Gene Therapy
The Promise of a Cure?

Improving Patient-Doctor Communication

Understanding and Treating ITP

CVID Questions and Answers

Traveling with PI Kids
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Influenza vaccine

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ACIP recommended for those with egg allergies
Approval in 50+ expected this Fall

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No antibiotics

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Triple strength

To order Flublok, contact
FFF Enterprises: www.MyFluVaccine.com or
(800) 843-7477

CPT Code
90673
Flublok (Influenza Vaccine)
Sterile Solution for Intramuscular Injection
Initial U.S. Approval: 2013

BRIEF SUMMARY OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Flublok safely and effectively. See full prescribing information for Flublok available at www.Flublok.com.

INDICATIONS AND USAGE
Flublok is a vaccine indicated for active immunization against disease caused by influenza virus subtypes A and type B contained in the vaccine. Flublok is approved for use in persons 18 through 49 years of age.

DOSAGE AND ADMINISTRATION
A single 0.5 mL dose for intramuscular injection.

DOSAGE FORMS AND STRENGTHS
A sterile solution for injection supplied in 0.5mL single dose vials.

CONTRAINDICATIONS
Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine.

WARNINGS AND PRECAUTIONS
If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of potential benefits and risks.

ADVERSE REACTIONS
In adults 18 through 49 years of age, the most common (≥10%) injection-site reaction was pain (>37%); the most common (≥10%) solicited systemic adverse reactions were headache (>15%), fatigue (>15%) and myalgia (>11%).

To report SUSPECTED ADVERSE REACTIONS, contact Protein Sciences Corporation at 1-888-855-7871 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

USE IN SPECIFIC POPULATIONS
• Safety and effectiveness of Flublok have not been established in pregnant women, nursing mothers, children, or adults 50 years of age and older.
• A pregnancy registry is available for Flublok. Contact: Protein Sciences Corporation by calling 1-888-855-7871.

Revised: October 2013
PAULINA BROOKS
Blogger, Writer and Founder of A Journey Home

**IG Chronicles — Firing Your Doctor: Is it as Simple or Easy as It Sounds?**

“As much as we want to foster a relationship with those who care for us, in the end, they provide a service for a fee, and, as such, we have the power to make hiring and firing decisions as we see fit.”

CAROLINE Y. KUO, MD
Clinical Instructor of Allergy and Immunology, UCLA School of Medicine

TORI M. MOSES
Medical Director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences

**Gene Therapy for Primary Immunodeficiency**

“Mere fanciful imagination a few decades ago, the idea of manipulating or repairing genes has evolved from science fiction to a real hope for those with serious incurable diseases, including primary immunodeficiencies.”

ROGER H. KOBAYASHI, MD
Clinical Professor, UCLA School of Medicine

**Diagnosing an Antibody Deficiency: Case 6, Part 4**

“Functional deficiencies in antibody production have been more difficult for physicians, patients and third-party payers/insurance providers to reconcile, especially when the quantitative values appear to be otherwise normal.”

MARC RIEDL, MD, MS
Associate Professor of Medicine, Division of Rheumatology, Allergy and Immunology, University of California, San Diego

**Commonly Asked Questions About Common Variable Immunodeficiency**

“Historically, it has been a challenge to get the proper testing for diagnosing CVID because it is a rare condition.”

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

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

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

In addition to connecting with others, IG Living’s patient advocate can help you determine if there’s a patient organization support group in your area.

Sign up for the Teleconferences now by emailing patientadvocate@IGLiving.com or calling (800) 843-7477, ext. 1366.
Searching for a Cure

Using biomedical therapeutics to cure inherited or acquired diseases dates back to the 1940s. Today, cell and gene therapy are overlapping fields of biomedical research, with cell therapy the older discipline and gene therapy showing great promise. Bone marrow transplantation (also known as stem cell transplantation) is the most common treatment of choice for severe combined immune deficiency (SCID). And, during the past 17 years, it has also been used more frequently as a potential cure for patients with severe autoimmune diseases who have an expected poor prognosis and lack of alternative treatment options.

This is the case for Jamie Stewart who was diagnosed in 2010 with an atypical presentation of chronic inflammatory demyelinating polyneuropathy that caused him ongoing nerve pain. After being told by his doctors that there were no other treatment options and that stem cell transplantation for his disease was “voodoo medicine,” Jamie was unsuccessful in his attempt to obtain a hematopoietic stem cell transplantation (HSCT) in the U.S. Eventually, he opted to undergo HSCT in Moscow in April. Now, six months later, Jamie describes in our Let’s Talk column his journey to undergo HSCT and his “roller-coaster” ride as he waits to find out if he is cured. His doctors give him an 80 percent to 90 percent chance of remission.

While still considered experimental, gene therapy has made important medical advances in the last two decades, and it is now being successfully used in clinical trials to treat a number of genetic disorders, including ADA-SCID, X-linked SCID, chronic granulomatous disorder, Wiskott-Aldrich syndrome and hemophilia, as well as acquired diseases such as cancer. Gene therapy has also been demonstrated in animal models to cure neurodegenerative diseases, viral infections, heart disease and diabetes, for which clinical trials in humans are being started. In our article “Gene Therapy: The Cutting Edge of PI Treatment,” two physicians who specialize in gene therapy for primary immunodeficiencies explain how this promising new therapeutic cure works, the challenges that remain and its realistic potential for curing serious, life-threatening diseases.

Of course, gene and cell therapy carry many different risks. So, it’s not surprising that Jamie was discouraged from pursuing HSCT. Jamie’s numerous attempts to establish a dialogue with his doctors about undergoing HSCT illustrates just how difficult communication can often be between patients and their doctors. So, in our article “Improving Patient-Doctor Communication,” we delve into how interaction between patients and doctors has evolved and provide strategies for breaking down the barriers of information exchange that should result in shared decision-making and patient-centered care.

I hope you gain insight from the information presented and enjoy the many other articles in this edition of IG Living.

Ronale Tucker Rhodes, MS

Sources


Reader: I have multifocal motor neuropathy and have been receiving intravenous immune globulin (IVIG) treatments for three years, which seems to be effective at slowing the progression of my disease. However, the dose I am receiving has had to be adjusted upward several times to maintain efficacy. Currently, I receive IVIG in a single session every three weeks. To attempt to decrease the number of hospital visits, my neurologist suggested two consecutive days of treatment. However, this was not successful, and my strength did not improve as much as it did with the more concentrated dose. By the end of four weeks, I was very weak in my affected limbs. Returning to a three-week regimen reverted me back to the previously seen gains. On that basis, I would like to experiment with a single higher-dose session every four weeks, but so far, my neurologist has been unwilling to take that next step, citing concerns about hyperviscosity and renal and thrombotic risks. I have had no significant side effects from the IVIG (I use maltose-stabilized), I’m relatively young (late 30s) and otherwise healthy, which suggests I am not in a high-risk group. Is hyperviscosity a significant concern? If so, how can the risk be assessed, and what signs and symptoms should be watched for during and after IVIG to help avoid longer-term complications? Additionally, are there any studies on the effects of single-session IVIG dose sizes and frequency, and their relative risks?

Leslie: IVIG does have the potential to increase blood viscosity due to the large protein load in the drug. The risk of developing thrombotic events/clots has been associated with several factors, including large doses, underlying hydration status, activity during infusion and osmolarity of the IVIG solution. There are ways to decrease the risk of developing thrombotic events with any dose of IVIG such as making sure you are well-hydrated before, during and after the infusion. This is best accomplished by drinking a lot of non-caffeinated, nonalcoholic beverages, preferably water, starting a few days before and through the infusion. If adequate hydration can’t be obtained from drinking water, then an IV hydration can be added before and after IVIG treatments, or at the same time when compatibility allows. Most IVIG products are compatible with dextrose 5% in water solution.

A second way of reducing the risk of thrombotic events is to move around occasionally during the infusion rather than staying in a seated or lying position throughout. Choice of IVIG product is a third way. Some IVIG products have osmolarity similar to blood, which is ideal. Others are very hyperosmolar and historically have been more associated with the development of clots than others. From a dosing standpoint, it is commonly thought that infusing large doses over more than one day will decrease the risk, but I don’t believe this has been prospectively studied. The signs and symptoms of a clot depend on where the clot forms. Things to watch for are pain and swelling in an extremity (deep venous thrombosis), shortness of breath or chest pain (clot in the lungs or heart), confusion, drooling or inability to speak (clot in or near the brain).

From a renal risk standpoint, acute renal failure has historically been associated with products stabilized with sucrose. Many of the same tactics to reduce clots can reduce the risk of developing renal issues (adequate hydration, breaking the dose into a few days and product selection to avoid sucrose stabilizers). Periodic monitoring of your serum creatinine with a subsequent calculation to determine your creatinine clearance (how well your kidneys are functioning) is recommended by most of the IVIG manufacturers. Things to watch for include a change in urination directly following infusion (such as a decrease in urine volume), a decrease in frequency and the color of the urine. If the urine darkens to a brown/tea color, this is a sign of renal insufficiency and should be addressed immediately.

From a dosing standpoint, neurologists do dose differently. Many dose at 2 gram/kg every four weeks. From my experience, some people have a better result with smaller doses more frequently than with larger doses farther apart. One option to consider is checking with your neurologist to see if he/she will allow you to receive your IVIG dose at home every three weeks rather than in the hospital. Many patients are treated at home without any serious issues or side effects. When treating patients at home, the nurse stays with them through the entire infusion to assess tolerance and to manage any side effects as they occur.

Leslie J. Vaughan, RPh, is senior vice president of clinical services at NuFACTOR Specialty Pharmacy.
LAST ISSUE, we continued the discussion of a 2-year-old-boy, whose symptoms began with an apparent respiratory infection before 1 month of age that persisted year-round but worsened during the winter months. He was treated with multiple courses of antibiotics, and he was hospitalized for a few days each winter. Family members who had been similarly ill during early childhood had outgrown the tendency to become ill later in childhood, so his physician was trying to reassure the parents that he, too, would outgrow the tendency to become ill so often.

An initial immunologic evaluation showed that a more severe form of primary immunodeficiency was not present. Indeed, the numerical, or quantitative, values were all normal for his age (in particular, normal white blood cell counts and normal immunoglobulin levels). Additionally, allergy testing was suggestive of mold hypersensitivities, which could be contributing to the respiratory symptoms.

However, most relevant were the pre-/post-immunization studies. Only 33 percent of the post-immunization pneumococcal titer values were in the protective range of greater than or equal to 1.3 µg/mL, and only 8 percent achieved more than or equal to a two-times increase over the pre-immunization titer values. By definition, an abnormal response was found, since normal for age is defined as greater than or equal to 50 percent of the post-immunization titer values greater than 1.3 µg/mL and more than or equal to a two-times increase over the pre-immunization titer values.

Therefore, this child appeared to have a functional deficiency in the ability to make antibodies to the pneumococcal polysaccharide vaccine.

Functional deficiencies in antibody production have been more difficult for physicians, patients and third-party payers/insurance providers to reconcile, especially when the quantitative values appear to be otherwise normal. For example, a normal quantitative IgG level for a 2-year-old is approximately 600 mg/dL. So, if his quantitative level had been 200 mg/dL, it would be somewhat obvious that his IgG level is low and could be causing recurrent infections. Yet, even though his IgG quantitative level is normal, a deficiency can still be present. What most are not considering is that there are millions of different antibodies present in each of us directed toward a myriad of potential pathogens. At a very conservative estimate, one antibody directed against a certain pathogen comprises less than 0.00001 percent of the total number of individual antibodies present (the actual value for some may be hundreds of times lower!). Thus, the inability to make antibodies against polysaccharide antigens to a limited number of pathogens may be hidden in the large numbers of different antibodies present. Even if this inability were to include 5 percent of all the antibodies, the total IgG level for a 2-year-old would fall from about 600 mg/dL to 570 mg/dL (or for a normal adult from 1,000 mg/dL to 950 mg/dL) and still be considered normal (not recognized as a deficiency). Ultimately, though, the functional ability to make appropriate antibodies is most critical when considering whether an immunodeficiency may be present, not merely the quantitative values. This is why a pre-/post-immunization assay is performed. The assay will show that while some individuals may have essentially normal serum levels of IgG, they may have a specific deficiency in the ability to make appropriate protective antibodies — and thereby have an antibody deficiency.

Thus, in this child, there appears to be a functional deficiency in the production of polysaccharide antibodies, which would seem to be a reason for recurrent infections. This means treatment needs to be initiated.

Yet, there are several questions still to consider: What role, if any, is there for the mold allergies? Since other family members had similar histories, but outgrew the tendency to have infections, will this be the same for him? (Could the other family members have had a similar inability to respond appropriately to the pneumococcal vaccine at an earlier age, but were never tested?) Should he be started on replacement immunoglobulin therapy? (And/or, should other therapies be used?) Is there only one correct approach to his treatment?

We will attempt to answer these questions as we continue with the discussion of this case in the next issue.

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

Midwest PANS/PANDAS Support Group Launches in October

The Midwest PANS/PANDAS Support Group will launch in October with the first annual meeting on Saturday, October 18. The event will be held from 9:00 am to 12:30 pm at the Omaha Marriott Regency, Omaha, Neb., and will include a continental breakfast, a medical overview of PANS (Pediatric Acute-Onset Neuropsychiatric Syndrome)/PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections), discussions about the role of tonsillectomy in treating PANS, neurological movement disorders with PANS, psychiatric and behavioral features of PANS, and a panel discussion and box lunch. Supervised entertainment will be provided for children attending the conference, and families are invited to attend the Omaha zoo afterward. Attendees are asked to RSVP before October 15 by emailing Allergy, Asthma and Immunology Associates at jennifer@allergynebraska.com, mindy@allergynebraska.com or laura@allergynebraska.com, or by phoning (402) 391-1800. Information about the meeting also can be found at www.igiveforkids.com.

PANS/PANDAS is a mysterious and controversial childhood disease in which a normal, healthy child quite suddenly and unexpectedly develops obsessive-compulsive behavior or tics or both with an undulating clinical course. PANDAS was first observed in the 1980s. However, because it is often difficult to demonstrate the relationship between strep infections and obsessive-compulsive disorder (OCD)/tic symptoms, the PANDAS diagnostic criteria were modified to describe PANS, which encompasses the larger class of acute-onset OCD cases.

The support group will be run by Dr. Roger Kobayashi and his associates at Midwest Allergy, Asthma and Immunology Associates, as well as by doctors at Boys Town National Research Hospital. Its purpose is to answer questions regarding PANS/PANDAS, provide patient information, facilitate interaction between patients, physicians and parents, help with insurance questions and information on the appeals process, and provide patient and family support.

Insurance

Medicare IVIG Demonstration Project Begins October 1st

On October 1, patients who applied and were accepted to participate in the Medicare IVIG Demonstration Project are now covered to receive intravenous immune globulin (IVIG) home infusions. Eligible participants included those who were covered under Medicare Fee-For-Service and enrolled in Medicare Part B, have a diagnosis of primary immunodeficiency (PI) and were not covered under a home health episode of care.

In January 2013, the Medicare IVIG Access Act was signed into law by President Obama, creating a three-year demonstration project allowing for the payment of home infusion services for up to 4,000 Medicare patients with PI. During the project, Medicare will pay a bundled payment for supplies and related nursing services to administer IVIG in the home to enrolled patients. Participation does not affect any other Medicare benefits, and patients can withdraw from the project at any time. The project’s purpose is to determine the cost effectiveness of allowing Medicare patients with PI access to home IVIG infusions.

The J codes for IVIG drugs that are rendered in the home (or home-like setting) for PI patients and covered under the demonstration are as follows: Bivigan (J1556), Flebogamma (J1572), Gammagard liquid (J1569), Gammaplex (J1557), Gamunex (J1561), IVIG NOS lyophilized (J1566), IVIG NOS non-lyophilized (J1599), Octagam (J1568) and Privigen (J1459). The HCPCS code for billing for the administration (services, supplies and accessories used in the home) of IVIG drugs is Q2052. Q2052 is for use with the IVIG demonstration project only. The nationwide payment amount is $300 for 2014 and may be updated annually.
Exercise

New Home Exercise Video Tailors Program to Individuals

Freedom2Move is a home exercise video program that is tailored to individuals regardless of physical condition, age or medical diagnosis. The program’s creator, Matt Hansen, a doctor of physical therapy and writer for IG Living, uses principles of positioning to adapt the difficulty of an exercise, yet that use the same muscles. Individuals are shown which muscles each exercise is targeting, what they do and how making them stronger can improve day-to-day function. Features of the video include a welcome message, the fundamentals (concepts), the classroom (that explains the muscles and actions), the exercise session (stretching and strengthening) and options (to play the video with or without commentary). Ten percent of the proceeds from video sales benefit the health and wellness community. IG Living’s subscribers can receive 10 percent off the video’s price with the purchase code IGL10. For more information, go to www.freedom2move.org or email info@freedom2move.org.

Patient Support

Autoimmune Neuropathies Facebook Chat Scheduled for October 22

The Neuropathy Association (TNA) is hosting an “Autoimmune Neuropathies” Facebook chat event on October 22 from 7:00 pm to 8:30 pm Eastern Standard Time. Co-sponsored by IG Living, the event offers the neuropathy community an opportunity to learn about and discuss autoimmune neuropathies. Guest hosts include Todd Levine, MD, and David Saperstein, MD, of Phoenix Neurological Associates. These experts will field questions posed by chat participants, while also discussing the importance of recognizing the symptoms, the value of partnering with neurologists specializing in neuromuscular diseases to get a prompt diagnosis and determine treatment strategies that work, and ways to improve access to care and quality of life. TNA’s Facebook page can be accessed at www.facebook.com/NeuropathyAssociation. Those who do not use Facebook can still access the chat live by visiting TNA’s Facebook page, but they will not be able to join the conversation by posting comments.

Medicines

FDA Approves Baxter’s HYQVIA for Treatment of Primary Immunodeficiency

The U.S. Food and Drug Administration (FDA) has approved HYQVIA (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase), Baxter’s subcutaneous treatment for adult patients with primary immunodeficiency (PI). HYQVIA is the first subcutaneous immune globulin (IG) treatment approved for PI patients with a dosing regimen requiring only one infusion up to once per month (every three to four weeks) and one injection site per infusion to deliver a full therapeutic dose of IG. “The availability of HYQVIA has a significant impact on the treatment of PI, allowing for effective delivery of a full therapeutic dose of IG less frequently than other subcutaneous treatments (up to once a month), while maintaining the efficacy, safety and tolerability profile that is most important for patients,” said Ludwig Hantson, PhD, president of Baxter BioScience. “This approval highlights the support of the patient community for new treatment options.”

HYQVIA was approved in Europe in 2013 for adults 18 years and older with PI and myeloma or chronic lymphocytic leukemia with severe secondary hypogammaglobulinemia and recurrent infections. It is currently available in several European countries, including Germany, Netherlands, Sweden, Norway, Denmark, Ireland and Italy.
Why Is CVID Referred to as “Common Variable” When It Is Not Common?

The prevalence of CVID is about one in 25,000 people, which makes CVID a rare medical condition. However, when looking at the genetic causes of primary immunodeficiency diseases (PIs), CVID is one of the most prevalent. Therefore, in the realm of PIs, CVID is quite common. CVID is referred to as variable because of the symptoms associated with it — infections, gastrointestinal (GI) issues, lymphoma, etc. — that vary from person to person. As such, there are many different symptoms and different clinical courses in people who have the same disorder.

Why Does CVID Take So Long to Diagnose?

Historically, it has been a challenge to get the proper testing for diagnosing CVID because it is a rare condition. According to the most recent studies, diagnoses are being made earlier, but we have a long way to go to get CVID diagnosed quickly after the onset of symptoms in most patients. Older studies showed it took a decade or more to diagnose CVID. Today, on average, it takes about five to seven years to diagnose CVID; however, some patients still aren’t diagnosed for 10 to 20 years or more.

There has been a lot of effort to raise awareness about PIs over the years. And, while awareness has improved, CVID is still very rare. So, one reason it takes so long to diagnose is because most physicians and healthcare practitioners are either not familiar with the disease, or they may have heard about it in their training, but have forgotten about it. Therefore, CVID is not something they’re thinking about or testing for.

Another reason CVID can take so long to diagnose is that there is a perception that PIs are a pediatric problem — something that is diagnosed at birth or early in life. So, many adults have to battle the myth that it doesn’t happen to adults or that they would have already been diagnosed.

In addition, finding the right doctor to diagnose CVID can be a challenge. The symptoms of CVID can be similar to other common conditions: sinus infections, bronchiectasis, bowel issues, etc. These are conditions that a lot of physicians see as run-of-the-mill; but they’re not, if they keep recurring. It takes a certain healthcare practitioner to know that recurring infection is not normal. And, while infection is the hallmark of CVID, there are also many other symptoms and complications. For instance, if the primary symptom is GI problems or granulomatous disease, physicians don’t equate that to an immune deficiency, and CVID gets overlooked.

Finally, today, doctors specialize in certain areas of medicine, and through no fault of their own, they often don’t look at the big picture. As such, individuals have to run into the right specialist or seek out the physician who will look at the big picture of various symptoms and conduct the appropriate testing.

Yet, even when physicians think of CVID as a possible diagnosis, they often don’t know what tests to conduct or how to interpret those tests. This is a particular challenge, so physicians who are not familiar with CVID are being encouraged to refer patients to a practitioner who is familiar with the disease. Unfortunately, there is a relative shortage of specialists who have a strong interest in this kind of immunology.

How Is the Time of CVID Diagnosis Calculated?

Studies that look at the time to diagnose CVID base it on the date from when a patient first started to record recurrent infections or presenting symptoms to when they were tested and diagnosed. This is an inexact science, however, because it relies on backward tracking and recollection.
Introducing

HyQvia

[Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]

For adults with primary immunodeficiency

What is HYQVIA?
HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] is a liquid medicine containing immune globulin and recombinant human hyaluronidase indicated for the treatment of Primary Immunodeficiency (PI) in adults. This includes, but is not limited to, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Limitation of Use:
Safety and efficacy of chronic use of recombinant human hyaluronidase in HYQVIA have not been established in conditions other than PI.

HYQVIA is infused under the skin into the fatty subcutaneous (subQ) tissue, in 1 infusion site, up to once every 4 weeks. A second infusion site may be used if needed.

For more information about HYQVIA, talk to your doctor or visit www.HYQVIA.com

Detailed Important Risk Information
HYQVIA can cause serious side effects. Call your healthcare professional or go to your emergency department right away if you get:

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a severe allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of swelling in your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s). These could be signs of a blood clot.
- Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver or blood problem.
- Chest pain or trouble breathing, blue lips or extremities. These could be signs of a lung problem.

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

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

- HYQVIA can cause blood clots.
- Call your healthcare professional if you have pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s), unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body.
- Your healthcare professional may perform blood tests regularly to check your IgG level.
- With your consent, your healthcare professional may provide blood samples to Baxter Healthcare Corporation to test for antibodies that may form against the hyaluronidase part of HYQVIA.
- Do not infuse HYQVIA into or around an infected or red swollen area because it can cause infection to spread.
- Talk to your healthcare professional if you become pregnant. Women who become pregnant during HYQVIA treatment are encouraged to enroll in the HYQVIA Pregnancy Registry by calling Medical Information at 1-866-424-6724.

What are the possible or reasonably likely side effects of HYQVIA?
After HYQVIA infusion a temporary, soft swelling may occur around the infusion site, which may last 1 to 3 days, due to the volume of fluid infused. Mild or moderate pain, redness, swelling or itching may occur at the site of infusion and generally go away in a few hours. Local reactions are less likely after the first few infusions. The most common side effects of HYQVIA are headache, fatigue, nausea, fever, and vomiting. Antibodies to the hyaluronidase component of HYQVIA were formed in some patients taking HYQVIA. It is not known if there is any long term effect. In theory, these antibodies could react with your body’s own PH20. PH20 is present in the male reproductive tract. So far, these antibodies have not been associated with increased or new side effects.

What is HYQVIA?
HYQVIA is a liquid medicine containing immune globulin and recombinant human hyaluronidase. HYQVIA contains IgG antibodies, collected from human plasma donated by healthy people. The antibodies help your body to fight off bacterial and viral infections. The hyaluronidase part of HYQVIA helps more of the immune globulin get absorbed into the body to fight infection.

Before starting HYQVIA, tell your healthcare professional if you have or had any kidney, liver, or heart problems, a history of blood clots, because HYQVIA can make these problems worse. Also tell your doctor if you have IgA deficiency or a history of severe allergic reactions to immune globulin IgG or other blood products, or are pregnant, trying to become pregnant or are breast feeding.

How should I take HYQVIA?
HYQVIA is infused under the skin (subcutaneously) up to once every 4 weeks. You can get HYQVIA at your healthcare professional’s office, clinic, or hospital. You can use HYQVIA at home. You and your healthcare professional will decide if home self-infusion is right for you. Do not use HYQVIA at home until you get instructions and training from your healthcare professional.

Who should not take HYQVIA?
Do not take HYQVIA if you are allergic to IgG, hyaluronidase, or other blood products, or have IgA deficiency with antibodies to IgA.

To report suspected side effects, contact Baxter Healthcare Corporation at 1-866-888-2472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of HYQVIA Prescribing Information on following page, including Boxed Warning.

Baxter and Hyqvia are trademarks of Baxter International Inc.
September 2014 USBS/MG89/14-0163
Brief Summary of Prescribing Information
HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]

The following summarizes important information about HYQVIA (pronounced Hi-Q-via). Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare professional. If you have any questions after reading this, ask your healthcare professional.

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

- HYQVIA can cause blood clots.
- Call your healthcare professional if you have pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s), unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body.
- Your healthcare professional may perform blood tests regularly to check your IgG level.
- With your consent, your healthcare professional may provide blood samples to Baxter Healthcare Corporation to test for antibodies that may form against the hyaluronidase part of HYQVIA.
- Do not infuse HYQVIA into or around an infected or red swollen area because it can cause infection to spread.
- Talk to your healthcare professional if you become pregnant. Women who become pregnant during HYQVIA treatment are encouraged to enroll in the HYQVIA Pregnancy Registry by calling Medical Information at 1-866-424-6724.

What should I tell my healthcare professional before I start using HYQVIA?

Before starting HYQVIA, tell your healthcare professional if you:
- Have or had any kidney, liver, or heart problems or history of blood clots because HYQVIA can make these problems worse.
- Have IgA deficiency or a history of severe allergic reactions to IgG or other blood products
- Are pregnant, trying to become pregnant or are breast feeding.

What is HYQVIA?

HYQVIA is a liquid medicine containing immune globulin and recombinant human hyaluronidase. HYQVIA contains IgG antibodies, collected from human plasma donated by healthy people. The antibodies help your body to fight off bacterial and viral infections. The hyaluronidase part of HYQVIA helps more of the immune globulin get absorbed into the body to fight infection.

Who should not take HYQVIA?

- Do not take HYQVIA if you: Are allergic to IgG, hyaluronidase, or other blood products
- Have IgA deficiency with antibodies to IgA

How should I take HYQVIA?

- HYQVIA is infused under the skin (subcutaneously) up to once every 4 weeks.
- You can get HYQVIA at your healthcare professional’s office, clinic, or hospital.
- You can use HYQVIA at home. You and your healthcare professional will decide if home self-infusion is right for you.

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

After HYQVIA infusion a temporary, soft swelling may occur around the infusion site, which may last 1 to 3 days, due to the volume of fluid infused.

The following local reactions may occur at the site of infusion and generally go away in a few hours. Local reactions are less likely after the first few infusions: mild or moderate pain, redness, swelling, and itching.

The most common side effects of HYQVIA are headache, fatigue, nausea, fever, and vomiting.

Antibodies to the hyaluronidase component of HYQVIA were formed in some patients taking HYQVIA. It is not known if there is any long term effect. In theory, these antibodies could react with your body’s own PH20. PH20 is present in the male reproductive tract. So far, these antibodies have not been associated with increased or new side-effects.

Call your healthcare professional or go to your emergency department right away if you get:
- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of swelling in your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s). These could be signs of a blood clot.
- Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver or blood problem.
- Chest pain or trouble breathing, blue lips or extremities. These could be signs of a lung problem.

These are not all of the possible side effects for HYQVIA. For more information about HYQVIA, go to www.HYQVIA.com. For more information on patient resources and education, please visit www.immunedisease.com.
Does CVID Run in Families, and Is There Genetic Testing for It?

Even though it is believed CVID is caused by genetic mutations, only about 10 percent of diagnoses are clearly familial. Ninety percent are sporadic, which means the disease shows up in only one person in the family. Therefore, only a small minority of patients have inherited CVID. The problem with such testing, though, is that a genetic mutation can be identified in only about 15 percent of all CVID cases. In the other 85 percent, the genetic mutation is unknown. Genetic testing is relatively expensive, so without a high rate of success, it is often not clinically useful outside of the research setting. Much more research needs to be conducted to understand the genetics related to CVID.

What Is the Difference between Hypogammaglobulinemia and CVID?

Hypogammaglobulinemia is a nonspecific diagnosis. Basically, it describes a laboratory value that shows antibody levels are low, but gives no other information on the condition. CVID, on the other hand, has specific criteria: low IgG plus low IgA and/or IgM levels. Therefore, hypogammaglobulinemia is a general diagnosis, whereas CVID is a more specific diagnosis.

It’s possible for children to have transient hypogammaglobulinemia, which means their IgG levels are low, but they become normal as they age. This sometimes occurs in children under 5 years old because the development of the immune system is delayed. Therefore, because it could be transient, physicians generally don’t like to diagnose children with CVID until they’re older than 5 years. In most patients, CVID is diagnosed after puberty.

What Is the Risk of Serious Disease with CVID, and What Can Be Done to Prevent It?

Historically, the major risk of CVID is overwhelming infection (bacteria in the bloodstream, meningitis, etc.). The good news is that infections have dramatically been reduced in patients who are diagnosed and properly treated with immune globulin (IG). And, these days, serious complications such as chronic lung disease (which occurs in 25 percent to 30 percent of patients) resulting from bronchiectasis may be prevented or slowed with IG therapy.

But, there are other conditions, like granulomas and lymphoma, that aren’t likely related to infection and cannot be prevented with IG treatment. There are also autoimmune diseases (ADs) associated with CVID, ranging from low blood cell counts and arthritis to lupus. Additionally, 20 percent of CVID patients also have serious GI problems, ranging from irritable bowel disease, Crohn’s disease, ulcerative colitis, malabsorption, giardia, etc. A final serious complication occurs with the spleen and lymph nodes. A third of CVID patients will develop problems with the spleen and lymph nodes, but these problems are largely benign. Approximately 8 percent of the time, these problems can result in lymphoma. Unfortunately, we don’t have any way to prevent any of these conditions; we can only recognize them early and treat the symptoms as they arise.

In short, infectious problems can be treated with IG; other conditions can’t. Therefore, it’s important for CVID patients to have regular follow-up with their physician to identify any other conditions that may arise and treat them early.

Can CVID Patients Have an Autoimmune Disease but Test Negative for It?

One of the challenges in dealing with CVID and its associated complications is that patients don’t make antibodies well. This includes autoantibodies, and because ADs are typically diagnosed based on autoantibody assays, CVID patients may have all the signs and symptoms of an AD, but their autoantibody lab tests may be normal. In addition, IG therapy may interfere with the lab tests that look for autoimmunity, which can make them unreliable for CVID patients. Therefore, these patients need to find a rheumatologist who will conduct a comprehensive physical examination for an AD and recognize that the lab tests won’t necessarily test positive for it.

Are CVID Patients Treated with Medications Other Than Immune Globulin?

IG is the primary treatment for CVID. It is the only proven treatment for preventing infectious complications. However, there are a lot of other medications that might be used to treat complications of CVID. These include antibiotics (although chronic prophylactic antibiotics are not commonly prescribed), immunosuppressant drugs to treat ADs, GI problems or lung problems, and chemotherapy to treat lymphoma, which rarely occurs.
Gene Therapy

The Cutting Edge of PI Treatment

Some PIs are currently being treated and cured with gene therapy, and as advancements with this life-saving technology progress, there is hope for many others.

By Caroline Y. Kuo, MD, and Roger H. Kobayashi, MD
Gene therapy, or the use of genetic material such as DNA or RNA to treat disease, has received growing attention in recent years and is becoming a recognized form of medical therapy. Mere fanciful imagination a few decades ago, the idea of manipulating or repairing genes has evolved from science fiction to a real hope for those with serious incurable diseases, including primary immunodeficiencies.

History of Gene Therapy

The concept of gene therapy developed during the 1960s, when scientists discovered enzymes that could essentially cut and paste DNA, allowing them to manipulate and potentially repair sequences of genetic material in a test tube. Around the same time, immortal cell lines were also developed that permitted testing of these DNA sequences, demonstrating that modified foreign DNA could be reintroduced into an individual in a stable manner. In addition, manipulated, or “transformed,” cells could continue to grow while permanently maintaining the change in their genome. This set the stage for realizing that gene manipulation and repair was indeed possible.

Although the transfer of genetic material into cells was met initially by frustrating technical difficulties, pioneering researchers observed that virally infected cells stably inherited small amounts of genetic information from the virus. This led to the hypothesis that it might be possible to modify viruses to transfer therapeutic genes instead of the virus’ own genes. Since then, many gene therapy studies have utilized these modified viral carriers (adenovirus, retrovirus, lentivirus) to insert corrected gene sequences, thus creating a transgene. These modified viruses are no longer infectious, but they retain their inherent ability to enter cells and desirably insert the “corrected gene” in the right location. These discoveries set the stage for future experiments in gene therapy to address human disease, allowing scientists to correct disease-causing DNA mutations in the laboratory, package them into viral vectors (the tools used to deliver genetic material into cells), and deliver the corrected transgene into diseased cells.

Over time, it has been learned that a number of factors need to be taken into consideration before attempting gene therapy: 1) The defective gene(s) need to be identified and their location carefully mapped out, which is not as simple as it sounds. 2) In many diseases in which there is a defect in manufacturing a functional protein (proteins within a cell determines its health and function), there may be multiple genes regulating different portions of a large protein. What this means is that even if it were possible to repair the defective gene, the final protein product may not be fully functional. For instance, in X-linked lymphoproliferative syndrome characterized in males by fatal susceptibility to the Epstein Barr virus, there may be missense (an incorrect genetic code sequence) or insertion mutations (permanent transmissible changes in the genetic material) that impair the function of a vital protein or prevent its manufacturing altogether. Therefore, not only is there the enormous problem of identifying one of potentially many mutations in a gene, but there also is the problem of inserting it in the correct position in the chromosome and ensuring that it is stable and functions correctly. At best, the procedure might work, thus resulting in manufacturing proteins that function correctly. At worst, the gene might be inserted in a wrong location or incorrectly, resulting in malignant or defective cells.

Although the first attempt at gene therapy in humans did not result in a permanent cure, it established the foundation that using DNA as a form of treatment could be safe and that the potential to cure disease existed.

Therefore, it became clear that the ideal target disease for initial gene therapy is one in which blood cells can be used (rather than heart, liver or brain cells), and one that has one and not multiple gene mutations, and in which insertion is “technically simple.” Severe combined immunodeficiency (SCID) is one such disease. Thus, an initial trial was attempted in a 4-year-old girl with adenosine-deaminase deficiency (a variant of the “bubble boy” disease known as SCID), which is characterized by profound T-cell deficiency and early death from overwhelming infection. Without the ADA enzyme, she could not detoxify DNA byproducts that damaged her T cells, causing profound
immunodeficiency. In 1990, physician scientists at the National Heart, Lung and Blood Institute and the National Cancer Institute inserted the gene into defective white blood cells collected from the patient and re-infused these “corrected cells,” which then produced ADA, thus detoxifying fatal byproducts. The treatment was safe and the corrected cells were able to produce ADA enzyme, but the cells were not long-lived, and the patient continued to require intermittent gene therapy, as well as additional treatment with exogenous ADA enzyme replacement.

Although the first attempt at gene therapy in humans did not result in a permanent cure, it established the foundation that using DNA as a form of treatment could be safe and that the potential to cure disease existed. Since that time, there have been significant advances in understanding gene delivery methods and the ability to stably correct genetic defects in multiple cell types such as bone marrow stem cells, tumor killing T cells, muscle cells and many others.

Safety of Gene Therapy

Work in gene therapy boomed after the initial clinical trial for ADA deficiency. However, in 1999, an 18-year-old male who enrolled in a protocol for treatment of ornithine transcarbamylase (OTC) deficiency died due to a severe immune reaction to the adenovirus carrier used to insert the correct gene. This was the first time death could be directly associated with the viral vector, and patient safety issues remain a priority for any gene therapy research or clinical trial to this day, accounting for what seems to be slow progress clinically.

Although the general concept of gene therapy is simple — replace or fix a mutated gene to allow proper protein expression — carrying out this process is highly complex. While viral vectors can efficiently transfer modified DNA, certain viruses can insert the genetic material at actively expressed sites that may result in abnormal proliferation (the growth of cells), called insertional oncogenesis. Therefore, efforts in using a more targeted approach for gene therapy and additional modifications to viral vectors have made gene transplantation safer, but not necessarily failsafe.

While it is understandable that patients and doctors are desperate for a genetic cure for potentially fatal diseases, many years of pre-clinical work are required to ensure and confirm the safety profile of gene therapy agents before they are allowed in clinical trials. Additionally, there has been heightened monitoring for malignant (deadly) events. Adequate safeguards are in place to control gene delivery and hopefully pre-empt gene therapy-related cancers. The Food and Drug Administration (FDA) and Recombinant DNA Advisory Committee (RAC) are intimately involved in trials involving gene therapy and play important roles in maintaining rigorous scientific, as well as ethical, standards in the field.

Clinical Trials Worldwide

More than 1,800 gene therapy clinical trials are either ongoing or have been completed worldwide involving 31 countries. The large majority of trials have been conducted in the United States, followed by Europe and, increasingly, Asia. The diseases most commonly addressed are cancer, cardiovascular disease and monogenic diseases that are due to a single, identifiable gene defect.

Thus far, most clinical trials (60 percent) have revolved around treating cancer, including those that affect the pulmonary, neurologic, gastrointestinal, hematologic and dermatologic systems. Multiple strategies have been employed in this approach such as inserting genes that are known to suppress tumors or engineering immune cells to specifically recognize and kill an individual's malignant cells. These clinical trials have shown early promise.

Advancements have also occurred in monogenic diseases, with more than 160 clinical trials conducted to date. Cystic fibrosis, which is commonly inherited in the U.S. and Europe and carries a life expectancy of less than 40 years, as well as SCID, which is generally fatal within the first year of life if untreated, are examples of gene therapy attempts that are actively being pursued and show
More than 10,000 patients and providers put their confidence in Hizentra.

Hear perspectives from our patients and prescribers at:
www.Hizentra.com/Perspectives

Important Safety Information

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

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

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

Please see additional Important Safety Information on reverse side and brief summary of full prescribing information for Hizentra, including boxed warning, on adjacent page.
Important Safety Information (continued)

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

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

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

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

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

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

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

Please see brief summary of full prescribing information for Hizentra, including boxed warning, on adjacent page.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
HIZENTRA®, Immune Globulin Subcutaneous (Human), 20% Liquid

Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

WARNING: THROMBOSIS

See full prescribing information for complete boxed warning.

- Thrombosis may occur with immune globulin products, including Hizentra.
- Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, 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.

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INDICATIONS AND USAGE

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

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DOSE AND ADMINISTRATION

For subcutaneous infusion only. Do not inject into a blood vessel.

Administer weekly or biweekly (every two weeks).

**Dosage**

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

**Weekly:** Start Hizentra 1 week after last IGIV infusion

Initial weekly dose = Previous IGIV dose (in grams) x 1.53

<table>
<thead>
<tr>
<th>No. of weeks between IGIV doses</th>
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<tr>
<td>1-4 weeks</td>
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- Biweekly: Start Hizentra 1 or 2 weeks after the last IGIV infusion or 1 week after the last weekly Hizentra infusion. Administer twice the calculated weekly dose.
- Adjust the dose based on clinical response and serum IgG trough levels (see Dose Adjustment).

**Administration**

- Infusion sites – 1 to 4 injection sites simultaneously, with at least 2 inches between sites.
- Infusion volume – First infusion, up to 15 mL per site. Fifth infusion, up to 20 mL per site, then to 25 mL per site as tolerated.
- Infusion rate – Up to 15 mL per hr per site. Increase to 25 mL per hr per site as tolerated.

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ADVERSE REACTIONS

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

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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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.

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USE IN SPECIFIC POPULATIONS

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

Based on September 2013 version
promise. The general aim of gene therapy with monogenic disorders is to deliver the functional gene to stem cells, which are long-lived and can continue to give rise to cells that contain the corrected gene. This would result in a permanent cure since corrected stem cells can divide and ultimately differentiate into different cell types that serve various functions in the body. Significant progress also has been made in the field of primary immunodeficiency diseases (PIs), and new trials continue to improve upon previous work (see Table 1).

There are still many more indications too long to list. Briefly, they include treatment of infections, notably the human immunodeficiency virus, neurological diseases such as Alzheimer’s disease and multiple sclerosis, ophthalmologic diseases such as glaucoma and retinitis pigmentosa, inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease, and blood diseases such as sickle cell disease.

**Advancements in Gene Therapy**

Traditional forms of gene therapy have focused on the delivery and incorporation of functional genes to diseased cells without targeting them to their natural location in the genome (an individual’s complete DNA set). However, genes in their endogenous locations are surrounded by intricate control elements that affect their expression (their ability to produce functional genes). Random incorporation of corrected genes into cells is acceptable only when

<table>
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<tr>
<th>Primary Immunodeficiency</th>
<th>Overall Outcomes</th>
<th>Future Directions</th>
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<tbody>
<tr>
<td>ADA-SCID</td>
<td>• 100% survival with most achieving protective immune function</td>
<td>• Can soon be considered standard of care for patients without matched sibling bone marrow donors</td>
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<tr>
<td></td>
<td>• No complications due to viral vector</td>
<td>• New trial underway using a new generation of self-inactivating gene delivery vectors lacking elements that can result in insertional oncogenesis</td>
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<tr>
<td>X-Linked SCID</td>
<td>• 95% engraftment with immune reconstitution in infants. Four of five older patients age 10 years to 20 years did not engraft with gene modified stem cells, although several of these patients also failed traditional bone marrow transplant</td>
<td>• Newer modified viral vectors are being used to decrease/eliminate the risk of insertional oncogenesis</td>
</tr>
<tr>
<td></td>
<td>• 5 patients developed acute T cell leukemia, 4 of whom were treated successfully</td>
<td>• Promising results in canine models represents potential for human clinical trials in the near future</td>
</tr>
<tr>
<td>Chronic Granulomatous Disease (CGD)</td>
<td>• Early trials were not able to achieve enough gene correction or resulted in insertional oncogenesis</td>
<td>• Newer modified viral vectors are being used to decrease/eliminate the risk of insertional oncogenesis</td>
</tr>
<tr>
<td></td>
<td>• Clinical trial ongoing in Europe may be followed by similar trials in the U.S.</td>
<td>• Majority of patients achieved permanent correction of their immunodeficiency</td>
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<tr>
<td>Wiskott-Aldrich Syndrome (WAS)</td>
<td>• Majorit of patients achieved permanent correction of their immunodeficiency</td>
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<tr>
<td></td>
<td>• Leukemia occurred in 7 out of 10 patients due to the retroviral vector</td>
<td>• No adverse events resulted from the gene therapy</td>
</tr>
<tr>
<td>Leukocyte Adhesion Deficiency (LAD)</td>
<td>• A few patients were treated with a retroviral vector, but there were no corrected cells found in circulation</td>
<td>• Promising results in canine models represents potential for human clinical trials in the near future</td>
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expression of the gene is not tightly regulated. Therefore, a targeted approach can significantly decrease the risk of insertional oncogenesis that can potentially occur with random integration of genetic material by a viral vector.

In recent years, there has been a strong focus on site-specific gene therapy using engineered genome editing tools to locate specific sequences of DNA, create a cut in the DNA near the location of a mutation, and make appropriate changes such as inserting or cutting out a sequence of DNA that affects expression of the gene. TALENs, or Transcription Activator-Like Effector Nucleases, are one such tool discovered in the 2000s from a type of plant bacteria. They can be designed and assembled in the laboratory to bind specific gene sequences and create a double-stranded break in the DNA. When a break in DNA occurs, natural repair mechanisms are activated that can use a provided DNA template to fix the break and incorporate a corrected gene sequence to override the diseased gene.

Another genome editing platform that has gained significant momentum in the last few years is the CRISPR/Cas-9 system, or Clustered Regularly Interspaced Short Palindromic Repeats. It is derived from a form of bacterial immunity, and it has been engineered so that researchers can utilize it to target almost any gene. Similar to TALENs, CRISPRs also create breaks in the DNA that can be repaired using a template containing the correct DNA sequence. However, both techniques can still result in off-target effects, cutting unintended sequences of DNA, so efforts are ongoing to further understand and decrease this complication.

Ongoing research has begun to gain a deeper understanding of which specific cells are best treated with gene therapy to provide a more permanent source of corrected cells to patients. These cells can be sorted out of the general population of cells through modern advancements in technology such as flow cytometry (which provides rapid analysis of multiple characteristics of single cells). In terms of DNA delivery, modifications have been made to viral systems to decrease the risk of infection and insertional oncogenesis. Non-viral methods of gene delivery are also underway, including the permeabilization of cell membranes with an electric pulse (electroporation), ultrasound-mediated transfer and chemical delivery, among many more.

The Future of Gene Therapy

Clinical trial and research activity in gene therapy continue to grow, and the future of the field is even brighter than before. It offers the promise of a cure for those with serious illnesses, and it may be only a matter of time before it becomes the standard of care for certain diseases.

In the area of immunodeficiency, recent results in utilizing gene therapy have shown promise in diseases such as X-linked hyper-IgM syndrome (XHIM), X-linked agammaglobulinemia (XLA), X-linked lymphoproliferative disease (XLP) and X-linked agammaglobulinemia (XLA). The goal is to translate this work into clinical trials. Although the path from the research bench to the clinic has not been entirely smooth, and the process to bring efforts to fruition takes years and significant investment, the knowledge that there is a realistic potential to cure serious, life-threatening diseases makes this effort entirely worthwhile.

CAROLINE Y. KUO, MD, is a clinical instructor of allergy and immunology at the UCLA School of Medicine, Los Angeles, Calif., who specializes in gene therapy research for primary immunodeficiencies.

ROGER H. KOBAYASHI, MD, is a clinical professor at the UCLA School of Medicine and a national consultant to the Immune Deficiency Foundation.

References

When 1,000 Americans were asked what bothers them most about going to doctor office visits, communication was the chief complaint. On top of gripes about long waits and billing disputes, they complained about being rushed, not being heard or failing to understand what they were being told. Surprisingly, doctors also cite communication as their chief complaint when seeing patients. Competing interests that limit the time doctors are able to spend with patients is a major reason. Yet, other reasons stem from a breakdown in the doctor-patient relationship caused by a lack of good communication skills on the part of both patients and doctors. It takes two for miscommunication to occur, and it takes two to correct the problems.

Benefits of Effective Communication

Doctor-patient communication has come a long way over the years. The medical model has evolved from paternalism to individualism, spurred by the growth of the Internet and by the health consumer movement. Today, the dominant communication model is information exchange comprised of shared decision making and patient-centered care, which includes “respecting and responding to patients’ wants, needs and preferences, so that patients can make choices in their care that best fit their individual circumstances.”

Many studies show that good doctor-patient communication benefits both patients and doctors. It has the potential to help regulate patients’ emotions, facilitate comprehension of medical information, and allow for better identification of patients’ needs, perceptions and expectations. It also leads to patients who are more likely to be satisfied with their care, especially to share pertinent information for accurate diagnosis of their problems, follow advice and adhere to the prescribed treatment (agreement with treatment and the need for follow-up is strongly associated with recovery). In addition, there are correlations between patients’ sense of control and their ability to tolerate pain, recover from illness and function daily. For doctors, good communication leads to satisfied patients who are less likely to lodge formal complaints. It also provides advantages for doctors in terms of greater job satisfaction, less work-related stress and reduced burnout.

By Ronale Tucker Rhodes, MS
Barriers to Good Communication

Doctors and patients face a number of different barriers to communicating effectively with each other.

Avoidance behavior. Some physicians avoid discussing the emotional and social impact of patients’ problems because it distresses them, either because they feel unable to handle the issues or because they simply don’t have the time. In turn, patients may be unwilling to disclose problems that could delay their recovery.4

Language barriers. Doctors spend years learning to speak in medical jargon, some of whom specialize in certain dialects, which becomes second nature to them. The use of technical terms, rather than plain English, makes them difficult to understand and creates a language barrier with patients, which undermines the communication process.4

Different perspectives. Compounding the language barrier is a different understanding of even plain English words. Peoples’ backgrounds, experiences and emotions influence how they interpret what is being said, and the same words spoken by someone to two different people may have entirely different meanings to each of them. For instance, how a doctor defines a successful surgery is likely very different from how a patient would. The result is doctors and patients entering the room with entirely different perspectives.4

Intimidation. How patients and doctors view each other is another issue. The patient-doctor relationship is very uneven, with the physician in a powerful position. In fact, oftentimes, from the beginning of an office visit, every step has the effect of making a patient feel at the mercy of staff members.5 In focus groups that explored how patients discuss healthcare issues with their physicians, researchers found that even well-educated patients feel intimidated in the physician’s office. “In the context of a medical consultation, people feel uniquely vulnerable,” says Dominick Frosch, PhD, an associate investigator at the Palo Alto Medical Foundation’s Research Institute and associate professor at the University of California, Los Angeles. “Asserting their views might require disagreeing. Patients fear that will lead to negative consequences that might impact their care in the future.”6

Patient anxiety. People who are ill or who think they are ill may suffer from heightened anxiety, which also chips away at their self-confidence.6 In addition, as much as 20 percent of the population suffers from white coat syndrome. Anxiety prevents patients from getting vital care.7 This is especially true for those with rare diseases. In the U.S., it can take up to eight years to receive an official medical diagnosis for a rare disease. The uncertainty, conflicting information, wrong diagnoses, frequent trips to different doctors and specialists cause stress and anxiety.8

Distrust. Patients with rare conditions, who have been bounced around the medical system, have been misdiagnosed and have seen specialist after specialist, may grow to distrust doctors. As a result, they may go into an appointment feeling guarded and with low expectations, which leads to poor outcomes in a cycle of self-fulfilling prophecies.
the coin, when doctors are presented with a situation that is outside the norm of their experience, they tend to distrust what patients are telling them. Doctors are scientists, and they are trained to rely on objective tests and treat patient reports with skepticism.4

Internet. While 21st century technology is a good thing in today’s patient-centered care model, it can pose problems for both patients and doctors. After researching conditions on the Internet, patients sometimes think they know more about a subject than their doctor. In addition, there tends to be a pessimistic and worst-case bias in medical information on the web, with the worst outcomes reported more than successes. This can lead to heightened concerns for patients that, in turn, causes them to be labeled alarmists. Doctors are responding to the shift in patients taking part in their diagnoses and treatments, but some are more willing that others to accept it.4

The patient-doctor relationship is very uneven, with the physician in a powerful position.

Shortage of physicians. Numerous forecasts have predicted shortages of physicians in the United States, particularly in light of the expected increase in demand from the Affordable Care Act (ACA). The share of primary care providers who are physicians is expected to shrink from 71 percent to 60 percent in 2025. In 2010, there were nearly four primary care physicians for every nurse practitioner in primary care, but in 2025, it is estimated there will be just more than two physicians per nurse practitioner.9 “As harried clinicians, we have a lifetime of learning in our heads that we immediately try to use to diagnose and treat before we run from one visit or operation to another,” says Atul Grover, MD, chief public policy officer of the Association of American Medical Colleges. “This pressure will only get worse as the shortage of physicians grows.”5

Competing agendas. Time is the fundamental prerequisite for good doctor-patient communication, and with the changes brought about by the ACA, competing agendas are limiting doctors’ time. “In the U.S., the median duration of visits to office-based physicians is less than 15 minutes,” says John Sotos, a cardiologist and flight surgeon. “So, it’s unsurprising that communication … is reduced to bare minimums.” According to Dr. Larry Shore of My Health Medical Group in San Francisco, “There’s some data to suggest that the average patient gets to speak for between 12 and 15 seconds before the physician interrupts them.”

A new poll by NPR, the Robert Wood Johnson Foundation and Harvard School of Public Health found that three out of five patients think their doctors are rushing through exams. But, for the most part, a doctor’s impatience is driven by competing agendas. For one, reimbursement rates for a primary care visit are notoriously low.10 The reimbursement pressures and frequency of patients per hour are creating new justifications for some doctors not to connect with their patients at a deeper level, says Fred Hassan, chairman of Bausch & Lomb.5

Another competing agenda is electronic health records, which have compounded the time problem because they, too, demand communication time from the physician. Electronic health records in the office requires many doctors to spend much of a patient exam looking at a computer screen instead of the patient in order to record information. “As legal documents, their need trumps the patient’s need,” says Sotos.5

Also with the ACA, doctors now have to demonstrate high-quality care by encouraging vaccination, further lowering blood pressure, ordering additional tests, adding new medications, initiating referrals, persuading patients to be screened (like mammograms) or discussing its pros and cons (like PSA). “The longer our agenda gets, the less time patients have to raise issues that matter to them,” explains Gilbert Welch, a general internist at the White River Junction VA and a professor of medicine at the Dartmouth Institute for Health Policy and Clinical Practice in the Geisel School of Medicine. “Physicians are increasingly distracted by being compelled to meet the needs of the system — rather than the needs of the patient.”5

Solo doctoring. Traditionally, physicians have been taught to function solo in medical school. With the new medical model, this is changing by teaching them to work with a variety of disciplines with a focus on teamwork. Unfortunately, patients often expect “Dr. Lone Ranger,” and doctors hate to disappoint them or diminish their own reputation with patients. “Patients have this expectation about doctors because they watch TV,” says Leah Binder, president and CEO of Leapfrog Group, a national organization representing employer purchases of healthcare. “In a given year, millions more people watch programs about hospitals than enter an actual hospital. With all due respect to my fellow commentator from ‘House,’ hospital dramas reinforce public expectations of the doctor-hero, who needs little or nothing from his colleagues.”5
Strategies for Doctors to Improve Communication

Physicians who are good communicators have empathy and respect for patients, and they understand that those who are sick are highly vulnerable. That means not interrupting patients even when time is short or when they are in a hurry to ensure patients are given sufficient time to explain their problems and symptoms. According to Dr. Gurpreet Dhaliwal, an associate professor of clinical medicine at the University of California, San Francisco, and a staff physician at the San Francisco VA Medical Center, “Doctors can improve their communication by seeking to understand the perspective of the patient. Active listening or the careful study of facial expression and body language can go a long way, but this critical duty can be simplified by always asking patients three simple questions: What is the patient’s idea about what is going on? What is the patient most worried about? And, what is the patient expecting the doctor to do? These open-ended questions, he says, “creates attunement, not agreement…. It signals ‘I hear you, I understand you, and I respect what you are saying.’”

The computer is here to stay, which means physicians can’t get around entering medical data into the computer while seeing patients. Therefore, says Robert M. Wachter, MD, professor and associate chair of the Department of Medicine at the University of California, San Francisco, and chair of the American Board of Internal Medicine, “the most important thing we can do is to remind our clinicians … that the real patient is more important than the iPatient, [and] that the human connection is essential to the art of healing.”

Physicians also should avoid the “tendency for a ‘quick fix,’ which often means ordering a test or writing a prescription,” says Rita Redberg, a professor of medicine and a cardiologist at the University of California San Francisco Medical Center. And, they need to be sure they are treating the symptom or problem that brought the patient to their office.

Doctors who are good communicators have the ability to share information in terms patients can understand, eliminating the “med-speak.” By putting themselves in the heads of the patients, says Sotos, doctors will
use language that matches the faculties of the patient, minimizing distractions and interruptions and anticipating questions.\(^5\)

And, doctors need to encourage patients to ask questions. Studies show that up to 80 percent of the medical information patients receive is forgotten immediately, and nearly half of the information retained is incorrect.\(^5\) Doctors who are good communicators effectively manage patients’ expectations by helping them understand what the next steps are and what the possible outcomes and ramifications are.\(^1,11\) One strategy doctors can use is the “teach-back” method, which asks patients and their caregivers to demonstrate that they understand what they heard by explaining it in their own words.

Finally, solo doctoring needs to go by the wayside. While most of the research on healthcare communication focuses on a two-person, patient-physician dynamic, today, a team-based approach, commonly known as integrated care or patient-centered care, is gaining popularity.\(^6\) Shore is making everything about the team. Each morning, he and his medical assistants have a “care huddle,” during which they strategize about the patients coming in that day. His assistants play a bigger role in care, renewing prescriptions and briefing him before he enters the exam room.\(^10\) One big advantage to the group approach is that team members can reach out to patients to provide information and answer questions that time-crunched physicians aren’t able to.\(^6\)

**Strategies for Patients to Improve Communication**

Because doctors have limited time, patients need to ensure that they are mindful of that by preparing ahead. They should think in advance about the questions they want answered and prioritize them, highlighting the main three of four issues they want to discuss, so they don’t get nervous and forget something important. Too many issues will likely cause their doctor to get behind and cause other patients longer waits. Another appointment can be scheduled for other, less important issues patients want to discuss.\(^11,12\)

Before the visit, patients should familiarize themselves with their medical history, keep a diary of their symptoms and concerns, list medications they are taking and their dosages, and notify the scheduler ahead of time if they think their questions will take an extended time to answer.\(^13\)

During the visit, it’s important that patients don’t provide a lot of superfluous information, but instead get right to the point. They should accurately describe their symptoms so the doctor has the necessary tools to diagnose their condition and prescribe appropriate treatment. Useful items to disclose are a list of medications and supplements being taken, recent symptoms and the dates they occurred, recent tests and names of other doctors they are seeing. Most importantly, patients should be sure they are describing their symptoms rather than diagnosing them. The same is true with medical records. Patients need to let doctors review the records rather than hearing an interpretation of them.\(^11,12,13,14\)

Some studies say it takes 23 seconds before doctors interrupt their patients. If interrupted, patients should ask their doctor to stop and listen to the entire list of symptoms or to the entire question. Sometimes, simply holding up a hand will alert the doctor to stop and listen.\(^11\)

Being assertive is important, so patients shouldn’t be afraid to ask questions. If they feel their questions haven’t been answered, they should ask if an additional appointment can be made, whether an appointment can be extended or if there are other staff members who can address the questions. However, they should also balance assertiveness with respect and understanding. It’s equally important to voice appreciation for positive aspects about their communication and treatment.\(^13\)

If doctors use a lot of “med-speak,” patients need to stop their doctors and ask them for a definition or description of what they are talking about. And, patients should always ask what to expect next so that they can understand what is going on immediately and what the outcomes might be. For example, if a doctor sends a patient for a medical test, he or she can ask what the doctor expects the results will be or what the possible outcomes might be and what they would mean. By managing expectations, patients will have more confidence about the process.\(^12\)

Before leaving the appointment, patients need to find out how to best keep in touch between office visits, whether it is through the nurse, via email or by leaving messages at the front desk.\(^13\)

**A Two-Way Street**

A substantial amount of research supports the benefits of effective communication and health outcomes for patients and healthcare professionals. Yet, effective patient-doctor communication is a two-way street. According to the Institute of Medicine, “the patient-centered care model underscores the essential features of healthcare communication, which relies heavily on core communication skills such as open-ended inquiry, reflective listening and empathy as a way to respond to the unique needs, values and preference of individual patients.”\(^15\) But, patients also
have a responsibility to learn good communication skills, especially in this age when the Internet empowers them to be active participants in their own care. An understanding of the causes of communication breakdown and mutual respect will help patients and doctors overcome the barriers to communicating well with each other.

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

References

Imagine caring for your child with hemophilia with no factor, refrigerator, running water, electricity, or transportation to a clinic. This is the reality for thousands of families in developing countries. For just $20 a month, you can help an impoverished child with hemophilia. Become a sponsor today!

www.saveonelife.net / contact@saveonelife.net
Caring for people with hemophilia around the world—one at a time.
Nearly 300 years ago, German physician Paul Gottlieb Werlhof discovered a disorder he labeled morbus macululosus hemorrhagicus. Today, the condition is known as idiopathic (immune) thrombocytopenic purpura, or ITP for short. It is estimated that among adults in the U.S., 66 cases per million are diagnosed with ITP each year, and among children, approximately 50 cases per million are diagnosed.

**What Is ITP?**

Idiopathic means the cause is unknown. Thrombocytopenic refers to a decreased number of platelets in the blood, and purpura pertains to the purple discoloring of the skin, much like a bruise. In a nutshell, ITP is an autoimmune disease that mistakes the body’s platelets as foreign and destroys them. Platelets are sticky cells that act as plugs to stop bleeding episodes. Those with ITP have fewer platelets, so they bleed longer than individuals with normal platelet levels. Platelets also play a role in storing serotonin, a brain neurotransmitter that is responsible for appetite and mood regulation, as well as sleep/wake cycles. Thus, a decrease in platelet counts may negatively affect these functions as well.

There are two types of ITP: acute and chronic. Acute ITP is most frequently seen in children between 2 years and 6 years following a viral illness such as rubella, chicken pox or hepatitis. Acute ITP generally has a very sudden onset,
Idiopathic Thrombocytopenic Purpura

It is estimated that 116 out of one million individuals are diagnosed with ITP each year. While no one knows for sure what causes this autoimmune disease, ITP patients can enjoy a fairly normal life with proper treatments and lifestyle adjustments.

Symptoms of ITP

Platelets are produced in the bone marrow by cells called megakaryocytes. As megakaryocytes mature into larger cells, they undergo a process of fragmentation that results in the release of more than 1,000 platelets per megakaryocyte. These platelets have proteins on their surface that make them sticky, allowing them to bond to each other and adhere to breaks in blood vessel walls. They also can change shape and extend long filaments to fill and stop a bleeding blood vessel.²

Typically, treatment is not required, and the disorder does not usually recur.³ According to the National Organization for Rare Disorders, acute ITP accounts for approximately 50 percent of cases, with 80 percent of children experiencing this form.⁷

Chronic ITP can occur at any age, and the symptoms can last a minimum of six months, several years or a lifetime. Adults are more likely to experience chronic ITP, but it can affect children and adolescents as well. Females, in general, are diagnosed two to three times more often than males. ITP can recur often and require continual follow-up care with a hematologist.³

There are two types of ITP: acute and chronic.

There are two types of ITP: acute and chronic. Individuals with moderate ITP might exhibit numerous petechiae; bruises larger than 5 centimeters; intermittent nose bleeds that last longer than 15 minutes despite pressure; recurrent bleeding from the gums, lips, mouth, esophagus and intestines; prolonged bleeding of cuts; and blood in the urine, known as hematuria. If a patient suffers from severe ITP, symptoms can include extensive petechiae, large bruises and continuous bleeding from the gums, lips, mouth and throat. Severe ITP can be life-threatening if bleeding occurs in the brain, lungs, muscles or joints.⁶

In some instances, frequent bleeding episodes might result in anemia, which could produce fatigue and weakness.
Some women may suffer from prolonged and heavy menstrual bleeding. Additionally, people with ITP may experience fevers and abnormal enlargement of the spleen.

Diagnosing ITP

Doctors often diagnose ITP by ruling out other potential causes of bleeding or low platelet count such as infection, acute leukemia, aplastic anemia, medication side effects or bone marrow failure. If test results are normal with healthy red and white blood cells and otherwise healthy bone marrow, then the attending physician can order a number of tests to diagnose ITP. First, a complete blood count (CBC) will measure the size, number and maturity of red and white blood cells and platelets. In ITP, the red and white cell counts are normal. Second, a blood smear test, in which a drop of blood is placed onto a slide and then observed under a microscope, will confirm the number of platelets in the CBC. Third, an antiplatelet antibody test looks for platelet antibodies in the blood. If the antibodies have destroyed a considerable number of platelets, the doctor may diagnose the individual with ITP. Last, a bone marrow exam also can help determine the cause of low platelet count. The exam might include a bone marrow biopsy, which removes a sample of solid bone marrow, or a bone marrow aspiration, which removes the liquid portion of the marrow. Usually, the samples are taken at the same time under local anesthetic, and are performed by inserting a needle into the hipbone through an incision.

Treating ITP

Currently, there is no cure for ITP; however, there are a number of conventional treatments available to help manage it and increase platelet count. Physicians usually prescribe a round of prednisone, an anti-inflammatory oral steroid, as the first line of defense to gradually increase platelet levels. Prednisone also has the additional benefit of strengthening vein and artery walls, which helps prevent unwanted bleeding. The dose of prednisone is slowly diminished over a course of weeks or months. With this treatment, some individuals experience increased platelet levels, but most require a long-term low dose to keep their platelet counts within an acceptable range.

In 1981, scientists observed that certain fractions of antibodies from healthy blood donors could be used therapeutically to increase platelet counts and slow the destruction of platelets in patients with acute and chronic ITP. These antibodies, known as immune globulins (IGs), have now become one of the standard therapies to treat severe or chronic ITP. Seven IG products have been approved by the U.S. Food and Drug Administration (FDA) to treat ITP: Baxter Healthcare’s Gammagard S/D, Bio Products Laboratory’s Gammaplex, CSL Behring’s Carimune NF and Privigen, Grifols’ Gamunex-C, Kedrion Biopharma’s Gammaked, and Octapharma’s Octagam 10%. All of these IG products are administered intravenously (IVIG). IVIG has also been approved for use by pregnant women with ITP because of the decreased risk to the health of the mother and the baby compared with other ITP treatments. Although IVIG is a temporary treatment that must be repeated every 10 to 21 days to maintain adequate platelet levels, it is effective in blocking platelet removal.

When an individual’s platelet count is below 100,000/µL, that person is considered thrombocytopenic.

In addition to these diagnostic tests, a doctor can look at an individual’s medical history to determine if he or she has ITP. The Platelet Disorder Support Association (PDSA) has a helpful list of 25 items that patients can mention about their symptoms and activities to help their doctor determine the right diagnosis. The list includes platelet count history; whether the person has ingested bitter melon, wood ear mushrooms or quinine (tonic) water; any new prescriptions, non-prescriptions or supplements that could be linked to a drop in platelet count; shots or vaccinations in the month prior to the decrease; conditions like hepatitis C, lymphoma, lupus or HIV; recent out-of-country travel; family members with a bleeding disorder; recent change in diet and/or exercise regimen; animal bite or scratch; recurrent stomachaches or ulcers; exposure to chemicals; hearing problems; thyroid problems; swelling joints; sun sensitivity rashes; hair loss; feeling of numbness in extremities; excessive alcohol consumption; or recent hospitalizations. The doctor also may perform a physical exam by looking for petechiae or bruising of the skin or mucous membranes.
The drug anti-D (WinRho SDF), a form of IG, also was approved by FDA to treat individuals with ITP who are Rh positive (approximately 85 percent of people are) and have a spleen. Similar to IG, the drug is administered intravenously with short-term effects that last about one month. However, sometimes the therapy results in long-term platelet count increase. Anti-D can be administered repeatedly in affected individuals, including children, who have acute or chronic ITP. Unlike IVIG, anti-D antibodies are not suitable for pregnant women.7,12

In 1916, the first splenectomy (removal of the spleen) was performed in Prague, and it is now an approved surgical procedure for chronic ITP.6 Since the destruction of platelets generally takes place in the spleen, its removal often results in increased platelet levels. A splenectomy is effective in about two-thirds of ITP patients who undergo the procedure. Because the spleen plays an important role in cleansing the blood of bacteria, tumor cells and other foreign materials, individuals who undergo a splenectomy are more susceptible to infections and are generally vaccinated against the most common ones. Occasionally, those who have a splenectomy experience a relapse, and their platelet counts drop again. There is no reliable way to predict how effective this procedure will be for an individual. However, some studies have shown that people age 40 and younger typically have better results.12

In 2008, FDA approved two thrombopoietin (TPO) receptor agonists to treat ITP. Romiplostim (Nplate, manufactured by Amgen Inc.) is a subcutaneous injection that stimulates bone marrow megakaryocytes to produce platelets. It is for patients with ITP who have had a poor response to corticosteroids, IGs or splenectomy. Eltrombopag (Promacta, manufactured by GlaxoSmithKline) is a pill-form therapy for patients with chronic ITP to help boost platelet levels and reduce bleeding.7

A number of other treatment options and available drugs are also available to help patients manage ITP. These include immunosuppressant drugs, antibiotics, Danazol, Rituxan and chemotherapy drugs.12

Living with ITP

Combining lifestyle changes with ongoing care can help patients better manage complications associated with ITP. Hematologists, doctors who specialize in diagnosing and treating blood disorders, can be especially helpful with lifestyle changes because they are familiar with treating people with ITP.14

In its free publication, Living with ITP: Answers to Common Questions, PDSA recommends a macrobiotic diet for those who have ITP because it eliminates “many foods that can cause allergic reactions. Following the macrobiotic diet reduces the allergic load on the body and reduces strain on the immune system.” A macrobiotic diet is a high-fiber, vegetarian, non-dairy, whole-foods diet that is similar to a Mediterranean or paleo diet.15

Patients are advised to avoid medications that contain ibuprofen or aspirin because they may negatively affect the body’s platelets, increasing the risk of bleeding.14

Currently, there is no cure for ITP.

Physicians also recommend that individuals stay away from contact sports like boxing, football or karate because they may increase the risk of injury, including life-threatening head wounds, and can put patients at risk for bleeding.14

Safe activities can include walking, swimming, Pilates and dancing.16

However, before patients make any changes to their diet or exercise regimen, it is important that they discuss these changes with their doctor. If a child is diagnosed with ITP, the child’s parents should ask their doctor to see whether certain activities should be restricted.

It’s wise for patients to watch for signs of infection such as fever, especially if they have undergone a splenectomy.14

Having a splenectomy makes it difficult for most adults to handle three types of bacterial infections, so doctors frequently vaccinate them with polyvalent pneumococcal, meningococcal C conjugate and haemophilus influenzae type b (Hib) vaccines before the procedure. Younger patients may be asked to take small daily doses of prophylactic antibiotics.15

Patients with ITP often experience bleeding gums when they undergo dental procedures. According to the medical advisors from PDSA, a stable platelet count of 60,000/µL is acceptable for “orthodontic procedures to be done without additional hemostatic support. Uncomplicated extractions can also be performed without additional agents. However, some doctors would prescribe epsilon aminoacproic acid (a drug used to control bleeding) every four to six hours starting the morning of the extractions and for two to three days afterward.”15

Having ITP does not prevent a woman from becoming
pregnant and delivering a healthy baby. But, pregnancy does require special consideration and close management between the woman’s hematologist, obstetrician and pediatrician. A woman’s platelet count may drop in the third trimester or she may relapse. Treatments like IVIG can be given to raise the platelet count for delivery. For delivery, most physicians recommend maintaining a platelet level between 20,000/µL and 30,000/µL through pregnancy and above 50,000/µL near term. A higher count between 80,000/µL and 100,000/µL is required for epidural anesthesia.17

Combining lifestyle changes with ongoing care can help patients manage complications associated with ITP.

Some drugs that are used to treat ITP, including immunosuppressants (except azathioprine) and platelet production stimulants, are not favorable choices for pregnant women because they could harm the fetus. In addition, TPO agents are not recommended during pregnancy because they can cross the placenta. Women should wait up to a year after Rituxan treatments end before becoming pregnant. Some studies link prenatal corticosteroids like prednisone to mental health problems later in the child’s life.17

ITP Outlook

For most children and adults, ITP is not a serious or life-threatening condition.16 Approximately 90 percent of children with ITP gain complete remission within three to seven years, and the severity of bleeding decreases with time.6 In some patients, platelet counts recover spontaneously, usually within the first few weeks. These patients may have another cause of thrombocytopenia such as a viral illness.

About 5 to 10 percent of patients have a stable disease, with platelet levels between 30,000/µL and 100,000/µL, which may persist for months to years and rarely requires treatment. Of the patients who have a consistently low platelet count between 25,000/µL to 30,000/µL, approximately 75 percent go into remission with the use of either corticosteroids or a splenectomy. Most of the remaining patients can manage their ITP with other forms of treatment. The mortality rate for chronic ITP is only between 1 percent and 4 percent, and is generally attributed to intracranial hemorrhage.19

No one knows for sure what causes ITP, but with proper treatments and lifestyle adjustments, individuals can enjoy a fairly normal and fulfilling life. ■

CARLA SCHICK is a staff writer for IG Living magazine.

References

13. FFF Enterprises, Inc. IG Immune Globulin (Human) Reference Chart.
“You can lament what is lost to you, whether it’s opportunity, a person or your health, but clinging to anger is no way to experience life.” — Rebecca Zook in “Life Lessons,” excerpted from Chronic Inspiration.

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Let’s Talk!

By Trudie Mitschang

Jamie Stewart was diagnosed with an atypical presentation of chronic inflammatory demyelinating polyneuropathy (CIDP) in October 2010. Frustrated by his lack of treatment options, Jamie made the difficult decision to travel to Moscow and undergo hematopoietic stem cell transplantation (HSCT). Jamie shares his experience and explains why he believes the potential benefits outweighed the risks of this controversial treatment plan.

Trudie: Why did you decide to pursue HSCT?
Jamie: I made the decision when I realized that I was not going to receive additional care besides immune globulin therapy and symptomatic relief such as pain killers and muscle relaxers. I had seen many neuromuscular specialists and all of them suggested a more aggressive treatment plan. Unfortunately, my local doctors would not follow those recommendations. After many hours of research and worsening symptoms, I decided if I wanted to get better, I had two choices: either move to another state to gain access to a CIDP specialist, or pursue a procedure that could put my CIDP into remission.

Trudie: What type of HSCT did you receive?
Jamie: I received nonmyeloablative allogeneic HSCT. It basically means that my immune system was reset, like rebooting a computer. My own stem cells were collected and used to help reboot my immune system, and my bone marrow was not damaged during the procedure.

Trudie: Why did you choose to go to Moscow for treatment?
Jamie: I initially applied to the Feinberg School of Medicine in Chicago as part of their ongoing HSCT U.S. Food and Drug Administration (FDA) trial. I have an atypical presentation of CIDP and, therefore, did not meet all of the study’s criteria. I then applied to HSCT facilities in Israel, Moscow and Italy. I was contacted by Israel and Moscow, and I was told I was a candidate. I emailed patients who had been at each facility, researched costs, aftercare and ease of communicating with the physicians, and in the end, we chose Moscow.

Trudie: What kind of support did you receive from colleagues, family and friends?
Jamie: My wife and I have had excellent support from both of our places of employment. Our families are very supportive, and they even set up a fundraiser to help with defraying some of the costs of treatment.

Trudie: What kind of skepticism did you encounter?
Jamie: The biggest pushback I received was from many of my doctors. I was repeatedly told: “You are not sick enough to try something so risky. This procedure will most likely kill you.” It was, and is, very frustrating talking with a specialist about something they are unwilling to learn about. I would send studies and details on the protocols used for HSCT to my doctors, but instead of reading them and trying to understand, I was told it was “voodoo medicine.” Sadly, these same doctors had no suggestions for better treatment options.

Trudie: HSCT is expensive. How did you handle the out-of-pocket costs?
Jamie: The two facilities I considered were Moscow (approximately $40,000) and Israel (approximately $96,000). Those prices are the cost of treatment. Additional expenses include plane tickets, time lost from work, hotel and meal costs, and foreign transaction fees. I was very fortunate because my cousin demanded that I set up a GoFundMe campaign. It was very successful. My family and friends also organized a local fundraiser. I recommend starting early with fundraising and, if you are like me, swallowing your pride. People want to help, but
sometimes don’t know how. I don’t recommend trying to do this alone.

**Trudie:** What was the most difficult part of the treatment?

**Jamie:** For me personally, the pain has been the worst. One reason I sought out HSCT was to hopefully rid myself of the ongoing nerve pain, and I didn’t fully understand that my symptoms would get worse before they improve. The first 12 months after HSCT are referred to as the “roller coaster” months, and during this time, I can expect really good and very bad days. I like to remind people that HSCT is not a sprint, but rather a marathon. Patience is crucial to a successful outcome. Also, the majority of people undergoing HSCT will not have the pain that I have; this is unique to my atypical presentation of CIDP.

**Trudie:** What is your prognosis?

**Jamie:** My treating doctor in Russia gave me an 80 percent to 90 percent success rate at putting my CIDP into remission. At the six-month mark, I am required to get a lumbar puncture to see if proteins have dropped in my spinal fluid. If my proteins are in a normal range, then my immune system should no longer be attacking my peripheral nervous system. An added benefit of HSCT is that if my immune system is successfully reset, many of the functions that I lost might be regained.

**Trudie:** You’ve expressed a desire to advocate for access to HSCT. Tell us about that.

**Jamie:** I have shared my story with as many people as possible. I have shared the studies and research with my local doctors and participated in a couple of TV interviews for the local networks. I have created a blog to share my experiences. I have also contacted my state congressional representatives asking for their help in moving this through FDA in a faster manner. I sent my story to national news organizations, talk shows, etc. Unfortunately, there has been little interest. I find that confusing and maddening. I will continue sending emails, and maybe, someday, someone will read it and want to know more about HSCT. Currently, HSCT can treat many different autoimmune disorders, including multiple sclerosis, diabetes, lupus, Crohn’s disease, rheumatoid arthritis, CIDP, pemphigus, dermatomyositis, Devic’s disease, myasthenia gravis, polymyositis and scleroderma, with more autoimmune diseases being added all the time.

**Trudie:** What advice do you have for patients who want to learn more about HSCT?

**Jamie:** HSCT is a procedure that has been used since the 1960s to treat cancer and in the early 1990s to treat hematologically-rooted autoimmune diseases. Your own stem cells are used to help you recover faster from the procedure. Do your own research because there are many treatment centers claiming cures by using stem cell therapy, but any HSCT patient will tell you that without chemotherapy, there is no remission. Also, you will need to be your own advocate as many healthcare professionals are not informed about HSCT. If you truly want this, don’t give up. Fight for access to the best care possible. It is your quality of life that is at stake.

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**If your life depends on immune globulin and you have a unique experience to share, we want to feature you in this column! Email us at editor@IGLiving.com.**

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**TRUDIE MITSCHANG** is a staff writer for IG Living magazine.
WE’VE ALL BEEN there: the days when we put on our best pair of cranky pants and are being the best cranky person we can be. Nothing is right; everyone and everything is annoying us. But, then we share our woes with our friends or loved ones and, all of a sudden, what seemed crummy becomes funny. The moment has passed, and there’s no need to hold onto those negative feelings.

But, recently, I’ve had the pleasure of being in contact with people who thrive on being miserable and aren’t satisfied until I am too. Their cranky moments are permanent, and they like it that way. Most of the time, we get to choose the kind of people we want to surround ourselves with and avoid those we don’t. The world’s a big place; we should be able to avoid the people who suck the life out of us. Every now and then, though, there are people we are thrown together with and can’t avoid, whether it’s for business or social occasions, or they just keep crossing our paths. Like gum on the bottom of our shoe that is aggravating and annoying, we can’t shake them off.

They poke, prod and use every method they can to upset us so we’re finally in just as foul a mood as they are. Then, we feel stressed out, which will probably cause flare-ups, leading to a chain of negative health effects spiraling out of control. Mission accomplished on their end! Misery loves company, and they’ve made us part of their crowd.

The older I get, I think I’ve finally gotten rid of “those people” and, yet, they keep turning up like a bad penny. So I’d like to share a few of my personal tools for dealing with the downer duds in life:

1) Don’t engage with them or how I like to put it: “Don’t poke the beast.” Being hostile is the only way they know how to communicate. If you need to answer them, as one of my friend’s says, “hit them over the head with the feather pillow of love.” Kind words always leave a good taste in my mouth.

2) I am blessed with many wise friends. Here’s a gem of advice from one: “There will always be those people who test you. Let them test you and pass!” Life is too short, as we know, to fill our hearts and heads with negative feelings. We fight enough with our own bodies; save your energy for those important battles.

3) Find a type of meditation to help ground and calm you. I’ve been practicing tai chi for several months now. It’s a physical and mental release for me. There isn’t just one path for getting some balance in your life. It could be watching movies, taking your dog for a walk, getting crafty with a hobby or just getting out and people watching. When you stop obsessing about what’s wrong and engage in an activity, your mind and body benefit.

Eleanor Roosevelt once said: “No one can make you feel inferior without your consent.” Be kind to yourself, and don’t let negative words hold sway over you. There will always be people who feel the need to put others down to lift them up. We are chronic illness warriors, and we have faced much worse than a few harmful words being hurled at us. So, the next time Negative Ned bothers you, just smile and drown out the verbal tantrum with MC Hammer’s song “You Can’t Touch This,” because you’ve made the choice not to let him.

STACY OLIVER was diagnosed in 2008 with multifocal motor neuropathy (MMN). She is the assistant director of the Center for the Writing Arts at Northwestern University, and she is working on her supersecret identity as Neuropathy Girl, who will one day save the world after her infusion and a nap.
THIS IS WHAT  my wedding day is supposed to look like: I’m wearing the perfect dress, I’m gliding down the aisle, and the only thing on my mind is getting to the other end to say my vows.

Here comes the bride,
Immunoglobulin levels aside,
She’s ready for the wedding,
As long as sick guests stay outside!

This is what my wedding day is probably going to look like: I’m frantically waving over the makeup artists to help me powder my nose after sneezing six times in a row. I’m wobbling, fatigued in high heels I didn’t practice walking in, and I’m gratefully nodding at my maid of honor as she remembers to rip the hospital ID bracelet off of my wrist just before I’m pushed into the ceremony.

Planning to produce or even simply lugging a swaying, hanging bag of 0.9% sodium chloride behind me? Will I have the energy to dance my first dance? Or hold that smile for every picture when the vertigo is making me see six photographers and five more bridesmaids than I’d picked out dresses for?

It would be very easy to call off the whole thing and have a quiet, inexpensive and more flexible event. (Just the three adjectives that I wanted to describe my big day.)

And it is a “big day.” But, in reality: My illness complicates every day. And whether I’m switching to online classes, holding the parties at my house, delegating chores or using a wheelchair — I’ve made friendships, relationships, school, jobs and holidays all work around the complications. So, why would I ever let being a bride slow me down now?

I’m here. I’m living. And, if the big day comes and I’m walking down the aisle with an IV trailing behind me, we’re going to dress it up in flowers and put some vapor rub in the bouquet. It’s all just part of the plan.

ILANA JACQUELINE is a 24-year-old 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.
CROWDED SHOPPING centers and malls. Oceans, rivers and lakes. Public showers, bathrooms and (gasp!) porta-potties. Hospitals, physician offices and medical laboratories. Now, sing with me like your life depended on it: “These are a few of the immune-deficient body’s most unfavorable places to be!”

Since our kids, 17-year-old Calvin, 15-year-old Caleb and 13-year-old Molly, were diagnosed with common variable immunodeficiency (CVID) as babies, we’ve done all we can to avoid the above-mentioned places. We’ve been lucky; we’ve suffered with only one cryptosporidium infection five times, being the 2,005th persons to have been infected, according to our local governmental germ-chasing agency.

Needless to say, water and splash parks are not on our family’s bucket list of places to visit. But, when sending our children to a STEM (science, technology, engineering and mathematics) academy, we take the risk of our children being exposed to a protozoan or two. For the past eight years, our CVID kids have thrived in one of Idaho’s finest public schools: Galileo STEM Academy. I have helped in the classrooms, volunteered for PTA activities and stuffed envelopes until I knew everything there was to know about the moms who failed to show up to stuff envelopes. But, when one of my favorite sixth-grade teachers, Mrs. Carden, asked if I’d chaperone a field trip, my response should have been, “Where to?” instead of “Why not!”

“Lunches packed?”
“Check!” Molly confirmed with age-appropriate excitement.
“Sweatshirts?”
“Double check!”
“Hand sanitizer?”
“Mom, can we pul-eeeeeze go? I
don’t wanna be late!” Molly begged, with age-appropriate annoyance.

As we headed to school, we talked about all the fun we were going to have: the yummy snacks I packed for lunch and what boy du jour she wanted me to rate on the cuteness scale. I couldn’t help but think how quickly kids grow up, while Molly giggled on about boys in her class and romances between her friends she’s known since kindergarten, when boys were “icky.” Pulling into school and seeing the throng of tweeners mop-headed boys and blushing young ladies, I thought: I don’t think we’re going to the zoo today! Little did I know how right I was!

We packed the buses to the gills, making sure everyone was in the right place next to the right person for the right reasons. Mrs. Carden blew into the handheld mic, making sure it was working.

“Can everybody hear me?” Mrs. Carden asked, speaking forcibly into the ancient mic. A collective and obnoxious “YEEEEEEEES!” rattled our bus driver, causing him to tilt his head back so he could glare into the face, and she fought a laugh trying to explain that “it’s a waste water plant, Cheryl. You do know what waste water is, right?”

A sick feeling grew in my stomach as the bus bumped and jumped over the rocky driveway leading us to the Water Shed.

“Waste water, as in the soapy water I use to wash dishes or maybe the runoff from washing the car?” I asked with great concern in my tone.

“You’re missing one very important type of waste water, perhaps the most important one, Cheryl!” Mrs. Carden snickered.

I can’t begin to tell you how many ways I tried to get out of being a chaperone through the “poo-poo plant.” Of course, had I known this was how I was going to be spending my day, I’d have insisted Molly not go as well due to her immune system’s inability to fight off what was being processed. And, for heaven’s sake, how does one chaperone hormonal sixth-graders through human, er, um, crap! The freak-out feeling began to sweep over me, and all I could think of was how much money I was going to sue somebody for inviting me and my immune deficient daughter to a crypto-sporidium’s stag party! Who’s crazy idea was it to allow innocent children to tiptoe through the poo-poo!

Suddenly, I felt a warm and familiar hand grab mine and lead me to the next station. Molly seemed to have a deeper understanding about this day beyond the mega-germs. I looked my daughter in the eyes and witnessed an undeniable confidence in trusting her immune system (and the immune body) to protect her from any type of badass bug that dare mess with her.

From that moment on, Molly and I were exploring every station of the waste water treatment plant on the edge of insanity. We were learning and living dangerously! The skimming treatment was my favorite: poop was bubbling as enzymes engulfed the “bad stuff.” Molly’s favorite came at the end when the water is exposed to ultraviolet rays in order to kill anything left (a very science-y process I can’t explain). Then, our guide dips a cup into the water and takes a drink to prove it’s clean enough to drink. No one else dared, but it sure made for a spectacular finale.

When we got back to school, I had a great chat with one of the teachers who remained with the kids who didn’t go on the field trip.

“Why didn’t you go, Mrs. Sohn?” I asked. “It really is fascinating.”

“Well, I didn’t go because I’m a massive germaphobe, and I’m so worried I’ll get some nasty intestinal thing from that place,” she replied.

The next day, when I picked Molly up from school, she couldn’t stop talking about the Water Shed.

“I didn’t think engineering was that entertaining!” Molly laughed.

“What about the rest of your day, dear?” I asked.

“We had a sub in Mrs. Sohn’s class.”

“Oh, really? Do you know why?”

“Rumor has it she’s got a nasty stomach bug,” Molly answered nonchalantly.

CHERYL L. HAGGARD is a stay-at-home mom and has three children who have common variable immune deficiency.
Parenting

Family Adventures and Travels with PI

Traveling with primary immune deficient kids can be safe and enjoyable with a little planning.

By Mark T. Haggard

ABOUT 10 YEARS ago, our family traveled to the Immune Deficiency Foundation (IDF) national conference at Walt Disney World, and a funny situation occurred that started with an ear infection in my then-3-year-old primary immune deficient (PI) daughter. While we were waiting for a doctor in the ER at a hospital in Old Oak, Fla., my wife engaged a Southern woman in a conversation concerning an activity that once landed her in the ER. To this day, my wife swears she heard her new friend say she did “witchcraft” and was “drilling a hole in a bird.” I still believe the woman said she did “woodcraft” and was “drilling a hole in a board.” We have gotten a lot of mileage out of that story, and there were a number of lessons we learned on that trip for families traveling with PI kids. The physical demands of travel can be stressful with healthy kids, but add an immune deficiency, and travel can almost seem not worth the effort. But, if you prepare and are proactive, you and your PI kids can enjoy a safe, enjoyable and well-deserved vacation.

Be Aware of Your Surroundings

We stayed overnight in Old Oak on our drive from Pensacola to Orlando. When Molly started screaming from the pain of her ear infection, we took her to the ER. An hour and a half later, we were back in our hotel room with a bottle of Augmentin.

From this, we learned to keep our immune-compromised children out of areas that are breeding grounds for germs such as gnoshing at out-of-town fast-food places or swimming in public pools. I’m not sure if that was the actual culprit, but Molly and I spent a good hour in the hotel pool before the incident at Old Oak.

Play the Immune Deficiency Card Early and Often

A full ER waiting room can be as much a germ factory as the ball pit at a fast-food playground or the water in a little-serviced hotel pool. Out comes the PI card. “My daughter has an immune deficiency, and I’m afraid she might become infected by one of the diseases that one of your Old Oak waiting room crowd might have.” That trumps the waiting room, and we get set up in a room next to radiology.

Anytime we are in waiting areas with large crowds, we play the PI card. We have been given special arrangements while going through airport security lines, special seating at U.S. Navy Blue Angels air shows and a place at the front of the line of people going to the top of the Space Needle.

On another front, the possibility of discounted services increases when a vacation is in conjunction with a medical conference or appointment. My wife is on a first-name basis with the manager of one of the major rental car outfits at Seattle-Tacoma Airport; on any of our trips to Seattle Children’s Hospital, we can get discounts and upgrade to a better car. We have received significant discounts at Disney World hotels while attending IDF conferences. Keep in mind that most of the expenses of a medical conference or appointment can be written off on federal income taxes.

What the Experts Recommend

There is no reason to be limited to within a 100-mile radius of your PI child’s immunologist. The Centers for Disease Control and Prevention advises the following for those traveling with a chronic illness:

1. Ensure your illness is well-controlled; see your physician to ensure the management of your illness is optimized.
2. When in doubt, seek a pre-travel consultation four to six weeks before departure to ensure adequate time to respond to immunizations and to try new medications.
3. Ask your physician about previous health-related issues encountered during travel.
4. Get a physician’s letter outlining existing medical conditions, medications prescribed and any equipment required to manage the condition. Some travelers should consider a medical assistance company that offers medical history storage that can be accessed worldwide if necessary.
5. Pack medications in their original containers in carry-on luggage, and carry a copy of prescriptions. Also,
ensure you have sufficient quantities of medications for the entire trip, plus extra in case of unexpected delays. Since medications should be taken based on elapsed time and not time of day, travelers may need guidance on scheduling when to take medications during and after crossing time zones.

6. Educate yourself regarding drug interactions. Some medications may interact with others prescribed for self-treatment of travel-associated sickness (particularly travel abroad). Discuss all medications used, either daily or on an as-needed basis, with your doctor.

7. Consider buying travel insurance. Three types of insurance policies can be considered: 1) trip cancellation in the event of illness; 2) supplemental insurance if traveling overseas so that money paid for healthcare abroad may be reimbursed; and 3) medical evacuation insurance.

8. Devise a health plan that gives instructions for managing minor problems or the exacerbation of underlying illnesses and that includes information about medical facilities available in the destination area.

9. Consider wearing a medical alert bracelet, or carry medical information on your person.

10. Keep well-hydrated, wear loose-fitting clothing and walk and stretch at regular intervals during long-distance travel.

11. Pack a health kit.

Michael Zimring, MD, a specialist in travel medicine at Mercy Medical Center in Baltimore, Md., and co-author of the book Healthy Travel: Don’t Travel Without It! makes a few additional recommendations. First, he recommends patients get their doctor’s approval to travel. He also recommends checking out medical facilities at your destination to ensure they can manage your specific health issues. He stresses the importance of having all relevant documentation related to any illnesses translated into the local language when traveling overseas. And, he suggests parents bring any medication a child has been prescribed for occasional use, even if they have not needed it in a while. Your pharmacist can be consulted about the best way to store medication since some drugs are sensitive to temperature and may not survive a trip in an airplane baggage compartment intact.

Finally, Dr. Zimring recommends considering the effects of your destination on your health. Breathing conditions are aggravated at high altitudes, and high humidity can exacerbate fatigue. That does not mean you should not visit such places, but you may need to adjust your schedule to allow time for extra rest, if needed. Parents should know their child’s abilities and limitations; planning beyond a child’s limits can be a disaster.

Other Thoughts

Allow children to bring something comforting. For my daughter, Molly, it was a pink blanket. For my son, Caleb, it was his stuffed dog, Josh. This settles the anxiety of waiting in an airport terminal or on a long car trip, as well as the potential trip to an ER in a far-off place. Caleb is 15 now, and he still has a special place in his bedroom for Josh. Molly plans on having part of her pink blanket sewn into her wedding dress.

Seek the help of a travel agent. While you can research any destination on the Internet, it is better to work with travel professionals. They can get you the best deals at the best prices (there are some not-well-advertised gems on the Disney campus), and many also have experience in organizing travel for people with health issues. In addition, they can help you find the small, little-known travel organizations that are better at targeting individual needs, as long as you are honest about your medical needs and ask questions about health facilities in the area.

Don’t Be Afraid of Vacationing with Your PI Kids

Families should not let a primary immune deficiency be an excuse to not get away. By using the wisdom of your immunologist and travel experts, you can take your PI kids on a vacation that will change their lives and yours; do not let those opportunities pass you by. Oh, and if your vacation takes you to Old Oak, Fla., tell them that the Haggards say “hi.”

MARK T. HAGGARD is a high school teacher and football coach, and has three children with PI, two of whom have CVID.
WHEN WE FIRST met, I was relieved. Finally, someone who was attentive, genuinely concerned and who really listened. Sadly, after five years, our relationship changed. It became overly familiar. Due to personal problems that he would disclose in moments of vulnerability, he became moody and distracted. His priorities shifted. I no longer knew what to expect. At times, he was rude and condescending, but he also had a compassionate side that kept me coming back. Finally, he lied — and cheated. I had enough. But had I reached that point too late?

My suspicions that something was off started a year ago, when my case manager requested a copy of my medical records, to no avail. I kindly asked the office staff to comply, but they became masters of avoidance. Was his ego that easily bruised that he would not want his treatment plan questioned by my other physicians? Or, did he suspect I wanted my file so I could seek care elsewhere? Months went by without results. I had to pick my battles, I thought. Exhausted, I gave up and stopped asking for what was rightfully mine.

Additionally, whenever I questioned the efficacy of a drug, my patience was tested. Rather than giving me an answer, he would compare me to other patients: “The woman who just walked out is doing fine on your same medication and dosage.” (Good for her, but how was that relevant to me?) And, if I brought up new symptoms or concerns, he would tell me about others who were “worse off but had such great attitudes,” as if trying to shame me for what he deemed to be baseless complaints. “You worry too much. You’re such a firecracker!” he would say.

Equally disturbing was his sudden refusal to give me refills on my medications, even though they had remained unchanged. This forced me to make an appointment at least every three weeks. Although it was inconvenient to make the two-hour drive to his office that often, I felt I had no other choice. With no medical records to corroborate my diagnosis and treatment, what new doctor was going to write orders for intravenous immune globulin (IVIG) and continue my pain-management regimen based solely on my word? He knew he had me cornered, and he took advantage of it.

But the writing was on the wall, or more accurately, on my Medicare claim summary. I was at the end of my rope and decided to examine each statement carefully; I figured that if nothing else, this could prove to a new doctor that I was already receiving IVIG infusions and that diagnostic tests to support my monthly treatments had already been done. Suddenly, the light bulb went off, and the madness made sense. I was shocked to find out that with each visit, he was billing for treatments he never provided!

I now understood why he needed me to come in so frequently. As for his lack of cooperation with my other providers and refusing to release medical records, the reason was as clear as the day is long: They were likely falsified to match what was billed. Insurance fraud not only costs us millions of dollars each year, but it has serious ramifications. Aside from being illegal, my care — as I now suspect is the case with many of
his other patients — became secondary to his pursuit of “supplemental income” (yes, I am being kind in my wording).

As much as we want to foster a relationship with those who care for us, in the end, they provide a service for a fee, and, as such, we have the power to make hiring and firing decisions as we see fit.

I get that he may have fallen into hard financial times (who among us hasn’t?), but his assumption that our years of working together would make me look the other way was an insult, and one that I could not overlook. My situation may sound extreme, but it is not uncommon. No matter what the issue may be — from bedside manners to competency and everything in between — there is no reason to hang on to a doctor based on fear of change or a distorted sense of loyalty.

As much as we want to foster a relationship with those who care for us, in the end, they provide a service for a fee, and, as such, we have the power to make hiring and firing decisions as we see fit. Although change may be a challenging and lengthy process due to insurance restrictions and other factors, there is always a second opinion to be had and a new choice to be made. Regrettably, the complexity of my overlapping illnesses then. Admittedly, there are times when I still struggle with the way I ended that relationship, or perhaps failed to do so since there was no final confrontation. I simply went away, quietly, because it was my hope that my absence would have a much more profound impact than any heated words we could have exchanged. Or, maybe it is my endless hope in humanity and belief that people are intrinsically good. Then again, that approach may just be my own defense mechanism to help me cope with this experience and not become jaded by it.

I trusted this man with my life, and a betrayal of this magnitude was not an easy pill to swallow. If you were faced with a similar problem, what would you do? Would you have handled things differently? Sound off by sharing your own cautionary tales, and spread wisdom by sharing tips based on your success stories.

PAULINA BROOKS is a blogger, writer and the founder of A Journey Home, an organization dedicated to helping veterans and their loved ones heal from the silent wounds of war. Passionate about life, Paulina has spent more than 20 years committed to ongoing self-healing and transformation. She lives in San Diego, Calif., with her husband, David, of 16 years.
MOBILITY ISSUES CAN affect anyone with a chronic illness, including those with respiratory problems, poor balance, limited strength and advancing age. Fortunately, there are many different products available that can help people move around with ease, style and independence.

Travel Mobility
Folding canes can make traveling with a walking stick easier because they can be disassembled for storage and then easily snapped back together for use. The key is to select the right cane based on need. If a cane is needed for balance, a standard cane with a single tip should be considered. If it is needed to bear weight, then a four-tip cane may be the better choice.1

Easy transport chairs are nice to have on hand for wheelchair-bound patients who enjoy the outdoors. Chairs feature sturdy handles and rugged wheels so that those seated can be moved either over rough terrain or up and down stairs with relative ease. They are foldable, lightweight and small enough to fit in most vehicle trunks. And, they can be used as emergency evacuation devices to quickly move those with special needs away from unsafe situations.

For those who want to enjoy mobile independence without having to use a manual wheelchair, a travel scooter is an option. Travel scooters not only provide powered mobility, but also transportability. Many are compact, lightweight and can easily be disassembled into separate components to load into a vehicle. Four-wheeled models allow for enhanced stability on rough terrain, and an ergonomic delta tiller can provide increased usability for those with limited hand strength or dexterity.

Need a Lift?
Stairlifts are ideal for patients who have a tough time traversing household stairs. With just the toggle of a switch or the push of a button, patients can ride with ease while in a comfortable sitting position. Stairlifts have three basic components: a track, a power pack and a seat. Domestic models are usually fitted directly onto the staircase with either a straight or a curved track, depending on the layout of the staircase. Some models feature safety sensors on the power pack and footplate that are designed to stop the lift if it encounters an obstruction. Some lifts also come with a remote control that allow the user to send them up or down the stairs without having to sit on them.

New Technology
Manual reverse wheelchair wheel attachments are the latest in mobility technology. Instead of the standard push propulsion, reverse wheels allow riders to pull the handrims to move forward. This allows users to engage the larger muscle groups in the upper back and shoulders, thereby reducing repetitive stress injuries to shoulders and wrists. The reverse roll technology functions very much the same way as rowing a boat, and has the added benefit of enhanced performance through responsive turning and acceleration. The wheels attach to most current manual wheelchairs.

The Right Device
Those with a chronic illness do not need to let mobility issues prevent them from doing the things they love. Freedom in movement is possible with the right device. Speak with a physician or physical therapist for recommendations.

CARLA SCHICK is a staff writer for IG Living magazine.

Reference
Crosswind Freedom Chair
The Crosswind Freedom Chair transports users up and down stairs and over rough terrain. It features arm rests, safety restraints, a large storage pocket and non-slip rubber hand grips. Two wheel styles are included: 5-inch polyurethane wheels and 10-inch Worry Free wheels for outdoor use. The chair weighs 23 pounds, has a 650-pound weight capacity, is made from weatherproof open-weave polyester and features a sturdy aluminum frame. It measures 60 inches long, 24 inches wide and 37 inches high (11 inches high when folded).
(707) 523-7535, www.crosswindconcepts.com

Ez2care Adjustable Folding Quad Cane
The Ez2care Adjustable Folding Quad Cane features a folding mechanism for easy storage, an ergonomically designed contoured handle that is compatible with right and left hand usage, and an anodized aluminum body and specially engineered plastic quad base to distribute stress evenly and provide maximum safety and endurance. The cane is adjustable from 29 inches to 37 inches in height, and can hold up to 250 pounds.
www.ez2care.com/adjustable-folding-quad-cane

Rowheels
Rowheels are aftermarket wheelchair wheels that feature a ½-inch quick-release axel that makes the reverse wheels compatible with most wheelchairs. Rowheels are designed to improve posture and reduce repetitive stress injuries to shoulders and wrists by allowing the user to pull to move forward and push to roll backward. They weigh 4 pounds and are made from magnesium alloy, and they come with the following available handrims: natural-fit surge, Q-grip, vinyl or anodized aluminum. Wheel sizes include 22 inch, 24 inch, 25 inch and 26 inch, and they have a weight capacity of 275 pounds and a maximum camber of 6 degrees.
(608) 721-0170, www.rowheels.com

Spitfire Scout 4-Wheel Travel Scooter
The Spitfire Scout 4-Wheel Travel Scooter is compact, lightweight and easily disassembles into five sections. It features adjustable seat and arms, a free-wheel release knob, a quick-connect battery pack, a delta-style tiller, anti-tip wheels, a rear reflector, flat-free tires and a large front basket. Its top speed is 4.25 mph, and it has a 9-mile maximum cruising range.

Sterling 1000 Straight Stairlift
The Sterling 1000 is a slim stairlift that carries its user up and down a straight staircase. It is available in six upholstery colors and can be supplied with optional powered features to fold the footplate and swivel the seat. The slim aluminum track has a hidden gear rack that offers points of contact at the top and bottom of the stairs to charge the batteries. The stairlift has a maximum weight capacity of 350 pounds, a 26¾-inch swivel radius, a 16¾-inch seat depth and a 4½-inch staircase track intrusion.
**Ataxia Telangiectasia (A-T)**

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

**Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**

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

**Evans Syndrome**

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

**Guillain-Barré Syndrome (GBS)**

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

**Idiopathic Thrombocytopenic Purpura (ITP)**

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

**Kawasaki Disease**

**WEBSITES**
- American Heart Association: www.heart.org/HEARTORG/Conditions/More/CardiovascularConditions/ChildhoodKawasaki-Disease_UCM_308777_Article.jsp?ikT112boePWE0
- 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 Neuropathy Association: www.neuropathy.org

**Multiple Sclerosis (MS)**

**WEBSITES**
- All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
- Multiple Sclerosis Association of America: www.msaa.com
- National Multiple Sclerosis Society: www.nationalmssociety.org

**ONLINE PEER SUPPORT**
- Friends with MS: www.FriendsWithMS.com
- MSWorld’s Chat and Message Board: www.msworld.org

**Myasthenia Gravis (MG)**

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

**ONLINE PEER SUPPORT**
- Genetic Alliance: www.geneticalliance.org

**Myositis**

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

**ONLINE PEER SUPPORT**
- The Cure JM Foundation: www.curejm.com
- Michigan Immunodeficiency Foundation: www.facebook.com/groups/180048062584350

**Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)**

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

**Pemphigus and Pemphigoid**

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

**Peripheral Neuropathy (PN)**

**WEBSITES**
- Neuropathy Action Foundation: www.neuropathyaction.org
- The Neuropathy Association: www.neuropathy.org
- Texas Chapter of the Neuropathy Association: www.handsfortheheart.org

**Primary Immune Deficiency Disease (PI)**

**WEBSITES**
- Immune Deficiency Foundation: www.primaryimmune.org
- Jeffrey Modell Foundation: www.info4pi.org
- International Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organisation for Primary Immunodeficiencies (IPOPI) — UK: www.ipopi.org
- New England Primary Immunodeficiency Network: www.nepin.org
- Rainbow Allergy-Immunology: www.uhospitals.org/rainbow/services/allergy-immunology

**ONLINE PEER SUPPORT**
- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: idffriends.org/forum
- IDF Friends: idffriends.org
- Jeffrey Modell Foundation Message Board: www.info4pi.org
- Michigan Immunodeficiency Foundation: www.facebook.com/groups/108048062584350

**Scleroderma**

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

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

**Stiff Person Syndrome (SPS)**

**WEBSITES**
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.genetica.org
- Living with Stiff Person Syndrome (personal account): www.livingwithsp.com
- Stiff Person Syndrome: www.stiffpersonsindrome.net
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- Coagulation Products
- Hyperimmunes
- Albumin
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