Genetic Testing

Advancing Health Outcomes and Treatment

PI and Leaky Gut: Causes and Treatments

Isometric Exercise for the Mobility-Impaired

Understanding Stiff Person Syndrome

IVIG in Solid Organ Transplantation
Getting started

1. Contact your Specialty Pharmacy and express a financial need for Hizentra Co-Pay Assistance

2. Your Specialty Pharmacy will verify your eligibility and process your request through Medmonk, the company that administers the co-pay program on behalf of CSL Behring

3. Access your account anytime at the secure online patient portal: Hizentra.medmonk.com

If you have any questions, call the IgIQ resource hotline:

IgIQ®
Your single source for Ig solutions

1-877-355-IGIQ (4447)
Monday–Friday,
8 AM–8 PM ET

Important Safety Information

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

WARNING: Thrombosis (blood clotting) can occur with immune globulin products, including Hizentra. Risk factors can include: advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (blood thickness), use of estrogens, installed vascular catheters, and cardiovascular risk factors.

If you are at high risk of thrombosis, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor you for signs of thrombosis and hyperviscosity. Always drink sufficient fluids before administration.

Tell your doctor if you have had a serious reaction to other immune globulin medicines or have been told you also have a deficiency of the immunoglobulin called IgA, as you might not be able to take Hizentra. You should not take Hizentra if you know you have hyperprolinaemia (too much proline in your blood).

not work well if you are using Hizentra. Before receiving any vaccine, tell the healthcare professional you are being treated with Hizentra.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

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.

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

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

Tell your doctor about any side effects that concern you. Immediately report symptoms that could indicate a blood clot, including pain and/or swelling of an arm or leg, with warmth over affected area; discoloration in arm or leg; unexplained shortness of breath; chest pain or discomfort that worsens with deep breathing; unexplained rapid pulse; and numbness or weakness on one side of the body. Your doctor will also monitor symptoms that could indicate hemolysis (destruction of red blood cells), and other potentially serious reactions that have been seen with Ig treatment, including aseptic meningitis syndrome (brain swelling); kidney problems; and transfusion-related acute lung injury.

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

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

Before being treated with Hizentra, inform your doctor if you are pregnant, nursing or plan to become pregnant. Vaccines (such as measles, mumps and rubella) might
Hizentra® Immune Globulin Subcutaneous (Human), 20% Liquid

Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HIZENTRA safely and effectively. See full prescribing information for HIZENTRA.

INDICATIONS AND USAGE

Hizentra is an Immune Globulin Subcutaneous (Human) (IGSC), 20% Liquid indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.

DOSAGE FORMS AND STRENGTHS

0.2 g per mL (20%) protein solution for subcutaneous injection

CONTRAINDICATIONS

- Anaphylactic or severe systemic reaction to human immune globulin or components of Hizentra, such as polysorbate 80
- Hyperprolinemia (type I or II) (Hizentra contains the stabilizer L-proline)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

WARNINGS AND PRECAUTIONS

- IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions.
- Thrombosis may occur following treatment with immune globulin products, including Hizentra.
- Aseptic meningitis syndrome has been reported with IGIV or IGSC treatment.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of acute renal failure.
- Monitor for clinical signs and symptoms of hemolysis.
- Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])
- Hizentra is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

ADVERSE REACTIONS

The most common adverse reactions observed in ≤5% of study subjects were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, rash, pruritus, vomiting, abdominal pain (upper), migraine, and pain.

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.

DRUG INTERACTIONS

The passive transfer of antibodies may interfere with the response to live virus vaccines, and lead to misinterpretation of the results of serological testing.

USE IN SPECIFIC POPULATIONS

- Pregnancy: No human or animal data. Use only if clearly needed.
- Pediatric: No specific dose requirements are necessary to achieve the desired serum IgG levels.

As tolerated

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Advertising in IG Living
IG Living Magazine is read by 30,000 subscribers who are patients that depend upon immune globulin products and their healthcare providers. For information about advertising in IG Living, download a media kit at igliving.com/Advertise.aspx. Or contact advertising@igliving.com.

About IG Living
IG Living magazine brings together patients, advocates and caregivers in the immune globulin (IG) community.

IG Living, (ISSN 1949-4548), published bimonthly, is a community service provided by FFF Enterprises, 44000 Winchester Road, Temecula, CA 92590, (800) 843-7477 x1362, fax (951) 699-9655.

Subscriptions to IG Living are free, and readers may subscribe at IGLiving.com or by calling (800) 843-7477 x1351.

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Getting Answers You Want and Need

OVER A DECADE ago, we created IG Living magazine to provide advocacy, education and support for patients treated with immune globulin (IG) and their caregivers. Since then, we have expanded our efforts through our patient advocate, website, Facebook page and reader teleconferences to provide a network for patients to connect with each other, and to offer insight to healthcare professionals about often-misunderstood diseases. This issue aims to further our educational objective by providing answers to some of your more frequently asked questions.

For some time now, readers have expressed an interest in understanding more about genetic testing. We know most types of primary immunodeficiency (PI) diseases and some neurological and autoimmune disorders are hereditary. But, how can genetic tests help? In our article “Genetic Testing: A Growing Approach to Disease Diagnosis and Treatment,” we explain what genetic testing is, how it can be used and the ways results should be interpreted. For instance, genetic testing can help to identify whether there is, in fact, a hereditary link to a disorder or if there are other causes. It can be used to help make a diagnosis when symptoms overlap those of other diseases. And, test results can sometimes help to determine the best course of treatment. In addition, because genetic testing can often be confusing, we discuss the role genetic counselors play in helping patients address their concerns.

One of the more distressing side effects PI patients frequently ask about is their associated gastrointestinal (GI) issues. Immunologist Terry O. Harville explains in our article “Gastrointestinal Problems in Immunodeficiencies: What Is Leaky Gut?” that PI patients “seem destined to develop some extent of an increased leaky gut,” which results in GI distress. Since there are multiple causes of an abnormal leaky gut, treatment varies from patient to patient — from medications to surgery and special diets. Fortunately, says Dr. Harville, identifying the underlying cause can lead to the best course of treatment.

Worn down from side effects and symptoms, many patients often feel weak and suffer from pain, causing them to remain inactive for too long, which makes their situation worse. How, then, patients ask, can they counteract muscle atrophy due to inactivity? Isometrics may be a perfect option, says physical therapist Matthew D. Hansen in our article “Isometrics for the Mobility-Impaired.” Studies show that isometrics improve both muscle size and strength. As such, Dr. Hansen provides a series of isometric and self-resistance activities that can be performed in many different positions, making them suitable for almost everyone regardless of how limited their mobility is.

Another frequently asked question is whether to participate in clinical research. While participation offers many benefits, our patient advocate Abbie Cornett explains in her column “Participating in Clinical Research” why patients need to be well-informed about the type of study they are considering. She also provides a list of questions patients should ask before making a decision to take part.

As always, I hope you gain insight from the information presented and enjoy this edition of IG Living. We will continue to provide you with educational articles in upcoming editions.
Participating in Clinical Research

By Abbie Cornett

CLINICAL RESEARCH is an invaluable part of developing new strategies and treatments for diseases, but that doesn’t mean participation is the right choice for all. Before deciding to participate, patients need to understand the difference between the two types of studies, gather all available information and understand their rights.

Patients and their family members need to be well-informed about any trial they are considering, and they shouldn’t be afraid to ask questions.

Many times, the terms “study” and “trial” are used interchangeably. Yet, while they sound similar, they can be very different. In a clinical study, also called observational research, participants are observed through the collection of blood, tissue or other samples, but drugs are not used. While studies don’t test drugs or treatments, they are still a very important means of gathering data for treatment of diseases. Clinical trials, on the other hand, test drugs, treatments and interventions to prevent, detect, treat or manage various diseases or medical conditions. Usually conducted in five stages, they are carefully set up and follow strict scientific guidelines, and represent the final stages of a long research process.

Many patients with chronic illness choose to participate in trials and studies because of potential benefits such as receiving regular medical attention, gaining access to new research and treatments and being more active in their own care. But, patients need to be aware of potential downsides. While clinical trials have very strict protocols to protect participants’ health, they still involve a certain amount of risk, just as all medical care does. For example, there are possibilities of complications such as serious or life-threatening side effects that require medical treatment. Other drawbacks to both trials and studies are the requirement for frequent lab work, visits to the study site or even overnight stays in the hospital, all of which require a lot of time.

Patients and their family members need to be well-informed about any trial they are considering, and they shouldn’t be afraid to ask questions. The National Institutes of Health recommends asking some of the following questions prior to entering:

- What are the risks?
- Will patients be able to take regular medications while in the trial?
- Who approved the study, and how is it funded?
- How long will patients be required to participate?
- What is the financial obligation for treatment or participation such as travel costs?
- How will the data be interpreted, and who will check the safety and results of the gathered data?

As part of the informed consent process, patients have the right to know all of the important information about a study or trial so they can make informed decisions about participating. For instance, patients should be aware that once they become part of a trial, they can withdraw at any time.

Clinical trials and studies offer hope for thousands of people each year. It’s true that being part of this research can be a very rewarding experience, but patients should first have a complete understanding of what is involved before committing to it. Feel free to contact me if you are interested in participating in a trial or study, or have any questions about guidelines for participation.

ABBIE CORNETT is the patient advocate for IG Living magazine. She can be reached at patient advocate@igliving.com or (800) 843-7477 x1366.

References
Join the conversation! Connect with other immune globulin patients through IG Living’s Facebook page at www.facebook.com/IGLivingMagazine. See our daily posts of interesting articles and facts, as well as thought-provoking questions that you can chime in on. Following are some snapshots of what’s being discussed.

**Do you suffer from fatigue?**

Yes, very much so, especially after a treatment. I find that my body has to “process” the new proteins from the immune globulin. Because I do treatments twice a week, [I] can [feel] this way most of the week. If my body is fighting off germs, then it is in overdrive mode, causing fatigue also. So, my energy levels are lucky to be good two days a week.

— Janet S-D

I’ve been trying to fight off malaise for years. My doctor says I’m barely sustaining my body. I do walk a short distance daily with my dog. I take care of him and, thank goodness, he’s a little dog that likes to cuddle. I’m asleep 12 to 18 hours a day. I don’t have a life outside of my house and doctor appointments. I live with my 87-year-old mother and sister. I just don’t know how I would make it without them.

— Lia F

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— Lia F

I suffer immensely from fatigue and mental fog. Since I work in corporate America full time, I had to do something. I actually had a sleep study done, and results showed that after a full night’s sleep, I can still fall asleep at any hour of the day within two minutes. What helps me is low-dose Ritalin, a B vitamin, amino acid and a caffeine supplement called Spark. I also run three- to three-and-a-half miles each day and ride my bike 30 to 50 miles on weekends in the summer with my hubby. As this article says, it must be individualized, but it may be worth sharing what works. One pro: We never have to worry about tossing and turning at night, right?

— Kristy H-P

My 11-year-old daughter has common variable immunodeficiency (CVID), and when she gets tired, she sleeps for three to four hours. Those days, she is late for school. I won’t send her when she has a CVID-tired day. If she wakes up from her nap and goes to the couch and lays [sic] down, I know it is one of those days. She also has attention deficit hyperactivity disorder, so she is always doing something.

— Pamela B

**Do you use a healthcare app?**

I would like to say, “Yes, I don’t know what I ever did without it.” But that is not the case. I tried a few years ago, and I still do not know what went wrong, but it became a real hassle. Now let me give you full disclosure: I am anything but a techie, but because of the earlier experience, I have not even tried again. I think your information today will help me decide to give it one more shot. Thank you for the nudge.

— Jenny G

Yes, I do! I’m learning they help me keep myself accountable and to watch for patterns that could be not in my best interest for my quality of life. They are a great tool if you’re serious [about it and] take [the information with you to] your healthcare provider, so you don’t forget things you need to discuss.

— Janet S-D
According to immunologist Terry O. Harville, MD, a variety of side effects can occur with both SCIG and intravenous IG (IVIG) infusions, but especially with IVIG. In general, most of the systemic side effects are lessened or disappear with SCIG infusions.

Joint discomfort has been reported with some IG infusions, which may be caused by several things. Most likely, the patient already has some level of arthritis in the joints or previous joint injury, and the infusion is exacerbating this. On the other hand, IG infusions generally greatly diminish joint pain, swelling, redness and stiffness in patients with inflammatory arthritis conditions such as rheumatoid arthritis.

There have not been widespread reports of knee pain with HYQVIA. However, since you appear to be sensitive to headaches and chills, you may be at risk for unusual side effects with SCIG therapy. Issues that should be considered are:

1) Was knee arthritis present prior to beginning infusions, with some extent of pain and other symptoms?
2) Do the knees swell and become red, warm and stiff following the infusion, or were these signs present before the infusions?
3) Did the knees hurt with any other IG product?
4) Does blood appear in the urine after infusions?
5) Did the knee pain begin after a respiratory or gastrointestinal tract illness?

While ibuprofen can’t be taken in conjunction with Coumadin, there are other medications that can be taken, which is something you should discuss with your treating physician.

Medigap (supplemental) policies will cover the remaining 20 percent once Medicare pays for its portion. If Medicare does not cover the diagnosis, the Medigap policy will not cover it either. We have experience with a few secondary policies (true secondary, not supplemental) that require authorization even for the 20 percent, and in some cases, while Medicare Part B is paying for 80 percent, the secondary policy has denied the 20 percent for medical necessity.

It is important to make sure the provider of your infusion has a good understanding of Medicare coverage criteria. Medicare can review the clinical diagnosis at any time, and if it is not supportive of the treatment, it can/will deny the claim well after the infusion has been administered.

Have a question? Email us at editor@IGLiving.com. Your information will remain confidential unless permission is given.

ABBIE CORNETT is the patient advocate for IG Living magazine.

LESLIE J. VAUGHAN, RPh, is senior vice president of clinical programs at NuFACTOR Specialty Pharmacy.
DiGeorge Syndrome: Genetics of the Neurologic Issues

By Terry O. Harville, MD, PhD

In previous issues, we discussed features of DiGeorge syndrome (DGS) and partial DGS (PDGS) resulting from the consequences of improper timing of the sequence of events during early phases of embryonic development. In the last issue, we began with a discussion of chromosome 22q11.2 hemizygosity. In this column, we will discuss how some of the genes in chromosome 22q11.2 may be involved with neurologic features of this complicated disease.

With better and earlier testing, it is now reported that up to 90 percent of children with DGS/PDGS have some detectable cognitive or developmental delay. This higher-than-previously reporting is likely due to more sensitive detection assays. The majority of patients with DGS/PDGS have an IQ of between 70 and 84, which is just below the average range (most consider the average IQ for 68 percent of the population to be between 85 and 114). Mild mental retardation (an IQ between 50 and 70) is reported to occur in 30 percent of DGS/PDGS patients. It is expected that cognition in these patients will be affected, and learning difficulties will be encountered in school. As such, early intervention is required to try to mitigate as much as possible any problems with education. In general, DGS/PDGS patients have difficulty with mathematic skills, so this skill set needs the most attention, whereas reading skills are not greatly affected.

In children, attention deficit and autism-spectrum disorders are frequently diagnosed. Additionally, anxiety, temper outbursts and impulsivities may more commonly occur. As children age into adulthood, psychiatric disorders may be diagnosed. Some 60 percent of adults with DGS/PDGS are diagnosed with a nonpsychotic and treatable psychiatric disease. However, a major issue caregivers and clinical providers need to keep in mind is that as many as 25 percent of patients with DGS/PDGS exhibit potentially more severe neurologic/psychiatric disease in the form of schizophrenia (a psychotic disorder). This needs to be recognized early and treated appropriately, rather than merely assuming the neurologic condition is only cognitive delay or mental retardation, resulting in unusual behaviors. A correct and thorough evaluation by appropriate specialists is required so the most beneficial therapy is expediently begun.

The neurocognitive and underlying psychiatric conditions noted in the majority of DGS/PDGS children continue into adulthood and become diagnosed as psychiatric disorders that require intervention and treatment. The disorders are exhibited as poorer verbal, communication, learning and mathematic skills, although rote memory is often better than expected considering all the issues involved. These reduced skills may result in poor socialization and inability to obtain and maintain employment.

With better and earlier testing, it is now reported that up to 90 percent of children with DGS/PDGS have some detectable cognitive or developmental delay.

Alterations in the catechol-O-methyl transferase (COMT) gene are thought to be responsible for the cognitive and psychiatric disorders occurring in DGS/PDGS. COMT is found in chromosome 22q11.2, and is postulated to be affected by the partial deletion of this region. More recently, other genes from chromosome 22q11.2 have also been implicated in possibly contributing to the neurologic issues, some of which have been tested by performing mutations in mice.

We will continue with the discussion of the genetics of DGS/PDGS in the next issue.

Terry O. 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.
CLINICAL BRIEF

IVIG in Solid Organ Transplantation
By Michelle Greer, RN

INTRAVENOUS IMMUNE globulin (IVIG) can play an important role in solid organ transplants, both in preparation to enhance successful grafting and posttransplant to treat potential complications. Here, we take a look at some of the uses of IVIG in transplants.

Pretransplant
Much success has been had using IVIG in kidney transplantation over the last 20 years. IVIG may be used as part of a protocol prior to transplantation in both living and deceased kidney donors. When someone becomes a candidate for a kidney transplant (host), the workup includes a blood test called a panel reactive antibody (PRA). This test measures the amount of alloantibodies produced by the host immune system. Alloantibodies are antibodies produced when there is exposure to the tissue of another person. This may occur when pregnant, when receiving a blood transfusion or during a transplant.

The PRA tests host cells against various samples of other people, and the result may range from 0 percent to 100 percent. Zero percent means there are no alloantibodies, and the risk of rejection is low. One hundred percent means there would be a reaction to all potential donors, significantly decreasing the chance of a successful transplant. Higher PRA scores can have a significant impact on wait times for a compatible donor. However, highly sensitized patients may be eligible for desensitization therapy with IVIG to improve their chances of successful transplant.

Research over the last several years has shown that although IVIG has been extensively used in most desensitization protocols, use of IVIG alone is not sufficient to sustain low levels of alloantibodies. Therefore, desensitization therapy may vary depending on the transplant center, and may involve steroids, plasma exchange, high- and low-dose IVIG and/or other drugs (Table 1).

IVIG is used to suppress the immune response, known as immunomodulation. The mechanism of action of IVIG in this manner is not clearly understood. However, it is believed that because IVIG consists of antibodies from a large variety of human donors, the antibodies suppress the immune response and, ultimately, lower PRA levels.

Although there is much documented
success using IVIG as part of desensitization prior to kidney transplant, there is currently little data to support similar success in other organs. There is one recent Canadian study, which designed a protocol that included IVIG, plasma exchange, anti-thymocyte globulin and mycophenolic acid given during the transplant operation to patients with a PRA of 30 or more. The researchers concluded that by applying this perioperative treatment, lung transplantation can be safely performed in donor-specific HLA antibodies/PRA-positive patients, with similar outcomes to nonsensitized recipients.²

Posttransplant

Rejection is a potential complication after transplantation, so very close monitoring of various lab values and use of immunosuppressants that deplete B and/or T cells to keep a patient from rejecting the transplanted organ are required. Rejection can be acute, occurring in the first few months posttransplant, or chronic, happening slowly over time, and can be caused by cells or antibodies. Rejection caused by circulating antibodies is known as antibody-mediated rejection (AMR). If AMR is suspected, a treatment regimen is implemented to suppress the immune response and save the organ.

In kidney transplants, IVIG and other drugs used in a desensitization protocol pretransplant are also utilized posttransplant. In a series of studies over the last 10-plus years, graft survival was enhanced using IVIG in conjunction with rituximab and other medications.³ Additionally, IVIG in combination with other treatments and medications have been used to treat AMR in lung, cardiac and liver transplants.

Another potential complication posttransplant is secondary hypogammaglobulinemia resulting from the use of potent immunosuppressants in transplant recipients, a trend that appears to be increasing. When this occurs, patients present with recurrent or multiple infections similar to those seen in patients with primary immunodeficiencies.⁴ IgG levels are part of lab monitoring after transplant, and if levels are low and/or infections occur, IG replacement therapy, either IV or subcutaneous, is implemented.

Use of IG products in the liver transplant population is a little different than other organs. Liver transplants have some unique challenges. Special IG formulations are used specifically for liver transplantation. One is hepatitis B hyperIG, which has made transplantation for hepatitis B-related liver cirrhosis not only possible, but successful. It has also opened up a potential new pool of donors who have been previously exposed to the hepatitis B virus.

The introduction of specific hyperIGs against cytomegalovirus (CMV) infection approximately two decades ago resulted in a significant reduction of viral infection rates posttransplant.⁵ Various trials suggest a lower incidence of rejection and improved long-term survival using CMVIG.

The use of IVIG in highly sensitized liver transplant recipients is currently undefined, since comparative trials are still lacking.⁶

Great Success, Yet More Studies Are Needed

The No. 1 issue in organ transplantation is lack of appropriate donors, both living and deceased. IVIG formulations have played a major role in broadening the population of donors, making solid organ transplants more successful, decreasing wait times, improving long-term survival rates and preventing complications. As always, more studies in all solid organ transplants utilizing IVIG in combination with other therapies are needed to further improve outcomes.

MICHELLE GREER, RN, is senior vice president of sales for NuFACTOR Specialty Pharmacy.

Table 1. Drugs Used in Desensitization Therapy

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<th>Intravenous Immune Globulin</th>
<th>Rituximab</th>
<th>Obintuzumab</th>
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<th>Belimumab</th>
<th>Eculizumab</th>
<th>C1 Esterase Inhibitor</th>
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References

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“No one wants to think they will lose their insurance—even briefly—but when you’re dealing with a chronic disorder you always have to be prepared for the unexpected.”

— Lori K.
Parent

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8 AM to 8 PM ET
A Gap in Your Insurance Coverage Shouldn’t Mean a Gap in Treatment


How to enroll:
• Call the toll-free IgIQ Hotline at 1-877-355-4447

Earning and redeeming points is easy.
• Earn a point for every consecutive month of CSL Behring product use
• Redeem 3 points for a one-month supply of your CSL Behring product*
• Should you suffer a lapse in your insurance, simply contact a IgIQ Care Coordinator and we will take care of the rest

“At the Immune Deficiency Foundation, we often talk to patients who lose their insurance coverage and we see firsthand how stressful this situation can be. This program not only helps people continue their life-saving treatments but also provides security for the future. It is a valuable option for our patient community.”
— Marcia Boyle
President and Founder, Immune Deficiency Foundation

*Certain limitations apply—see program Terms and Conditions at www.cslbehringassurance.com.
IN THE NEWS

Initiatives

New Medicare Educational Initiative Introduced to Raise Awareness of Chronic Care Management

Connected Care is a new educational initiative to raise awareness of the benefits of chronic care management (CCM) services for Medicare beneficiaries with multiple chronic conditions and to provide healthcare professionals with support to implement CCM programs. It is a nationwide effort within fee-for-service Medicare that includes a focus on racial and ethnic minorities, as well as rural populations, who tend to have higher rates of chronic diseases.

According to the Centers for Medicare and Medicaid Services (CMS), which launched the initiative with the Federal Office of Rural Health Policy at the Health Resources and Service Administration, “two-thirds of Medicare beneficiaries have two or more chronic conditions, and one-third have four or more chronic conditions. Many healthcare professionals are providing these patients with chronic care management, non-face-to-face services such as reviewing test results or coordinating with other providers, but are not aware of the separate payments under the Medicare Physician Fee Schedule and are not receiving the full separate payments that are now available for CCM services under Medicare Part B.”

The initiative includes new resources to educate patients and healthcare professionals, including:

• A toolkit for healthcare professionals with detailed information about CCM and resources to help providers implement CCM;

• A partner toolkit that includes downloadable resources and suggested activities to get involved in the Connected Care initiative; and

• Patient education resources, including a poster and postcard that can be used in a clinical or community setting.

All resources are available at no cost online at go.cms.gov/ccm.


Did You Know?

The Kawasaki Disease Foundation of India has launched the world’s first free mobile app on Kawasaki disease. Part of the foundation’s public awareness program, the app provides all available information about the disease, which is often confused with other common conditions such as measles fever, scarlet fever and Stevens Johnson syndrome, and can result in fatal coronary artery disease if not treated within 20 days of acute illness. The app can be downloaded from Google Play store.

Campaign

Shire Launches #PIPostsThanks to Raise Awareness About PI

Shire, manufacturer of immune globulin for the treatment of primary immunodeficiency (PI), has launched a social campaign, #PIPostsThanks, to spotlight the unsung heroes who make a difference in the lives of people living with PI. The #PIPostsThanks campaign kicked off April 22 through 29 during the seventh World PI Week to bring the PI community together to share personal journeys and highlight the efforts of those who help ease the burden of living with PI. “As a leader in developing innovative treatments and support services for PI patients, Shire values the opportunity to serve this community,” said Kasha Witkos, global head of immunology at Shire. “Through awareness campaigns such as #PIPostsThanks, we hope to raise awareness of this devastating disorder and offer our own thanks and ongoing commitment to innovating on behalf of PI patients around the world. We are determined to make a meaningful difference for patients with PI.”


Campaign
Marcia Boyle, IDF’s Founder and President, Announces Retirement

In May, Marcia Boyle, the Immune Deficiency Foundation (IDF) founder and president, announced plans to retire from the organization after more than 37 years of leadership. Boyle co-founded IDF in 1980 after her son was diagnosed with a primary immune deficiency (PI). Since 2005, she has served as IDF’s president and is known for accomplishing several key milestones, including creating education materials; helping to establish PI advocacy groups in foreign countries; leading a team of advocates and legislators to advocate for the creation and enactment of the Medicare IVIG (intravenous immune globulin) Access Act (HR 1845); helping to launch a nationwide campaign to establish severe combined immunodeficiency newborn screening in all states; and being honored in 2015 by the White House as a Champion of Change in Precision Medicine.

Boyle’s commitment to the IDF community was celebrated at the IDF 2017 National Conference in Anaheim, Calif., June 15-17. At that time, it was announced she will continue to volunteer for the organization and will serve as a member of IDF’s Board of Trustees. “While Marcia will always be remembered for her vision and tenacity in establishing IDF, her true legacy within our community will be tied to her organizational leadership skills and innovative approach she took in re-establishing a positive trajectory for IDF when she came back a little over a decade ago,” said John Seymour, PhD, chair of the IDF Board of Trustees. “Thanks to Marcia’s leadership, IDF has experienced a resurgence in the past decade, expanding programs and services, diversifying and enhancing funding streams and building an endowment.”


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Autoimmune Corner

Medicines

First Drug Approved to Treat Severe Forms of MS

The U.S. Food and Drug Administration has approved Genentech’s ocrelizumab (Ocrevus), which is the first to have an effect on primary progressive multiple sclerosis (MS), the most severe form of MS, by targeting the body’s B cells. In the past, research has focused on T cells, which has often worked in mice models but doesn’t work in humans. The new drug was developed by a team of researchers at the University of California, San Francisco, that focused on B cells, the majority of which reside deep inside the brain, but about 2 percent of which circulate through the blood and cause inflammation in the nervous system of MS sufferers. In clinical trials, the drug effectively destroyed rogue B cells for several months. When tested against interferon beta-1a, the current standard for the most common form of MS known as relapsing-remitting, ocrelizumab reduced the annual relapse rates by 47 percent, reduced disability by 43 percent and shrank brain lesions by 95 percent. But even more impressive was that it showed promise in slowing down primary progressive MS, which researchers suspect is caused by the 98 percent of B cells located in the brain, making it much harder to treat.


Research

Researchers Receive Grant to Study Most Effective Treatment for Kawasaki Disease

Researchers at the University of California San Diego School of Medicine, Rady Children’s Hospital-San Diego and Betty Irene Moore School of Nursing at the University of California, Davis, have received a $2 million grant from the Patient-Centered Outcomes Research Institute (PCORI) for a three-year study to look at the effectiveness of two treatment options for children with Kawasaki disease (KD) who are resistant to initial therapy. Standard treatment for KD is intravenous immune globulin (IVIG), but 10 percent to 20 percent of patients are resistant to the therapy, putting them at a higher risk for serious complications such as coronary artery damage and aneurysms. Currently, there are no guidelines for the best secondary treatment. Most patients receive either a second infusion of IVIG or an engineered antibody called infliximab that inactivates a molecule that promotes inflammation. The PCORI grant will support a study to compare the effectiveness of these two approaches for IVIG-resistant KD patients.

“After talking to more than 100 parents, clinicians and researchers, we learned that their top priority for research is to test the effectiveness of treatments to prevent heart damage in this fragile patient population,” said Jane Burns, MD, co-principal investigator of the study and professor of pediatrics at the University of California San Diego School of Medicine “Our findings will further Kawasaki disease research and give insight into how to approach patients who do not respond to initial treatment.”

The KD study was selected for PCORI funding through a highly competitive review process. The goal of the nonprofit organization is to determine which of the many healthcare options available to patients and those who care for them work best in particular circumstances so they can make the most informed decisions.

In February, the U.S. Food and Drug Administration accepted CSL Behring’s biologics license application (BLA) for Privigen (immune globulin intravenous [human] 10% liquid) to treat chronic inflammatory demyelinating polyneuropathy (CIDP). If approved, Privigen would be indicated for the treatment of patients with CIDP to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse. This would be the third approved indication for Privigen in the U.S., after primary immunodeficiency and immune thrombocytopenic purpura.

Trial data supporting the supplement includes CSL Behring’s PRIMA study that showed Privigen may help decrease weakness and loss of motor function in people with CIDP. Data from the recently completed PATH study will be used to further support the efficacy, safety and tolerability of Privigen to treat CIDP.

“CSL Behring is committed to building a leading neurology franchise, and the approval of Privigen for CIDP will be a significant step in providing valuable options for patients and physicians to treat neurological conditions,” said Charmaine Gittleson, senior vice president of global clinical development at CSL Limited. “The possibilities for innovating new uses for IVIG [intravenous immune globulin] therapy are growing, and this expansion into CIDP is another way we can deliver on our promise to meet the needs of patients with rare and serious disorders.”

The growing interest in genetic testing has spurred the field of genetic counseling, leading to better health outcomes and treatment options.
WITH MORE THAN 1,800 genetic tests available through research centers and direct-to-consumer kits, and more than 10 million genetic variants, the interest in genetic testing is rapidly gaining momentum, with some estimates showing a market growth of as much as 25 percent annually. Alongside this rise comes increased access to information about health status and susceptibility to health concerns, diseases and potential expectations for projected life span. “The field of genetics has grown tremendously,” explains James P. Evans, MD, PhD, Bryson Distinguished Professor of Genetics and Medicine at the University of North Carolina, Chapel Hill. While the possibilities for this information seem endless, it is important to gain a better understanding of what genetic testing is, what can be gained from it and how results can best be interpreted.

What Is Genetic Testing and How Is It Used?

Genetic tests identify changes in chromosomes, genes or proteins that may be able to confirm or rule out a genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. For instance, scientists can look at a single gene’s short DNA strands to identify mutations that can lead to a genetic disorder. They can look at whole chromosomes or long lengths of DNA to see if there are large genetic changes such as an extra copy of a chromosome that can cause a genetic condition. Or, they may consider biochemical genetic tests to study the activity level or number of proteins since abnormalities can indicate changes to DNA that result in a genetic disorder.

In a clinical setting, genetic testing is generally a simple blood draw that allows for a better quality DNA sample. In some cases, only one gene is looked at such as with the rare condition of fragile X syndrome. In others, multiple genes are tested at once such as with suspected autoimmune disease in which a mutation or error in any number of genes collectively can increase a person’s risk. In some cases, doctors know which gene they are specifically testing for, but in others, they aren’t sure. Complex diseases such as those with known strong genetic and environment components make testing and forming conclusions more difficult. Multiple sclerosis (MS), for example, is known to be caused by both genetic and environmental factors. “The field of genetics doesn’t really understand what to test for with MS,” explains Erynn Gordon with the National Society of Genetic Counselors. “Research tells us there is clearly a genetic component, but we don’t yet know the gene to test for.” In these cases, testing multiple genes at one time can provide a cost-effective look at a number of genetic causes.

Genes are DNA inherited from parents that can tell one version of a person’s risk for disease, its potential severity and other factors. Typical reasons for genetic testing referrals differ between adults and children. For instance, in adults, the most common testing referral occurs because of an unusual cancer diagnosis such as young age or other suspicious factors. In children, a birth defect is the most common reason. Patients with suspected or familial immune disorders are frequently referred for genetic testing to assist with diagnosis and clinical prognosis and to narrow successful pharmacogenetic treatment options. “While most diseases aren’t genetic in nature,” explains Dr. Evans, “our development is driven by our genes.”

Understanding a person’s genetic makeup can help guide patients and physicians in making healthcare choices. It can guide families in deciding about future pregnancies by identifying genes that can be passed on to children, and it can better inform expectant and new parents about any conditions their newborn may be susceptible to both in utero and after birth. Obstetrics is an area in which genetic testing is common because it is a noninvasive prenatal look via amniotic fluid or placenta tissue samples. Once a child is born, a heel stick screening can identify any abnormalities that warrant further exploration.

Genetic testing can provide vast amounts of information to patients, as well as patients’ first-, second- and, in some cases, third-degree relatives who may also choose to undergo genetic testing multiple genes at one time can provide a cost-effective look at a number of genetic causes.

Direct-to-Consumer Genetic Testing

With the thousands, and by some reports tens of thousands, of genetic tests available, curiosity about direct-to-consumer (DTC) genetic testing is increasing. While the lure of quick and easy answers draw consumers, the U.S. Food and Drug Administration, Centers for Disease Control and Prevention, Federal Trade Commission and some healthcare associations such as the American College of Medical Genetics and the American Society of Human Genetics urge consumers to use caution and remember there are many complex layers of information surrounding both the decision to undergo a genetic test and how to interpret the results. Without the context of a medical evaluation, a full interpretation of the results and what to do next, DTC test results may be meaningless to the consumer. And, while many DTC test kits suggest contacting a professional to discuss results, the onus is on the patient to do so.
testing based on results. For example, while there may be a familial pattern of autoimmunity, autoimmune diseases seen in each family member may be different. The ability to genotype family members for their own genetic information and identify appropriate donors can be critical to patients’ health and healthcare. This information may inspire patients to make different decisions, which can be overwhelming because it can completely change the trajectory of their lives.

The good news is geneticists (doctors who specialize in genetics), genetic counselors (certified healthcare workers who counsel patients on genetic testing plans and results), nurses, social workers and other specialists trained in genetics can help patients evaluate the decisions surrounding testing and how to interpret the results. Patients can then be armed with the best available information and how to use it.

Help from Geneticists and Genetic Counselors Can Determine Clinical Utility, or Whether the Information Can Lend Insight into a Diagnosis, Management or Treatment.

What Genetic Test Results Mean

The term “genetic mutation” sounds scary. However, most disease-causing genetic mutations are rare. Mutations, or alterations, also apply to things as simple as eye color and blood type.

If a test comes back “positive,” it means the genetic alteration tested for was detected. If it comes back “negative,” it means it was not detected or it is inconclusive, which means either not enough information was gleaned or further testing may be warranted.

The terms “positive,” “negative” and “inconclusive” may also suggest a “bad result,” “good result” or “question mark.” For instance, testing positive for a gene mutation doesn’t mean the disease is inevitable (just as not everyone who carries the BRCA1 or BRCA2 genes develop breast or ovarian cancer). Also, the course or severity of a disease can’t be predicted. And, just because a test doesn’t reveal a gene mutation, it’s still possible the disease will develop (like those who develop breast cancer even though they don’t carry BRCA1 or BRCA2 genes).

Confusing results is just one reason it is so important for individuals making the decision to undergo genetic testing to do so under the guidance of healthcare professionals who can discuss family history, available tests and the analytical (accuracy) and clinical (whether they actually provide the information sought) validity of the tests. Taken together, help from geneticists and genetic counselors can determine clinical utility, or whether the information can lend insight into a diagnosis, management or treatment.

What to Expect from Genetic Testing and Genetic Counseling

Why is genetic testing important? Why not just diagnose the disease and treat it if possible? According to Gordon from the National Society of Genetic Counselors, there are many important reasons: “In some cases, the phenotype, what the patient is experiencing, can have multiple different causes as in the case of peripheral neuropathy. Sometimes it is caused by diabetes, and sometimes there are hereditary causes. Another example is Charcot-Marie-Tooth disease, which can have different versions and be inherited in different ways.”

Another reason is the symptom being tested for may be one of many, and an evaluation can help determine what other organ systems may be involved and whether an evaluation of family members may lead to a bigger picture of the disease. “Some diseases are more clearly genetic than others,” Gordon explains. “In many cases, the disorders of interest will be more diverse, and a test may rule in or rule out hereditary forms.”

Gordon says that, oftentimes, people are not referred to geneticists when they should be: “There is a tendency, rightfully so, for specialists to focus on their area of expertise, but that may mean multisystem disorders are missed. If you are a patient and have multiple systems involved in your disease, ask your doctor if something could be tying them all together. There are probably more genetic disorders than we realize because we tend to focus on the primary system rather than the bigger picture.”

Genetic counselors are facilitators and educators for both patients and primary care physicians. They primarily deal with face-to-face patient interaction to help address concerns and to ease patients into the process. It starts with a discussion of family history to better understand who else might be affected and whether other considerations need to be addressed. They then discuss the type of tests to be performed, any risks, how long the results will take and what types of information the tests will provide.
How the results are interpreted and what type of follow-up is required depends on each situation. For example, in pediatrics, genetic counselors provide “anticipatory guidance” to educate families and their doctors and ensure they are connected with all available resources. “In a pediatric setting, we help the family figure out if there is a genetic condition for what we are seeing,” explains Robin Grubs, assistant professor of human genetics and director of the genetic counseling program at the University of Pittsburgh. “We discuss all the possibilities with the patients and their families, including discussing possible outcomes and what a positive or negative result may mean, as well as treatment possibilities. We help patients understand the possible outcomes so they won’t be blindsided by the results. We must ensure they understand that this could be really serious.”

In adults, cancer is the most common type of referral to a genetic counselor, and the relationship between the counselor and patient is generally shorter term because the counselor becomes part of the precision medicine process of disease management. In those for whom increased surveillance is warranted, adapted screening recommendations and testing can help to keep on top of risks.

For prenatal patients, it is hoped the relationship is even shorter, says Janice G. Edwards, MS, CGC, clinical professor and director of the genetic counseling program at the University of South Carolina School of Medicine: “We never see them again if they are healthy.” But, when needed, genetic counselors follow the patient and help the parents get through the crisis.

Genetic Testing Costs

Genetic testing can run anywhere from a few dollars (in the case of some prenatal screenings) to a few thousand dollars. Many insurance companies cover genetic testing, at least in part, so it is important to verify which tests are covered and the co-pay amount.

Many genetic tests today are moving toward what is known as panel testing, or testing multiple genes at once. “Going back to the peripheral neuropathy example,” explains Gordon, “we might look at all the genes that could be associated, rather than guessing which gene could be the underlying cause.” According to Gordon, the field of genetics is moving so fast that costs of testing have dropped significantly: “If multiple genes can have a similar presentation, it makes sense to cast a wider net.”

No matter the results, the Genetic Information Nondiscrimination Act prevents both health insurers and employers (provided the employer has more than 15 employees) from discrimination based on test results. Even with this protection, however, some elect to undergo genetic testing without going through their insurer because it could affect the cost of insurance. Also, some types of coverage do not fall under this protective umbrella such as long-term care, disability and life insurance.

Genetics of the Future

Genetic disorders were once so rare, most pharmaceutical companies declined to invest in them. But now, pharmacogenetics is a promising field and is beginning to change the way medicine is prescribed, with a focus on tailored treatments. “Now, we are understanding the molecular mechanisms, what is broken and how that affects proteins,” says Gordon. “We can focus in, as is the case with cystic fibrosis and Duchenne muscular dystrophy, and we’ll see this increasing over time.”

“We are trying to better understand precision medicine,” says Grubs. “Our goal is to understand the factors that contribute to disease.” In the meantime, patients can play a role in their health, including the possibility of whether health-harming genes are triggered by environmental factors. For example, some drugs are associated with the development of immune disorders, and some suspect that certain viruses are associated as well. Even iodine has been attributed to the onset of thyroid disease. “We want to give patients a sense of agency in what they can do for their health,” adds Grubs.

In some genetic conditions, dietary changes or enzyme replacement therapy can help. Resources such as the American Cancer Society’s cancer prevention guidelines offer recommendations that should be adopted by most everyone. Eliminating tobacco, maintaining a healthy weight, performing physical activity and eating a healthy diet are important proactive steps people can take. “Everyone can reduce their cancer risk,” says Grubs, “even if they have a hereditary form of cancer.”

“One day, we’ll have lots of changes we can make, but we aren’t there yet,” explains Edwards. “Today, if patients know they have a genetic change that makes them more at risk, as in the case of increased risk for breast cancer, they can have a prophylactic surgery to reduce the risk.” And, in the future, we may have other means and protocols.

AMY SCANLIN, MS, is a freelance writer specializing in medical and fitness issues.

Resources
Gastrointestinal Problems in Immunodeficiencies:

Common among PI patients, leaky gut has many underlying causes that, when identified, can determine the best course of treatment.

By Terry O. Harville, MD, PhD
ALONG WITH THE skin, the gastrointestinal (GI) tract interfaces our bodies with the world. While we think of the GI tract as being “inside of us,” it is actually connected to the world “outside of us.” In simple terms, our bodies are a “tube,” with the mouth at one end and the anus at the other. Anything in the world can potentially enter the mouth (or anus), migrate through the GI tract and exit from the anus (or mouth). Thus, the GI tract is always in direct contact with the outside world.

The skin covers the outer portion of our bodies (the tube), and the mucosal cells of the GI tract cover the inner portion. Together, these two coverings protect all the cells, tissues and organs inside of our bodies. Like the skin, the mucosal cells of the GI tract come into contact with a myriad of microorganisms, acting as a barrier to keep them out of our bodies. It is estimated there are 10 times more microorganism cells in our GI tract than the total number of cells that make up our bodies. Thus, we are only about 10 percent of a community of organisms with which we must live in harmony or suffer some form of adverse consequence.

Under normal circumstances, the immune system becomes tolerized to the microorganisms that are present in the GI tract. Collectively, this is known as our microbiome. As long as the microorganisms remain outside the body in the open space of the intestines (the lumen), they are not perceived as a threat, and the immune system does not attack them. The relationship is commensal (neither is trying to hurt the other) and symbiotic (we provide them with food and a place to live, and the microorganisms provide certain nutrients we need). Additionally, some of the microorganisms may have important roles in the development of our immune system, as well as roles to help prevent conditions such as allergic diseases and autoimmune disorders from developing. Therefore, when our GI tract remains functionally intact, we have the correct microbiome present, and our immune system is functioning normally; we are healthy, and all is remaining well.

Unfortunately, things break down when immunodeficiencies are present or autoimmunity occurs. Further, antibiotics and some medications may alter the microenvironment of the GI tract resulting in problems with the microbiome.

Figure 1. Layers of Skin Cells

The skin, as a barrier, has multiple layers of cells to keep water and other molecules inside, while simultaneously keeping unwanted things out. (Modified from the original Grey’s diagram: en.wikipedia.org/wiki/Image:Gray941.png; public domain: commons.wikimedia.org/w/index.php?curid=1374564)

Functions of Skin and GI Mucosal Cells

Skin acts a barrier with multiple layers of cells and blood vessels to prevent loss of water and other molecules, as well as unwanted entities entering from the outside world (Figure 1).

In contrast, GI mucosal cells are typically one cell layer thick, which suggests it may be somewhat easier to lose the layer’s integrity and keep what should remain outside from what is inside. The relative thinness is by design, though. When food is digested and water is ingested, the mucosal cell...
layer can more readily transport the nutrients directly into the blood system just below the cell layer (Figures 2 and 3).

To maintain mucosal cell layer integrity, a specific mechanism creates a tight adherence between the cells. By analogy, the GI mucosal cell layer is a brick wall (each brick is a cell) with a front and back side. The front is the intestinal lumenal side to the outside world, and the back is the side to the body. The other four sides interact with the adjacent cells. Using this analogy, the mortar (desmosomes) between the bricks (cells) maintain tight integrity to keep things out or in (Figure 4).

Because the wall is only one cell thick, the GI mucosal cell layer is somewhat tenuous. Damage to the cells or breaks in the adhesion between the cells could readily allow for a leaky gut.

Is It Always “Abnormal” for the Gut to Become Leaky?

Throughout life, there is a need for cells to grow and divide to replace old, dying or injured cells. From infancy into adulthood, a tremendous amount of growth and cell division must occur.
And, during this process in the GI mucosal cell layer, adhesion between cells is temporarily lost in order to complete the division cycle. As such, early in life, excess normal leakiness of the gut naturally occurs as the cells grow and divide. When the normal and intact immune system and the correct microbiome of the intestines are in place, appropriate immune maturation occurs, despite the occasional normal leakiness. Therefore, evolutionary growth from infancy to adulthood results in some normal, extra leakiness of the intestines. It’s part of normal maturation of the immune system and for tolerance induction to allow symbiotic and commensal microorganisms to live in harmony.

**Causes and Consequences of the Gut Becoming “Abnormally” Leaky**

Unfortunately, the tenuous mucosal cell layer can undergo pathologic processes and become abnormally leaky due to a number of causes.

In some individuals (most typically children), some food item (e.g., peanuts) exposures early in life, when the GI tract is more normally leaky, or some alteration of the microbiome (e.g., antibiotic treatment) may enhance abnormal leakiness or alter the tolerization. When this happens, the food item can be mistaken by the immune system as a parasitic attack, and allergic disease may result. In the mistaken response to rid the GI tract of parasites, this reaction compounds itself in cycles of increased leakiness due to mediators released by the immune cells. Typically, avoidance of the offending food item allows the GI mucosa to heal and the immune system to retolerize and return to a less leaky state.

On another front, inflammatory bowel disease (IBD) is a major cause of a leaky gut. While this is not fully understood, it is believed that tolerization against certain microorganisms is lost early in the process. It’s not clearly understood, but possibly some microorganisms with a greater pathogenic potential became present and invaded the GI mucosa, initiating an immune system inflammatory response. Inflammation worsens the leakiness, which then compounds the effects of the microorganisms’ exposure to the immune system, perpetuating cycles of continuous leakiness and inflammation. The breakdown in tolerance to the microbiome of the intestines could also be due to the influence of specific genes, beginning with malfunction of the immune system, causing it to initiate inflammation in the mucosa and the leakiness, which again results in seemingly endless cycles perpetuating leakiness. Diarrhea typically occurs when tolerization against microorganisms is lost. Several useful treatment options can downregulate the immune system’s activation state, which can reduce the extent of inflammation and, in turn, reduce leakiness.

At least 10 percent of patients with common variable immunodeficiency (CVID) report symptoms of the GI tract. But, endoscopy and biopsy analyses indicate 50 percent or more have alterations suggestive of infectious or inflammatory diseases. Approximately 2 percent of patients with CVID may develop granulomatous disease, which can involve the GI tract. In granulomatous disease, nodules of immune cells aggregate into clusters in the tissues and disrupt the normal function of the specific tissue. Finding granulomas is one of the histopathologic criteria for the diagnosis of Crohn’s disease (one specific IBD found in approximately 0.2 percent of the population), but other conditions (e.g., sarcoidosis) may also present with granulomas. Use of IBD treatments may be beneficial for treating granulomatous disease.

Unfortunately, patients with primary immunodeficiency (PI) seem destined to develop some extent of an increased leaky gut. With an immune system...
that is not intact, tolerization to the microbiome may not occur. As stated previously, tolerization should occur early in life, when normal, excess leakiness may be present. Due to lack of tolerization, the symbiotic and commensal microorganisms may be perceived as trying to invade the body, or in some cases, may actually invade (opportunistic infections). At this point, most patients require antibiotics to treat respiratory infections. The antibiotics alter the normal microbiome, which may allow for potentially pathogenic organisms to become present (e.g., C. difficile). Indeed, antibiotic usage since the middle of the 20th century has altered the microbiome in such a way that we are not totally sure what is truly normal.

Additionally, parasites may become chronically present. For example, giardia (a microscopic parasite that causes diarrhea) can be commonly found in the normal water supply, or brought into the home by pets. Other bacteria and parasites may also take up residence in the GI tract (e.g., Isospora, Coccidia, Campylobacter, Salmonella, Shigella, Yersinia, Cryptosporidium, etc.), each of which can result in continuous inflammation and leakiness.

Another way microorganisms cause increased GI tract leakiness is through the release of toxic compounds, known as enterotoxins. Perhaps one of the best known is the cause of shigellosis through Shiga toxin from Shigella. Enterotoxins tend to produce extensive diarrhea by adversely affecting the mechanisms mucosal cells normally use to transport nutrients and electrolytes into cells, and then into the body. Some enterotoxins actually cause essentially a reversal of the transport process so that water, electrolytes and nutrients are pumped out of the body into the GI tract. When this happens, massive amounts of diarrhea may occur, resulting in extensive loss of nutrients and proteins from the body.

Viruses can also compound leakiness. Enteroviruses make up a large category of viruses that may enter the body and result in respiratory, GI and central nervous system symptoms (e.g., meningoencephalitis). Some are commonly called the “24-hour bug” or the stomach flu (not influenza). Norovirus is now more recognized as a cause of chronic diarrhea in patients with immunodeficiencies. Other viruses such as cytomegalovirus may also plague patients with immunodeficiencies. These viruses may directly infect intestinal cells, resulting in cells losing tight adherence, causing them to die and activating the immune system to kill the infected cells. In short, loss of the mucosal cell integrity occurs, which can cause extensive leakiness. Viruses may be difficult to treat, but for some, antiviral agents are available. An increase in replacement immune globulin (IG) may also be helpful.

Chronic diarrhea indicates the GI tract is leaking proteins and fluids from inside the body. This can result in loss of nutrients and specific proteins such as albumin, but in particular, loss of IgG. This can further impair immunodeficiency since the level of circulating IgG may not be able to be maintained at a sufficient level for good immune protection.

In addition, there is evidence of oxidative stress, which occurs in cells undergoing inflammation, in patients with leaky gut. Exposure of the immune system to microorganisms in the wrong manner (i.e., a break in tolerization), alterations of organisms’ molecular components due to oxidative damage (the generation of new antigens to which the immune system may respond) and alterations of one’s own tissues due to oxidative damage (likewise, possibly generating new auto-antigens to which the immune system may adversely respond) may continue a cycle of inflammatory responses with intestinal leakiness that can be difficult to break. In this case, antioxidative therapy is commonly recommended, which is unlikely to cause harm. Yet, even though it may be beneficial, it is unlikely to completely resolve the problem in all persons.

Also, gluten sensitivity may result in the diagnosis of celiac disease (CD), which has been shown to occur in approximately 1 percent of people and can be a major source of GI leak. In patients with CVID who had endoscopic and biopsy features similar to those found in patients with CD, only 20 percent had improvement with a gluten-free diet. Therefore, merely trying a gluten-free diet may not be beneficial for most patients with a leaky gut. However, those with the specific risk factors for CD may benefit. Specific testing for CD and its risk factors should be considered and discussed with a physician.

In summary, there are numerous causes of a leaky gut. Some may be attributed to normal circumstances during normal cell growth and division, as well as during normal growth from infancy to adulthood. There are abnormal circumstances due to the development of allergic disease, alterations in the microbiome due to antibiotic treatment, inflammation arising from IBD, altered tolerance to the microbiome due to immunodeficiencies,
opportunistic infections due to immunodeiciencies, toxins produced by microorganisms, viral infections, oxidative stress and conditions such as gluten sensitivity. Mutations may be present in the immune system, affecting how it responds to the microbiome interface. And, there may be mutations affecting the way mucosal cells function, further compounding the issues.

What Can Be Done for a Leaky Gut?

Unfortunately, due to the nature of the onset of a leaky gut and the inflammation that precedes and/or follows, endless cycles of the condition may occur that can be difficult to break. For those treated with IG replacement therapy, sometimes higher dosing may ease symptoms by helping to control the infectious processes and reduce inflammation, which in turn reduces leakiness.

Corticosteroids can be useful since they reduce inflammation and tend to reestablish the tight junctions between mucosal cells. Chronic corticosteroid use, though, can result in numerous adverse side effects. Therefore, a corticosteroid such as budesonide, which is poorly absorbed systemically, may be better to use.

If there are known mutations that are further promoting leakiness, specific therapies associated with these may be helpful. For example, specific genes upon activation can result in autophagy (damaging and killing of cells, and production of much inflammation), which is responsible for some IBD. Specific inhibitors of these pathways can be very useful in ameliorating a leaky gut in patients with specific mutations.

In some instances, probiotics can be useful, especially in those treated with antibiotics. The goal is to try to reestablish a normal microbiome. When parasites are present (e.g., giardia), the typically recommended course of treatment may be woefully inadequate; sometimes months of treatment are required to prevent relapses.

Gluten avoidance can be useful in some, but the specific risks for CD should be evaluated (since these are the patients likely to benefit) and fully discussed with a physician before attempting. It puts antibodies into the GI tract where they are needed, and some have used it successfully to improve leaky GI tracts. This product must be prescribed by a physician.

Fecal transplants, also known as fecal microbiota transplants, collect normal microorganisms from the GI tracts of nondiseased persons to treat patients with GI tract problems. This is a U.S. Food and Drug Administration-approved treatment for C. difficile. Use of fecal transplants in PI patients has not been widely studied, but many consider it relatively safe and likely beneficial. There is concern, though, that opportunistic pathogens could be present and create significant problems for those with PI. Once again, this approach requires very careful discussion of the pros and cons.

Helminthic therapy uses rat tapeworms introduced into the human GI tract to induce specific immune responses for down-regulating autoimmune disorders, asthma and allergic diseases. It has also been reported to benefit some neurologic disorders and autism. While it could benefit some forms of GI tract inflammation such as IBD in PI patients, it has not been studied fully. There are concerns that an immune system that cannot respond normally will not generate the desired beneficial effect of a decrease in inflammation, followed by a decrease in GI tract leakiness. Unfortunately, there is also potential for the opposite to occur: worsening of the leakiness.

Some specific diets (e.g., specific carbohydrate diet) have been touted as bringing remarkable changes in a leaky gut, but they have not been tested in a rigorous fashion. Major dietary changes should be undertaken with guidelines from a nutritionist and a physician.

Any therapeutic intervention should be carefully considered and thoroughly discussed with a physician before attempting.

A Major PI Disorder Complication

Leaky gut is a major complication in PI patients. There are multiple reasons for it to present, as well as causes for worsening symptoms. Identifying a treatable underlying cause or exacerbator is currently the best approach for improvement. Careful and thorough evaluations should be performed to determine how best to treat the condition. Full discussion with a physician is necessary to make sure individuals receive the correct treatment approach.

TERRY O. 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.

Resources
Listen, PI.
I’ll tell you who’s in charge.

Treat PI on your own terms with CUVITRU

For people living with primary immunodeficiency (PI) 2 years of age or older

CUVITRU™ [Immune Globulin Subcutaneous (Human) 20% solution gives you and your doctor control over your treatment—from the number of infusion sites to how much, how fast, and how often you infuse.1

Number of infusion sites
Infuse using 1 to 4 sites simultaneously

Infusion volume
Infuse up to 60 mL per site, as tolerated

Infusion rate
Infuse at rates up to 60 mL per hour per site, as tolerated*

Infusion frequency
Infuse daily up to once every 2 weeks, at regular intervals

Weekly infusions typically were completed in under an hour† using 1 or 2 sites.1

You and your doctor will determine if CUVITRU is right for you and if so, what regimen is best.

*Recommended to infuse first 2 infusions at 10-20 mL per hour per site.
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Please see the Indication and Important Safety Information on the adjacent page, and the Brief Summary of the FDA-approved patient labeling on the back page of this ad.
CUVITRU [Immune Globulin Subcutaneous (Human)] 20% Solution

Indication and Important Safety Information

What is CUVITRU?

- CUVITRU is a ready-to-use, liquid medicine that contains immunoglobulin G (IgG) antibodies, which protect the body against infection.
- CUVITRU is indicated for the treatment of primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age and older.
- CUVITRU is made from human plasma that is donated by healthy people. CUVITRU contains antibodies collected from these healthy people that replace the missing antibodies in PI patients.
- CUVITRU is given under the skin (subcutaneously).
- Most of the time infusions under the skin are given at home by self infusion or by caregivers. Only use CUVITRU by yourself after you have been instructed by your healthcare provider.

Important Safety Information

What is the most important information that I should know about CUVITRU?

CUVITRU can cause the following serious reactions:

- Severe allergic reactions causing difficulty in breathing or skin rashes
- Decreased kidney function or kidney failure
- Blood clots in the heart, brain, lungs, or elsewhere in the body
- Severe headache, drowsiness, fever, painful eye movements, or nausea and vomiting
- Dark colored urine, swelling, fatigue, or difficulty breathing

Who should not use CUVITRU?

Do not use CUVITRU if you:

- Are allergic to immune globulin or other blood products.
- Have selective (or severe) immunoglobulin A (IgA) deficiency with antibodies to IgA.

CUVITRU can cause serious side effects. Call your healthcare professional or go to the emergency department right away if you get:

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of irritation of the lining around your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms. These could be signs of a blood clot.
- Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver or blood problem.
- Chest pain or trouble breathing, or blue lips or extremities. These could be signs of a serious heart or lung problem.
- Fever over 100°F. This could be sign of an infection.

What are the possible or reasonably likely side effects of CUVITRU?

The following one or more possible side effects may occur at the site of infusion: mild or moderate pain, redness, and itching. These generally go away within a few hours, and are less likely after the first few infusions. The most common side effects that may occur are: headache, nausea, fatigue, diarrhea, and vomiting.

These are not all the possible side effects. Talk to your healthcare professional about any side effects that bother you or that don't go away.

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire at 1-800-999-1785.

The risk information provided here is not comprehensive. To learn more, talk about CUVITRU with your healthcare provider or pharmacist. The Brief Summary of the FDA-approved patient labeling can be found on the reverse side.


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S17659 02/17
Low rate of infusion site reactions even when infused at higher volumes and rates per site\(^1\,^2\)

- **2 out of every 3 people** who received CUVITRU had **no infusion site reactions**
- The most common infusion site reactions are mild or moderate pain, redness, and itching (these generally go away within a few hours, and are less likely after the first few infusions)
- The most common side effects that may occur are headache, nausea, fatigue, diarrhea, and vomiting

To learn more about CUVITRU, visit ListenPI.com and talk to your doctor to find out if CUVITRU is right for you.

**Important Safety Information**

**CUVITRU can cause blood clots** in the heart, brain, lung, and elsewhere in the body. Call your healthcare professional or go to your emergency department right away if you have pain, swelling, warmth, redness, a lump in your legs or arms, chest pain, trouble breathing, or blue lips or extremities. These could be signs of a blood clot.

**Do not take CUVITRU** if you are allergic to immune globulin or other blood products, or have selective (or severe) immunoglobulin A (IgA) deficiency with antibodies to IgA.

Please see the Indication and additional Important Safety Information on the inside of this fold out page, and the Brief Summary of the FDA-approved patient labeling on the back page of this ad.
IMPORTANT INFORMATION ABOUT
CUVITRU [Immune Globulin Subcutaneous (Human)], 20% Solution

The following summarizes important information about CUVITRU. Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare provider, and it does not include all of the important information about CUVITRU. If you have any questions after reading this, ask your healthcare provider.

What is CUVITRU?
CUVITRU is a ready-to-use, liquid medicine that contains immunoglobulin G (IgG) antibodies, which protect the body against infection. CUVITRU is used to treat adult and pediatric patients two years of age and older with primary immunodeficiency diseases (PI).

• There are many forms of PI. The most common types of PI result in an inability to make a very important type of protein called antibodies, which help the body fight off infections from bacteria or viruses. CUVITRU is made from human plasma that is donated by healthy people. CUVITRU contains antibodies collected from these healthy people that replace the missing antibodies in PI patients.

What is the most important information I need to know about CUVITRU?
CUVITRU can cause the following serious reactions:

• Severe allergic reactions causing difficulty in breathing or skin rashes
• Decreased kidney function or kidney failure
• Blood clots in the heart, brain, lungs, or elsewhere in the body
• Severe headache, drowsiness, fever, painful eye movements, or nausea and vomiting
• Dark colored urine, swelling, fatigue, or difficulty breathing

Who should not use CUVITRU?
• Do not use CUVITRU if you have a known history of a severe allergic reaction to immune globulin or other blood products. If you have such a history, discuss this with your healthcare provider to determine if CUVITRU can be given to you. Tell your healthcare provider if you have a condition called selective (or severe) immunoglobulin A (IgA) deficiency.

What should I avoid while taking CUVITRU?
• CUVITRU can make vaccines (like measles/mumps/rubella or chickenpox vaccines) not work as well for you. Before you get any vaccines, tell your healthcare provider that you take CUVITRU.
• Tell your healthcare provider if you are pregnant, or plan to become pregnant, or if you are nursing.

What are the possible or reasonably likely side effects of CUVITRU?
The following one or more possible reactions may occur at the site of infusion: mild or moderate pain, redness, and itching. These generally go away within a few hours, and are less likely after the first few infusions.

The most common side effects with CUVITRU are: headache, nausea, fatigue, diarrhea, and vomiting.

If any of the following problems occur after starting treatment with CUVITRU, stop the infusion immediately and contact your healthcare provider or call emergency services. These could be signs of a serious problem.

• Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
• Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of irritation of the lining around your brain.
• Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
• Pain, swelling, warmth, redness, or a lump in your legs or arms. These could be signs of a blood clot.
• Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver problem or a blood problem.
• Chest pain or trouble breathing, or blue lips or extremities. These could be signs of a serious heart or lung problem.
• Fever over 100°F. This could be a sign of an infection.

These are not all of the possible side effects with CUVITRU. You can ask your healthcare provider for physician’s information leaflet. Tell your healthcare provider about any side effect that bothers you or that does not go away.

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire at 1-800-999-1785.

The information provided here is not comprehensive. To learn more, talk about CUVITRU with your healthcare provider or pharmacist. The FDA-approved patient labeling can be found at www.CUVITRU.com or by calling 1-800-423-2090.

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Issue Date: 09/2016
16D028-CUV-US
S28017 01/17
Isometrics for the Mobility-Impaired

These exercises are the perfect option for individuals who have difficulty moving due to pain and/or weakness.

By Matthew D. Hansen, DPT, MPT, BSPTS

There are a number of reasons someone receiving immune globulin (IG) treatments may, at least temporarily, not be motivated or able to move much. Fatigue, joint pain, muscle cramps and dizziness may be directly related to the treatment itself or to the patient’s medical condition. Though taking it easy for a day or two following an infusion is certainly understandable, many conditions requiring IG therapy already include weakness and/or muscle atrophy as primary symptoms, and remaining inactive for too long can make the situation worse.

For patients who are unable to move, isometric exercises may be an option. Isometrics are a type of strength training that is performed “in place,” without the angle of the joint or length of the muscle changing during contraction. Resistance can be provided by structural items such as a wall, floor or furniture; holding an external weight in a fixed position; or using one’s own body weight. Though not technically true isometrics, dynamic tension or self-resistance (i.e., pushing or pulling against one’s own body for resistance) is a closely related strengthening technique.

Traditionally, isometric exercises have been used to help prevent disuse syndrome in a limb that is immobilized in a brace, sling or cast. However, they have also been shown to be beneficial for patients who are otherwise immobilized voluntarily or involuntarily. Depending on the method and purpose of the
routine, exertion with isometrics can vary in intensity. The force needed to hold a weight still, for example, is usually submaximal, or the weight would move. On the other hand, pushing/pulling against an immovable object or one’s own body, such as with dynamic self-resistance, may be performed to elicit a maximal contraction.

Research and Parameters

There are a few published scientific studies on the effectiveness of isometric exercise. Some of the most widely referenced studies were supported by NASA to investigate the theoretical effectiveness of isometric exercise on astronaut muscle atrophy due to prolonged weightlessness in space. Though the experiments were performed on lab rats and not on astronauts, the studies’ authors concluded that isometric exercises do promote muscle hypertrophy, but they also fail to prevent the wasting of contractile proteins in the muscle tissue at a molecular level. In other words, even though isometric exercises caused muscles to grow in their experiments, they didn’t appear to increase strength.1,2

In contrast to the NASA research, several studies have found isometric exercises do indeed improve not only muscle size, but also strength, though they are most effective in preventing atrophy of slow-twitch (e.g., endurance and postural) versus fast-twitch (e.g., jumping and running) muscle fibers.3 The angle of the joint is also important to help determine an isometric activity’s impact on strength. Training at only one joint angle does not increase the strength of the muscle as much as training through its entire range of motion. However, there is some cross-transference between joint angles, especially when the exercise is performed at an extended versus flexed joint angle.4

When the purpose of isometrics is to increase strength in the entire muscle, exercises should be repeated every 10 degrees to 30 degrees throughout the available range of motion. If there is only time to perform exercises in one position, the lengthened or extended position should be chosen to have the greatest impact on strength in the entire muscle.5,6

Research suggests both shorter isometric hold times with higher repetitions and longer hold times with fewer repetitions increase static strength.5,7 Because of the increased risk of muscle cramping with sustained contraction, I prescribe a hold of 10 seconds or less, with my preference for a three- to five-second hold, which corresponds well with the time required for someone to exhale slowly through pursed lips while performing the contraction. This is important because isometric exercises can raise blood pressure significantly during the duration of the exercise, which can be particularly dangerous if someone holds their breath while performing the contraction. Patients who have high blood pressure or any form of cardiovascular disease should first check with their doctor before performing any isometric exercises.

With regard to frequency and duration of isometric exercise, established optimal strengthening parameters should be used if possible: eight to 12 repetitions per set, two to three sets per session, at least three sessions per week. However, fewer repetitions and/or sets are certainly appropriate if a patient is not able to meet the optimal standards. In fact, if weakness or pain is a limiting issue, patients should not do more than they are able.

Examples of Isometric Exercises

One of the advantages of isometric exercises is they can be performed from just about any position. The following series of isometric and self-resistance activities can be performed without any special equipment, and have been selected because they emphasize the muscle groups that have a strong association with function and/or are the most vulnerable to atrophy with inactivity. Higher-level isometric exercises, which involve multiple muscle groups at the same time (e.g., some static-hold yoga positions) are not included in this article because if someone is able to perform them, their mobility likely isn’t limited due to pain or weakness.

**Shoulder abduction.** Position yourself with the right arm bent at the elbow and held across the chest. Now, grasp the right elbow with your left hand and pull both arms outward. Switch sides by bending the left elbow and grasping it with the right hand. This can also be performed by standing or sitting with a bent elbow held at the side of your body, and pushing into the wall.

**Shoulder flexion.** Lie face down with both arms held at the sides of your body and push into the surface of the bed or floor with your open palms. The exercise can also be performed while standing face forward and pushing into a stable wall or door frame, or from any position via self-resistance by attempting to
lift one of your arms in front of your body while pushing down on the targeted upper arm with the opposite hand.

Shoulder extension. Flip the position used for shoulder flexion by lying on your back or standing faced away from the wall or door frame and pushing into the surface with open palms.

Horizontal abduction (pecs). Firmly grasp your hands with curled fingers in front of your body, and pull apart without breaking the grasp.

Horizontal adduction (pecs). Push the palms of your hands together in front of the body.

Elbow flexion. Place both hands under either side of a chair, with bent elbows, and pull upward. If elbows are extended, the activity becomes isometric shoulder elevation instead of elbow flexion.

Elbow extension. Place both hands on top of a seat surface, with bent elbows, and push downward without lifting yourself up out of the chair. If elbows are extended, the activity becomes isometric shoulder depression instead of elbow extension.

Abdominals. Contract to pull the abdominal muscles inward as you slowly exhale through pursed lips. This can take some practice because the natural tendency is to push outward during exhalation. Squeeze tightly as you come toward the end of your breath, relax, inhale and repeat.

Knee extension. Keep your right leg straight and tighten the quadriceps (thigh muscles) by pushing your knee backward into extension. If performed while lying on your back in bed or on the floor, your knee would be pushed downward toward the supportive surface. Repeat the activity for the left leg.

Squats. These also target the quadriceps. They are performed by standing with your back against a stable wall and lowering the body toward the floor as if you were going to sit in a chair. Begin by lowering yourself to a point where you just can’t see the tips of your toes. If abdominal obesity is a factor, using the toes as a reference may not work, and because of the extra weight on the knees, it is probably not the best activity to perform. Regardless, don’t go past a position that you are able to stand back up from, and don’t perform this activity if you have a history of knee surgery or pain.

Hip extension. Gluteal sets are performed by simply squeezing the buttocks together and holding for a designated time. If you have a hard time initiating the contraction, as some people do, try imagining you are holding a quarter or cracking a walnut between the cheeks of your derrière. These can also be performed by standing with your heel against a wall and pushing backward into the baseboard, or by lying on your back and pushing down through your heel into the surface. Both of these positions can actually contract both the hip and knee extensors at the same time.

Hip abduction. The gluteus medius, one of the primary muscles responsible for hip abduction and side-to-side balance, is a smaller structure that is very prone to atrophy with prolonged inactivity or bed rest. To perform hip abduction exercises, sit or lie with hands placed on the outside of bent knees and attempt to spread the legs further outward while resisting the motion by pushing inward with the hands. A wall or sofa (back or arm) can be used instead of the hands to resist hip abduction, but only one leg at a time can be targeted in this manner. To perform the exercise while standing, place yourself so that the targeted leg is positioned parallel to a wall, and push the side of your foot into the baseboard while keeping the leg straight.

Plantar flexion (calves). Stand on your toes while holding onto a countertop or sturdy chair. If the activity is too easy, try standing on one foot at a time, then repeating on the other side. You can also perform the exercise while seated with your feet on the floor and pushing up onto your toes, or while lying on your back and pushing your toes first downward, and then pulling them back upward toward your body.

These exercises are just a few of the many isometric and self-resisted exercise options that exist. Though not mentioned here, there are also isometric exercises for the head/neck, back, hip flexors, knee flexors, hands/fingers and more. Just about any dynamic exercise can also be adapted to have an isometric component by holding the repetition statically at some point in the range of motion and contracting.

Do What You Can

If dynamic exercises are not currently an option, don’t distress. The important thing is to do what you can and increase activity as you are able. There can be hope and progress even in being still.■

MATTHEW DAVID HANSEN, DPT, MPT, BSPTS, is a practicing physical therapist in Utah and president of an allied healthcare staffing and consulting agency named SOMA Health, LLC. He completed his formal education at the University of Utah, Salt Lake City, and has additional training in exercise and sports science, motor development and neurological and pediatric physical therapy.

Reference
This neurological disease thought to be caused by an autoimmune response can leave patients unable to leave home. But treatment can help many to control the disease, and a possible cure may be on the horizon.

By Ronale Tucker Rhodes, MS

IN 2014, SALLIE Rhodes was a normal, happy 25-year-old “with an apartment, roommates, a passion for jogging and a good job as a pediatric nurse.” But, one day, her life was turned upside down. Her body kept locking up from searing spasms that made her legs stiff, her head and neck rigid and the muscles in her torso extremely tense, causing her to suffer concussions, cuts and other injuries. She suffered two years before finally being diagnosed with stiff person syndrome (SPS), a very rare disease of the nervous system.1

While SPS affects approximately only one in a million persons, for those few, it is a frightening disease that leaves some too afraid to leave home, fearing stimuli will trigger painful spasms, and others unable to leave home because they can’t walk or move. SPS, also known as “tin man syndrome,” can occur in people of all ages, even infants, although it mostly occurs in individuals between 30 years and 60 years of age. It is twice as prevalent in women than men, but there is no link to any race or ethnic group.2 And while no genetic link has been established, there have been isolated familial cases.3

SPS was first described by Frederick Moersch, MD, and Henry Woltman, MD, in a 1956 paper that covered 14 patients (10 men and four women with an average age of 41 years) collected over 32 years. Initially named Moersch-Woltman syndrome in their honor, the two coined the term stiff man syndrome.4 The name was later changed to SPS to reflect that the disorder can affect individuals of any age and of either gender.4

What Is SPS?

According to the National Organization of Rare Disorders, SPS is a rare acquired neurological disorder whose severity and progression varies from person to person. In addition to classic SPS, which is found in the majority of cases, there are several variants often referred to as “stiff-man plus syndromes”: 1) stiff limb syndrome characterized by a focal onset of stiffness and rigidity in one leg followed by more widespread involvement later on in some patients; 2) progressive encephalomyelitis with rigidity and myoclonus (PERM) that presents with more rapid neurological decline with features of brainstem dysfunction (nystagmus [involuntary eye movement], opsoconus [uncontrolled eye movement], ophthalmoparesis [weakness or paralysis of the eyes], deafness, dysarthria [poor speech articulation] and dysphagia [difficulty swallowing]) and profound autonomic dysfunction; 3) paraneoplastic SPS (approximately 5 percent of SPS cases), which presents with stiffness and rigidity in the neck, upper torso and arms, and is most commonly associated with breast, ovarian and lung cancer; and 4) others that present with a mixture of signs and symptoms superimposed on classic features of SPS, including cerebellar dysfunction, gait instability, oculomotor dysfunction, dysarthria, peripheral neuropathy, vertigo, parkinsonism and seizures.6

Because SPS symptoms vary so widely, a diagnosis is often difficult.

The exact cause of SPS is unknown, but it is believed to be an autoimmune response in the brain and spinal cord, and it often occurs alongside other autoimmune disorders. Related disorders
include diabetes mellitus (occurring in approximately 35 percent of SPS patients), thyroiditis, breast cancer, epilepsy, vitiligo, cerebellar ataxia and myasthenia gravis.5,7

Most people with SPS have antibodies to glutamic acid decarboxylase (GAD), a protein in inhibitory nerve cells involved in the creation of gamma-aminobutyric acid (GABA) that helps to control muscle movement. When the immune system mistakenly attacks certain nerve cells that produce GAD, this leads to a deficiency of GAD in the body. It is unknown what role a deficiency of GAD has in developing SPS. Some individuals with SPS have no detectable antibodies to GAD. But GAD-65 is the most common antibody produced by people with autoimmune diabetes.5

Less commonly, individuals with SPS will have antibodies to amphiphysin, a protein involved in the transmission of signals from one nerve cell to another. These antibodies pose a higher risk for developing breast cancer.3

In infants and young children, the disease is termed stiff baby syndrome, which is somewhat different because it typically affects the lower legs and arms and feet and hands. Spasms usually occur due to stress or being startled, and it may be more persistent or more frequently recurrent. In addition, the syndrome is dependent upon the presence of anti-GAD antibodies.6

Symptoms of SPS

SPS is characterized by progressive muscle stiffness (rigidity) and repeated episodes of painful muscle spasms, as well as back pain, sleep disturbance, impaired movement, emotional disturbances, lumbar lordosis, muscle and skeletal ruptures and fractures and joint deformity.4,8 In addition, symptoms reported by 80 percent to 99 percent of individuals with SPS include anxiety, EMG abnormality, falls and hyperhidrosis. And, 30 percent to 79 percent of individuals report agoraphobia [a fear of leaving home], autoimmune antibody positivity, difficulty walking, emotional liability, exaggerated startle response and paraspinal muscle hypertrophy.6

There are three different stages of SPS: early, advanced and end. Symptoms vary from case to case and depend on the stage in which the person is diagnosed.

In the early stage, individuals experience an exaggerated upright posture (rigidity) primarily in the trunk and abdomen that fluctuates. They may also have discomfort, stiffness or pain in the entire back that worsens with tension or stress. Sleep disturbance is common when transitioning from rapid eye movement to stage one or two sleep due to the loss of relief from spasms, which may awaken individuals. In some people, brief episodes of severe worsening symptoms resolve spontaneously within hours or days.

In the advanced stage, rigidity usually ensues in the proximal limb muscles along with muscle spasms that occur randomly and can be triggered by stimuli such as a sudden noise, touch or emotional stress. These stimuli cause individuals to begin to move very slowly to avoid rapid movement that induces severe spasms even in the distal extremities. In addition, exaggerated lumbar lordosis (inward curvature of the lower back) is present combined with contraction of abdominal muscles. Depression is a comorbidity since the individual’s quality of life is severely affected. Approximately 65 percent of SPS patients are unable to function independently during this stage.

Finally, in the end stage, facial and pharyngeal muscles may be markedly affected, and joint deformities may occur. During spasms, fractures and muscle ruptures may occur. And, eating, simple movement and other activities of daily living may be problematic.7

Diagnosing SPS

Because SPS symptoms vary so widely, a diagnosis is often difficult. Indeed, diagnosis is frequently delayed considerably by an average of 6.2 years.9

A diagnosis of SPS begins by identifying characteristic symptoms and obtaining a detailed patient history and thorough clinical evaluation.10 Table 1 provides a list of characteristics physicians look for when conducting an

Table 1. What Physicians Look for During an Examination for SPS

- Increased tone in the axial/trunkal muscle groups
- Increased tone in the legs (symmetric or asymmetric)
- Normal power in the upper and lower limbs, unless at an advanced stage of the disease
- Possible hyperreflexia, without plantar extension
- Normal sensory function and coordination
- Hyperlordosis of the lumbar spine (resulting from cocontraction of abdominal and paraspinal muscles)
- “Woody” feel on palpation of the muscles, due to spasms
- Slow, wide and cautious gait
- Intact cognitive function
- Normal sphincter function

examination. In addition to these, more specific tests are needed to support or confirm a diagnosis, as well as to rule out other conditions. This is because while SPS lacks any significant similarity to other neurologic diseases, it presents with overlapping symptoms. For instance, tetanus is perhaps the closely related disease to SPS because both conditions affect peripheral inhibition via central mechanisms and both inhibit central GABA systems.\(^\text{11}\)

Antibody testing can measure levels of GAD in the blood. While absence of GAD antibodies doesn’t rule out SPS, the presence of high levels of them strongly supports a diagnosis. In most people, GAD antibodies are commonly associated with diabetes, but these individuals have low levels making the distinction between high and low levels important. Very high GAD antibodies make SPS more likely.\(^\text{10}\)

Electromyography is another important diagnostic tool that measures electrical activity in skeletal muscles. In SPS, the typical finding is continuous (low-frequency) motor unit activity simultaneously occurring in agonist and antagonist muscles.\(^\text{10}\)

Additional tests that can support a diagnosis include hemoglobin A1C, complete blood count, comprehensive metabolic profile and thyroid-stimulating hormone. And, a lumbar puncture to detect oligoclonal bands that are seen in approximately two-thirds of SPS patients can rule out other diseases.\(^\text{3}\)

There are clinical criteria for diagnosing SPS that were established in 1967 by Edward E. Gordon, MD. Later, those criteria were expanded by other physicians, including Marinos C. Dalakas, MD, who broadened the criteria to include tightness of the axial muscles, the progression of stiffness to the limbs, painful spontaneous muscle spasms, and an elevation of positive GAD or amphiphysin antibodies. Today, the Dalakas criteria are used worldwide to diagnose classic and variants of SPS (Table 2).\(^\text{9}\)

### Treating SPS

The goal of treatment is to provide symptom relief and to modulate the immune response causing SPS. Unfortunately, because the disease is so rare, the quality of treatment is limited because clinical drug trials are hindered by the low numbers of patients.\(^\text{12}\)

Drugs known as benzodiazepines such as diazepam and clonazepam are used to treat muscle stiffness and episodic spasms. However, these muscle relaxants often need increasing doses for symptom relief, which sometimes cause troublesome side effects. In conjunction with benzodiazepines, baclofen is usually given to treat spasticity. Other options to treat spasticity include dantrolene and tizanide, which are commonly combined with other muscle relaxants. Anti-seizure medications such as tiagabine, valproate, carbamazepine and gabapentin have also shown to benefit a small number of people with SPS. However, vigabatrin, another anti-seizure medication, is rarely used because of its potential for visual field constriction.\(^\text{5,12}\)

Immune-modulating therapies include intravenous immune globulin (IVIG), plasmapheresis, rituximab and corticosteroids. IVIG is considered a second-line treatment for severe or refractory SPS, and in addition to its immune-modulating effects, it has shown to improve many SPS symptoms.\(^\text{11}\) The usual dose is 2 g/kg administered over two to five days, and the length of the series is variable and dependent upon patient response.\(^\text{13}\) Case reports show significant improvements in stiffness, startle, functional status and clinical examination, as well as radiographic and serological improvements. In a randomized, double-blinded, placebo-controlled crossover trial of monthly IVIG, results showed a significant decrease in stiffness, which stabilized during washout and increased again when switched to a placebo. Patients reported improvements in symptoms and ability to participate in activities of daily living, which lasted between six weeks and one year. And, GAD autoantibody titer also fell after IVIG.\(^\text{3,12}\)

With plasmapheresis (or plasma exchange), blood is removed from the patient and blood cells are separated from the plasma. The plasma is then replaced with other human plasma, and the blood is retransfused into the patient.\(^\text{3}\) There is no real prescribed

### Table 2. Dalakas Criteria for Diagnosis of Typical SPS

- Stiffness in the axial muscles, prominently in the abdominal and thoracolumbar paraspinal muscle leading to a fixed deformity (hyperlordosis)
- Superimposed painful spasms precipitated by unexpected noises, emotional stress, tactile stimuli
- Confirmation of the continuous motor unit activity in agonist and antagonist muscles by electromyography
- Absence of neurological or cognitive impairments that could explain the stiffness
- Positive serology for GAD-65 (or amphiphysin) autoantibodies, assessed by immunocytochemistry, Western blot or radioimmunoassay

dosage for plasmapheresis, and the time of plasmapheresis and other parameters are controlled on a patient-by-patient basis. However, a standard regimen for autoimmune diseases is a five-treatment series administered every other day. There are possible adverse effects, including hypotension, bleeding, arrhythmias and infection.\textsuperscript{13} While no controlled studies have been conducted of plasma exchange, case reports show conflicting results, with some patients’ symptoms and serological markers improving, and others showing no improvement.\textsuperscript{12}

Rituximab, which depletes mature B cells, has been shown to give symptomatic and serological remission in patients with refractory SPS.\textsuperscript{12} In 2010, a patient with SPS associated with a thymoma, diabetes mellitus, autoimmune thyroiditis and the presence of anti-GAD and anti-amphiphysin autoantibodies experienced a partial improvement following a thymectomy and the administration of prednisone, IVIG and mycophenolate mofetil. When treated thereafter with rituximab, the patient had complete sustained remission of SPS and the disappearance of serum anti-amphiphysin antibodies.\textsuperscript{14}

Corticosteroids have been used as either monotherapy or combined with other therapeutic agents and have shown to improve spasms and autoantibody titers. However, again, there have been no clinical trials performed to determine their overall role in treating SPS.\textsuperscript{12}

In addition to these therapies, physical and occupational therapy are critical to recovery since treatments may make patients feel weak. Exercise or physical therapy may also be helpful for preserving range of motion and relieving symptoms related to prolonged muscle tension. In addition, muscular biofeedback may be helpful.\textsuperscript{13}

**A Possible Cure?**

Most recently, autologous hematopoietic stem cell transplantation (auto-HSCT) has shown success in curing patients with SPS. In 2014, researchers at the Blood and Marrow Transplant Program at the Ottawa Hospital Research Institute in Ontario, Canada, performed transplants on three women with SPS, two of whom were in clinical remission following the transplant and have now returned to normal functioning.

During the first part of auto-HSCT, a patient’s cells that can regrow bone marrow are retrieved and put into a preservative and stored in liquid nitrogen. The patient is then given a conditioning regimen that includes chemotherapy and antilymphocyte antibodies to try to kill their immune system. The preserved cells are then thawed and reinfused into the patient, which redevelops their immune system from scratch. After the procedure, the patient is prescribed medications to prevent unusual viral or fungal infections. Six months posttransplant, the patient has to be revaccinated. While the patient’s blood counts recover within a few weeks after transplant, the immune system recovery can take from three months to six months.

The first woman to receive a transplant was diagnosed with SPS in 2005 at age 48. She presented with progressive leg stiffness, hyperreflexia and falls, and she walked with an abnormal “tin solder” gate. MRI findings were normal, but anti-GAD antibodies were present at a very high titer (127 U/mL). And, over the years, her symptoms worsened. A month following her transplant, her symptoms resolved. After two months, her GAD antibody titer was 87 U/mL. “Despite continued circulating anti-GAD antibodies, at six months, she was fully mobile, had returned to work and was enjoying skiing and biking.” And, as of 2014, she had remained asymptomatic four years and eight months following the transplant.

The second woman was 30 years old in 2008 when diagnosed and presented with episodic leg muscle stiffening with normal neurologic exams between attacks. She also had a low titer of anti-GAD antibody. After transplant, she experienced two episodes of severe muscle spasms in the first two-and-a-half months, followed by a third and a fourth, but those were less severe and shorter in duration. As of 2014, she had also returned to work and not had symptoms related to SPS in more than year.

Neither of these women had unexpected treatment-related toxic effects, and neither needs immunomodulatory or immunosuppressant medication.

The third woman was recovering and her symptoms were going away at the time of the reporting.

According to Christopher Bredeson, MD, head of malignant hematology and stem cell transplantation at Ottawa Hospital and senior scientist at Ottawa Hospital Research Institute, while the results so far are “favorable,” the treatment approach involves an approximate 5 percent mortality risk, the recovery period is long and it’s unclear if the effects are permanent. However, he
added, “In select patients who have sort of exhausted other things, it proves the principle, and we are encouraged to continue and try to develop the approach.”

In the U.S., the Fred Hutchison Cancer Research Center in Seattle, Wash., has an ongoing clinical trial testing the efficacy of high-dose immunosuppressive therapy and auto-HSCT in more than a dozen neurological autoimmune diseases, including SPS, that don’t respond to conventional therapy. Led by George Georges, MD, the trial accepted Sallie Rhodes after other treatments failed, and her condition deteriorated. While U.S. insurance doesn’t pay for the $450,000 procedure, Rhodes’ company made an exception and approved it.

On May 5, 2014, Rhodes underwent the procedure even though the doctors were worried her condition was so severe that muscle spasms could stop her breathing or that nausea from chemotherapy could result in her choking on her own vomit. However, more than five months after transplant, her symptoms were much better; her upper-body motion was much improved, and her spasms were less frequent and severe when they occurred. Unfortunately, improvement hasn’t been as dramatic as they’d hoped, and at the time of the reporting, she never entirely stopped having spasms, including episodes severe enough to send her regularly to the emergency room. But, the treatment is still deemed a success.1

References


Until more is discovered about SPS and how to cure it, patients are left with available treatments that help to manage their condition. Fortunately, symptoms of SPS can be well-controlled for many with appropriate treatment. Regrettably, that is not the case for all as many patients continue to live housebound out of fear of freezing or falling unexpectedly. At this point, because the immune system appears to be at the root of the problem, procedures like auto-HSCT, and even potentially others, could eventually lead to alleviating this traumatic disorder.

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.
LET’S TALK

PROFILE:
Ric Dolore

By Trudie Mitschang

IN 1993, Ric Dolore was blessed with his first instrument: a Fender Squier Stratocaster. With a small Fender practice amp and guitar lessons from a great jazz guitarist named Pace Connor, Ric opened his soul to music. After playing in cover bands throughout his youth, Ric made it his goal to pursue a career in music production. That is, until a diagnosis of common variable immune deficiency (CVID) at age 35 put those dreams on hold.

Trudie: Tell us about your journey to a diagnosis.

Ric: I was misdiagnosed several times with everything from scabies to athlete’s foot. During that time, I had strep throat four times in five months. My fevers were so severe that I sweated through an entire mattress and memory foam. At one point, I was admitted to the hospital and misdiagnosed with lupus. In the end, it took 11 doctors and four years to find out I had CVID. At the time, I still had the diagnosis of lupus and was dealing with a rampant skin infection. I was prescribed steroids and steroid creams, which only made things worse. Eventually, I was referred to a rheumatologist who reviewed my health history and suggested I quit work and “live in a bubble.”

Trudie: How did you respond to that advice?

Ric: It’s very hard to make a living working from home. It’s possible, but it’s very hard. You have to do quite a bit to be able to work from home; you need a quiet place to work, office furniture, a computer and Internet. It wasn’t really an option for me.

Trudie: How did you keep your music career going at that time?

Ric: At the time, I was pursuing a career as a music producer. When I became ill, I had to cancel my collaborations and DJ events, but I was not willing to give up, and I did not want being sick to keep me from pursuing my goals. I ended up launching a crowdfunding campaign to raise enough money to make music and work from home. I was hoping I could avoid being exposed to germs, and since music is a stress reliever for me, I was hopeful it would benefit my health as well.

Trudie: Were you successful?

Ric: Unfortunately, I was not able to raise enough money. I’m currently working full time as a trainer for a call center, but pursuing music on the side. I would love to finish the song I’m working on and release it. Any profit above costs would be donated to the Jeffrey Modell Foundation.

Trudie: Tell us about your other diagnoses.

Ric: When my immune system went wonky, the remaining parts became hyperactive, which is when I was diagnosed with psoriatic arthritis. I also developed allergies for things I’ve eaten and lived with my whole life: coffee, dairy, chocolate, cats, dogs — it’s been a struggle. To put some perspective on it,
I’m actually a master barista and have worked in coffee shops my whole life. I’ll never be able to do that again.

Trudie: What is your treatment plan?
Ric: I do not have a treatment plan at this time due to the out-of-pocket medical costs. I simply cannot afford it. I have not had an immune globulin infusion since September 2015. As a result, I’ve been sick for months with ear infections that may have caused permanent damage to my right ear, along with so many other illnesses along the way.

Trudie: Do you have health insurance?
Ric: I do have insurance, but I have not been to the immunologist due to the cost of an appointment (even with my insurance). Every treatment leaves me thousands in debt and, eventually, it could lead me to being dropped by my insurance plan. In 2015, I was dropped by a major insurance company and dropped again in 2016 due to the cost of treatment. I’ve concluded there is nothing I can do to get treatment, apart from going on 100 percent disability. I’m not prepared to do that.

Trudie: Are you part of any advocacy groups?
Ric: I’m on a Facebook page for CVID patients, and that’s been tremendously helpful. I’m a big proponent of advocacy groups; I think it would be a great thing to be able to bring awareness about this rare condition to the world using social media connections.

Trudie: Do you often have to explain your health challenges to others?
Ric: All of the time. If I get something simple like an ear infection or catch a cold, it’s a serious issue for me; I’ll end up in a local emergency room or urgent care. I always ask the doctor: “What is your experience with immune-compromised patients?” If the doctor can’t answer, I ask for another doctor. It’s a struggle because you almost have to educate people whose job it is to be educated about this. I do find some things helpful when explaining my disease to lay people. For instance, when my family and friends ask, I point them to the Immune Deficiency Foundation’s website at primaryimmune.org. There’s also an episode of the hit show “House” that does a great job of explaining my condition.

Trudie: Where do you find humor in your circumstances?
Ric: I like to use humor by posting funny pictures to make people think about CVID. I also have been known to quote the movie “Innerspace,” which was one of my favorites growing up; there’s a lot of neat stuff in that movie about the immune system. My wife has a nickname for me. She calls me “Captain Contagion.”

Trudie: What do you most hope for in the future?
Ric: I hope to raise awareness about CVID because with awareness, comes interest, and with interest, there will hopefully be more research into the genetic components of CVID. Although maybe not in my lifetime, it would be great if there were some type of gene therapy to help patients like me produce antibodies again on our own. There has to be a lot of change in the way we view chronic and rare diseases. We need a paradigm shift for our lawmakers and government to focus on prevention rather than treatment.

Trudie: Who has been your greatest support?
Ric: My wife, Janet. She’s been the reason I get up and go to work on days that I’m able to. We’ve been together for 15 years and married for 13. She’s been my biggest support, biggest fan and best friend.

Trudie: What is a favorite quote?
Ric: One of my heroes, Bruce Lee, said you must “become like water.” When water meets an obstacle, like a boulder in a river, it flows over, under and around it. Water always finds a way.

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.

I hope to raise awareness about CVID because with awareness, comes interest, and with interest, there will hopefully be more research into the genetic components of CVID.
Important Safety Information

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

WARNING: Thrombosis (blood clotting) can occur with immune globulin products, including Hizentra. Risk factors can include: advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (blood thickness), use of estrogens, installed vascular catheters, and cardiovascular risk factors.

If you are at high risk of thrombosis, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor you for signs of thrombosis and hyperviscosity. Always drink sufficient fluids before administration.

Tell your doctor if you have had a serious reaction to other immune globulin medicines or have been told you also have a deficiency of the immunoglobulin called IgA, as you might not be able to take Hizentra. You should not take Hizentra if you know you have hyperprolinemia (too much proline in your blood).

Infuse Hizentra under your skin only; do not inject into a blood vessel. Allergic reactions can occur with Hizentra. If your doctor suspects you are having a bad allergic reaction or are going into shock, treatment will be discontinued. Immediately tell your doctor or go to the emergency room if you have signs of such a reaction, including hives, trouble breathing, wheezing, dizziness, or fainting.

Tell your doctor about any side effects that concern you. Immediately report symptoms that could indicate a blood clot, including pain and/or swelling of an arm or leg, with warmth over affected area; discoloration in arm or leg; unexplained shortness of breath; chest pain or discomfort that worsens with deep breathing; unexplained rapid pulse; and numbness or weakness on one side of the body. Your doctor will also monitor symptoms that could indicate...
hemolysis (destruction of red blood cells), and other potentially serious reactions that have been seen with Ig treatment, including aseptic meningitis syndrome (brain swelling); kidney problems; and transfusion-related acute lung injury.

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

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

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

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

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

**Initial U.S. Approval: 2010**

**BRIEF SUMMARY OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use HIZENTRA safely and effectively. See full prescribing information for HIZENTRA.

**WARNING: THROMBOSIS**

See full prescribing information for complete boxed warning.

- **Thrombosis** may occur with immune globulin products, including Hizentra. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyeprviscosity, and cardiovascular risk factors.
- For patients at risk of thrombosis, administer Hizentra at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

**INDICATIONS AND USAGE**

Hizentra is an Immune Globulin Subcutaneous (Human) (IGSC), 20% Liquid indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.

**DOSAGE AND ADMINISTRATION**

For subcutaneous infusion only.

Administer at regular intervals from daily up to every two weeks (biweekly).

**Dose (2.2)**

Before switching to Hizentra, obtain the patient's serum IgG trough level to guide subsequent dose adjustments.

- **Weekly**: Start Hizentra 1 week after last IGIV infusion
  
  Initial weekly dose = Previous IGIV dose (in grams) \* 1.37
  
  No. of weeks between IGIV doses

- **Biweekly**: Start Hizentra 1 or 2 weeks after the last IGIV infusion or 1 week after the last weekly Hizentra/IGSC infusion. Administer twice the calculated weekly dose.

- **Frequent dosing (2 to 7 times per week)**: Start Hizentra 1 week after the last IGIV or Hizentra/IGSC infusion. Divide the calculated weekly dose by the desired number of times per week.

- **Adjust the dose** based on clinical response and serum IgG trough levels.

**Administration**

- **Infusion sites** – 1 to 4 injection sites simultaneously, with at least 2 inches between sites.

**Infusion Parameters**

<table>
<thead>
<tr>
<th>Infusion Number</th>
<th>Volume (mL/site)</th>
<th>Rate (mL/hr/site)</th>
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<tbody>
<tr>
<td>1st</td>
<td>≤ 15</td>
<td>15</td>
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<tr>
<td>2nd to 4th</td>
<td>≤ 20</td>
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<td>5th</td>
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<td>6th and above</td>
<td>≤ 25</td>
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As tolerated

**CONTRAINDICATIONS**

- Anaphylactic or severe systemic reaction to human immune globulin or components of Hizentra, such as polysorbate 80
- Hyperprolinemia (type I or II) (Hizentra contains the stabilizer L-proline)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

**WARNINGS AND PRECAUTIONS**

- IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hyperviscosity and anaphylactic reactions.
- Thrombosis may occur following treatment with immune globulin products, including Hizentra.
- Aseptic meningitis syndrome has been reported with IGIV or IGSC treatment.
- Monitor for clinical signs and symptoms of hemolysis.
- Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])
- Hizentra is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

**ADVERSE REACTIONS**

The most common adverse reactions observed in ≥5% of study subjects were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, rash, pruritus, vomiting, abdominal pain (upper), migraine, and pain.

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.

**DRUG INTERACTIONS**

The passive transfer of antibodies may interfere with the response to live virus vaccines, and may lead to misinterpretation of the results of serological testing.

**USE IN SPECIFIC POPULATIONS**

- **Pediatric**: No specific dose requirements are necessary to achieve the desired serum IgG levels.

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**Based on October 2016 revision**

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**Co-pay Assistance**

Co-pay assistance

**Questions?**

Call 1-877-355-IGIQ (4447) Monday–Friday, 8 AM to 8 PM ET.
Seize the Day
By Stacey Philpot

2016 tucked away in a cabin hidden in a winter wonderland in Minnesota. It was there a word dropped in my heart from nowhere. I heard a whispered invitation to “begin.” 2017 was to be the year I began really living again. Something deep inside of me shifted. How long had it been since I let myself want more than survival from life?

That afternoon, my 5-year-old daughter ran her bundled body up to my waist and pleaded, “Will you go down the hill on the snow tube with me?” I almost always said no to these requests. I considered the PICC line hidden within my jacket, looked at her expectant face and then said, “Yes.” I took my husband’s scarf and wrapped it around my PICC line within my jacket, rested my daughter on the other arm, and down the hill we flew. Tears of joy rolled down my face as my daughter squealed, “This is so fun, Mommy!”

The same day I sat in the cabin looking gleefully at that picture, I got a message from a precious friend who’d recently moved to London. Did I want to come visit for a bit? She’d disinfect everything. We could go at my pace. She’d make sure I had everything I needed. I am 38 years old. I had never been out of the county. I had no idea if my immunocompromised, medically complex body could withstand such a trip. I wrote her back. “Yes.”

In March, for my birthday, for the first time in my life, I visited overseas. I seized the day. For months, I quietly collected clearances from my various specialists, obtained a passport and made health-related contingency plans. Finally, I took a 10-hour flight that opened up a whole new world for me.

I wish I could tell you the only tears I cried on my trip were of joy, that I never woke up in pain at night so intense I wept. I wish I could say there were no medical repercussions. What I will say? I have no regrets about seizing the day. May this be the year we all begin again.

I heard a whispered invitation to “begin.” 2017 was to be the year I began really living again.

The next day, I stayed back in the cabin with an angry body and a full heart while my family went adventuring. I pulled out my phone and looked at a picture of my daughter and me at the top of that hill preparing for our descent. “Seize the day,” I thought.

Should you go tubing with a PICC line? Absolutely not. My doctor would kill me if he knew I’d done that. But, maybe we should all pluck the joy from life whenever we can. Maybe we should “seize the day” more often!

Stacey Philpot is an author, goofball and avid reader. You can find her blog at chronically whole.com, where she shares her journey of making the most of a life touched by common variable immunodeficiency, Lyme disease and rheumatoid arthritis.
**Making Your Hospital Room Your Haven**

By Ilana Jacqueline

**IT’S THAT TIME** again. You’re being wheeled into a hospital room. You have no idea how long you’ll be there. It could be a night. It could be a month. With an immune deficiency, it’s a guessing game how long an infection will take to clear up — and it’s no small hazard to be in the most infectious building in the city.

This room is going to be your home now, so you’ve got to make it work. Here are some of my top tips for keeping your hospital room cozy, clean and conducive to getting well.

1. **Disinfect.** A custodian has come through and wiped the same rag over the mouthpiece of your room’s phone, bed handles, toilet seat and eating tray. I’m sure he or she has also dragged that same grungy mop from room to room pushing dust and gunk and who knows what across the floor you’re now supposed to walk across in hospital socks. Don’t delude yourself into thinking your hospital room is sterile. It isn’t. So make sure your hospital bag includes Clorox wipes, Purell and disinfecting spray. Wipe down the phone, bed handles and eating tray. Get a pair of slippers so your socks don’t go from floor to bed dragging all that gunk with them. If you plan on sitting on the toilet seat, wipe it down first! You are vulnerable. So, if ever there was a place to let your obsessive-compulsive tendencies shine, this is it.

2. **Stay cool.** Or hot, if that’s your preference. Most hospital rooms now have their own thermostat for each patient to control. I generally like to keep my room cool; it helps keep the germ population at bay. But, it’s also easier for me to make myself warm at night than it is to cool myself down. My hospital kit always includes an extra-large throw blanket — something large enough to cover me, but small enough to fit in the washing machine at home. (Because the first thing you do when you get home is put every piece of clothing you wore at the hospital in the wash!) I also like to bring my electric heating pad. If nothing is actually hurting me, I just sleep on top of it. But if my IV is infiltrated or I have some kind of sore area, I’ll wrap the heat pack around it, and I’ll be glad the room is cold so I’m not overheated.

3. **Organize.** The truth is, when you’re in a hospital room, you’re just a marionette. You’re attached to an IV, heart monitors and, sometimes, feeding tubes or oxygen masks. Everything needs to be within reach. First thing first: Have someone help you plug everything into nearby outlets: phone charger, laptop, heating pad. You have two surfaces you need to make the most out of: your nightstand and your meal tray. The meal tray opens up into two sections. On one, I keep my laptop, headphones and a notebook with a pen (to take notes when doctors come in and I’m half asleep but need to remember their instructions). The other side of the table is for food, drinks and snacks. Try to put a lid on any beverages just in case you knock the tray while you’re sleeping or moving around. On the nightstand goes your phone, tissues, glasses/contact cases or any other personal items you might have. Make sure to wipe down these surfaces every day with a disinfecting wipe.

4. **Make it your own.** OK, as far as that statement goes, I realize how lame it is. Like the hospital room is some sick venue for a nightclub. I get it: This room is never going to be as comfortable as your home, but there are ways to make it less foreboding. Start with scents. I don’t know about you, but the smell of hospitals makes me nauseous. So I spray the sheets down with Febreeze (they sell it in a travel size, and Bath & Body Works also sells lavender linen spray). I also keep a small bottle of essential oils to add to my disinfecting wipes. Yes, I am that fancy. You can also add things like your own pillow case and a screensaver of your dog on your laptop.

5. **Gear up.** Everyone knows the hospital is not the place one goes to get rest. Not unless you sleep best with a nurse coming into your room every 10 minutes to poke you and take your temperature and blood pressure, doctors coming in to see you at the crack of dawn, and being told you’re being wheeled down for a test just as you’re about to fall into that deep sleep. The IV poles are beeping. Your roommate has a hacking cough that never ends. One of the nurses is on her phone right outside your door. How is anyone supposed to recover in this kind of atmosphere? Ear plugs and eye masks. There’s also a free app from Brookstone that acts as a sound soother; it really helps me sleep when I’m in need of a nap but in an unfamiliar bed. Block out that noise, and don’t worry about the roommate who keeps opening the curtains and letting the sunshine in. You control the smells, the temp, the noise, the light, the germs! You’ve got this **covered.**

It’s always the last place you want to be, but if you have to be there, stock your hospital bag with the tools mentioned above to keep you comfortable, sane and maybe even on your way to healing.
Download the *IG Living* eBook today—now available for iPad, Nook and Kindle!

“You can lament what is lost to you, whether it’s opportunity, a person or your health, but clinging to anger is no way to experience life.” — Rebecca Zook in “Life Lessons,” excerpted from *Chronic Inspiration*.

Download a daily dose of inspiration with this heartfelt compilation of writings on life with chronic illness. From coping strategies and parenting tips to “from the trenches” advice on dealing with family and friends who simply don’t get it, these personal stories are sure to uplift, challenge and inspire. Honest and candid, *Chronic Inspiration: Heartfelt Perspectives on Life with Chronic Illness* gives voice to those who refuse to let their diagnosis define who they are or what they can accomplish.

“For the patient community, this was invaluable. When I downloaded it, I knew this would be something I would refer to over and over again.”

— Jenny Gardner

*Chronic Inspiration* can be purchased on iTunes, Amazon and Barnes and Noble.com
LIFE CAN BE extra challenging for anyone living with a chronic illness or disability. To face those challenges, many people develop new routines or adapt their lifestyle to accommodate the illness or condition. But children, because of their young age, may lack coping skills and strategies, and the condition’s effects on their lives may, at times, be more challenging than the condition itself. Instead of coping and making lifestyle changes, children may adopt inappropriate behavioral practices or develop an emotional disorder that requires the help of a mental health professional.

How Chronic Illness Can Affect Children’s Mental Health

Chronic illness is defined as a condition that lasts longer than three months and can typically be managed but not cured. It is believed that approximately 8 percent of children in the U.S. under age 17 suffer from some form of chronic illness such as asthma, epilepsy, severe allergies and diabetes, as well as primary immunodeficiency. While all of these can be managed relatively well with medication and regular medical care, their effects can take a heavy toll.

Children may become tired easily or often be in pain, or they may suffer from undesirable side effects of necessary medication. Young children, especially, may find it difficult to understand why they have been affected by the illness, while their friends or siblings aren’t. They may also experience feelings of anger or depression, and can likely become frustrated by a strict regimen of medication or frequent doctor appointments and hospital visits.

Children and adolescents who have visible disabilities may be excluded by their peers or experience bullying from classmates. This may lead to feelings of insecurity, or the fear of not being accepted by others their age who are not affected by illness or disability.

Ten to 13 percent of teenagers who have a chronic illness say they experience limitations in their daily life as a result of their condition. It is difficult for young people to cope when they are unable to participate in the same events and activities as their peers, leading to feelings of frustration and resentment. As kids become older, body image concerns arise from certain chronic conditions that may have visible effects, which can have a negative impact on self-esteem.

Some teens may shy away from dating, and experience anxiety at the thought of social occasions like school dances, parties and sporting events. When young people feel isolated and misunderstood or experience teasing, conditions such as anxiety, stress or depression may develop.

When Is it Time to Seek Help?

If a child’s health condition isn’t going away, and he or she seems to struggle emotionally, mentally or in relationships with others as a result of the chronic illness or disability, it may be time for parents to seek professional help for their child. At the same time, no parent wants to send their child to treatment that costs both time and money if it’s not necessary. How do parents know when the time has come to seek professional help? What are the signs that indicate treatment is the next logical step?

Chronic illness in children can cause anxiety, trauma and frustration, which can in turn generate disruptive, explosive or dangerous behavior. If a child’s condition leads to unwanted and inappropriate behavior that disrupts family life or leads to trouble in school, it’s important to get help.
It’s normal for kids who are dealing with medical stress to struggle at times with their thoughts, feelings and behaviors. Chronically ill children are allowed to cry when they receive painful medical treatments, or ask “Why me?” from time to time. They may worry about their health or become fearful just before a doctor appointment. But there is a difference between sadness and depression, and worry and anxiety. Parents need to know these differences so they don’t miss a serious problem that requires consultation with a mental health professional. It is time to seek help when a child seems to experience depression or anxiety for a long period of time and it’s interfering with his or her ability to do age-appropriate things.

Signs of depression in children include sad or irritable mood most of the time; frequent bouts of crying without triggers, or not showing emotions appropriate to a situation; withdrawal and isolation from others; and rarely showing joy or interest in activities they used to enjoy.3 Common signs of anxiety in chronically ill children include an inability to follow through with necessary procedures (shots, X-rays, blood draws) even if they want to; general worries (about bad things happening, health and safety of loved ones) that feel out of control; difficulty falling asleep or sleeping through the night because of worries; behaving in ways that get in the way of treatment or worsen the condition such as not taking medications; complaining about aches and pains that exceed those expected from the medical problem; and excessive restlessness and fidgeting.3

While depression and anxiety are two of the most common mental health issues experienced by chronically ill children, behavioral outbursts may also occur. Oppositional behaviors that get in the way of medical care and relationships such as avoidance of necessary medical procedures or refusal of medication need to be addressed and treated. Other red flags include changes in school behaviors such as falling grades or refusal to go to school. Another behavioral warning sign is a change in relationships with friends such as withdrawal from friends and skipping activities to stay home instead. At home, increased arguing with family members or withdrawal from family activities should signal parents that something may be going on that needs to be addressed.3

When Is it Time to Wait and See
If treatment is necessary, it’s best to start as soon as possible. Unfortunately, family members, friends and maybe even the child’s doctor may recommend parents relax and wait to see if the child may grow out of it. If parents would rather wait to get help, with the hope that the child’s issues will resolve themselves, it is important they keep an eye on the problem, monitor the child’s behavior closely and be ready to act if it doesn’t improve. Even though the thought of therapy can be intimidating, it’s never a good idea to ignore a problem, pretending that it’s nothing.

One issue that can complicate matters is when parents disagree on the topic of therapy. One parent may think the child’s behavior is a problem that needs professional attention, while the other considers it normal “acting out” that only requires stronger parental discipline. This is one of the biggest reasons families wait to seek advice or care. If parents find themselves waiting on the therapy decision, they should do it actively by setting a timetable for when to bring up the issue again, and deciding which behaviors the child needs to change during that time period. If parents keep track of the issues that concern them, they’ll be better able to make a decision when the subject of therapy is revisited.2

What Is the Right Therapy for Your Child?
A therapist or other mental health professional may be able to offer help and support when problems arise that are beyond a parent’s ability to solve. There are therapies that can often be effective in teaching kids to understand their emotions and rein in their behavior if it is becoming a problem.

For behavior problems, parents can consult a mental health professional such as a behavioral psychologist who specializes in children and adolescents, or a child psychiatrist or social worker with expertise in treating young people. If a child begins to refuse medications and treatments, ignore medical recommendations or hinder treatment, behavioral therapy addressing “adherence behaviors” could be helpful.3

All kids have hard days, especially when living with a chronic illness. But when the hard days become more frequent than good days, or when children show big changes in how they function in their daily lives, they may benefit from the additional help of a licensed professional.

References

Jessica Leigh Johnson is a stay-at-home mom and mother of four kids, three of whom have X-linked agammaglobulinemia. She is a member of American Christian Fiction Writers and has written one book about the loss of her son to a primary immunodeficiency.
Germ Warfare: Sanitizing Solutions for a Healthier Home

By Trudie Mitschang

FOR IMMUNE-COMPROMISED patients, keeping the home free from disease-causing microbes and germs is essential. While wiping down countertops and keeping bathroom debris at bay are common-sense practices, many other simple steps can be taken to ensure the home is a haven from the outside world’s infectious organisms.

Pick the right products. Whether choosing traditional or “green” products for daily household chores, take note of whether the product is designed to disinfect or sanitize. Sanitizers are designed to remove 99 percent of bacteria within 30 seconds, while disinfectants are designed to kill all specified organisms within at least 10 minutes of product application. Certain household products already on hand such as chlorine bleach, rubbing alcohol and hydrogen peroxide can also be used to disinfect. Products with disinfectant capabilities can be easily identified by U.S. Environmental Protection Agency registration information on the packaging.

Target hard surfaces. Pay special attention to hard surfaces such as doorknobs, table tops, light switches, stair railings, chair backs and any other places hands tend to linger. Allow the disinfectant product to remain on surfaces for as long as necessary, then wipe the surfaces down with disposable towels. Be sure to grab a fresh towel each time you start wiping a new surface.

Disinfect electronic devices. In a 2013 study1 that inspected 50 cell phones, 100 percent showed contaminable bacteria, and 90 percent reported the same bacteria on users’ hands. Further, only 38 percent of participants cleaned their devices weekly. To disinfect handheld devices, spray a commercial spray disinfectant or a 50/50 solution of rubbing alcohol and water on a microfiber cloth and wipe down all surfaces front and back.

Remove shoes. In Japan, where it is a custom to remove shoes before entering a home, life expectancy is one of the highest in the world. Coincidence? Some studies have analyzed a typical household floor where residents did not remove shoes, and results showed rampant amounts of bacteria, including animal feces, urine, petrochemicals, viruses and pesticides. An alternative to leaving footwear in the entryway, an antimicrobial doormat can remove and trap debris, dust mites and other allergens from the bottom of shoes.

Vacuum often. A canister-style vacuum cleaner can remove pet dander, lead and everyday dirt from the carpet, and most come with a built-in HEPA (high efficiency particulate air) filter that captures lung-irritating air pollutants. A sanitizing vacuum with UVC light technology is another excellent way to reduce germs and deodorize furniture and mattress fabrics. Laboratory tests have shown sanitizing vacuums have the ability to eliminate MRSA and the H1N1 flu virus, as well as combat certain molds and allergens without the use of chemicals.

Disinfect laundry. Household linens, towels and clothes can harbor infectious bacteria for weeks and perpetuate the cycle of disease in the home. For thorough cleansing, soak soiled items in an oxygen-bleach powder solution before putting them in the washing machine. Then, wash them using laundry detergent and the warmest water as recommended on an item’s label.

Unmask hidden mold. Mold buildup in homes can cause allergic reactions in one in every three people, and significantly aggravate asthma and other breathing problems. Telltale signs of mold include faint musty smells and, of course, visible spots, even if they are small. Chronic physical symptoms such as sneezing, coughing, dry eyes or rashes could also indicate it is time to schedule a mold inspection.

Environmentally conscious options. Without shelling out a lot of green to get green products, consider all-natural household products that can double as standby sanitation solutions:

• White vinegar. This multi-tasker contains acetic acid, which gives it antimicrobial properties and is great for killing mold. Use it diluted with water to clean hard surfaces, disinfect sinks and toilets, and wash produce.

• Tea tree oil. This all-natural essential oil is naturally antibacterial, antifungal and antiseptic. A few drops added to water makes an effective natural cleanser for countertops and tile, and is also good for disinfecting pet accidents.

• Hydrogen peroxide. This natural product is a great stain remover for carpets and clothes and, in conjunction with vinegar, is an excellent scum buster for tub and tile. And unlike vinegar, it doesn’t have a noticeable smell.

Living with a compromised immune system, germ warfare can feel like a full-time job. By stocking the right products and maintaining vigilant cleaning habits, a home can be bacteria-free and sanitized, while protecting the health of all family members.

Reference


TRUDIE MITSCHANG is a contributing writer for IG Living magazine.
**Germ-Free Texting**

CleanTex Phone Wipe disinfectant pads are premoistened germicidal wipes that kill most germs on hard, nonporous surfaces. They are manufactured to kill all non-spore-forming bacterial strains, including Staphylococcus aureus, Pseudomonas aeruginosa and Salmonella choleraesuis. Box of 72 pads; $20.40; Amazon.com

**Breathe Easier**

The Advanced HEPA+ Jr air purifier is a medical-Grade HEPA filter plus 6.5 pounds of activated carbon that is designed to remove 99.97 percent of harmful particles, odors, gases and fumes from rooms up to 700 square feet. It is available in four colors. $399; www.natlallergy.com

**Shopping Guide to Sanitizers**

**Banish Laundry Bacteria**

Lysol Laundry Sanitizer is specially designed to sanitize clothes and can kill 99.9 percent of bacteria that detergents don’t address. It works in cold water, is safe for whites and colors and can be used in standard and high-efficiency machines. 41 fluid ounces; 5.99; Target.com

**Keep Mold at Bay**

My Mold Detective is a professional-grade and do-it-yourself mold test kit that utilizes the same method used by industry professionals to sample air quality in homes and businesses. The kit identifies what types of mold are present and determines whether mold concentration levels are normal, slightly elevated or elevated. Two-room test kit; $64.99; Homedepot.com

**Eliminate Microscopic Pests**

The UV Vacuum kills bed bugs and dust mites and is suitable for use on mattresses, sofas, pillows, curtains, rugs and carpets, or anywhere bacteria can live. It can be used as a handheld vacuum or a full-length vacuum cleaner using the in-built telescopic handle. $79.99; Amazon.com

**Freshen Up Floors**

The Dr. Doormat all-season utility mat is infused with an antimicrobial formula that creates a positive charge to disable microorganisms like bacteria, fungus and mold on contact. It comes in two sizes. $26.99-$46.99; www.drdoormat.com
The Autoimmune Fix: How to Stop the Hidden Autoimmune Damage That Keeps You Sick, Fat, and Tired Before It Turns Into Disease
Author: Tom O’Bryan, DC, CCN, DACBN
Publisher: Rodale Books

In *The Autoimmune Fix*, Dr. Tom O’Bryan examines the mechanisms underlying this modern-day autoimmune epidemic and takes a look at how these disorders are inadequately identified, diagnosed and treated. Written for both health practitioners and patients, the book includes two comprehensive three-week plans for patients to follow. The first three weeks focus on a paleo-inspired diet during which patients cut out gluten, sweets and dairy, which he believes are the three primary culprits behind autoimmunity. Once the dietary changes have been addressed, the book focuses on the other causes of autoimmunity such as genetics, other dietary issues and microbiome.

Antioxidant Smoothies: Sensational Smoothie Recipes That Promote Anti-Inflammatory, Anti-Aging and Immune System Health
Author: Jerry Newsome
Publisher: Amazon Digital Services

This book contains smoothie recipes that readers can make in the comfort of their homes to improve their lives. Each smoothie contains a different health benefit — from anti-aging to anti-inflammation. The book contains information about which antioxidants are the most powerful to consume, informs about the significance of including antioxidants in the diet, provides smoothie recipes with specific benefits, and uncovers ingredients that could help reduce stress and anxiety, detox the body and increase energy.

The Rheumatoid Arthritis Cookbook: Anti-Inflammatory Recipes to Fight Flares and Fatigue
Author: Caitlin Samson
Publisher: Rockridge Press

In this rheumatoid arthritis (RA) resource, nutrition expert Samson, who suffers from RA, shows how finding relief from RA symptoms through anti-inflammatory nutrition is possible. The book offers recipes specifically geared toward those with RA, offering 100 easy recipes that offer big flavors with little prep work; a two-week meal plan to get started right away, with guidelines for modifying calories to lose or gain weight; up-to-date information outlining the foods that fight (or worsen) inflammation; and a guide to the medicine-diet relationship to better understand how nutrition can balance the side effects of RA medications.

The Wahls Protocol Cooking for Life: The Revolutionary Modern Paleo Plan to Treat All Chronic Autoimmune Conditions
Authors: Terry Wahls, MD, and Eve Adamson
Publisher: Avery

In this book, Dr. Wahls shares essential paleo-inspired recipes to reduce and often eliminate chronic pain, fatigue, brain fog and other symptoms related to autoimmune problems, neurological diseases and other chronic conditions. With easy-to-prepare meals based on her pioneering therapeutic lifestyle clinic and clinical research that readers can customize to their own needs and preferences, this cookbook features breakfasts, smoothies, skillet meals, soups, wraps, salads and snacks that are inexpensive to prepare, nourishing and delicious. Also included are strategies for cooking on a budget, reducing food waste, celebrating the holidays without compromising health and helpful tips from fellow Wahls Warriors.
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<th>Disease</th>
<th>WEBSITES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ataxia Telangiectasia (A-T)</td>
<td>- A-T Children’s Project: <a href="http://www.atcp.org">www.atcp.org</a></td>
</tr>
<tr>
<td>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)</td>
<td>- GBS/CIDP Foundation International: <a href="http://www.gbs-cidp.org">www.gbs-cidp.org</a></td>
</tr>
<tr>
<td>Evans Syndrome</td>
<td>- Evans Syndrome Research and Support Group: <a href="http://www.evanssyndrome.org">www.evanssyndrome.org</a></td>
</tr>
<tr>
<td>Guillain-Barré Syndrome (GBS)</td>
<td>- GBS/CIDP Foundation International: <a href="http://www.gbs-cidp.org">www.gbs-cidp.org</a></td>
</tr>
<tr>
<td>Idiopathic Thrombocytopenic Purpura (ITP)</td>
<td>- ITP Support Association – UK: <a href="http://www.itsupport.org.uk">www.itsupport.org.uk</a></td>
</tr>
<tr>
<td>Kawasaki Disease</td>
<td>- American Heart Association: <a href="http://www.heart.org/HEARTORG/Conditions/More/CardiovascularConditions/Childhood/Kawasaki-Disease_UCM_308777_Article.jsp#T1T2oePWE0">www.heart.org/HEARTORG/Conditions/More/CardiovascularConditions/Childhood/Kawasaki-Disease_UCM_308777_Article.jsp#T1T2oePWE0</a></td>
</tr>
<tr>
<td>Multiple Sclerosis (MS)</td>
<td>- All About Multiple Sclerosis: <a href="http://www.multi-sclerosis.org/index.html">www.multi-sclerosis.org/index.html</a></td>
</tr>
<tr>
<td>Peripheral Neuropathy (PN)</td>
<td>- Neuropathy Action Foundation: <a href="http://www.neuropathyactionfoundation.org">www.neuropathyactionfoundation.org</a></td>
</tr>
<tr>
<td>Myasthenia Gravis (MG)</td>
<td>- Myasthenia Gravis Foundation of America (MGFA): <a href="http://www.myasthenia.org">www.myasthenia.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- Genetic Alliance: <a href="http://www.geneticalliance.org">www.geneticalliance.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- The Myositis Association: <a href="http://www.myositis.org">www.myositis.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- International Myositis Assessment and Clinical Studies Group: <a href="http://www.niehs.nih.gov/research/resources/imacs">www.niehs.nih.gov/research/resources/imacs</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- The Cure JM Foundation: <a href="http://www.curejm.org">www.curejm.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- Myositis Association Community Forum: tmacommunityforum.ning.com</td>
</tr>
<tr>
<td>Myositis</td>
<td>- Myositis Support Group – UK: <a href="http://www.myositis.org.uk">www.myositis.org.uk</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- A-T Children’s Project: <a href="http://www.atcp.org">www.atcp.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- United Mitochondrial Disease Foundation: <a href="http://www.umdf.org">www.umdf.org</a></td>
</tr>
<tr>
<td>Myositis</td>
<td>- MitoAction: <a href="http://www.mitoaction.org">www.mitoaction.org</a></td>
</tr>
<tr>
<td>Pemphigus and Pemphigoid</td>
<td>- The International Pemphigus and Pemphigoid Foundation: <a href="http://www.pemphigus.org">www.pemphigus.org</a></td>
</tr>
<tr>
<td>Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)</td>
<td>- PANDAS/PANS Advocacy and Support: <a href="http://www.pas.care">www.pas.care</a></td>
</tr>
<tr>
<td>PANDAS</td>
<td>- PANDAS Network: <a href="http://www.pandasnetwork.org">www.pandasnetwork.org</a></td>
</tr>
<tr>
<td>PANDAS</td>
<td>- Midwest PANS/PANDAS Support Group: <a href="http://www.midwestpandas.com">www.midwestpandas.com</a></td>
</tr>
<tr>
<td>Primary Immune Deficiency Disease (P1)</td>
<td>- Immune Deficiency Foundation: <a href="http://www.primaryimmune.org">www.primaryimmune.org</a></td>
</tr>
<tr>
<td>Stiff Person Syndrome (SPS)</td>
<td>- American Autoimmune Related Diseases Association Inc.: <a href="http://www.aarda.org">www.aarda.org</a></td>
</tr>
<tr>
<td>Stiff Person Syndrome (SPS)</td>
<td>- Genetic Alliance: <a href="http://www.geneticalliance.org">www.geneticalliance.org</a></td>
</tr>
<tr>
<td>Stiff Person Syndrome (SPS)</td>
<td>- Living with Stiff Person Syndrome (personal account): <a href="http://www.livingwithspsp.com">www.livingwithspsp.com</a></td>
</tr>
<tr>
<td>Stiff Person Syndrome (SPS)</td>
<td>- Stiff Person Syndrome: <a href="http://www.stiffpersonsindrome.net">www.stiffpersonsindrome.net</a></td>
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</tbody>
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