

GI Problems for IG Patients

**Diagnosing and
Treating Myositis**

**Funding Research
for Cures & Treatments**

Leaving the Nest: Preparing
IG Kids for Independence

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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MATTHEW DAVID HANSEN, DPT, MPT, BSPTS
Physical Therapist and President,
Allied Healthcare Staffing and
Consulting Agency

Funding Research to Find Cures/Treatments

“One of the hottest topics globally in immunological research is the establishment of a connection between immune deficiencies and specific genes.”



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

How Antibodies Develop

“It is believed that we retain a ‘useful repertoire’ of approximately 15 million different antibodies by generating a ‘new repertoire’ of B lymphocytes each week.”



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

Leaving the Nest

“The way to prepare young adults for independence is not to coddle them until the last minute. We can’t do everything for them until the day they leave. Instead, they should learn to deal with the intricacies of their disability at a young age.”



JILL WEISENBERGER, MS, RD, CDE
Registered Dietitian

GI Problems for IG Patients

“For someone with an immune disorder, the immune system’s defenses have holes or gaps that allow outside infections to infect and thrive inside the body.”

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

IG Living isn’t just a magazine; it’s an interactive community of people with interesting stories. And, we want you to be a part of it! Our blog, which has a new entry posted each Friday, provides interesting perspectives on topics such as living with IG, people to be admired, support and encouragement, current news of interest and things you just need to know. We encourage you to comment with your opinions and stories. And, better yet, if you have a blog you’d like to post, send it our way!

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

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



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



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

- Email *IG Living* to be added to our email invitation list for the teleforums.
- *IG Living* will send you invitations to let you know when the 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.



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

A community service from
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Research and IVIG's Future

You've heard the question: "If we can send a man to the moon, why can't we find a cure for ...?" The answer: research. According to the National Institutes of Health, research is the key to unlocking the knowledge we need to find cures and new treatments for so many of the diseases that plague our society. That includes autoimmune diseases and those diseases caused by immune deficiencies. And, while research has already helped many in the *IG Living* community, new findings suggest that treatments can be improved and there might one day even be a cure.

In this issue, we explore how research studies are funded and how, collectively, we all can get involved to support continued and increased funding of these crucial studies. What's more, author Matthew Hansen discusses what he and a number of immunologists call "one of the hottest topics globally in immunological research" that focuses on gene sequencing, which could eventually result in stem cell replacement leading to the cure for immune and autoimmune diseases.

In the meantime, many other ongoing research studies have resulted in the development of more effective treatments. For instance, scientists are increasingly learning the benefits of immune globulin (IG) for non-FDA indicated diseases. And, of course, manufacturers are continually working to improve IG products by increasing their potency, resulting in decreased infusion frequencies, rates and durations.

Yet another interesting development might improve intravenous IG (IVIG) potency by a rate never seen before. Virdate Pharmaceuticals, founded by Rockefeller University's Jeffrey Ravetch, has found that adding sugar molecules,

or sialic acid, to purified IVIG could boost the anti-inflammatory potency of the treatment.

Dr. Ravetch's discovery was founded on his identification of billions of different antibodies in IVIG, only a small population of which are anti-inflammatory, while the majority of them are pro-inflammatory. According to an article in *Life Science Leader*, "What makes the minority different is that they have sugar molecules, sialic acid, on the stem region." So, Virdate has introduced a new manufacturing step to add the sialic acid back onto the purified IVIG, creating sIVIG, which increases the anti-inflammatory potency of the IVIG and reduces dosing tenfold. In effect, only one-tenth of the product is needed to treat a patient.

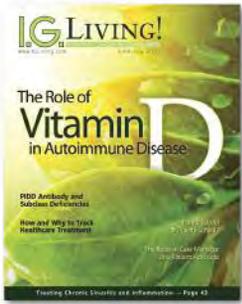
According to biotechnology industry consultant Martin Ashdown, this discovery "is probably one of the most important discoveries in medical science in recent times and exceedingly promising." It could be a win-win situation for all involved. Some existing patients would have improved outcomes, healthcare savings for governments could be significant, and, as IG demand increases with off-label treatments, the amount of IG product available to treat this growing demand might not be the problem it once was.

While this research is in its early stages, it's just one more example of the value that research provides. We sent a man to the moon; surely we can better treat or even cure immune diseases. ■

To your health,

Ronale Tucker Rhodes, MS, Editor

Readers Say, “Thanks!”



Thanks for the article on vitamin D. I had my primary care doctor check my levels and mine were almost nonexistent [thus, probably all my sickness issues]!

— Gloria

Thank you so much for your last issue. It came ... when I was suffering a really bad reaction

from supposedly a better and safer pain medication for some compressed vertebrae in my neck. I felt so depressed because it takes so long for me to get over what used to be minor body reactions to less-than-perfect medicines. Somehow, it was a comfort to know that I am not alone in struggling with the confusing intricacies of the human immune system.

It is hard to find someone who understands the enormity of the effect [that] a less-than-perfect immune system has on one's life. I believe that coping with loss has less to do with one's attitude than it is a question of having energy enough to devise a plan A, B, etc., to deal with the days when you are so tired that you cannot even add numbers correctly or remember words to convey issues to your doctors or other important people in your life.

I feel as if I never know what will make me feel better or worse, or if I'll react differently this time. But reading your magazine makes me realize that part of this struggle is [about] weathering these episodes as graciously as possible.

— Brian Burke

IVIG Home Access

My name is Dana “Dane” Currie and I have common variable immune deficiency [CVID] (diagnosed 15 years ago [and] treated with 50 grams of IVIG every two and a half to three weeks), Sjogren's syndrome (diagnosed this past year) and celiac disease (diagnosed 10 years ago). My particular issues related to CVID have been fairly serious (I've been told that I must have “more lives than a cat” because I've come so close to losing my life many times). After three and a half years of appeals, I was finally granted disability and Medicare coverage last fall. This was definitely for the best, but for several months, I was really depressed — feeling like I was a burden, not contributing to society, etc.

I've been receiving the Immune Deficiency Foundation's (IDF) newsletter for as long as I can remember. A few months ago, I noticed a blurb about volunteer/advocacy opportunities. It was like I was given a shot of some amazing drug; here was my chance to make a difference, to use my years of struggling to help and educate others. So, I went through the required screening and am proud to represent the state of Maine as an IDF volunteer/patient advocate.

I recently had the opportunity to travel to Washington, D.C., to speak with legislators about the 2009 Medicare Patient IVIG Access Act. Currently (without getting into confusing technical details), Medicare is not reimbursing patients who are better off getting their IVIG at home. There have also been issues with patients not being referred to hospital settings for infusions, as this is expensive. This needs to be fixed *now*; the current situation is unacceptable, and patients are becoming seriously ill and dying because of this. I am extremely fortunate to be covered by my mother's private insurance in addition to my Medicare, but [I] am quite worried about what will happen if I lose that when she retires in a few years.

Unfortunately, primary immunodeficiencies are not well known to the voting public, which is why advocacy is more important now than ever before. I urge you to please address this serious issue in your publication, *IG Living*.

I always enjoy the articles and such in *IG Living* and am excited when I see the latest issue in my mailbox!

— Dana L. Currie



The Editor replies:

Thanks for being an advocate for our community! We also want to spread the word about what people can do to help others. As soon as we heard about this issue, we posted a news item on our *IG Living* website (www.igliving.com) about a bill that was introduced in June regarding this. That same news item appears on page 11 of this issue. 📌

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 Be Heard/Feedback page to send your comments.

Life with IG

Living with a chronic illness poses many challenges. And, it often helps to hear about those challenges, including stories, ideas and issues, that confront those of us in the *IG Living* community — especially when they come with a personal perspective. That's what *IG Living's* blog is all about. Below is a sample posting on our blog, where a new one is added each Friday. If you haven't yet visited the *IG Living* blog, we invite you to do so at www.igliving.com/blog engine. And, we invite you to not only comment on the blogs, but to submit your own blog to be included on the site by writing us at editor@igliving.com.



Immune Disease: Are You Sure It's Not Depression?

By Kris McFalls

I often hear from *IG Living* readers who are frustrated with questions and advice from well-meaning, but slightly misguided friends and family. When trying to show support, they offer advice and make suggestions that make us want to scream. But, instead, we bite our tongues and give a pleasing response in hopes of making them feel better for having helped. For your entertainment, I've listed some of the more popular questions posed by these well-meaning people, along with some suggested responses.

Do you think you might be depressed?

What we would like to say: Wow, imagine being depressed after years of being poked and prodded, having chronic infections and unrelenting pain, only to find out that a simple blood test could have solved the mystery years ago.

What we do say: Wow, I never thought of that. Thanks for your concern.

Do you think more exercise would help?

What we would like to say: Yea, the cane is for self-defense, the walker is so that I can get better parking and, for extra attention, I use a wheelchair.

What we do say: Maybe working with a physical therapist would help, thanks for the advice.

Have you tried taking Echinacea? It can really boost the immune system.

What we would like to say: Do you really think big insurance companies would pay thousands of dollars for a plasma product if a simple herb could make my immune system whole again? You cannot boost what you don't have. What part of zero times zero do you not understand?

What we do say: That really works for you? Huh, imagine that.

Are you sure you don't have any allergies?

What we would like to say: Well, I felt like I had just been attacked by a porcupine after I left the allergist's office, but maybe you're onto something.

What we do say: Maybe I should try some Benadryl.

How are you feeling? You look good to me.

What we would like to say: Let me think about that for a moment. I spent over an hour in the bathroom and that was just to use the toilet; it took me three cups of water to get all my pills down, and I want to spew my breakfast on the next person that asks me how I feel and then tells me what my answer should be.

What we do say: Oh I feel pretty good today, thanks.

Do you think your faith is strong enough?

What we would like to say: Seriously? The devil made me do it.

What we do say: I'll pray about that one.

Now it's your turn. Give us your feedback. What comments and questions, if stated one more time, would send you over the edge? As much as you would like to fire off a snappy comment, how do you reply and turn those well-meaning suggestions around so that you truly feel supported? Post your replies on our site — let's start a discussion!

As of this writing, this blog has received 45 responses. Log onto www.igliving.com/blogengine now to read the comments!

How Antibodies Develop

By Terry O. Harville, MD, PhD

THIS ISSUE, we continue the discussion of antibodies introduced in the August-September column. As a reminder, antibodies are sometimes called gamma-globulins or immunoglobulins (Igs), or they may be referred to by their specific class names, such as IgG (immunoglobulin G), IgA, IgM, IgE and IgD. Each plays specific roles in immune system development and function.

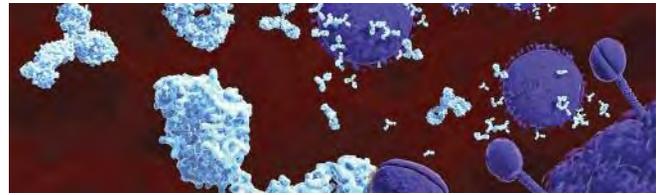
How IgG Develops in the Body

IgG — the immunoglobulin found in the highest concentration in the body — is the only immunoglobulin to pass through the placenta, so that at birth, the infant's level is the same as the mother's, which is approximately 1,000 mg/dL. After birth, transplacentally acquired maternal immunoglobulin has a normal half-life of approximately 21 to 28 days (to approximately 500 mg/dL after the first month, and then approximately 250 mg/dL after the second month, etc.). During this time, the infant with "normal" immunity begins to make his/her own IgG. The level dips to its lowest value between three and six months (three and six half-lives) after birth, on average approximately 300 to 325 mg/dL (representing a combination of maternal antibodies and infant antibodies). At that point, there are fewer maternal antibodies than those being made by the infant. The lowest accepted "normal" range value for this age is about 125 mg/dL. A value less than 125 mg/dL would represent a deficiency of IgG.

While the "average" half-life of all the antibodies is usually 21 to 28 days, any individual antibody may have a shorter or much longer half-life, and some maternal antibody titers can be detected as far out as 18 to 24 months after birth. From its nadir, the IgG level begins to increase to approximately 500 mg/dL, on average, by about 1 year of age. And, there continues to be a steady increase both in the quantity, as well as function (quality), typically reaching "normal" accepted adult values after about 6 years of age. In some children, the process is somewhat more delayed, so that the "normal" adult values are not achieved until about the time of puberty — around 10 to 12 years of age.

How Ig Is Made

Antibodies, or Igs, are produced by B lymphocytes, and individuals are capable of making more than 200 million different B lymphocytes, each producing a different antibody



(by a mechanism to be discussed later). Once created, antibodies fall into one of three categories: 1) useful (capable of binding to a pathogen and providing immune protection), 2) useless (incapable of binding to a pathogen and, therefore, providing no immune protection) and 3) harmful (having the potential to bind to self-tissues and cause autoimmune diseases). Therefore, in an effort to retain the useful antibodies and eliminate the useless and harmful ones, more than 90 percent to 95 percent of all developing B lymphocytes (and thereby, individual antibodies) being formed during the normal developmental process are destroyed.

It is believed that we retain a "useful repertoire" of approximately 15 million different antibodies by generating a "new repertoire" of B lymphocytes each week. To do that, the body produces more than 200 million different new B lymphocytes (antibodies) weekly to try to eliminate the 90 percent to 95 percent of those that are useless or harmful — all in an effort to retain approximately 15 million potentially useful ones. It is likely that the body produces about the same 200 million different B lymphocytes each week, while trying to select for the same 15 million potentially useful ones. For instance, if a recently formed, naive B lymphocyte can recognize a specific antigen it encounters, the immune system appropriately activates it to preserve it for future antibody production (memory B lymphocyte). In contrast, a non-stimulated B lymphocyte will die. Therefore, on an ongoing basis, we continue to need to replace the supply of naive B lymphocytes to provide us with potentially useful antibodies.

However, complications can arise during the developmental processes. One is that the process of forming new B lymphocytes on an ongoing basis raises the risk for B-cell leukemia or lymphoma, which results when certain errors occur during the formation process. What's more, if the potentially harmful B lymphocytes are not eliminated, there is the potential to develop autoimmune disease. Indeed, we can measure the accumulation of autoimmune antibodies in most individuals as they grow older.

This discussion will continue in the next issue. ■

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

Research

IVIG Shown to Relieve CRPS



A small study conducted at the Pain Research Institute at the University of Liverpool in England found that intravenous immune globulin (IVIG) was effective for alleviating chronic regional pain syndrome (CRPS). Researchers administered a half gram of IVIG per kilogram of body weight to 13 people who had been suffering from CRPS between six and 30 months and who reported pain intensity of at least five on an 11-point scale for seven consecutive months. All had failed to achieve significant relief from conventional treatments, including acetaminophen, nonsteroidal anti-inflammatory drugs,

opioids, antidepressants, gabapentin or pregabalin, and physical therapy.

Beginning six days after the infusion, when discomfort from the injection and transient side effects had subsided, subjects rated their pain every day for two weeks. Five of the 12 subjects reported median pain scores at least two points lower with IVIG than with the saline placebo, and three of the five reported pain scores at least 50 percent lower. The average drop in pain after receiving IVIG was 1.55 points. "To our knowledge, we have shown for the first time that low-dose IVIG reduces pain in patients with longstanding, refractory CRPS, with few adverse reactions," say the study's authors.

Because the number of subjects in the study were so few, pain researchers say that these results need to be replicated by larger and more rigorous research. The study was reported on in the Feb. 2 issue of the *Annals of Internal Medicine*. ■

Research

Multiple IVIG Doses Benefit CIDP Patients

Patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) may need two doses of intravenous immune globulin (IVIG), 10 percent caprylate/chromatography purified (IVIG-C), every three weeks for initial improvement, and additional therapy may be needed to reach and maintain a maximal response, according to research published online May 10 in the *Archives of Neurology*.

Researchers examined data on 117 individuals with CIDP who received IVIG-C or a placebo in the IVIG-C CIDP Efficacy (ICE) trial. Those in the IVIG-C group

received a 2 g/kg loading dose and then a 1 g/kg dose every three weeks for as long as 24 weeks. Of the 30 responders to IVIG-C, the researchers found that 14 (47 percent) had improved adjusted inflammatory Neuropathy Cause and Treatment disability scores by week three, and 16 (53 percent) improved at six weeks after a second infusion. In patients who improved, the number reaching maximal improvement increased for the duration of maintenance therapy, up to 24 weeks.

The ICE trial was funded by the Talecris Biotherapeutics Center for Science and Education. ■

Conference

First Neuropathy Summit Scheduled

In conjunction with its 15th anniversary as the leading national organization serving the peripheral neuropathy community, the Neuropathy Association is hosting the 2010 Neuropathy Summit, a first-of-its-kind event that features back-to-back conferences for patients, physicians and other healthcare professionals. The summit will be held December 3 through 5 in Washington, DC. Its theme is "Proving the Paradoxes of Neuropathic Pain" since a large majority of neuropathy patients suffer with chronic and debilitating pain.

The physicians' conference, scheduled for December 3 through 4, will be a dynamic forum for healthcare professionals, scientists, investigators and clinicians working in the neuropathy field to exchange and share scientific knowledge; accelerate translational research; explore applications in clinical practice to enhance patient care; and foster collaboration and share new ideas in addressing peripheral neuropathy. The patients' conference will be held December 4 through 5 and is intended for all neuropathy patients, caregivers and family members to take part in interactive informational sessions with featured experts and company representatives in the field of neuropathy. Attendees will learn about the latest research advances; review treatment approaches for neuropathy and neuropathic pain; and connect with and learn from their peers. The event also includes a joint 15th anniversary banquet.

For more information and to register for the event, go to <http://www.neuropathysummit.org>. Or, contact Chris Cherkis, registration and exhibit manager, at (202) 973-8616. ■

Legislation

IVIG Access Bill Introduced in House



On June 24, H.R. 5597, a bill to establish a Medicare patient IVIG access demonstration project, was introduced in the U.S. House of Representatives. If approved by both the House and Senate, the bill would establish and implement a demonstration project under title XVIII of the Social Security Act to evaluate the benefits of providing payment for items and services needed for the

administration, within the homes of Medicare beneficiaries, of intravenous immune globulin (IVIG) for the treatment of primary immune deficiency diseases (PIDD).

The demonstration project would begin no later than Jan. 1, 2011, would last for a period of three years and would enroll no more than 4,000 Medicare beneficiaries who have been diagnosed with PIDD. The Secretary of Health and Human Services would establish an hourly rate of payment for items and services needed for the administration of IVIG based on low-utilization payment adjustment under the prospective payment system for home health services established under section 1895 of the Social Security Act.

The bill is intended, not later than 24 months after the date of enactment, to establish an interim evaluation

of the impact of the demonstration project on access for Medicare beneficiaries to items and services needed for the administration of IVIG within the home; to analyze the appropriateness of implementing a new methodology for payment for IVIG in all care settings; to analyze the feasibility of reducing the lag time with respect to data used to determine the average sales price of IVIG; and to update the report titled *Analysis of Supply, Distribution, Demand, and Access Issues Associated with Immune Globulin Intravenous (IGIV)*, which was issued in February 2007 by the Office of the Assistant Secretary for Planning and Evaluation of the Department of Health and Human Services. A final evaluation and report of the impact of the demonstration project would be required no later than July 1, 2014. ■

Research

New Center Established for Immunology Research

The Immune Tolerance Institute (ITI) and the David H. Murdock Research Institute have established a Kannapolis, N.C., research center designed to speed up the discovery and development of treatments for people with a broad range of immune system-related conditions.

The Center for Critical Path Research in Immunology (CCPRI) will operate at the Murdock Institute's facility within the North Carolina Research Campus, a \$1.5 billion, 350-acre laboratory/office site developed by Murdock — a real estate and food magnate who is chairman of Dole Foods — to

accommodate health, nutrition and agricultural research. CCPRI will integrate “genomic, cellular, proteomic and bioinformatics technology platforms to discover and develop novel biomarkers,” as well as “match patients with therapies that will provide them the greatest benefit.” Its goals are “to accelerate the translation of basic discoveries into medical practice, and to become a major resource for a range of academic and industry partners.”

The ITI is a nonprofit corporation founded in partnership with the University of California, San Francisco, to translate scientific discoveries into



new therapies for diseases related to the human immune system, including autoimmune diseases, allergy, asthma, cancer and cardiovascular and infectious diseases. ■

A photograph of a man and a young girl smiling at each other. The man is on the left, wearing a light blue shirt, and the girl is on the right, wearing a pink shirt. They are standing behind a wooden table with a plate of fruit, including strawberries and green grapes. The background is a bright, textured wall.

GI Problems for IG Patients

By Jill Weisenberger, MS, RD, CDE

Immune disorders often cause inflammation and infection that affect nutrient absorption. Understanding these effects and taking action can help to keep patients healthy.

The belief that good nutrition feeds the immune system is nothing new. Hippocrates said, "Our food should be our medicine, and our medicine should be our food." This seems simple enough to understand, but it's not so simple for those with intestinal problems.

Individuals with chronic infections often experience stomach irritation, inflammation and diarrhea, leaving their intestinal wall inflamed and unable to adequately absorb the nutrients their body craves for good health. These individuals are highly prone to nutrient deficiencies from malabsorption. And, since optimal immune function demands optimal nutrition, this can become a self-perpetuating cycle of disease: Inflammation or infection hinders nutrient absorption, which weakens the immune system, which further lessens absorption and so on and so on. Therefore, the discomfort, diarrhea and dashing to the bathroom — even when fairly mild — are more serious than the inconvenience or embarrassment they cause.

Immune Disorders

Pummel the Intestines

An immune deficiency disease disrupts the normal functions of the intestines in several ways, says Neil L. Kao, MD, allergist and immunologist in Greenville and Spartanburg, S.C. Lack of antibody production provides opportunities for infections in the intestinal tract, and these infections damage the gut, he explains. In addition, the side effects of treatment can hinder nutrient absorption, and other defects in the immune system can lead to autoimmune diseases, such as ulcerative colitis and Crohn's disease, further damaging the intestines. Actually, an individual with an immune disorder may be burdened with some or all of these problems, leading to nutrient absorption issues that range from mild to severe.

Common Infections and Causes of Inflammation

For someone with an immune disorder, the immune system's defenses have holes or gaps that allow outside infections to infect and thrive inside the body, says Kao.

Among the invaders are giardia and cryptosporidia, single-celled parasites that cause much of the diarrhea in humans. These tiny organisms enter the body with contaminated water or food and set up home in the small intestine, where they multiply in massive quantities. Similarly, the bacteria campylobacter and yersinia, common in undercooked foods, also invade and grow in the small intestine. This swarm of trespassers then inflames or injures the intestinal walls. Likewise, Crohn's disease and ulcerative colitis, which are common among individuals with immune deficiency diseases, cause chronic inflammation of the intestines.

When Malabsorption Occurs

Because of its specialized cells and incredible length of about 20 feet, a healthy small intestine is remarkably capable of absorbing more nutrients and calories than the body needs. But damaged or irritated tissue loses its

ability to extract the nutrients from food and move them into the bloodstream. Being denied entrance into the cells that depend on them and with nowhere else to go, these unabsorbed nutrients and particles of food travel to the large intestine, where they are eventually excreted with the feces.

The symptoms of malabsorption are many and range from unnoticeable to frequent diarrhea, severe weight loss, dehydration, irregular heartbeats and more. Symptoms depend on the severity of malabsorption

and the site of diseased tissue. Importantly, even those immune disorder patients who appear well-nourished may have one or more nutrient deficiencies, notes registered dietitian Colleen Gill, MS, RD, CSO, of the University of Colorado's Oncology Services and Integrative Medicine. According to Gill, there are many nutrients of special concern.

Individuals with chronic infections often experience stomach irritation, inflammation and diarrhea, leaving their intestinal wall inflamed and unable to adequately absorb the nutrients their body craves for good health.

Common Nutrient Deficiencies

Dietary changes are often enough to improve nutritional status, but frequently, malabsorption is severe enough to warrant supplementation. However, supplementing with

any nutrient has risks, including interfering with medications, causing toxic symptoms and decreasing the absorption of other nutrients. Before taking any supplement, immune disease patients should talk to a physician, registered dietitian or pharmacist.

Vitamin B12. This water-soluble vitamin is absorbed in the ileum, the lowest portion of the small intestine. If this section of the digestive tract is affected by illness, the vitamin is poorly absorbed. Additionally, some patients with immune deficiencies are at risk for atrophic gastritis, a condition in which the stomach lining fails to produce enough acid, says Kao. Without adequate acid, the body cannot extract vitamin B12 from proteins in food. Long-term lack of vitamin B12 leads to a form of anemia and to nerve damage that may eventually be irreversible.

Fat-soluble vitamins and essential fatty acids. Signs of fat malabsorption include “stools that float on the surface of the toilet basin,” explains Gill. This is similar to fat separating from water when oil is poured into pasta while cooking, she adds. The fat-soluble vitamins are A, D, E and K. These vitamins have multiple roles in immune function, blood clotting, bone health, vision, growth and more. Some pharmacies supply vitamins A, D, E and K in a special highly absorbable, water-soluble form just for those individuals with fat malabsorption problems.

Calcium. This bone-building mineral depends on adequate vitamin D for its absorption. Additionally, calcium and other minerals may bind with fats in the digestive tract, hindering uptake, says Gill. Patients who need a calcium supplement should choose calcium citrate over calcium carbonate if they produce inadequate stomach acid; calcium carbonate requires



some acid for absorption.

Other minerals. Zinc, magnesium, selenium and other minerals also bind with fats, forming a chemical “soap,” blocking absorption. Some minerals that are lost in diarrhea also can cause or aggravate diarrhea when taken in excess, so caution should be used with these and other nutrient supplements.

Medications and Nutrient Losses: A Double-Edged Sword

Anyone who takes medications for chronic diseases can relate to the refrain: “Sometimes the treatment is worse than the disease.” Many medications for immune disorders or for the infections they cause increase malabsorption problems or otherwise raise the risk for nutrient deficiencies.

Prednisone. Prednisone decreases the inflammation of the gastrointestinal tract, but sabotages nutritional status. This corticosteroid and others decrease calcium absorption, leaving the bones vulnerable to weakening. This drug further damages the bones by accelerating bone loss and by increasing calcium excretion in the urine. Protein needs also may increase because of increased breakdown of body proteins.

Cholestyramine. This drug decreases diarrhea, but also blocks the absorption of calcium, iron and the vitamins A, D, E, K, folate and B12.

Sulfasalazine. This anti-inflammatory impedes the absorption of folate, a B vitamin important in the formation of red blood cells and in cell growth and division.

Antibiotics. While attacking the bacteria that have caused a respiratory infection or any infection, antibiotics also kill the good bacteria in your gut that contribute to a

The symptoms of malabsorption are many and range from unnoticeable to frequent diarrhea, severe weight loss, dehydration, irregular heartbeats and more.

healthy gastrointestinal tract, says Gill. If this leads to diarrhea, food and food particles run through the digestive tract more quickly than usual — so quickly that they don't get absorbed.

Take Action

A gentle rain gradually soaks into the soil, but a hurricane dumps so much rain that it floods the neighborhood. A comparison can be applied to the size of meals, suggests Gill. Eating too much at once floods the gastrointestinal (GI) tract. Instead of eating three large meals that can overwhelm the intestines, individuals with an immune disease need to slow down the assault by eating smaller, more frequent meals.

If diarrhea is a problem, limiting irritants like caffeine also is a smart idea. While a daily latté may help someone else manage constipation, caffeine isn't a good idea for those with frequent trips to the bathroom. Hot coffee compounds the problem, Gill adds. "Extremes in temperature, whether cold or hot, will trigger more contractions," speeding the passage of food through the GI tract and limiting absorption.

Some people with diarrhea have trouble digesting the sugars in dairy products. If this is a problem, they should try eating only small amounts at a time or use lactose-free milk. Lactase supplements (sold as Lactaid) also help. Finally, fluids lost with diarrhea need to be replaced. "Dehydration makes everything worse: fatigue, nausea and pain control," Gill adds.

Sometimes discomfort or the fear of embarrassment prevents individuals from eating adequately. It's important for these people to take action and to seek the help of their physician or a registered dietitian.

When Food Alone Isn't Enough

In some cases, malabsorption is so severe that food — and even standard or high-dose vitamin-mineral supplementation — isn't enough. Frequently, physicians and dietitians recommend high-protein or high-calorie supplemental beverages such as Peptamen 1.5, which is pre-digested and, thus, more easily absorbed. For those with fat malabsorption problems, Gill recommends Resource Fruit Breeze or Enlive. However, these products should only be used under the guidance of a healthcare professional. Whatever product is chosen, it should first be

drunk at room temperature or only slightly cold to avoid the gastrointestinal contractions brought on by temperatures above or below room temperature.

Short-term tube feedings may be necessary for some individuals. Either a thin, flexible plastic tube is placed down the nose into the stomach or a tube is surgically placed into the small intestine. A prescribed amount of liquid feeding is administered through the tube. Tube-feeding products vary in nutrient composition. They may be high-protein, high-fiber, low-fiber, low-fat and many other versions. A physician or registered dietitian will select a product specific to a patient's needs. And, like some supplemental beverages, some tube-feeding products contain nutrients that do not need to be digested before absorption. In some cases, tube feedings may be used for supplemental nutrition, and in others, they may be the sole source of nutrition.

Total parenteral nutrition (TPN) is reserved for individuals whose GI tracts are so inflamed or damaged that only minimal nutrients can be absorbed, or for those people who need to allow their bowels complete rest in order to heal. In TPN, all essential nutrients, including calories, fluids, vitamins,

minerals, amino acids and carbohydrates, are delivered through an intravenous catheter placed directly into the bloodstream, completely bypassing the stomach and small intestine.

Planning an Individualized Diet

Nutritional status affects all facets of health and daily living. Immune disease patients should visit the American Dietetic Association (www.eatright.org) website to find a registered dietitian near them to help them or a family member plan an individualized diet. ■

JILL WEISENBERGER is a registered dietitian, certified diabetes educator, nutrition and health writer, speaker, spokesperson and culinary expert based in southeast Virginia. Her website, *All That's Nutrition*, can be accessed at www.allthatsnutrition.com.

Sources

University of California San Francisco, patient education. Accessed June 5, 2010.
<http://www.ucsfhealth.org/adult/edu/inflammatoryBowelDiseaseNutrition/index.html>.

If diarrhea is a problem, limiting irritants like caffeine also is a smart idea.



Funding Research to Find Cures/Treatments

Scientific research to identify, diagnose and treat PIDD and autoimmune diseases continues to increase with the combined efforts of doctors, organizations and individuals.

By Matthew David Hansen, DPT, MPT, BSPTS

The hopes and prayers of people living with a primary immune deficiency disease (PIDD) and/or autoimmune disease are to someday be cured of the condition or, at the very least, to find a way to stay healthy and improve their quality of life. Although the prospect of an individual miracle cannot be — nor should it ever be — discounted, the potential future eradication of PIDDs and autoimmune diseases will likely be due to the combined effort and enlightened discoveries of medical research.

Groundbreaking scientific advances have taken place during the last 10 to 15 years that are leading to the enhanced identification and diagnoses of PIDDs and autoimmune diseases, as well as the development of new vaccines and new and improved therapies for the disorders and their symptoms. Yet, how many of the tens of millions of people worldwide with one of these diseases are aware of the research that is taking place? And, how many are actively participating, supporting and/or promoting the cause? The thousands, perhaps tens of thousands, of patients and families who are, are making a *big* difference; however, when considering the needless suffering, disability and loss of life that occurs every day due to these diseases, progress cannot come fast enough. It is one thing to hope, but quite another to continue that hope while getting involved. Only collectively can we bring change.

Advances in Research

One of the hottest topics globally in immunological research is the establishment of a connection between immune deficiencies and specific genes. In fact, the Centers for Disease Control and Prevention (CDC) reports that many PIDDs are due to a single gene defect. As a result of improved and expanded gene sequencing, “there are about 160 to 165 mutations in different genes that have been identified in PIDD,” explains Dr. Troy Torgerson of the University of Washington and Seattle Children’s Hospital, and co-director of the hospital’s Immunodeficiency Molecular Diagnostics Laboratory, who is participating in the clinical care of patients with immune deficiency and autoimmune disorders. “We’re learning why particular genetic defects make patients susceptible to certain infections or make patients develop autoimmune diseases. ... You can now sequence someone’s entire genome for a relatively reasonable cost, and it’s getting cheaper and cheaper.”

Dr. Torgerson is excited that, along with more specific diagnoses, comes the prospect of more effective treatments and potential cures for PIDDs and autoimmune diseases. In his estimation, one of the fruits of gene sequencing that is on the not-too-distant horizon involves stem cells that are taken from a patient’s own peripheral blood, bone marrow, preserved umbilical cord blood or other potential sites in their body. “With traditional gene repairs, in the

neighborhood of only one in a million cells is repaired and then put back," Dr. Torgerson explains. "But, it's not enough cells to completely fix the problem." The body's stem cells are unique because they are able to renew themselves by dividing and differentiating into specialized cell types, like the blood cells that are so important to our immune system. "We would like to take stem cells from a patient, select and repair them [with a normal copy of the defective gene], grow and expand them up in the lab and then put them back in the patient," he adds.

Whereas current therapies for PIDDs and autoimmune diseases focus on controlling symptoms, stem cell transplantation may offer a future cure for many of the conditions. The technique still faces several hurdles in the laboratory before it can become common practice in the clinic. However, society's best and brightest scientists are working hard to develop stem cell transplantation and other disease-specific therapies, and to both reduce the cost and increase the effectiveness of current treatments like immunoglobulin infusions. The greatest hurdle to the rate and height of their success may not be limitations on the human mind or the bounds of science but, instead, limitations on the pocket-book.

Funding Research

An overwhelming majority of funding for PIDD and autoimmune disease research (estimated by Dr. Torgerson to be at least 95 percent) comes from the federal government through grants approved by the National Institutes of Health (NIH). However, Dr. Hans Ochs, also of the University of Washington and Seattle Children's Hospital, who is widely considered a pioneer in the field of PIDD research and is a primary investigator for the NIH contract supporting the United States Immune Deficiency Network (USIDNet), elaborated that getting projects approved is "highly competitive" and "presently very difficult, with less than 10 percent being funded." During the Clinton years, the administration had a goal of doubling the NIH budget, with 20 percent to 25 percent of projects being funded. Increased funding continued into the first or second year of the Bush presidency, though budgets have experienced only modest, if any, increases since that time. "Consequently," declares Dr. Torgerson, "a lot more time is put into grant writing that could be used

otherwise. People are trying to find ways to scrape by and keep their labs open and keep going."

As disappointing as the current funding challenges may be, it's important to realize how far the funding of PIDD and autoimmune disease research has come. According to Dr. Ochs, "As PIDD became more prominent, the patient organizations started to make their voices heard, and the experts in PIDD banded together. There were very few grants from NIH supporting research directly related to PIDD until some 15 years ago when NIH started to support registries and began to notice that research fell behind in the U.S. compared with Europe." As a result, a task force recommended more funding and the USIDNet was charged with the tasks of providing small two- to three-year grants, establishing a new web-based PIDD registry, setting up a repository of DNA and cell lines and organizing meetings. Dr. Torgerson acknowledges one individual in particular, the late Dr. Josiah F. Wedgwood, MD, as a

powerful force behind specific funding opportunities for PIDD research. "Prior to his work with the NIH (as a program officer) in developing this specific area of interest, you would submit your grant to the general NIH and there wasn't much recognition," explains Dr. Torgerson.

Although most of the direct funding for PIDD and autoimmune disease studies comes from the government, several other organizations serve as significant sources of

monetary and non-monetary support for research. One group, the Clinical Immunology Society (CIS), just organized its first North American PIDD Conference in May 2010. The organization also is responsible for hosting an annual PIDD Summer School, which they began eight years ago, for future scientists who have a potential interest in clinical immunology. Companies that make immunoglobulin products also often give money to help fund research and to sponsor fellows in programs like the PIDD Summer School. And, other important organizations, including the Immune Deficiency Foundation (IDF), the Jeffrey Modell Foundation (JMF) and the American Autoimmune Related Diseases Association (AARDA), are nonprofit patient advocacy groups that provide invaluable opportunities for others to get involved in the promotion of PIDD and autoimmune disease research.

One of the most important ways that anyone can advocate for research funding is to lobby their political representatives.

Getting Involved

So, how can someone who doesn't put on a white lab coat to go to work each day make a difference in research? Fortunately, there are a number of opportunities to get involved, most of which don't include pulling out the checkbook.

One of the most important ways that anyone can advocate for research funding is to lobby their political representatives. "Patients can provide a tremendous role by getting to know their congress members and telling them their story, and letting them know what they struggle with and how medical research can really change their lives or has changed their lives," says Dr. Torgerson. "They [congressional representatives] have people from all sides telling them how to spend the money, and our voices need to be heard too. ... [They] need to hear about the importance of funding NIH and understand that for every dollar that they put in there, it generates more income in the long run because new discoveries generate new companies, new therapeutics and all kinds of things that generate jobs, etc."

The IDF and AARDA websites (www.primaryimmune.org and www.aarda.org, respectively) both have tools to help you contact your congressional representatives, as does the *IG Living* website (www.igliving.com). The IDF even has a "Grassroots Advocacy Toolkit" that teaches the basics of letter and email writing, telephoning legislators, writing letters to the editor and other skills. According to its website: "You don't need to be a professional lobbyist to influence how policy and legislation are created. ... All you need is personal experience, factual information to back up your personal experience, knowledge of who the key decision-makers [are] and what is most likely to influence them. IDF can provide the factual and political information necessary for a successful advocacy campaign."

Another way to support research is to participate directly by filling out questionnaires and surveys or taking part in clinical trials. The IDF, AARDA and JMF (www.info4pi.org or www.jmfworld.org) have online surveys, which can be completed anonymously, in support of gathering data that can be used for a number of purposes. The USIDNet (www.usidnet.org) also offers surveys and maintains a national patient registry for

the purposes of "providing a minimum estimate of the prevalence of each disorder in the United States, providing a comprehensive clinical picture of each disorder and providing a resource for clinical and laboratory research." To learn more about clinical trial opportunities in the U.S., visit the USIDNet or NIH-sponsored website at www.clinicaltrials.gov.

Finally, if individuals are able to donate money or participate in fundraising events, there are a number of options. For those interested in funding a specific area of research or a specific researcher, the best way to give may be directly to their institution. For instance, a gift fund can be given to a hospital and designated how it is to be spent. The JMF website has a map of the Jeffrey Modell Centers Network, a system of more than 50 diagnostic and research centers worldwide and physicians at 138 academic teaching hospitals and medical schools. At Children's Hospital in Seattle, the families and some of the older patients run a local immunodeficiency research guild.

They have several events each year to raise funds for research at the hospital. Activities in the past have included barbecues, Mariners baseball games and a day at the zoo. Individuals also can contribute to one of the aforementioned nonprofit organizations. Although there may not be a lot of input on how the money gets spent unless contributing a substantial amount, the foundations do lots of wonderful things with the donations.

"Just get involved," says Dr. Torgerson. "I know that it's difficult

and it's just one more thing to add to a busy schedule, but these things won't move forward unless people get involved. We are so incredibly grateful for the willingness of people to give of themselves whether it is research samples or money, or time to run a guild or participate in events, or write to their congress members."

There is power in numbers, and our voices need to be heard. ■

Whereas current therapies for PIDDs and autoimmune diseases focus on controlling symptoms, stem cell transplantation may offer a future cure for many of the conditions.

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



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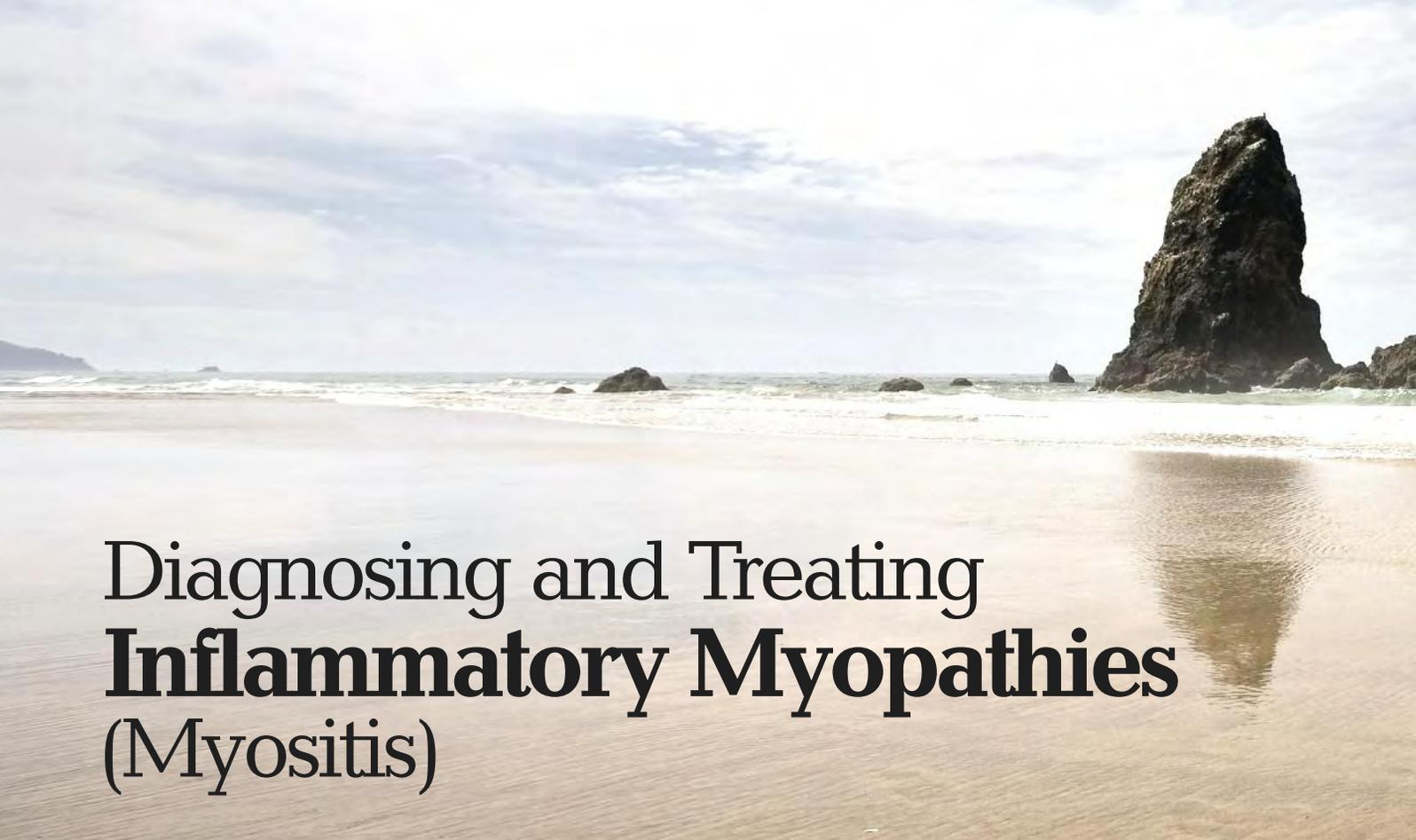
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Diagnosing and Treating Inflammatory Myopathies (Myositis)

Once myositis is diagnosed, there are several methods for treating and managing it, as well as many ways in which patients can seek help and get involved.

While more is becoming known about inflammatory myopathies, they are still rare and making a diagnosis can often be a lengthy process. Myositis is the medical term used to describe a number of inflammatory myopathies, including dermatomyositis (DM), polymyositis (PM), inclusion-body myositis (IBM) and juvenile forms of myositis (JM).¹ In the U.S., myositis affects about one out of every 100,000 people. PM and DM are most common in women, with symptoms often occurring at about age 50, whereas IBM affects men more often, usually occurring around age 60.²

Myositis causes a swelling of the muscles and is believed to be an autoimmune disease, which means the body's immune system mistakenly attacks its own normal, healthy tissue through inflammation. It can be caused by injury, infection, certain medicines and even exercise. But, most forms of myositis are temporary and the swelling goes away after treating the injury or infection, after resting the muscles from exercise or after discontinuing the use of the medication.¹

Myositis Symptoms

While all forms of myositis can cause muscle weakness, all differ in their symptoms.¹

DM signs include a rash on the eyelids, cheeks, nose, back, upper chest, elbows, knees and knuckles; scaly, dry or rough skin; trouble rising from a seated position or getting up after a fall; and general tiredness. Individuals who have DM often experience a painful and/or itchy rash; sudden or progressive weakness in muscles in the neck, hip, back and shoulder; difficulty swallowing or a feeling of choking; hardened lumps or sheets of calcium under the skin; and a hoarse voice.

Sudden or gradual weakness in the muscles, difficulty swallowing, falling and difficulty getting up from a fall and general feelings of tiredness all are signs of PM. Individuals who have PM often experience weakness in the muscles closest to the center of their body, such as their forearms, thighs, hips, shoulders, neck and back. Sometimes they experience weakness in their fingers and toes. And, there could also be a thickening of the skin on their hands.

Common signs of IBM include frequent falling episodes,



By Ronale Tucker Rhodes, MS

trouble climbing stairs or standing from a seated position, a foot that drops while walking, weakened hand grip and difficulty swallowing. Muscle weakness is the main symptom, and occurs in the forearm muscles, muscles below the knees, flexor muscles of the fingers, throat muscles and quadriceps. The quadriceps also noticeably shrink. And, as the muscles weaken, there is often pain and discomfort.

JM signs include a visible, reddish-purple rash over the eyelids or joints; tiredness; moodiness or irritability; stomachaches; difficulty climbing stairs, standing from a seated position or getting dressed; difficulty reaching up; and trouble lifting the head. Kids suffering from JM usually experience a rash, gradual muscle weakness, hardened lumps or sheets of calcium under the skin, trouble swallowing, a hoarse-sounding voice and stomach problems.

Making a Diagnosis

While all forms of myositis are difficult to diagnose, DM is the easiest to diagnose because a skin rash often appears before muscle weakness. Both the rash, which

looks patchy, dusky and reddish or purple, and the muscle weakness are caused by inflammation in the blood vessels under the skin and in the muscles, which is also known as vasculitis. Individuals who experience the rash but not the muscle weakness have amyopathic DM (or DM sine myositis).¹

When diagnosing PM, it is common for each case to be quite different from the others. Individuals who have PM often have one or more other autoimmune diseases. And, in some instances, cases originally diagnosed as PM that do not respond to treatment are later found to be IBM. With IBM, a small number of cases may be hereditary (h-IBM), but most are sporadic (s-IBM), which means there is no genetic link.¹

JM may be diagnosed as either juvenile dermatomyositis (JDM) or juvenile polymyositis (JPM). The difference is that with JDM, there also is a rash.¹

To diagnose myositis, a number of tests and examinations can be conducted. Conventional blood tests will be conducted to look for elevated levels of muscle enzymes in patients' blood samples. Muscle and skin biopsies will show abnormalities in muscles, including inflammation,

damage and abnormal proteins. Electro-diagnostic tests also will be conducted and include muscle resonance imaging (MRI) scans to reveal inflammation in muscles, as well as electromyograms (EMGs) to detect changes in muscles' electrical patterns that indicate muscle disease and which muscles are affected. And, last, antibody testing will confirm a myositis diagnosis and provide insight into the possible course of the disease and its potential complications.³

Getting Treatment

Since myositis is such a rare disease, the medical community does not have a standard approach to treating the illness. And, it can be a challenge for doctors to decide how best to address the symptoms. Myositis affects individuals differently, and no one type of medication works for all patients.⁴

However, what is known is that there is no cure for myositis. And, it is necessary to manage the disease to reduce inflammation and to prevent muscle weakness from progressing. Managing the disease involves two approaches: medical treatment and lifestyle management changes.⁵

All forms of myositis are treatable, with the exception of IBM. Those with IBM get progressively weaker with time and need to prepare for the imminent limitations in their strength and mobility. While doctors sometimes prescribe prednisone (corticosteroids) for IBM, followed by methotrexate or azathioprine, if there is no improvement in their condition, the treatment is discontinued.⁶

Individuals with DM, PM and JM have active periods of the disease that occur as "flares," and typically respond to treatment in a month or two and generally regain strength after two to three months.⁵ The first line of treatment, which is mandated by insurance companies, is corticosteroids or prednisone, which dampens inflammation and the immune response by interfering with the processing of antigens and with the early triggering of T cell and B cell production and, later, proliferation of B cells and T cells (cells that are produced by the immune system in autoimmune disease).⁷ For long-term control of the disease and

to reduce the long-term side effects of prednisone, methotrexate or azathioprine is usually prescribed. Both of these drugs also interfere with the proliferation of B cells and T cells.^{6,7}

If individuals fail to respond to prednisone or have serious side effects from the drug, intravenous immune globulin (IVIG) and other immunosuppressive medications may be prescribed. These other medications include cyclosporine (Neoral, Sandimmune); tacrolimus (Prograf) or mycophenolate (Cellcept). All of these also keep T cells from stimulating the production of more T cells and B cells.^{6,7}

Successful IVIG Treatment for Myositis

The use of IVIG to treat DM and PM is controversial, and myositis is not a U.S. Food and Drug Administration (FDA)-approved indication for IVIG. However, many reports have shown that IVIG has been a successful therapy in the management of this disease. In one case, a 66-year-old Caucasian female with primary idiopathic PM was admitted to the hospital. On the eighth day of hospitalization, she was started on a pulsating dose of 500 mg of intravenous methylprednisolone. The next day, she had progressive muscle weakness, hypotension and respiratory failure and was transferred to intensive care. Treatment with methylprednisolone was continued, as well as 60 mg of prednisone and pulsating treatment of cyclophosphamide — all of which were unsuccessful. On her 13th day in the hospital, she was treated with IVIG 0.04 kg/day for five days, and her clinical state started to improve with mild improvement of dysphagia and muscle strength. After five weeks in intensive care, the patient was transferred back to the internal clinic, and it was determined that IVIG was an effective therapeutic strategy.⁸

In a double-blind, placebo-controlled trial, 15 patients with DM were randomly selected to receive one monthly infusion of high-dose IVIG or a placebo for three months, at the end of which they had the option to cross over to the other treatment. Initially, eight were assigned to IVIG and seven to the placebo. After crossing over, a total of 12 patients had received IVIG. Nine of the patients, who were severely disabled, experienced major improvement and

Since myositis is such a rare disease, the medical community does not have a standard approach to treating the illness.

resumed almost normal function, two patients showed mild improvement and one had no change in condition. Of the 11 patients on the placebo, none showed a major improvement, three had mild improvement, three had no change in condition and five had a worsening of the condition. In addition, four of the patients who crossed over to the placebo after major improvement with IVIG returned to their original condition of disability, and two returned to wheelchairs. The only reported side effects to the IVIG were headaches during the course of the 12-hour infusion.⁹

It should be noted that while it is said that there is no treatment for IBM, there have been studies conducted to determine the effectiveness of IVIG in treating the disease. In one double-blind, placebo-controlled, cross-over study, 22 IBM patients ages 32 to 75 received IVIG or a placebo for six months each, followed by the alternative treatment. After six and 12 months, the response to treatment was evaluated using a modified Medical Research Council scale known as Neuromuscular Symptom Score (NSS), the patient's own assessment of improvement, arm outstretched time and electromyography. Overall, there was no progression of the disease in 90 percent of the patients. A mild and significant improvement (11 percent) in clinical symptoms was found using NSS, but not with the other test procedures. There was a trend in mild improvement in treated patients when using other tests. And, there were no serious side effects.¹⁰

In a second study of IVIG treatment for IBM using the same study design, 19 patients were given monthly infusions of 2g/kg IVIG or a placebo for three months. Patients crossed over to the alternate treatment after a washout period, and responses were evaluated at baseline and at the end of each treatment period using expanded (0-10) MRC scales, the Maximum Voluntary Isometric Contraction (MVIC) method, symptom and disability scores and quan-



titative swallowing studies. Of the 19 patients, nine were randomized to IVIG and 10 to the placebo. During IVIG, the patients gained a mean of 4.2 MRC points, and during the placebo, they lost 2.7 points. Similar results were obtained with the MRC and MVIC scores when the patients crossed to the alternative treatment. Six patients had a functionally important improvement by more than 10 MRC

points that declined when crossed over to the placebo. Limb-by-limb analysis demonstrated that during IVIG, the muscle strength in 39 percent of the lower-extremity limbs significantly increased compared with the placebo, while a simultaneous decrease in 28 percent of other limbs was detected. In addition, the duration of swallowing functions measured in seconds with ultrasound improved statistically in the IVIG patients compared with the placebo.¹¹

Both of these studies determined that IVIG may be mildly effective in treating IBM by preventing disease progression or inducing mild improvement. However, whether those modest gains justify the high cost of trying IVIG remains unclear.^{10,11}

Most insurance companies have medical policies outlining IVIG coverage.

The Insurance Component

The high cost of treatment is often a factor when determining whether to treat myositis with IVIG, and as stated earlier, IVIG is not an FDA-approved indication. Most insurance companies have medical policies outlining IVIG coverage. The guidelines to establish those medical policies are based upon peer-reviewed published studies, also referred to as evidenced-based medicine.¹²

In addition, most insurance companies have coverage guidelines for both PM and DM that determine whether IVIG will be covered. These guidelines mandate that the patient and/or their physician provide the company with a history of disease, muscle biopsy, lab results and other medications that have been tried but that failed, such as steroids and immunosuppressants. Once an insurance company agrees to cover IVIG for PM or DM, continued

coverage depends upon the patient's response, including whether symptoms diminish and/or resolve and ensuring that IVIG isn't making the condition worse. Currently, IVIG for IBM is considered investigational only; studies are not conclusive enough to warrant coverage.¹²

The Lifestyle Management Component

Lifestyle management changes can help patients to restore their strength. These include exercise, rest, stress reduction and nutrition.

Once drug treatment has been started, physicians

A Man on a Myositis Mission

When Steve Morris was diagnosed with giant cell myositis in 2006, he was determined. At first, he was determined to beat it. Then, he was determined to raise money to find treatments and raise awareness of the disease. Now, he's determined to reach out to others to help them overcome the obstacles they face.

After his diagnosis, Morris searched the Internet for any information that would help him to better understand his disease. He discovered The Myositis Association (TMA) website and its discussion board, on which he posted that, someday, he wanted to start his own foundation (Mo Beta Foundation) to help those with myositis. Since he went into remission six months after his diagnosis, he also posted that he was planning a benefit ride on his Harley motorcycle to Sturgis, S.D. In response, someone at TMA headquarters contacted him, and Morris decided to raise funds through the association's website "since they had everything in place to do that."

Morris decided to take his fundraising mission to Canada, riding 4,500 miles in 14 days to Vancouver. "This time, I had the great pleasure of meeting people along the route that actually suffered from myositis," Morris explains. "In Vancouver, we rode up on the busiest street corner in the city, and we were greeted by numerous people. They had a band playing, banners up and were doing some fundraising of their own. We felt like rock stars!" The ride raised \$10,000.

Morris has two more fundraising events planned. The first is a 90-minute endurance race at Pole Position, an indoor kart racing company, in which teams of three to five people will race as a tag team, and the team with the most laps wins. The second is a golf tournament to be held some time in 2011 or 2012. More information about both events can be found on his website at www.riding4thosewhocant.org.

After his first fundraising event, Morris was contacted again by TMA and asked to speak on its patient panel at its 2007 National Conference in Seattle. He has continued to speak at TMA's conference annually. When he speaks, he says, "I always do about 10 to 15 minutes of humor. I always say [that] if you ain't laughing, you're crying! Most of the humor is just life stuff that might not have been funny at the time, but is now hilarious. Sometimes I think we get too caught [up] in our disease that we forget to laugh." To hear some of Morris' humor at the 2009 Charlotte, N.C., conference, go to www.youtube.com/watch?v=5yXTXpjGWIA.

According to Morris, he always ends his speeches with a couple of ideas that he takes to heart in his own life. The first is: I have myositis, but myositis does not have me. "I try not to let my disease consume me and dictate how I will live life," Morris explains. "I have a life that is truly blessed. My disease has opened my eyes to what I can do for others, instead of always thinking about what I can do for myself. I now feel more fulfilled. If not for this disease, I would not have been able to do some of the most incredible things that I have had the pleasure of doing." The second thing he always ends his speeches with: Any day you wake up on this side of the dirt is a pretty good day.



In 2007, Morris went on his first "Riding for Those Who Can't ... Yet" fundraiser, riding from his home in Southern California to Sturgis, S.D., and raising \$15,000, not to mention a great deal of awareness about myositis. In 2008,

can prescribe a program of regular stretching exercises to help maintain range of motion in weakened arms and legs. Individuals may also want to enroll in physical therapy to help prevent permanent muscle shortening. In addition, it can be beneficial to add whirlpool baths, heat and gentle massage as part of their treatment.⁵

Getting enough rest also can help to manage myositis. Frequent breaks should be taken throughout the day, and activity should be limited. In addition, myositis patients need to find outlets to release daily stress in their lives. Relaxation exercises, such as yoga or biofeedback, can help.⁵

What individuals eat also can affect their overall health. Because treatment for myositis often requires courses of steroids to fight muscle inflammation, weight gain is frequently a result, which can make symptoms even more difficult to deal with.⁵ As such, a healthful diet is extremely important. Also, individuals with PM may be at increased risk of celiac disease. If so, a gluten-free diet may be necessary to improve signs and symptoms of celiac disease. However, a gluten-free diet will not improve signs and symptoms of polymyositis. Individuals who have PM, as well as unexplained diarrhea, may want to get tested for celiac disease.¹³

Participating in Clinical Trials

Doctors can greatly benefit from additional information about medications that treat myositis, but “the ability of scientists to study effective treatments for the illness ... is limited by the small number of patients that participate in rare disease studies,” says Lawrence J. Kagan, MD, attending rheumatologist at the Hospital for Special Surgery and professor of medicine at Weill Cornell Medical College. Research studies on the effectiveness of treatments for myositis are unlike those for other diseases, such as lupus or rheumatoid arthritis, which have hundreds or even thousands of patients. Yet, for the FDA to approve a drug, such as IVIG, a proven track record clearly illustrating patient benefit must be present.⁴

Therefore, individuals with myositis are highly encouraged to take part in research. For information about new, ongoing and completed studies, visit The Myositis Association website at www.myositis.org or visit the U.S. National Institutes of Health's ClinicalTrials.gov website at <http://www.clinicaltrials.gov/ct/search;jsessionid=D9D2A78BB81C717131DA90D4EDBB3E54?term=inflammatory+myopathy&submit=Search>.

Getting More Information

A host of resources are available to individuals interested in finding out more about myositis. The *IG Living* website has a list of resources at www.igliving.com. And, The Myositis Association also has a list of resources at <http://www.myositis.org/template/page.cfm?id=105>.

While there are still many unknowns about diagnosing and treating myositis, it can be managed. Patients must take an active role in their own treatment, and they should get involved to improve the diagnosis and treatment options for the future. ■

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

References

1. The Myositis Association. About Myositis. Accessed at <http://www.myositis.org/template/page.cfm?id=2>.
2. Everyday Health. Myositis: What Is It? Accessed at <http://www.everydayhealth.com/health-information/myositis-what-is-it.aspx>.
3. The Myositis Association. About Myositis: Diagnosis. Accessed at <http://www.myositis.org/template/page.cfm?id=>
4. Kagen, Lawrence J. A Doctor's Perspective on Treating Patients with Myositis. Accessed at http://www.hss.edu/conditions_Doctor's-Perspective-Treating-Myositis-Patients.asp.
5. Johns Hopkins Medicine. Myositis Treatment Information. Accessed at www.hopkinsmedicine.org/myositis/differences/treatment.html.
6. The Myositis Association. About Myositis: Frequently Asked Questions. Accessed at <http://www.myositis.org/template/page.cfm?id=13>.
7. MDA Publications. Facts About Inflammatory Myopathies (Myositis): PM and DM Treatments. Accessed at <http://www.mdaua.org/publications/fa-myosi-pmdmchart.html>.
8. Kristofova, B, Oetterova, M, Valocikova, I, Macejova, Z, Pidanicova, A, Firmont, J, Majernik, M, and Lazurova, I. Successful therapy with intravenous immunoglobulin in the management of polymyositis. *Bratisl Lek Listy*, 2008; 109(9).
9. National Institute of Neurological Disorders and Stroke. Study Shows IVIG Safe, Effective Treatment for Muscle Disease. December 29, 1993. Accessed at www.ninds.nih.gov/news_and_events/news_articles/presrelease_dermatomyositis_122993.htm.
10. Walter, MC, Lochmuller, H, Toepfer, M, Schlotter, B, Reilich, P, Schroder, M, Muller-Felber, W, and Pongratz, D. High-dose immunoglobulin therapy in sporadic inclusion body myositis: a double-blind, placebo-controlled study. *Journal of Neurology*, January 2000, 247(1).
11. Dalakas, MC, Sonies, B, Dambrosia, J, Sekul, E, Cupler, E, and Sivakumar, K. Treatment of inclusion-body myositis with IVIG: a double-blind, placebo-controlled study. *Neurology*, 1997 Mar; 48(3): 712-6.
12. Vaughan, Leslie J, RPh. IVIG Therapy. Slideshow presentation. Accessed at <http://www.myositis.org/pdf/IVIG%20in%20service%20for%20TMA%20mtg.pdf>.
13. MayoClinic.com Polymyositis: Can a gluten-free diet reduce symptoms? Accessed at <http://www.mayoclinic.com/health/polymyositis/AN00572>.

Flebogamma® 5% DIF

Immune Globulin Intravenous
(Human)



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*Laser etched identifier number may at times be covered by the label.

(1) Mean value from 97 consecutive lots, data on file, Instituto Grifols, S.A.

(2) Berger M et al. A Multicenter, Prospective, Open Label, Historically Controlled Clinical Trial to Evaluate Efficacy and Safety in Primary Immunodeficiency Diseases (PID) Patients of Flebogamma 5% DIF, the Next Generation of Flebogamma. J Clin Immunol 2007;27:628-633.



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Flebogamma® 5% DIF is indicated for replacement therapy in primary humoral immunodeficiency disorders

Important Safety Information

Immune Globulin Intravenous (Human) (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. 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. Flebogamma® 5% DIF does not contain sucrose. See PRECAUTIONS and DOSAGE AND ADMINISTRATION sections for important information intended to reduce the risk of acute renal failure.

Flebogamma® 5% DIF is made from human plasma. As with all plasma derived products, the risk of transmission of infectious agents, including viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated. Flebogamma® 5% DIF should not be administered to individuals with a history of severe or anaphylactic reactions to blood or blood-derived products. Patients with severe selective IgA deficiency (IgA < 0.05 g/L) may develop anti-IgA antibodies that can result in a severe anaphylactic reaction. Anaphylaxis can occur using Flebogamma® 5% DIF even though it contains low amounts of IgA (typically < 50 µg/mL). If patients are known to be intolerant to any component of Flebogamma® 5% DIF, such as sorbitol (i.e., intolerance to fructose), they should not receive the product. An aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with IGIV treatment. AMS may occur more frequently in association with high-dose (e.g., > 1.0 g/kg body weight) and/or rapid-infusion IGIV treatment. Thrombotic events have been reported in association with IGIV. Patients at risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired

cardiac output, and/or known or suspected hyperviscosity. There have been reports of non-cardiogenic pulmonary edema [Transfusion-Related Acute Lung Injury (TRALI)] in patients administered IGIV. Immune Globulin Intravenous (Human) (IGIV) products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Reported adverse reactions with Flebogamma® 5% DIF and other IGIV products include: headache, chills, fever, shaking, fatigue, malaise, anxiety, back pain, muscle cramps, abdominal cramps, blood pressure changes, chest tightness, palpitations, tachycardia, nausea, vomiting, cutaneous reactions, wheezing, rash, arthralgia, and edema, often beginning within 60 minutes of the start of the infusion. Rarely, Immune Globulin Intravenous (Human) can induce a severe fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with IGIV. In the case of shock, the current standard medical treatment for shock should be implemented. **Please refer to adjacent Brief Summary of the Prescribing Information.**

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**Immune Globulin Intravenous (Human)
Flebogamma® 5% DIF
For intravenous use only
Rx only**

BRIEF SUMMARY

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INDICATIONS AND USAGE

Flebogamma® 5% DIF is indicated for replacement therapy in primary (inherited) humoral immunodeficiency disorders.

DOSAGE AND ADMINISTRATION

The usual dose of Flebogamma® 5% DIF for replacement therapy in primary humoral immunodeficiency diseases is 300 to 600 mg/kg body weight administered every 3 to 4 weeks.

An in-line filter with a pore size of 15 to 20 microns is recommended for the infusion. Antibacterial filters (0.2 micron) may also be used. Discard unused contents and administration devices after use.

The infusion of Flebogamma® 5% DIF should be initiated at a rate of 0.01 mL/kg body weight/minute (0.5 mg/kg/minute). If, during the first 30 minutes, the patient does not experience any discomfort, the rate may be gradually increased to a maximum of 0.10 mL/kg/minute (5 mg/kg/minute).

For patients judged to be at risk for developing renal dysfunction or considered to be at increased risk of thrombotic/thromboembolic events, it may be prudent to limit the infusion rate to a maximum rate less than 0.06 mL/kg body weight/minute (3 mg/kg/minute). Reduction in dose, concentration, and/or rate of infusion in patients at risk of acute renal failure, which includes patients over 65, has been proposed in the literature in order to reduce the risk of acute renal failure.

CONTRAINDICATIONS

Flebogamma® 5% DIF should not be administered to individuals with a history of severe or anaphylactic reactions to blood or blood-derived products. Patients with severe selective IgA deficiency (IgA < 0.05 g/L) may develop anti-IgA antibodies that can result in a severe anaphylactic reaction. Anaphylaxis can occur using Flebogamma® 5% DIF even though it contains low amounts of IgA (typically < 50 µg/mL). Such patients should only receive intravenous immune globulin with utmost caution and in a setting where supportive care is available for treating life-threatening reactions. If patients are known to be intolerant to any component of Flebogamma® 5% DIF, such as sorbitol (i.e., intolerance to fructose), they should not receive the product.

WARNINGS

Immune Globulin Intravenous (Human) (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. 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. Flebogamma® 5% DIF does not contain sucrose. See PRECAUTIONS and DOSAGE AND ADMINISTRATION sections for important information intended to reduce the risk of acute renal failure.

Flebogamma® 5% DIF is made from human plasma. As with all plasma derived products, the risk of transmission of infectious agents, including viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated. The risk that such products will transmit an infectious agent has been greatly 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. ALL infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Grifols Biologicals at 888-GRIFOLS (888-474-3657).

All patients, but especially individuals receiving Flebogamma® 5% DIF for the first time or being restarted on the product after a treatment hiatus of more than 8 weeks, may be at risk for the development of inflammatory reactions characterized by fever, chills, nausea, and vomiting. Careful monitoring of recipients and adherence to recommendations may reduce the risk of these types of events.

Appropriate supportive care, including immediate access to epinephrine injection, should be available for the management of acute anaphylactic reactions.

PRECAUTIONS

General:

Any vial that has been entered should be used promptly. Partially used vials should be discarded and not saved for future use because the solution contains no preservative. Do not use if turbid. Solution that has been frozen should not be used. Ensure that patients are not volume-depleted before the initiation of the infusion of IGIV.

Renal Function:

Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk for developing acute renal failure. Renal function, including measurement of blood urea nitrogen (BUN)/serum creatinine, should be assessed before the initial infusion of Flebogamma® 5% DIF and again at appropriate intervals thereafter. If renal function deteriorates, discontinuation of the product should be considered.

For patients judged to be at risk for developing renal dysfunction, it may be prudent to reduce the amount of product infused per unit time by infusing Flebogamma® 5% DIF at a maximum rate less than 0.06 mL/kg (3 mg/kg) body weight/minute.

Aseptic Meningitis Syndrome:

An aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with IGIV treatment. The syndrome usually begins within several hours to 2 days following IGIV treatment. It is characterized by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, and nausea and vomiting. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per cubic milliliter, predominantly from the granulocytic series, and with elevated protein levels up to several hundred mg/dL. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. AMS may occur more frequently in association with high-dose (e.g., > 1.0 g/kg body weight) and/or rapid-infusion IGIV treatment. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.

Hemolysis:

Immune Globulin Intravenous (Human) (IGIV) products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration [See ADVERSE REACTIONS]. IGIV recipients should be monitored for clinical signs and symptoms of hemolysis [See PRECAUTIONS: Laboratory Tests].

Thrombotic Events:

Thrombotic events have been reported in association with IGIV (See ADVERSE REACTIONS). Patients at risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, and/or known or suspected hyperviscosity. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies [See PRECAUTIONS: Laboratory Tests].

Transfusion-Related Acute Lung Injury (TRALI):

There have been reports of non-cardiogenic pulmonary edema [Transfusion-Related Acute Lung Injury (TRALI)] in patients administered IGIV. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever and typically occurs within 1 to 6 hours after transfusion.

Patients with TRALI may be managed by using oxygen therapy with adequate ventilatory support. IGIV recipients should be monitored for pulmonary adverse reactions. If TRALI is suspected, appropriate tests should be performed for the presence of antineutrophil antibodies in both the product and patient serum [See PRECAUTIONS: Laboratory Tests].

Information For Patients:

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.

It is recommended that the lot number of the vials used be recorded when Flebogamma® 5% DIF is administered.

Laboratory Tests:

Renal function, including measurement of blood urea nitrogen (BUN)/serum creatinine, should be assessed before the initial infusion of Flebogamma® 5% DIF in patients judged to have a potential increased risk for developing acute renal failure and again at appropriate intervals thereafter.

Following infusion of Flebogamma® 5% DIF, there may be a transitory rise of various antibody titers that may result in misleading positive results in serological testing. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. If TRALI is suspected, appropriate tests should be performed for the presence of antineutrophil antibodies in both the product and patient serum.

Pregnancy Category C:

Animal reproduction studies have not been performed with Flebogamma® 5% DIF. It is also not known whether Flebogamma® 5% DIF can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Flebogamma® 5% DIF should be given to a pregnant woman only if clearly needed.

Drug Interactions:

Antibodies in Flebogamma® 5% DIF may interfere with the response to live viral vaccines, such as measles, mumps, and rubella. Physicians should be informed of recent therapy with Immune Globulin Intravenous (Human) so that administration of live viral vaccines, if indicated, can be appropriately delayed 3 or more months from the time of IGIV administration.

Pediatric Use:

The above mentioned clinical trial with Flebogamma® 5% DIF enrolled only a very limited number of children (0) and adolescents (3) with primary humoral immune deficiency, a number insufficient to fully characterize and establish the efficacy and safety in pediatric patients.

Geriatric Use:

Subjects over 65 are at increased risk of renal failure with IGIV treatment. For these subjects, and for any other subjects at risk of renal failure, the infusion rate of Flebogamma® 5% DIF should be limited to < 0.06 mL/kg/min (3 mg/kg/min).

Adverse Reactions

Increases of creatinine and blood urea nitrogen (BUN) have been observed as soon as 1 to 2 days following infusion of IGIV. Progression to oliguria and anuria requiring dialysis has been observed, although some patients have improved spontaneously following cessation of treatment. Types of severe renal adverse reactions that have been seen following IGIV therapy include: acute renal failure, acute tubular necrosis, proximal tubular nephropathy, and osmotic nephrosis.

Certain severe adverse reactions may be related to the rate of infusion. The recommended infusion rate [See DOSAGE AND ADMINISTRATION] must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. Adverse reactions may occur more frequently when a high infusion rate is used, the treatment is the initial exposure to immunoglobulin, the immunoglobulin product has been changed to that of a different manufacturer, or there has been a long interval (more than 8 weeks) since the previous infusion. Slowing or stopping an infusion usually results in the prompt disappearance of symptoms.

Post-Marketing:

The following adverse reactions have been identified and reported during the post-approval use of IGIV products.

Respiratory	Apnea, Acute Respiratory Distress Syndrome (ARDS), Transfusion-Related Acute Lung Injury (TRALI), cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm
Cardiovascular	Cardiac arrest, thromboembolism, vascular collapse, hypotension
Neurological	Coma, loss of consciousness, seizures, tremor
Integumentary	Stevens-Johnson Syndrome, epidermolysis, erythema multiformae, bullous dermatitis
Hematologic	Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs) test
General/Body as a Whole	Pyrexia, rigors
Musculoskeletal	Back pain
Gastrointestinal	Hepatic dysfunction, abdominal pain

Because post-marketing reporting of these reactions is voluntary and the at-risk populations are of uncertain size, it is not always possible to reliably estimate the frequency of the reaction or establish a causal relationship to exposure to the product. Such is also the case with literature reports authored independently.

Adverse events were reported in a study of 46 individuals with primary humoral immunodeficiency diseases receiving infusions every 3 to 4 weeks of 300 to 600 mg/kg body weight. Forty-three (94%) subjects experienced at least 1 adverse event

irrespective of the relationship with the product, and these subjects reported a total of 595 adverse events. None of the 46 subjects who participated in this study discontinued the study prematurely due to an adverse experience related to the study drug. One subject had treatment-emergent bronchiectasis, mild, ongoing, after infusion #10; and one subject had recurrent moderate leukopenia after the 7th and 12th infusions. No adverse events occurred with an incidence of > 2% on a per infusion basis.

Table 1. Adverse Events Occurring with an Incidence of > 15%

Adverse Event	Number of AEs	Number of Subjects with AEs	Percent of Subjects with AEs
Combined Bronchitis	19	14	30
Cough and productive cough	10	10	22
Diarrhea NOS ^a	14	9	20
Headache NOS and sinus headache	46	16	35
Nasal congestion	11	7	15
Injection site reaction NOS	13	7	15
Pyrexia	27	17	37
Arthralgia	11	7	15
Sinusitis NOS	38	20	44
Pharyngitis	9	8	17
Upper respiratory tract infection	24	15	33
Wheezing and asthma aggravated	24	10	22

a. NOS = not otherwise specified

The total number of AEs (regardless of attribution) reported whose onset was within 72 hours after the end of an infusion of Flebogamma® 5% DIF was 216. There were a total of 709 infusions, resulting in a rate of 0.305 (95% confidence interval 0.225 to 0.412) temporally associated AEs per infusion. There were 144 infusions (20.1%, 1-sided 95% upper bound confidence interval = 24.4%) associated with 1 or more AEs that began within 72 hours after the completion of an infusion.

Table 2. Summary of Infusions with Mild, Moderate, and Severe Treatment-Related Adverse Events

Severity of AE	No. Infusions with AE	Adjusted % ^a	Confidence Interval ^b
Mild	58	7.9	10.4
Moderate	25	3.6	4.9
Severe	1	0.1	0.3

a. Adjusted % = average of the % of infusions with a treatment-related adverse event for each individual subject.

b. The 95% upper bound for the adjusted % of infusions for which at least 1 treatment-related adverse event was reported was derived by using the t-statistic.

The number and percent of subjects with treatment-emergent rises in AST or ALT are in Table 3.

Table 3. Number (%) of Subjects with Treatment-Emergent Rises in AST or ALT (N = 46)

Laboratory Test	Assessment Criteria	n	%
AST	Above 3x the ULN^a	3	6.5
ALT	Above 3x the ULN	1	2.2

a. ULN = upper limit of normal.

None of these subjects had a concomitant treatment-emergent rise in total bilirubin.

Reported adverse reactions with Flebogamma® 5% DIF and other IGIV products include: headache, chills, fever, shaking, fatigue, malaise, anxiety, back pain, muscle cramps, abdominal cramps, blood pressure changes, chest tightness, palpitations, tachycardia, nausea, vomiting, cutaneous reactions, wheezing, rash, arthralgia, and edema, often beginning within 60 minutes of the start of the infusion.

Rarely, Immune Globulin Intravenous (Human) can induce a severe fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with IGIV. In the case of shock, the current standard medical treatment for shock should be implemented.

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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.



Immune globulin (IG) patients see their share of physicians. But, depending on where and how they get their infusions, they may not have regular contact with their pharmacist. As a result, they may be losing out on a valuable resource within their health maintenance team. This month, we sat down with Amy Ehlers, pharmacist at NuFACTOR FFF Specialty Pharmacy. NuFACTOR is a subsidiary of FFF Enterprises, Inc. Amy offers some valuable insights on how IG patients can best cultivate a mutually beneficial patient/pharmacist relationship.

Trudie: For *IG Living* readers who are unfamiliar with your role at NuFACTOR FFF Specialty Pharmacy, please tell us about your background and training.

Amy: I've been with NuFACTOR since February 2007. I have my bachelor's degree in pharmacy from Ohio Northern University, my doctorate

in pharmacy from the University of Florida, and I am board certified in pharmacotherapy. I worked mainly in a hospital pharmacy prior to coming on board with NuFACTOR.

Trudie: As a specialty pharmacist, how do you build relationships with your patients?

Amy: Building trust and open communication with them is the first and most important step. I can't help a patient if I don't know they are having a problem. I have found it is usually a larger problem that first prompts the patient to contact me, but after that, they are more

While pharmacy is often the last step in the healthcare process, it is often the step that helps put the pieces all together.

likely to call for smaller issues.

Trudie: What are the advantages, from a patient perspective, of developing a relationship with their pharmacist?

Amy: Patients have the ability to

stop small problems from turning into big problems. Pharmacists have long been among the most trusted and accessible members of the healthcare team. There is a reason for this. While pharmacy is often the last step in the healthcare process, it is often the step that helps put the pieces all together. IG patients may only see their physician once a year, but they may see or speak with their pharmacist once a month. This allows the pharmacist to have the most complete and recent picture of the patient's overall health and well-being.

Trudie: What are a few important questions IG patients might ask their pharmacist?

Amy: Most important is to ask questions about anything that is unclear or doesn't make sense regarding their therapy. A patient should feel comfortable with all aspects of their medical care. They should never do something — whether it's a medication, treatment or procedure — just because someone told them to do so. They should get a second opinion if needed. Also, if something doesn't feel right or is out of the normal routine, they need to ask questions! As unfortunate as it is, mistakes happen every day in the U.S. healthcare system. In the aftermath of many of these cases, someone inevitably says that something didn't seem right,

but they didn't stop to question it.

Trudie: Can you share any stories about instances where a patient/pharmacist relationship resulted in a more positive patient outcome?

Amy: I had a patient who was fairly new to Vivaglobin call me. She was having what she described as fairly significant leakage and large red welts that lasted for several days following her infusion. She was getting quite discouraged and was ready to transition back to her monthly intravenous IG (IVIG) infusions, even though she was enjoying the freedom the subcutaneous IG (SCIG) infusions were providing. We worked together to go through the various options to deal with these common side effects. It took several infusions until we found the right combination, which in her case, was a longer needle, slowing the infusion rate and increasing the number of infusion sites. This patient continues to be successful with Vivaglobin today.

Trudie: Many patients think their



Shortly after the earthquake in Haiti in 2009, Amy reached out to the victims when she joined other healthcare providers to care for the injured.

pharmacist needs to be informed only about what other drugs they are taking and their list of allergies. What else is important for a pharmacist to know about a patient?

Amy: It's best to be as thorough with the pharmacy as possible,

It's best to be as thorough with the pharmacy as possible, especially when it comes to IG patients.

especially when it comes to IG patients. It's important for the pharmacist to know how often IG patients are having infections, as this may mean a dose change is needed. Significant changes in weight also are important to note. Also, if a patient is having a problem, being able to provide as much detailed information as possible is helpful, especially when troubleshooting over the phone.

Trudie: Why is it important for a patient to tell the pharmacist about vitamins and herbs and not just medications?

Amy: Vitamins and herbs, while available over the counter and without a prescription, can and do have effects on how prescription medications work. Patients sometimes feel that "it's just a vitamin," but that's not always the case. If the pharmacist doesn't know about it, they

can't account for how it may or may not affect the care they are providing.

Trudie: What kinds of mistakes can a pharmacist help the patient prevent?

Amy: IG patients are very knowledgeable about their disease state and their treatments. However, with the Internet, there are so many websites that no one is policing to make sure that the information is accurate. Sometimes patients read something on a less-than-reliable site and make decisions based on it. If a patient doesn't have the correct knowledge to assess the information and make an informed decision, negative outcomes can occur. It's always best to get a professional opinion before trying something new.

Trudie: How can IG patients better reach out to their own pharmacists?

Amy: They should call or email the pharmacist and introduce themselves. Ask the pharmacist if there is a good time to contact them to ask a few questions about their treatment. Most pharmacists are fairly outgoing and enjoy speaking with patients. And if the pharmacist has been especially helpful, be sure to let them know. While we are always available to solve problems, it's nice to hear how what we do every day impacts a patient's life in a positive way. ■



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: How does selective immunodeficiency affect the digestive system?

Kris: Gastrointestinal (GI) problems are a common complaint in patients with primary immune deficiency disease. I asked Dr. Terry Harville to address your question, and found his answer very informative.

Dr. Harville: This is a very important issue. How antibody deficiencies affect the GI tract is somewhat complex. First, it's important to remember that the GI tract, by some accounts, is the largest immune organ in the body. Throughout the GI tract, aggregates of lymphocytes are collected into areas known as Peyer's patches, which function as food antigen monitors. Even though the GI tract is inside the body, it has tremendous exposure to the outside world, which includes organisms that are not harmful, as well as those that are harmful. The GI tract is highly populated with bacteria, most of which are important for the maintenance of good health. For example, there are bacteria that produce vitamin K, which clots blood and prevents hemorrhage. Without the presence of bacteria, spontaneous bleeding would result.

Throughout the history of human beings, food mostly was consumed raw (i.e., not cleaned or cooked) and was naturally full of bacteria and parasites, giving the immune system the activity it needs to discriminate between harmful and non-harmful

organisms. As a result, much immunity is located along the GI tract to carry out this function. Further, a "normally" functioning immune system prevents organisms that would otherwise not be pathogenic from invading into the tissues. In this way, it helps to maintain a proper balance in the intestines, allowing

How antibody deficiencies affect the GI tract is somewhat complex.

so-called "good" bacteria to remain present, but preventing them from creating a problem by accidentally invading into the tissues.

When an immune system fails to work properly, this normal balance at the interface between the outside world and inner body becomes disrupted, allowing otherwise harmless bacteria to try to invade into the tissues. In addition, pathogenic organisms have an easier time invading into the tissues, which activates the remaining immunity in the GI tract. This results in more localized inflammation, which, in turn, injures the tissues more and allows further invasion of organisms, causing more immune activation and more inflam-

mation. The physical results of this are symptoms such as loose stools, diarrhea, gas, cramping, etc. This chronic activation also may promote the development of autoimmune disease, such as inflammatory bowel disease or celiac disease.

Therefore, in summary, "normal" immunity maintains the integrity of the interface between the outside world and the inner body at the intestines. Immunodeficiency breaks down this integrity, resulting in excessive activation of immunity and inflammation in the intestines in an effort to control the possible invasion of pathogenic organisms, as well as to maintain control of the organisms that are normally present. This excessive inflammation causes GI symptoms, and chronic inflammation can promote the development of autoimmune intestinal disease.

What all this means is that, due to the underlying immunodeficiency, patients with CVID, antibody deficiency, XLA, etc., remain at great risk for developing GI disease. ■



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.

Dr. 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.

Coping with the Non-Coping

By Ever Feckske

I HAVE BEEN living with my common variable immune disease diagnosis for more than five years now, and I am finally settling into it. Yes, my world has been turned upside down, but I have come to peace with it in my mind. My career and going out with friends, which were of paramount importance before my diagnosis, are no longer my first and second priorities. Now, I focus more on what is right for my health and for my body. And, as I am settling in, my family also is getting used to having this new person around, and they are becoming more sensitive to and aware of my disease. They have changed alongside me and have become more accustomed to making accommodations and adjustments that are better for my health.

Yet, while a smooth transition to a new way of being is something all immune-disease patients strive for, there are still people who make things difficult. Most with our condition can relate to dealing with a loved one who is not completely on board — the one who doesn't really understand or doesn't even try to understand. Better yet, the loved one who is in complete denial about the whole thing. So, in addition to coping with our illness, we now have to cope with the people who refuse to cope with it. It's exhausting!

Personally, I have dealt with many hurtful responses made about my illness by individuals like these. I ran into some high school friends who asked, "What happened to you?"



Clearly, they were reacting, rudely, to what the prednisone has done to me physically. It's funny how that situation just made me want to have a cheeseburger. In another instance, a woman in the doctor's office asked me if I was having a boy or a girl. I couldn't decide whether I wanted to run away or kick her in the knee. Instead, I just said, "I don't know." Instead of telling her how I really felt, I decided to protect her so she wouldn't feel embarrassed. It caught me completely off guard. In situations like this, I never come up with the right response, until I get home, of course, and I am able to make up a whole speech of what I would have liked to have said. How does one react in that kind of situation? Should I understand that it's just another awkward situation, or should I be confrontational? It may be educational for them, but I think it would just be strange and uncomfortable for me.

I have had distant family members call me antisocial because I can't work and lazy because I have to take naps on some days. They have tried to get me to work out with a trainer, and they suggest that I should skip lunch. Clearly they don't understand pred-

nisone! If I skip lunch, I may end up eating somebody's arm!

It's most hurtful when family members trivialize what I have to go through. But, I've come to realize that this reaction is their own coping mechanism. I call it "coldness in order to cope." They are hurt and feel bad that I am sick, and they feel defeated and helpless because they can't do anything about it. So they react the way they do to make themselves feel better. Unfortunately, in the end, people who react this way hurt us by denying all we have to go through or by projecting on to us their solution to our condition.

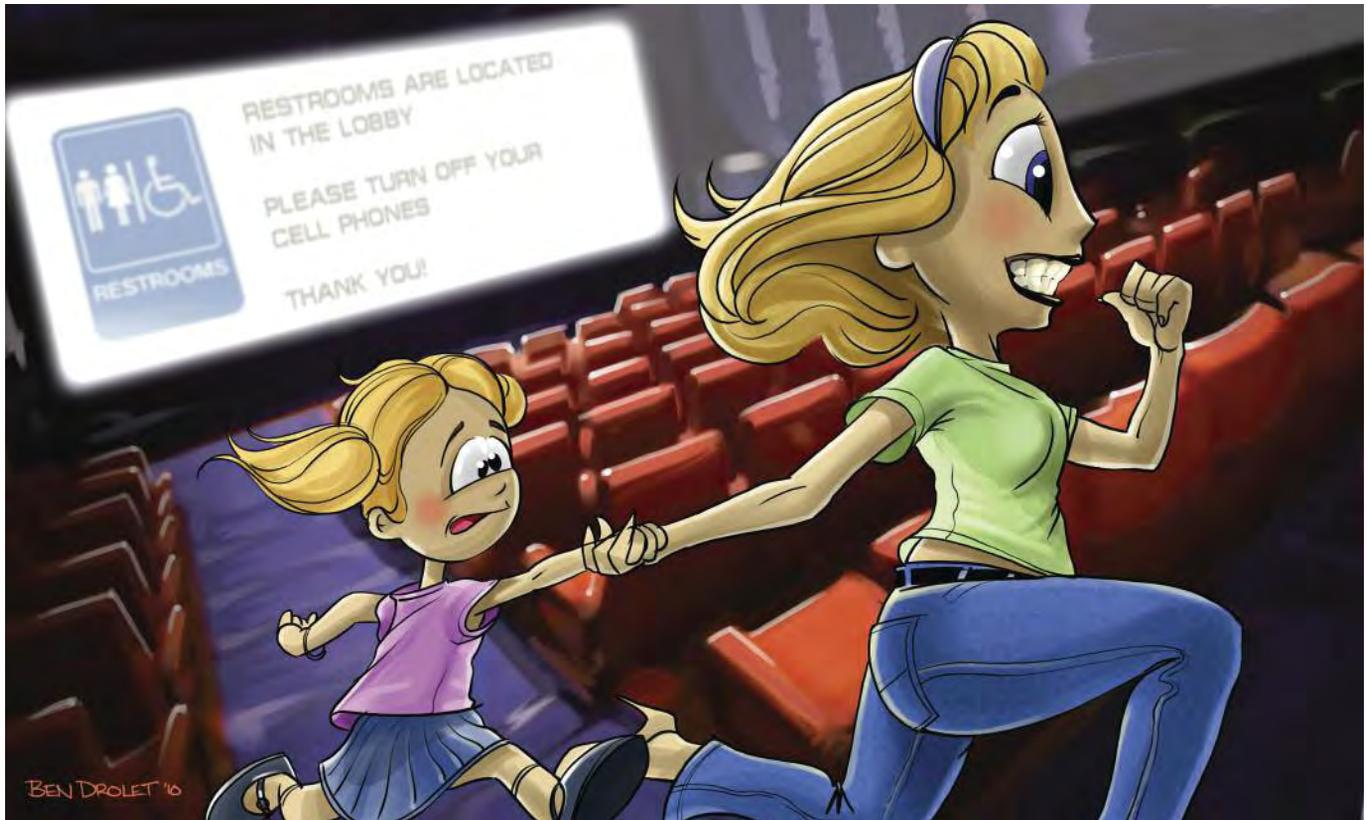
So here is one more thing that we have to add to our "deal with it" list. When people say hurtful things, try to understand it's because they can't cope with the reality of our condition. And if there are times that it would make you feel better to come out and say what you are feeling, do it! Just say, "I have a chronic condition and I can't just get better because you want me to, so deal with it!" Perhaps honesty will help us cope with our reality. All we can do is our best in the moment. ■



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!

Fear This!



By Cheryl L. Haggard

“MOM, CAN WE go to the movies?” my daughter, Molly, begged. “We need a break,” she insisted, and who was I to argue?! Molly had been fighting an unrelenting sinus infection, thanks in part to her common variable immune disease (CVID) and 25 other 8-year-olds from Room 15 at Sunnyside Elementary School.

“Pleeeeeease Mom? We deserve it!” Molly emphatically whined.

The other half of “we” she’s talking about is me, her mom. My recent diagnosis with ankylosing spondylitis and reactive arthritis has turned me into a reluctant weatherwoman fore-

casting rainfall by the intensity of my aches and pains. Studying our scenic Idaho skies, I concluded we were in for a doozie of a thunderstorm, and maybe a chick flick with a bucket of melt-in-your mouth, grease-disguised-as-melted-butter popcorn, Goobers and a frozen Coke to wash it all down wasn’t such a bad idea after all. Perhaps losing ourselves in someone else’s romance might make our icky-snotty-nose-stiff-and-painful-joints-pity-party-no-one-wants-to-join at least go away for a few madcap hours.

But as you know, the immune disorder community doesn’t just go

to the theater; we *adventure* to the theater. Why all the traveling drama? Because all it takes to tick off our T cells (and everything else in our immune systems) is to enter a public place. We must be prepared and arm ourselves with the best germ-fighting paraphernalia available to us: hand sanitizer — bright blue goo that turns germs black for the kids and moisturizing almond and juniper berry scent for me. We also pack plenty of Kleenex, masks, ice packs, Band-Aids, Neosporin sponges, alcohol wipettes and a generous handful of both children’s and adult Motrin. And, depending on who

is on the adventure with us: a six pack of individual servings of chablis.

So after I took out a small personal loan from the credit union to pay for Girls' Day Out (why are popcorn and a pop more expensive than the movie tickets themselves?), I "unhooked" Molly from her Vivaglobin and packed our "adventure basket." Molly crawled into the back seat of the family Suburban and gave me a thumbs up and a cheeky smirk, letting me know her requested "break" was going to go just fine (well, at least for her).

When we entered the lobby of the 60-year-old Egyptian Theater, my feet sank into the plush red carpet while the excitement all around seemed to melt my worries about both of us contracting double pneumonia from this historical place. I stood for a moment studying the gold-painted walls and became caught up in the stories they might tell. I had heard the Egyptian was haunted by a former disgruntled operating engineer who lurks among the heavy, deep purple velvet curtains. A chill crept up my spine as the ticket line grew longer and Molly's patience shorter.

"Come on, Mom! Let's get our tickets before they sell out!" Molly demanded.

"OK, OK! Just a min..."

"Mom! Please!" Molly interrupted, as my fears grew about the boogeyman lurking among the curtains. Some break this is, I whispered to myself. At least if I were at home, I wouldn't be freaking out about ghosts flying around or my scary checkbook.

After Molly and I got our tickets, a familiar female nether-region "twinge" required a necessary detour. And, because I was expecting Molly's 8-year-old bladder to hold 16 ounces of pop through two-and-a-half hours of

watching \$32 million of Hollywood's most beautiful fall in and out of love at least three times over, I figured one trip to the ladies room might be warranted for both of us.

Using public bathrooms is something I try to avoid at all costs. "Normal" folks exit a public bathroom relieved; we leave with rotovirus. So, I take all the necessary precautions, like using paper towels to turn faucets on and off. My most overly cautious trick is to use just about every potty protector before sitting down to do business. But being a sitter isn't very "green"; an entire tree must be sacrificed in order for me to, uh, pee.

I used to be a squatter. In fact, I come from a long line of squatters. Grandma Schwander was a squatter (came naturally to her because she was the outdoorsy type). My mom is the no-nonsense squatter: in, out and done. I was more your athletic-type squatter. I'd actually get in a pretty good leg workout while doing my "thing." As for Molly, she's just about got the Schwander squat down and I (sniff) am very proud of her progress.

"Mom, are you done yet?" Molly hollered from three stalls down. "I wanna get snacks before the movie starts."

"I'll be out in a minute! I'm going as fast as I can!" I replied.

Struggling to get myself all zipped up without touching anything public, I was as anxious as Molly to get to the fun part: FOOD!

Standing in line at the concession stand was overwhelming. Everything looked so good! My mouth began to water at the sight of pretzels dipped in cinnamon sugar and uber-juicy sausages spinning. Classics like Ju Ju Bees, Dots and Junior Mints glistened under the lighted case. Even my lactose-

intolerant entrails coveted a waterfall of soft-serve ice cream cascading slowly into sugar cones. I was officially snack-smitten until a soft tap on my shoulder pulled me away from Candyland.

I turned toward the tapper thinking it was Molly. It wasn't.

"Please tell me you are my long-lost cousin and you are shoving a wad of toilet tissue in my hand because I'm going to start crying."

"No, but I'd want someone to tell me if I had, well, uh..." The tapper struggled, pointing me to the ultimate of human humiliation: a toilet tissue trail running from my derriere to the entrance of the ladies room.

"Well, at least you and your husband will have something to talk about if your movie is a flop!" I laughed, trying to convince the tapper that toilet tissue problems happen to me on a daily basis.

The tapper nodded and quickly found her husband hiding behind a butter kiosk.

Molly and I eventually found our seats and settled in with snacks galore in our laps. We feasted through the previews, desperately trying to forget the previous events and remember what we were there for in the first place: a "break" from our illness.

Then, minutes before the feature film began, Molly and I looked deep into each other's eyes and, in perfect harmony, said, "I have to go to the bathroom!" ■



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



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GAMUNEX[®], Immune Globulin Intravenous (Human), 10% Caprylate/Chromatography Purified, safely and effectively. See full prescribing information for GAMUNEX.

GAMUNEX (Immune Globulin Intravenous [Human], 10% Caprylate/Chromatography Purified) 10% Liquid Preparation

Initial U.S. Approval: 2003

WARNING: ACUTE RENAL DYSFUNCTION and FAILURE

See full prescribing information for complete boxed warning.

- **Renal dysfunction, acute renal failure, osmotic nephrosis, and death may 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 **PROOF** is everywhere you look

GAMUNEX is the IGIV therapy supported by robust clinical trials

- Proven efficacy in more FDA-approved indications (CIDP, PI, and ITP)* than any other liquid IGIV¹

Important Safety Information for GAMUNEX

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).

Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. 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.

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

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

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

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

Reference: 1. Data on file. Talecris Biotherapeutics, Inc.

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

Please see adjacent page for brief summary of GAMUNEX full Prescribing Information.

Evidence based. Patient proven.

gamunex[®]
immune globulin intravenous (human), 10%
caprylate/chromatography purified

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www.gamunex.com

July 2010

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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.

Keeping the Faith



JADE LINN HAD been sick off and on with colds and sinus infections all her life, but it wasn't until the summer before her sophomore year of college that she became seriously ill with abdominal pain. Sent to an infectious disease doctor who tested her for primary immune deficiency disease (PIDD), she then was diagnosed with common variable immune deficiency (CVID). According to Jade, the immunologist who treated her told her, "I was one of the worst cases he had ever seen, and he had no idea how I wasn't in the hospital with a serious infection. I also found out that most of my other health

problems, such as [my] GI [gastrointestinal] problems are because of CVID."

That was in October 2006, when she was 19. It was an accidental diagnosis, but it ended Jade's lengthy search for an answer. Quite simply, her family doctor just "never thought to test me for PIDD," Jade explains. Throughout all her health problems, her parents never gave up when the doctors told her there was nothing wrong with her. "They saw how sick I was, and they took me to every doctor they could think of," she says. "They always believed me, and never doubted that I was sick."

Getting the Support She Needs

Right after Jade was diagnosed with CVID, her mother started researching the disease on the Internet, and she even subscribed

mother who helped educate Jade. "Having the support of my parents made my diagnosis so much easier," Jade says.

In fact, Jade's parents have kept her going in many ways. "My family has always been very supportive and would always listen when I needed to talk about it," she explains. "They always ... told me I could do anything I put my mind to." When Jade first began getting her intravenous immune globulin (IVIG) infusions, one of her parents would go with her, but eventually she felt comfortable going on her own.

And, when several people told Jade they thought she was too sick to make it through college, her parents encouraged her to continue. "They would advocate for me when I couldn't advocate for myself, whether it [was] at school or at the doctor's

When several people told Jade they thought she was too sick to make it through college, her parents encouraged her to continue.

to *IG Living* magazine. So, rather than Jade trying to make her parents understand her disease, it was her

office," she adds. Jade attended the University of Findlay in Ohio, and lived on campus until she graduated.

During college, her mother would make the 45-minute drive each week to collect her laundry and bring it home to wash. Her mom also brought her hand sanitizers to carry with her and to keep in the living room of her on-campus house for her friends to use. And, if she wanted to come home but was too sick to drive, one of her parents would go and get her no matter what time it was. "Some semesters were really hard, and having my family's help was great," Jade says. "Some people don't realize how small things like that help when you don't feel well. [They] would do anything to help me, because at the end of the day, I didn't feel like doing anything but going to bed."

Jade also had very supportive friends to help her through college. She was open with her friends, and especially her roommates, about her disease. "It's important for them to know you have this disease so they can help you," she explains. Luckily for Jade, her friends were interested in the disease and wanted to help in any way they could. "When my roommates were sick, they would always use hand sanitizer and stay in their rooms as much as possible," she adds. Jade's professors also were instrumental in getting her through school. "Kim Forget, an education professor, helped me the most," Jade remembers. "She was like my mom away from home and would always check up on me to make sure I was doing OK."

Getting On with Life

Since her recent college graduation, Jade is now back living at home. She

was going to her monthly infusions by herself until recently, when her mother also was diagnosed with CVID. In June, they received their first infusion together. Jade's 19-

year-old sister also has an immune deficiency, but she is not on IVIG. "I have always been told that CVID is not hereditary, but that confuses me since my mom has it, too," Jade says.

What's in Jade's future? "My parents are currently in charge [of] the finances until I get a full-time job," she says. But that shouldn't be long as she is currently working part time as a special education teacher. And, while she is a little worried about being around children every day who often get sick, she has a positive outlook. "Thankfully, I didn't have any problems during my field experiences," she says. "I believe that God's plan for me is to be a teacher, and that is the reason I have not had problems with getting sick working with children. He will make my way!"

A Whole New Outlook

Having CVID has definitely shaped Jade's future. She originally wanted to be in the medical field, but realized that it was a bad idea to work in a hospital. She also wanted to be a missionary and travel to Third World countries before being diag-

nosed, but she can no longer do that, either. But, Jade says that's OK, because teaching is something she really loves. "My goals before my disease were much more self-centered,

Right after Jade was diagnosed with CVID, her mother started researching the disease on the Internet.

but now I want to advocate for other people with illnesses, and I want to use my illness to help others," Jade says. "It has opened my eyes to so many things, and it has made me a better, stronger person."

When asked what advice she would give to parents whose children are going through the same thing, Jade says, "Mostly, just listen to them and advocate for them. It's very scary at first to receive this diagnosis, and your child will probably want to talk." She also suggests that parents do some of their own research to become well-informed about the disease. "And, don't be too afraid to let your children live life and go off to college," she adds. "It will be rough at first to adjust, but your child will grow so much, and [will] have the opportunity to help others because of the disease."

Sounds like Jade has learned a lot from this transition in her life. "My family always encouraged me to never give up and to stay positive," Jade says. "My dad always says, 'Keep the faith!'" And, she has. ■

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

Leaving the Nest

Teaching kids to become independent at an early age will help them succeed when it comes time to leave home.

By Mark T. Haggard

“EXPECT THE BEST, but prepare for the worst.” That’s what many parents think when their children move out of the family home for the first time. During this turbulent time, questions swirl in parents’ heads as their chicks leave the nest. Questions such as: Will they find a good job? How will they pay for their housing? Will they be hanging out with the right people? Have we done all that we can to prepare them for life on their own?

That list of questions grows significantly longer for parents of children with immune deficiencies: Will they remember to do their infusions? Will new friends understand the challenges my children face? Will insurance cover the cost of infusions? Will they stay healthy? Will they have to return home because of their ill health?

We parents expect the best, but we prepare for the worst. We hope that we have done enough to prepare our children for a difficult and sometimes unforgiving world. It’s certainly difficult out there: Even people without immune issues find themselves having to return home after leaving for college or work. How much more concerned must we be for children with an immune disease as they leave the nest?

After all, teenagers tend to see themselves as superhuman, and they



are often too preoccupied or too busy to do the things that need to be done. Some tasks just aren’t “cool,” and, unfortunately, this sometimes includes infusions. In more than a few cases, without mom or dad constantly reminding them, young adults have missed infusions, become sick and were forced to return home. “When they’re healthy, they’re not thinking about their medicine,” one father of a young adult with primary immune deficiency disease (PIDD) told me.

Deciding to Leave Home

Jordan Leventhal was diagnosed with selective IgA deficiency at age 13, and then teenage-onset common variable immune deficiency (CVID) at age 16. Nevertheless, he chose to leave home in suburban Cleveland, Ohio, as a teen to attend the American Hebrew Academy, a boarding school in Greensboro, N.C. He successfully navigated his way through school, coordinating his IVIG infusions through the high school medical center and a specialty pharmacy.

Now 21 years old, Jordan is a few years removed from school and has returned to Ohio, on his own accord, to live with his parents. Jordan's role model is his father, Mark, who also lives with CVID. Father and son get their IVIG infusions together once a month, which Jordan calls "an infusion party with Dad!" In fact, it is his father's words that encouraged Jordan during his time away from home: "You have CVID; CVID does not have you."

According to Jordan, "You run it as well or as bad as you want to." Jordan has run it well; he played three sports in high school and is now working in Cleveland as a paramedic. He has found that consistency is the name of the game when it comes to infusions. Jordan keeps his own calendar and sets his own appointments. He also is open about his CVID, sharing information about his condition with his friends and employers.

What concerns Jordan most as he heads toward independence and leaving the nest is his future employment. He wonders how understanding potential employers will be about his condition.

Tyler Yates was diagnosed with CVID as a child growing up in Chico, Calif. His father left the family soon after learning of the diagnosis and it was up to his mother, Suzie, to raise him. With a background as a medical assistant and a phlebotomist, Suzie was able to administer Tyler's intravenous immune globulin (IVIG) infusions at home every 14 days. But, as the expense of his therapy mounted, she had to take extra jobs for insurance and income purposes.

At 17, Tyler left home after receiving

a full scholarship to play soccer at the University of Redlands in Southern California. Suzie was concerned that her only child was moving "a million miles away." One hang-up Suzie encountered was with her insurance carrier, which determined "a college dormitory was not a legal dwelling" and therefore denied Tyler an infusion nurse. This is when Suzie stepped in. Every two weeks, Suzie woke up after four hours of sleep and made the 589-mile drive ("a million miles away" to a mother) from Northern California to Southern California to watch a soccer game, start Tyler's infusion and then drive 10 hours back home to start her next shift.

We parents expect the best, but we prepare for the worst.

One of the things that Suzie "harped on" was that Tyler had to take care of himself; otherwise, "a small thing could turn huge." She encouraged her son to become familiar with and use the resources afforded him, particularly Redlands' "disabled student services."

Another concern of Suzie's was that Tyler's classmates and teammates would not understand that "they could not come and hang with Ty in his room if they had a cough." Or, that his classmates wouldn't accept him: "Not so much making friends; he can do that anywhere. But a majority of people around him who accept him for who he is." Tyler's

roommate and soccer teammate, Kody, relieved many of Suzie's fears when he became a close friend and part-time nurse, pulling Tyler's IVs at the end of his infusions.

Without doubt, the physical fitness benefit that Tyler gained from soccer was countered by potential illness due to even the slightest injury he might suffer. A first-aid kit remained on the sidelines for Tyler all the time, and he wore elbow pads and kneepads to cushion any injurious blows. Kody became skilled with an Epi pen. But, for the most part, soccer was a "sanctuary" for Tyler, where he could forget about the troubles created by PIDD.

Tyler's experience with PIDD motivated him early on to study the immune system. He started studying his mother's microbiology textbooks as a child and, in the fourth grade, he created a model of the immune system with all of its components for a science fair project (a professor still uses it in her class). Tyler is now in his second year studying pediatric immunology at Georgetown Medical School.

When asked what advice he would give to those going out on their own for the first time, Tyler said, "It is important to not be overly cautious or overly naive" about their condition. He echoed his mother when adding, "Know what services are available to you."

Preparing Kids for Independence

Taking advantage of available services seems to be a recurring theme for families with kids preparing to leave the nest. And now, as part of this year's healthcare reform bill, the U.S. government has made a few

more services available to families with children. As of September 2010, insurance companies must guarantee coverage to dependent children until age 26, and insurance companies can no longer turn down new enrollees because of a pre-existing condition, such as an immune deficiency. Essentially, families have earned another few years to get “junior” employed and working for his own insurance. In the meantime, kids continue to get the same coverage they had under their family’s insurance plan.

However, having insurance does not keep independent children healthy. The way to prepare young adults for independence is not to coddle them until the last minute. We can’t do everything for them until the day they leave. Instead, they should learn to deal with the intricacies of their disability at a young age.

The way to prepare young adults for independence is not to coddle them until the last minute.

To become self-reliant, they need to practice taking responsibility for keeping up with medications and infusions. Teaching them to “know their body” also is important — to recognize the signs of becoming sick so that they can immediately get treatment before a small sickness

gets out of hand and they land back at home.

Both Jordan and Tyler were actively involved in their treatment at a young age. Rather than letting someone else (mom or dad) do all of the work concerning their treatment, they took charge themselves, researching what was occurring inside their bodies, scheduling infusions and making their own contacts. They were proactive rather than reactive, and they continue to be proactive as adults.

Mark Leventhal’s long history with CVID contributes to his assertive attitude about his son living with his condition. “CVID does not define us,” he told Tyler. “If you let it, CVID can become all encompassing [and] emotionally debilitating.” When asked to advise parents of children with PIDD, he says that young adults need to be self-sufficient. “If we allow them to, they will become a victim. Instead, let them go for everything they can go for.”

That sentiment was echoed by Suzie Yates: “Critically ill or not,” she says, “I raised Tyler to never, ever use his disease as an excuse to not exceed his potential — not achieve his potential, but to exceed it — as we all have that capability regardless of our health.”

This really is all that we can do for our children, precious gifts given to us for 18 to 20 years (26 years, according to the federal government). While in our care, we need to instill life skills: money management, work ethic, and how to choose good friends. We need to encourage them.

Ultimately, the time comes when our kids will have to act on their own. Success or failure is up to them. Best results happen when parents avoid



creating a psychology of dependence in their children, fight the urge to overprotect them because of their illness, but instead encourage and prepare them to stand on their own. The reality is that it is better to let kids fail early in their learning process when we can still help them. Guiding our kids to be proactive in their sickness rather than reactive and relinquishing the reins to them at an early age makes for a smoother transition to life on their own. Young adults need to know how to fly when it finally comes time to leave the nest. ■



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

Going Gluten-Free

By Kris McFalls

GLUTEN IS A protein found in wheat, rye and barley. Most grain-based products, such as pasta, bread and cereals, contain gluten. Unfortunately, many people suffer symptoms such as abdominal pain, diarrhea, bloating, weakness, weight loss and malnutrition as the result of their body's struggle to process gluten. That struggle can be the result of either a gluten intolerance, a wheat allergy or celiac disease.

What Is Gluten Intolerance?

Gluten intolerance is a digestive response in which the body has trouble breaking down gluten proteins. Gluten intolerance is not an autoimmune disease or an allergy. Patients with gluten intolerance will have discouraging digestive symptoms, but will have negative biopsies and blood work. In general, patients sensitive to foods containing gluten will have transient symptoms but will not have long-term or permanent tissue damage.

When Is a Gluten Reaction an Allergy?

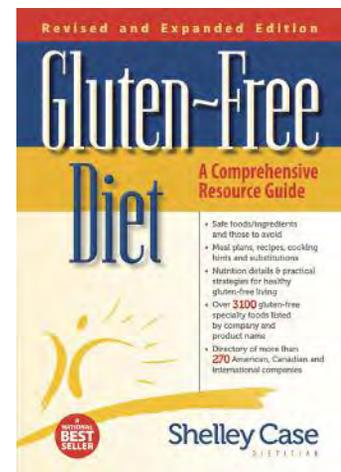
Patients sometimes are allergic to the grains that contain gluten. An allergy is an immune response to a substance the body views as a foreign invader. In response to this foreign invader, the body overreacts and sends unusually large amounts of IgE antibodies to fight it, ultimately causing the body harm. Yet, even though a grain allergy is an overreaction of the immune system, it is not thought to be an autoimmune disease.

Patients may notice symptoms such as itchy, watery eyes, rash or breathing difficulties, in addition to digestive symptoms. Reactions caused by an allergy usually begin much quicker than those caused by gluten intolerance. And, because people with a grain allergy avoid gluten-containing grains, such as wheat, rye or barley, they often can follow a gluten-free diet.

When Is a Gluten Reaction Celiac Disease?

Celiac disease is an inflammatory autoimmune disease caused by gluten. It causes damage to the intestinal villi responsible for absorbing nutrients derived from the food we consume. Although there are blood tests that screen

for celiac disease, the only definitive diagnostic test is a small intestinal biopsy. Patients with certain autoimmune diseases, such as thyroid disease, liver disease or diabetes, are at higher risk for celiac disease. Left untreated, it can cause malabsorption, nutritional deficiencies, chronic diarrhea and nerve damage.



Treating Gluten Intolerance

Whether individuals are gluten-intolerant, have a grain allergy or celiac disease, their treatment is the same. They need to avoid eating the foods that cause the problem. Historically, it was thought that celiac disease was a rare disease. Consequently, gluten-free products, diets and cookbooks were difficult to find. But, with current estimates of the prevalence of celiac disease at one in 133 people, the market for gluten-free products has exploded and these products are widely available, found in just about every local grocery. However, buyers need to beware, as gluten-free labeling does not always mean the product is totally gluten-free. In response to these content concerns, the U.S. Food and Drug Administration (FDA) has proposed labeling rules. To read more about FDA gluten-free labeling, go to www.fda.gov/Food/LabelingNutrition/FoodAllergensLabeling/GuidanceComplianceRegulatoryInformation/ucm111487.htm.

Consult a Reliable Source

For individuals who need to learn about gluten-free products, it's best to talk to a doctor and consult with a registered dietitian specializing in gluten-free diets. ■

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

Directory of Gluten-Free Websites

Celiac Disease Foundation

This foundation is a nonprofit, public benefit corporation dedicated to providing services and support regarding celiac disease and dermatitis herpetiformis through programs of awareness, education, advocacy and research.

www.celiac.org

Celiac Sprue Association

The Celiac Sprue Association/United States of America Inc. (CSA/USA Inc) is a member-based 501(c)(3) nonprofit organization dedicated to helping individuals with celiac disease and dermatitis herpetiformis worldwide through research, education and support.

www.csaceliacs.org/AACSAF/CSAFoundation.php

Gluten-Free Diet

Dietitian Shelley Case developed this comprehensive resource guide for a gluten-free lifestyle. Patients and doctors living with gluten-free diet restrictions will find information about how to read and understand labels, find creative

ideas for snacks and meals, tips for eating out and more.

www.glutenfreediet.ca

Gluten Free Foundation

This foundation exists to facilitate gluten-free living by raising public awareness and funding for the purpose of providing resources to enhance the lives of people living a gluten-free lifestyle. It was founded in 2006 and is a tax-exempt, nonprofit corporation.

www.jackshouse.org

National Foundation for Celiac Awareness (NFCA)

The NFCA was formed as a national 501(c)(3) not-for-profit organization to raise awareness of celiac disease among the general public and the healthcare community, as well as to facilitate research to better understand the causes, mechanisms and treatment of celiac disease. Awareness brings treatment that, in turn, brings improvement of the quality of life for those with celiac disease and gluten intolerance.

www.celiaccentral.org



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Whether you follow blogs already or are new to social media, the IG Living blog is destined to become one of your favorites. We tackle topics that range from touching and thought-provoking to downright funny, and new blogs are posted every Friday. Check it out at www.igliving.com.

Happy reading and be sure to leave comments; we want to hear from you!



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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

Evans Syndrome

Online Peer Support

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

Guillain-Barré Syndrome (GBS)

Websites

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

Online Peer Support

- GBS & 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_Whats.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

THE MYOSITIS ASSOCIATION

- 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

Jeffrey Modell JM Foundation

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.uhhospitals.org/tabid/132/Default.aspx
- Team Hope (for families and patients in New England): www.teamhope.info

Online Peer Support

- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: my.primaryimmune.org/forum
- IDF Friends: my.primaryimmune.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/topics/foodallergy/Pages/default.aspx
- 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

1. Cayco AV, Perazella MA, Hayslett JP. Renal insufficiency after intravenous immune globulin therapy: a report of two cases and an analysis of the literature. *J Am Soc Nephrol* 1997;8:1788-1793.
2. Dalakas MC. High-dose intravenous immunoglobulin and serum viscosity: risk of precipitating thromboembolic events. *Neurology* 1994;44:223-226.
3. Woodruff RK, Grigg AP, Firkin FC, Smith IL. Fatal thrombotic events during treatment of autoimmune thrombocytopenia with intravenous immunoglobulin in elderly patients. *Lancet* 1986;2:217-218.
4. Wolberg AS, Kon RH, Monroe DM, Hoffman M. Coagulation factor XI is a contaminant in intravenous immunoglobulin preparations. *Am J Hematol* 2000;65:30-34.
5. Gabor EP. Meningitis and skin reaction after intravenous immune globulin therapy. *Ann Intern Med* 1997;127:1130.
6. Copelan EA, Strohm PL, Kennedy MS, Tutschka PJ. Hemolysis following intravenous immune globulin therapy. *Transfusion* 1986;26:410-412.
7. Thomas MJ, Misbah SA, Chapel HM, Jones M, Elrington G, Newsom-Davis J. Hemolysis after high-dose intravenous Ig. *Blood* 1993;15:3789.
8. Wilson JR, Bhoopalam N, Fisher M. Hemolytic anemia associated with intravenous immunoglobulin. *Muscle Nerve* 1997;20:1142-1145.
9. Kessary-Shoham H, Levy Y, Shoenfeld Y, Lorber M, Gershon H. *In vivo* administration of intravenous immunoglobulin (IVIg) can lead to enhanced erythrocyte sequestration. *J Autoimmun* 1999;13:129-135.
10. Rizk A, Gorson KC, Kenney L, Weinstein R. Transfusion-related acute lung injury after the infusion of IVIG. *Transfusion* 2001;41:264-268.
11. Pierce LR, Jain N. Risks associated with the use of intravenous immunoglobulin. *Trans Med Rev* 2003;17:241-251.

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%)

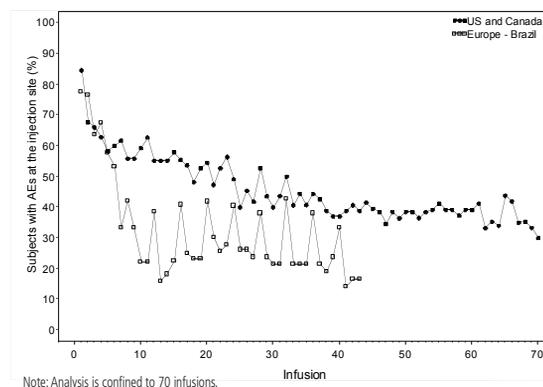
*Excluding infections

**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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