Maximizing Quality of Life
How to Balance Life, Health and Finances

December-January 2020

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Guidelines for Proper Nutrition

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Up Front

5 Editorial
Chronic Illness: A Delicate Balancing Act
By Ronale Tucker Rhodes, MS

6 Abbie’s Corner
What Caused the Recent Shortage of IG Products?
By Abbie Cornett

7 Faces of IG
From our Facebook page

Departments

8 Ask the Experts
Healthcare professionals’ responses to patient questions

9 Immunology 101
The Peculiarities of Hypersensitivities and Allergic Reactions
By Terry O. Harville, MD, PhD

10 Therapeutic Helpline
My Feelings Have Too Much Control Over Me! Part 2
By Erika Lawrence, PhD, LCP

12 Clinical Brief
Clinical Presentation of CVID
By Michelle Greer, RN

14 In the News
Research, science, product and insurance updates

Columns

40 Let’s Talk! — Heidi Plavecsky
By Trudie Mitschang

42 Patient Perspective — Holding Steady
By Stacey Philpot

43 Life as a 20-Something — Everyday Anxieties with Chronic Illness
By Ilana Jacqueline

44 Parenting — Resources for Educating Children About PIs
By Jessica Leigh Johnson

Features

18 Tips for Balancing Life, Health and Finances
By Trudie Mitschang

22 East Meets West: Complementary and Alternative Therapies for Chronic Pain and Autoimmune Disorders
By Rachel Colletta, BSN, CRNI, IgCN, VA-BC

28 What Is Proper Nutrition?
By Mindy Hermann, MBA, RDN

31 SCID Bone Marrow Transplant: A Follow-Up After 47 Years
By E. Richard Stiehm, MD

34 Understanding Hyper IgE Syndrome
By Ronale Tucker Rhodes, MS

46 Product Guide
Managing IVIG Adverse Effects
By Michelle Greer, RN, and Leslie J. Vaughan, RPh

48 Book Corner
New and useful reading

50 Resource Center
Community foundations, associations, forums and other resources

Sources

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Chronic Illness: A Delicate Balancing Act

MANAGING THE day-to-day challenges of a chronic, lifelong illness can be a delicate balancing act. Choices have to be made about how to prioritize health, family, friends, work, and the list goes on — all in an effort to accomplish as much as possible while healthy and having enough energy to do so. While things may not always go as planned, we can at least begin each day with the intent of making it better. And, heck, if it doesn’t work out, it’s important to maintain a positive outlook and keep things in perspective. Let’s face it: Balance requires constant adjustment!

Balance is the focus of this issue, beginning with “Tips for Balancing Life, Health and Finances” (p.18) in which we share lessons learned by others about how to achieve balance in four areas of life: energy, finances, health and mood. Most people with chronic illness have heard of the Spoon Theory, a concept borne out of one person’s battle to grapple with the challenges of lupus. Simply put, it’s a “pacing strategy” to get through each day with energy to spare. Also included are resources for gaining as much knowledge about our conditions, methods of empowering ourselves to juggle the tasks of our healthcare to-do lists and utilizing the mind’s power over the immune system.

Balance is also important for achieving wellness, which according to modern-day alternative medicine practitioners can only be achieved by focusing on the person as a whole. In our article “East Meets West: Complementary Alternative Therapies for Chronic Pain and Autoimmune Disorders” (p.22), we explore how combining Western and Eastern medicinal practices, known as complementary and alternative medicine (CAM), can restore balance by addressing how the mind, body and spirit work together. A number of CAM therapies such as supplements, meditation and acupuncture have proved to work for treating chronic pain and autoimmune disorders.

And, while nutrition needs and benefits differ for each person, the foundation for a well-rounded diet is a balanced one. Every five years, the U.S. government publishes the Dietary Guidelines for Americans, which we outline in our article “What Is Proper Nutrition?” (p.28). We also discuss the nutritional benefits of different types of foods, including vegetables, grains, protein, dairy and fat. We hope this information will help you with planning healthy, balanced meals that also meet your food likes and dislikes.

As always, we hope you enjoy these articles, as well as the many more educational and insightful topics presented in this issue of IG Living.
What Caused the Recent Shortage of IG Products?

By Abbie Cornett

IN RECENT MONTHS, many patients in the U.S. have been notified their scheduled immune globulin (IG) infusions were either being delayed or canceled due to a shortage of product. Understandably, this has caused concern for patients who depend on these lifesaving treatments for their acute and/or chronic conditions.

Since 1951, when Ogden Bruton, MD, first treated an 8-year-old boy with congenital agammaglobulinemia with serum IG, the market for these products has evolved considerably. Dr. Bruton’s work was the basis for developing the first U.S. Food and Drug Administration-approved intravenous IG (IVIG) product in 1981. Since then, the demand for plasma protein therapies used to treat rare and chronic conditions has grown at a rapid rate. Indeed, the worldwide demand for IVIG and subcutaneous IG products more than doubled between 2008 and 2016, and it is projected to continue growing at more than 8 percent a year (Figure).

I am frequently asked by patients why the use of IG therapy has expanded so quickly. Mainly, it is because physicians are prescribing IG to treat a growing number of disease states — not only for its ability to fight infection as a replacement therapy, but also for its anti-inflammatory and immunomodulating effects. For instance, while IVIG was originally developed to treat immune deficiencies, its use has expanded to treat several other chronic illnesses such as chronic inflammatory demyelinating polyneuropathy, hypogammaglobulinemia, multifocal motor neuropathy, myasthenia gravis, Guillain-Barré syndrome, Miller Fisher syndrome, acute motor axonal neuropathy, acute motor-sensory axonal neuropathy, Kawasaki disease and immune thrombocytopenia purpura, among others.

The increased demand for these products is further compounded by an aging population prone to antibody deficiency disorders due to weakened immune systems that is increasingly being treated with IG. According to the United States Census Bureau, the number of people aged 65 years and older in the U.S. was approximately 46.2 million in 2014, and their numbers are expected to reach more than 98 million by 2060. Undoubtedly, this geriatric population will propel the demand for IG therapies in the near future.

It is critical for patients to understand the pharmaceutical industry is doing everything it can to meet patient therapy needs. Foremost, manufacturers are developing ways to improve the product yields derived from donor plasma. And, the number of IG products available to treat patients is increasing with the introduction of new products and reintroduction of a once-removed product to the market this year. It is hoped these efforts will help fulfill patient demand in the near future.


Figure. U.S. Intravenous Immunoglobulin Market Size, by Application, 2014-2025 (USD Billion)

For additional information on this topic, listen to IG Living’s podcast titled “The Increased Demand for Immune Globulin and Its Effects on Patient Access” at www.igliving.com/life-with-ig/ig-living-advocate-podcast.html.

If you have been told your IG product is not available, please contact me at patientadvocate@igliving.com. ☐

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

References
Now, there is a question for the ages. I think I have forgotten what it is like to not be tired. — Jenny G

I have learned to adjust my activities accordingly and not beat myself up emotionally because of it. — Debbie K

I was just thinking this as I sit on my La-Z-Boy couch in my nightgown. I’m not motivated to get dressed, take a shower or go exercise. I didn’t go anywhere yesterday, either. Chronic fatigue is a side effect of my polycythemia, when my hematocrit and hemoglobin levels get too high. It just means I need a phlebotomy at my next hematologist-oncologist appointment. Also, [fatigue] is a side effect of a brand-new medication the pulmonologist just [prescribed for] me that I’m supposed to [take] twice a day, but I started with once a day because of the side effects. The other thing that causes chronic fatigue for me is having fibromyalgia and myofascial pain syndrome. — Rachel D

Why am I tired all the time?

I was just thinking this as I sit on my La-Z-Boy couch in my nightgown. I’m not motivated to get dressed, take a shower or go exercise. I didn’t go anywhere yesterday, either. Chronic fatigue is a side effect of my polycythemia, when my hematocrit and hemoglobin levels get too high. It just means I need a phlebotomy at my next hematologist-oncologist appointment. Also, [fatigue] is a side effect of a brand-new medication the pulmonologist just [prescribed for] me that I’m supposed to [take] twice a day, but I started with once a day because of the side effects. The other thing that causes chronic fatigue for me is having fibromyalgia and myofascial pain syndrome. — Rachel D

Who cares about patient advocacy?

Anyone who is a patient has a story to share and has lessons they have learned. Sharing these stories and lessons helps others, including our doctors, nurses and administrators. I believe very strongly in patient advocacy, and I volunteer at our local hospital on various committees that give patients a voice. So important! — Donna G

Patient advocacy is extremely important. When possible, I think the person we are contacting needs to put a face to the need. I’m hoping that makes it harder for the legislators to say no! — Jenny G

Is your provider HIPAA-compliant?

Most likely not. I just went through this when one dropped me because his wife mucked up the billing of my account. When I requested a copy of my record should the next doctor in that specialty need it, they sent me a bill for $75. I sent a complaint to the Centers for Medicare and Medicaid Services (CMS) as [it was a] Medicaid and Medicare provider at some point during the time I was seen. And, CMS sent back that they found the doctor in violation of unreasonable and excessive charges for records requests. Even Alabama law is murky on this matter. It doesn’t set any limits beyond “reasonable charge.” Alabama law also stipulates a doctor’s office cannot charge if the person is low income and the fee would provide a hardship. Of course, now that I know this, the next time some hospital wants to charge me $100 for a record request, I’m just going [to say], “Nope, because I legitimately cannot afford that, but I need this for whatever doctors may need this outside your system.” — Susan ES

I’m pretty sure all my doctors and hospital systems are in compliance because I’m continually having to fill out HIPAA forms on a regular basis. — Rachel D
**Abbie**  I spoke with Terry O. Harville, MD, PhD, medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, about your concern. He said PANDAS is associated with streptococcus, which is treated by various therapies, including IVIG. Patients with PANDAS do not have excessive susceptibility to infections. Unfortunately, though, infections can trigger flares in the disease activity. But, overall, there is no need to avoid normal contact with most persons.

My 6-year-old granddaughter has had one intravenous immune globulin (IVIG) treatment for pediatric autoimmune neuropsychiatric disorder associated with streptococcus (PANDAS). Her parents keep her in the house all the time to avoid illness. I am concerned about this and would like to know if she can be around healthy people who have not been vaccinated.

**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.
The Peculiarities of Hypersensitivities and Allergic Reactions

By Terry O. Harville, MD, PhD

THE DISTINCTION between hypersensitivities and allergic reactions is often confusing. And frequently, the medical profession contributes to this confusion. For example, if a patient is treated with erythromycin for an infection and then experiences a stomachache, he or she may be told it is an allergy to the drug and not to take it in the future. However, that statement is inaccurate. The stomachache is not an allergic reaction nor a hypersensitivity to erythromycin since it is well-known erythromycin has a direct action on the cells of the stomach that can cause a stomachache. As such, stomachache is a well-known side effect of erythromycin.

Misperceptions about allergies and hypersensitivities date back many decades. In 1963, Gell and Coombs reported on a system of classification of histopathologic reactions observed in tissues through a microscope. It should be noted at that time the underlying mechanisms of these reactions were not fully known or understood. For example, IgE, which is responsible for what we typically consider an allergic reaction, had not yet been discovered. The Gell-Coombs classification defined four patterns of tissue reactivities or hypersensitivities. Type I hypersensitivity is what we now know is a true allergic reaction mediated via IgE and its effects on mast cells. Type II hypersensitivity is due to antibodies (other than IgE) that can bind to and injure cells and tissues. Type III hypersensitivity is due to antibodies (other than IgE) binding to their targets in the blood and body fluids, which then become circulating immune-complexes (CIC) that are subsequently deposited into tissues where they may cause injury or damage. The medical condition caused by CICs is commonly referred to as serum sickness. Type IV hypersensitivity is not due to antibodies, but rather to the migration of mononuclear cells we now know as monocytes and T lymphocytes into the affected tissue area. This type is also known as cell-mediated immunity or delayed-type hypersensitivity (DTH). DTH was named for the response time to the tuberculosis skin test, which takes a couple of days before the reaction can be observed. Types I, II and III hypersensitivities could occur with IVIG and SCIG infusions.

A true IgE-mediated allergic reaction that results in mast cell activation from the nonallergic hypersensitivities is dose-independent. Understanding these issues is very important for those receiving IVIG or SCIG therapy. It’s important to determine whether a hypersensitivity or an allergic reaction is occurring to more effectively treat or prevent it.

In the next issue, we will continue to distinguish between hypersensitivities and allergic reactions, as well as place each in the correct clinical context.

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.

Reference
IN MY LAST column, I talked about the ways in which we try to distract ourselves from uncomfortable or unwanted feelings. Known as away moves, those strategies may be helpful sometimes, unhelpful at other times and may even make things worse.

The opposite of away moves is willingness, which means being willing to experience your thoughts, feelings and urges. Willingness is something you can do anywhere at any time. It’s not a feeling or a thought: it’s a choice. Willingness is not ignoring your emotions, but rather being aware of them and still being willing to move forward and live your life. Following are two willingness activities you can practice.

Activity #1: The Ice Cube Metaphor1
To illustrate, get an ice cube and let it sit in one open hand. What does it feel like? What’s the temperature? How heavy is it? You might have sensations of cold, heat, burning, tingling, moisture or numbness. And those feelings may differ from moment to moment. Does it still feel the same as it did at the beginning, or has it changed?

Now, notice your thoughts. You might be thinking, “Why am I doing this?” or “This is stupid, what’s the point?” What are your feelings? Do you have any urges to do anything? Maybe to put the ice down or throw it away?

Let the ice move around slightly in your hand. Notice the sensations in your hand while also noticing what your mind is doing. Notice what’s happening to the size and shape of the ice. If there’s water now, notice how it moves and feels in your hand. Simply notice it without trying to change anything. Notice if you are judging it as good or bad.

Now, put the ice down and dry your hand. What was it like to hold the ice cube? What thoughts and feelings did you notice? What was the most difficult part? Did you learn anything about your responses to unwanted or uncomfortable sensations? Why did you decide to participate in this activity? Why did you hold the ice for the whole time? You could have chosen to set it down and not participate, so something must be motivating you to participate even though holding the ice is uncomfortable.

You may have noticed struggling with the ice made it hard. Struggling against our feelings often makes it hard to move forward in our lives. Moving forward in our lives and doing the things that matter to us sometimes requires us to experience unwanted and uncomfortable emotions.

Activity #2: Practice Observing Emotions
Think about the last time you felt a really intense emotion. It may be anger, sadness or anxiety, for example. Imagine where you were, what happened right before you felt that way, who was there and what was said. Try to put yourself back in that moment. Let yourself feel that emotion all over again. Now, hold on to that emotion and go through the following steps:

1) Take a deep breath and scan your body from head to toe. Notice all of the uncomfortable sensations that come along with that feeling. Look for the strongest one, the one that bothers you most. Maybe it’s your face getting warm, a knot in your stomach or your fists starting to clench.

2) Focus your attention on that sensation. Take a couple of breaths and breathe into that sensation. Imagine your breath is flowing in and around it. Make room for it. Allow it to be there. You don’t have to like it or want it, just let it be.

3) Notice whether you are having any thoughts while focusing on the sensation. Notice whether you become distracted by those thoughts. Don’t try to get rid of the sensation or alter it. If it changes by itself, that’s OK. If it doesn’t change, that’s OK, too. Changing or getting rid of it is not the goal.

You may need to focus on this sensation for as long as a few seconds to a few minutes until you completely give up the struggle. Be patient. Take as long as you need. You’re learning a valuable skill.

The Bottom Line
Willingness takes practice, especially when our instinct may be to avoid, get rid of, distract or try to change an overwhelming emotion. Try using these activities to practice willingness when you feel overwhelmed. These are not easy techniques. It’s like learning to drive a car. It takes time and practice, but you can get there if you’re willing.

ERIKA LAWRENCE, PhD, LCP, is director of translational science at The Family Institute at Northwestern University, Evanston, Ill.

References
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Specialty Solutions in Chronic Care

- Immune Globulin
- Factor
- Infliximab

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Clinical Presentation of CVID

By Michelle Greer, RN

**COMMON VARIABLE IMMUNODEFICIENCY (CVID)** is one of more than 350 forms of primary immunodeficiency diseases (PIs), each of which presents with varying symptoms, clinical courses and treatment. CVID occurs when there is an antibody deficiency that impairs the immune system from providing a proper defense against antigens such as bacteria, viruses or fungi, resulting in multiple and recurring infections. Although several genes have been identified as the cause of CVID, environmental factors can also play a role. And, while the exact cause of CVID is unknown, family history does not seem to play much of a role since most cases are sporadic with no family history.

CVID can be diagnosed at any age. Diagnosis is confirmed by a variety of laboratory tests that reveal a low immunoglobulin G (IgG) and other immunoglobulin levels and an impaired immune response to vaccine antigens. The IgG level can vary widely from person to person, ranging from mildly low to just below normal and profoundly low. Pneumococcal pneumonia, tetanus and diphtheria vaccines are typically given to assess immune response.

Infections are the hallmark of all PIs, including CVID. Infections can range in severity and mostly occur in the ears, sinuses and respiratory tract. Infections of the gastrointestinal tract are also common. CVID patients are frequently ill with severe infections requiring frequent doctor visits and multiple rounds of antibiotics, resulting in missed work and/or school and even hospitalization. Because such infections can occur in all people, a PI is not typically suspected, nor tested for. Therefore, CVID patients often go years without receiving a definitive diagnosis, which can be frustrating and also concerning since recurrent infections can result in permanent damage, especially infections of the respiratory tract, which can damage the lungs (known as bronchiectasis).

Autoimmune diseases in conjunction with CVID occur in approximately 25 percent of cases. There are more than 100 forms of autoimmune diseases, which occur when the immune system recognizes itself as foreign and attacks it. Sometimes, an autoimmune disease is diagnosed prior to CVID. The more common types of autoimmune diseases seen in conjunction with CVID are those affecting other blood cells (such as what occurs with immune thrombocytopenia, which destroys platelets and results in bleeding) or those that cause anemia, which affects red blood cells. Rheumatoid arthritis and autoimmune conditions of the endocrine system such as the thyroid gland are also common.

Table 1. 10 Warning Signs of PI

| 1) Four or more new ear infections within one year. |
| 2) Two or more serious sinus infections within one year. |
| 3) Two or more months on antibiotics with little effect. |
| 4) Two or more pneumonias within one year. |
| 5) Failure of an infant to gain weight or grow normally. |
| 6) Recurrent, deep skin or organ abscesses. |
| 7) Persistent thrush in the mouth or fungal infection on skin. |
| 8) Need for intravenous antibiotics to clear infections. |
| 9) Two or more deep-seated infections, including septicemia. |
| 10) A family history of PI. |

Source: Jeffrey Modell Foundation: info4pi.org
CVID patients have a higher risk of certain forms of cancer, with malignancies seen in roughly 40 percent of patients. This increased risk is mainly for blood cell cancers, most commonly lymphoma and gastrointestinal cancers; there is no increased risk of solid organ cancers. A recent study of people with cancer enrolled in a national registry found a 42 percent increase in cancer incidence among PI patients, the majority of whom were CVID patients who comprised 70 percent of those in the database, including an increased risk of non-Hodgkin lymphoma, gastric cancer and skin cancer.

CVID is treated with immune globulin (IG) replacement therapy administered either intravenously or subcutaneously. Based on test results, the physician will decide if IG therapy is warranted, and the patient and physician will together determine the appropriate route of administration and site of care, which is based on age, lifestyle and tolerability. IG treatment almost always requires prior authorization by health insurance. However, while all payers generally require proof of diagnosis, including history of infections, IgG levels and tests showing an inability to mount an immune response to vaccines, requirements vary from payer to payer. Some payers state in their medical policies that IgG levels must be below 400, while some state two standard deviations below normal for the person’s age, and some ask for two tests for IgG levels. Even Medicare recently changed its local coverage determination and requires levels below 200 or a history of infection along with a low IgG level and a poor vaccine response. The most common test that is not required by payers is the vaccine test.

In summary, each CVID patient presents differently, and the results of testing to diagnose CVID are unique to each person. The number, type and severity of infections vary, and other complications of CVID may or may not be present. Therefore, it is important to understand the warning signs (Table 1) of CVID and for suspected patients to be tested (Table 2) by a physician who specializes in immune deficiencies so the best treatment protocols can be implemented as early as possible before permanent damage occurs.

**MICHELLE GREER** RN, is senior vice president of sales for Nufactor, a Specialty Infusion Company.

**Reference**


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**Table 2. Four Stages of Testing for PI**

<table>
<thead>
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<th>Stage</th>
<th>Tests</th>
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<td>1. History and physical examination, height and weight</td>
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<td>2. Complete blood count and differential</td>
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<tr>
<td>3. Quantitative immunoglobulin levels IgG, IgM, IgA (related to age)</td>
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<tr>
<td>4. Specific antibody responses (tetanus, diphtheria)</td>
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<td>5. Response to pneumococcal vaccine (pre/post) (for ages 3 and up)</td>
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<td>6. IgG subclass analysis</td>
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<tr>
<td>7. Candida and tetanus skin tests</td>
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<tr>
<td>9. Mononuclear lymphocyte proliferation studies (using mitogen and antigen stimulation)</td>
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<tr>
<td>10. Neutrophil oxidation burst (if indicated)</td>
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<tr>
<td>11. Complement screening CH50, C3, C4</td>
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<tr>
<td>12. Enzyme measurements (adenosine deaminase, purine nucleoside phosphorylase)</td>
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<td>13. Phagocyte studies (surface glycoproteins, mobility, phagocytosis)</td>
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<td>14. NK cytotoxicity studies</td>
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<td>15. Further complement studies, AH50</td>
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<td>16. Neoantigen to test antibody production</td>
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<tr>
<td>17. Other surface/cytoplasmic molecules</td>
<td></td>
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<tr>
<td>18. Cytokine receptor studies</td>
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<tr>
<td>19. Family/genetic studies</td>
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Source: Jeffrey Modell Foundation: info4pi.org
IN THE NEWS

Medicines

FDA Transfers Bivigam and Nabi-HB Licenses from Biotest Pharmaceuticals Corp. to ADMA Biologics

The U.S. Food and Drug Administration (FDA) has revoked the licenses for Bivigam and Nabi-HB from Biotest Pharmaceuticals Corporation (BPC) and transferred and issued the licenses to ADMA Biologics.

“We are very pleased to announce the U.S. License transfer of Bivigam and Nabi-HB from BPC to ADMA, as this was the final remaining regulatory item from the acquisition of the Biotest Therapy Business Unit [BTBU] transaction,” stated President and Chief Executive Officer Adam Grossman. “It is important for patients, prescribers and investors to recognize that FDA regulatory licensing is complex, particularly with respect to ADMA’s acquisition of the BTBU assets. Since ADMA’s ownership and operation of the BTBU, we have received an acceptable FDA inspection classification, FDA approvals for two product submissions and now licenses issued in ADMA’s name for two FDA-approved biologic drugs.”


Medicines

Orchard Therapeutics Receives RMAT Designation from FDA for WAS Gene Therapy

The U.S. Food and Drug Administration (FDA) has granted Orchard Therapeutics’ OTL-103 ex vivo autologous hematopoietic stem cell (HSC)-based gene therapy regenerative medicine advanced therapy (RMAT) designation to treat Wiskott-Aldrich syndrome (WAS). RMAT designation was based on data from an interim analysis of a registrational trial in patients with severe WAS that showed recovery of the immunological and platelet abnormalities associated with WAS with a consequent significant reduction in the major complications of the disease. Specifically, following treatment with OTL-103 gene therapy, patients with follow-up ranging from 0.5 to 5.6 years showed a decrease in the frequency of severe infections, as well as elimination of severe bleeding episodes and a reduction in moderate bleeding episodes.

An investigational drug or therapy is eligible for RMAT designation if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates the drug or therapy has the potential to address unmet medical needs for the disease or condition. “Securing RMAT designation for OTL-103 is an important step in expediting the product development and review of our planned biologics license application and recognizes the unmet need for children and young adults afflicted with Wiskott-Aldrich syndrome,” said Anne Dupraz-Poiseau, PhD, chief regulatory officer at Orchard. “We remain on track to file for regulatory approval of our WAS gene therapy program in the U.S. and Europe in 2021 in the hope of bringing this potentially curative therapy to patients as soon as possible.”

IN THE NEWS

Research

Orchard Gene Therapy Effective in Treating ADA-SCID

Three-year follow-up data on 20 patients with adenosine deaminase deficiency-severe combined immune deficiency (ADA-SCID) treated with Orchard Therapeutics’ OTL-101, an autologous hematopoietic stem cell gene therapy, showed positive results. At month 24, the overall survival and event-free survival rates were 100 percent. Overall survival was 12 percent better than hematopoietic stem cell transplantation (HSCT), while event-free survival was 44 percent better. Ninety percent of treated patients were able to stop immune globulin replacement therapy compared with 55 percent treated with HSCT. There were no cases of graft-versus-host disease in the OTL-101 group compared with eight in the HSCT control group (including one death). There were 27 serious adverse events in nine of the 20 OTL-101 patients, the most frequent of which were infections and gastrointestinal events. And, there was one treatment-related case of bacteremia (bacteria in the bloodstream) that was resolved with antibiotics. 


Research

New Bone Marrow Transplantation Approach Is a Potential Cure for PI Patients

A recent study showed a novel radiation-free and serotherapy-free reduced-intensity conditioning T-cell replete bone marrow transplantation (BMT) approach for primary immunodeficiency disease (PI) patients yielded promising results, even for high-risk patients. In the study, 20 high-risk PI patients with a median hematopoietic cell transplantation-comorbidity index of 3, ranging in age from 4 years to 58 years, were treated in a prospective clinical trial of the BMT approach using pentostatin, low-dose cyclophosphamide and busulfan for conditioning with posttransplantation cyclophosphamide-based graft-versus-host-disease (GVHD) prophylaxis. At median follow-up of survivors at 1.9 years, the one-year overall survival rate was 90 percent, and grade III-IV acute GVHD-free, graft failure-free survival was 80 percent at day +180. Graft failure incidence was 10 percent. Split chimerism was frequently observed at early post-BMT timepoints, with a lower percentage of donor T cells that gradually increased by day +60. The cumulative incidences of grade II-IV and grade III-IV acute GVHD (aGVHD) were 15 percent and 5 percent, respectively. All aGVHD was steroid-responsive, no patients developed chronic GVHD, and few significant organ toxicities were observed. Evidence of phenotype reversal was observed for all engrafted patients, even those with significantly mixed chimerism or with unknown underlying genetic defect. All six patients with pre-BMT malignancies or lymphoproliferative disorders remain in remission.

A new study has found combined primary therapy with intravenous immune globulin (IVIG) and ciclosporin is safe and effective for favorable coronary artery outcomes in Kawasaki disease patients who were predicted to be unresponsive to IVIG. In the randomized, open-label, blinded endpoints trial involving 175 patients (one of whom was excluded because of lost echocardiography data) at 22 hospitals in Japan between May 29, 2014, and Dec. 27, 2016, eligible patients predicted to be at higher risk for IVIG resistance were randomly assigned to IVIG plus ciclosporin (5 mg/kg per day for five days; study treatment) or IVIG (conventional treatment) groups, stratified by risk score, age and sex. The primary endpoint was incidence of coronary artery abnormalities using Japanese criteria during the 12-week trial, assessed in participants who received at least one dose of study drug and who visited the study institution at least once during treatment.

Findings showed incidence of coronary artery abnormalities was lower in the study treatment group than in the conventional treatment group (12 [14 percent] of 86 patients versus 27 [31 percent] of 87 patients). And, no difference was found in the incidence of adverse events between the groups (9 percent versus 7 percent).


Researchers at the Karolinska Institute in Stockholm, Sweden, have found the risk of developing seven autoimmune diseases is largely inherited, but some diseases are more closely related than others. By using data on 116,320 twins from the Swedish Twin Registry, which is managed by the Karolinska Institute, they found Addison’s disease, celiac disease and type 1 diabetes are strongly influenced by genes with heritability greater than 85 percent, while environmental factors contribute to disease for Hashimoto’s hypothyroidism, vitiligo, Graves’ disease and atrophic gastritis. In addition, they found autoimmune clustering was high in Addison’s disease and vitiligo, but low in celiac disease. “Our results indicate that Addison’s disease and vitiligo often overlap with other disorders, whereas celiac disease more rarely associates with the other diseases,” said Jakob Skov, MD, the study’s lead investigator and a PhD student at the Karolinska Institute.

Since autoimmune diseases tend to run in families, the basis of twin studies is to examine concordance rates, the likelihood of both twins in a pair having the same disease. Higher concordance rates in identical rather than in nonidentical twins point to genetic influence. This information is typically used to calculate heritability. The researchers also looked at the likelihood of both twins in a pair having different autoimmune diseases, which they named “pseudoconcordance,” and compared these rates to measure autoimmune clustering.

“These results contribute to our understanding of what causes autoimmunity and how autoimmune diseases are related,” said Dr. Skov. “We examined the risk of acquiring not only one specific disease, but any one in a cluster of conditions. The findings may be helpful in patient education and autoimmune risk counseling.”

Research

New SCIG 16.5% Effective in Preventing Infections in PI Patients

A study that evaluated a new 16.5% subcutaneous immune globulin (SCIG) therapy, Cutaquig (Octanorm), was shown to be effective in preventing infections in primary immune deficiency disease (PI) patients and was well-tolerated.

In the study, patients who were previously treated with intravenous immune globulin (IVIG) received a total of 64 weekly SCIG infusions, including 12 weekly infusions during the wash-in/wash-out period, followed by 52 weekly infusions during the evaluation period. Results showed 61 patients ages 2 years to 73 years received 3,497 infusions of Cutaquig, with a mean dose of 0.175 g/kg per infusion per patient. The mean calculated dose conversion factor from the patients’ previous IVIG dose was 1.37. No serious bacterial infections developed during the study, and the rate of other infections per person-year during the primary observation period was 3.43. All but one nonbacterial infection were mild or moderate in intensity. And, IgG trough levels were constant during the course of the study. Eleven patients (18 percent) experienced mild or moderate systemic adverse events related to Cutaquig, at a rate of 0.004 adverse events per infusion. In 76.7 percent of infusions, no infusion site reactions were observed, and only two reactions were deemed severe. In addition, the incidence of site reactions decreased with successive infusions.

Medicines

FDA Approves First Drug to Treat Children with LEMS

The U.S. Food and Drug Administration (FDA) has approved Ruzurgi (amifampridine) tablets to treat Lambert-Eaton myasthenic syndrome (LEMS) in patients 6 years to less than 17 years of age. This is the first FDA approval of a treatment specifically for pediatric patients with LEMS. The only other treatment for LEMS is approved for use in adults only.

Approval of Ruzurgi is based on a randomized, double-blind, placebo-controlled withdrawal study of 32 adult patients who were taking Ruzurgi for at least three months prior to entering the study. Researchers compared patients continuing on Ruzurgi to patients switched to placebo. Effectiveness was measured by the degree of change in a test that assessed the feeling of weakening or strengthening. Scores indicated greater perceived weakening in patients who were switched to placebo. The most common side effects experienced by pediatric and adult patients taking Ruzurgi were burning or prickling sensation (paresthesia), abdominal pain, indigestion, dizziness and nausea. Side effects reported in pediatric patients were similar to those seen in adult patients. Seizures have been observed in patients without a history of them.

LEMS is a rare autoimmune disorder that affects the connection between nerves and muscles and causes weakness and other symptoms. In people with LEMS, the body’s immune system attacks the neuromuscular junction and disrupts the ability of nerve cells to send signals to muscle cells. The application for Ruzurgi was granted priority review and fast track designations, and it also received orphan drug designation.

“We continue to be committed to facilitating the development and approval of treatments for rare diseases, particularly those in children,” said Billy Dunn, MD, director of the division of neurology products in the FDA’s Center for Drug Evaluation and Research. “This approval will provide a much-needed treatment option for pediatric patients with LEMS who have significant weakness and fatigue that can often cause great difficulties with daily activities.”


Not unlike a demanding toddler, chronic illness commands attention. But, with proper tools and resources, patients can achieve much-needed balance and keep sickness and its symptoms from dominating their time, energy and attention.

By Trudie Mitschang

**BEING DIAGNOSED WITH** a chronic illness can be both frightening and overwhelming. For many, it’s as if the illness itself becomes an entity that must be managed, planned for and navigated, in addition to juggling life’s everyday responsibilities such as work, relationships and finances. And, while everyone deals with varying degrees of stress, living with a long-term health condition presents a host of unique stress triggers, including:

- Coping with pain or discomfort from symptoms;
- Adjusting to new limitations the condition puts on life;
- Managing increased financial pressures and insurance questions; and
- Feelings of frustration, confusion or isolation.

The good news is, no matter where patients find themselves on their journey with chronic illness, there are steps they can take to maximize quality of life.

**Balancing Energy: The Practice of Pacing**

Chronic illness and fatigue go hand-in-hand, sometimes limiting life in ways most healthy people will never truly understand. There is always so much to do, but so little energy to do it. For many, it’s hard to properly budget what little bit of energy they have.

In the early stages of diagnosis, patients might consider keeping a health journal to track symptoms and get a snapshot of any patterns attached to energy highs and lows. Close attention should be paid to what seems to ease symptoms or make them worse, making special note of dietary changes, activity levels and sleep patterns. A notebook or calendar can be used to record trends and other insights that might help manage symptoms. Over time, as patterns develop, patients will be able to better anticipate high energy days, putting
them in the driver’s seat when it comes to making plans and social commitments.

Christine Miserandino, a writer, blogger, speaker and lupus patient advocate, perfectly describes the limited energy reserves people with chronic illness face in her popular Spoon Theory object lesson. The concept was born when Miserandino was asked by a friend to describe life with lupus. Sitting in a café at the time, she reached over and gave her friend a handful of spoons, using them to illustrate finite units of energy. She then walked her friend through an average day’s tasks, taking spoons (or energy) from her after each activity. Take a shower? One spoon. Cook breakfast and eat it? Two spoons. Leave the house? Three spoons. In short order, her friend was out of spoons and had a much clearer picture of what life was like for Miserandino and millions of others who live with chronic illness.

“Until Spoon Theory, no one else had explained the trials of chronic illness so simply and, yet, so effectively. It’s been accepted across the world as this amazing tool to describe what life with illness is really like,” says Kirstin Schultz, a blogger and patient advocate who has been living with multiple chronic illnesses since childhood. “The Spoon Theory has done some great things since its inception — one of which is providing a way for people to meet others dealing with illness. A quick search on social media will pull up hundreds of thousands of posts from people who identify as a ‘Spoonie’.”

Toni Bernhard, author of How to Live Well with Chronic Pain and Illness: A Mindful Guide, is no stranger to the energy depletion dilemma. Bernhard advises patients navigating recurrent exhaustion to practice a technique called “pacing,” a method she says is extremely effective in helping her and others get through the day with energy to spare. “Pacing refers to spacing out your activities during the day so you’re able to stay within the limits of what your body can handle without exacerbating your symptoms,” she explains. “Another way to think of it is that pacing is a way to keep you inside your ‘energy envelope’ — the envelope that contains your energy stores for any given day.”

While the theory sounds simple enough, Bernhard is quick to admit it’s a lot more difficult than it seems, since most of us have a tendency to overdo it when we feel good, only to pay the price later when energy levels crash. In her blog on the topic, she offers tips for developing a successful pacing strategy, beginning with alternating activity with rest.

“This approach to scheduling has helped me tremendously since becoming chronically ill,” Bernhard says. “For example, if I put on the schedule for the morning, ‘10:00-10:30: work on article,’ but then wind up working until 11:00, I revise the schedule and move on with the day. Simply having that schedule in front of me keeps me from deviating from it too much. Without set time frames, I’m likely to lose track of time and work for several hours straight; then, of course, I suffer the consequences. Some people find it helpful to set a timer; when it goes off, they know it’s time to stop the activity and rest for a while.” Bernhard also recommends slowing down when performing chores like folding laundry or doing dishes to keep from expending precious energy on mundane tasks.

Additionally, she advises following something she calls the 50 percent rule: “With this pacing tool, given how you feel on a particular day, you decide what you can comfortably do, and then only do 50 percent of it. One reason this is a great strategy is that I tend to overestimate what I can comfortably do, so this keeps me safely within my energy envelope. I also recommend that you think of that unexpended 50 percent as a gift you’re giving yourself to help you feel less sick and in less pain.”

Managing Money: Staying Fiscally Fit

While managing personal finances is universally challenging, people who live with a chronic illness often experience a unique set of monetary concerns, making it a wise idea to consult with a professional financial planner. Even if patients were highly adept at managing their money prior to the onset of illness, chronic conditions can be unpredictable, and investing in the help of a trained advisor can help them make sure they have all their bases covered now and in the future.

For example, when it comes to developing a comprehensive plan, a professional advisor can assist in creating a budget for healthcare savings, disability coverage and long-term care

In the early stages of diagnosis, patients might consider keeping a health journal to track symptoms and get a snapshot of any patterns attached to energy highs and lows.
insurance. Prior to crunching the numbers, it’s also a good idea for patients to research the likely progression and symptoms of their illness so they can make informed decisions. For instance, will home healthcare be required at some point? If a wheelchair will be needed, will they need to widen doorways or make additional home modifications? Additionally, retirement may come earlier than planned, or a spouse may need to leave work to become a caregiver; these are all scenarios a financial adviser can use to help prepare for projected costs.

According to Cyndi Hutchins, director of financial gerontology at Bank of America Merrill Lynch, keeping good financial records is also important, including a tracking system for medical expenses and insurance claims. She advises making a list of instructions that includes where to find important household and financial information, and providing these documents to a trusted friend or relative who can access them in an emergency. Another step to consider is streamlining finances by consolidating various accounts. Having everything in one place can make it easier and quicker to manage. Remember, when it comes to finances, knowledge is power, and staying on top of expenses, although time-consuming, can pay big dividends when it comes to peace of mind.

“The fear factor is a real factor when it comes to the financial balancing act,” says patient advocate and author Ilana Jacqueline. “You’re getting collection letters and calls from billing departments and debt collectors constantly. Once you familiarize yourself with your insurance plan, your deductible and your co-pays, you’re going to feel less intimidated. You need to constantly be asking questions when you’re asked to pay a bill: When was the date of service? Who was the treating physician? How much of the bill did insurance cover? Why didn’t insurance cover all of it? If they can’t answer these questions, tell them you’ll pay when they have all the data. Errors in billing are made constantly; don’t be a financial victim of someone else’s incompetence!”

Managing Health: Becoming an Empowered Patient

No matter the diagnosis, ignorance is not bliss when it comes to health. Learning everything one can about symptoms and treatment options is always wise. Patients should ask their doctors specific questions about their condition, and they shouldn’t stop there. Online resources and patient associations for specific diagnoses are excellent places to start when it comes to increasing one’s knowledge base. But, patients should be careful to get their online facts from trusted sources. With the overwhelming amount of information just a click away, it can be hard to distinguish science-backed information from sales pitches and personal opinions. To ensure information is reliable, consider limiting online research to government and nonprofit websites such as these:

- U.S. Department of Health and Human Services’ Healthfinder: www.healthfinder.gov
- Centers for Disease Control and Prevention: www.cdc.gov
- American Academy of Family Physicians: familydoctor.org
- Medscape: www.medscape.com/today

When patients empower themselves as the manager of their own health, it can help them regain a sense of control at a time when things feel very chaotic. Some of that empowerment also comes from being a compliant patient. Following recommended treatment plans, taking prescribed medications as directed and attending scheduled healthcare appointments goes a long way when it comes to patients feeling their best. It may help for patients to set up a reminder system in their calendar or daily planner, or to consider any number of mobile apps that can help them juggle the tasks on their healthcare to-do lists. Here are a few apps worth checking out:

- Medisafe is an app that helps patients manage medications.
It helps with dosage and reminds them when they need to take their meds, increasing adherence rates. The information can also be shared with the healthcare team and pharmacy.

• Pain Diary works for anyone with a chronic illness by allowing patients to chart and score pain, as well as record and track other symptoms of the disease such as fatigue and mood swings. This app also has a feature that allows patients to connect with others living with the same chronic illness and swap best practices.

• ZocDoc is another popular app that allows patients to search for local specialists who are approved by their insurance company. The app will even tell them when the doctor is available.

• My Medical Info is a helpful app that stores all relevant health history and insurance details. This makes filling out those endless forms a little less challenging, since patients won’t have to rely on their memory for all the details.

• Fooducate helps patients keep track of their diet and allows them to program how many calories they want to consume a day and then add in the food choices they make. The app will work out the nutritional values of everything they eat and tell them how many calories they’ve consumed. It also works in conjunction with many fitness apps to add in details of any physical activities and calories burned.

• Sleep Cycle analyzes how much sleep and the quality of sleep patients get each night. Plus, they can also have the alarm set to wake them when they’re in their lightest sleep, leaving them feeling less groggy and more refreshed.

Managing Mood: Maintaining a Positive Outlook

When struggling with pain, fatigue and other chronic disease symptoms, maintaining a positive attitude is probably the last thing on patients’ minds. Still, it’s worth noting that mental health research indicates attitudes like optimism and hope help people recover faster from surgery and cope better with serious diseases — even diseases as serious as cancer, heart disease and AIDS. Increasingly, evidence suggests these effects may have something to do with the mind’s power over the immune system. One insightful study, for example, polled healthy first-year law students at the beginning of the school year to find out how optimistic they felt about the upcoming year. By the middle of the first semester, the students who had been confident they would do well had more and better functioning immune cells than the worried students.6

In her new book, _Surviving and Thriving with an Invisible Chronic Illness: How to Stay Sane and Live One Step Ahead of Your Symptoms_, Jacqueline offers a wealth of tips to help patients advocate for themselves at their most vulnerable moments. She is currently working on multiple projects to help connect chronically ill patients with remote employment opportunities, financial and emotional support and creating new programs for patient empowerment and awareness efforts. “Managing chronic illness means developing strategies to assist you in moving forward with your life’s greater focus with as minimal suffering as possible. Don’t head-but your disease, outsmart it,” she says. “Life with chronic illness is just like any other — a life full of obstacles. It’s easy to lie down and not get back up. But if you’re not moving, you’re not living. So, even when the obstacles become too great, the treatment stops working, the doctors stop telling you the good news, even when you lose support, you lose sight of what you’re moving toward, you keep moving.”

TRUDIE MITSCHANG is a contributing writer for _IG Living_ magazine.

References

THOUSANDS OF YEARS before the dawn of Western medicine, ancient Chinese cultures used practices like acupuncture, herbal remedies, massage and meditation to treat a variety of conditions — from pain to mental illness. During that period, these practices were the only form of medical care available, and they have continued to evolve over the centuries. Chinese medicine focuses on the importance of the mind-body connection in the healing process. Dating back 3,000 years, traditional Chinese medicine practitioners treated the root of the illness using a holistic approach to bring about a state of complete healing. Today, modern-day alternative medicine practitioners believe the body’s energy forces must be in balance to achieve wellness. The process of restoring balance is accomplished by focusing on the person as a whole, not as a disease state or a group of symptoms. Understanding how the systems of mind, body and spirit work together enables practitioners to develop a treatment plan that addresses the imbalances in these energy forces to bring the body into a state of harmony. Only then can healing begin.

What Are Alternative and Complementary Therapies?

What do the terms “complementary therapies,” “alternative medicine” and “integrative treatments” mean, and how can these ancient practices be used to treat patients with chronic pain and autoimmune disorders?

Alternative medicine is any of a range of medical therapies not regarded as orthodox by the medical profession such as herbalism and acupuncture. Complementary medicine is any of a range of medical therapies that fall beyond the scope of scientific medicine, but may be used alongside it in the treatment of disease. Examples include acupuncture and osteopathy (a therapy involving manipulation of the bones). Integrative medicine is a form of medical therapy that combines practices and procedures from alternative medicine with conventional medicine.

Complementary and alternative medicine (CAM) is a term used to describe a group of healthcare practices and/or products that are not considered a part of conventional Western medicine. While there is a lack of scientific evidence supporting the effectiveness of many of these treatments, more people than ever are integrating these practices into their treatment plan. Indeed, many patients may already be incorporating some form of CAM into their daily healthcare regimen.

Types of CAM

The National Institutes of Health (NIH) reports approximately 38 percent of adults and 12 percent of children are practicing some form of CAM. In 2012, a nationwide survey conducted by NIH found Americans spent more than $30 billion out of pocket for complementary and alternative therapies, representing more than nine percent of overall out-of-pocket expenses paid that year. The following are therapies for which Americans are spending their money (Figure).

Fish oil/omega 3. These are fatty acids that can be found in fish and plant oils, but may also be taken as a supplement. In clinical trials, omega 3 has been shown to lower both triglyceride levels and blood pressure.

Probiotics. Probiotics are bacteria similar to existing bacteria in a healthy gut. These bacteria, that number in the trillions, are the first line of defense against unwanted invaders to the gastrointestinal (GI) tract. Frequent or overuse of antibiotics can kill healthy bacteria, leaving the gut vulnerable to infections. Probiotics may be ingested as supplements, or they can be found in certain foods such as yogurt. Evidence suggests probiotics may slow the growth of certain tumors, particularly of the colon; however, more studies are needed to fully understand their role.

Echinacea. Echinacea is a flower found in regions of North America that is primarily used to treat common colds and to stimulate the immune system. It may be taken as a supple-
ment, or it can be ingested as tea or juice. There is conflicting data about the effectiveness of this supplement in treating or preventing the common cold.

Natural herbal remedies. Because of their anti-inflammatory effect, herbal and plant-based products have been used for thousands of years as an effective pain remedy. Commonly used herbal remedies include turmeric, willow bark, green tea, cat’s claw and ginger. The anti-inflammatory effect of these products has also been shown to help with GI issues. However, because the supplement industry is not regulated by the U.S. Food and Drug Administration, it is essential for patients to use quality products and to inform their physician and pharmacist of all herbal supplements taken to ensure there are no potential drug interactions.

Deep breathing techniques or meditation. Meditation is one of the oldest forms of alternative medicine in the world, thought to have started around 3500 B.C. on the continent of India. It is a mind-body practice that allows the body to calm, the breath to slow and the mind to still. Meditation comes in a variety of forms, but each has several commonalities: a quiet space, a comfortable position, a focus of attention and a willingness to be open to the practice. Meditation can be used as a relaxation technique; however, it has also been shown to assist with issues such as insomnia, high blood pressure, pain, anxiety and depression, to name a few. Meditation does not have to be a structured activity, and there is no right or wrong way to meditate. It involves merely breath and focus.

It is thought meditation actually changes the chemistry of the brain, which allows for the healing process to take place. Just a few minutes a day of meditation may start to relieve stress and help relieve symptoms of chronic illness. A beginner’s guide to meditation can be found at www.yogajournal.com/meditation/let-s-meditate.

Acupuncture. Acupuncture is an ancient practice that predates history. Evidence of the use of acupuncture dates back to the Stone Age, when sharp stone objects were used to puncture and drain wounds. The practice of acupuncture was first recorded in Chinese history around the 13th century and documented in European history around the 17th century.

Practitioners of Chinese medicine in ancient times understood that inside every human body is a series of channels or meridians. These meridians are like a superhighway through which the body’s energy flows. Unlike the circulatory system with its veins and arteries, meridians can’t be seen in the physical sense. Rather, meridians are invisible pathways within the body that connect, flow and transfer energy.

Figure. Out-of-Pocket Spending on Complementary Health Approaches in the U.S. (Total Health Care Spending, 2012: $2.82 Trillion)
Important Safety Information

**WARNING:** Thrombosis (blood clots) 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 blood clots, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor for signs of clotting events and hyperviscosity. Always drink sufficient fluids before infusing Hizentra.

See your doctor for a full explanation, and the full prescribing information for complete boxed warning.

Hizentra is a prescription medicine used to treat:

- Primary immune deficiency (PI) in patients 2 years and older
- Chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

Treatment with Hizentra might not be possible if your doctor determines you have hyperprolinemia (too much proline in the blood), or are IgA-deficient with antibodies to IgA and a history of hypersensitivity.

Tell your doctor if you have previously had a severe allergic reaction (including anaphylaxis) to the administration of human immune globulin. Tell your doctor right away or go to the emergency room if you have hives, trouble breathing, wheezing, dizziness, or fainting. These could be signs of a bad allergic reaction.

Inform your doctor of any medications you are taking, as well as any medical conditions you may have had, especially if you have a history of diseases related to the heart or blood vessels, or have been immobile for some time. Inform your physician if you are pregnant or nursing, or plan to become pregnant.

Infuse Hizentra under your skin only; do not inject into a blood vessel. Self-administer Hizentra only after having been taught to do so by your doctor or other healthcare professional, and having received dosing instructions for treating your condition.
Immediately report to your physician any of the following symptoms, which could be signs of serious adverse reactions to Hizentra:

- Reduced urination, sudden weight gain, or swelling in your legs (possible signs of a kidney problem).
- Pain and/or swelling or discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, or numbness/weakness on one side of the body (possible signs of a blood clot).
- Bad headache with nausea; vomiting; stiff neck; fever; and sensitivity to light (possible signs of meningitis).
- Brown or red urine; rapid heart rate; yellowing of the skin or eyes; chest pains or breathing trouble; fever over 100°F (possible symptoms of other conditions that require prompt treatment).

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

The most common side effects in the clinical trials for Hizentra include redness, swelling, itching, and/or bruising at the infusion site; headache; chest; joint or back pain; diarrhea; tiredness; cough; rash; itching; fever, nausea, and vomiting. These are not the only side effects possible.

Before receiving any vaccine, tell immunizing physician if you have had recent therapy with Hizentra, as effectiveness of the vaccine could be compromised.

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.

Biotherapies for Life®  CSL Behring
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. Risks factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, 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 indicated for:

- Treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years and older.
- Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to prevent relapse of neuromuscular disability and impairment.

Limitation of Use: Maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Continued maintenance beyond these periods should be individualized based on patient response and need for continued therapy.

For subcutaneous infusion only.

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, including HIZENTRA 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 infusion site reactions, headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, upper respiratory tract infection, rash, pruritus, vomiting, abdominal pain (upper), migraine, arthralgia, pain, fall and nasopharyngitis.

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.

Based on March 2018 revision
The process of acupuncture involves inserting very tiny needles at specific points along the lines of the body’s multiple meridians. There are more than 300 acupuncture points that access this energy highway. Placing needles in these points are thought to rebalance the body’s energy flow that has been disrupted by disease or illness. Western medicine scientists believe the benefits of acupuncture come more from the release of neurotransmitters and the anti-inflammatory effect than from rebalancing the body’s energy. Regardless of which school of thought is believed, acupuncture is one of the few alternative medicine practices that is widely accepted in Western medicine. In fact, many commercial insurance plans cover acupuncture therapy.

Due to the increased popularity of acupuncture, the practice has become state-regulated. Each state has its individual requirements for the practice’s training and administration. The World Health Organization has established guidance for practitioners regarding the amount and kind of training providers should receive to practice safely. It is vital for patients to find a qualified practitioner. The National Certification Commission for Acupuncture and Oriental Medicine has both a practitioner registry and directory that may assist in locating qualified acupuncturists.

### CAM for Autoimmune Disorders and Pain

There are thousands of published clinical trials and ongoing studies touting the benefits of acupuncture for a variety of conditions, including autoimmune disorders. Following is how acupuncture and other forms of CAM work for treating chronic pain and autoimmune disorders.

Autoimmune disorders occur when the immune system attacks, instead of protects, the body. Autoimmune disorders can impact any area of the body from the joints to the blood vessels. NIH estimates up to 23 million Americans suffer from some form of autoimmune disorder, which is close to three times more people than those affected by cancer. There is no cure for many autoimmune disorders, which are characterized by cycles of worsening symptoms, called flare-ups, followed by periods of calm or remission. Much of the treatment plan involves symptom management with conventional medicine like steroids and immunosuppressant therapy. While these medications can help to alleviate symptoms associated with autoimmune disorders, long-term use of these medications is associated with diminished function of the immune system and potential effects to the muscular and skeletal systems and GI system.

Each autoimmune disorder is unique in its clinical presentation; however, many have similar symptoms such as joint pain and swelling, fatigue, skin rashes, abdominal pain or digestive issues, fever and swollen glands. When flare-ups occur, conventional medicine may not provide adequate relief. This is when alternative medicine practices can be effectively used to complement medication.

Both acupuncture and massage therapy have been shown to decrease pain and inflammation for patients with autoimmune disorders. Research has shown acupuncture causes a physical effect on the nerves and parts of the brain. These responses cause the body to release hormones, proteins and chemicals that control body functions such as temperature and blood pressure. Additionally, acupuncture is thought to block the body’s pain receptors by releasing neurotransmitters. Massage therapy has been proven to reduce joint and muscle stiffness and fatigue, as well as promote sleep and reduce stress. Another benefit of massage therapy is a decrease in cortisol, the stress hormone, and an increase in serotonin, which may help with depression. Herbal supplements such as turmeric and willow bark may also help with joint pain and inflammation. And, ginger and probiotics may help to relieve GI distress from the disease or the medications used to treat the illness.

### Still Relevant Today

Because chronic pain and autoimmune disorders can be devastating to both patients and families, anything that can be done to relieve symptoms and improve quality of life is an important step to take. Many CAM therapies have been in use for hundreds and even thousands of years, and they are still relevant in the practice of medicine today. Patients should take the time to have a discussion with their physician about how these practices may help. And, patients should only begin CAM therapy after discussing it with their physician. Importantly, these therapies are not meant to replace an existing treatment plan; they are intended to complement that plan.

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**Resources**

While proper nutrition differs from person to person, a solid foundation can be established by eating a balanced diet as outlined in the Dietary Guidelines for Americans.

By Mindy Hermann, MBA, RDN

**IN THIS ERA** of personalized nutrition, we’re learning more and more about how each of us may have different nutrition needs. For example, one person might thrive on a diet high in carbohydrates, while another might fare better with more protein. One person might absorb certain vitamins and minerals easily while another does not. However, despite our individual differences, all of us fall within a general range of nutrition needs that can be met by eating a balanced diet with a variety of foods.

The U.S. government has been issuing Dietary Guidelines for Americans every five years since the 1970s to educate the population and policymakers about food and nutrition. The guidelines also address the health of American adults, since about half of them have one or more diet-related diseases such as cardiovascular disease, high blood pressure, type 2 diabetes, overweight and obesity, some cancers and poor bone health, many of which (obesity in particular) can trigger or worsen symptoms of an autoimmune disease.

While these guidelines provide a broad framework and are not specifically tailored to individuals, they create a solid foundation for a basic diet that can be adapted to individual needs and intolerances. A revision of the current guidelines will be released sometime in 2020.

**Key Recommendations**

Following are the key recommendations from the 2015-2020 Dietary Guidelines for Americans:

*Follow a healthy eating pattern throughout life.* Good nutrition matters at all ages. This means making smart food and beverage choices in childhood, the teen years and throughout adulthood. It’s easy to make less healthy food choices as a teen or young adult or when life gets busy, but months and years of a poor diet can impact health down the road. Eating a balanced diet at the right calorie level for a person’s metabolism and activity level, along with getting regular physical activity, can maintain a healthy body.
weight, provide good nutrition and lessen the chances of chronic diseases such as heart disease and diabetes.

Choose a variety of foods with a lot of nutrition per serving. The body needs a certain number of calories to maintain weight; eating too many calories over a prolonged period of time causes weight gain and can eventually lead to obesity. The goal is to choose foods with plenty of vitamins, minerals and key nutrients but without too many calories, and to have indulgent foods with a lot of calories and not much nutrition occasionally and only in small portions. Here is an example: A small baked potato has fewer than 100 calories, is satiating and supplies fiber and several key vitamins and minerals. A one-ounce bag of potato chips has less potato and more oil, supplying about 160 calories, a lot of which comes from fat, and lower amounts of important nutrients. Potato chips are also not as filling as a baked potato.

Limit calories from foods with ingredients detrimental to health. In addition to recommending high nutrition foods, the guidelines caution against ingredients and nutrients that can be detrimental to health. These include sugars people add to foods and beverages such as breakfast cereal and coffee, as well as sugars added to processed foods and beverages. Some processed foods and beverages are surprisingly high in added sugar. A single serving bottle of a sugar-sweetened soft drink may have 12 or so teaspoons of sugar, much more than a person would add to a drink at home. Foods high in saturated fats include well-marbled beef, sausage, high-fat cuts of pork, whole milk and whole milk dairy products, coconut and many fast food entrées. Restaurant foods and fast food tend to be higher in sodium (the main mineral in salt) than foods prepared at home. Fresh foods generally have less sodium than packaged canned or frozen foods and take-out foods from the deli counter or buffet.

Switch to healthier food and beverage choices. Many foods and beverages can be swapped for healthier options without making major changes in eating habits. Some swaps cut calories. For example, choosing skim milk instead of whole milk saves about 80 calories, choosing oat ring cereal instead of granola saves at least 100 calories, and choosing seltzer over sugar-sweetened soft drinks can save up to 200 calories. Other swaps can reduce saturated fat such as using a lean cut of beef instead of a fatty one.

Fundamentals of Good Nutrition

A healthy and balanced diet includes selections from six different food groups: vegetables, fruits, grains, dairy, protein and oils. Body size, desired weight status (gaining, maintaining, losing) and age affect the body’s metabolism and the number of calories and amount of food a person should eat.

The vegetable family includes dark green leafy vegetables such as kale, spinach and Romaine lettuce; red and orange vegetables such as red peppers, beets, carrots and sweet potatoes; white vegetables like cauliflower, onions and turnips; kidney beans, chickpeas, split peas and other legumes; and starchy vegetables such as potatoes and yams. Different colors mean different beneficial nutrients and plant compounds, which is why the guidelines call for eating a variety of vegetables every day.

As with vegetables, different colors of fruit provide different beneficial plant compounds. Enjoy red-skinned and green-skinned apples; red, green and black grapes; white and yellow peaches and nectarines; berries of all types and colors; and the various citrus fruits available in the winter months. Unsweetened frozen fruits are picked and frozen on the farm, so they have just as much nutrition as fresh fruit and are a great option when fresh fruit is not in season.

A healthy and balanced diet includes selections from six different food groups: vegetables, fruits, grains, dairy, protein and oils.

The grains family includes both whole grains and refined grains, and a balanced diet includes both. Whole wheat is a well-known whole grain used in bread, cereal and pasta. Whole grains such as brown rice and quinoa are popular in side dishes. Refined white flour is a common ingredient in bread, cereal, pasta and pizza. In the U.S., refined white flour is fortified with several important vitamins and minerals. However, many people eat too many refined grains in large portions of indulgence foods such as cake, cookies, crackers, pizza and pasta.
People who cannot tolerate gluten, the main protein in wheat, can choose from a wide variety of gluten-free alternatives, including brown or white rice, quinoa and “ancient grains.” Gluten-free pasta, desserts and bread incorporate flours made from rice, beans, peas and other gluten-free ingredients. Portion control is extremely important since gluten-free options often provide as many or more calories and less nutrition than their conventional counterparts.

In dairy products, fat-free or lower-fat dairy products are preferred over full-fat products to manage calories and saturated fat. Dairy products provide protein, calcium and other extremely important nutrients. The guidelines recommend three daily servings.

People who cannot tolerate either the carbohydrate (lactose) or protein (casein) in traditional dairy products have multiple options, including lactose-free dairy products treated to break down lactose or A2 milk obtained from cows that produce only a better-tolerated form of casein. The dairy aisle also offers a broad range of plant-based milks, beverages, yogurts and cheeses. Plant-based products generally are not nutritionally equal to or better than products made from cow or goat milk. They tend to have less protein, along with a form of calcium that is harder for the body to absorb. Still, many people prefer to switch to plant-based products.

Protein foods are derived from animals (lean meats and poultry, fish and seafood, eggs) and from plants such as beans and peas, nuts, seeds, soy products and plant-based meat alternatives. Although protein is widely called out on food and beverage packages, most people in the U.S. and Canada get enough protein in their diet without having to eat overly large portions. The guidelines recommend about half a pound (before cooking) daily of animal-based protein or the equivalent in plant-based protein.

Healthy oils and fats include olive oil, canola oil, nut oils, nuts, olives and avocados. These are considered healthier than butter, other forms of dairy fat and fats from meat because they are lower in saturated fat. Still, all pure fats have the same number of calories so they should be consumed in moderation.

The benefits and drawbacks of alcohol continue to be debated. The guidelines state that if alcohol is consumed, it should be consumed only in moderation, defined as up to one drink per day for women and two for men. One drink equals a 12-ounce beer, 5-ounce glass of wine or 1.5-ounce shot of 80 proof distilled spirits.

Putting Guidelines Into Action

The U.S. Department of Agriculture created a website, ChooseMyPlate.gov, to help people plan healthy, balanced meals that coincide with their food likes and dislikes, as well as their lifestyle, culture and traditions. The site depicts a plate divided into sections for each major type of food with vegetables and fruits filling half the plate and grains and protein each filling a quarter of the plate. A nutritious meal also includes a serving of dairy along with healthy fats. The day’s meals should provide the right amount of calories based on age, sex, height, weight and physical activity level. The site also offers instructions for managing sugar and saturated fat by using Nutrition Facts labels and ingredient lists to find amounts of saturated fat, sodium and added sugars and then look for foods and beverages lower in those items.

Good nutrition may seem overwhelming, which is why small changes are so important. ChooseMyPlate.gov encourages small changes such as making over one meal at a time, learning how to make healthful choices at a buffet, ordering healthier takeout foods and beverages, planning meals when going to a potluck or party, and choosing wisely when eating restaurant foods.

Because individuals with autoimmune diseases have multiple symptoms and are on various medications and treatment protocols, food tolerance may be a very real challenge. It is important to track reactions to meals and snacks by keeping a diary of foods and beverages consumed and any discomfort after eating or drinking. Make diet changes slowly and one by one to identify which specific food or drink might be causing problems, and increase healthful foods such as vegetables, legumes and whole grains gradually to allow the digestive system to adapt.

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Resources

- Choose My Plate: www.choosemyplate.gov
In 1970, shortly after my arrival at the University of California, Los Angeles (UCLA), 5-month-old Maurice Elias was referred to me with pneumonia and a mouthful of oral thrush. Little did I know this was the start of a 48-year odyssey.

By E. Richard Stiehm, MD

IN 1970, Maurice Elias was the fifth child born to a healthy mother and father; however, two maternal uncles had died in infancy. Maurice was normal at birth, and he had received his 2-month-old vaccinations without a problem. But, at 3 months old, he developed a respiratory infection and oral thrush. He was admitted to a local hospital and given ampicillin for pneumonia and nystatin for the thrush. He remained unwell with respiratory symptoms, he was referred to UCLA at 5 months old at which time he had gained no weight and the thrush had returned.

A chest X-ray disclosed bilateral pneumonia and no thymic shadow. His blood count was normal, but he had very low levels of all three immunoglobulins. His lymphocytes, although normal in number, did not proliferate when stimulated with the potent mitogen phytohemagglutinin (PHA). A needle biopsy of his lungs disclosed Pneumocystis jiroveci, formerly Pneumocystis carinii or PCP, a rare fungal infection that only affects patients with poor immunity. He was started on Pentamidine for the pneumonia and Amphotericin for the oral thrush.

Maurice was diagnosed with SCID, also known as the bubble boy syndrome. Infants with SCID have no cellular or antibody immunity and, if unrecognized or untreated, they generally succumb from infection in the first year of life. The only cure for SCID is a bone marrow (stem cell) transplant, which at that time had been performed successfully only once in a SCID infant.¹

For the bone marrow transplant to be successful, Maurice would need a donor with lymphocytes that exactly matched his cells. Unlike red blood cells for which there are only four types, lymphocytes have thousands of types known as human leukocyte antigen (HLA) types. Therefore, the best chance of finding a perfect match is from a sibling with common parents.
The Need for a Bone Marrow Donor

By good fortune, UCLA had the premier tissue typing laboratory in the world, led by Paul Terasaki, MD. I spoke with Dr. Terasaki about Maurice, and he was optimistic about finding a perfect match among Maurice’s four siblings. Unfortunately, repeated typing resulted in three different results, none of which matched his parents or siblings. “It’s never happened before,” said Dr. Terasaki. “Don’t do a transplant.”

Performing a mismatched transplant can cause graft-versus-host disease, which occurs when the new cells reject the patient, often resulting in death. Therefore, I delivered the sad news to Maurice’s parents and sent the child home on antibiotics, antifungals and weekly immune globulin (IG) injections. Maurice remained sick, and he returned to the hospital at 9 months old with persistent vomiting. The fungal infection had extended into his esophagus, preventing him from swallowing and necessitating tube feedings.

I called Dr. Terasaki again about finding a donor, and he requested more blood. After receiving three more samples, Dr. Terasaki typed Maurice repeatedly and up to 16 different types showed up (a normal result has no more than four types, two from each parent). After comparing the typing results, he noted three types showed up repeatedly, and these were identical to his 13-year-old sister Tami. “I think Tami might be a match,” Dr. Terasaki told me. We can test that by mixing their blood together to see if Tami’s cells recognize Maurice’s cells as foreign (a procedure known as a mixed leukocyte test). One week later, Dr. Terasaki said: “I think Tami is a perfect match. But, I can’t be 100 percent sure.”

Maurice’s parents agreed to go forward with the bone-marrow transplant. The child’s father, who was a Hollywood actor and stuntman, had kept his coworkers informed about his child’s illness and proposed transplant. One coworker told a Life magazine reporter of the proposed transplant, who contacted the parents to see if they would agree to a story about Maurice before, during and after the procedure.

The Bone Marrow Transplant

With a Life photographer present, Tami was admitted to the hospital, where under general anesthesia, a hematologist used a large-bore needle at multiple sites to extract four ounces of marrow from her hip and breast bones. The cells were taken to Maurice’s crib and injected into his abdominal cavity from where they would migrate to the bone marrow liver and spleen.

Two weeks passed, and overnight, the oral thrush disappeared. It was determined the new cells were working! But, then, there was a crash. Maurice’s face and abdomen swelled, a generalized rash appeared, his breathing became labored and his liver and spleen enlarged. He was undergoing a graft-versus-host reaction.

Maurice was admitted to the intensive care unit for oxygen, antibiotics and corticosteroids. Two weeks later, he gradually improved and his body was producing immunoglobulins. A test of his lymphocytes showed them to be XX, identical to those of his donor sister. The rash and swelling disappeared, and his chest X-ray normalized.

Three months later, Maurice was discharged apparently cured. Life magazine photographed every step of the transplant from admission to discharge, which appeared in the May 28, 1971, issue titled “Gift of Life From a Big Sister.”

Reappearance After Three Decades

I followed Maurice through high school, and he did well, even joining the school’s wrestling team. Thereafter, I lost track of him, even after hiring a student to search for him.

Last summer, at age 48, Maurice reappeared in the office of Manish Butte, MD, an immunologist and colleague of mine, to investigate why he had rejected two corneal transplants. After his hospital discharge in 1971, Maurice had been living a normal life and working as a plumber. He didn’t require IG treatment or continuous antibiotics. But, he had persistent eye problems, one pneumonia, several sinus infections, poor dentition and recurrent warts. An examination showed he was normal except for the warts on his hands and toes.

Advanced immunologic studies not available in the 1970s were
performed. A TREC (T cell receptor excision circles) test was negative, indicating his thymus was not producing T cells. Genetic analysis showed he had a mutation of the interleukin-2 receptor gamma chain on his X chromosome, indicating he had X-linked SCID. This is the most common form of SCID that occurs only in boys of an unaffected carrier mother. This explained the early deaths of his two maternal uncles.

The test also showed he had normal immunoglobulins and near normal T and B cells, but his natural killer cells (CD16/56) were very low. His T cells (CD3) were all from the donor, and these were functioning well, responding to PHA (a potent stimulus) and some vaccine antigens. His B cells (CD19) were those of the patient, but they were now making immunoglobulins and antibodies with the help of the donor T cells. His natural killer cells (CD16/56) were those of the patient, and they had very poor activity, probably explaining his predisposition to warts.

One interesting aspect was why his own abnormal B cells could make some antibodies. This is not uncommon when the transplant includes unfractionated marrow without pretransplant conditioning. We showed his B cells could respond normally to cytokines produced by normal T cells.

When Maurice returned for his next visit, he was accompanied by his mother and sister Tami, the donor for his transplant 47 years ago. Since Maurice still has some immune problems, one consideration was to give him a booster transplant from his sister using a new monoclonal antibody against stem cells that will make room for the sister’s cells, which may augment his less-than-perfect immune system.

**Evolution of Immunodeficiency Transplants**

If Maurice were born today, a SCID diagnosis would be made at birth from a heel-stick blood test, which is performed on every U.S. newborn. The TREC test would indicate he was not making T cells, and he would be referred to a center for confirmation of the SCID diagnosis and treatment by bone marrow or other stem cell source. But, in 1970, unlike today, we could not identify the genetic defect, delineate the various types of lymphocytes, assess natural killer cell function or filter the bone marrow cells for intravenous infusion.

With today’s technology, if Maurice did not have a matched sibling, other donors could be used, including those from an unrelated HLA-identical adult from an international registry or from a cord blood bank of typed and stored umbilical cord blood cells. Another option would be gene therapy for this form of SCID and a few other immunodeficiencies.

Worldwide today, there have been more than 2,000 stem cell transplants and more than 200 gene therapies for patients with primary immunodeficiency.

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**References**

Understanding Hyper IgE Syndrome

While HIES, which appears in infancy, often results in death at an early age, more has been discovered about it over the years, and experimental treatments for this disease show promise.

By Ronale Tucker Rhodes, MS

HYPER IGE SYNDROME (HIES) was first called Job’s syndrome in 1966, named after the biblical character Job whose entire body was covered in boils and sores. Later in 1972, when it was recognized those with the disease had extremely high serum IgE levels, it was renamed HIES. Until 2007, the syndrome remained the last of the major immune deficiencies without a known genetic etiology or a comprehensive understanding of the associated immune dysfunction.¹

HIES is listed as a rare disease by the National Institutes of Health, meaning it affects fewer than 200,000 people in the U.S.² More than 200 cases of HIES have been described in the medical literature, affecting males and females in equal numbers and all ethnic groups. However, it often goes unrecognized or misdiagnosed, making its true frequency in the general population difficult to determine. Although HIES is present during infancy, diagnosis may not be made until adolescence and, in some cases, adulthood.³

What Is HIES?

HIES is a very rare primary immunodeficiency disorder characterized by the triad of highly elevated serum IgE, dermatitis and recurrent skin and lung infections. There are two forms of HIES: autosomal dominant (AD) (the more common form), some of which are caused by mutations in the STAT3 gene, and autosomal recessive (AR), with the majority of cases caused by mutations and deletions of the DOCK8 gene and the remaining for which a genetic cause is unclear.¹

For years, researchers considered AD-HIES and AR-HIES different expressions of the same disorder; however, it is now known they are similar, yet distinct disorders.⁴ In fact, each presents differently in courses and outcomes, and they share little in terms of pathogenesis other than elevated IgE serum. AD-HIES is characterized by nonimmunologic features, including skeletal, connective tissue and pulmonary abnormalities, as well as recurrent infections and eczema. Whereas, AR-HIES lacks the somatic features and has marked viral infections and neurologic complications.¹

Causes of HIES?

Most cases of AD-HIES and AR-HIES are sporadic, but some genetic cases of HIES have been reported.⁵

As mentioned, some AD-HIES are caused by mutations in the STAT3 gene responsible for producing one of the signal transducer and activator of transcription (STAT) proteins involved in alerting the immune system to respond to
pathogens. While the mutations result in a normal amount of STAT3 protein, the function of the protein is affected making it unable to properly defend against pathogens. Only 60 percent of AD-HIES patients have mutations of the STAT3 protein, so it is believed other gene mutations may be associated with the disease. In dominant genetic disorders, only a single copy of an abnormal gene is necessary to cause the disease, and the gene can be inherited from either parent or it can mutate in the affected individual. The risk of passing the abnormal gene from an affected parent to an offspring is 50 percent for each pregnancy in both males and females.

The majority of cases of AR-HIES are caused by mutations and deletions of the DOCK8 gene, which helps maintain the structure and integrity of T cells and NK cells that recognize and attack pathogens. However, recessive genetic disorders occur when an individual inherits the same abnormal gene for the same trait from each parent. If the individual receives one normal gene and one abnormal gene, the person will be a carrier for the disease but will not usually exhibit symptoms. The risk for two carrier parents to both pass the defective gene onto the child is 25 percent with each pregnancy. The risk for the child to become a carrier like the parents is 50 percent with each pregnancy. And, the chance a child will receive two normal genes from both carrier parents is 25 percent. These percentages are true for both males and females.

Symptoms of HIES

Symptoms for both types of HIES usually begin during infancy.

Common symptoms of AD-HIES include respiratory infections, newborn rash, eczema, recurrent skin abscesses, and ear, sinus and lung infections. A newborn rash is typically the first manifestation, with pustular and eczema-like rashes on the face and scalp beginning within the first month of life. Skin abscesses are typically caused by a susceptibility to infections with Staphylococcus aureus. Recurrent bacterial pneumonias usually start in childhood caused by Staphylococcus aureus, Streptococcus pneumoniae and Haemophilus influenzae. Fungal lung infections, especially with Aspergillus fumigatus, are common. Because the pneumonias often present with fewer symptoms than occur in persons with intact immunity, they often advance and cause significant tissue damage before treatment is begun. And, the severity of lung tissue damage and the subsequent emergency of chronic lung disease are higher in patients with AD-HIES, which may lead to large cavities in the lung (pneumatocele formation), a distinguishing feature of AD-HIES.

Other important features of AD-HIES patients include involvement of both skeletal and connective tissues, as well as abnormalities with teeth. Patients have an asymmetrical facial appearance with prominent forehead and chin, deep-set eyes, broad nose, thickened facial skin and a high arched palate, all of which evolve during childhood and become more established by adolescence. They also have hyperextensibility of the joints causing bone fractures from insignificant trauma, and bone density may be reduced. Scoliosis is also common, typically emerging during adolescence or later in life. And, fused skull bones and extra or abnormally formed ribs or vertebrae occur more often in AD-HIES patients than in the general population. Teeth abnormalities caused by reduced resorption of primary tooth roots include retention of primary (baby) teeth even after the permanent teeth have erupted.

AR-HIES symptoms are similar to AD-HIES with eczema, skin abscesses, recurrent respiratory infections, candidiasis and other fungal infections. Skin infections, however, usually start early in life but not during the newborn period. Unlike AD-HIES, AR-HIES exhibits severe recurrent or persistent skin viral infections and recurrent respiratory infections are usually caused by pathogens such as herpes simplex, herpes zoster and Molluscum contagiosum, possibly leading to chronic lung disease with damage to the airways and lung tissues. AR-HIES patients are also susceptible to allergic and autoimmune manifestations, including food allergy, hemolytic anemia (due to red blood cell destruction by antibodies) and vasculitis (inflammation within blood vessels). A high frequency of neurologic complications, including encephalitis and vascular brain lesions, is also common in AR-HIES patients, which may be caused by viral infections of the
central nervous system and autoimmunity. In addition, they may experience neurologic manifestations such as facial paralysis and hemiplegia (one side of the body paralyzed). And, unlike AD-HIES patients, AR-HIES patients do not experience connective tissue or skeletal abnormalities.

Both AD-HIES and AR-HIES patients are at increased risk for malignancies, especially lymphomas. They are also more prone to other cancers such as leukemia, cancers of the vulva, liver and lung, and papilloma virus-induced squamous cell carcinoma. Autoimmune diseases are also associated with both types of HIES but most often in AR-HIES.5

**Diagnosing HIES**

Diagnosing HIES is made via a combination of clinical and laboratory findings, as well as a detailed patient history. For both types, blood tests will show elevated levels of IgE in the blood and elevated levels of blood cells known as eosinophils. Importantly, diagnosis of HIES cannot be made solely on elevated IgE since patients with other conditions such as severe eczema also present with elevated IgE levels. Also for both, X-ray studies such as computed tomography can detect lung infections, and in AD-HIES, the development of pneumatoceles (thin-walled, air-filled cysts) within the lungs. Serum IgG, IgA and IgM are typically normal; however, some individuals will have deficiencies in one or more of these.4,5,6

There are some important differences between AD-HIES and AR-HIES. In AD-HIES, IgE levels may drop to normal or near normal in adulthood, so that does not rule out an HIES diagnosis. In AR-HIES patients, IgM concentrations and peripheral blood T-cell counts are decreased. And, the DOCK8 protein is absent in more than 95 percent of AR-HIES patients, which can be useful in diagnosing the disease in suspected patients, but it also can’t rule out a diagnosis if the protein expression is normal.5,6

After HIES was determined to be a multisystem disorder, the National Institutes of Health devised a clinical scoring system mainly useful for diagnosing AD-HIES that combines immunologic/infectious manifestations and skeletal/connective tissue abnormalities. Immunologic/infectious features include elevation of serum concentration of IgE, eosinophilia, recurrent skin abscesses, pneumonias, destructive parenchymal lung lesions following infection, other serious or fatal infections, newborn rash, eczema, sinusitis or otitis, and mucocutaneous candidiasis. Nonimmune features include three or more retained primary teeth, scoliosis, bone fractures following minimal trauma, hyperextensibility of joints, characteristic facial appearance, increased nasal width, high palate, congenital skeletal anomalies and lymphoma. Scores are weighted to reflect the severity of a finding and to emphasize findings specific for AD-HIES. Individuals with a high likelihood of AD-HIES have a combination of both types of features. A score of greater than 40 is suggestive of AD-HIES, a score of 20 to 40 is considered indeterminate, and a score of less than 20 is considered unlikely.7 It should be noted that this scoring system can be used for diagnosing AR-HIES. However, a definitive diagnosis for either needs to be made with genetic analysis of the STAT3 and/or DOCK8 genes.5

**Treating and Managing HIES**

Treatment of HIES is directed at specific symptoms and is mostly supportive, and patients often require the coordinated efforts of a team of specialists, including pediatricians, dermatologists, pneumologists, immunologists and other healthcare specialists.
Most important for HIES is preventing bacterial infections with prophylactic antibiotic therapies. For AD-HIES, common antibiotics include dicloxacillin or cotrimoxazole. For severe infections, recombinant interferon-gamma may be given subcutaneously as adjuvant therapy. Common antibiotics to treat AR-HIES include dicloxacillin, trimethoprim-sulfamethoxazole, cephalosporin, cotrimoxazole and penicillin.

AD-HIES patients may require antifungal drugs such as fluconazole or itraconazole to treat mucocutaneous candidiasis. For both types of HIES, skin lesions may require surgical drainage followed by antibiotics. And, in some cases, topical steroids and moisturizing creams can be used.

Drug treatment for chronic lung infections that may lead to the formation of air cavities in AD-HIES patients is difficult, so management often requires surgically opening the chest to remove or drain infected pneumatoceles. AD-HIES patients may also need to have primary teeth removed, be regularly monitored for scoliosis and be evaluated for fractures following minor trauma.4,6

Most experimental therapies for HIES are for individuals who are unresponsive to other forms of treatment. These include cyclosporin-A (CSA), immune globulin (IG) supplementation and interferons for AD-HIES and AR-HIES, as well as antibodies directed against IgE for AD-HIES and bone marrow transplant for AR-HIES.

A recent study examined the effect of a small dose of CSA on the clinical course, and the excessive production of IgE and other immunologic parameters and infection in patients with HIES. Three patients, two females and one male (two were brother and sister) between 10 months and 3 years, were suffering from severe eczema, recurrent sinopulmonary infection, lung and skin abscesses, chronically draining ear and failure to thrive since the first few weeks of their lives. Their serum IgE was more than 10 times upper normal for age. Serum IgE, cytokine IL-4, and IFN-γ and serum immunoglobulins were measured before and after treatment, and skin score of dermatitis and the number of infections were evaluated before and after treatment with CSA. Following treatment with 2 mg/kg to 4 mg/kg per day of...
CSA in two divided doses, after standard treatment failed, there was a dramatic and sustained clinical improvement, especially dermatitis associated with marked drop in serum IgE, IL-4 and IFN-γ. And, there was no significant change in serum levels of IgG, IgA and IgM, indicating immune imbalance in HIES can be modulated by CSA that leads to a marked drop on IgE and IL-4 synthesis and clinical remission. However, the researchers did recommend the treatment be repeated in a larger number of patients.8

While there is limited data suggesting improvement in some patients with high-dose IG therapy, researchers do suggest some form of controlled trial is probably warranted.

Bone marrow transplantation is curative for AR-HIES patients with DOCK8 deficiency, and it is recommended due to the severity of the disease and the lifelong risk of developing fatal complications, including infections, autoimmunity and malignancies.5

To date, bone marrow transplantation has also been tried in four patients with AD-HIES. The first patient was a 46-year-old man with recurrent pneumonias who received a peripheral stem cell transplant for B cell lymphoma. However, he died six months following transplant with interstitial pneumonitis. Subsequently, a 7-year-old girl was transplanted to treat her severe HIES, and her skin lesions improved. However, she developed recurrence of symptoms after four years. Her serum IgE also returned to pretransplant levels. Interestingly, this occurred despite full donor engraftment in all lineages, suggesting the reasons for recurrence may have been somatic or not just confined to the haematopoietic system.

More recently, two unrelated male children with sporadic STAT3 mutations were transplanted for high-grade non-Hodgkin’s lymphoma. At 10 years and 14 years following transplantation, both patients were reported to be well with continued resolution of both immunological and nonimmunological features. Of particular note, both osteoporosis and the characteristic facies improved following transplant. According to the researchers, “the successful transplant in these two individuals is significant because this potentially represents a means of preventing the long-term complications of chronic lung disease, vascular aneurysms and brain lesions.”9

It is recommended AD-HIES and AR-HIES patients and their families receive genetic counseling.4,6

HIES Prognosis

The long-term outlook for HIES patients depends on whether it is the AD or AR form and its severity. Most individuals with AD-HIES survive into mid-adulthood, but a shortened life span is common. The oldest reported affected individual was approximately 60 years of age. Deaths in the second and third decades of life are mostly due to severe pulmonary disease and infection of pneumatoceles. Other reported complications include myocardial infarction (heart attack) related to coronary artery aneurysm and subarachnoid hemorrhage related to intracranial (brain) aneurysm. Lymphomas also occur more commonly, and other cancers have been reported.

Most individuals with AR-HIES do not reach adulthood if untreated. It has high mortality due to sepsis, central nervous system infections and early onset of malignancies. Those with mutations in the DOCK8 gene have frequent complications with cutaneous viral infections caused by varicella-zoster, herpes simplex viruses, HPV and molluscum contagiosum virus at a younger age. Individuals with AR-HIES are also known to develop severe chronic refractory molluscum contagiosum infections resistant to treatment.10

The Future of HIES?

While HIES was first described more than half a decade ago, it is now known the disease has two genetic defects

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**Diseases/Conditions Sharing Some Symptoms of HIES**

- Atopic dermatitis
- IPEX syndrome
- Wiskott-Aldrich syndrome
- Cornelia-Netherton syndrome
- DiGeorge syndrome
- Chronic granulomatous disease
- Common variable immunodeficiency
- Chronic mucocutaneous candidiasis
- Parasitic disease
- HIV-AIDS
- Hematological malignancies – Sézary’s syndrome
- Aspergillosis
- ABPA
- Churg-Stauss syndrome
- Omenn syndrome

resulting in two separate syndromes: STAT3 mutations that cause AD-HIES and DOCK8 mutations and deletions that result in AR-HIES. While symptoms of both types of HIES are similar, there are some distinguishing features in each. And, although the disease is present in infants, it sometimes goes undiagnosed until adolescence and even adulthood. Treatment is mostly supportive, although a number of investigative therapies are being studied. Unfortunately, prognosis is often a shortened lifespan.

Currently, there are only five ongoing studies on ClinicalTrials.gov evaluating the genetics, symptoms and treatments for HIES. It’s clear much more needs to be understood about the disease to enable researchers to create better therapies and prevent its morbidity and mortality. Perhaps the greatest help to researchers is for patients and their families to become involved in registries to examine the causes and characteristics of HIES. For more information about becoming involved, contact the United States Immunodeficiency Network, a research consortium established to advance scientific research in the field of primary immunodeficiency diseases, at usidnet.org.

RONALE TUCKER RHODES is the editor of IG Living magazine.

References
Profile: Heidi Plavecsky

By Trudie Mitschang

AS A PATIENT advocate for the Immune Deficiency Foundation (IDF) and a primary immunodeficiency disease (PI) patient, Heidi has been privileged to serve alongside her mother and son who is also a PI patient. Noting that career options for patients with PI have expanded significantly since she was a young adult, Heidi is currently pursuing her nursing degree.

Trudie: Tell us your diagnosis story.
Heidi: I was sick pretty much from the day I was born. Pneumonia, bronchitis, ear infections, every virus that came through the house. I was born in 1977, and I was known as the sick kid. At the time, PIs weren’t on anyone’s radar. Before I went to kindergarten, though, a man named Marty who lived about two miles from my family went to the National Institutes of Health because he kept getting sick. He was part of a study that ultimately ended up diagnosing him with a PI. When he returned and educated his family doctor about his condition and how to test for it, the doctor thought of me. Thank God we had the same family doctor, and he was thinking outside the box. I was born in 1977, and I was known as the sick kid. At the time, PIs weren’t on anyone’s radar. Before I went to kindergarten, though, a man named Marty who lived about two miles from my family went to the National Institutes of Health because he kept getting sick. He was part of a study that ultimately ended up diagnosing him with a PI. When he returned and educated his family doctor about his condition and how to test for it, the doctor thought of me. Thank God we had the same family doctor, and he was thinking outside the box. In a time when only the very sickest were being diagnosed, I was able to get diagnosed at a relatively young age. Unfortunately, only very painful intramuscular immune globulin (IG) injections were available then, so I was instead treated with prophylactic antibiotics and other aggressive treatment regimens. I didn’t start IG therapy until many years later.

Trudie: How did your family get involved with IDF?
Heidi: My mother first joined an IDF family support group when I was in elementary school. Marty, the man I attribute with educating my doctors and leading them to my early diagnosis, was one of the primary organizers. In a world where so few patients are diagnosed, we were able to find solace in the friendships and understanding that was available through our newfound relationships. The support group met for many years, but because only the sickest were diagnosed at that point, many of the patients in the group eventually grew too ill to attend meetings and/or plan the functions. I developed a very grim outlook on what my future might look like based on that experience, yet I learned so much from the patients there. Marty would constantly tell my Mom, “Elaine, you’ve got to let her live. When we have a chronic illness, we never know just how long we have. Let her know the consequences, but then let her make her decisions.” As a result, if I wanted to be in Girl Scouts or spend the night with friends, my mom allowed it. I learned it came with a cost. Becoming overly tired, being out of my routine or being in environments where not everyone thought to warn me they had a cold often meant I would get sick and be down for a few days. But, I had a childhood with many memories, and I will always cherish that advice.

Trudie: Did having a PI concern you when you started planning your family?
Heidi: Fast forward 20 years later to 1999: I was told since my brothers didn’t have a PI neither would my children because at the time it was thought only X-linked PIs were passed on to future generations. Despite that advice, we knew almost immediately my son Alex had inherited my PI. It took almost two months for him to return to his birth weight, he had his first ear infection at 2 weeks old, and he never went more than 14 days between sick visits at the doctor’s office in his first 18 months of life. We were hoping it was just lack of maternal immunity, but he never outgrew it.
**Trudie:** How did your childhood experience with PI impact Alex?

**Heidi:** I tried to use the same advice Marty gave my mom: to let him live life without limitations. Fortunately, he was started on subcutaneous IG (SCIG) therapy when he was only 6 years old, so he didn’t have quite so many sick days as I did.

**Trudie:** What is your treatment plan today?

**Heidi:** Alex and I are both treated with SCIG. Alex is treated with Cuvitru, and I am treated with Hizentra.

**Trudie:** What was it like attending the 2018 IDF Advocacy Day as three generations?

**Heidi:** Alex and I attended Advocacy Day in 2009, and my mom and I attended it in 2018. This year, with the three of us attending together, it felt like our team was complete. For years, we have performed advocacy work together by going to plasma centers to encourage redonation. The insurance landscape is changing so fast, and I can bring my 21 years of insurance industry experience to the table, but I can’t really make the legislators feel the impact on those around us. With all of us at the table together, I felt the legislative aides were really able to see exactly how chronic illness affects a family such as how much extra support it requires and how expensive it is when multiple people in one household have chronic illness and less-than-ideal insurance. Every time we can get in front of policymakers by phone, in person or by mail to remind them that chronic illness affects real people, real families and real voters, we are one step closer to finding a health insurance solution that can work for everyone. I highly encourage others to bring more of their tribe into their inner circle to let them be a part of fighting along with them. We are stronger when we combine our voices; everyone benefits from the wider insight we offer together.

**Trudie:** What do you find most rewarding about advocacy work?

**Heidi:** My mom fell asleep every night reading all the medical journals she could get her hands on. She always taught me to seek out your own answers if the doctors aren’t finding them for you fast enough. By performing advocacy work, I like to think I am helping to educate lawmakers, get funding for research and ensure future generations will have doctors with answers. I’m hoping children will be diagnosed quicker, and once diagnosed, they will have viable and affordable treatments.

**Trudie:** What are your goals for the future?

**Heidi:** Because treatments have come so far, I now have career options that are opened up to me that, when I was a teen deciding what to do with my life, weren’t available. For example, I was told I could never go into the medical field. I have been an insurance agent for the past 21 years because I was drawn to a career path where I could help people, and it was the closest my medical team would allow me to healthcare. I am now back in school to become a nurse! My hope is to guide others the way empathetic and creative medical staff have helped me over the years.

**Trudie:** What’s next for Alex?

**Heidi:** Alex is a commercial carpenter in a time when the sky is the limit for young contractors. He travels extensively for work and because he can take his infusions on the road with him, his PI doesn’t slow him down.

**Trudie:** How do you maintain a positive outlook?

**Heidi:** I remind myself and others how far medical science has come in the 37 years since my diagnosis. I remind myself and my son that although the treatment is expensive, and sometimes inconvenient, we have full and satisfying lives and are relatively healthy. We have the energy to get out and experience life and can travel the world. With dreams and aspirations within reach because of the amazing medical science available, I can’t help but look forward to where treatments will be in the future! This keeps me advocating to legislators and teaching every doctor, medical student or nurse I encounter everything I know (or at least what they’ve got the patience to listen to). In fact, I’ve perfected the three-minute elevator speech of the most important points needed to encourage medical professionals to seek more information on their own.

**TRUDIE MITSCHANG** is a contributing writer for *IG Living* magazine.
I RUSH TO my gate where I proceed to wait among the throngs of tired travelers fighting for a seat closest to the charger. Expending no small amount of effort, I go to the restroom one last time before we all will be herded onto the plane like less-than-compliant cattle. I hope for ideal seatmates, the kind who do not repeatedly release offensive odors, listen to music without headphones or sneeze on my snacks mid-flight. Once onboard, and I’ve sanitized everything in sight, I settle in and listen to the flight attendant’s safety message. Before long, the plane is pushing into the air, its wings fighting to steady themselves against the wind, the resistance and shear force pressing against them. I exhale a long sigh of relief when the captain’s voice booms overhead to announce the plane has reached its cruising altitude, and he has now turned off the fasten seatbelt sign. I am holding steady, high above the earth.

I can’t help but compare this liftoff with the journey the chronically ill take each time they encounter challenges. I visualize the shear force pushing against our community, and the overwhelming beauty of our community’s ability to steady itself despite all that may oppose it. I feel the turbulence of those unexpected words spoken in an office or on a phone that may alter our lives forever. I picture the flare, the infection, the worsening of symptoms, the new diagnosis we never saw coming. But then, I see us regaining balance, normalizing and holding steady. We are a resilient people.

A popular definition of resilience is “the process of, capacity for or outcome of successful adaptation despite challenging or threatening circumstances.” To me, this means things may not be OK, but I can still be OK. There have been moments when symptoms came from seemingly nowhere or illness stole a particularly special moment from me, and I did not feel OK, but knew I would get there in time.

But, what about those days, months or seasons when I’m not feeling particularly resilient? According to life counselors, “Protective factors, such as having a positive level of self-efficacy and self-esteem, positive future expectations, good coping skills, personal control, problem-solving abilities, initiative, optimistic thinking, and internal motivation can increase the ability to be resilient.” In other words, resiliency can be cultivated. When I’m not feeling convinced I’ll be OK in spite of all that’s far from OK around me, I usually ask myself two questions:

1) How have I coped with and overcome these adverse situations in the past? When the call came, and the answer was precisely what I was hoping it wouldn’t be, how did I navigate the emotions, financial hurdles and logistical issues this new diagnosis, flare or infection brought? What previous experience can I apply to my current situation? What coping skills did I learn that I might want to apply now? What did I do then that I don’t want to repeat now? Did I wallow in self-pity or push others away? How will I improve my responses in my current situation?

2) What support networks or protective factors have I relied on in the past? Do I have a particularly supportive friend I could talk with about my situation? Am I connected with a religious or community organization that provides comfort, peace or assistance at this time? Do I have pasttimes, hobbies or interests that could provide stress relief during this time? Do I have friends or family who will help me think and talk through my options without pressure? Do I need to set some time aside to think or process before making any decisions?

When I draw on my experience of holding steady in the past, it enables me to hold steady in the face of new less-than-ideal circumstances. In short, I can be OK, even when things aren’t OK. And, when I’m not OK, I know that in time, I will get there. All of us in this chronically ill community can foster resilience within ourselves, and marvel at our own ability to take flight, pushing back against all that stands in our way.

Reference

Everyday Anxieties with Chronic Illness

By Ilana Jacqueline

OUR 20S ARE a time to live, learn and get over our fears. After all, we are now the captains of our perpetually sinking ships of poor health! It can be intimidating to be the one in charge of our disease, to be the decision-maker, the demander of change and the only one left to blame if things fall through the cracks. We need to practice constant self-forgiveness and patience as we learn to develop skills that help make us more confident when managing our disease.

Let’s break down some common anxieties in our everyday living with a complex chronic illness:

Calling doctors to ask questions. Many patients experience phone anxiety. Anytime we have to call our doctor to ask a question, refill a medication or schedule an appointment, we feel inexplicable fear waiting for the person on the other end of the line to pick up. We can’t remember what we were going to ask, we feel pressured the person answering the phone won’t fully understand our message, or we worry we’ll forget an important detail or face some kind of backlash for calling. The best way to fight this fear is simply with practice and preparation. If you’re the kind of patient who experiences phone anxiety (and you’re not alone!), write down the bullet points of what you’re going to ask before picking up the phone. Decide whether you need to speak with the receptionist, the medical assistant or the billing department. It’s possible you still may forget something in your message and need to call back, and that’s OK! No one is going to yell at you for calling in two or even three times. It’s their job to help you with tasks outside the exam room. Your care comes before their inconvenience.

Speaking up in the exam room. We’ve covered this topic before, but it’s important to reiterate that respectfully asserting yourself in the exam room is a necessity. With doctor appointments getting shorter and shorter, we must come prepared and refuse to leave without having all of our questions answered. It’s not uncommon to have fears about overstepping or asking too many questions when it comes to managing our health. If a doctor refuses to answer any of your questions or outright states he has other patients to see and doesn’t have time for you, then you are seeing the wrong doctor. Politely inform the doctor that if your questions can’t be answered during your appointment, you’d be happy to email them to him or call him after-hours when he has more time.

Facing medical debt collectors. Dealing with medical debt collectors can be exhausting, infuriating and anxiety-producing. The best way to deal with debt collectors is with all the facts in hand. When patients have complex illnesses that require them to see multiple specialists, frequent emergency rooms and require multiple hospital admissions, it can be very hard to keep track of what is owed. It doesn’t help that debt collectors constantly buy and sell debt, and you may receive calls from both billing departments, hospitals and debt collection agencies. But, before you whip out your credit card, make sure to get all the facts straight and ask the following questions: When was the date of service for this bill? Who was the treating physician? Was my insurance billed? If the callers are unable to give you any of this information, tell them to call back when they can. If they are able to give you this information and you’re unsure why you’re being charged that amount, tell them you will give them a call back after you’ve spoken with your insurance company to verify the claim went through. You are not obligated to pay a debt over the phone if you haven’t received a bill in the mail. If all seems legitimate and your anxiety stems from not having the funds to pay the bill, you still have options. Ask to begin a payment plan, and tell them how much you’re able to put toward this debt each month.

We all deal with anxiety around the big and little interactions in our everyday lives as patients, but the more we face our fears head-on, the less scary they become.

ILANA JACQUELINE is a dysautonomia and primary immune deficiency disease patient from South Florida. She’s been writing professionally since 2004 on everything from health and wellness to celebrities and beauty. Her blog www.letsfeelbetter.com is both a personal collection of anecdotes about life with chronic illness, as well as a resource for patients of all ages.
WHEN CHILDREN are diagnosed with a chronic disorder, a lot of information is provided about the condition to parents and families. Sometimes, the diagnosis comes after a time of crisis such as a major infection or a lengthy hospital stay, and it comes as quite a shock to the family. Other times, the diagnosis isn’t so unexpected since there may be a family history of the disease, and it is diagnosed shortly after birth with the help of genetic testing. Either way, parents can spend many hours in doctors’ or genetic counselors’ offices discussing the condition and what its impact may be on the child’s life, health and future.

While the diagnosis may be overwhelming for parents and families, it can be especially confusing for children. This is because doctors tend to speak in a language that’s not so easy for kids to understand. When parents bring their children home from appointments, they may find themselves faced with questions they have to answer on a more age-appropriate level. So, how can parents take the information they’ve learned and pass it on to their children in a way young minds can understand?

Thanks to two organizations that have done the hard work of compiling an abundance of medical information and converting it into child-friendly material, parents of primary immunodeficiency disease (PI) children don’t have to look very far for help.

Immune Deficiency Foundation (IDF)

When dealing with a PI, the first place parents should look for information is IDF. Founded in 1980, IDF is “the national nonprofit patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with PI through advocacy, education and research.” Its website offers many helpful resources for educating parents and patients about PI.

On the IDF’s website, parents can check out the “Kids Connection,” which provides links to all of the resources, books and games designed for children with PI and their families. From this central hub, parents and kids can make their way to the “Zebra Zone,” where they will find coloring pages and an explanation of why the zebra is the mascot of PI and other rare diseases. Also in the “Kids Connection” is a link to the informative publication *Our Immune System*, written by Sara LeBien, which helps PI kids better understand how the immune system works, what happens when part of that system is missing, and what some of the more common terms such as B cell, T cell, immunoglobulin and IgG mean. Using fun, child-friendly illustrations,
Our Immune System explains what the treatment for PI is and how it works. This book helps children and their families to get a grasp of the immune system and PI, and it can be downloaded for free directly from the IDF website.

After kids and their parents have read the book, there is a link on the IDF website to an app called “Whack-a-Germ” that features the characters from the story in a game for use on tablets and smart phones available on Google Play and iTunes.

Another children’s book produced by IDF available free for download is A Zebra Tale by Katherine Antilla. In this story, Flash, the zebra who discovers he has a PI, explains why he has stripes while the rest of his family are just regular horses. This book would be a helpful tool for parents of young children who enjoy bedtime stories or looking at picture books. It does an excellent job of generally explaining disorders of the immune system in kid-friendly terms while providing colorful illustrations to grab children’s attention.

At the IDF National Conference, held every two years, there are sessions for adults, as well as special programs designed just for kids ages 6 months to 18 years. These programs include hands-on activities designed to help children understand their condition and connect them with other children who have the same or a similar condition.

Occasionally, local IDF Education Meetings include youth events geared toward kids ages 5 years through 18 years in venues throughout the U.S. To view a calendar of events listing the next IDF Education Meetings including an event for children, access the IDF’s website at www.primaryimmune.org/events and click on the Education Meeting nearest you.

Jeffrey Modell Foundation (JMF)

Another outstanding resource for educating children about everything related to PI is JMF’s website at info4pi.org. Established in 1987 by Fred and Vicki Modell in honor of their son, Jeffrey, who died at age 15 from complications of hypogammaglobulinemia, JMF is “a public charity devoted to early and precise diagnosis, meaningful treatments and, ultimately, cures through clinical and basic research, physician education, patient support, advocacy, public awareness and newborn screening.”

The foundation’s website provides an abundance of information regarding PI. Created with kids in mind, this website offers such things as answers to common questions about PI; a descriptive online encyclopedia explaining how the immune system works and the parts of the body involved; and a glossary of commonly used medical terms defined in a way that helps children understand the medical terminology used to describe their condition.

In the website’s “Kids Zone,” parents can find downloadable coloring pages, printable word searches using PI terms, and trivia games that test kids’ knowledge of the immune system. This website is one of the best resources available for teaching kids about the immune system and its diseases in a way that keeps things light and fun without overwhelming them with hard-to-understand terminology.

Teens

For teens, IDF’s website offers links to media channels on YouTube that include videos such as “In Tune with Your Immune System,” which is geared toward older children. This particular cartoon-style video compares the human immune system to a rock band with every instrument playing a different part. In addition, IDF offers an informative four-part podcast for older teens and young adults that is available on the iTunes store. This podcast deals with issues specific to older teens and young adults with PI who are learning to navigate the world on their own while facing issues such as college concerns, employment and healthcare management.

Valuable Resources Are Now Available

When the Modell’s son Jeffrey first began to suffer from frequent infections, they struggled to find ways to explain to him what was happening. At that time, they had very little information available to them, virtually no support network and knew of no one else with the same disease. But because of the efforts of their foundation, along with those of IDF, parents today have access to valuable resources to help educate their children about disorders of the immune system.

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.
Managing IVIG Adverse Effects

By Michelle Greer, RN, and Leslie J. Vaughan, RPh

**INTRAVENTOUS IMMUNE globulin (IVIG)** is a very effective treatment that frequently provides disease improvement for people who have suffered years of misdiagnosis and medications that did not help. For some people such as those with primary immunodeficiency, IG therapy is the only treatment for their condition. But, because IVIG evokes an immune response, side effects can be expected. Fortunately, there are ways to mitigate and even eliminate them. Additionally, there are more serious reactions that are rare, so it’s imperative to understand what these are and how to take steps to decrease their occurrence. It’s also important to ensure nurses who administer IVIG have received education and training on how to safely and effectively infuse IVIG.

**Side Effects of IVIG**

The most common reactions to IVIG are flu-like symptoms, including headache, fatigue, body aches and fever. Headache is the most commonly reported side effect, with pain ranging from mild to severe. For most people, premedication with acetaminophen is routine, and if headache occurs, the dose may be repeated. People who experience frequent headaches or even migraines prior to starting IVIG may be at a higher risk for a more severe headache. In this case, steroids or the person’s current prescribed migraine treatment may also be given as premedication. A severe headache along with other symptoms such as nausea, vomiting and neck pain or stiffness can signal a more serious adverse reaction known as aseptic meningitis. If these symptoms are reported, the physician should be notified, and the person may need to seek emergency medical attention.

Blood pressure fluctuation is another potential side effect. If the person is known to have hypertension, it is especially important to take blood pressure medications exactly as prescribed. And, the nurse administering the IVIG should take a baseline blood pressure prior to starting the infusion. IVIG infusions are started slowly and ramped up at predetermined intervals to a maximum rate. Blood pressure should be monitored throughout the infusion, and is typically taken right before an increase in the rate of infusion. If at any point in the infusion the person does not feel well, blood pressure and other vital signs such as pulse, breathing rate and temperature should be reassessed. If blood pressure is high, the infusion should be paused and restarted when symptoms or blood pressure normalize. Many reactions can be resolved simply by slowing the rate or pausing the infusion and resuming when symptoms subside.

A rash or other dermatological reaction occurs in about 6 percent of persons treated with IVIG. The rash may present as redness, papules (small red bumps) and itching. This reaction does not necessarily indicate an allergic reaction, nor does it mean IVIG should be discontinued. Typically, a premedication of steroids is added.

More severe reactions are rare, but a physician and/or pharmacist or nurse should perform a risk assessment prior to initiating treatment to formulate the best plan to prevent the reactions. Additionally, people receiving IVIG should be educated about the potential for developing side effects so they will be aware of which signs and symptoms they should promptly report to the physician or pharmacist. These reactions can include aseptic meningitis, as mentioned earlier, as well as impaired renal function, thrombotic event and hemolytic anemia. Preventive measures can be instituted for these severe reactions; however, if these side effects occur, consideration may be given to changing the brand of IVIG.

One of the most important ways to reduce side effects is to hydrate. Drinking an adequate amount of water several days prior to the infusion, on the infusion day and a few days after the infusion is key. Unless there is a clinical reason someone should not have increased fluids, the person should drink 64 ounces (8 cups) of water each day. Some physicians may prescribe intravenous fluids to be infused just prior to the IVIG infusion. Prehydration with normal saline is also used to prevent IG-induced adverse effects. Many studies have proposed prehydration can be helpful to reduce the risk of headache, thrombolyis (blood clots), renal impairment (decreased kidney function) and hemolysis (destruction of red blood cells).

If the potential for side effects is great, or if they have already occurred, the subcutaneous (SC) route of administration can be considered. With the exception of injection site reactions, side effects are generally much less frequent with SCIG.

**A Safe Therapy**

All in all, IVIG is very safe, and many people tolerate this treatment with minimal or no side effects.

**MICHELLE GREER**, RN, is senior vice president of sales for Nufactor, a Specialty Infusion Company.

**LESLIE J. VAUGHAN**, RPh, is senior vice president of clinical programs at Nufactor, a Specialty Infusion Company.

**Reference**

**Snuggle Up**

The Lavender Spa Blanket helps soothe everything from aches to anxiety. Add in some lavender and a dash of the calming shade of violet, and it’s the perfect side-effect-combatting comfort. Pop it in the microwave or freezer for hot or cold therapy. The removable insert is filled with flax seed and lavender blossoms, and the cover is washable. $68; [www.uncommongoods.com/product/lavender-spa-blankie](http://www.uncommongoods.com/product/lavender-spa-blankie)

**Drink Up**

The best way to stay hydrated: Drink a lot of water. Need help? Get a cute and functional water bottle. The HydroFlask bottle, emblazoned with that cute little spikey-haired guy, will keep water cold (or hot) for hours. It’s equipped with a strong seal that won’t leak and is available in a rainbow of bright colors. $79.99-$89.98; [amazon.com](http://amazon.com)

**Rash Relief**

Applying a topical steroid cream to the skin after IVIG treatment can help patients deal with rashes by relieving redness, itching and swelling. Topical hydrocortisone valerate cream targets the inflammation of the skin caused by allergic reactions, eczema or other issues. Available by prescription only

**Headache Remedy**

Tylenol, the brand name for the drug acetaminophen, can help alleviate headaches that often accompany IVIG treatments. Although Tylenol isn’t an anti-inflammatory like ibuprofen, it’s an effective option to lessen headaches for patients who may have issues with aspirin due to acid reflux, ulcers, etc. Available at drug stores and supermarkets

**OTC Pain Relief**

Pain can be kept at bay with a nonsteroidal anti-inflammatory drug, and that old standby ibuprofen is a great option. This over-the-counter medication will help ease infusion issues by reducing pain and inflammation. Available at drug stores and supermarkets

**Gentle Reminder**

Ramping up the fluids in the days leading up to an infusion is crucial. Something as simple as the Ultra Smart Hydration Reminder can serve as that necessary reminder. The smart tracker, which straps onto water bottles of all shapes and sizes, reminds the user to take a sip at least once per hour with a gentle blink. $25; [amazon.com](http://amazon.com)
**NEW AND USEFUL READING**

**Plot Your Health: A Journey to Wellness Planner**
Author: C.J. Ellison
Publisher: Red Hot Publishing

This wellness planner is developed for people who are struggling to stay on top of multiple medications, symptoms and self-care requirements throughout each day; manage mood and energy levels; manage day-to-day appointments; and juggle treatment details. Each planner contains an owner’s information page with room for doctor information, personal data, emergency contacts, allergies and more; condition detail pages; medicine and supplement records pages; tests/scans/bloodwork results pages; undated monthly calendar pages for jotting down medical appointments, wellness visits, physical therapy, IV infusions, etc.; doctor/wellness visit pages for questions to ask at each appointment; room for notes and an area to jot down tests needed; treatment record pages; two-page symptom trackers; three-page medicine and supplement tracking grids; mood-tracking coloring images; blank two-page grids for tracking sleep, food, blood pressure, habits, blood sugar, oxygen levels and more; lined pages per month for additional needs; and a future planning area on the last page for appointments and scheduling for the months to come.

**End Chronic Disease: The Healing Power of Beliefs, Behaviors and Bacteria**
Author: Kathleen DiChiara
Publisher: Hay House Inc.

Millions of people are struggling through the vicious cycle of chronic symptoms associated with internal inflammation and immune dysregulation. And yet, determining the root cause of inflammation can be challenging. Nutrition educator, researcher and health advocate Kathleen DiChiara aims to answer the question of what truly conditions the body to overcome illness. She shares her passion for functional medicine, microbiology and growth mindset, and helps readers discover the key strategies that impact the three driving forces for optimal health: beliefs, behavior and bacteria. In this book, readers will find a health-conscious and practical guide to build physical health and immunity.

**Caregiving: Hope and Health for Caregiving Families**
Authors: Sharon Wegscheider-Cruse and Pat Egan
Publisher: Health Communications Inc.

While some people choose to take care of loved ones after they can no longer take care of themselves, many others must do so for a myriad of other reasons, often financial. It can be a crisis situation, such as an accident, or the long-term effects of aging. In this book filled with practical, easily implementable advice, the authors help readers sort through the puzzle that forms the caregiving world. Chapter topics include identifying the roles of caregivers; how to deal with burnout; finding ways to compartmentalize and separate without guilt; using technology to make life easier; building bridges through teamwork; downsizing; and navigating end-of-life issues. Most importantly, the book offers readers invaluable suggestions for navigating tough issues with positivity and optimism. It is also the first book to provide stories from the perspective of not just the caregiver, but the patient, enabling caregivers to better understand their fears and feelings.

**The Autoimmune Brain: A Five-Step Plan for Treating Chronic Pain, Depression, Anxiety, Fatigue and Attention Disorders**
Author: David S. Younger, MD
Publisher: Rowman and Littlefield Publishers

*The Autoimmune Brain* connects common brain health symptoms to changes in the immune system, and particularly bacterial, viral and parasitic infections. In this book, Dr. Younger explains his groundbreaking research and adds a new component: how traumatic stress (whether physical or emotional) and genetics affect this same triad as inextricable factors in initiating disease and brain health symptoms. In fact, a change in personality, behavior, coping style and one’s emotional state may be the first clue there is a health problem brewing somewhere else in the body. Readers will find new answers to dozens of troubling conditions.
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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
Ataxia Telangiectasia (A-T)

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

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

WEBSITES
- GBS/CIDP Foundation International: www.gbs-cidp.org

Evans Syndrome

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

Guillain-Barré Syndrome (GBS)

WEBSITES
- GBS/CIDP Foundation International: www.gbs-cidp.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

Idiopathic Thrombocytopenic Purpura (ITP)

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

Kawasaki Disease

WEBSITES
- American Heart Association: www.heart.org/HEARTORG/Conditions/More/ CardiovascularConditionsOfChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#T1T2boePWE0
- Kawasaki Disease Foundation: www.kdfoundation.org
- KidsHealth: kidshealth.org/parent/medical/heart/kawasaki.html

Mitochondrial Disease

WEBSITES
- United Mitochondrial Disease Foundation: www.umdf.org
- Mitochondrial Action: www.mitoaction.org

Multifocal Motor Neuropathy (MMN)

WEBSITES
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

Multiple Sclerosis (MS)

WEBSITES
- All About Multiple Sclerosis: www.mult sclerosis.org/index.html
- Multiple Sclerosis Association of America: mymsaa.org
- Multiple Sclerosis Foundation: www.msfocus.org
- National Multiple Sclerosis Society: www.nationalmsociety.org

Myasthenia Gravis (MG)

WEBSITES AND CHAT ROOMS
- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org
- Genetic Alliance: www.geneticalliance.org

Myositis

WEBSITES
- The Myositis Association: www.myositis.org
- International Myositis Assessment and Clinical Studies Group: www.niehs.nih.gov/research/resources/imacs

ONLINE PEER SUPPORT
- The Cure JM Foundation: www.curejm.org
- Myositis Association Community Forum: tmacommunityforum.ning.com
- Myositis Support Group – UK: www.myositis.org.uk

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

WEBSITES
- PANDAS/PANS Advocacy and Support: www.pas.care
- PANDAS Network: www.pandasnetwork.org
- Midwest PANS/PANDAS Support Group: www.midwestpandas.com

Peripheral Neuropathy (PN)

WEBSITES
- Neuropathy Action Foundation: www.neuropathyaction.org
- Western Neuropathy Association: www.pnhelp.org
- Neuropathy Alliance of Texas: neuropathyalienecb.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

Primary Immune Deficiency Disease (PI)

WEBSITES
- Immune Deficiency Foundation: www.primaryimmune.org
- Jeffrey Modell Foundation: www.info4pi.org
- The National Institute of Child Health and Human Development (NICHD): www.nichd.nih.gov/Pages/index.aspx
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organisation for Primary Immunodeficiencies (IPOD) — UK: www.ipod.org
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.uhospitals.org/rainbow/services/allergy-immunology

ONLINE PEER SUPPORT
- IDF Friends: www.idffriends.com
- Jeffrey Modell Foundation Facebook Page: www.facebook.com/JMFworld
- IDF Peer Support Program: www.primaryimmune.org/idf-peer-support-program
- Michigan Immunodeficiency Foundation: www.primaryimmune.org/idf-peer-support-program
- Michigan Immunodeficiency Foundation: www.idffriends.com
- National Institute of Child Health and Human Development (NICHD): www.nichd.nih.gov/Pages/index.aspx
- Primary Immune Deficiency Disease Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- Living with Stiff Person Syndrome (personal account): www.livingwithspss.com
- Stiff Person Syndrome: www.stiffpersons.net

Scleroderma

WEBSITES
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Johns Hopkins Scleroderma Center: www.hopkinsscleroderma.org

ONLINE PEER SUPPORT
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Stiff Person Syndrome (SPS)

WEBSITES
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Johns Hopkins Scleroderma Center: www.hopkinsscleroderma.org

ONLINE PEER SUPPORT
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Stiff Person Syndrome (personal account): www.livingwithspss.com
- Stiff Person Syndrome: www.stiffpersons.net

Pemphigus and Pemphigoid

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

Peripheral Neuropathy (PN)

WEBSITES
- Neuropathy Action Foundation: www.neuropathyaction.org
- Western Neuropathy Association: www.pnhelp.org
- Neuropathy Alliance of Texas: neuropathyalienecb.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

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- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organisation for Primary Immunodeficiencies (IPOD) — UK: www.ipod.org
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.uhospitals.org/rainbow/services/allergy-immunology

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- Jeffrey Modell Foundation Facebook Page: www.facebook.com/JMFworld
- IDF Peer Support Program: www.primaryimmune.org/idf-peer-support-program
- Michigan Immunodeficiency Foundation: www.primaryimmune.org/idf-peer-support-program
- Michigan Immunodeficiency Foundation: www.idffriends.com
- National Institute of Child Health and Human Development (NICHD): www.nichd.nih.gov/Pages/index.aspx
- Primary Immune Deficiency Disease Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
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- Scleroderma Research Foundation: www.srfcure.org
- Johns Hopkins Scleroderma Center: www.hopkinsscleroderma.org

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- Stiff Person Syndrome: www.stiffpersons.net

Pemphigus and Pemphigoid

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

Peripheral Neuropathy (PN)

WEBSITES
- Neuropathy Action Foundation: www.neuropathyaction.org
- Western Neuropathy Association: www.pnhelp.org
- Neuropathy Alliance of Texas: neuropathyalienecb.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com
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