16-17]. The first is

that there are several very bona fide options for accreditation other than the Joint Commission [on Accreditation of Healthcare Providers]. Although [the commission] has been around for a long time, many home infusion and specialty pharmacies are choosing to become accredited by others, including the Accreditation Commission for Healthcare (ACHC) or Healthcare Quality Association on Accreditation (HQAA). These organizations should be considered acceptable as well. Second, the issue of payer authorizations is a sticky one. We have, on countless instances, verified the benefits of a patient, received pre-authorization, and then received a denial after the claim was processed. As illogical as that sounds, it happens routinely to most providers in our industry. The best voice to quickly and effectively settle a payment issue is always the patient himself. Although we hesitate to involve the patient in a billing dispute, it is generally the voice that is heard the loudest by the payer.

— *Grace Sierchio, MSN, CRNI, CPHQ*

Kris McFalls replies:

In hindsight, it would have been a good idea to mention other recognized agencies. We are happy to clarify that in a future issue of *IG Living*. The purpose of this particular article was to inform patients of their choices and give them tools to use when choosing a provider. Unfortunately, we hear from many patients that some specialty pharmacies and homecare companies refuse to assist patients in appeals. I agree that patients and their doctors are going to be the strongest voice when communicating with an insurer. However, patients are not as experienced as the providers, and it is quite reasonable to expect that providers, who are making the money,

assist with patient appeals, regardless of who is at fault for mistakes that delay treatment and/or payments. If the provider is not going to provide this assistance, the patient has a right to know before agreeing to the service.

I am grateful for your comments and would encourage you to keep reading and writing.

Writing for "Go Juice"

I have been getting [this magazine] for three years and have read every page. I started having immune issues when I was 20 (I'm 45 now), and for the last 16 years, I've received IVIG every three weeks (I've nicknamed it "Go Juice"). So many of the stories and articles are "me." I know I'm not going crazy. Thanks for doing the magazine; keep up the good work.



— *Lisa*

I managed to pick up a copy of your June-July 2009 magazine today and couldn't get over how informative a lot of the articles were! My son who is 8 has CVID [common variable immune disease], and I will usually get the latest magazine at the infusion clinic. This practical issue was sitting out, and I felt it was all very informative.

We just got through running an autoimmune panel on my son for leg/muscle issues he has been having. I found a lot of information in this issue explaining the autoimmune process and its association with PIDD [primary immune deficiency disease]. I also enjoyed the article on side effects. What grabbed my attention initially was the cover page [title] PIDD and Sinusitis, since that is one my son battles frequently, even on infusions. I have read over the last year several of your issues, but for whatever reason I felt the June-July issue really related to me more on a personal level.

— *Laura*

Your feedback, opinions, suggestions and anything else you'd like to share are important! Email us at editor@IGLiving.com or visit www.IGLiving.com and go to the Contact Us page to send your comments.



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

Immunology 101: Parts of the Immune System that Protect Against Infection

“Protection from infections is a broader process, and our immune system contains components that we may not typically have considered as relevant for immunity.”



AMY SCANLIN, MS
Freelance Writer

PIDD Antibody and Subclass Deficiencies

“Intravenous IG (IVIG) therapy can be a controversial topic for patients who have antibody and subclass deficiencies.”



KRIS MCFALLS
Patient Advocate, IG Living magazine

The ABCs of Tracking Healthcare Treatment

“When physicians and infusion nurses are asked whether IG patients should keep track of their treatments, their answers will vary.”



JIM TRAGESER
Freelance Writer

The Roles of a Case Manager and Patient Advocate

“To streamline the bureaucratic process inherent to medical care, as well as to clarify the choices available to patients and to control costs, a mitigating party can help.”



JILL WEISENBERGER, MS, RD, CDE
Registered Dietitian

PIDD Antibody and Subclass Deficiencies

“The sooner an immunologist can order the correct tests, the sooner a diagnosis can be made and treatment can begin.”

Vitamin D and Autoimmune Disease

“The question is whether autoimmune diseases cause low levels of vitamin D, or whether poor vitamin D status leads to autoimmune disease.”

Connect with Other *IG Living* Readers through Monthly Teleforums!



IGL's Readers Group Teleforums allow readers to connect with others to share their experiences living with chronic diseases. Here's how you can participate:

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

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

Sign up for the Teleforums now by emailing kmcfalls@IGLiving.com or calling (888) 433-3888, ext. 1349.

Faces of IG Living

There are many faces in the IG Living community, representing hundreds of immune-mediated diseases and countless medical and lifestyle issues. IG Living's magazine, website, Facebook page and blog are the ways in which our community can connect with one another. Be a part of the community by interacting with us. Your comments could lead you to others who share similar issues, and vice versa. Monday through Friday, we pose a new question on the IG Living Facebook page. Here is what some of our faces of IG Living are saying in response.

Question: April is Primary Immunodeficiency Awareness Month. What do you do to raise awareness in your community about your disease state?



Susan Giorgi-Branch

This year has been a very busy year for me, however last year, our group here in Rhode Island handed out information at local stores. We also did an in-town dinner to raise awareness and funds for the Immune Deficiency Foundation (IDF). We also had planned on visiting the local blood bank to thank plasma donors for their time and plasma donation that is so appreciated. We then did the 5K Walk/Run Blue Jeans for Healthy Genes to raise awareness and funds for IDF.

Question: When you are seeking medical care for chronic illness, knowledge is power. What have you done to educate yourself about your disease?



Dale Manning Cook

Research, research and more research on the Internet. Staying in contact through Facebook with people who have the same chronic illness.



Linda Schatz

We have a medical homecare plan for our son. This way, when someone is [working] who doesn't know him, I can refer them to the careplan, and not be the pushy mom. Being in the undiagnosed stage is frustrating, but research [and] peer-to-peer contact helps a lot. Finding a doctor who listens is hard, but your best bet too!

Question: When your life revolves around illness, it can keep you from the pursuits that bring joy to life. What passions have you let slip away? What can you do now to begin to incorporate more personal pleasures into your daily activities?



Christopher L. Sallay

I have my IVIG tomorrow. Here's how my life is normal: Tonight, my men's ice hockey team has a must-win game to make the playoffs and my wife and kids are coming to cheer me on. I still work for a great company and only miss one day a month for treatment. I will be celebrating Easter with my family this weekend. Next weekend, I start coaching my kids' T-ball and softball teams. I refuse to let this disease make me feel anything but normal.

Question: Art. Music. Reading. Travel. When your life revolves around illness, it can keep you from the pursuits that bring joy to life. What passions have you let slip away? What can you do now to begin to incorporate more personal pleasures into your daily activities?



Laura Guenther

Having things to look forward to is hard because the nature of CVID is so unpredictable. However, I have subscription tickets to the symphony and ballet, and the nice thing is if I'm sick the date of the performance, as a subscriber, I can trade them in for another day! This has worked nicely even though it's more expensive, because now I can safely look forward to special events that bring me pleasure, without having to be too worried about whether I can go.

Our mission is to support the IG community through education, communication and advocacy

A community service from
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It Takes a Village

THERE IS an African proverb that states, "It takes a village to raise a child." This proverb's first four words, "It takes a village," have frequently been used to describe how a cause can only be as successful as the efforts of a great many.

How true it is, then, to say that "it takes a village" to raise awareness of the diseases faced by those who are immune-compromised. This is especially valid as the number of disease states and the many faces in the *IG Living* community continue to grow. Fortunately, for more than a decade, the many ways in which a village can be tapped into also have grown — mainly made possible with the Internet.

We at *IG Living* magazine have been expanding the many ways in which we can act as a village to support our community. In April, we launched our redesigned *IG Living* website (www.IGLiving.com) to help you tap into the great many resources needed to find information about your diseases and connect with others. The new site offers much more in-depth content, including weekly news updates about research, clinical trials, newly approved medicines and more. In addition, the entire issue of *IG Living* is available to peruse page-by-page online or to download. We've also archived all of our back issues in case you have misplaced your magazine or are looking for something not in the current issue.

IGLiving.com also is much more interactive, providing you with more ways to make your voices heard. For instance, we have a form for you to email us your stories, another to ask your questions and yet another to provide us with feedback. We also regularly post information about how to participate in our upcoming monthly reader teleforums, as well as information about past teleforums. And, we have started a blog with insightful weekly postings.



There also is a link to the *IG Living* Facebook page where hundreds of fans regularly post questions and comments. Check out our Facebook question of the day, which we post Monday through Friday — intended to inspire conversation among fans about *IG Living*-related issues. On page 7, you'll find our newest column, Faces of *IG Living*, with a sampling of the types of questions we post daily, as well as some of the comments in response to those questions.

To reiterate the importance of being a voice of the village, I want to mention one shining example: Andy Lutzenhiser, a 25-year-old with ataxia telangiectasia (A-T). As part of the A-T Cure Team, Andy is taking part in the Disneyland Half Marathon and 5K Family Run (to be held Labor Day weekend in Anaheim, Calif.) to raise money to find a cure for A-T. He is challenging everyone in the *IG Living* community and beyond to support his fundraising goal or to raise funds of their own. You can find more information on Andy's fundraising page at www.communityatcp.org/AndyL. I, personally, will do my part to be a voice of the village by running the Disneyland Half Marathon to support Andy and others with A-T in spirit.

Andy's goal is one of many great ways to spread the word about and support research for immune-mediated diseases. Numerous other organizations are doing similar things. To help you find them, we've restructured our resources section on our website where you can access and share information with others, and where you can connect for a cause.

The *IG Living* community is strong and growing. But, we know that to continue to make it better, it will take a village. ■





Parts of the Immune System that Protect Against Infection

By Terry O. Harville, MD, PhD

LET'S REDEFINE THE term “immunity.” Immunity is commonly referred to in a broad sense to represent the processes of providing protection. In people, though, we tend to think of it in narrow terms, frequently focusing on the adaptive components — T and B lymphocytes. Yet, in reality, protection from infections is a broader process, and our immune system contains components that we may not typically have considered as relevant for immunity.

Skin and Mucosal Cells

Foremost is our skin, a critical barrier that keeps pathogens out of the body. The outer layers of skin are made from layers of flattened dead cells that are held together, making it a more or less waterproof barrier, impervious to minor trauma. There are numerous sweat glands throughout the skin, and sweat contains chemicals that may have antimicrobial properties.

A seemingly unlikely component of immune protection is our urine. The urethra provides an opening for which organisms may enter and cause bladder and, in worse cases, kidney infections. Frequent urination can keep the organisms “flushed” from the urinary tract, preventing infections.

Another component is tears, which flush away organisms from the eyes, as well as help defend against organisms in the nose. In the early search for antimicrobial agents, Sir Alexander Fleming, a Scottish bacteriologist, noted that tears would cause bacteria to break apart (lyse). It was found that tears contain digestive enzymes that are capable of digesting the cell walls of bacteria. Saliva, yet another component, is capable of doing the same. Saliva contains many digestive enzymes capable of lysing the cell walls of microorganisms. Therefore, tears and saliva “bathe” our upper respiratory tract with antimicrobial protection.

We also have several conduits into or through the body, which may be pathways for pathogenic organisms to invade our bodies. These include the ear canals, Eustachian tubes, nose, tear ducts, mouth, lungs,

esophagus, stomach, intestines, anus, bladder and urethra. Like the skin, these conduits are lined with cells, albeit different from the skin, that are collectively known as the mucosa. An interesting concept is that the open areas bounded by these mucosal cell linings are actually “outside the body,” even though we may think of them as “in” the body. In other words, the mucosal cells are like the skin, but they line the otherwise open areas found “inside” the body to protect them from the invasion of organisms, and these cells connect directly to the outside world via the mouth, anus, nose, etc. The mucosal cells do not form the stratified layers of flattened cells like the external skin, but they do have help from specialized cells that secrete mucous. The mucous provides an additional barrier over the cells, making it more difficult for organisms to invade. In the ear canals, a waxy material is produced for the same purpose. When considering the scale of size of the milieu in which microorganisms live, the movement of bacteria in water is comparable to humans swimming through tar. And, mucous adds to this viscosity, further impeding invader organisms.

Critical Protective Barriers

Clearly, the barrier provided by skin and mucosal cells is a critical component of normal immune system protection. Further, the flow of fluids can help “flush” away microorganisms, and many of the fluids have intrinsic antimicrobial activities. In addition, the secretion of mucous helps to further protect the mucosal cell layers. Although not always recognized for their protective qualities, these immune system components serve as our first line of defense against infections.

Next time, we will explore more components of the immune system. ■

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.

Medicine

FDA Warns About WinRho Use for ITP



In the June-July issue of *IG Living*, we incorrectly reported that the FDA had issued a warning about intravenous immune globulin (IVIG) use to treat ITP. While the FDA did issue a warning, it was about using human intravenous immune globulin (WinRho SDF). In March, the U.S. Food and Drug Administration (FDA), Baxter Corp. and Cangene Corp. notified healthcare professionals that cases of intravascular hemolysis (IVH) and its complications, including fatalities, have been reported in patients treated for immune thrombocytopenic purpura (ITP) with WinRho(r) SDF [Rho(D) Immune Globulin Intravenous (Human)]. Fatal outcomes associated with IVH and its complications have

occurred most frequently in patients 65 years of age and older with co-morbid conditions. In addition, serious complications that include severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation also have been reported.

The notification comes in the form of a boxed warning that informs healthcare professionals that 1) patients should be closely monitored in a healthcare setting for at least eight hours after IVIG administration; 2) a dipstick urinalysis should be performed at baseline, two hours and four hours after administration, and prior to the end of the monitoring period; 3) patients should be alerted to and monitored for signs and symptoms of IVH, including back pain, shaking chills, fever and discolored urine or hematuria (absence of these signs and/or symptoms of IVH within eight hours does not indicate IVH cannot occur subsequently); and 4) if signs and/or symptoms of IVH are present or if IVH is suspected after administration, post-treatment laboratory tests should be performed, including plasma hemoglobin, urinalysis, haptoglobin, LDH and plasma bilirubin (direct and indirect). ■

Conference

2010 Myositis Patient Conference

The Myositis Association's (TMA) 2010 Annual Patient Conference will be held Sept. 23-25 at the Hilton St. Louis at the Ballpark in St. Louis, Mo. The conference will focus on research and is designed to present patients and their caregivers with an opportunity to hear from those most knowledgeable about myositis and to provide answers to their questions. For the first time,

the entire 20-member TMA medical advisory board will attend to share their expertise. Conference sessions are interactive, and questions are encouraged. The three-day conference costs \$125 and covers all meals and materials, and a special room rate at the Hilton at the Ballpark has been negotiated for \$99 per night for conference attendees. ■

Research

APS-I Patients' Antibodies Attack Cytokines

According to two recent studies, patients with a rare autoimmune disease known as autoimmune polyendocrine syndrome (APS-I) produce antibodies that attack microbe-fighting immune proteins called cytokines. The two teams of researchers in the United Kingdom, one at the National Institute for Biological Standards and Control and the other at Newcastle University, found that patients with APS-I produce autoantibodies that bind to and disarm these yeast-fighting cytokines.



Normally, the immune system produces cytokines that help protect the body against airborne yeast and other environmental pathogens. The findings may help explain why these patients suffer recurrent yeast infections. In addition, they suggest that cytokine replacement therapy might be considered in the treatment of APS-I patients.

APS-I afflicts one in 100,000 people and is characterized by disrupted thyroid and adrenal gland function and recurrent skin infections with one type of yeast. The studies were published online on Feb. 1 in the *Journal of Experimental Medicine* (www.jem.org). ■

Medicine

CSL's Hizentra SCIG Receives FDA Approval

CSL Behring has received U.S. Food and Drug Administration (FDA) approval for its Hizentra immune globulin (IG) subcutaneous (human) 20% liquid for treating patients diagnosed with primary immunodeficiency (PI). The once-weekly IG replacement therapy is the first 20 percent subcutaneous IG (SCIG) approved in the U.S.

Hizentra is a high-concentration product stabilized with L-proline, a naturally-occurring amino acid. It can be stored at room temperature, requiring no refrigeration, making it ready to use by patients who can safely self-administer it. "As the first SCIG treatment with a 20 percent concentration of immunoglobulin, Hizentra

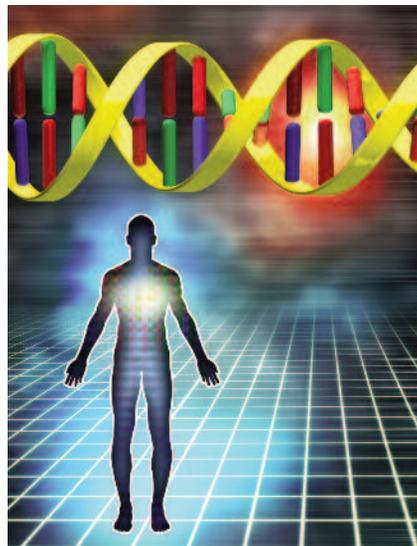
represents an effective, convenient choice of at-home IG therapy that will allow people with PI to schedule treatment around their busy lives, instead of scheduling their lives around treatment," says Robert Lefebvre, vice president and general manager, U.S. Commercial Operations at CSL Behring. ■

Research

B-Cell Self-Reactivity Increased in CVID Mutation

An aberrant gene identified in patients with common variable immune deficiency (CVID) may help explain why these patients also may carry an autoimmune complication. A mutation in the gene encoding the transmembrane activator, calcium modulator and cyclophilin ligand interactor (TACI) appears to give new B cells, which have not yet been programmed to bind to a specific antigen, the tendency to bind to DNA and other self-antigens, making them self-reactive. Self-reactivity is the hallmark of autoimmunity.

CVID is a primary immune deficiency that usually is diagnosed in young to middle-age adults who, after a few serious infections, discover they have no gammaglobulin in their blood. The pathway that the TACI mutation falls within may help explain what happens not only in this subset of primary immune deficiency, but also in lupus, rheumatoid arthritis and other autoimmune conditions. According to Mark Ballou, MD, of the State



University of New York in Buffalo and incoming president of the American Academy of Allergy, Asthma and Immunology, the study of this relatively rare disorder "has important implications for a number of other disorders — autoimmunity, but even allergic disorders like asthma — because there are a lot of immunological and inflammatory pathways involved in that as well." ■

Medicine

Arthritis Drug Suspended After Deaths

Ocrelizumab, the experimental drug used to treat rheumatoid arthritis (RA) and lupus, was suspended in March after it caused deaths. Swiss drugmaker Roche Holding AG and U.S. biotechnology company Biogen Idec stopped using the drug for the two diseases after a safety monitoring board said it had seen serious infections in studies involving the drug and that some were fatal. A late-stage trial of ocrelizumab showed it significantly reduced the signs and symptoms of RA, a painful joint disease, but that it was associated with a higher number of serious infections. The drug was expected to succeed Rituxan when its patent expires. ■

Did You Know?

Climate changes may affect many aspects of human health, including respiratory allergic diseases such as allergic rhinitis (hay fever).

— American Academy of Allergy, Asthma & Immunology

Disease

New Report Examines Autoimmune Disease



A Briefing Report on Autoimmune Disease and AARDA: Past, Present and Future is a new, comprehensive report from the American Autoimmune Related Diseases Association that presents an up-to-date assessment of all of the most current data available on autoimmune disease, including its incidence (frequency of disease development), prevalence (the

number of people affected) and etiology (cause). The report also outlines current and pipeline treatment therapies, trends in research funding and the impact of autoimmune disease on the U.S. health-care system. It was presented at the National Autoimmune Diseases Summit held in March to kick off National Autoimmune Disease Awareness Month. ■

People and Places in the News

Octapharma AG has started the first of a series of Phase III studies for its new 10% high-purity intravenous immunoglobulin (IVIG). The Phase III study represents the start of a series of planned studies to investigate Octapharma's new 10% IVIG for a range of neurologic and hematological conditions including idiopathic thrombocytopenic purpura (ITP), Guillain-Barré syndrome (GBS), Kawasaki disease and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

CSL Behring has started a global clinical trial program called SWIFT (Studies with von Willebrand factor [VWF]/Factor VIII) to evaluate the pharmacokinetics, efficacy and safety of Biostate, a low-volume, highly active, plasma-derived VWF/FVIII concentrate for the treatment of

von Willebrand disease (VWD) and hemophilia A. The SWIFT program, which will include centers in Europe, North America and South America, comprises four open-label studies in adults/adolescents and children with VWD and hemophilia A. CSL Behring is performing the SWIFT studies to meet the regulatory requirements for making Biostate available in multiple countries. Biostate has been available in Australia since 2003.

Grifols has received approval from the FDA for its new sterile albumin filling plant in Los Angeles. This approval is the culmination of a three-year project to transform the entire process of obtaining, purifying and filling albumin vials at Grifols Biologicals Inc. In October 2009, Grifols also obtained FDA approval for its new plasma fractionation plant, known as "Minifrac." The capacity to

process 700,000 liters of plasma brings the total fractionation capacity of the Los Angeles plant to 2.2 million liters per year. In addition to the work in Los Angeles, Grifols also is constructing a second plasma analysis laboratory in San Marcos, Texas. Grifols hopes to start operations there at the start of 2011.

The Neuropathy Association has awarded two scientific research grants for 2010, each for \$80,000 over a two-year period. This year's grant recipients are Dennis Paul, PhD, and co-principal investigator Harry J. Gould, MD, PhD, of Louisiana State University Health Sciences Center for New Orleans, and Glauca C. Furtado, PhD, of Mount Sinai School of Medicine. The two recipients were chosen from 13 applicants involved in neuropathy research at medical institutions across North America. ■

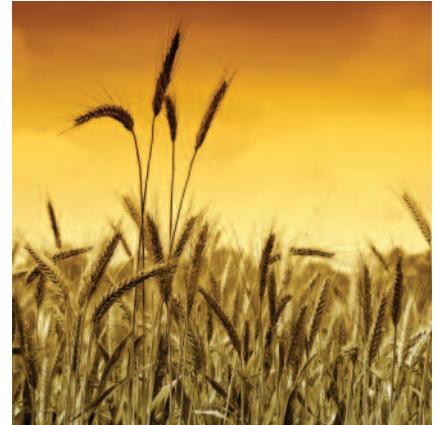
Research

Celiac Genes Identified in Immune System

A United Kingdom-led international study, which was published in the Feb. 28 online issue of the journal *Nature Genetics*, has identified four types of genetic disturbance in the immune system that lead to celiac disease, bringing to 40 the total number of known inherited factors that increase a person's risk of developing the disease.

Researchers performed a second-generation genome-wide association study that included 4,533 people with celiac disease and 10,750 people who did not have the disease. They also genotyped more than 130 sequences

of DNA (single-nucleotide polymorphisms, or SNPs) in a separate group of 4,918 people with the disease and 5,684 controls. By comparing what they found in the genomes of people with the disease to those of people without the disease, the researchers concluded there is robust evidence of SNP variants in 13 new regions of the genome, most of which contained genes with immune functions and four having key roles in thymic T-cell selection. They also found evidence to suggest there is a shared risk between the gene linked to celiac disease and many other common chronic diseases



involving the immune system.

It is hoped that the findings will help to improve diagnostic tools and treatments for celiac disease, as well as give new clues about related autoimmune diseases, such as type 1 diabetes. ■

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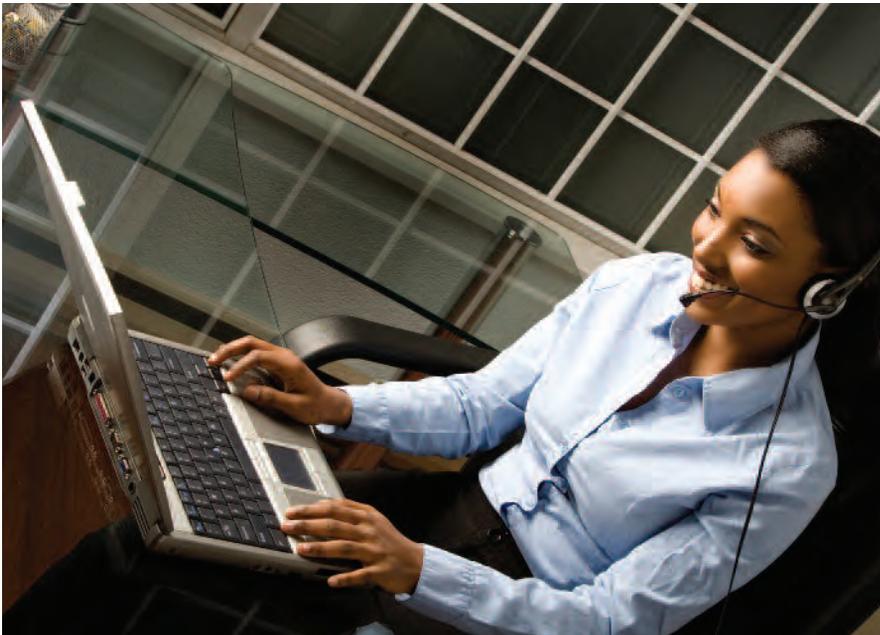
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The Roles of an Insurance Case Manager and Patient Advocate

By Jim Trageser



Anyone with a medical condition that requires ongoing care knows well the many frustrations that have nothing to do with medical care itself. Dealing with the insurance company, doctors' staff, pharmacies and other providers can be a headache all its own. And all too often, the many choices — from the treatment plan to selecting a provider for that treatment — can seem overwhelming to patients and their families for whom the entire process is unfamiliar.

To streamline the bureaucratic process inherent to medical care, as well as to clarify the choices available to patients and to control costs, a mitigating party can help. This party can be either a case manager or an independent patient advocate, or, in some

cases, both. But, before deciding whether to utilize one or both, it will be helpful for patients and their families to understand what roles a case manager and a patient advocate play.

loyalty is to the insurer.

From an insurance company's perspective, a case manager's salary and benefits are another expense to be paid for out of plan members' contributions and deductions. Jose Santoro, director of managed care with NuFACTOR, the specialty pharmacy of FFF Enterprises Inc., says there are good reasons why insurance companies utilize the services of either staff or a contract case manager. For instance, they "ensure appropriate care for a member's disease state, reduce inpatient hospital stays, minimize duplicity of tests and increase utilization of a contracted provider network," he explains. "The insurance company can steer the member to the appropriate resources, can have an active role in care coordination and [can] manage cost-effective care."

From a patient's point of view,

From a patient's point of view, having a case manager means having a familiar face or voice to deal with at the insurance company.

The Role of a Case Manager

A case manager works for the insurance company. While that individual can help clarify the choices available to a patient, as well as take some of the red tape out of the process, they are paid by and their

having a case manager means having a familiar face or voice to deal with at the insurance company. Rather than calling customer service and having to repeatedly explain their situation to a different company representative, patients can interact with the same

person who is familiar with their case history and can provide quick, accurate information about their account.

A case manager is commonly used to help oversee the treatment of people with cancer, HIV and other serious chronic diseases and conditions with high-cost ongoing therapy, such as patients who rely on immune globulin (IG). And, even if they are not automatically assigned a case manager, patients can request one. According to Santoro, assignment of a case manager often occurs when hospitalization is required, particularly when ongoing post-hospitalization treatment or home equipment is also necessary.

Many large companies that are self-insured (i.e., they pay their employees' medical bills out of a pool of money from their profits and hire an insurance company to administer the program) are increasingly relying on case managers to help control costs. A case manager can ensure that the patient isn't receiving duplicate tests, is receiving treatment from in-network providers (thus saving the company money), and is on track with treatment to prevent more serious complications.

But, even with a case manager to fully explain all of the options and to act as a regular conduit to the insurance company, it remains important for patients to ask the correct questions so they can get accurate answers. For some families, this is where a patient advocate comes in.

The Role of a Patient Advocate

Whereas a case manager works for the insurance company, a patient advocate works for the patient. "The

patient does not know what they don't know," explains Santoro, which is why they may need a patient advocate to help them map out their treatment options. A patient advocate should have expertise and experience in both medical care and insurance company bureaucracy, making them better equipped than the family to sort out the best course of action.

A patient advocate should have expertise and experience in both medical care and insurance company bureaucracy, making them better equipped than the family to sort out the best course of action.

But, while a patient advocate's loyalty is to the patient, that person may not always have the same access to the decision-making process at the insurance company that a case manager would have. And, caution is advised in hiring a patient advocate, since no licensing is required for the profession. In addition, many individuals and firms advertising their patient advocacy services emphasize their ability to negotiate better financial terms with the insurance company and/or care providers — which isn't always what a patient or their family is looking for.

When considering whether to hire a patient advocate, some precautions should be taken. For instance, before agreeing to services, patients should find out exactly how much they will

be paying and the specifics of what they will get for that money. Those items should be drawn up in a contract so there are no misunderstandings later. In addition, the patient advocate should provide documentation of their expertise that will allow them to assist patients in negotiating the maze of insurance requirements and treatment options. Referrals from previous clients should be requested.

A Team Effort

Whether a case manager and/or patient advocate is utilized depends upon each patient's needs. However, if a patient advocate is hired, and the patient also has a case manager assigned from their insurer, it's important that the two work as a team. "The advocate would serve the patient better by interacting *with* the insurer's case manager," says Santoro. "It would not be in lieu of the patient; it would be in conjunction with the patient." ■

JIM TRAGESER *edits the film, religion and books sections for a daily newspaper in the San Diego, Calif., area, and has contributed to two reference books on the blues.*

PIDD ANTIBODY AND SUBCLASS DEFICIENCIES

It is often a long road to diagnose these two less severe forms of PIDD, and while treatment is available, it is sometimes controversial and has its share of insurance issues.

By Kris McFalls and Amy Scanlin, MS

The World Health Organization recognizes more than 150 diseases classified as a primary immune deficiency disease (PIDD), affecting as many as one in 500 individuals. While some disease states require immediate hospitalization and even bone marrow transplants, others can cause minor illnesses and even go undiagnosed. Two of the less severe forms of PIDD that may require immune globulin (IG) treatment are selective antibody deficiency (SAD) and IgG subclass deficiency. Unfortunately, these two forms are difficult to diagnose, but once they are detected, with the proper treatment, patients can lead relatively normal lives.



Diagnosing SAD and IgG Subclass Deficiency

Typically, when a primary care provider (PCP) has a patient that presents with sinus or respiratory infections, the PCP will likely treat each infection with appropriate antibiotics. However, if the patient returns time and again with chronic infections that won't heal, don't respond well to antibiotics or increase in frequency, the PCP will suspect something more. At this point, the PCP will likely take a complete blood panel (CBC) to screen for infections, anemia and other possible diseases.

In many cases, a CBC for a mild PIDD patient generally will not sound alarm bells. So, if infections persist, increase in frequency and respond poorly to antibiotics, the PCP may suspect allergies, environmental factors such as smoke, mold or even gastrointestinal reflux, and again try to treat the patient symptomatically. For PIDD patients, these measures may help, but they will not stop the onslaught of infections. Finally, after years of failing to get infections under control, the PCP may refer the patient for further evaluation.

The hope is that the patient will be referred to an immunologist for testing. But, the reality is that the patient will likely see an otolaryngologist, allergist or infectious disease specialist. The Jeffery Modell Foundation (JMF) and the Immune Deficiency Foundation (IDF) have taken very active roles to try to educate PCPs and medical students to think outside the box, notice the warning signs and seek an immunology consult before long-term damage from infections occur. Unfortunately, according to one IDF study, it takes, on average, more than nine years for a PIDD patient to be diagnosed. Perhaps further education and heightened awareness can help decrease considerably the average time to achieve diagnosis.

Once a patient is referred to an immunologist, patient history, labs and other testing will be reviewed. In addition, further blood testing will likely be ordered to look at immunoglobulin G (IgG) subclass levels named IgG1, IgG2, IgG3 and IgG4, as well as antibody function. A deficiency in any of these typically may be found in association with frequent respiratory infections, including ear, sinus, bronchitis and pneumonia, as well as excessive viral infections. The sooner an immunologist can order the correct tests, the sooner a diagnosis can be made and treatment can begin.

IgG Subclass Deficiencies

There are four subclasses of the IgG antibody, named in order of their concentration in the blood serum. In most people, IgG1 constitutes 60 percent to 65 percent of total

IgG, followed by IgG2 at 20 percent to 25 percent, IgG3 at 5 percent to 10 percent and IgG4 at 3 percent to 6 percent. However, these ranges vary. It's possible for a person to be deficient in one or more subclasses but have a normal serum IgG level due to compensation from the other IgG subclasses.

Because IgG1 levels are so high, a person who is low in this subclass will typically have a low overall IgG level.¹ IgG1 and IgG3 are the primary protectors against tetanus and diphtheria, and a deficiency in one often coincides with a deficiency in the other.

Approximately 60 percent of PIDDs can be diagnosed with a simple blood test, yet 70 percent to 90 percent remain undiagnosed.

A deficiency of IgG2, which is most common in children, is often associated with respiratory infections and asthma. IgG2 is responsible for making antibodies to the polysaccharide in cell walls of bacteria. It protects against bacteria and is the primary protector against pneumococcus, which can cause bacterial meningitis, pneumonia and infections in the bloodstream and sinuses. Often, an IgG2 and either an IgA or IgG4 deficiency will be found alongside each other. A person with an IgG2 deficiency may be asymptomatic. Yet, for those who do present with infections, encapsulated bacteria are often the cause due to the antibody response to polysaccharides.²

IgG3 deficiencies are most common in adults and are commonly associated with upper and lower respiratory tract infections. IgG3 is a primary response to viral respiratory agents. A significant fraction of the IgG antibodies against pneumococcal polysaccharides may be of the IgG3 subclass.

IgG4 deficiencies occur with surprising frequency. Fifteen percent of children and 10 percent of adults have completely undetectable IgG4. Since its role in infection susceptibility is unknown, its absence is not considered clinically significant by itself when looking for a cause of a patient's symptoms.³

According to Dr. Francisco Bonilla, immunologist at Boston Children's Hospital, "Doctors are more likely to look more closely at patients who have more than one

deficiency. For instance, treating a patient with IG who only has an IgG3 or an IgG4 deficiency may be controversial. However, if a patient has an IgG2 and an IgG4 deficiency, plus an IgA deficiency, doctors may be willing to give it more consideration.”

Also, it’s important to note that because the levels of circulating IgG subclasses vary throughout people’s lives, age must be taken into account when analyzing the results of subclass testing.

Selective Antibody Deficiency (SAD)

SAD is just as it sounds: The body produces too little of a certain antibody and normal amounts of others, which causes a patient to be more susceptible to encapsulated bacteria and enteroviruses, and conditions such as respiratory infections with bacteria and viruses.

While there are five main classes of antibodies, the IgG class has the highest concentration in the blood and fluids that surround the tissues and cells. Interestingly, IgG is the only immunoglobulin that can cross from the mother to the placenta and fight infection in utero.



Testing

Approximately 60 percent of PIDDs can be diagnosed with simple blood tests, yet 70 percent to 90 percent of patients remain undiagnosed.⁴ To simplify the explanation of testing, JMF has classified the tests into four stages, yet because they can overlap, there is no set sequence.⁵ “The stages are not necessarily sequential and may occur simultaneously, but should be based on the initial information obtained from the history, physical examination and previous

laboratory testing,” explains Dr. Terry O. Harville, medical director of immunology at the Departments of Pathology and Laboratory Services and Pediatrics at the University of Arkansas for Medical Sciences. “These stages are more or less possibilities, but have no particular time scale.”

A typical immune evaluation likely would include a vaccine challenge, which helps assess the immune system’s ability to function as expected. The most common is a pneumococcal vaccine challenge. In this test, several (usually 12 to 14 depending on the lab) antibodies against 23 pneumococcal serotypes are measured before the pneumococcal vaccine is given. Three to four weeks following, the patient’s blood is again tested and antibodies are remeasured. A level of 1.3 micrograms/milliliter or higher is considered protective. However, immunologists also like to see an increase in antibody levels of two to four times the starting level for at least half of the serotypes.

If more information is needed, the specialist will look further at the four subclasses, IgG1 through IgG4. However, some specialists feel that the subclass information is not particularly helpful because it doesn’t provide any information about the patient’s ability to produce antibodies to protein, polysaccharides or viral antigens.

Assessment of antibody responses to polysaccharide antigens also must be considered, because responses may be deficient in some who otherwise respond normally to protein antigens. Antibodies measured after a pneumococcal capsular polysaccharide vaccine are useful in children over 2 years of age and can provide information about a patient’s immunocompetence.⁶

A patient’s symptoms will guide which tests a doctor chooses. “[If] the patient presents with recurrent boils, furuncles, poor wound healing, etc., the evaluation would not necessarily require measurement of IgG levels or lymphocyte enumeration, but does require neutrophil counts and oxidative burst assay,” explains Dr. Harville. “The most common evaluation would be for recurrent sinopulmonary disease/infections. This implies humoral immunodeficiency. Therefore, the evaluation would consist of IG levels (IgG, IgA, IgM, and IgE), CBC with differential to determine the lymphocyte count, pre-immunization diphtheria, tetanus and pneumococcal titers, and CH50. Most also will assess lymphocyte enumeration to determine the extent of B lymphocyte lack and the alterations in B lymphocyte subpopulations.”

Treatments

Intravenous IG (IVIG) therapy can be a controversial topic for patients who have antibody and subclass



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deficiencies. Some clinical immunologists believe that patients with only SAD or a subclass deficiency should not be treated with IG. When deciding whether to treat with IG, doctors should consider a patient's quality of life and infection history. According to Dr. Bonilla, the SAD and subclass deficiencies are still considered to be at the mild end of the immune deficiency spectrum. As a result, many patients are managed with antibiotics.

"Some patients can be managed with extra immunizations and/or antibiotics alone," says Dr. Melvin Berger, MD, PhD, division chief, allergy and immunology at University Hospitals Case Medical Center. "It depends on the pattern of infections the patient has experienced, the exposure of the patient to infectious agents, and the response and tolerance to antibiotics." Also, some patients have good success using a prophylactic antibiotic to prevent infections, and once they get an infection, they can then be moved to another antibiotic.

In some cases, such as chronic sinusitis, IV treatment may be warranted because antibiotics will not be effective due to a hampered humoral immune response.⁷ In addition, some patients develop resistance and sensitivities to entire

classes of antibiotics. For those patients in particular, IG may be the best option to prevent infections.

Before a patient with a subclass deficiency will be considered for IVIG therapy, antibody responses to polysaccharides and proteins will be tested for clinical significance. If the subclass deficiency is considered to be clinically significant, the patient will have both recurrent infections and impaired functional antibody responses.⁸ According to Dr. Bonilla, "When a patient gets to the point where they are always on antibiotics and are still getting sick and they are missing work or school, then it may be appropriate to start IG therapy."

The controversy over treating patients with IG can be very confusing. Dr. Bonilla encourages patients to talk with other patients and find a doctor that will work with them. The IDF is a good place to start the search. Patients can go to www.primaryimmune.org and click on Patients and Families to find information about joining the foundation's free peer support network. The IDF will determine the patient's needs, then work closely to find a peer support. Trained volunteers are partnered with patients and family members who share similar situations to provide information and support. And, all correspondence is confidential.

IG Living (www.IGLiving.com) also has a fan page on Facebook where patients are able to participate in discussions. On the site's homepage, there is a Facebook link at the bottom left.

Precautions

Because patients with antibody deficiencies do not produce a good antibody immune response, they should speak with their doctor about their particular risks of receiving live vaccines while undergoing IVIG treatment. For most, the risk is low. According to Dr. Bonilla, patients with SAD generally do not have a problem with live vaccines: "In my 15 years of practice, I cannot think of one patient with SAD who suffered serious complications from a live vaccine."

Dr. Berger adds, "In general, the precaution of avoiding live vaccines is recommended for patients with T-cell defects (an exception being live nasal influenza vaccine in IgA-deficient patients). Therefore, these vaccines may be given to specific antibody deficiency patients who may still produce antibodies to protein antigens and whose T cells may be stimulated by the vaccine antigens. Individual patients should discuss immunization plans with a doctor who is familiar with their exact immunologic defects."

Patients with SAD or subclass deficiency need to take



reasonable precautions to avoid interaction with people they know to be sick, and they need to have good hygiene, a healthy diet and get plenty of exercise and rest.

Insurance Issues

Dealing with insurance companies can be as confusing as testing and treatment. It can be a challenge to get IVIG approved because, as Dr. Bonilla explains, although there are quality-of-life issues, SAD or subclass deficiencies still are considered to be at the mild end of the immunodeficiency disease spectrum. However, copious notes, lab reports, culture results, radiological confirmation of infection and persistence in determining what documentation and verification a patient's insurance company needs will help.

In addition, doctors must show that they have tried reasonable alternatives to IG before it will be approved. It is not uncommon to see patients develop allergies or intolerance to certain classes of antibiotics, leaving few treatment options should a severe infection develop. In addition, patients may require IV antibiotics to clear a recurrent infection. But, in order to show that infections are recurrent and a switch to IG is necessary, specific documentation will need to be provided to the insurer. In fact, some insurers specifically state in their policy that "calling in a prescription is not proof enough of infection."

Children with SAD and/or subclass deficiency may be required by some insurers to go through a trial period during which they go off of IG after one year for re-evaluation. This is because it is possible that children's immune systems could further mature and, therefore, they could "grow out" of their immune deficiency. "Particularly when specific antibody deficiency is diagnosed in young children, it may be a delay in development of the full repertoire of antibody responses, and the patient may well grow out of the problem as their immune system matures," explains Dr. Berger.

While growing out of an immune deficiency may be possible for a child, Dr. Bonilla says, "I can count on one hand the number of adults who have had apparent spontaneous remission of PIDD."

Research

New research could shed additional light on SAD and subclass deficiencies. At the 2009 Immune Deficiency National Patient Conference, Dr. Bonilla reported that some patients may produce antibodies, but those antibodies may not be of sufficient quality. He and his colleagues have been studying this theory and were scheduled to

present an abstract regarding this topic at the First Clinical Immunology Society's North American Primary Immune Deficiency National Conference, which took place May 20-23 in Philadelphia, Pa.

Some clinical immunologists feel that patients with only SAD or a subclass deficiency should not be treated with IG.

Patience Helps Patients

Because of the often misunderstood symptoms of SAD and subclass deficiency, finding the cause and appropriate treatment is rarely easy. Patients and doctors most often spend countless hours working together to find the appropriate tests and protocols for treating the disorder. But, with proper management, patients can enjoy work and play, and avoid future complications despite their reduced immune capacity. ■

KRIS MCFALLS is the full-time patient advocate for IG Living, and **AMY SCANLIN** is a freelance writer specializing in medical and fitness writing.

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Vitamin D

and Autoimmune Disease

The connection between vitamin D and autoimmune disease is becoming better established, and new information and recommendations are continually emerging.

By Jill Weisenberger, MS, RD, CDE

Vitamin D, the fat-soluble vitamin that aids calcium absorption and assists with bone growth and remodeling, is well known for its role in bone health. But that's just a small part of the vitamin D story. Today, researchers recognize that vitamin D is critical to immune function and a deficiency in vitamin D can play a role in the development of multiple health problems, including autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes, Crohn's disease and others.

What is surprising is the number of people believed to be vitamin D deficient. Researchers estimate that in the United States, approximately 41 percent of men and 53 percent of women have blood levels of vitamin D too low for optimal health.¹ According to a recent report in *Pediatrics*, 70 percent of the population between ages 1 and 21 years has inadequate levels of vitamin D in the blood.² Generally, blacks and Hispanics have lower levels than whites.¹ And, individuals with one or more autoimmune diseases are especially likely to be vitamin D deficient.³

In autoimmune diseases, the immune system attacks itself instead of foreign pathogens only, such as bacteria and viruses. There are more than 80 known autoimmune disorders. And, while the causes and cures of most remain a mystery, scientists agree that both genetic and environmental factors play important roles. What's more, vitamin D may be one of those environmental factors.

Shedding Light on Vitamin D

In recent years, scientists have made a connection between vitamin D and autoimmune diseases after statistics showed that multiple sclerosis, Crohn's disease and other autoimmune diseases are more common in Canada, the northern United States and Europe than in southern areas where there is more sunlight, especially in the winter months. In fact, people who were born and lived the first 10 years of their lives in the South have a lower risk of developing multiple sclerosis at any time throughout their lives.⁴

Vitamin D is known as the sunshine vitamin because, unlike other vitamins, it is synthesized from cholesterol in the skin in the presence of the sun's ultraviolet rays. Therefore, those living in the northern latitudes are more likely to have lower vitamin D levels. In addition to season and latitude, a person's skin color, age, use of sunscreen and the length of time spent outdoors influence the synthesis of vitamin D in their skin.

Intrigued that both autoimmune diseases and low vitamin D levels are more common in the northern latitudes, researchers looked for more associations between vitamin D and autoimmune disease. They discovered that immune cells have vitamin D receptors that allow the vitamin to enter these cells, further supporting the connection. Researchers also have observed low vitamin D levels in patients with systemic lupus erythematosus, type 1 diabetes and Crohn's disease compared with the healthy population.^{4,5} In 2008, Hungarian researchers reported that patients with

early signs of and at high risk for autoimmune connective tissue diseases, such as rheumatoid arthritis, systemic lupus erythematosus and Sjogren's syndrome, were more likely to convert to the full-blown disease if they had low vitamin D status.⁶ And, they discovered that in patients with rheumatoid arthritis, vitamin D levels are associated with disease activity; the lower the vitamin D levels, the greater the disease activity.⁴

Which Came First?

The question is whether autoimmune diseases cause low levels of vitamin D, or whether poor vitamin D status leads to autoimmune disease. Though scientists are still teasing out the answers, Margherita T. Cantorna, PhD, associate professor at Pennsylvania State University, suggests that vitamin D levels modify other risk factors that lead to autoimmune diseases. "If you don't have other risk factors (genetic and environmental factors), you won't get autoimmunity even if vitamin D is very low," she explains. Likewise, maintaining adequate vitamin D status may slow or prevent the development of lupus, multiple sclerosis or any other autoimmune disorder in individuals who are at high risk for developing these diseases.

Unfortunately, once individuals are diagnosed with an autoimmune disease, vitamin D is unlikely to offer a cure. As such, these individuals and their physicians should discuss vitamin D supplementation in addition to, but not instead of, standard therapies. "Based on what we know, there should be benefits of vitamin D even in patients using other treatments," explains Cantorna. "Supplemental vitamin D may lessen the symptoms of multiple autoimmune diseases." Solid proof that vitamin D supplements help any

Individuals with one or more autoimmune diseases are especially likely to be vitamin D deficient.

autoimmune disease in humans, however, is not yet evident. Much more research is necessary, Cantorna cautions. Family members also should discuss vitamin D supplementation with their physicians, since autoimmune diseases run in families.

D's Many Benefits

Vitamin D is linked to more than autoimmune diseases and bone metabolism.

- **Mortality:** In a study of more than 13,000 Americans, researchers found that those with the lowest vitamin D levels in the blood were the most likely to die during the median 8.7 years of follow-up.¹⁴
- **Heart disease:** In the Framingham offspring study of more than 1,700 individuals, those with the lowest vitamin D levels were the most likely to have a heart attack or other cardiovascular event in the five-year study period.⁸
- **Type 2 diabetes:** Vitamin D may have roles in insulin secretion and action. Low vitamin D levels are linked to type 2 diabetes.⁸
- **Falls:** Several studies have shown that vitamin D supplements decrease falls among the elderly, possibly because of improved muscle function.⁸
- **Cancer:** In the National Health and Nutrition Examination Survey of more than 16,000 men and women, those with higher vitamin D levels were less likely to have colorectal cancer. In a separate study of nearly 1,100 men, higher vitamin D levels were associated with less total cancer cases. Some, but not all, studies demonstrate lower rates of breast and prostate cancers with higher vitamin D levels.⁸

Vitamin D Deficiency

Low levels of vitamin D are likely related to a combination of factors, including low vitamin D intake, poor absorption, genetic factors, time spent in direct sunlight and more. As little as five to 10 minutes of sunlight on the arms and legs or face and arms between 11 a.m. and 2 p.m. three times per week should provide adequate vitamin D status for an average healthy person. Unfortunately, although it is proven to reduce skin cancer, sunscreen decreases vitamin D synthesis in the skin. Sunscreen with a sun protection factor (SPF) of 15 reduces the production of vitamin D in the skin by 99 percent.⁷ Cloud cover, shade and pollution further inhibit vitamin D synthesis. And, while tanning beds are thought to provide vitamin D, they are an unreliable source.⁸ In addition, individuals with dark skin produce less vitamin D when exposed to sunlight than light-skinned people. And, as people age, they also are less efficient at synthesizing vitamin D from sunlight. For instance, a dark-skinned octogenarian living up north is at greater risk of being vitamin D deficient than a light-skinned young adult residing in the South.

What seems to be an adequate intake from food and supplements may be inadequate in people with fat malabsorption diseases, such as cystic fibrosis, or diseases of the gastrointestinal tract, such as Crohn's disease, ulcerative colitis and celiac disease, as each of these health problems causes decreased nutrient absorption. Gastric bypass surgery and small bowel resections also will limit nutrient absorption.

Carrying extra pounds raises the risk of vitamin D deficiency, too. The greater an individual's body fat, the more likely this fat-soluble vitamin will be trapped in fat stores instead of circulating in the blood and making itself available to the various cells and body systems.⁹

Some medications also increase an individual's risk of vitamin D deficiency. Corticosteroids, such as prednisone, and anti-seizure medications, such as phenobarbital and phenytoin, may impair vitamin D metabolism. In addition, the weight-loss drug orlistat (Xenical and Alli) and the cholesterol-lowering drug cholestyramine inhibit absorption of vitamin D and other fat-soluble nutrients.¹⁰

Whether from food or sun, vitamin D must be metabolized in both the liver and the kidney before becoming activated, so having diseases of either of these organs will further lower an individual's vitamin D status.

A blood test can determine the level of vitamin D circulating in a person's bloodstream. However, scientists are still

The question is whether autoimmune diseases cause low levels of vitamin D, or whether poor vitamin D status leads to autoimmune disease.

debating the ideal amount. Many, however, believe the current recommendations are too low. Until researchers unravel this vitamin's roles in each body system, controversy is likely to remain. For now, many scientists recommend serum levels of at least 30 ng/ml.¹¹ With vitamin D so critical to multiple body systems, including the immune function, and with inadequate levels so common, individuals should consider asking their physician for this blood test.

D in the Diet

Food is an unreliable source of vitamin D. Oily fish, such as salmon, tuna, mackerel and sardines, and UV-irradiated mushrooms are good sources. Egg yolks supply moderate amounts. Fortified foods provide most of the vitamin D in the American diet. In the U.S., most milk is vitamin D fortified. Some fruit juices, yogurts, breakfast cereals and margarines also are fortified. Many people assume that because milk is a good source of added vitamin D that other dairy products also supply this vitamin. But, cheese, ice cream and some yogurts are not good sources of vitamin D because they are generally not made with fortified milk. Individuals who drink soymilk regularly should make sure their brand is fortified with both vitamin D and calcium.

How Much Is Enough?

The current vitamin D recommendations were set in 1997. These recommendations established the Adequate Intake (AI) for infants, children and adults under 51 years to be 200 IU of vitamin D. The AI increases to 400 IU for adults between the ages of 51 and 70 and to 600 IU for those over age 70.¹⁰

D's Discovery

Scientists recognized the association between sunlight and bone health during the industrial revolution in Europe when pollution blocked direct sunlight. This caused children living in polluted areas to suffer growth abnormalities and a bone disease called rickets. On the other hand, children living in rural areas continued to grow properly. When the children with rickets received sunlight on the rooftop of a hospital for several months, their rickets improved.

Eventually, scientists learned that sunlight and a compound produced by it (named vitamin D) could both eradicate and prevent rickets.¹⁵ By the 1930s, vitamin D was the new miracle vitamin added to numerous foods, including milk, hot dogs, peanut butter and even a variety of Schlitz beer marketed as the beer with sunny energy in both summer and winter. Today, milk and some cereals and juices are fortified with vitamin D in the United States.

But, with so much new research about vitamin D's many roles, the Food and Nutrition Board (FNB) at the Institute of Medicine has established an expert committee to re-evaluate adequate vitamin D intakes. Many experts believe the recommended intake levels will increase, and the FNB report is expected by midyear.

Yet, some experts and expert panels are not waiting for the FNB report. In fact, in 2008, the American Academies of Pediatrics recommended that all infants, children and adolescents receive a minimum of 400 IU beginning the first days of life.¹¹ Other scientists recommend 1,000 IU daily. John Jacob Cannell, MD, executive director of the Vitamin D Council, suggests as much as 5,000 IU for healthy adults.¹² Currently, however, the FNB set the maximum upper limit at 1,000 IU for infants and 2,000 IU for everyone else.¹⁰

Despite this, individuals should not jump on the D bandwagon too quickly. The vitamin looks promising, but concrete evidence is scant, and not enough is known about the side effects of higher-than-usual doses. Because there are so many unanswered questions, all individuals should speak with their physician before supplementing.

When Diet and Sun Aren't Enough: Picking a Supplement

Vitamin D supplements are available both by prescription and over the counter. Vitamin D₃, or cholecalciferol, is the form your body makes in response to ultraviolet light. In plants, ultraviolet light triggers the synthesis of vitamin D₂, also called ergocalciferol. Vitamin D₃ may be more potent,¹³ so this is the form many recommend. Individuals should be certain to ask the proper dosage for their specific concern.

Too Much of a Good Thing

The body cannot synthesize too much vitamin D from spending time in the sun, and individuals are unlikely to consume too much through food, except perhaps from large amounts of cod liver oil.¹⁰ However, taking supplements long term is associated with toxicity symptoms. Common symptoms of vitamin D overload include nausea, vomiting, poor appetite, constipation and weakness.¹⁰ More seriously, high vitamin D levels can raise calcium concentrations in the blood, resulting in confusion and abnormal heart rhythms. Phosphorus levels also may rise, and both calcium and phosphorus may become deposited in the kidneys and other soft tissues.¹⁰

According to the Natural Medicines Comprehensive Database, individuals with kidney disease, sarcoidosis, histoplasmosis, lymphoma, overactive parathyroid gland or ather-

osclerosis (hardening of the arteries) must take extra precautions. Vitamin D supplements could make any of these conditions worse or lead to an increased risk of kidney stones.

As with any nutrient supplement, vitamin D can interfere with medications, including certain cholesterol drugs, diuretics (water pills), heart medications and aluminum-containing antacids. Individuals are advised to talk to both a physician and pharmacist about nutrient-drug interactions. ■

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Initial U.S. Approval: 2003

WARNING: ACUTE RENAL DYSFUNCTION and FAILURE

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- **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. GAMUNEX does not contain sucrose.**
- **Administer IGIV products at the minimum concentration available and the minimum infusion rate practicable.**

INDICATIONS AND USAGE

GAMUNEX is an immune globulin intravenous (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. Epinephrine should be 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.

- 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 GAMUNEX 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.

ADVERSE REACTIONS

- **PI** – Most common drug related adverse reactions during clinical trials were headache and cough.
- **ITP** – Most common drug related adverse reactions during clinical trials were headache, vomiting, fever, and nausea.
- **CIDP** – Most common drug related adverse reactions during clinical trials were headache and fever.

To report SUSPECTED ADVERSE REACTIONS, contact Talecris Biotherapeutics, Inc. at 1-800-520-2807 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

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

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- The most clinically studied liquid IGIV, with >600 patients and >4100 infusions²

*CIDP=chronic inflammatory demyelinating polyneuropathy; PI=primary humoral immunodeficiency; ITP=idiopathic thrombocytopenic purpura.

References: 1. Data on file. Talecris Biotherapeutics, Inc. 2. GAMUNEX® [package insert]. Research Triangle Park, NC: Talecris Biotherapeutics; 2008.

The most common drug-related adverse reactions observed at a rate $\geq 5\%$ were headache, fever, chills, hypertension, rash, nausea, and asthenia (in CIDP); headache, cough, injection site reaction, nausea, pharyngitis, and urticaria (in PI); and headache, vomiting, fever, nausea, back pain, and rash (in ITP).

The most serious adverse reactions observed in clinical study subjects receiving GAMUNEX 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).

Important Safety Information—Gamunex, Immune Globulin Intravenous (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). Gamunex is contraindicated in individuals with known anaphylactic or severe systemic response to Immune Globulin (Human).

Immune Globulin Intravenous (Human) (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients should be instructed to immediately report symptoms of decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath (which may suggest kidney damage) to their physicians.

While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IGIV products, those containing sucrose as a stabilizer accounted for a disproportionate share of the total number. Gamunex does not contain sucrose. Glycine, a natural amino acid, is used as a stabilizer.

There have been reports of noncardiogenic pulmonary edema [Transfusion-Related Lung Injury (TRALI)], hemolytic anemia, and aseptic meningitis in patients administered with IGIV. 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, and/or known or suspected hyperviscosity. Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy.

Gamunex is made from human plasma. As with all plasma-derived therapeutics, the potential to transmit infectious agents, such as viruses and theoretically, the Creutzfeldt-Jakob (CJD) agent that can cause disease, cannot be totally eliminated. There is also the possibility that unknown infectious agents may be present in such products.

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The



of Tracking Healthcare Treatment

The best way to ensure that IG treatments are working is to maintain good health records. Here's why and how.

By Ronale Tucker Rhodes, MS,
and Kris McFalls

Gone are the days of patients placing blind faith in doctors and the healthcare system. In this age of ever-expanding and complex diseases, as well as the plethora of information available online to all, individuals can and should now take a proactive approach to their healthcare. This approach extends from keeping up to date on disease state issues, to playing a role in diagnoses and, even more important, maintaining health records. And, while keeping good records of healthcare treatment applies to all patients, it is of paramount importance to individuals who rely on immune globulin (IG). As IG patients well know, information pertaining to their health, including symptoms, side effects, medications, allergies, lab results, surgical procedures and more, is the only way to ensure that their IG treatment therapy is working. Following are the ABCs of tracking treatment.



Accounting for One's Own Health

When physicians and infusion nurses are asked whether IG patients should keep track of their treatments, their answers will vary. According to Heather Lawson, RN, an independent infusion nurse, it's common when patients have their infusions in the hospital or in an infusion clinic for doctors not to recommend patients track their treatments. This is because the facility is required to keep the information so that the doctors can easily access it if necessary. And, she says, even if patients have their infusions at home, the home healthcare company keeps the information on file via the nurse's paperwork. "However," she explains, "the patient should keep their own book, because it is easy to obtain the information ... regardless of location ... and then the patient has a record and continuity of care."

In fact, it also is the experience of Dr. Carol Koski, MD, retired professor of neurology at the Maryland University School of Medicine and medical board member of GBS-CIDP Foundation International, that “most doctors do not recommend patients keep their own records of intravenous immune globulin (IVIG) use.” But he, along with other physicians, agrees with Lawson that patients should. Records “can be very helpful, particularly when moving, seeing a new physician and for [making] the patient aware of which products, rates, etc., they tolerate best,” says Koski. In addition, for physicians to monitor safety and tolerance of a product, as well as that product’s effectiveness in preventing infections and other complications, record keeping by patients “is imperative,” says Dr. Ricardo Sorenson, MD, chairman of the Department of Pediatrics at Children’s Hospital, New Orleans, La. “If you don’t know which product was used and how it was given, it hinders taking corrective measures.” For instance, says Koski, if an adverse reaction occurs, a patient being seen for the first time may mention an allergic reaction to IVIG, but may not be able to remember the type of reaction, the timing or the brand they were on.

Even for the doctors who regularly see the same IG patients, personal records “can be very helpful during clinic visits for identifying problem areas and making any necessary changes in the treatment plan,” says Dr. Marc Riedl, MD, MS, section head of clinical immunology and allergy at the University of California, Los Angeles, David Geffen School of Medicine. But, that doesn’t mean it happens. “I haven’t had much success in actually getting patients to track or provide this specific information,” adds Riedl, and “because so few actually do this, I’ve come to rely on the home healthcare companies or infusion centers to provide the data on infusions, reported side effects and history of infections/antibiotics” — information that can be helpful in making dose adjustments, changing products or lots in the event of side effects, and tracking the efficacy of the treatment over time.

In case patients underestimate the importance of tracking their treatments, Lawson says she’s seen all kinds of mistakes occur with poor records or in situations where records don’t exist. “I have had the wrong medication shipped to the home. I have had the wrong dose sent. I have had patients have some very severe reactions to the medications,” she says. “I have had patients who receive one brand of IVIG at home only to be given a different brand of medication when the patient was in the hospital. [And,] I have patients who don’t tolerate infusions in

certain locations on their arms or [who have] certain veins that don’t work well. This is why continuity of care is so important, and being your own advocate is essential.”



Best Accounting Practices

The best accounting practices are detailed. Records should include not only treatment details and notes, but also other healthcare information. While this may seem a little tedious, once information has been initially recorded, it can become routine to regularly add information to keep it current.

Basically, this will be a “health diary.” It will include all essential information, as well as diet and exercise regimens, symptoms, infusion timelines, side effects, medications, allergies, surgeries/procedures, lab results, insurance information, etc. Here’s what to include:

Personal information. Start by logging all personal information, such as height, weight in pounds and kilograms (divide pounds by 2.2 for kilograms), address, home and cell phones, occupation and travel history.

In case patients underestimate the importance of tracking their treatments, Lawson says she’s seen all kinds of mistakes occur with poor records or in situations where records don’t exist.

Symptoms. Any PIDD-related symptoms, such as infections, response or lack of response to antibiotics, joint pain, change in bowel habits and increased fatigue, should be logged, including the type of symptom, when it occurred, how long it lasted and what was done, if anything.

Medication. List the names of all medications with the dose and frequency (prescribed doses for medications can



be found at www.accessdata.fda.gov/Scripts/cder/DrugsatFDA), and how the medications are taken (i.e., subcutaneously, intravenously, orally). Note why the medication is being taken, and list whether the dosage differs from what is normally prescribed. The brand name as well as the generic name should be included, if applicable. Also, make a note about whether the medications cause interactions when taken with other medications. And, don't forget supplements; they are drugs, too.

Allergies. If allergies to medicines exist, the type of reaction (e.g., rash, breathing difficulties) should be recorded, as well as how quickly the allergy developed after taking the medication. List the name of the medication causing the allergy and any similar medicines that may cause the same kind of reaction. (For instance, if a patient is allergic to Ceclor, are they allergic to all cephalosporins?) Also list whether the reaction resolves on its own or whether medical intervention is required and what type. Is the reaction serious enough to require the patient to carry an EpiPen? If so, note whether any type of medical alert identification is worn.

Surgeries/procedures. If hospitalizations have occurred, list when and why. List the types of surgeries and procedures that have been undergone, as well as the dates they occurred. In addition, all immunization dates should

be logged, and if unable to receive immunizations, indicate which ones and why.

Lab results. Lab results should be kept side by side to show trends (this is especially important because what is considered the normal range may not be normal for the patient). Also list the names of the doctors and their contact information (including office and fax numbers and email addresses), and their lab diagnoses.

IG treatment. Last, but certainly not least, is a thorough list of all IG infusion treatments. This is important so that doctors can better assess whether treatment is working and whether the dosage is correct. In addition, these records will help justify continued therapy and help to decrease the expense of repeat and unnecessary testing.

What should be tracked during treatment? The date of the treatment; the product, lot number and dose (usually in grams); rate of infusion (usually in milligrams per hour) and infusion time; infusion site (rotating the placement of the IV keeps veins as healthy as possible); side effects and/or reactions; interval history with intercurrent infections; other medications given; and days of school/work missed.

Insurance. Insurance information should include the name of the company, the identification and group numbers, and the name of the case manager (if there is one), as well as their contact information. If possible, keep a copy of the insurance card with the records.



Choosing a Tracking Method

There is no reason to start from scratch when creating health records. Many existing logs, both in paper and electronic form, are available. Here is just a sampling of what patients can choose from (many other record keeping products also are available):

- NuFACTOR Health Diary. Patients can track symptoms side by side with their infusions so their doctors can quickly see the response to treatment and make any needed adjustments. This diary is great for people who like to be short and sweet, and it charts an entire month on one sheet, making it simple to spot trends in symptoms and how they relate to infusions. NuFACTOR also offers a paper infusion log and an emergency medical card containing information needed in an emergency on www.nufactor.com or by calling (800) 323-6823.
- IG manufacturers' infusion logs. Most manufacturers

of IG provide some form of infusion logs to patients. For instance, Baxter offers patients a complimentary Wellness Kit 2010, which includes both the Wellness Tracker and Wellness Organizer. The kit was designed by primary immunodeficiency patients and caregivers to help patients get organized, track infusions and communicate with their treatment team. It can be obtained at www.immunedisease.com/patients-and-families/help-and-support/baxter-resources/wellness-kit.html. Patients should check with their product's manufacturer to see what kind of logs they provide.

- **HealthHuman.** This in-depth online solution (available at www.healthhuman.com) allows patients to track and analyze all areas of health, from medical history and records to diet, exercise, lifestyle and more. Membership to the site is free, although upgrades are offered for more extensive record keeping.

Patients Setting an Example

With the right tools, patients can easily maintain their own health records, and we found that many do. *IG Living* conducted a poll on its Facebook page (which can be accessed at www.IGLiving.com) to assess whether, where, when and how patients keep their records. While responses varied, here's a sampling of what we heard from the respondents who do keep records:

"I keep a binder with all of my son's blood-work results, vitals, discussions with the doctor on treatment days, as well as the identification information on all bottles of IVIG," says Nicole Bird Kofoed. "When we go to the pediatrician or other specialists, everything they ask questions about is right there in my binder. It is not only helpful, but comforting as a parent to know that all that information is at my fingertips if it is ever needed."

"I have a list of all my medications, doses, etc., in my computer, [have] shrunk it down to business card size, laminated it and keep it in my wallet with doctors' names and phone numbers," explains Lisa Wooding. "I have labs every week [and] one of my doctors suggested I make a spreadsheet so when I see my immune deficiency doctor, who I only see twice a year, or get sent to a new doctor, they can look at [it] ... instead of flipping through the multiple pages of labs. [I] have also kept track of all my surgeries, dates, doctors, locations, any complications, etc.... When I have to see [a] new doctor or need another surgery, I just take a printout so I don't have to rewrite it in the three blanks they provide. Same with my medication list.... [And,] when I go to the doctor, I will take copies of the latest labs in case they

have not received [them]. It's not a wasted appointment that way."

"When I was on IVIG, the hospital and, then, my at-home nurse kept my infusion logs. Now that I am on subcutaneous IG, I keep it (Vivaglobin supplies one, and you can also get one on the Immune Deficiency Foundation site, if I remember correctly)," says Sheri Hewson Rader. "There, I track the globulin batch numbers, days I received the infusion, what I took before and during, and how I felt afterward. Oh, and where I had the infusion, which helped me find the best spots to have them with the least topical problems! I also write about any colds, infections, fevers or any problems I've been having, and there's a spot for questions for the doctor. I never go to an appointment without the log. And, I now save them to see how I have progressed. I highly recommend taking the few minutes to do this!"

Tracking IG treatments is important so that doctors can better assess whether treatment is working and whether the dosage is correct.

As our poll samples demonstrate, everyone has their own tracking style. Some patients will choose to track a lot of details, while others will choose to log just a few items. The key is for patients to pick their own comfortable level of detail and to be consistent about tracking it.

As Easy as ABC

The bottom line is that patients are their "own best medical professional," says Lawson. "Ask questions, talk to your doctors and infusion nurses, take notes and keep a record of all your care. Be an active part of your own care." It's as easy as ABC: accountability, best practices and choosing the right tools. ■

RONALE TUCKER RHODES, MS, is the editor of *IG Living* magazine, and **KRIS MCFALLS** is the full-time patient advocate for *IG Living* magazine.

Let's Talk!

By Trudie Mitschang

If your life depends on immune globulin, this column is for you! Here, we have an opportunity to network and share our experiences about all of the ramifications of our illnesses, and to learn from one another. If you have a question, comment or experience to share for a future column, email it to us at editor@IGLiving.com.

Davis Sabo and Debbie Cyranski have been married for 12 years. Along the way, they have adopted two children, provided caregiving to elderly parents and managed to stay connected as a couple. They also have created a united front when it comes to managing Debbie's primary immune deficiency disease (PIDD). In this month's column, we talked to both Davis and Debbie about what it's like to be a husband and caregiver, a role Davis has wholeheartedly embraced and one that has made their relationship even stronger.

Trudie: Tell us about Debbie's diagnosis.

Davis: Debbie was diagnosed with PIDD with subclass IgG deficiency after a long journey of misdiagnoses. Despite a history of major respiratory infections, Debbie maintained a healthy lifestyle with exercise and good nutrition. During that time, she was seen by a variety of physicians, including immunologists and allergists. Finally, in 2008, she saw a hematologist who recommended monthly intravenous immune globulin (IVIG) infusions. One month later, we began monthly visits to the hospital for seven- to eight-hour infusions, and within a short time, Debbie's IgG levels were in a normal range, and she was feeling much better. But, we could see that the infusion process was going to be a long-term commitment and would require a significant time investment.



Davis Sabo and Debbie Cyranski are managing Debbie's PIDD together as a couple.

That's when we started investigating our options and learned about subcutaneous IG (SCIG).

Trudie: How did you discover SCIG?

Davis: We both work in healthcare as occupational therapists, so we had an advantage in terms of knowing what questions to ask and where to look for answers. And, Kris McFalls, *IG Living's* patient advocate, has been a tremendous help! We signed up for a teleconference on subcutaneous infusions and took copious notes, and then brought all of that information back to our hematologist. We told the doctor that we needed to pursue this line of treatment for Debbie's health and overall quality of

life. And, while we led the way with pursuing this line of treatment, our doctor was very supportive. You really do have to become an advocate in your own treatment plan.

Trudie: Was it difficult to transition to SCIG?

Debbie: I was the first PIDD patient in our area to get approved for SCIG, so not only did we have to learn about the infusion process itself, we had to educate ourselves on the billing codes, figure out which distributors carry which products, learn who the area product managers are and incorporate all of those things into our care plan. There was nobody who could give us the protocol for how this worked, and Davis went through that process with me for nine months. We really had to pioneer it.

Trudie: Describe your role in Debbie's care.

Davis: I do whatever I can to support her emotionally and physically to make sure that things go smoothly. I try to be supportive of her success and progress with this life change. I assist her with the start-up of most infusions. I keep track of her shipments and call the pharmacist if we're low on something. This saves her the hassle of that since she has to do the infusions. I also try to take stress away from her life by helping more around the house and with the kids. I tell everyone, "We all need to step up and do what we need to do; mom

works and is dealing with SCIG.” The motto in our house is that everybody does their part.

Trudie: How does Davis help during infusions?

Debbie: My infusions take about two hours once a week, and Davis helps me with everything from setting up the kit on the bathroom sink to monitoring the pump and providing moral support. It’s important to note that we do not let my infusions interrupt our lives; sometimes, I sit at the dinner table with the pump running. The kids are used to it, and it’s just something we all manage as a family.

Trudie: As the caregiver, how do you “refuel” and take care of yourself to avoid burnout?

Davis: I like to exercise and play golf, and get out and do something recreational with my kids. I used to run 5Ks with my son, and as soon as I recover from hernia surgery, I’d like to start doing that again.

Trudie: What advice can you offer other caregivers?

Davis: I think the key thing is if you’re facing this as a couple, communication is really important. You both have to be honest about how you feel. And, as the caregiver, even if you are having a tough day, you have to remember that you still have the easier role. One question I always ask Debbie is, “What else can I do to help?” Also, don’t go it alone. Get connected with some good support groups, and be sure to ask for help when you need it. Family and friends often don’t know what you need unless you tell them.

Trudie: How has having this illness changed your relationship?

Debbie: We had a good marriage



Davis and Debbie have been married for 12 years and have two children, Violet and Matthew.

already, and facing this challenge together has made it even better. We have a tremendous amount of love and respect for each other and we feel so blessed. I’m really proud of us.

Trudie: What do you appreciate most about Davis?

Debbie: Davis is extremely loyal and committed. He voluntarily goes with me to every doctor’s appointment, and he’s as well versed about my disease process as I am. We are totally in this together. The other thing I really appreciate is that I’m completely confident that Davis would make the right decisions for me if I could not make those decisions for myself. He knows where we keep all of our lab tests, he knows exactly what I take and why, and if I was ever in an accident, he’d be able to talk to the medical staff and make sure I received the highest quality care. That’s very reassuring.

Trudie: What have you learned through all of this?

Davis: This has been a challenging medical journey, but it has also been a success story. Debbie has succeeded in getting past the chronic infections and being really sick. The whole experience has reinforced to me how important Debbie is in my life — I’ll do whatever I need to do to make sure she stays healthy in her body and spirit. This illness revealed the love and care we really have for each other. This is the reason we found each other. ■



TRUDIE MITSCHANG is a staff writer for IG Living magazine.

Ask Kris

By Kris McFalls

Have a question? Kris McFalls, IG Living's patient advocate, is eager to find answers. Email them to editor@IGLiving.com. Your confidential information will not be used for any purpose but to communicate with you about your questions.

Reader: Can you explain the term “half-life” and why I have to be off of treatment for so long until new testing can be done?

Dr. Harville: Depending on the individual, the normal half-life of IgG in the blood is approximately 21 to 28 days. This means that if no IgG is infused (e.g., from intravenous immune globulin [IVIG] infusions) and none is made (e.g., a patient with X-linked agammaglobulinemia), then the level in the blood will decrease by approximately 50 percent in three to four weeks, and then again and again every three to four weeks. For instance, if the starting serum level of IgG is 1,000 mg/dL, and no IgG is infused and none is made, then in about a month, the level of IgG in the blood would decrease to about 500 mg/dL. In two months, it would decrease to 250 mg/dL; in three months to 125 mg/dL; and so on. This is one reason why infusions are given every three to four weeks on average — to keep the serum level at a good value and to prevent the individual from experiencing infection or relapse.

Testing patients' ability to make antibodies to specific immunizations is scheduled approximately four to six months after they stop their infusions of IVIG, when their values are low enough not to interfere with pre/post-immunization response testing. This is necessary to ensure that the testing reflects the patient's own immune responsiveness, and is not due to the passive immunity being provided by the IgG infusions.

Carolyn: When I first met with my doctor to discuss treatment for multifocal motor neuropathy (MMN), he said that if I started intravenous immune globulin (IVIG), I could never stop. He explained that two of his patients stopped IVIG infusions when they regained function, then lost that function and went back on IVIG, but the results were never the same. So, he said IVIG works well as long as it is received regularly, but treating symptoms as they occur is not a good idea.

Kris: To be honest, this is not something I have heard of before. Given how tough reimbursement can be and the delays it can cause, I can only imagine the worries it would cause you and others in your situation. I asked Dr. Todd Levine to address your concerns.

Dr. Todd Levine: Most people with MMN require some lifelong type of immunomodulatory therapy. IVIG is probably the safest long-term solution. If it works well, it will need to be continued. However, patients can often slowly lower the dose of the medication or even spread out the infusions. But, this needs to be done very slowly and while working closely with the neurologist.

Reader: My infusion nurse insists on turning up the rate of my infusion, even though my doctor set a limit on how fast the infusion can go. As a result, I had a reaction. What should I do?

Kris: If your physician wrote the prescription for a certain rate and the nurse does not follow the prescription,

you need to report that to both your doctor and the hospital administration. In talking with a pharmacist, I was told: “While I cannot cite a specific regulation, as there are federal, state, Medicare and Medicaid guidelines, a statement like this from a physician is the same as a prescription, and no one, not a pharmacist or a nurse, can supersede that order or prescription. The nurse clearly overstepped her legal authority and could easily be cited by the State Board of Nursing, resulting in a verbal warning or a temporary license suspension. An instance such as this would be comparable to a physician writing a prescription for Lipitor 20 mg daily and the pharmacist saying, ‘Oh, you only need 10 mg, so I am going to fill it for that.’ Physician orders or prescriptions cannot be changed by anyone without a physician's approval.”

Result: This patient did report the problem to her doctor and her hospital administrator. In return, she got a phone call from the hospital administrator assuring her the nurse would follow the prescription as it is written. ■



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

Terry Harville, MD, PhD, is medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences.

Dr. Todd Levine is director of the Department of Neurophysiology at Good Samaritan Hospital, Phoenix, Ariz.

Circling the Drain

By Ever Feckske

SINCE BEING DIAGNOSED five years ago with common variable immune deficiency (CVID), I had never experienced the stereotypical symptoms of the disease. I never got sick when I was around sick people. I never had a life-threatening infection, and I had never been hospitalized because of an infection. Yet, I'd heard about the scariest situations with bacterial meningitis and pneumonia. So, it made me wonder why I was so lucky. Why wasn't I in the club?! Was I above all this? Was my body actually stronger than I realized? I thought that perhaps I was the exception — some kind of mutant of primary immune deficiency disease (PIDD) patients.

Well, I thought wrong! One recent morning, I woke up with excruciating pains in my stomach. I ran to the bathroom and couldn't decide what to do first: sit down or put my head in the toilet. Both ends had an uncontrollable mind of their own. I kept thinking, "Oh, it will pass; I have things to do today." But it didn't pass. In a matter of two hours, I had been to the bathroom 20 times and all that was coming out of both ends was bright red blood. I was freaking out. I needed to get to a doctor.

My fiancé wheeled me into urgent care as my mom parked the car. I was hiding under a hooded sweatshirt dry-heaving into a kitchen pot on my lap. Let's just say that I was making a really gross scene. My mind was whirling, I couldn't focus on anything but the pain, and I just wanted help! I made it into the triage holding area

and somehow made it onto a bed. The nurse began taking my vital signs, and while I heard the blood pressure machine, I couldn't feel it tightening on my arm. I wanted to jump out of my skin. I was begging the nurse to do something, anything, to help me. I was yelling for the doctor, all while running to the bathroom and trying not to fall over. When the doctor walked in, his face looked panicked when the nurse told him that my blood pressure was 60 over 30. "We have to get her out of here," he said. "We have nothing to help her — no medication, no blood." That was when my fiancé's face turned white, and my mom began rubbing my legs in hopes that I would calm down. But, in my heart, I felt I was dying.

Before I knew it, there were 10 big tall men with dirty pants standing around my bed. Why I remember their dirty pants, I don't know. I guess most firemen wear dirty yellow pants. It seemed like they were playing a game of telephone; the doctor told one what was going on, then that one told another one and he told the next. In a matter of minutes, I had an IV in my arm, and I was being wheeled outside to an ambulance — sirens and all!

I spent 12 hours at the nearest hospital emergency room being stabilized, scanned, medicated and tested before I was transferred again, by ambulance, to another hospital where I spent the next three days. Between the liquid diet, vampires waking me up in the night to suck

my blood (ha-ha) and the endless tests and procedures, I was ready to be better and go home.

The most ridiculous part of all of this was the overall diagnosis: I had the stomach flu! And because the vomiting was irritating my esophagus, it began to bleed. I was bleeding from the other end because of a hemorrhoid! Ahh, so embarrassing!

But I did learn something from this awful situation. When feeling something out of the ordinary, don't wait and think it will just go away. CVID makes my body much more sensitive to even something as common as the stomach flu. For a couple of days, I was circling the drain. But, thankfully, I am here and healthy-ish. Not to mention that I have a newfound appreciation for the complications of PIDD and how the disease needs to be handled.

I also learned that I find strength in my peers. And, I applaud everyone with this disease for having such strength, because I now know that being in the hospital with all the uncertainty is unnerving.

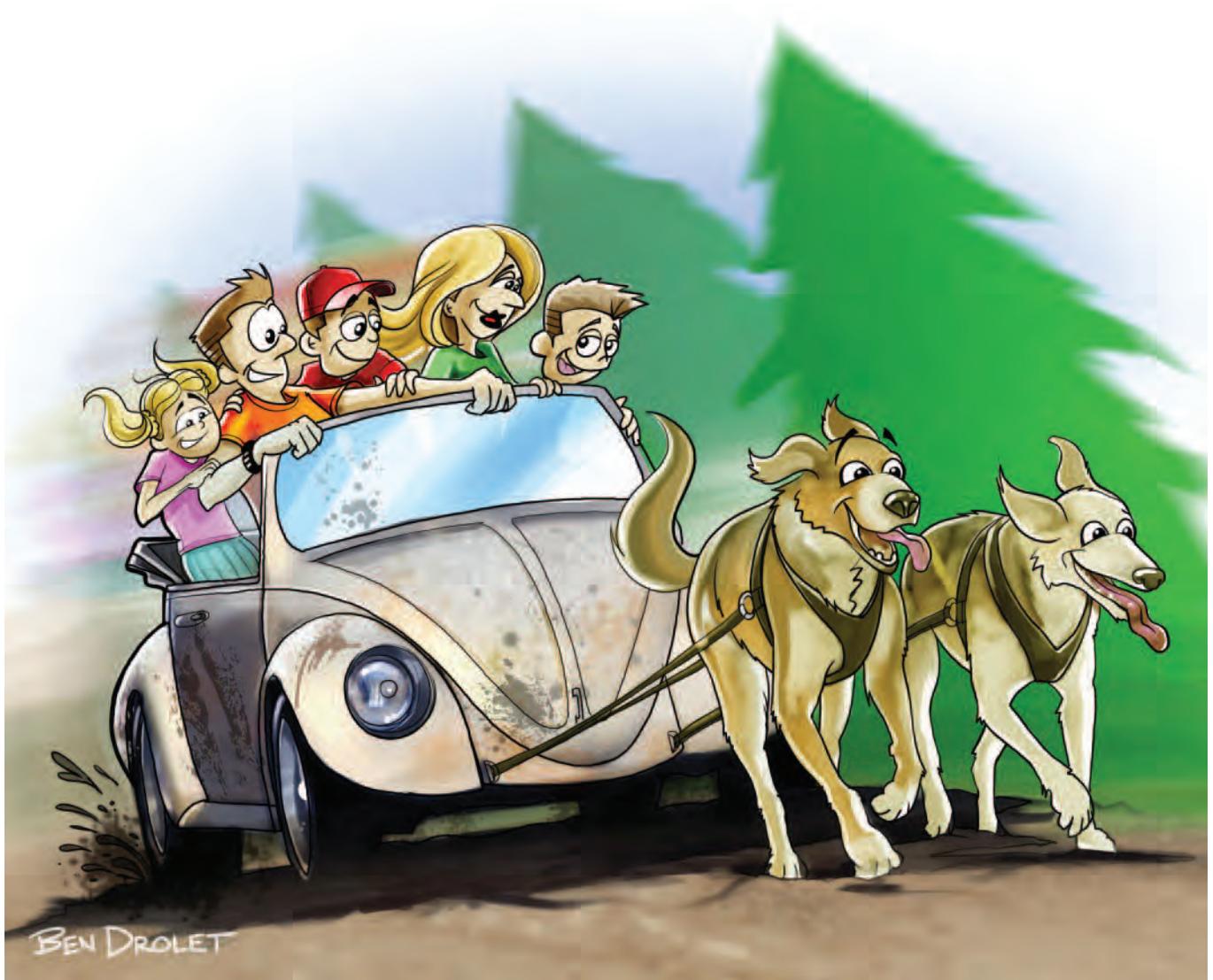
P.S.: I would like a formal induction into the club! ■



EVER FECKSKE was diagnosed with CVID and interstitial lung disease in 2004.

She is a fashion design student, loves spending time with her fiancé, family and bulldog, Dunkin, and can't get enough of writing, cake decorating and anything that sparkles!

Name That Dog!



By Cheryl L. Haggard

YOU CAN'T SWING a dead cat here in Idaho without hitting a yellow Labrador retriever, or so the saying goes to indicate how plentiful the hounds are in our neck of the woods. And naming man's best

friend is just as important as our time-honored rough-and-ready lifestyle. Four-legged Tanks, Bucks and Rexes live and retrieve just about anything you can shoot out of the air or throw into the creek

(pronounced "crick"). One rarely hears, "Fetch, Fifi, fetch!" in these parts. That's just not right!

Our family's Norman Rockwell moment happens 'round 3:30 each weekday afternoon when our own

black Lab, Jax, sits patiently on the porch, leash in mouth, waiting for the kids to come home from school. We can't picture Fifi doing that either. She'd get her perfect, perky poodle "do" all doo-doodie.

Canine companionship is especially important in our primary immune deficient (PIDD) family, as I know is true in many other families touched by chronic illness. Infusion day doesn't seem as scary for our PIDD kids, Caleb and Molly, since our black, hairy and slobbery friend joined in our craziness. For our special PIDD pooch, it was essential that we find the right name. So, when Jax came to us as "Junior," we knew his name had to change. Saying "Junior" is tongue torture, as it feels like you're pulling an elephant through mud with your pinkie toe. But, Jax fit! His name is one syllable, simple to say, especially when our PIDD kids have an IV needle coming their way.

Poochie passion runs deep in our family, especially for Caleb. Second grade is where he was introduced to the Iditarod, the re-enactment of the "serum run" from Anchorage to Nome, Alaska, when a diphtheria epidemic broke out in 1925. The brutal "race" pitted brave dogs, mushers and sleds against nature's frozen fury so lives could be saved. I doubt the heroic hounds of the Iditarod were named Daisy, Droopy or, ahem, Junior.

Two lucky summers ago, my dad — who valiantly fought common variable immune disease (CVID) — and my mom blessed our family with a 13-day vacation of a lifetime in Alaska. Of course, we could not come home until we had gotten a small taste of the thrill of the Iditarod. So, one sloppy-wet summer day in

Juneau, we boarded the hulled-out chassis of a Volkswagen Beetle. This "dry" training vehicle mimicked a wintry sled, giving tourists a memorable one-time ride of a lifetime. The dogs were mangy mutts, not the glorified Husky breed we expected. We didn't care; the dogs' piercing barks and yowls told us they were ready to run no matter where they came from. There are no words to express the experience I had being rushed through pine trees with dogs for an engine. There also is no way I can express how it felt seeing my PIDD kid living his dream.

Drying off as best possible after our ride, we conversed with our musher, Ted, asking him many questions to keep him and his satisfied dog-brood around. After "What do they eat?" and "Do they like being all wet and cold?" we made our way to the puppy nursery. Somehow, puppy dander has a way of melting your shivering body. As we passed one pup around and snuggled with another, Caleb piped up: "How do you name so many dogs? Don'tcha run out of things to call them?"

"That's a great question!" Ted responded. "Our dogs are all on teams, and we give that team a theme. For example, our team has been named after spices." Patting the side of our lead dog, Ted exclaimed, "This is Cin, for Cinnamon. And this guy right back there is Cin's brother Ty, for Thyme."

To prolong hanging out with the puppies, we asked the other mushers what they named their teams. One told us cereals like Kellogg and Shredder for shredded wheat. There wasn't a froufrou name in the bunch. We were having a great

time with the name game, until the drivers turned to us for ideas.

"What would you name your team, Caleb?" Ted asked.

Cogs were churning in my son's mind.

"I'd name my team after luncheon meats!" a thin man from another group interrupted. He held his puppy over his head and exclaimed, "This one's name is 'Header,' get it? For head cheese?"

Thankfully, Caleb "came to" with his answer: "Ya' know, Iditarod dogs are the bravest dogs I know. They saved lives! Lots of them." The beginning of Caleb's answer was an unintended retort for the "meaty man's" sarcasm. "My team will also fight disease like the first team did. So I'll name my team for germs I wanna get rid of like Crypto (cryptosporidium) and, uh, Strep (streptococcus)."

It's been two years since that trip, and a year ago in April, my dad, Doug Harlan, lost his battle with complications of CVID. Watching my kids fight chronic illness, and recently handed my own diagnosis, I wonder what is stronger: the disease itself or the person fighting it? Mark, my husband, often tells the kids, "It's not the size of the dog in the fight, it's the size of the fight in the dog."

Me? Well, all I know is you better not call me "Fifi." ■



CHERYL L. HAGGARD is a stay-at-home mom and has three children, two of whom have CVID. She and her husband, Mark, also operate Under the Hood Ministries at www.underthehoodministries.org.

Transitions

By Ronale Tucker Rhodes, MS

Immune globulin (IG) is a miraculous therapy, and no one knows this better than patients who receive it for an immune-mediated disease. Indeed, without IG, these individuals would fail to make the transition from living in a constant state of illness, struggling to survive, to a healthy, happy lifestyle. That is what this column is about — the unique and sometimes extraordinary stories of people of all ages whose lives have positively transitioned with the help of IG. We want to hear your stories! Email us at editor@igliving.com.

From Private Insurance to Medicare

“MY INSURANCE ISSUES were difficult for so many years!” exclaims Nancy Hoffman who was diagnosed with common variable immune deficiency (CVID), thrombocytopenic purpura (low platelets) and neutropenia (low white cells) in 1995. Like Nancy, most individuals diagnosed with immune-mediated diseases are all too familiar with the hassles of insurance — from therapy choice to reimbursement issues and rates that threaten their personal and financial lifestyles. But, Nancy’s story, in particular, may help to shed some light on what others in the immune globulin (IG) community may encounter when transitioning from private insurance to Medicare.

From IVIG to SCIG

Nancy was very ill for eight years before being diagnosed. After her diagnosis, she found out about intravenous immune globulin (IVIG), and she was thrilled with its results. According to Nancy, her IVIG infusions came with “many side effects, but you learn to deal with them, as it’s just part of what happens when you get that wonderful stuff (gamma) inside of you!” After years of being tired all of the time and unable to do much, IVIG gave her a new life.

However, after eight years of IVIG, Nancy’s veins stopped cooperating. “To have eight to nine sticks each

treatment time was not unusual,” she explains. “My veins would blow or collapse or roll too much. I guess they just didn’t want to be stuck anymore.” Plus, her reactions were very uncomfortable, ranging from headaches to backaches, chills, tiredness and lots of bruising. So, she sought information about subcutaneous IG (SCIG). “I wanted the ability to be in control of my care, and to be able to work it around my schedule,” says Nancy.

Because her doctor of eight years would not help her with the switch to SCIG, she found a new doctor who would. In addition, she met another SCIG patient who became her mentor and friend, and who helped ease her concerns about self-infusing. “I was concerned about actually sticking myself, so I thought about it a long time,” says Nancy. But, with her friend’s help, the homecare company she uses (NuFACTOR) and her nurse, Kim, “I started my new life again!”

And a new life it was for Nancy. According to her, she had no ups and downs, no highs and lows and no side effects other than some minor redness around the needle sites. And, she was able to do more than ever. Being able to bring her infusion supplies with her wherever she went allowed her to spend a month in Africa in 2007 and to trav-

el to Canada in 2009 to find her mother’s birthplace. “Something I probably would not have done on IVIG,” explains Nancy.

The SCIG Snag

And, while the switch to SCIG didn’t affect her insurance coverage, it was at this time that she was repeatedly denied coverage and finally was accepted on a state-funded program of high-risk insurance, which cost her family \$1,500 a month. While Nancy says she feels it was good insurance coverage, she also says, “How we did this for three years, I don’t know — only by the



Nancy traveled in 2007 to the Hyumbani Children’s Home in Kenya, Africa, for HIV children where she worked for a week.

grace of God, believe me!" The high payments were a drain on her marriage and life. And, despite those payments, the plan still did not pay for everything, so they were forced to come up with extra money to pay for the balance, which typically was for the remainder of the IG.

Then, last year, Nancy turned 65. She was eligible for Medicare, and she thought her insurance issues were over. "My transition to Medicare was relatively easy," says Nancy. "Because I had chosen to take my Social Security at age 62, I was already in the system. So when I turned 65, I just received my Medicare card in the mail!" Then, all she had to do was to decide which supplemental insurance to go with, and she decided upon AARP. "My homecare company (NuFACTOR) took care of setting up everything as far as payment, and it seemed to flow quite easily," adds Nancy. "I feel blessed, actually, that I pay an affordable amount each month and am well-covered."

Unfortunately, while Nancy's insurance issues were over in terms of cost, Medicare actually proved to pose a problem for her with her medication. Medicare will cover only the Food and Drug Administration (FDA)-indicated IG product, which was not the product she was infusing and was doing so well with. Unhappily, she was forced to switch to the FDA-indicated product, which causes her bad reactions, including large red, hard and hot lumps around the infusion sites, aching in her legs, chills and tiredness. "After I do my [infusion], I am very uncomfortable, so I put aloe gel on the swollen sites and just try to work through it," explains Nancy. "It usually lasts overnight and is better the next day — only to start all over again, though, the following



Nancy and husband Moe took their first safari in 2007 to Sumburu in Kenya, Africa.

week." Nancy also has experienced more illness with the new product than ever before. "I have had to take many rounds of antibiotics for bronchitis and sinus infections and was hospitalized this past February with severe lung infection and fever — very close to pneumonia," says Nancy. "So, I don't think this product has been as good a protector for me."

Yet accessing the product that worked better seemed to be just out of her reach. Despite contacting the manufacturer of the product that did keep her healthy, as well as having her immunologist write a letter stating he believed she should go back to infusing with her old product, Medicare refused to cover it. Instead, Medicare's determination was that the only way her original product would be covered would be for her to infuse intravenously, rather than subcutaneously. But, that is not an option for her because of the problems she has with her veins.

"What I've had to do mostly is try to accept and have an attitude of gratitude for what is good for me," says Nancy. "And, because Medicare has paid regularly, as has AARP, I decided it was best to 'suck it up' and not rock the boat. It's not the

best, but it's where I'm at right now."

A Happy Ending on the Horizon?

Could there be a solution on the horizon for Nancy? It appears so. The product that worked so well for her may soon be approved by the FDA for subcutaneous infusions. In the meantime, Nancy says she believes in our Medicare system. And, she encourages others who are dealing with this same issue or who may soon be getting ready to transition to Medicare to not be afraid. "Be aware, and do your homework!" encourages Nancy. "Talk to others who have enrolled with the program, and talk to the Medicare reps about the coverage. Then, be sure to do the same for the supplemental [insurance]. There are so many options ... and there are lots of different payment amounts and plans, so it's important to find what works best for you!" ■

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

Editor's note: Every patient reacts differently to different IG therapies, and Nancy's reaction may not be typical of another patient's experience.

Education: Home School or Public School?



By Mark T. Haggard

Home school or public school? That is one of the questions that parents of children with primary immune deficiency disease (PIDD) face. Home school and public school both have their merits and strengths, whether your children are immune compromised or not. But for those in the immune-deficient community, a number of issues must be taken into consideration, including health, cost, socialization and others.

Pros and Cons of Home School and Public School

According to Brian D. Ray, PhD, of the National Home Education Research Institute, an estimated two million children are home-schooled in the United States, and that number has grown by 5 percent to 12 percent each year in the past four years. Ray's research suggests that home-schooled children score approximately 20 percent to 25 percent higher on

standardized achievement tests and typically fare "as well or better than their institutional public or private school peers in terms of social, emotional and psychological development." In a survey of 7,000 adults who were home-schooled, 95 percent say they were glad that they were home-schooled, and 92 percent say that home schooling has been advantageous to them.

For parents with immune-deficient

children, home schooling is an attractive alternative to public education. For one, it may be in their best interest to keep their child in an environment free of the billion-or-so germs and pathogens that infest our schools. No matter how many bottles of hand sanitizers are posted throughout the campus, germs find a way into our children's systems. And this, of course, leads to many more days absent from school for immune-compromised children. In addition, in the home-school environment, both the curriculum and the schedule are based more upon choice and less on state mandates, and, obviously, there is a smaller student-teacher ratio than the 30-or-more-to-one in the public schools.

One of the criticisms of home schooling is that children are not socialized as well as they would be in the public school environment. There also is a large expense involved in home schooling, and few teachers are certified to teach specific subjects. On the other hand, the public school system provides more curriculum opportunities, more diversity in social education and a larger selection of extracurricular activities from which to choose. For parents of PIDD kids, though, the most important advantage may be the opportunity to get an eight-hour break from the ongoing battle that they face every day.

A Home School Success

Terri and Chuck Cerda have two immune-compromised daughters. When oldest daughter Molly was 18 months old, she became sick with mycoplasma pneumonia, the result of combined immune deficiency

syndrome (CID) and cystic fibrosis. By age 5, Molly had irreversible lung damage. Molly's sister, Maggie, also was diagnosed with CID. Despite their intravenous immune globulin (IVIG) treatments, exposure to even the slightest cold could turn into pneumonia within 36 hours. "For our daughters," Terri says, "the choice to home school became the only option in order to protect the fragile health of our children."

Despite their sickness, Terri believes

of other children their age. "I am realizing that my gifted children, at the tender ages of 7 and 9, know more than I do. I am content in the notion that we must be doing something right," Terri says. "The mere fact that my daughters are here with me each and every day is a cause for celebration. I am thankful that I am gifted with their presence all day long, each and every day. Their lives are so fragile, and I know how quickly things can change."

For parents with immune-deficient children, home schooling is an attractive alternative to public education.

that her daughters are receiving an incredible education, far superior to what they would receive at an average public school. They can set their own schedule, allowing for the inevitability of an illness or a hospital trip at some time during the year. The Cerdas pay for all of the girls' educational resources, and Terri finds herself playing numerous roles in their lives: mother, nurse, teacher and social director. "I'm learning things I never expected to have to know, like curriculum mapping and planning," she explains. In addition, Terri has taken on a new role as a manager for the National Children's Homebound Education Foundation.

Within the home-school environment, the Cerda girls are thriving. Presently, they are two grades ahead

A Public School Success

Rich and Lori Riggins of Visalia, Calif., have three children: Roxanne, a healthy daughter, and Rhett and Zachary, sons with adenosine deaminase deficiency severe combined immunodeficiency (ADA SCID). At one point in their lives, after years of living in the proverbial — and literal — bubble, watching everything they did, avoiding crowds and carrying their life and death issues on their sleeves, Rich and Lori were determined to allow their sons a well-rounded, enjoyable life. School was a huge consideration. "I love the idea of home schooling," says Lori. "It just wasn't for us."

Obviously, health concerns weigh heavily on parents of PIDD kids; open lines of communication are a must

when placing immune-compromised children into a public school. "We live in a small community and have gotten to know their teachers, administrators and health service personnel," explains Lori. "We found everyone very willing to go the extra mile to keep us informed." Lori became very good friends with every school nurse, and they developed a system where the nurse would call if there was an outbreak of any communicable disease at school. "I was the expert regarding the boys' disease," she adds, "and advocated many, many times, but we always

for children that they might not have otherwise. Lori agrees: "Involvement in school has enriched their lives. Friends, sports, band, Future Farmers of America, teachers — all have written something on their heart that they will carry forever. But I have watched something powerful in them that I haven't seen in some of their friends. I have seen compassion for the outcast, helping someone in trouble or hurting, and simply being a strong support when things have gotten shaky. Their disease, the pain, facing a difficulty most will never face,

Having children who are immune compromised changes the parameters of where we make that investment. Both the public school and home school option have their merits. Rich and Lori chose to give their boys the opportunity to have a "well-rounded, enjoyable life," despite their compromised immune systems. Children with immune deficiencies can survive and thrive in the public schools, as long as teachers and administrators understand the position in which they are being placed. At the very least, your child should have an Individualized Health Plan for the school days they will inevitably miss. In extreme cases, you have the legal right to an Individualized Education Plan, which allows your child specific academic accommodations. Rich and Lori did public education right, and their boys are the better for having done it.

Circumstances forced Terri to home-school her daughters, an education that has been a true blessing for her and her girls. The sacrifice of time and financial resources to home-school is a significant part of their lives, but the results are far beyond what the family expected. The girls are thriving in both their health and their education, and as Terri says, "Every day is a celebration." ■

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

Source

National Homebound Children's Education Foundation, www.my4walls.org

One of the criticisms of homeschooling is that children are not socialized as well as they would be in the public school environment.

had a very good response from all involved in the boys' lives."

This system was not always fool-proof, though. Rhett came down with whooping cough and spent seven days in the hospital with chickenpox. Zack went to the hospital three different times with chickenpox. "They had every respiratory thing that is out there," says Lori. "They missed school with illness and doctor visits, but if we had to do it all over again, we would."

Supporters of public school say that school creates opportunities

have produced young men who are deeper than the average young men their age."

Rhett graduated from high school last year, and Zach is now a junior, "and at the close of this side of education, we can honestly say we are happy with our decision. We are very content with their school experience. It wasn't perfect, but it was a good one — a very good one."

The Best Option?

Our children's education is the greatest investment we will make.

Treating Chronic Sinusitis and Inflammation

By Kris McFalls

CHRONIC SINUSITIS AND inflammation are probably the most common complaints among patients with a primary immune deficiency (PIDD). Beyond the usual advice to eat right, sleep tight and drink lots of non-caffeinated beverages, some regimens can help to keep infections down and make breathing clearer. But, before starting any medical regimen, patients should discuss treatment options with their physicians.

Prevention Is Foremost

The best way to deal with sinusitis and inflammation is to keep it from happening in the first place. To do this, many PIDD patients are advised to use a saline nasal irrigation system to help remove daily irritants and rinse away excessive mucous buildup. While the process of irrigating looks as disgusting as it sounds, patients who do it, swear by it. Saline can be made by combining pre-mixed packets and distilled water. Pre-mixed packets are pH balanced, and if mixed properly, patients should not experience stinging. Care should be taken to ensure only distilled water is used to make the saline rinse. And, equipment should be stored in a position that allows for residual water to drain rather than pool. In addition, equipment needs to be kept clean. Instructions on proper use and cleaning of equipment can be found on the pre-mixed package insert.

Keeping inflammation down in order to breathe freely is just as important as keeping the nasal passageways clean. Patients are frequently prescribed steroidal nasal sprays to use in combination with nasal irrigation. When using both products, it is important to first use the nasal spray, followed by nasal irrigation. Steroidal nasal sprays are generally approved for nasal allergies. Yet, because PIDD patients have symptoms of swelling and mucous buildup similar to allergy patients, it is quite common for PIDD patients to use the same products. However, maximum benefit may not be achieved for up to two weeks after

starting treatment. And, for maximal relief, the product needs to be used exactly as directed.

Treating Infection

No matter how compliant patients are with preventive treatments, bacterial infections can still set in. And, chronic, recurring bacterial sinusitis can be particularly frustrating to treat with oral antibiotics. If the sinuses are the main area of concern, some physicians may choose to treat patients with a nebulized antibiotic. Nebulizers are commonly used for asthma. However, the same principle of using a fine mist to distribute medication via inhalation is a possible alternative to systemic medication for bacterial sinusitis. Inhaled antibiotics and sinus nebulizers used to dispense the medication are available only via prescription. And, both should be covered by insurance, with the nebulizer being covered under the durable medical benefit and the antibiotic being covered under the prescription benefit. Of course, as with any medication, it is best for patients to request a predetermination of benefits to understand their financial responsibilities before agreeing to treatment.

Persistence Leads to Breathing Freely

No matter what regimen patients' doctors prescribe, the key to success is sticking to it and following up with the doctor as quickly as possible when problems occur. Sinus inflammation and infections are very uncomfortable, but with a little persistence, many patients can breathe freely. ■

KRIS MCFALLS is the full-time patient advocate for IG Living magazine.



Directory of Sinus Products

Nasonex

Nasonex is a prescription nasal allergy spray approved for the treatment of seasonal and perennial nasal allergy symptoms in adults and children 2 years of age and older. Taken just once a day, Nasonex helps relieve nasal allergy symptoms, including itchy nose, runny nose, sneezing and congestion. Improvement can occur within 11 hours of initial treatment (based on studies done in a park during the pollen season and in a controlled pollen exposure room). The maximum benefit of Nasonex is usually achieved within one to two weeks. The product is non-drowsy, won't keep individuals awake at night, scent-free and alcohol-free.

www.nasonex.com/nasx/application?gclid=CJrt6dDLsaACFRQWawodhCDwTA

NeilMed

Sinus Rinse nasal wash is a large-volume low-positive pressure nasal wash designed to irrigate the nose to clean away mucous and make medication more effective. It can be used by individuals of all ages, and is available in isotonic, pediatric and hypertonic concentrations. The adult kit contains one custom 8-ounce nasal irrigator and 50 regular pre-mixed packets of pH balanced sodium chloride and sodium bicarbonate mixture (USP grade, natural ingredients, isotonic, preservative and iodine free). The pediatric kit contains one custom 4-ounce nasal irrigator, as well as 50 regular pre-mixed packages. Both come with an educational brochure, and a starter kit for both also is available.

www.neilmed.com/usa/index.php

Simply Saline

Simply Saline nasal and sinus irrigation is designed to help clear congestion, dust and debris while improving the ability to smell and gain clearer breathing. It is made of purified water and 3 percent sodium chloride. The product comes in six styles: Sterile Saline Nasal Mist, Baby Simply Saline, Nasal Moist Gel, Nasal Mist Cold Formula, Nasal Mist Cold Formula with Menthol and Saline Nasal Wash.

www.blairex.com/SimplySalineReg.php

SinusDynamics

The SinusDynamics nebulizer is designed to produce a mist with ultra-consistent particle size for maximum distribution of medication in the nasal cavity and sinuses. It is lightweight (weighs less than a pound), has no tubing (resulting in no trapped bacteria), is completely silent, has no dead volume (100 percent of the medication is nebulized) and comes with an optional battery pack for portability.

www.sinusdynamics.com

SinuPulse Elite

The SinuPulse Elite Advanced Sinus Irrigation System cleanses and clears sinuses for the maintenance of clear and healthy sinuses. Developed and engineered in Switzerland, it features a pulsating irrigation system that has a patented dual spray and rinse operation, and it has been designed to be clog-free and leak-resistant. Features include an electronic touch switch and LED display, a dual spray option (gentle pulsating mist spray or pulsating cleansing rinse) and IntelliPulse technology for accurate pulse rate.

www.sinupulse.com/sinus-irrigation-system.html

Veramyst

Veramyst treats allergy symptoms with a gentle fine mist that is scent-free. For people ages 12 years and older, the usual starting dosage is two sprays in each nostril once a day. Once individuals feel better, their healthcare provider may tell them that one spray in each nostril once a day may be enough. For children ages 2 to 11 years, the usual starting dosage is one spray in each nostril once a day, although healthcare providers may tell children to take two sprays in each nostril once a day. An adult should help a young child use this medicine.

www.veramyst.com/using_veramyst/how_to_use_veramyst_nasal_spray.htm

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

General Resources

Other Organization Websites

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
- Alliance for Plasma Therapies (fair access to plasma therapies): www.plasmaalliance.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
- Cleveland Clinic: www.clevelandclinic.org/health
- eMedicine from WebMD: emedicine.medscape.com
- FamilyDoctor.org: www.familydoctor.org
- Johns Hopkins Medicine: www.hopkinsmedicine.org
- KeepKidsHealthy.com (pediatrician's guide to children health and safety): www.keepkidshealthy.com
- Kids Health (medical and emotional impact of caring for an ill child): www.kidshealth.org/parent/system/ill/seriously_ill.html
- Mayo Clinic: www.mayoclinic.com
- National Committee for Quality Assurance (detailed report cards on health plans, clinical performance, member satisfaction and access to care): www.ncqa.org
- National Institute of Neurological Disorders and Stroke (NINDS): www.ninds.nih.gov/disorders/disorder_index.htm
- National Institutes of Health: www.niams.nih.gov/hi/topics/pemphigus/pemphigus.htm
- 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



The nonprofit Patient Services Incorporated, www.needpsi.org, specializes in health insurance premium, pharmacy co-payment and co-payment waiver assistance for people with chronic illnesses. (800) 366-7741

- WebMD (medical reference): www.webmd.com

IG Manufacturer Websites

- Baxter: www.baxter.com
- CSL Behring: www.cslbehring.com
- Grifols: www.grifolsusa.com
- Octapharma: www.octapharma.com
- Talecris: www.talecris.com

Disease-State Resources

Ataxia Telangiectasia (A-T)

Websites

- A-T Children's Project: www.atcp.org

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Websites

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

Online Peer Support

- Barbara's CIDP/GBS Site: www.geocities.com/HotSprings/Falls/3420

Evans Syndrome

Online Peer Support

- Evans Syndrome Research and Support Group: www.evanssyndrome.net

Guillain-Barré Syndrome (GBS)

Websites

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

Online Peer Support

- GBS & CIDP Discussion Forum – UK Bulletin Board (For Ireland and England): www.gbs.org.uk/cgi-bin/ikonboard3/ikonboard.cgi
- GBS/CIDP Foundation International Discussion Forums: www.gbs-cidp.org/forums
- GBS Support Group and Chat Room – UK: www.jsmarcussen.com/gbs/uk/chat.htm

Idiopathic Thrombocytopenic Purpura (ITP)

Websites

- ITP Support Association – UK: www.itpsupport.org.uk
- National Heart, Lung and Blood Institute: www.nhlbi.nih.gov/health/dci/Diseases/Itp/ITP_Whats1.html
- Platelet Disorder Support Association: www.pdsa.org

Kawasaki Disease

Websites

- American Heart Association (how the disease affects the heart): www.americanheart.org/presenter.jhtml?identifier=4634

- Kawasaki Disease Foundation: www.kdfoundation.org
- KidsHealth: <http://kidshealth.org/parent/medical/heart/kawasaki.html>

Mitochondrial Disease

Websites

- United Mitochondrial Disease Foundation: www.umdf.org

Multifocal Motor Neuropathy (MMN)

Websites

- The Neuromuscular Center at Washington University: www.neuro.wustl.edu/neuromuscular
- 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
- Multiple Sclerosis Foundation: www.msfacts.org
- 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

- Autoimmune Information Network Inc.: www.aininc.org

Myositis

Websites



The mission of The Myositis Association, www.myositis.org, is to find a cure for inflammatory and other related myopathies, while serving those affected by these diseases. (703) 299-4850

- International Myositis Assessment and Clinical Studies Group: <https://dir-apps.niehs.nih.gov/imacs/index.cfm?action=home.main>



The Cure JM Foundation www.curejm.com (760) 487-1079

Online Peer Support

- Juvenile Myositis Family Support Network: www.curejm.com/family_support/index.htm
- Myositis Association Community Forum: www.myositis.org
- Myositis Support Group: www.myositissupportgroup.org
- Myositis Support Group – UK: www.myositis.org.uk

Pemphigus and Pemphigoid

Websites

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

Peripheral Neuropathy (PN)

Websites



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

- Neuropathy Action Foundation: www.neuropathyaction.org

Online Peer Support

- Calgary Neuropathy Support Group: www.calgarypnrs.org

Primary Immune Deficiency Disease (PID)

Websites



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



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

- The National Institute of Child Health and Human Development (NICHD), www.nichd.nih.gov, is part of the National Institutes of Health. Go to the "Health Information and Media" tab on the website and do a search under
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organization for Primary Immunodeficiencies (IPOPI): www.ipopi.org
- Michigan Immunodeficiency Foundation: www.midf.org

- National Institute of Child Health and Human Development (NICHD) (Click on "Health Information and Media" tab and search for "primary immunodeficiency": www.nichd.nih.gov)
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.rainbowbabies.org/immunology
- Team Hope (for families and patients in New England): www.teamhope.info

Online Peer Support

- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: my.primaryimmune.org/forum
- IDF Friends: www.idffriends.org
- Jeffrey Modell Foundation Message Board: www.info4pi.org
- Rhode Island peer group: <http://health.groups.yahoo.com/group/RhodelslandPIDD>

Scleroderma

Websites

Scleroderma Center: <http://scleroderma.jhmi.edu>

- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org

Online Peer Support

- CureZone.com: curezone.com/forums/f.asp?f=404
- 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
- Autoimmune Information Network Inc.: www.aininc.org
- Living with Stiff Person Syndrome (personal account): www.livingwithsps.com

Other Resources

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.
- Continuation of Health Coverage — Consolidated Omnibus Budget Reconciliation Act (COBRA): www.dol.gov/dol/topic/health-plans/cobra.htm
- DisabilityInfo.gov: www.disabilityinfo.gov
U.S. Federal government's disability-related information and resources.
- Individuals with Disabilities Education Improvement Act of 2004: <http://idea.ed.gov/explore/home>
- National Disabilities Rights Network: www.ndrn.org
This website offers a search tool to find resources in your state to assist with school rights and advocacy.
- Social Security: www.ssa.gov/disability

- U.S. Department of Education Website: www.ed.gov
This federal government website offers a parents section titled "My Child's Special Needs."
- U.S. Department of Health and Human Services, Office of Civil Rights: www.hhs.gov/ocr/office/news/2008/discrimdisab.html
Spells out your rights under Section 504 of the Rehabilitation Act.

Medical Research Studies

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

Food Allergies

- Allergic Disorders: Promoting Best Practice: www.aaaai.org
- American Partnership for Eosinophilic Disorders: www.apfed.org
- Food Allergy and Anaphylaxis Network: www.foodallergy.org
- National Institutes of Health, National Institute of Allergy and Infectious Diseases (2004). Food Allergy: An Overview (NIH Publication No. 04-5518): www.niaid.nih.gov/publications/pdf/foodallergy.pdf
- Sicherer, S.H. (2006). "The Complete Peanut Allergy Handbook: Understanding and Managing Your Child's Food Allergies," Johns Hopkins Press.
- 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 Carimune NF: www.carimune.com
- IVIG Flebogamma: www.grifolsusa.com/pdfs/flebo_14Jun05.pdf
- IVIG Gammagard Liquid: www.gammagardliquid.com
- IVIG Gammagard S/D: www.immunedisease.com
- IVIG Gamunex: www.gamunex.com
- IVIG Octagam: www.octapharma.com
- IVIG Privigen: www.privigen.com
- SCIG (subcutaneous immune globulin) Vivaglobin: www.vivaglobin.com

Pump and Infusion Sets Websites

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

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

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

1 INDICATIONS AND USAGE

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

4 CONTRAINDICATIONS

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

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

Hizentra is contraindicated in 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 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.¹ If renal function deteriorates, consider discontinuing Hizentra. For patients judged to be at risk of developing renal dysfunction because of pre-existing renal insufficiency or predisposition to acute renal failure (such as those with diabetes mellitus or hypovolemia, those who are overweight or use concomitant nephrotoxic medicinal products, or those who are over 65 years of age), administer Hizentra at the minimum rate practicable.

Thrombotic Events

Thrombotic events may occur with use of human immune globulin products.²⁻⁴ Patients at increased risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and/or known or suspected hyperviscosity. Because of the potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Hizentra at the minimum rate practicable.

Aseptic Meningitis Syndrome (AMS)

AMS may occur with use of human immune globulin products.⁵ The syndrome usually begins within several hours to 2 days following IGIV treatment. AMS is characterized by signs and symptoms including 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, with 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 IGIV.

Conduct a thorough neurological examination, including CSF studies, to rule out other causes of meningitis in patients exhibiting signs and symptoms of AMS. Discontinuation

of IGIV treatment has resulted in remission of AMS within several days without sequelae.

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.⁶⁻⁸ Delayed hemolytic anemia can develop subsequent to immune globulin therapy due to enhanced RBC sequestration, and acute hemolysis, consistent with intravascular hemolysis, has been reported.⁹

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

Transfusion-Related Acute Lung Injury (TRALI)

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

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

5.3 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.

5.4 Laboratory Tests

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

6 ADVERSE REACTIONS

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

6.1 Clinical Trials Experience

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

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

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

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

Table 2 summarizes the most frequent adverse events (AEs) (experienced by at least 4 subjects), *irrespective of causality*. Included are all AEs and those considered temporally associated with the Hizentra infusion, i.e., occurring during or within 72 hours after the end of an infusion. Local reactions were the most frequent AEs observed, with injection-site reactions (i.e., swelling, redness, heat, pain, and itching at the site of injection) comprising 98% of local reactions.

Table 2: Incidence of Subjects With Adverse Events (AEs)* (Experienced by 4 or More Subjects) and Rate per Infusion, Irrespective of Causality (ITT Population)

AE (≥4 Subjects)	All AEs*		AEs* Occurring During or Within 72 Hours of Infusion	
	Number (%) of Subjects (n=49)	Number (Rate ¹) of AEs (n=2264 Infusions)	Number (%) of Subjects (n=49)	Number (Rate ¹) of AEs (n=2264 Infusions)
Local reactions [†]	49 (100)	1340 (0.592)	49 (100)	1322 (0.584)

Table 2: (Continued)

AE (≥4 Subjects)	All AEs*		AEs* Occurring During or Within 72 Hours of Infusion	
	Number (%) of Subjects (n=49)	Number (Rate [†]) of AEs (n=2264 Infusions)	Number (%) of Subjects (n=49)	Number (Rate [†]) of AEs (n=2264 Infusions)
Other AEs:				
Headache	13 (26.5)	40 (0.018)	12 (24.5)	32 (0.014)
Cough	8 (16.3)	9 (0.004)	5 (10.2)	6 (0.003)
Diarrhea	7 (14.3)	8 (0.004)	5 (10.2)	6 (0.003)
Fatigue	6 (12.2)	6 (0.003)	4 (8.2)	4 (0.002)
Back pain	5 (10.2)	11 (0.005)	4 (8.2)	5 (0.002)
Nausea	5 (10.2)	5 (0.002)	4 (8.2)	4 (0.002)
Abdominal pain, upper	5 (10.2)	5 (0.002)	3 (6.1)	3 (0.001)
Rash	5 (10.2)	7 (0.003)	2 (4.1)	3 (0.001)
Pain in extremity	4 (8.2)	7 (0.003)	4 (8.2)	6 (0.003)
Migraine	4 (8.2)	5 (0.002)	3 (6.1)	4 (0.002)
Pain	4 (8.2)	5 (0.002)	3 (6.1)	4 (0.002)
Epistaxis	4 (8.2)	6 (0.003)	2 (4.1)	3 (0.001)
Pharyngolaryngeal pain	4 (8.2)	6 (0.003)	2 (4.1)	2 (<0.001)
Arthralgia	4 (8.2)	5 (0.002)	2 (4.1)	3 (0.001)

* Excluding infections.

[†] Rate of AEs per infusion.

‡ Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.

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

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

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

Adverse Reaction (≥2 Subjects)	Number (%) of Subjects (n=49)	Number (Rate*) of Adverse Reactions (n=2264 Infusions)
Local reactions [†]	49 (100)	1338 (0.591)
Other ARs:		
Headache	12 (24.5)	36 (0.016)
Vomiting	3 (6.1)	3 (0.001)
Pain	3 (6.1)	4 (0.002)
Fatigue	3 (6.1)	3 (0.001)
Contusion	2 (4.1)	3 (0.001)
Back pain	2 (4.1)	3 (0.001)
Migraine	2 (4.1)	3 (0.001)
Diarrhea	2 (4.1)	2 (<0.001)
Abdominal pain, upper	2 (4.1)	2 (<0.001)
Nausea	2 (4.1)	2 (<0.001)
Rash	2 (4.1)	2 (<0.001)
Arthralgia	2 (4.1)	2 (<0.001)

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

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

Injection-Site Reaction	Number [†] (Rate [‡]) of Reactions (n=683 Infusions [§])
Edema/induration	467 (0.68)
Erythema	346 (0.50)
Local heat	108 (0.16)
Local pain	88 (0.13)
Itching	64 (0.09)

* 15 to 45 minutes after the end of infusions administered at regularly scheduled visits (every 4 weeks).

[†] For multiple injection sites, every site was judged, but only the site with the strongest reaction was recorded.

[‡] Rate of injection-site reactions per infusion.

[§] Number of infusions administered during regularly scheduled visits.

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

6.2 Postmarketing Experience

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

The following adverse reactions have been identified and reported during the postmarketing use of IGIV products¹¹:

- **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.

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

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

7.2 Serological Testing

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

8.3 Nursing Mothers

Hizentra has not been evaluated in nursing mothers.

8.4 Pediatric Use

Hizentra was evaluated in 10 pediatric subjects (3 children and 7 adolescents) with PI. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels. Hizentra was not evaluated in neonates or infants.

8.5 Geriatric Use

Of the 49 subjects evaluated in the clinical study of Hizentra, 6 subjects were 65 years of age or older. No overall differences in safety or efficacy were observed between these subjects and younger subjects.

15 REFERENCES

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Manufactured by:

CSL Behring AG
Bern, Switzerland
US License No. 1766

Distributed by:

CSL Behring LLC
Kankakee, IL 60901 USA
Based on March 2010 version

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Vivaglobin®

Immune Globulin Subcutaneous (Human)

Manufactured by:
CSL Behring GmbH
 35041 Marburg, Germany
 US License No. 1765

Distributed by:
CSL Behring LLC
 Kankakee, IL 60901 USA

CSL Behring

R only

Before prescribing, please consult full prescribing information, a brief summary of which follows:
INDICATIONS AND USAGE

Vivaglobin® Immune Globulin Subcutaneous (Human), is indicated for the treatment of patients with primary immune deficiency (PID).

CONTRAINDICATIONS

As with all immune globulin products, Vivaglobin® Immune Globulin Subcutaneous (Human) is contraindicated in individuals with a history of anaphylactic or severe systemic response to immune globulin preparations and in persons with selective immunoglobulin A (IgA) deficiency (serum IgA < 0.05 g/L) who have known antibody against IgA.

WARNINGS

Patients who receive immune globulin therapy for the first time, who are switched from another brand of immune globulin, or who have not received immune globulin therapy within the preceding eight weeks may be at risk for developing reactions including fever, chills, nausea, and vomiting. On rare occasions, these reactions may lead to shock. Such patients should be monitored for these reactions in a clinical setting during the initial administration of Vivaglobin® Immune Globulin Subcutaneous (Human).

If anaphylactic or anaphylactoid reactions are suspected, discontinue administration immediately. Treat any acute anaphylactoid reactions as medically appropriate.

Vivaglobin® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Vivaglobin® is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically, the CD agent. The risk that such plasma-derived products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses during manufacture (see **DESCRIPTION** section for virus reduction measures). Stringent procedures utilized at plasma collection centers, plasma-testing laboratories and fractionation facilities are designed to reduce the risk of virus transmission. The primary virus reduction steps of the Vivaglobin® manufacturing process are pasteurization (heat treatment of the aqueous solution at 60°C for 10 hours) and ethanol - fatty alcohol / pH precipitation. Additional purification procedures used in the manufacture of Vivaglobin® also potentially provide virus reduction. Despite these measures, such products may still potentially contain human pathogenic agents, including those not yet known or identified. Thus, the risk of transmission of infectious agents cannot be totally eliminated. Any infections thought by a physician to have been possibly transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring at 1-800-504-5434 (in the US and Canada). The physician should discuss the risks and benefits of this product with the patient.

During clinical trials, no cases of infection due to hepatitis A, B, or C virus, parvovirus B19, or HIV were reported with the use of Vivaglobin®.

PRECAUTIONS

General-Administer Vivaglobin® Immune Globulin Subcutaneous (Human), subcutaneously. Do not administer this product intravenously. The recommended infusion rate and amount per injection site stated under **DOSE AND ADMINISTRATION** should be followed. When initiating therapy with Vivaglobin®, patients should be monitored for any adverse events during and after the infusion.

Laboratory Tests - After injection of immunoglobulins, the transient rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation. Passive transmission of antibodies to erythrocyte antigens, e.g., A, B, D may cause a positive direct or indirect antiglobulin (Coombs') test.

Drug Interactions - Immunoglobulin administration can transiently impair the efficacy of live attenuated virus vaccines such as measles, mumps and rubella. The immunizing physician should be informed of recent therapy with Vivaglobin® Immune Globulin Subcutaneous (Human), so that appropriate precautions can be taken.

Vivaglobin® should not be mixed with other medicinal products.

Pregnancy Category C - Animal reproduction studies have not been conducted with Vivaglobin® Immune Globulin Subcutaneous (Human). It is also not known whether Vivaglobin® can cause fetal harm when administered to a pregnant woman, or can affect reproduction capacity. Vivaglobin® should be given to a pregnant woman only if clearly needed.

Pediatric Use - Vivaglobin® was evaluated in 6 children and 4 adolescents in the US and Canada study and in 16 children and 6 adolescents in the non-IND study. There were no apparent differences in the safety and efficacy profiles as compared to adult subjects. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels. The safety and efficacy of Vivaglobin® was not studied in pediatric subjects under two years of age.

Geriatric Use - The clinical study of Vivaglobin® Immune Globulin Subcutaneous (Human), did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ADVERSE REACTIONS

In clinical studies, administration of Vivaglobin® Immune Globulin Subcutaneous (Human), has been shown to be safe and well tolerated in both adult and pediatric subjects. Reactions similar to those reported with administration of other immune globulin products may also occur with Vivaglobin®. Rarely, immediate anaphylactoid and hypersensitivity reactions may occur. In exceptional cases, sensitization to IgA may result in an anaphylactic reaction (see **CONTRAINDICATIONS**).

Should evidence of an acute hypersensitivity reaction be observed, the infusion should be stopped promptly, and appropriate treatment and supportive therapy should be administered.

In the US and Canada clinical study, the safety of Vivaglobin® was evaluated for 15 months (3-month wash-in/wash-out period followed by 12-month efficacy period) in 65 subjects with PID. The most frequent adverse reaction was local reaction at the injection site. Table 5 summarizes the most frequent adverse events by subject reported in the clinical study, and Table 6 summarizes the most frequent adverse events by infusion.

Table 5: Most Frequent Adverse Events by Subject Irrespective of Causality* in the US and Canada Study

Adverse Events (≥ 10% of subjects)	No. of Subjects (% of total)
Adverse Events at the Injection Site	60 (92%)
Non-Injection Site Reactions	
Headache	31 (48%)
Gastrointestinal disorder	24 (37%)
Fever	16 (25%)
Nausea	12 (18%)
Sore throat	11 (17%)
Rash	11 (17%)
Allergic reaction	7 (11%)
Pain	6.7 (10%)*
Diarrhea	6.7 (10%)*
Cough increased	6.7 (10%)*

*Excluding infections

† Due to missing subject diary information, values listed are estimates.

Table 6: Most Frequent Adverse Events by Infusion Irrespective of Causality* in the US and Canada Study

Adverse Events (≥ 1% of infusions) (Number of Infusions: 3656)	No. of Adverse Events (Rate**)
Adverse Events at the Injection Site	1789 (49%)
Mild	1112 (30%)
Moderate	601 (16%)
Severe	65 (2%)
Unknown Severity	11 (< 1%)
Non-Injection Site Reactions	159 (4%)
Headache	59 (1.6%)
Gastrointestinal disorder	40.3 (1.1%)*

*Excluding infections

**Rate = number of reactions/infusion

† Due to missing subject diary information, values listed are estimates.

Table 7 summarizes the most frequent related adverse events by subject reported in the clinical study, and Table 8 summarizes the most frequent related adverse events by infusion.

Table 7: Most Frequent Related Adverse Events by Subject* in the US and Canada Study

Related Adverse Event (≥ 2 subjects)	No. of Subjects (% of total)
Adverse Events at the Injection Site	60 (92%)
Non-Injection Site Reactions	
Headache	21 (32%)
Nausea	7 (11%)
Rash	4 (6%)
Asthenia	3 (5%)
Gastrointestinal disorder	3 (5%)
Fever	2 (3%)
Skin disorder	2 (3%)
Tachycardia	2 (3%)
Urinary abnormality	2 (3%)

*Excluding infections

Table 8: Most Frequent Related Adverse Events by Infusion* in the US and Canada Study

Related Adverse Event (≥ 2 AEs) (Number of Infusions: 3656)	No. of AEs (Rate**)
Adverse Events at the Injection Site	1787 (49%)
Non-Injection Site Reactions	
Headache	59 (1.6%)
Rash	9 (0.2%)
Nausea	9 (0.2%)
Nervousness	4 (0.1%)
Asthenia	3 (0.1%)
Gastrointestinal disorder	3 (0.1%)
Skin disorder	3 (0.1%)
Urinary abnormality	3 (0.1%)
Fever	2 (0.1%)
Dyspnea	2 (0.1%)
Gastrointestinal pain	2 (0.1%)
Tachycardia	2 (0.1%)

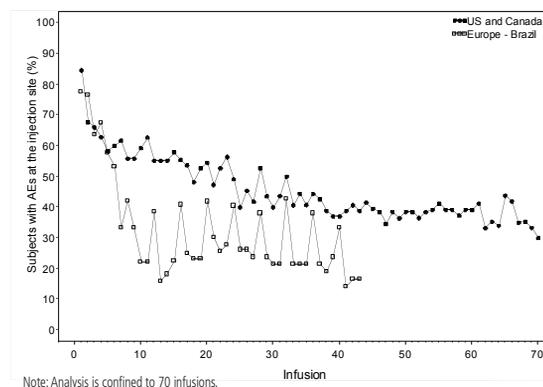
*Excluding infections

**Rate = number of reactions/infusion

In the non-IND Europe and Brazil clinical study, the safety of Immune Globulin Subcutaneous (Human), Vivaglobin® was evaluated for 10 months in 60 subjects with PID. The adverse events and their rates reported in this study were similar to those reported in the US and Canada study, with two notable exceptions for the related adverse events. These events were 59 episodes of headache (1.6%) and 2 episodes of fever (0.1%) in the US and Canada study and no episodes of headache and 18 episodes of fever (0.8%) in the Europe and Brazil study.

Local (Injection Site) Reactions - Local injection site reactions consisting of mostly mild or moderate swelling, redness and itching, have been observed with the use of Vivaglobin®. No serious local site reactions were observed. The majority of injection site reactions resolved within four days. Additionally, the number of subjects reporting local injection site reactions decreased substantially after repeated use (see Figure 1). Only three subjects in the US and Canada study and one subject in the Europe and Brazil study discontinued due to local site reactions.

Figure 1: Subjects Reporting Local Site Reactions By Infusion



Note: Analysis is confined to 70 infusions.

After administration, discard any unused solution and administration equipment in accordance with biohazard procedures.

HOW SUPPLIED

Vivaglobin® Immune Globulin Subcutaneous (Human), is supplied in single-use vials containing 160 mg IgG per mL. The following dosage forms are available:

- NDC 0053-7596-01 3 mL carton
- NDC 0053-7596-03 Box of ten 3 mL vials
- NDC 0053-7596-10 10 mL carton
- NDC 0053-7596-15 Box of ten 10 mL vials
- NDC 0053-7596-20 20 mL carton
- NDC 0053-7596-25 Box of ten 20 mL vials

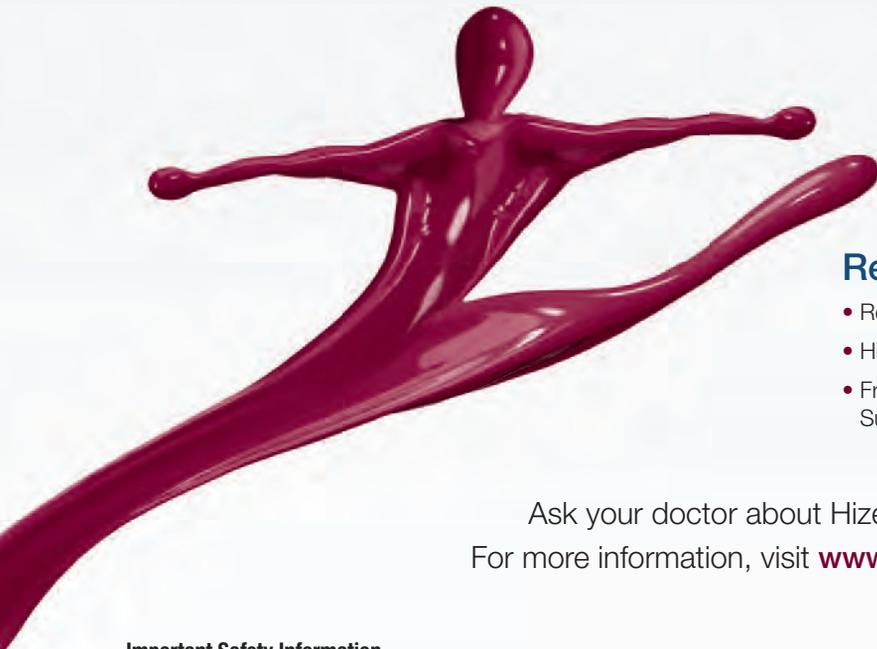
STORAGE

Store in the refrigerator at 2 - 8°C (36 - 46°F). Vivaglobin® Immune Globulin Subcutaneous (Human), is stable for the period indicated by the expiration date on its label. Do not freeze. Keep vials in storage box until use.

Based on April 2009 revision

If you live with primary immunodeficiency disease (PIDD)...

Make the leap to Hizentra



Ready-to-use Sub-Q Ig therapy

- Room temperature storage—no refrigeration required
- Hizentra can be infused in approximately 2 hours*
- From the maker of Vivaglobin®, Immune Globulin Subcutaneous (Human)

Ask your doctor about Hizentra today.

For more information, visit www.Hizentra.com

Important Safety Information

Hizentra and Vivaglobin are indicated for the treatment of patients with primary immunodeficiency (PI).

If you have a history of anaphylactic or severe systemic response to immune globulin preparations or selective immunoglobulin A deficiency, check with your physician as neither Vivaglobin nor Hizentra should be used. If your physician suspects you are having anaphylactic or anaphylactoid reactions, treatment will be discontinued. Because Hizentra contains the stabilizer L-proline, you cannot be treated with Hizentra if you have hyperprolinemia.

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

In separate clinical trials for Hizentra and Vivaglobin, the most frequent adverse event was injection-site reaction, consisting of mild or moderate swelling, redness, and itching. With Vivaglobin, no serious local site reactions were observed, and reactions tended to decrease substantially after repeated use. Other adverse events with Vivaglobin, irrespective of causality, included headache, gastrointestinal disorder, fever, nausea, sore throat, and rash.

Adverse reactions to Hizentra, observed in 5% or more of clinical trial subjects, were local injection-site reactions, headache, vomiting, pain, and fatigue.

Hizentra is manufactured by CSL Behring AG and distributed by CSL Behring LLC. Hizentra is a trademark of CSL Behring AG.

Vivaglobin is manufactured by CSL Behring GmbH and distributed by CSL Behring LLC. Vivaglobin is a registered trademark of CSL Behring GmbH.

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

Patients receiving Ig therapy for the first time, receiving a new product, or not having received Ig therapy within the preceding eight weeks may be at risk for developing reactions, including fever, chills, nausea, and vomiting. On rare occasions, these reactions may lead to shock.

Ig administration could impair the effect of live virus vaccines, such as measles, mumps and rubella. Before getting any vaccination, inform your doctor that you are being treated with Hizentra or Vivaglobin.

In their clinical studies, Hizentra and Vivaglobin were effective in pediatric patients without specific pediatric dose adjustments. With either treatment, no overall differences in safety or efficacy have been observed in patients over 65 or in pediatric patients.

Please see brief summary of full Prescribing Information for Hizentra and Vivaglobin, including Patient Product Information, on previous pages.

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

*In a clinical study, the median length of a weekly infusion ranged from 1.6 to 2 hours.


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