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IG Living magazine brings together patients, advocates and caregivers in the immune globulin (IG) community. For information about advertising in IG Living, download a media kit at igliving.com/Advertise.aspx. Or contact advertising@igliving.com.

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Celebrating a Decade of IG Living Magazine

HAPPY ANNIVERSARY IG Living magazine! This issue celebrates 10 years of our resolve to help inform you about your diseases and treatment options, give you strategies for communicating about your struggles with complicated illnesses, and assist you in advocating for yourself to get the care you need and deserve.

In this special anniversary issue, we recount the developments we’ve reported on during the past decade in the areas of diagnosis, treatment, safety, reimbursement and legislation — developments that have been crucial to the support of members in the IG community who rely on improvements in healthcare policy safeguards and enhanced treatment.

To be sure, there have been many successes, yet some disappointments, too. On the plus side, enhanced awareness about the rare diseases affecting our community has shortened diagnosis time for many. IG treatment has been augmented with new and improved therapies and administration options that have reduced side effects and increased site-of-care choice. IG therapy has also been found to be a viable treatment for many more diseases, including autoimmune and neurological disorders. And, extensive study has revealed that for some patients, hematopoietic stem cell transplants may offer a cure, and perhaps in the future, gene therapy may be a feasible alternative as well.

To make IG therapies safer, biopharmaceutical companies have continued to improve their manufacturing processes, and government and industry associations have adopted policies that essentially eliminate the risk of exposure to pathogens in products. Additionally, as more diseases are treated with IG therapies, innovative methods are being developed that may one day yield increased production of the drug from plasma donations.

Safeguards for those with rare diseases continue to increase. A number of laws have been enacted at the local and federal levels to curtail discrimination and unfair taxation. And clinical guidelines, published by industry associations, assist healthcare providers in treating your diseases.

Still, disappointing sticking points remain in the midst of all the progress as reimbursement issues continue to plague the IG community. Many patients still fight to access treatment due to insurance denials, reduced Medicare reimbursement rates and the implementation of Tier IV and V categories that require high co-payments, the latter of which are being challenged in many states.

While it’s pretty straightforward to recount developments we’ve reported on during the past decade, we also want to highlight the myriad educational features and stories shared in this magazine’s pages that have resonated with others experiencing similar hardships and triumphs — stories that have helped you to connect with one another and have given you a sense of belonging and a place to find answers. These are the stories that make us so proud of what IG Living magazine has accomplished over the past 10 years. On page 30, we list our top feature article picks, which we hope will provide a quick reference to the information most important to you. You can find these articles on our website, along with a countless number of columns written by and featuring IG patients and caregivers in every issue.

Just as it has been our mission to provide you with an abundance of helpful information over the past decade, we will continue to be your trusted resource going forward. As always, I hope you gain insight from the information presented and enjoy this edition of IG Living.

Ronale Tucker Rhodes, MS
Keeping an Eye on Predatory Drug Pricing Practices

By Abbie Cornett

RECENTLY, THE NOW-DISGRACED former CEO Martin Shkreli of Turing Pharmaceuticals brought the case of artificially inflated drug prices to the center stage of national news when he increased the price of the drug Daraprim (pyrimethamine) from $13.50 to $750 per tablet — more than a 5,000 percent increase. Turing Pharmaceuticals purchased the rights to the 60-year-old off-patent drug in August 2015. Daraprim is the only drug available to treat toxoplasmosis, an infection contracted from cat parasites that can cause birth defects. It is also used as a co-treatment for HIV infections, some cancers and malaria.¹

Unfortunately, a drastic increase in the price of a drug is not as uncommon as one might think.

Un fortunately, a drastic increase in the price of a drug is not as uncommon as one might think. It does not occur as often with common drugs or drugs for which there is a large market such as cholesterol medication. The larger the market, the more competition there is to keep the price lower. Rather, these types of increases tend to occur when there is only one medication or a small number of medications available to treat a disease. This means it is more likely to occur with drugs that are used to treat rare diseases, because there is a smaller market and less competition to produce new treatments.

Inflated increases in drug prices are usually triggered when one company purchases another or when a company purchases the rights to an existing drug, as in the case of Daraprim. Frequently, these purchases give the buying company a monopoly on the treatment for a chronic condition or rare disease — a practice that makes the medically vulnerable and often underinsured patient populations unable to afford their medications. It further drives up the overall cost of healthcare for everyone.

In September, as a result of the National Alliance of State and Territorial AIDS Directors contacting the House Committee on Oversight and Government Reform, Shkreli was sent a request for information on the company’s pricing practices.² The letter stated that Turing’s practices had violated the Health Resources and Services Administration’s nondiscrimination requirements. It also stated that it was reprehensible to boost corporate profits at the expense of patients.

In response to the public backlash, Shkreli announced Turing would reduce the price of the drug to a much lower level that would still allow the company to make a profit. However, at the end of November, the company reversed its decision to lower the price of the drug. Fortunately, a pharmacy that compunds prescription drugs for individual patients has stepped in, and it is selling a capsule version of Daraprim for 99 cents.³

While Turing’s actions caught the attention of the media, predatory pricing practices were already under investigation by Congress. And, what is important to remember is that while there are bad actors in the pharmaceutical industry, the actions of a few should not color our view of the entire industry. The majority are there to help patients and to offer programs for patients who are unable to pay for their medications.

As the patient advocate for IG Living, I will be closely following this issue and will keep you up to date on the actions of Congress and anything that may adversely affect your access to lifesaving medications.

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

References
Would you hide your illness from an employer?

I was five months pregnant and didn’t tell my employer until after I was hired. After being hired, I went to human resources and told them, because it’s illegal to be fired for an illness or pregnancy. I doubt they would have hired a pregnant woman knowing I would have to take leave within a few months. I ended up working there for 15 years until my myasthenia gravis got too bad.

— Laurie L.J.

Everyone should check the Americans with Disabilities Act laws. They can help protect you.

— Jan S.W.

 wsp;

Does your doctor listen?

My story takes much longer, and being a retired nurse practitioner, I make sure the doctor is listening by asking if he/she understands what I’m explaining. Of course, my immunologist always sets me up with a longer appointment.

— Lia F.

Dr. William Osler, a Canadian physician, is known as the father of modern medicine. He said that if you listen carefully to a patient’s story, you are more than likely to make a diagnosis based on what the patient has said.

— Connie K.

Both my primary care physician (PCP) and immunologist listen. They both give me longer appointments, and they usually answer all of my questions. Or, they tell me they don’t know and [either] show me the best place to search or search with me on the computer. My PCP is learning along with me. He says he had another patient who came in years later, and he can help her now.

— Suzan B.R.

How did you react when you were told you had a chronic illness?

I was prepared for it to be cancer. At least there are huge networks and charities, and everyone knows someone and understands what you’re going through. And, there’s a chance of a cure. After 10 years of misdiagnosis and suffering, the last two have given me an answer with common variable immunodeficiency and IG therapy, but I’m still so unwell and in pain that I can’t lead anything akin to a normal life.

— Laura W.

I waited so long to get a diagnosis that, when I was told, I was relieved that it wasn’t cancer. Don’t get me wrong. I was scared, but happy that there was a treatment for it.

— Sharon B.D.

I guess because I was relieved to have a diagnosis and treatment plan, I was more relieved than despairing. I accepted it, and was determined to fight, but I probably didn’t give the finality of it a lot of thought.

— Kris H.M.
**Ask the Experts**

**Abbie** » Both Hizentra and Atenolol can cause the symptoms you are describing. While some patients become elated and energetic with an infusion, others become tired. Generally, after receiving several doses of immune globulin, these symptoms may subside to allow for better tolerance. Another possible explanation could be that the tiredness is due to antibodies in the Hizentra product that are finding targets to attack.

**Question »** Should my child who has SAD stay home from school if she can’t be treated with antibiotics?

My 4-year-old daughter was just diagnosed with specific antibody disorder after having pneumonia two times earlier this year. Prophylactic antibiotics were the first thing recommended; however, my daughter is allergic to amoxicillin and is resistant to all others except Bactrim and clindamycin. We feel that a daily dose would limit her treatment in the event she does get an infection. We are also concerned about the possibility of C. diff. She goes to preschool five days a week and, as usual, children are always getting sick. Since we are heading into the viral season, we are wondering if we should reduce the days that she is at school. We aren’t sure what else we can do to prevent her from getting another infection.

**Abbie** » After speaking with one of our experts, we suggest that your daughter be tested for an allergic reaction to amoxicillin if she has not yet been tested. If she is allergic, there is a relatively straightforward process to desensitize her to an antibiotic, which then allows it to be tolerable. This would give your daughter a wider range of available antibiotics. Our expert did say that C. diff is possible, but it really isn’t as common as many people believe. The risk of taking a prophylactic antibiotic is something you should thoroughly discuss with your immunologist.

There are many things you can do to help protect your daughter while at school. We have published a number of articles in *IG Living* that provide useful tips, which can be found at www.IGLiving.com/magazine/archive.html.

- Education: Home School or Public School?: June-July 2010, p40.
- School Site Programs for K-12 Health-Impaired Students: August-September 2013, p14.

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

**ABBIE CORNETT** is the patient advocate for *IG Living* magazine.
DiGeorge Syndrome Development: “The Timing Is Off”

By Terry O. Harville, MD, PhD

THE OLD SAYING “timing is everything” could not be more accurate for individuals with DiGeorge syndrome (DGS). During the past few years, it has been shown that deletions of DNA from chromosome 22, in the region of 22q11.2, during events in the first trimester (typically in the second month) are likely responsible for most cases of DGS. These are frequently called microdeletions since the overall size of chromosome 22 may not appear to be affected. And, only one of a person’s pair of chromosome 22 needs to be affected. This region contains specific DNA structures that correspond to a timing mechanism. Thus, the 22q11.2 DNA provides the timing signals for part of early embryonic normal development, and if in disarray, results in the many features associated with DGS.

During the first month, the early human embryo forms as a tube with one end that will become the mouth and the other the anus. The “head” end folds inward to fill in the opening of the tube and create what will become the front of the face, with positioned openings remaining for the nose and mouth. If these folding events or if the extension of the tissue that is to reach the other side begins earlier or later, then the tissues do not develop and connect in the correct time sequence. A cleft lip, bilateral cleft lip and/or cleft palate (characteristics that may also be found in patients with DGS) are the most common examples of this. In addition, what will become the eyes are on opposite sides of the tube, and as the folding occurs, they are brought forward into the face. Commonly in DGS, this may be delayed, and the eyes will remain somewhat farther apart than expected.

While these events are occurring, areas in the neck, commonly called “gill slits” (since they look like what is seen in fish), develop and are known as pharyngeal pouches. Between the pharyngeal pouches are structures known as branchial arches (or pharyngeal arches). The first branchial arch develops into the mandible of the jaw and parts of the ear. The third pharyngeal pouch develops into the thymus and the two inferior parathyroid glands. The fourth pharyngeal pouch develops into the two superior parathyroid glands. (Many other structures come from the pharyngeal pouches, but we will not be discussing them since they are not necessarily relevant for DGS. Further, the branchial arches contain blood vessels that may be affected in DGS resulting in cardiac abnormalities, and these will be discussed later.) If the timing is off with the first branchial arch, the mandible may be small in size and the ears may develop “notches” and appear to be pointed at the top. Together with the position of the eyes, this is the characteristic face of DGS, commonly called an “elfin” face. If the timing is off during the development of the third and fourth pharyngeal pouches, the thymus and parathyroid glands may not fully develop. The lack of fully developed parathyroid glands results in low serum calcium levels. And, the lack of a fully developed thymus may result in reduced or lack of development of T lymphocytes resulting in potential immunodeficiency.

We will continue next issue describing what further steps and events should normally occur during fetal development, but — when their timing is off — result in other features of DGS.

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.
MYASTHENIA GRAVIS (MG), derived from the Latin term that means grave muscle weakness, is a serious condition with a high mortality rate. The good news is that much has been learned about this condition. Several treatment options have been identified, one of which is rituximab (Rituxan, MabThera and Zytux), which is currently being considered.

What Is MG?

MG is believed to be an autoimmune disorder in which the immune system malfunctions and creates antibodies that attack and cause damage to a part of the body. In MG, acetylcholine receptors at the junction between the nerve and the muscle are attacked. A few antibodies have been identified as responsible for this attack. The most common antibody is anti-acetylcholine receptor. Another is anti-muscle specific tyrosine kinase (MuSK); however, this is less common, and controlling MG caused by an attack by MuSK has been more challenging.

Acetylcholine is a neurotransmitter. If its receptors are attacked, the nerve transmission is interrupted or ineffective at the junction from nerve to muscle, causing muscle weakness. The hallmark of MG, muscle weakness increases with activity and improves upon resting. Because MG affects the voluntary muscles, movements such as blinking, chewing, swallowing and holding one’s head up become difficult. Additional symptoms may include droopy eyes and slurred speech. In some cases, the symptoms are confined only to the ocular nerves and muscles and are not generalized. People with MG can experience periods when symptoms are relatively controlled, as well as periods of exacerbation, or worsening. In some cases, exacerbations can happen rapidly and require quick intervention. Severe exacerbations can affect swallowing to the point where aspiration (inhaling something such as food into the lungs) can occur and can become dangerous. Breathing can also become affected.

Treating MG

Treatment of MG varies and depends on the presenting symptoms and their severity, causative antibody and presence of thymoma.

Table 1. Current Treatments for Myasthenia Gravis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyridostigmine</td>
<td>Boosts acetylcholine levels at the neuromuscular junction. Results in improved muscle strength. Routinely used in maintenance of MG.</td>
</tr>
<tr>
<td>Steroids</td>
<td>Has an immunosuppressive effect and can decrease antibody levels. Dose is individualized and may be adjusted when symptoms worsen or improve.</td>
</tr>
<tr>
<td>Immunosuppressive agents: azathioprine (Imuran); mycophenolate mofetil (CellCept); cyclosporine</td>
<td>Suppress the production of the antibodies responsible for MG.</td>
</tr>
<tr>
<td>Immune globulin</td>
<td>Mechanism of action is not clearly understood. Used during periods of exacerbation for quick stabilization.</td>
</tr>
<tr>
<td>Plasmapheresis or plasma exchange</td>
<td>A process in which the liquid in the blood (plasma) is separated from the cells and replaced with good plasma, or a plasma substitute. Used during periods of exacerbation for quick stabilization.</td>
</tr>
<tr>
<td>Thymectomy</td>
<td>The thymus plays a role in the development of the immune system. It is larger during childhood and decreases during growth and development to adulthood. In MG, the thymus remains large, and there may be presence of a benign tumor, known as thymoma. In these cases, the thymus may be removed.</td>
</tr>
</tbody>
</table>
of a thymoma. See Table 1 for the current treatment options.

In recent years, rituximab has become increasingly popular for treating autoimmune diseases, and it may one day be a treatment option for MG. Rituximab is a monoclonal antibody. An antibody is a protein produced by the immune system in response to something foreign entering the body. Antibodies are made by B cells, and each B cell makes only one kind of antibody. A monoclonal antibody is produced in a lab and is designed to replicate the response of naturally produced antibodies. As such, introducing a monoclonal antibody into the system will interrupt the immune response and essentially prevent the antibodies from being produced in the first place. This whole process is known as immunomodulation.

The current U.S. Food and Drug Administration (FDA)-approved indications for rituximab include:

- non-Hodgkin’s lymphoma
- chronic lymphocytic leukemia
- rheumatoid arthritis (RA) in combination with methotrexate in adult patients with moderately- to severely-active RA who have inadequate response to one or more tumor necrosis factor-antagonist therapies
- granulomatosis with polyangiitis (Wegener’s granulomatosis) and microscopic polyangiitis in adult patients in combination with glucocorticoids.

While use of rituximab in MG has shown to be very effective in refractory cases, it remains a non-FDA-approved therapy. However, there have been a few clinical trials to determine its effectiveness in treating MG. Currently, a Phase II trial is comparing rituximab with a placebo to determine whether its therapeutic benefit for MG warrants further study in a Phase III efficacy trial. An initiative by NeuroNEXT, an organization that conducts trials specific to neurological conditions, the trial has 26 locations around the country and is currently recruiting.

Rituximab is infused intravenously with dosage based on weight. For MG, the dosing is four courses of 375 mg/m² (per meter squared), which is repeated after six months. Side effects can occur during and after an infusion, some of which can be serious (see Figure 1). As such, many factors need to be considered prior to starting rituximab therapy to ensure tolerability and to ensure any potential risks of adverse reactions are addressed and minimized, if possible.

Due to the potential for hepatitis B virus (HBV) reactivation, all patients should be screened for HBV prior to treatment with rituximab. The cardiovascular, digestive and nervous systems can be affected by rituximab. Since rituximab interferes with immune response, once it is discontinued, patients are monitored to ensure normal immune function resumes. In some cases, B cells are not produced in sufficient quantities, and patients can experience hypogammaglobulinemia that may even require treatment with immune globulin therapy to protect against recurring infections.

Because adverse reactions can occur, rituximab infusions are typically conducted in a controlled setting. The first infusion should be carefully monitored, since 80 percent of fatal infusion reactions have occurred during this time. After patients have received a first dose in a controlled setting without incident, some physicians feel home infusions can then be allowed.

An Alternative Therapy

For cases of MG that become refractory with severe symptoms despite treatment with current therapies, rituximab may be an alternative treatment option that can effectively control the disease. According to NeuroNEXT, there is a need for another agent in the management of MG, as there are few effective drugs. Safe, well-tolerated, effective and steroid-sparing therapeutics are those that are most desirable.

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

Sources
In a recent study, primary immunodeficiency disease (PI) patients scored significantly lower on a number of the instruments of health-related quality of life (HRQOL) assessments compared with normal controls and other chronic disease patients. HRQOL assessments range from generic health status questionnaires that are applicable to all populations to more specific questionnaires that evaluate particular aspects of disease or treatment modalities.

To better understand what factors affect HRQOL in patients with PI, the researchers reviewed the published literature that used standardized instruments that measure HRQOL. They found that PI patients experience measurably lower general health with higher hospitalization rates and increased physical, school and social activity limitation. They also scored lower with respect to perception of general health compared with other chronic disease patients.

In one literature review, the researchers found that PI patients’ QOL changed in the six years between the first and final assessments, with a significant decline noted in scores relating to bodily pain, general health, limitation due to emotional problems and limitation in physical and social functioning. It also found that patients’ relative risk of death, independent of age, was affected by their perceived physical and social function. Another study showed that a long delay in diagnosis and a large number of infectious episodes further negatively impacts HRQOL and leads to permanent functional impairments prior to the start of treatment. Other factors that influenced HRQOL were unemployment, infections in more than four organs, two or more additional diseases, and more than two occurrences of stress in the last two to three months.

In addition to measuring HRQOL, the researchers sought to determine whether the route and site of immune globulin administration affects HRQOL. They found that choices about the route of administration have a significant impact on HRQOL, most specifically being able to self-administer subcutaneously.

The researchers concluded that “by further analyzing what factors impact HRQOL, therapy adjustments can be made to maximize patient well-being and minimize disease impact on daily functioning.”

Jiang, F, Torgerson, TR, and Ayars, AG. Health-Related Quality of Life in Patients with Primary Immunodeficiency Disease. Allergy, Asthma & Clinical Immunology, 2015, 11:27.

A study conducted by the National Institute of Allergy and Infectious Diseases found that gene therapy can safely rebuild the immune systems of older children and young adults with X-linked severe combined immunodeficiency (SCID-X1). In the study, researchers tested the safety and effectiveness of gene therapy combined with low-dose chemotherapy in five SCID-X1 patients aged 7 to 24 years with worsening immune systems despite one or more previous transplants from a parent. The investigators removed stem cells from the patients’ bone marrow and used a lentiviral vector to deliver a normal IL2RG gene to the cells. The corrected cells were infused back into the patient after a low dose of chemotherapy to help the stem cells establish themselves and begin producing new blood cells.

The first two patients to receive the therapy showed substantial improvements in immunity and clinical status, with one patient continuing to improve three years after therapy. Despite improvements in immunity, the second patient died of pre-existing, infection-induced lung damage two years after receiving gene therapy, suggesting the importance of early treatment before organ damage becomes irreversible. The three other patients, who more recently received the therapy, are beginning to show improvements in immune function.

IN THE NEWS

Research

Phase III Trial to Begin of IVIG Product to Treat PI

In October, the U.S. Food and Drug Administration cleared the investigational new drug application for ProMetic Life Sciences’ intravenous immune globulin (IVIG) product for the treatment of primary immunodeficiency disease (PI). The Phase III clinical trial, which was slated to begin in the fourth quarter of 2015, is an open-label, single-arm, two-cohort multicenter study to investigate the safety, tolerability, efficacy and pharmacokinetics of ProMetic’s plasma-purified IVIG in a total of 75 patients with PI, including 50 adults (cohort one) and 25 children (cohort two).

ProMetic utilizes a proprietary platform, the Plasma Protein Purification System (PPPS), a multi-product sequential purification process originally developed in collaboration with the American Red Cross that employs powerful affinity separation materials in a multi-step process to extract and purify plasma proteins in high yields. “The yield advantage provided by our PPPS technology for more mainstream plasma-derived products such as IVIG is of great importance to our commercial strategy,” said Pierre Laurin, president and chief executive officer of ProMetic. “The significant financial contribution from products like IVIG will greatly facilitate the pursuit of our strategy, namely the development of much needed and more affordable orphan products addressing rare diseases.”

Putting the Right Pieces Together for Your Home Infusion Therapy

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For adults with primary immunodeficiency

Schedule an appointment with your physician to see if HYQVIA is right for you.

* subQ Ig, also known as subcutaneous immune globulin.

Reference
1. HYQVIA [prescribing information]. Westlake Village, CA: Baxter Healthcare Corporation, September 2014

Please see the Detailed Important Risk Information on the adjacent pages and the Brief Summary of HYQVIA Prescribing Information, including Boxed Warning, on the reverse side.

To learn more about HYQVIA, visit www.HYQVIA.com
HYQVIA (Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase) is the only once-a-month subQ Ig with recombinant human hyaluronidase (hy•ah•RON•ah•dase) and Ig. The hyaluronidase temporarily opens the subQ space, allowing a larger amount of Ig to reach the subQ tissue and be absorbed into the bloodstream to help fight infection. It’s the reason you can infuse your monthly dose of HYQVIA using 1 needle, 1 infusion site, 1 time a month.

**INDICATION AND USAGE**

HYQVIA (Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase) is an immune globulin with a 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.

**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 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 swelling in your brain.
- 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.
You may be eligible
to save up to $4,000
on HYQVIA

If you are starting or currently receiving treatment with HYQVIA
(Immune Globulin Infusion 10% (Human) with Recombinant Human
Hyaluronidase) for PI, you may be eligible to save up to $4,000 on
your deductible/co-payment/co-insurance costs over 12 months.

To enroll, call us.
We'll take care of the rest.

Terms and Conditions
- To be eligible, patients must: 1) be starting or receiving treatment with (and have
  a current prescription for) HYQVIA with an ICIB9 or IC10, as applicable, for
  adult (≥16 years of age) Primary Immunodeficiency (PI); and 2) have medical
  insurance that covers medication costs for HYQVIA treatment and allows for
  co-pay/coupon assistance.
- This manufacturer coupon program is not valid for prescriptions reimbursed
  in whole or in part, by Medicaid, Medicare, Medigap, VA, DoD, IRCAH, or any
  other federal or state healthcare programs, including state pharmaceutical
  assistance programs, and where prohibited by the health insurance provider
  or by law.
- The coupon program provides a maximum benefit of $4,000 for eligible out-
  of-pocket costs and expires 12 months from date of activation. Eligible costs
  include deductible, co-payment, and co-insurance costs for HYQVIA. Non-
  medication expenses, such as ancillary supplies or administration-related costs,
  are not eligible.
- Patients are eligible for a maximum benefit of $4,000 in total Baxalta sup-
  port in any 12-month period, including any amount received as part of the
  GAMMA/GAMLIQ/LIQUIL/SIUQ/CoPay Program.
- Acceptance of this offer must be consistent with the terms of benefits provided
  by your health insurance provider.
- Offer limited to one card per person and expires 12 months from date of activa-
  tion and may not be combined with any other coupon, discount, prescription
  savings card, rebate, tree trial or other offer.
- This program is only valid for residents of the United States, excluding Puerto
  Rico and other U.S. territories.

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 moder-
ate pain, redness, swelling, or itching may occur at the site of infusion and gener-
ally 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 prod-
ucts, 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 Baxalta US Inc.
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 follow-
ing page, including Boxed Warning.
**More free time with HYQVIA**

Infusing 1 time a month with HYQVIA doesn’t mean your infusions will take longer. Typically, infusions take less than 3 hours with HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]. Instead, you’ll have more free time.

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**INDICATION AND USAGE**

HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] is an immune globulin with a 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.

**Selected Important Risk Information about HYQVIA**

**HYQVIA can cause blood clots.** Call your healthcare professional or go to your emergency department right away 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. These could be signs of a blood clot.

**Do not use HYQVIA** if you are allergic to immune globulin (IgG), hyaluronidase, or other blood products, or have IgA deficiency.

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.
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 Baxalta 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.
Technology

New Mobile App for PI Patient Community

The Immune Deficiency Foundation (IDF) has launched a mobile app for its IDF ePHR, an electronic personal health record powered by Get Real Health’s InstantPHR. The app allows patients with primary immunodeficiency diseases (PI) to easily track their health information, including symptoms, diagnoses, medications, infusions and other critical health data. The desktop and mobile web version of IDF ePHR was rolled out last fall and is used by more than 1,600 people. Now, with the app, patients will be able to manage their health on-the-go by tracking goals and setting reminders and notifications, in addition to viewing their information and keeping track of all their health conditions through easy-to-read charts and graphs.

Get Real Health customized many of the components of IDF ePHR to make it user-friendly and relevant for the PI population. Because the approximately 250,000 PI patients living in the U.S. vary widely in their symptoms and treatments, a portal that is flexible and entirely patient-centered is necessary. InstantPHR met those requirements with the addition of customized infusion logs that allow patients to track their infusions on a regular basis, either by date, product or lot number. In addition, a new calendar feature allows patients to log their daily records, as well as track side effects and allergies.

IDF ePHR is connected to the IDF Patient-Powered Research Network, PI CONNECT, which allows consenting patients to share anonymous data with the U.S. Immunodeficiency Network (USIDNET) for research. The long-term goal of PI CONNECT is to boost the efficiency of research and shift away from investigator studies to patient-centered studies, where patient experience is the driver toward change.

More information about the IDF ePHR and PI CONNECT can be found at primaryimmune.org/services/idf-ephr. The app can be downloaded to any smartphone.

Medicines

Baxalta Files for Approval of SCIG 20% for PI

Baxalta has submitted an application to the U.S. Food and Drug Administration for its investigational 20% concentration subcutaneous immune globulin (SCIG) treatment for patients with primary immunodeficiencies (PI). The filing is based on positive results of a Phase II/III study of SCIG 20% in North American patients at least 2 years old with PI. In the study, SCIG 20% met the primary endpoint as measured by the rate of acute serious bacterial infections (ASBIs). A single ASBI was reported, equating to 0.012 ASBI per patient-year compared with the reference threshold of one ASBI per patient year. The rate of all infections was 2.41 per patient-year. Nearly all infusions (99.8 percent) were completed without a reduction, interruption or discontinuation for tolerability reasons, and 84.9 percent of infusions were administered using two infusion sites.

The rate of local adverse reactions was 0.022 per infusion, and all local adverse reactions were either mild (92.5 percent) or moderate (7.5 percent) in severity. The most common adverse reactions were local and systemic, including headache, nausea, fatigue, diarrhea and vomiting. Regulatory reviews of SCIG 20% are now underway in both the U.S. and Europe.

IN THE NEWS

Autoimmune Corner

Research

INIM Conducting Study on ME/CFS Genetics

The Institute for Neuro Immune Medicine (INIM) has started a gene study for patients with myalgic encephalopathy (ME) and chronic fatigue syndrome (CFS). According to Dr. Nancy Klimas, director of INIM, the goal of the study is to “better understand which gene mutations give people a better shot or worse shot at therapy.” The study aims to collect genetic data from a minimum of 1,000 ME/CFS patients (and preferably more than 10,000 patients).

To participate, patients can email MECFSGenes@Nova.edu to have a personalized link to a secure website emailed to them. The encrypted email will explain how to proceed. A pre-screening questionnaire consisting of 11 questions will determine if patients are eligible to participate. If eligible, patients will complete an additional two surveys and will be asked to upload their genetic data to the study’s website. Genetic data can come from any publicly genetic testing site, including 23andme.com, Ancestry.com, Family Tree DNA, Gene by Gene, Pathway Genomics, GeneSight and any genetic test conducted by patients’ physicians.

There is no cost to participate in the study. The only cost is for the genetic test. In addition, all communication is conducted via a secure email server, and no travel is necessary. For more information, go to www.nova.edu/nim/research/mecfs-genes.html.

Research

CRPS May Be Effectively Treated with Plasma Exchange

While there is currently no single therapy that controls the pain levels in patients with complex regional pain syndrome (CRPS), a new study has found that plasma exchange (PE) therapy in combination with other therapies may work. PE therapy is an extracorporeal therapy in which the whole blood of the patient is extracted and separated into plasma and blood cells. The plasma is replaced with another solution such as human albumin in saline or specially prepared donor plasma, which along with the blood cells is then returned to the patient.

For the study, the researchers conducted a retrospective case series study of 33 patients with CRPS who received PE treatment at Drexel University between September 2012 and June 2014. The patients completed a medical and pain evaluation, the short-form McGill questionnaire, quantitative sensory testing (QST) and a skin punch biopsy. Then, all patients had a series of five to 11 PE therapies performed over a two- to three-week period, followed by a pain evaluation and the short-form McGill questionnaire. During PE, patients continued their medication therapy with no change, and no new medications were started. Those who responded to PE were offered maintenance therapy consisting of either weekly PE or other immune-modulating agents.

Significant pain reduction (64 percent) was experienced among 30 of the 33 patients following the initial series of PE, 24 of whom are receiving maintenance therapy with either weekly PE, oral immune-modulating agents or intravenous immune globulin. The remaining six patients are not receiving maintenance therapy, and their pain has returned to pre-treatment levels. While the researchers are unsure why PE reduces pain in CRPS patients, they speculate that it could be because PE has shown to decrease plasma pro-inflammatory cytokines and increase the anti-inflammatory cytokine IL-10. “The efficacy of PE could also be due to reduction of plasma fibrinogen,” the study authors wrote. “We found a significant correlation between the reduction of plasma fibrinogen following PE and pain relief.” Fibrinogen is a glycoprotein found in blood that is involved in the formation of blood clots and also plays an important role in inflammation.

Researchers at the Chromatin and Disease Group from the Bellvitge Biomedical Research Institute and La Paz Hospital have identified epigenetic alterations in common variable immunodeficiency (CVID) using genetically identical monozygotic twins, one of whom has CVID and the other does not.

In the study, which compared epigenetic marks in B cells in a pair of identical twins discordant for the disease, the researchers identified a group of genes important for the functioning of B lymphocytes that had epigenetic alterations (higher DNA methylation levels) in the twin with CVID that are not present in the healthy twin. DNA methylation is related to the ability of cells to allow their genes to be expressed. Subsequently, the same genes were investigated in a cohort of healthy individuals, which showed that CVID patients have partially lost the ability of demethylating those genes during the process of generating mature lymphocytes. This indicates that patients not only produce less CVID memory B cells (the mature form that produces antibodies) but also these cells are altered and have not properly completed their maturation.

The exact cause of low levels of serum immunoglobulins in CVID patients is not known. In recent years, geneticists have described mutations in several genes related to the biology of lymphocytes in CVID patients, but for several patients, there are no identified mutations. The results of this study are the first evidence of such epigenetic alterations in the field of primary immunodeficiencies, which could open the door to future research avenues for the diagnosis and treatment of patients with CVID.

The study was published in the June 17 issue of Nature Communications.

By Ronale Tucker Rhodes, MS

IT WAS 10 years ago when we asked “Yoo-hoo! Anybody Out There?” in the February-March 2006 debut issue of IG Living magazine that mailed to nearly 16,000 specialty physicians, including allergists, immunologists, neurologists, hematologists-oncologists and pediatric allergists, as well as to members of the U.S. Congress. The decision to publish this magazine was based on our recognition that there was a great need among immune globulin (IG) patients for information and a sense of belonging to a community. Our goal was to provide support for underserved and isolated patients by first informing legislators and providing doctors with a resource for education, communication and advocacy to recommend to their patients.

In just a decade, IG Living has grown and is now read by upwards of 30,000 patients, physicians and others tied to the IG community. We’ve heard back from a great number of you over the years. We know that the majority of our readers have a common variable immunodeficiency (CVID) diagnosis; however, diagnoses span all of the primary immunodeficiency (PI) diseases, as well as autoimmune and neurological disorders. Most of you also infuse IG intravenously (IVIG) in the home setting, but the number of individuals infusing subcutaneously (SCIG) is slowly gaining ground. We’re proud that most readers have been receiving IG Living for more than five years and report reading each issue cover to cover. What’s more, you are active on our IGLiving.com website and Facebook page.

It’s so rewarding to see how much the magazine and the landscape of the IG community have continued to evolve, especially in how you now support each other! While many of the challenges affecting our community in 2006 still remain today, in this special anniversary issue, we want to share with you some snippets of community developments reported on in IG Living over the past decade in the areas of diagnosis, treatment, safety, reimbursement and legislation.
According to Immune Deficiency Foundation (IDF) surveys, the average time to diagnose a PI was 9.2 years, during which time 37 percent of patients developed permanent impairments such as loss of hearing, pulmonary function, digestive function, mobility, vision or neurological function. This delay in diagnosis resulted in delay of treatment for 21 percent, an inability to see a specialist as often as needed for 11 percent and treatment denial by insurance carriers for 17 percent.

To increase awareness and speed diagnosis of PI in children, the American Academy of Pediatrics, the Jeffrey Modell Foundation and Talecris Biotherapeutics announced a new continuing medication education series titled “Immunodeficiency in Pediatrics.” The program, which featured a panel discussion, addressed the concern that PI may be more common than previously thought, and that pediatricians need to have a high degree of suspicion when evaluating certain key signs and symptoms such as recurrent or resistant infection in patients.

At the national level, Secretary of Health and Human Services Kathleen Sebelius announced the addition of SCID to the core panel of 29 genetic disorders, as part of her recommendations to adopt the national Recommended Uniform Screening Panel. SCID was the first nominated condition to be added to the core panel of disorders.

During that year, five states and one territory (California, Louisiana, Massachusetts, New York, Wisconsin and Puerto Rico) began offering SCID screening. Seven other states — Colorado, Delaware, Iowa, Michigan, Minnesota, North Carolina and Rhode Island — also voted to recommend the addition of SCID to their newborn screening panels to begin at a later date. And, proposals to add SCID screening were made in Connecticut, Nebraska, Ohio and Pennsylvania.

It took two years after Florida Governor Rick Scott’s veto in 2011 for the state to add SCID screening to its uniform set of newborn screening tests.

Following Florida’s decision were Iowa and Texas. Texas added SCID screening to its standard newborn panel, while Iowa launched a pilot screening program to ensure the screening process met all necessary standards.

As more forms of PI have been identified over the years, the International Union of Immunological Societies Expert Committee on Primary Immunodeficiency published an updated classification of human primary immunodeficiencies (PIs), the most current and complete catalog of known PIs. The report serves as a reference for these conditions and provides a framework to help in the diagnostic approach to patients suspected of having a PI.
There were two administration options for IG, intravenous (IVIG) and port access, until the U.S. Food and Drug Administration (FDA) expanded the options to three with its approval of the first subcutaneous immune globulin (SCIG) therapy, Vivaglobin 16%. Still, IVIG was the preferred method of treatment except in cases where physicians determined that patients didn’t tolerate IVIG well.

With the addition of Vivaglobin, there were 10 FDA-approved IG products manufactured by five companies. Further, these products were determined only to be “definitely useful” by the primary immunodeficiency committee of American Academy of Allergy, Asthma and Immunology to treat five diseases: PI, idiopathic thrombocytopenic purpura (ITP), Graves’ ophthalmopathy, demyelinating polyneuropathies and Kawasaki disease.

Yet, for every FDA-approved indication for IG therapy, it was estimated there were 10 non-FDA-approved indications. In fact, there were 18 clinical trials being performed in the U.S. by both manufacturers and clinical researchers to determine the safety and efficacy of IG therapy for PI, multiple sclerosis, ITP, chronic inflammatory demyelinating polyneuropathy (CIDP), hemolytic disease, myopathy, severe C. diff, West Nile encephalitis and others.

The next IG product to be approved by FDA in the U.S. was CSL Behring’s Privigen, a new IVIG that requires no refrigeration or reconstitution.

FDA approved yet another IVIG product, Gammaplex ready-to-use 5% for the treatment of PI.

Shortly thereafter, CSL Behring received approval from FDA for its Hizentra SCIG 20% liquid for treating patients diagnosed with PI. The once-weekly IG replacement therapy is the first 20% SCIG approved in the U.S.

Most IG patients were receiving infusions in hospital outpatient clinics, infusion suites or doctor offices, but a growing number had started receiving infusions at home. It was estimated that as many as one million people across the U.S. were receiving home infusions.

The success of IG in treating patients led to publication of a paper by Dr. Jeffrey Ravetch, Theresa and Eugene M. Lang professor and head of Rockefeller’s Laboratory of Molecular Genetics and Immunology, that explains what makes IG effective. According to Dr. Ravetch, a small fraction of the IgG antibodies in the IG solution carry a sugar called sialic acid that is required for its protective ability. The discovery, he said, paved the way to generate a recombinant form of IgG that, by virtue of a sialic acid molecule attached in the right place, would be anti-inflammatory and could act as a novel treatment for autoimmune disorders.

But, IG therapy came with side effects. So, researchers at the University of California, Los Angeles, Medical Center and David Geffen School of Medicine began studying ways to minimize those effects. In their studies that used already approved IG products, they discovered ways in which patients were able to remain on their routine IG therapy schedule and dosage.

Then, FDA approved Gamunex as a treatment for CIDP, the first and only therapy approved to treat CIDP and the only IVIG approved to treat a neurological disorder in the U.S.

Researchers then began wondering about the clinical efficacy of SCIG versus IVIG in treating CIDP. In two different studies, they found a sustained effect of SCIG in CIDP in a 1:1 dose ratio compared with IVIG, which is corroborated by another case report describing effective treatment with SCIG in a patient with multifocal motor neuropathy (MMN).

Four more case studies described how PI patients successfully switched from IVIG to SCIG therapy. Those patients, who were diagnosed with CVID and agammaglobulinemia, were treated weekly with Vivaglobin, then the only approved SCIG therapy.
FDA then approved Talecris Biotherapeutics' Gamunex-C 10%, the third SCIG therapy for the treatment of PI in the U.S.

And, with the approval by FDA of Flebogamma 10% DIF IVIG to treat PI, Grifols became the first company in the U.S. to offer patients and clinicians two concentrations of liquid IVIG (5% and 10%).

There were then 11 IG products FDA approved (with some removed and new products added) for five indications: PI, ITP, CIDP, B-cell lymphocytic leukemia and Kawasaki syndrome. While all IG products carried an indication for PI, no one product carried an indication for all five. In addition, the number of off-label uses for IG had greatly expanded, far exceeding that of labeled indications. Diseases most commonly treated off label were Guillain-Barré syndrome, polymyositis, dermatomyositis, MMN, stiff person syndrome, relapsing-remitting multiple sclerosis and pemphigus. What's more, there were a number of studies being conducted to look at the efficacy of IG in other non-FDA-approved indications, including Alzheimer's disease, secondary recurrent miscarriage and chronic regional pain syndrome.

Due to delays in supply, CSL Behring discontinued distribution of Vivaglobin in the U.S. market, once again reducing the number of approved IG products to 10.

The number quickly returned to 11 with FDA approval of Kedrion Biopharma's Gammaked 10% for intravenous treatment of PI, ITP and CIDP, and for subcutaneous treatment of PI.

Since IG is a lifetime therapy for CVID, a group of physicians at the 37th annual meeting of the European Group for Blood and Marrow Transplantation in Paris, France, reported that they believed hematopoietic stem cell transplants (HSCTs) were feasible in CVID patients and would result in an improvement of the condition. Their conclusion was based on a cohort of four CVID patients who underwent HSCTs with peripheral stem cell grafts, all of whom presented with a host of other medical issues in addition to CVID and in whom no graft failure occurred.

Today, several clinical trials are underway that are examining the efficacy of SCIG treatment for neuromuscular conditions. These include the PATH (polynephropathy and treatment with Hizentra) study for CIDP patients and another evaluating SCIG for the treatment of patients with dermatomyositis.

Two additional IG products were added to the market when FDA approved Octapharma's Octagam 10% IVIG for the treatment of chronic ITP and Baxter's HYQVIA SCIG with recombinant human hyaluronidase for the treatment of PI. HYQVIA became the first SCIG 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.

In other treatment news developments, an international consortium of scientists perfected gene therapy in promising clinical trials that they said might lead to an eventual long-term cure for X-linked SCID. The mechanism used to deliver the gene therapy was designed to prevent the serious complication of leukemia that developed in one-quarter of boys treated a decade ago in a similar trial in Europe.

A different study showed that patients with SCID have improved survival when they undergo HSCT within a few months after birth, before the onset of infection or after the infection resolves. It was hoped that this would put pressure on states that have resisted adding SCID to their newborn screening programs.

And, according to another study, HSCT could be considered in some instances for patients with CVID, specifically “in patients in whom there has been extensive characterization of the immunologic and/or genetic defect underlying the CVID diagnosis.”

With four SCIG products now on the market, CSL Behring sought a new dosing option for Hizentra SCIG 20% that was approved by FDA to allow PI patients to individualize therapy with flexible dosing, meaning treatment at regular intervals from daily to once every two weeks.
Grifols set the stage for deterring adulterated and mislabeled IG products with its laser-etched vial technology. With laser etching, each vial of IG was laser inscribed with the product’s lot number that includes such information as date of production, expiration of product and vial size. Grifols also took additional protective steps by etching a filling sequence number on each vial that corresponds with a recording of the entire filling sequence.

Focus on the safety of the drug supply chain at this time was heightened. The Prescription Drug Marketing Act (PDMA), the federal drug pedigree requirement that called for documentation of every entity that had possession of a vial or bottle of medication handled by a distributor, was an effort to secure the supply channel and prevent drug counterfeiting and diversion, but it was on hold due to a constitutional challenge. In response, states began considering their own legislation, and Florida became the leader in the nation with its passage of the Prescription Drug Protection Act (PDP Act), which required all distributors of prescription drugs to prepare, authenticate and distribute drug pedigrees whenever they transacted prescription medicine. However, the pharmaceutical industry neutralized the Act by supporting legislation that eliminated the pedigree requirements.

Unfortunately, after the publication of that study, Octapharma USA initiated a voluntary withdrawal of all lots of Octagam IVIG 5% from the U.S. marketplace due to an unusually high number of thromboembolic events that were associated with people being administered the drug. The withdrawal followed an initial announcement earlier in the year of a voluntary withdrawal of selected lots of Octagam 5%.

Through examination, it was determined that the increase of thromboembolic events was due to FXIa procoagulant activity. Following this discovery, Octapharma removed FXIa through corrective and preventive measures in the manufacturing process, and FDA and the Committee for Medicinal Products for Human Use in Europe approved the return of Octagam 5% to the market.

Due to concerns about the Ebola virus outbreak, especially among persons with immunodeficiencies who are more vulnerable to infections, the Plasma Protein Therapeutics Association endorsed the recommendation by the EU Center for Disease Prevention and Control that travelers or residents returning from Ebola virus disease-affected areas be deferred for donation of plasma for fractionation two months after return.

To help increase the availability of plasma therapies to treat immune disorders, autoimmune disease, neuropathies and others, Plasma Tech Biopharmaceuticals reported it developed a new and innovative method to extract plasma proteins from pooled human plasma samples.

An additional improvement in the fractionation process came with FDA approval of the Intercept Blood System for plasma, the first pathogen-reduction system for use by blood establishments in the preparation of plasma to reduce the risk of transfusion-transmitted infections. The system can be used to reduce pathogens in plasma derived from whole blood and plasma obtained by apheresis, a collection process that separates red blood cells from plasma and then returns the red cells to the donor.
Because of the genetic link to many diseases that respond to IG therapy, the importance of genetic testing to the IG community was determined likely to grow, resulting in concerns about losing health benefits or having to pay more for coverage as a result of information found by genetic testing. In response, President Bush signed the Genetic Information Nondiscrimination Act, popularly known as GINA, into law. GINA prohibits health insurers and employers from discriminating against individuals based on their genetic information.

Protections for people with disabilities expanded again when Congress passed the Americans with Disabilities Act Amendments Act (ADAAA). The portions of the amendment's changes that apply specifically to patients treated with IG include 1) the phrase “major life activity” now includes operation of major bodily functions, including but not limited to functions of the immune system, normal cell growth, digestive, bowel, bladder, neurological, brain, respiratory, circulatory, endocrine and reproductive functions; 2) an impairment that is episodic or in remission is a disability if it substantially limits a major life activity when active; and 3) the question of whether an impairment is disabling must be made without regard to whether medication, equipment, prosthetics, assistive technology or other treatment, devices and supplies improve the impairment.

To encourage more participation in clinical trials, President Obama signed into law the Improved Access to Clinical Trials Act, which amends the Social Security Act to provide for an exclusion under the Supplemental Security Income (SSI) program and Medicaid for certain compensation of individuals who participate in clinical trials for rare diseases and conditions. The law excludes “the first $2,000 received during a calendar year by such individual (or spouse) as compensation for participation in a clinical trial involving research and testing of treatments for a rare disease or condition, and the first $2,000 received by an individual (who has attained 19 years of age) as compensation for participation in a clinical trial meeting the requirements of section 1612(b)(26) for purposes of determining the income eligibility of such individual for medical assistance under the state plan or any waiver of such plan.”

The ADAAA of 2008 was also expanded upon when the Equal Employment Opportunity Commission published final regulations that protected many more employees from disability discrimination in the workplace than had previously been the case under the courts' narrow interpretations of the ADA and ADAAA. Specifically favorable for the IG community were that an “impairment need not prevent or severely or significantly restrict performance of a major life activity to be considered a disability,” that “impairments that are episodic or in remission are disabilities if they would be substantially limiting when active” and that “major life activities” includes “major bodily functions” such as immune system, normal cell growth, and brain, neurological and endocrine functions.

And, with concern about which vaccines immunocompromised individuals should receive, the Infectious Diseases Society of America issued the "Clinical Practice Guideline for the Vaccination of the Immunocompromised Host" to recommend that individuals with compromised immune systems get the flu shot and other vaccinations.

With the growing use of IVIG for neuromuscular disorders, the American Academy of Neurology (AAN) released an evidence-based guideline on the efficacy of IVIG for neuromuscular disorders, based on a comprehensive review of the literature by the AAN Therapeutics and Technology Assessment Committee in the 43-year period between 1966 and 2009.
Reimbursement

Changes established in 2005 for Medicare reimbursement of IG therapy threatened the care and lives of many patients in the U.S. A congressionally mandated reduction in Medicare Part B reimbursement rates and the two-tier rates for liquid and lyophilized IG established two different rates for administering IG, depending on where treatment was received. This new reimbursement methodology significantly lowered the rate paid to physician offices and homecare companies, creating a dangerous situation for seriously ill, low-income patients with PIs or neuropathies. The reduced rate at which physicians were reimbursed was so devastating that many had no choice but to refer patients to hospitals where co-pays were as high as $649 per treatment. And, what many people predicted would happen did: One patient unable to receive his IG treatments died.

Another issue also prevented many patients with autoimmune diseases such as Guillain-Barré syndrome and neuropathies from receiving coverage for IG therapy. Even though these diseases were discovered more than 100 years ago, and the use of IVIG to treat these disorders was known to be beneficial, insurance companies mandated evidence from controlled medical clinical trials, which didn’t exist, versus experimentation and observation. This made getting reimbursed extremely difficult.

Effective Jan. 1, the final rules for reimbursement changes issued by CMS went into effect. The changes included 1) the elimination of the preadministration fee for the hospital outpatient setting and the physician’s office that was established to help locate product for patients who had shifted to other treatment sites because of earlier reimbursement changes; and 2) a reduction in the reimbursement for the hospital outpatient setting from ASP plus 5 percent to ASP plus 4 percent.

Patient access to IG therapy in states across the country was further reduced when the majority of Medicare carriers (private insurance companies that implement Medicare benefits at the local level) implemented local coverage determinations. The determinations varied by state and carrier, and were not based on accepted medical guidelines for treatment and dosing.

In the private healthcare sector, some insurance companies transitioned the management of chronically ill patients’ homecare and delivery of their specialty pharmaceutical products and services to a single, company-designated specialty pharmacy and/or homecare company. Under this new policy, patients started receiving product from a specialty pharmacy either owned or designated by the insurance company and nursing services from the homecare company selected by the insurer, rather than by the patient. While the effects of the policy were not yet known, analysts predicted that patients would have increased cost barriers to out-of-network providers.

But a report titled “Specialty Pharmacy Management Insights” indicated that specialty pharmacies were becoming more important as insurance companies, managed care providers and other payers sought ways to streamline specialty pharmaceutical dispensing and cut costs. According to the report by Wyeth Healthcare Systems, more specialty pharmacies would be acquired by larger companies and would offer more services. What wouldn’t change is their role: providing the special needs of patients that are peripheral to the actual administration of their medicine.

Also that year, the Centers for Medicare and Medicaid Services (CMS) reduced reimbursement for all drugs offered in the hospital outpatient setting, including IVIG, from the manufacturer’s average sales price (ASP) plus 6 percent to ASP plus 5 percent, as well as reduced the IVIG hospital outpatient preadministration fee by 50 percent — at a time when IVIG patients were shifted to hospitals as the site of care of last resort. CMS was also scheduled to eliminate coverage for treatment of certain infections that are acquired while patients are hospitalized, which would have severely affected immune-compromised patients, many of whom have no other site-of-care option.
Then, insurance companies, including private healthcare plans, Medicare Part D plans, Tricare and the Federal Employees Health Benefit Program, announced that patients who need chronic lifesaving therapies such as IG may have to pay for them under Tier IV and Tier V categories. Previously, these therapies that were covered by a health insurance company’s major medical plan were switched to be covered only under Tier 1, II and III categories; the higher the tier number, the higher the co-pay. Under Tiers IV and V, patients would be required to pay a 10 percent to 30 percent co-pay for their therapy.

Access to IVIG therapy continued to be a concern due to Medicare reimbursement changes, prompting President Obama to sign into law the Medicare IVIG Access Act, a demonstration project to assess whether adding coverage for nursing services and supplies to administer IVIG for patients with PI in the home will impact issues currently faced by Medicare patients. Under current law, Medicare Part B covers IVIG treatment only in the home for some PI patients.

In response, the state of New York passed a law that prohibits commercial health insurance plans from creating specialty tiers within their prescription drug formularies. According to New York law, specialty tiering is contrary to the original purpose of insurance, which is to spread the cost; instead, it creates a structure where those who are most sick pay more, which is an unlawful discriminatory practice.

California joined New York by passing a bill that protects patients with life-threatening diseases from escalating insurance costs for medication. It placed a $150 co-payment cap for a one-month supply of medication, prohibited health plans and insurers from using co-insurance and placed an annual out-of-pocket limit on prescription drug costs if a plan or insurance policy maintains an annual limit. Many other states were considering similar legislation.

The Department of Health and Human Services also sought to protect consumers from exorbitant insurance costs when it issued a regulation to ensure that large health insurance premium increases would be thoroughly reviewed and consumers would have access to clear information about those increases. The rule requires independent experts to scrutinize any proposed increase of 10 percent or more for most individual and small group health insurance plans.

With the Medicare IVIG Access Act underway, the Centers for Medicare and Medicaid Services held an open-door forum to get input from key stakeholders on questions related to the design and implementation of the demonstration project. The main questions under discussion during the forum were:

- Should billing for demonstration-covered nursing services and supplies be permitted by organizations that are not supplying the drug?
- What types of organizations should be eligible to participate in the demonstration?
- Who should CMS reach out to to inform about this demonstration?
- How can CMS best reach out to beneficiaries and their providers?
- Should CMS have an open enrollment period during which applications would be submitted on an equal basis for consideration, rolling enrollment or some combination?
- Should a patient’s physician be required to sign a beneficiary’s application to confirm the diagnosis and awareness of the demonstration and locus of service?
- Should the beneficiary’s application specify a particular drug or supplier?

The outcome of this initiative is still being awaited.

Editor’s note: The above information is what was reported on in IG Living magazine during the past decade, and is not meant to be representative of all events that occurred in the highlighted areas.
IG Living is indeed unique. Not only does each issue provide insight on the issues of greatest importance to our readers, but it is an educational resource chock-full of information that cannot be found elsewhere. Over the years, we have teamed with talented writers, dedicated healthcare professionals, patients and caregivers in the IG community who have dedicated countless hours during the past decade to write articles to help you better understand your diseases and cope with the many issues you face living with chronic illness. The sheer number of articles published in IG Living totals in the thousands, many of which detail how diseases treated with IG are diagnosed and treated. Here, though, we list our picks for the top educational articles on disease management, lifestyle management, parenting/caregiving, communication, insurance/reimbursement and research — all of which (and much more!) you can find on our website at www.IGLiving.com/magazine/archive.html.

**Top Educational Picks!**

### Communication
- Improving Patient-Doctor Communication, by Ronale Tucker Rhodes, MS
  October-November 2014, p22
- Paging Dr. Right!
  by Trudie Mitschang
  October-November 2011, p22
- Telling It All: How to Share the News of Your Diagnosis,
  by Dana Martin
  June-July 2015, p18

### Lifestyle Management
- Exercise Success, by Matthew D. Hansen, DPT, MPT, BSPTS
  June-July 2014, p16
- Financial Planning for Patients with Chronic Illness, by Trudie Mitschang
  August-September 2015, p32
- GI Problems for IG Patients, by Jill Weisenberger, MS, RD, CDE
  October-November 2010, p12
- How Exercise Benefits the Immune System, by Matthew D. Hansen, DPT, MPT, BSPTS
  April-May 2010, p22
- How to Cope, by Erika Lawrence, PhD
  December-January 2010, p16
- How to Successfully File for Disability, by Cynthia Perry
  June-July 2015, p22
- Job Interviewing Strategies for the Chronically Ill, by Dana Martin
  April-May 2015, p32
- Patient Advocacy: How Patients Can Gain Control,
  by Annaben Kazemi
  April-May 2014, p26

### Insurance/Reimbursement
- A Review of Medicare and Disability Programs, by Jennifer Kester
  August-September 2010, p29
- How the ACA Impacts the Chronically Ill,
  by Ronale Tucker Rhodes, MS
  August-September 2014, p26
- How to Write an Effective Appeal Letter, by Kris McFalls
  December-January 2011, p14
- Transitioning IG Coverage to Medicare, by Michelle Greer, RN, and Leslie J. Vaughan, RPh
  October-November 2015, p28
Parenting/Caregiving

- School Site Programs for K-12 Health-Impaired Students, by Ronale Tucker Rhodes, MS
  August-September 2013, p14

- The Impact of Chronic Illness on the Family, by Erika Lawrence, PhD
  June-July 2012, p20

- Treating PIDD Kids — Post-Diagnosis, by Amy Scanlin, MS
  October-November 2012, p18

Disease Management

- An Overview of Immune Globulin Dosing, by Kris McFalls
  February-March 2011, p14

- Diagnosing PIDD: Problems and Solutions, by Kris McFalls
  June-July 2011, p22

- Fungal Infections in PIDD Patients, by Alexandra F. Freeman, MD, and Anahita Agharahimi, MSN, CRNP
  December-January 2014, p16

- Overcoming SCIG Needle Anxiety, by Amy Ehlers, BS, PharmD, BCPS
  April-May 2013, p16

- Preventive Healthcare for Patients with Chronic Illness, by Ronale Tucker Rhodes, MS, and Kris McFalls
  August-September 2010, p16

- Routine Primary Immunodeficiency Lab Reports: What Do They Mean? by Bob Geng, MD, MA
  October-November 2015, p36

- The ABCs of Tracking Healthcare Treatment, by Ronale Tucker Rhodes, MS, and Kris McFalls
  June-July 2010, p28

- Understanding and Treating IG Side Effects, by Ronale Tucker Rhodes, MS, and Kris McFalls
  April-May 2010, p26

Research

- Funding Research to Find Cures/Treatments, by Matthew D. Hansen, DPT, MPT, BSPTS
  October-November 2010, p16

- Gene Therapy: The Cutting-Edge of PI Treatment, by Caroline Y. Kuo, MD, and Roger H. Kobayashi, MD
  October-November 2014, p16

- Individual IG Dosing Strategies, by Ronale Tucker Rhodes, MS, and Kris McFalls
  December-January 2012, p18

- Long-Term Effects of PIDDs, by Annaben Kazemi
  December-January 2013, p24

- Screening for Severe Combined Immunodeficiency Disease, by Amy Scanlin, MS
  June-July 2014, p26

- Severe PIs: Cutting-Edge Science Turns Tragedies to Cures, by Keith Berman, MPH, MBA
  April-May 2015, p16
A brief overview of prescription drug labeling for patients and providers.

By Amy Scanlin, MS

SINCE 2006, the U.S. Food and Drug Administration (FDA) has mandated both content and format of full prescribing information (FPI) and highlights for pharmaceuticals and biological products through a regulation commonly referred to as the Prescription Labeling Rule (PLR). These standards have created a label that is more concise, easier to read and more accessible to electronic prescription methods.

A “quick reference” of the drug in the highlights of the FPI is a detailed snapshot of the most pertinent information practitioners and patients should be aware of. Both the FPI and highlights provide information and instructions that may pertain to the specific needs of the patient, with the what and how clearly articulated. The intent is for the drug to be more safely prescribed to a population for which it is intended, with additional details, if any, for those with special considerations.

While the full FPI for any drug should be reviewed thoroughly, following is an overview of the basics of drug labeling, as well as three key sections containing information of importance to specific populations.

Content Ordering

The FPI and highlights sections are laid out as mandated by the PLR, which contains 17 sections (see Prescription Label FPI Contents and Section Numbers). Should one or more of the 17 sections not pertain to a specific drug, they may be eliminated from the label; however, the sequential ordering of the sections must not be changed. For example, if there are no known drug interactions to be concerned with, section 7 may be omitted from the label, and the panel would move directly from section number 6 (adverse reactions) to section number 8 (use in specific populations).

Highlights and Boxed Warning

The highlights of a drug label are most often referred to, therefore, it is essential that the highlights provide immediate access to the most important information. Should the drug company determine more detailed information should be referenced beyond what is listed in the highlights, it may refer to and cross-reference other sections in the FPI that contain more detailed data.
At the top of the highlights section is the boxed warning, critical information that the prescriber must be aware of. A boxed warning is also a required part of a label if the information is listed in the FPI. Boxed warnings inform consumers about possible adverse reactions to the drug that are so significant that the risks of the drug must be carefully weighed against the benefits. In the boxed warning, specific guidances for appropriate use to avoid those adverse reactions (such as specific monitoring, awareness of certain drug interactions and patient selection) and restrictions to ensure safe use are also included. Of special interest to providers is the inclusion of information specific to effective use in certain patient populations, if necessary. However, this information is usually found in the warnings and precautions section.²

Optional Content and Cross-Referencing
The only optional sections are the warnings and precautions, drug interactions and use in specific populations, though FDA highly recommends including warnings and precautions. The recent major changes section is required only if there are changes to the boxed warning, indications and usage, dosage and administration, contraindications or warnings and precautions, since these important updates must be conveyed.³

Prescribers should also be aware that section 2, dosing and administration, may be cross-referenced in any number of sections if the information may alter the dose. For instance, if a provider monitors for any specific therapeutic blood levels or metabolites for adverse events (section 6), if there are any details of the dosage with regard to specific populations (section 8), or if there are any specific drug interactions of concern due to concomitant medications (section 7), that information must be explained in multiple sections as needed.

Dosage and Administration
The dosage and administration section of the FPI contains subsections that are invaluable to prescribers of patients with special needs. Subsections include:
- Instructions for monitoring to assess effectiveness
- Monitoring to assess safety
- Monitoring therapeutic blood levels
- Dosage modifications because of drug interactions
- Dosage modifications for specific patient populations
- Important considerations concerning compliance with a dosage regimen
All of these subsections paint a detailed picture for occurrences such as when to anticipate possible side effects in certain patients, how to adjust the drug therapy to help eliminate side effects, when to return to normal dosing and how to adjust the dosage in the future.

The dosage and administration section also gives information to help providers and patients understand the importance and the reason for any additional instructions. If there are reasons for compliance with specific instructions such as timing of the dosage or instructions for taking complex dosage forms, or if there are specific infusion administration details and possible reactions, that information is explained.4

**THE DOSAGE AND ADMINISTRATION SECTION OF THE FPI CONTAINS SUBSECTIONS THAT ARE INVALUABLE TO PRESCRIBERS OF PATIENTS WITH SPECIAL NEEDS.**

Adverse Reactions

FDA labels require the inclusion of only those adverse reactions for which there appears to be a direct causal link to the drug or drugs in the same pharmacologically active and chemically related class. The adverse reactions are arranged by body system, severity of reaction and in order of decreasing frequency. Those reactions with clinically severe implications will also be cross-referenced in other sections, as appropriate, such as the boxed warning, warnings and precautions and contraindications sections.

These reactions are also further separated by those reported during clinical trials and by both foreign and domestic post-marketing spontaneous reports. Post-marketing reports include a statement that helps practitioners understand the significance of any data.

It is important to note the distinction between adverse reactions and adverse events. Adverse reactions are those that have a causal relation between the use of the drug and the adverse event. Drug labels may also contain serious adverse events if those events have an unlikely occurrence in the absence of the drug therapy.5

**Use in Specific Populations**

This optional section is of special importance to providers because it provides details on any clinically significant differences in response or usage by population. Should there be detail for multiple populations, those populations must be listed in the same order in the highlights section and the FPI. While this section is optional and may be omitted in cases where there is no available data, sometimes that lack of data in and of itself is important if the drug has not been evaluated in certain populations. In those cases, this section should be retained with this detail included.

It should be noted that information regarding use of the drug by pregnant women is not included in the highlights section because FDA recommends instead a conversation between the provider and patient that includes all available data. However, any pertinent details on a drug’s use during pregnancy are to be included in the FPI under subcategory 8.1: pregnancy.6

**More Information Is Available**

While this is merely a brief overview of what the information on drug labels includes, a more thorough review of all labeling details can be found on both FDA’s website at www.fda.gov and on the drug manufacturer’s website. Any serious adverse events should be reported to FDA’s Medwatch at www.fda.gov/Safety/MedWatch/HowToReport/default.htm.

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**References**

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A chronic illness diagnosis can strain a marriage beyond its limits, but learning communication skills and seeking support can help couples survive and even thrive.

By Trudie Mitschang

APPROXIMATELY 35.3 MILLION Americans are limited in their daily functioning because of a chronic mental health or physical health condition, according to the American Association for Marriage and Family Therapy.1 For the vast majority of these individuals, family members in general and spouses in particular are often the primary caregivers, and it’s a role that can take a toll on even the strongest relationships. For married couples, navigating a “new normal” can be especially daunting, particularly when the illness becomes like a third-wheel personality, interrupting the couple’s communication, hobbies, lifestyle and even bedroom activities.

Dr. Toni Bernhard, author of several books on chronic illness, including How to Live Well with Chronic Pain and Illness: A Mindful Guide, says of all the areas in a marriage impacted by an illness diagnosis, communication breakdowns seem to be the most problematic. “We do a poor job in this culture of preparing people for the inevitability of health problems. Because of this, when one partner becomes ill, couples are caught off guard, and both of them are likely to start living in ‘crisis mode,’” she explains. “Couples need to be rational and calm in order to effectively evaluate how chronic illness may affect their relationship, and in order to decide what steps both of them can take to make their lives as easy and as pleasant as possible, given their new limitations.”
For many couples, the person who is ill becomes the center of attention, and while some spouses may step comfortably into the caregiver role, others struggle with the title and responsibility. In his book Beyond Chaos: One Man’s Journey Alongside His Chronically Ill Wife, author Gregg Piburn describes how his wife’s struggle with fibromyalgia and other health problems changed not only her life, but their life together as well. He describes his feelings of anger, frustration and guilt, and how the experience ultimately led him to reevaluate his expectations and priorities. In an interview about his journey, Piburn says he and his wife eventually allowed the diagnosis to draw them together, becoming allies against the illness they dubbed “the intruder.” “Like an intruder, chronic illness sneaks into your house unexpectedly and robs valuable items from everyone who lives there. I find value in personifying the illness because it creates an impetus to fight back,” says Piburn. “We go to war against ‘the intruder’; however, we fight wars on several fronts. My book focuses on how to fight chronic illness on the emotional and relational fronts.”

Understanding the Strain

Illness, whether temporary, chronic or terminal, demands time and attention from everyone impacted. A once-healthy couple used to juggling the daily demands of work, childrearing and social obligations may suddenly find themselves straining under the burden of endless medical appointments, mounting insurance bills and complex health regimens. For spouses who find themselves suddenly ill, the additional need for rest and even assistance in showering and dressing can provoke feelings of guilt and helplessness, while putting tremendous pressure on the healthy partner. This is where communication can begin to break down and resentments may begin to build; sadly, many marriages simply disintegrate under the pressure.

In the general population, the lifetime divorce rate has long been reported at 50 percent, and some studies suggest a chronic illness may bump that number up to as high as 75 percent (a figure that remains unsubstantiated). Still, there’s no question that the impact of chronic illness can be detrimental to matrimonial harmony. And, for those marriages that do survive, it can be tough and go — a day-to-day decision to tough things out — with unique challenges for both the caregiver and patient. “Caregivers often make the mistake of trying to be ‘super caregiver.’ This can easily lead to caregiver burnout and depression,” says Dr. Bernhard. “It’s important for caregivers to recognize that it’s OK for them to have days when they feel weary of their role. In my experience, the life of the caregiver is affected as much by chronic illness as is the life of the partner who is struggling with health issues.”

Dr. Bernhard adds that partners who are chronically ill tend to make the mistake of entertaining a “pity party” mentality, believing that their loved one doesn’t care enough about them: “Those who are chronically ill often make the mistake of expecting too much from their caregiver/partner — of not realizing that their partner is as confused and shocked as they are over this unexpected change in their lives and their relationship.”

The Influence of Gender Roles

Studies show that men and women react differently to a diagnosis of chronic illness, and may exhibit different coping skills. One study, which analyzed 20 years of data on 2,717 marriages from the Health and Retirement Study conducted by ISR since 1992, examined “the role of serious physical illness onset in subsequent marital dissolution via either divorce or widowhood.” The study found an elevated risk of divorce at the wife’s illness onset, but not the husband’s. There is “evidence that when wives become sick, marriages are at an elevated risk of divorce,” says Amelia Karraker, a researcher at the University of Michigan Institute for Social Research (ISR), and one of the study’s authors, “whereas we don’t see any relationship between divorce and husbands’ illness.”

Elvira Aletta, PhD, a licensed clinical psychologist who was diagnosed with a rare kidney disease in her 20s, and later diagnosed with scleroderma, a chronic connective tissue disease, says the problem can come down to an inability to deal with displaced emotions. “Men, in particular, are programmed from birth to fix things. Our healthy spouses hate that in the face of chronic illness, they can’t fix things,” she explains. “Their frustration can come out as irritability, sniping, overcompensation, co-dependent, enabling-type behavior, throwing themselves into..."
work (an area where they can feel competent) and/or shutting down emotionally, appearing kind of flat. All of these can be masking depression.”

Another study published in the journal Cancer found that a married woman diagnosed with a serious disease is six times more likely to be divorced or separated than a man with a similar diagnosis. Among study participants, the divorce rate was 21 percent for seriously ill women and 3 percent for seriously ill men. A control group divorced at a rate of 12 percent, suggesting that if disease makes husbands more likely to split, it makes wives more likely to stay. Scientists point to a few possible explanations for the disparity. For one, being a caregiver is not a traditional role for men, says Dr. Marc Chamberlain, director of neuro-oncology at the Seattle Cancer Care Alliance and one of the authors of the study. “The majority of husbands take excellent care of their partners, but men on the whole tend to be less comfortable doing so,” he says.

Studies show that men and women react differently to a diagnosis of chronic illness, and may exhibit different coping skills.

Seeking Help and Support

A diagnosis of chronic illness often comes with a confusing mix of emotions, including anger, grief and even shame. When an individual suffers from an invisible illness such as an immune deficiency disease, those feelings can be compounded. Dr. Aletta encourages couples who sense long-term illness is threatening the stability of the marriage to seek outside support and help sooner rather than later. Getting toxic feelings and fears out in the open by discussing them with a neutral third party can give both the patient and caregiver improved coping and communication skills. In her article, “10 Ways to Care for Your Marriage When You Have a Chronic Illness,” she advises:

1. Be honest with yourself. Only you in your heart can know how much you reasonably can and cannot do. When you know your limits, there is no need to be defensive.

2. Remember you are on the same team. Your marriage is a cart being drawn by two horses: you and your spouse. Being a team, when you pull in the same direction with the same speed, your cart goes forward. If you run in opposite directions, the cart falls apart.

3. Keep the chronic illness outside of yourself. Keep it figuratively “out there.” That way the problem isn’t you; the illness is another problem to face and deal with, like the mortgage. That way, it’s easier for the two of you to face it together and problem solve shoulder to shoulder.

4. Let your partner take responsibility for his or her own emotional life; don’t try to shoulder the burden.

5. Remember, we cannot change them. We can only ask ourselves: “Am I being the best partner I can be?” Miraculously, by not responding defensively to their provocations, for example, not yelling back when we are yelled at, we role model real versus pseudo communication.

6. Be creative. I know a couple who uses a non-verbal signal for pain levels. You can also be creative about “lightening the load.” Are there other community, friend or family supports that can be utilized better? The two of you can also Internet search healthy, easy recipes for dinner.

7. Find a routine you both can count on. Stress thrives in chaos. Health — emotional as well as physical — loves regularity. The more you can plan your day and week, the easier for both of you. Take a few minutes at least once a week to go over what will be happening the week ahead.

8. There’s always therapy. I know I can be a broken record about this, but couples counseling is for more than just couples who are fighting and heading for divorce. A good couples’ counselor can help you loosen up your creative energy when you are too deep in bad habits. A lot of spouses will go to couples therapy “for you” and then get help for their own adjustment problems or depression.

9. Let him know, every day, in small but direct ways, when he is appreciated. The carrot, rather than the stick, is the most powerful tool for positive change.

10. The book The Power of Two by Susan Heitler is a favorite of mine. It is a practical resource that helps even the best marriages by teaching couples to pay attention to how they are communicating, talking and listening to each other.

Pulling Together When a Child Is Sick

When chronic illness strikes a marriage partner, the road ahead can be a difficult one. But when illness impacts a couple’s child, a whole different level of stress bombards even the happiest unions. Jessica Johnson is the mother of three
boys with X-linked agammaglobulinemia (XLA), a rare immunodeficiency disease. A fourth son passed away from XLA, a tragedy that has taken a toll on her 16-year marriage. “Chronic illness, specifically XLA, has somewhat taken away our positive outlook for the future. It’s positive enough ‘given the circumstances,’ but there is definitely a shadow of doubt when it comes to how long our kids will maintain healthy and active lives,” she explains. “It has also had an effect on how many kids we had. I think if we hadn’t continued to have sons afflicted with XLA, we might have had one more child. We’ve also lost one child to XLA, and that loss has affected our family in so many ways. We have one less child in the house. We may feel like we’re busy, running four kids here and there, but we should be even busier.”

While some couples are able to unite in the face of tragedy, Jessica says her and her husband’s different coping styles have created a gulf between them: “It has definitely created a wedge. I’m a worrier and I tend to place my concerns for the kids above everything else, particularly my husband’s needs. I can’t live in the moment if they’re sick or if I’m preoccupied with thoughts of their illness. If it’s flu season, for example, I’m pretty mentally checked out, and that creates distance in my relationship with my husband.”

Taking care of a child, or in Jessica’s case, multiple children, with ongoing health problems can be one of the most difficult tasks a parent can face. Relationships within the family will be altered, and sometimes strained, as everybody adjusts to the situation and perhaps takes on additional responsibilities. Sometimes other children get a lot less time and attention. In addition to worry and concern about the child’s health, there may also be financial worries. The cost of medical treatments and procedures can be expensive for families, and sometimes parents need to go back to part-time work, or not work, to care for their child, which can create additional financial strain.

**When chronic illness strikes a marriage partner, the road ahead can be a difficult one.**

According to the Women’s and Children’s Health Network, these types of pressures can lead to stress, exhaustion and tensions within family relationships. However, there are some things that adults can do to help support the family and prevent the situation from destroying the marriage. Some suggestions include joining a support group, asking for help from extended family members, giving yourselves “time out” from caregiving to just be a couple again, and considering professional help from counselors and therapists. “The initial diagnosis of chronic illness can be pretty shocking, and it may seem life-altering at first,” says Jessica, “but as you get used to incorporating the treatments and/or therapies into your daily and weekly routine, you can start returning to life the way it used to be, with a few adjustments.”

TRUDIE MITSCANG is a contributing writer for IG Living magazine.

**References**


AFTER SUFFERING through years of chronic illness, Deborah Sevett was finally diagnosed with common variable immunodeficiency (CVID). Unfortunately, after battling with her insurance company over immune globulin (IG) treatment, Deborah lost everything, including her career, marriage, family and friends. What she didn’t lose, fortunately, was hope. Today, this talented artist has found a way to turn her experiences into dynamic artistic creations that were recently featured at the UCLA David Geffen School of Medicine.

Trudie: When did you know you were ill?
Deborah: I knew something was very wrong with me around age 12. I began having sore throats and was told I was fine, [it was] just a little allergy. As I kept complaining, I was then labeled a hypochondriac. I learned much later that my instincts were correct: I have CVID, a diagnosis that would lead to a lifetime of self-research and psychological pain for me.

Trudie: How were you finally diagnosed?
Deborah: When antibiotics mostly failed, I tried all types of natural therapies. You name it, I have tried it! I felt awful all the time, but hey, at least I looked OK! How could I be sick? Then came multiple bouts of pneumonia. This really scared me and set off warning signals. I knew I had to become proactive or end up in a place I did not want to think about. Fortunately, I found a specialist in Kansas City who informed me there was good news and bad news. The good news was I have had this genetic issue most of my life; it was not in my head. The bad news was I would require infusions of IG for the rest of my life. I was relieved. My first infusion went to work and kicked in on the pneumonia. The next day, I felt 100 percent better. Then, the insurance wars began. It was an exhausting battle, and I lost everything: my career as an instructor, my marriage, my family and many friends. I went through a deep depression, and I turned to art as an outlet. I knew my art would never in any way leave me or abandon me.

Trudie: What is unique about your artistic style?
Deborah: I love the color black. I know other people reject the color for being “dark and depressing.” Not me. I find so many other colors within this color, and I made this my focus and exploration for many years.

Trudie: Tell us about your art show “But … You Look Okay!” at the UCLA David Geffen School of Medicine. How did that come about?
Deborah: I was approached by a local curator for a show at UCLA. He wanted my work to be displayed when the students were in the genetics semester of school, and since CVID is a genetic condition, it was perfect timing. They really enjoyed it and learned a lot. I was anxious to ask what they would do if they had a patient with persistent and chronic infections. They all shook their heads and said they would act on their suspicion, not think twice, and send the patient to an allergist/immunologist. Many had further questions and came up to talk after the lecture. As a young patient and for much of my adult life, most of my physicians did not know about nor had they heard of CVID. This was truly a revelation for the students.

Trudie: What has been the public reaction since the show?
Deborah: Favorable. Personally, the most shocking was from people I know.
They wrote heartfelt letters stating: “How could I know you my entire life and not know this?” They had no idea I was ever ill. They were sorry and sad that I felt I could not share, but understood. My personal aim was to bring awareness to the UCLA medical school students. After sharing my personal story, I asked the students if anyone knew what CVID was. To my surprise, only one out of the 50 students knew the answer. Mission accomplished.

**Trudie:** What is your goal with your artwork?

**Deborah:** My intention as a student and painter was not to set out to highlight illness. Looking back, however, it’s just what I did in the 1990s. Those years allowed me to communicate subconsciously. Today, I paint much the same. I am in shows in Los Angeles and very active in the art community. There are also many layered meanings in my work. My hope through the UCLA exhibit is to bring awareness to CVID because so many suffer silently while being labeled hypochondriacs.

**Trudie:** What has chronic illness taught you about yourself?

**Deborah:** I have learned from experience that if CVID is not diagnosed, many other related co-diseases, infections or viruses may present. For example, I have had two severe bouts of Epstein-Barr virus. This left me with unpredictable chronic fatigue syndrome. I learned my limits long ago, and now say “no” to many requests.

Sadly, many of us endure family members who refuse to see the debilitating side of CVID and, in my case, still view me as lazy and passive. I know I am none of those things. Still, it brings anguish and sadness. I have learned that I am not alone and that many are misunderstood. I also learned that I must work hard to present an upbeat persona. This is probably most confusing to family members and friends.

Finally, chronic illness taught me to reach out. One night about five years ago, I started a CVID discussion group on Facebook. Today we have a very tight and caring group. We have shared some of life’s deepest tragedies and some of life’s most amazing strides. One man remarked that he learned more in two weeks than he did in 25 years of seeing numerous physicians who had no answers for him. The intrinsic value that comes from this group is to help others while helping myself. Win-win!

**Trudie:** What advice do you have for other CVID patients?

**Deborah:** My advice is listen to your body and listen to your gut. They are not wrong! Find a supportive group of people who have the same condition as you. No one understands better than those who have walked alongside you on this trail. Stay with your tribe, and know that they may not be your blood relatives but they “get” you. If they are blood, consider yourself one who hit the jackpot! Discard those who are careless of your condition. Keep your spirits up and stress low in any and every way you find necessary. Seek joy, and know that nothing is more important than that you feel good. Lastly, if a health professional treats you shabbily, calmly stand up and walk out. There are many knowledgeable and compassionate doctors out there. Check the Immune Deficiency Foundation and CVID websites for names of physicians. Above all, do not stop reading and educating yourself. Be proactive.

**Trudie:** How has being an artist sustained you during the most difficult seasons of life?

**Deborah:** When I was in art school, I was often very ill. Art and music would soothe me. Over the years, I have faced wearying conditions, desolation and difficult people. In my life, my art is my one true love and will never ever leave me. I rest knowing this in every single cell of my three-dimensional self. ☐

**TRUDIE MITSCHANG** is a contributing writer for IG Living magazine.

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Editor’s note: More of Deborah’s work can be viewed at www.deborahsevett.com.
What a Lulu!

By Stacy Oliver

I HAVE A confession to make. I have become one of those people. What kind of person, you ask? Well, I’ll proudly sing the praises of being a dog owner and a lover of these four-legged creatures that are truly one of humans’ best friends. Dogs bring joy, love and comfort in ways that are magical and healing.

This journey started three years ago, when on top of dealing with having multifocal motor neuropathy for several years, I was diagnosed with lupus and Sjögren’s syndrome. Yay, two more autoimmune issues for me! As you can imagine, I was incredibly anxious and depressed. I was in a funk, feeling unmotivated to be active. My husband and I started discussing getting a dog for therapy purposes. He had one many years ago, and I had never owned one. In fact, I used to be afraid of dogs. But I was open to the suggestion. We also knew it had to be a rescue dog.

Time went by, and we still had taken no action. Of course, when you’re not looking, the best things come into your life. One weekend, my guy found the dog of our dreams at a shelter. It was completely unplanned. I got a text with a picture of the doggie that said: “Me likey, me want.” I looked at our dog and said yes. She was adopted on April 1 — no joke. I remember reading everything I could about the American Staffordshire breed. I even chose her name since she didn’t have one. My husband has a funny phrase he says when something amuses him: “What a lulu!” In the first picture he took of our angel, she had a big dopey smile on her face. She was a Lulu.

It’s been a love affair ever since. She is love and she wants to be loved. The fur on her chest is in the actual shape of a heart. I met people in the neighborhood I never knew before because of Lulu. On our walks, I discovered new places. We had Lulu for a few days when on a walk with her, I fell. Foot drop — one minute you’re fine, the next you’re kissing concrete. I gathered myself up and assessed the damage, and then realized, “Where’s Lulu?” I thought she’d be long gone. Nope. She was sitting right next to me looking all concerned about what happened to her mama, and she licked my face.

She’s a certified Good Citizen by the American Kennel Club and also a therapy dog. She brings joy everywhere she goes. People giggle when they see her. This could be because we take her for walks sometimes with glittery angel wings on or a big flower on her collar. Never in my life would I believe folks driving by would slow their cars down to shout out the window: “What a beautiful dog!” Every month, I receive two eight-hour days of intravenous immune globulin infusions at home. Lulu is by my side the whole time comforting me. She senses when I’m not feeling well, and she helps relieve so much stress.

So, I implore you fellow immune globulin users. If you are able to do so, I highly recommend bringing a pet into your life. I can’t imagine a more positive action you can take for yourself. Lulu got me back to living life! She unlocked my happiness that had been buried in despair and sorrow. She opened the door to explore new social activities and make new friendships. Long walks with her keep me active. Lulu is a reminder that we all want to love and be loved. What a Lulu!

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.
I’LL BE THE first to say that I was lucky. I may have a rare disease and more disruptive symptoms than I can handle, but in terms of my disease causing me to declare bankruptcy, I made out like a bandit! Cigna, Aetna, Humana, Blue Cross. I jumped from plan to plan seamlessly. Nobody questioned my existing conditions. Sure, I was billed for every medication, hospital visit and doctor appointment. I even had medical debt like every other chronically ill patient in the United States. But compared with most, I knew I had it good.

I’d been coasting on my parents’ insurance plan throughout my entire life. If there was a doctor I needed to see, I saw him or her. If there was a medication I needed to take, I got it. But, then, age 26 came roaring at me like a freight train. I knew that I was about to take the plunge into the most perilous part of chronically ill young adulthood: finding health insurance without my parents. It didn’t help that my stepfather switched jobs, and I suddenly found myself with just one month to avoid a gap in coverage. I’m a freelance worker, a job that doesn’t come with benefits. So, attempting to afford COBRA was laughable.

And even then, in my moment of uncertainty, I managed to luck out one more time. My fiancé was able to add me to his insurance plan at his work. And, although the human resources person completely butchered the process of putting my name on the plan for an entire month, the benefits were pushed through in the nick of time. It’s not a great plan, but if I have a crisis, I’m not going to owe student debt-sized paychecks to the hospital.

Yesterday, I went to pick up one of my medications that is excluded from the plan. The pharmacy asked me to pay $500 for a month’s supply. Another medication that I had been taking for seven years was also excluded, and it was going to cost me $200. That’s when I thought: “Well, is not having a 24-hour migraine that important to me?” I’d like to think I’m the kind of responsible patient who would say: Yes, here, take all my savings because it’s the health-conscious thing to do! But let’s face it, I’m not. And with most other 20-somethings already struggling with being uninsured, you can bet they’re skipping out on important medications as well.

An example: A year or two ago, a friend of mine sprained both wrists working as a waitress. The pain was constant, but because she lacked insurance, she refused to see a doctor. She would sling her wrists up in stiff ace bandages and deal with it. Eventually, after a lot of searching and suffering, she finally was able to obtain a healthcare plan under the Affordable Care Act (ACA). With the ACA, things are taking a turn for the better. Historically, according to ObamaCareFacts.com, 37 percent of people ages 19 years to 25 years and 25 percent of those ages 26 years to 35 years were uninsured — far higher than any other age group. Now, according to the Centers for Disease Control and Prevention’s National Health Interview Survey, the current uninsured rate is 9.2 percent — the lowest in more than 50 years.

This doesn’t mean much if you end up with a plan that covers virtually nothing beyond the assurance that you won’t get fined for not being insured when you do your taxes this upcoming year. So, here are some things to help you stay one step ahead of the insurance game:

• Start putting away small sums of money each week toward an emergency medical fund.
• Speak with different health insurance agencies about what they can offer you. Ask them to send you information packets, and go over them thoroughly with someone who is insured and can help analyze them.
• Ask your friends. What better resource is there than the entire age group of people going through the exact same issue? Ask what their insurance plans are, how much they cost and how the process of applying for them went.

As your 26th birthday draws nearer, be on the alert. Lucky or not, informed is always the best way to be. IG Living has a list of resources that can help you learn more about how to get the right insurance for you at www.igliving.com/resources/insurance.html.

ILANA JACQUELINE is a 26-year-old dysautonoma 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.letsfeelsbetter.com is both a personal collection of anecdotes about life with chronic illness, as well as a resource for patients of all ages.
A Child’s Doctor Appointment Checklist

By Jessica Leigh Johnson

PARENTS OF CHILDREN who suffer from primary immunodeficiency (PI) are all too familiar with doctor appointments. Indeed, because PI kids have a higher occurrence of infections, their families may think of the clinic as a second home. As such, going to the doctor becomes so routine, it may be standard practice to head to an appointment with little forethought. However, there are several things that every PI kid should take to clinic visits to make them go as smoothly as possible.

Medical records. Your child’s regular doctor should have his or her complete medical history on file, but this won’t be the case if your child is seeing a specialist for the first time, or if you’re traveling or visiting an emergency room. Parents of PI kids should be prepared for the unexpected, so it’s a good idea to make a folder containing key health information in case you’re visiting the doctor under less-than-ideal circumstances.

Some things to include are a list and explanation of medical conditions, dates of past surgeries, hospitalizations, current medications, primary care doctors’ and specialists’ names and contact information, a few close relatives’ names and their contact information, health insurance card, and any known drug allergies. Websites such as MedID.com offer free medical card templates that can be filled in and printed out for a convenient way to carry important information. Keep a card in your wallet or purse so you’ll have it with you wherever you go.

Recent test results. PI kids often have X-rays of their chest and sinuses, and they’re no strangers to blood work. It is important to bring lab test or X-ray results to each and every clinic appointment. This is especially important when seeing multiple doctors or visiting a specialist for the first time. Up-to-date information will help the doctor get a more complete picture of the child’s overall health. And, unless an infection is suspected, it will reduce the need for additional or redundant testing that will expose the child to more radiation and the risk of unnecessary side effects.

An infusion log. No matter the reason for the appointment, the doctor needs to know the date of your child’s last infusion. The clinic where your child receives intravenous immune globulin (IVIG) should have that information on file, but if the child is visiting a new clinic, or if he receives subcutaneous IG (SCIG) infusions at home, the doctor’s office will have no record. Knowing when your child’s infusions occur will ensure that blood work, such as testing for trough levels, is done at the appropriate time.

Also, in the case of SCIG infusions, the doctor may want to check your child’s skin to make sure his body is tolerating the treatment. If the tissue is hard, or if lumps and welts don’t disappear within a few days, the doctor may recommend changing needle insertion sites or adding to the number of sites to give certain areas of the skin a rest. Because some PI patients tolerate one IG manufacturer’s brand better than another, bringing your child’s infusion log (including brand name and lot numbers) will help the doctor know which product the child has been receiving, and aid in determining if another product may work better or have fewer side effects.

A list of prescription drugs. When a child sees multiple doctors, it is possible that one doctor isn’t aware of drugs another doctor has prescribed, especially if the prescription is new. Knowing the names of the drugs your child takes isn’t enough. The dosage and strength of the prescribed medication is vital information to pass on to the doctor. The best thing to do is to bring the bottles with the labels on them to each appointment. Also, be sure to mention any natural remedies, vitamin pills and supplements your child takes, as there may be harmful interactions between alternative therapies and prescription drugs.

Be sure to tell the doctor if your child has stopped taking any prescribed drugs. If the doctor assumes your child is still taking allergy medicine, for example, yet
notices he still has a clear runny nose, he may assume the drug isn’t working and prescribe a higher dose or stronger medication. Also, do an inventory of your medicine cabinet and check for any prescriptions that need refilling. It’s a lot easier to get a refill from the doctor when he’s sitting in front of you at his computer rather than leaving him a string of phone messages or emails once you get home.

Entertainment. In a perfect world, we would enter the doctor’s office at our scheduled appointment time and be done within half an hour. But most parents know from experience that clinic appointments usually take longer than expected, and they require patience on the part of both the children and parents. Snacks, drinks, toys, books and iPads can keep children entertained and happy (relatively happy, under the circumstances) while waiting for the doctor to arrive in the room, or while waiting for test results.

A notebook and pen. So often when we take our children to see the doctor, we have a list of questions we want to ask. “What is that rash on my son’s skin?” “Should he be getting so many eye infections?” But if, at appointment time, traffic is heavy and we’re running late, we may arrive at the clinic in such a frazzled state, those questions flee our minds, only to return once we get back home.

It’s better to prepare for the child’s appointment ahead of time by jotting down a list of questions in a notebook. Think ahead to the next six months. What sports are coming up? Any family trips? What do you need to know regarding your child’s illness and these activities? Having these questions written down will ensure that you won’t forget them when you’re face-to-face with the doctor.

Also, keep that notebook handy during the appointment to jot down any instructions or new information the doctor gives. After receiving a medical information dump, it’s easy for us mere mortals to forget the technical details. “How many times was my son supposed to puff on this newfangled inhaler?”

No matter the reason for the appointment, the doctor needs to know when your child had his last infusion.

A family member or friend. If possible, bring someone to the appointment, other than the child, for moral support. This can be a spouse or a close friend or relative. Raising a child with PI can be emotionally draining for parents, especially when receiving unpleasant news from the doctor. Having another adult in the room while you and the doctor discuss diagnosis, testing or treatment will ensure that your primary questions and concerns are addressed. If you’re not satisfied with the answers the doctor gives, it’s easier to voice your objections when you have the support of someone close to you.

Write this down! There is one number no PI parent should be without, but many may not know about it. Whether you’ve moved to a new area or are simply on a vacation, there may be times when your child has to see a doctor who is unfamiliar with his or her condition. Because treating an infection must be done more aggressively for PI kids, be sure to ask every new doctor if he is familiar with PI. If he is not, or if he simply wants a second opinion, request the doctor contact the IDF Consulting Immunologist Program at (877) 666-0866. According to the IDF website, “The IDF consulting immunologist program offers free physician-to-physician consults; consults or second opinions on issues of diagnosis, treatment and disease management; and access to a faculty of recognized leaders in clinical immunology.”

No matter how long you’ve been dealing with PI, you probably already know to expect the unexpected. So the next time your child has a clinic appointment, it’s better to be overprepared and bring something you don’t need than to show up without something vital. Being organized will help you and the doctor get the most out of your time together, and ensure that your child receives the best care possible.

JESSICA LEIGH JOHNSON is a stay-at-home mom and mother of four kids, three of whom have X-linked agammaglobulinemia. She is a member of American Christian Fiction Writers and has written one book about the loss of her son to a primary immunodeficiency.

Sources
Managing IG Co-Pays

Out-of-pocket sticker shock for immune globulin (IG) therapy can add insult to injury for many primary immunodeficiency (PI) patients. But for those who qualify, patient assistance programs and co-pay assistance can help ease the burden.

By Trudie Mitschang

THERE HAVE BEEN significant advancements in the diagnosis, treatment and care of PI patients. What has not improved in recent years, unfortunately, is the cost of care. IG infusions, whether done in the hospital setting, in an infusion center or at home, are extremely costly, and even patients with the best insurance coverage can find themselves burdened with hefty co-pays that can make ongoing care difficult if not impossible. For some, the increased financial burden leads to some very tough decisions that could put their health and financial stability at risk. It’s no surprise, then, that more and more patients are seeking assistance when it comes to footing the bill for out-of-pocket IG expenses.

Am I Covered?

The challenge for most newly diagnosed PI patients (and their family members) is that there are so many unknowns. Between treatment decisions and navigating side effects, asking the right insurance coverage questions may not become a priority until the first unpaid claim statement arrives, an event that leads to time-consuming appeals, frustration and possible interruption in care.

When it comes to paying for IG treatments, key questions to ask your insurance provider include whether a particular treatment is covered, and whether details such as where treatments are administered, whether they are intravenous or subcutaneous, and how the treatments are coded for billing will change the bottom line. Next, be sure to ask what costs are covered by the policy and what costs are considered the patient’s responsibility. Lastly, patients should find out whether their policy has a lifetime maximum on benefits, since once the maximum is exceeded, insurance may no longer pay for treatment or medical care. Because the high cost of IG can very rapidly deplete even the most generous policies, this is a question you will want answered sooner rather than later. It is not uncommon for chronically ill patients who do not fully understand their out-of-pocket obligation to suddenly discover after starting treatment that they are unable to afford their medication, forcing them to put their health and/or financial future at risk.

Offsetting the Cost of Care

In 2014, the Affordable Care Act (ACA) required all health-care plans that were not grandfathered to implement an out-of-pocket expenses maximum to help patients who could not afford the cost of care. Last year, the maximum expenses were capped at $6,600 per individual and $13,200 for families, but these benefits are not readily available to patients with chronic diseases and expensive treatments like IG. Many insurance plans place medications for the chronically ill into specialty tiers that obligate patients to high out-of-pocket costs, with co-insurance rates as high as 30 percent to 40 percent. So while the ACA’s cap on out-of-pocket expenses for patients may benefit some, the co-pay portions remain a very heavy burden for chronically ill individuals.

In response, patient advocacy groups, drug manufacturers and other stakeholders have been looking at ways to help offset the skyrocketing cost of care for IG patients. For those who meet certain income thresholds, there are several patient assistance programs offered by IG manufacturers that provide free or low-cost drugs to individuals who are unable to pay for them. These programs have been called indigent drug programs, charitable drug programs or medication assistance programs, and while they are not for everyone, they can offer temporary help for those in severe financial straits. Keep in mind that while all the major drug companies have patient assistance programs, each one has different eligibility and application requirements. (Grifols, for example, requires patients be uninsured with income levels that fall below 250 percent of the federal poverty line.)

In addition to patient assistance programs, IG patients can look into qualifying for co-pay assistance. For example, Grifols provides Gamunex-C patients with PI or chronic inflammatory demyelinating polyneuropathy financial assistance that includes up to $2,500 toward deductibles and co-payments; the Hizentra Co-Pay Relief program offered by CSL Behring helps eligible patients afford their therapy by assisting with monthly out-of-pocket expenses up to $4,000 annually; and eligible adult patients with PI starting or currently receiving HYQVIA with
commercial insurance may be able to save up to $4,000 on their deductible/co-payment/co-insurance costs over 12 months with Baxalta’s co-pay card program.

The diagnosis of a PI is frightening and overwhelming. The improvement in quality of life many patients discover after embarking on an IG treatment plan is often short-lived once the cost-of-care reality begins to sink in. Finding ways to manage these costs is a high priority for patients who hope to remain compliant with prescribed treatment plans without bankrupting their family’s financial future.

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.

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**Co-Pay and Patient Assistance Resources**

**Baxalta U.S. Inc.**
Products: Gammagard Liquid, Gammagard S/D and HYQVIA.
Offers co-pay cards for selected products.
(855) 250-5111; www.MyIgSource.com

**Biotest Pharmaceuticals Corp.**
Product: Bivigam
Bivigam Cares Program
(855) 248-4426; www.bivigamcares.com

**Bio Products Laboratory**
Product: Gammaplex
+44 (0) 20 8957 2342; www.bpl.co.uk

**CSL Behring**
Products: Hizentra, Carimune, Privigen
IgIQ Resource Hotline
(877) 355-4447; www.cslbehring-us.com/patient-services/patient-assistance.htm

**Grifols**
Products: Flebogamma DIF, Gamunex-C
Patient Assistance for Flebogamma (888) 474-3657; Gamunex Connexions Program (888) 694-2686; www.grifols.com

**Kedrion**
Product: Gammaked
(855) 353-7466; www.kedrionusa.com

**Octapharma**
Product: Octagam
(800) 554-4440; www.octapharma.com

**Immune Deficiency Foundation (IDF)**
IDF provides manufacturer assistance program listings and resources.
(800) 296-4433; www.primaryimmune.org/treatment-information/manufacturers-and-assistance-programs

**National Organization for Rare Diseases (NORD)**
NORD provides assistance programs that include medication, financial assistance with insurance premiums and co-pays, diagnostic testing assistance, and travel assistance for clinical trials or consultation with disease specialists.
(800) 999-6673; www.rarediseases.org/for-patients-and-families/help-access-medications/patient-assistance-programs

**Jeffrey Modell Foundation (JMF)**
JMF’s website includes a list of resources related to primary immunodeficiency diseases.
(212) 819-0200; www.info4pi.org/internet-cafe/resources

**Patient Services, Inc. (PSI)**
A premium and co-payment foundation, PSI offers assistance in a variety of diagnosis areas for prescribed products.
(800) 366-7741; www.patientservicesinc.org
new and useful reading

**The Autoimmune Solution: Prevent and Reverse the Full Spectrum of Inflammatory Symptoms and Diseases**

Author: Amy Myers, MD  
Publisher: HarperOne

In *The Autoimmune Solution*, Dr. Amy Myers, a leader in functional medicine, offers her medically proven approach to prevent a wide range of inflammatory-related symptoms and diseases, including allergies, obesity, asthma, cardiovascular disease, fibromyalgia, lupus, irritable bowel syndrome, chronic headaches and Hashimoto’s thyroiditis. Her method is built on four pillars: 1) eliminating toxic foods such as sugar and caffeine, and inflammatory foods like dairy, gluten and grains that disrupt the digestive system, 2) introducing restorative ingredients and supplements such as quality proteins, healthy fats and probiotics to repair the gut, 3) identifying environmental toxins in everyday products like shampoo, soap, cosmetics, detergent and other household products and 4) healing autoimmune-related infections while relieving the mental, emotional and physical stress that exacerbate the immune system’s response to external toxins.

**My Victory Over Neuropathy: Life After Guillain-Barré and CIDP**

Author: David Dakroub  
Publisher: Amazon Digital Services

David Dakroub was plagued with nerve pain for five years before he woke up in the hospital paralyzed from the waist down. David’s doctors provided him with no hope of ever walking or living without pain again. Finally, according to David, there came a glimmer of hope that he pursued, and he walked into complete recovery from the disorder and its accompanying symptoms. While he is not a doctor, David wrote this book to give hope to individuals suffering from a neuropathy or a neurological disorder. He believes he has tools that anyone can use to help others overcome their afflictions and that can be applied with immediate results. He does suggest that individuals consult a doctor first before implementing any of his treatment options.

**When the Immunocytes Get Sick … : Primary Immunodeficiencies**

Author: Juan Carlos Aldave, MD  
Publisher: Amazon Digital Services

A clinical immunologist living in Lima, Peru, who cares for children with allergies and primary immunodeficiencies, Dr. Aldave believes that “everyone should understand about the importance of a proper functioning of our immune system.” A major interest in his career is to teach immunology in a funny way to every person, from physicians and medical students to young children and their families. This book is a funny explanation of how “immunocytes” (the immune cells that protect individuals) get sick and stop working.

**Primary Immunodeficiency Disorders**

Editor: Anthony Montanaro, MD  
Publisher: Elsevier

This issue of Immunology and Allergy Clinics of North America is devoted to primary immunodeficiency disorders. The book is written by a group of experts who review the following topics: overview of immunodeficiency disorder; severe combined immunodeficiency disorder; specific antibody deficiencies; common variable immunodeficiency; pulmonary manifestations of primary immunodeficiency disorders; approach to the child with recurrent infections; immunoglobulin treatment for primary immunodeficiency; bone marrow transplantation for primary immunodeficiency; and autoimmune manifestations of primary immunodeficiency.
For a more comprehensive list of resources, visit the Resources page at IGLiving.com.

**Ataxia Telangiectasia (A-T)**
- **WEBSITES**
  - A-T Children’s Project: [www.atcp.org](http://www.atcp.org)

**Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**
- **WEBSITES**
  - GBS/CIDP Foundation International: [www.gbs-cidp.org](http://www.gbs-cidp.org)
  - The Neuropathy Association: [www.neuropathy.org](http://www.neuropathy.org)

**Evans Syndrome**
- **ONLINE PEER SUPPORT**
  - Evans Syndrome Research and Support Group: [www.evanssyndrome.org](http://www.evanssyndrome.org)

**Guillain-Barré Syndrome (GBS)**
- **WEBSITES**
  - GBS/CIDP Foundation International: [www.gbs-cidp.org](http://www.gbs-cidp.org)
  - The Neuropathy Association: [www.neuropathy.org](http://www.neuropathy.org)
  - GBS Support Group: [www.gbs.org.uk](http://www.gbs.org.uk)
  - GBS/CIDP Foundation International Discussion Forums: [www.gbs-cidp.org/forums](http://www.gbs-cidp.org/forums)

**Idiopathic Thrombocytopenic Purpura (ITP)**
- **WEBSITES**
  - ITP Support Association – UK: [www.itpsupport.org.uk](http://www.itpsupport.org.uk)
  - Platelet Disorder Support Association: [www.pdsa.org](http://www.pdsa.org)

**Kawasaki Disease**
- **WEBSITES**
  - American Heart Association: [www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#.T1T2boePWEO](http://www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#.T1T2boePWEO)
  - Kawasaki Disease Foundation: [www.kdfoundation.org](http://www.kdfoundation.org)
  - KidsHealth: [kidshealth.org/parent/medical/heart/kawasaki.html](http://kidshealth.org/parent/medical/heart/kawasaki.html)

**Mitochondrial Disease**
- **WEBSITES**
  - United Mitochondrial Disease Foundation: [www.umd.org](http://www.umd.org)
  - MitosAction: [www.mitosaction.org](http://www.mitosaction.org)

**Multifocal Motor Neuropathy (MMN)**
- **WEBSITES**
  - The Neuropathy Association: [www.neuropathy.org](http://www.neuropathy.org)

**Multiple Sclerosis (MS)**
- **WEBSITES**
  - All About Multiple Sclerosis: [www.mult-sclerosis.org/index.html](http://www.mult-sclerosis.org/index.html)
  - Multiple Sclerosis Association of America: [www.msaa.com](http://www.msaa.com)
  - National Multiple Sclerosis Society: [www.nationalmssociety.org](http://www.nationalmssociety.org)
  - **ONLINE PEER SUPPORT**
    - Friends with MS: [www.FriendsWithMS.com](http://www.FriendsWithMS.com)
    - MSWorld’s Chat and Message Board: [www.msworld.org](http://www.msworld.org)

**Myasthenia Gravis (MG)**
- **WEBSITES AND CHAT ROOMS**
  - Myasthenia Gravis Foundation of America (MGFA): [www.myasthenia.org](http://www.myasthenia.org)
  - **ONLINE PEER SUPPORT**
    - Genetic Alliance: [www.geneticalliance.org](http://www.geneticalliance.org)

**Myositis**
- **WEBSITES**
  - The Myositis Association: [www.myositis.org](http://www.myositis.org)
  - **ONLINE PEER SUPPORT**
    - The Cure JM Foundation: [www.curejm.com](http://www.curejm.com)
    - Michigan Immunodeficiency Foundation: [www.facebook.com/groups/108048062584350](http://www.facebook.com/groups/108048062584350)
    - Myositis Support Group: [www.myositis.org.uk](http://www.myositis.org.uk)
    - Myositis Support Group – UK: [www.myositis.org.uk](http://www.myositis.org.uk)

**Peripheral Neuropathy (PN)**
- **WEBSITES**
  - Neuropathy Action Foundation: [www.neuropathyauction.org](http://www.neuropathyauction.org)
  - Western Neuropathy Association: [www.pnhelp.org](http://www.pnhelp.org)
  - Texas Chapter of the Neuropathy Association: [www.handsfeetheart.org](http://www.handsfeetheart.org)

**Primary Immune Deficiency Disease (PI)**
- **WEBSITES**
  - Immune Deficiency Foundation: [www.primaryimmune.org](http://www.primaryimmune.org)
  - Jeffrey Modell Foundation: [www.info4pi.org](http://www.info4pi.org)
  - American Academy of Allergy, Asthma & Immunology: [www.aaaai.org](http://www.aaaai.org)
  - International Patient Organisation for Primary Immunodeficiencies (IPPO) — UK: [www.ipopi.org](http://www.ipopi.org)
  - New England Primary Immunodeficiency Network: [www.nepin.org](http://www.nepin.org)
  - Rainbow Allergy-Immunology: [www.uhospitals.org/rainbow/services/allergy-immunology](http://www.uhospitals.org/rainbow/services/allergy-immunology)
  - **ONLINE PEER SUPPORT**
    - IDF Common Ground: [www.idfcommonground.org](http://www.idfcommonground.org)
    - IDF Discussion Forum: [idffriends.org/forum](http://idffriends.org/forum)
    - IDF Friends: [idffriends.org](http://idffriends.org)
    - Jeffrey Modell Foundation Facebook Page: [www.facebook.com/JMFworld](http://www.facebook.com/JMFworld)
    - Michigan Immunodeficiency Foundation: [www.facebook.com/groups/108048062584350](http://www.facebook.com/groups/108048062584350)

**Scleroderma**
- **WEBSITES**
  - Scleroderma Foundation: [www.scleroderma.org](http://www.scleroderma.org)
  - Scleroderma Research Foundation: [www.srfcure.org](http://www.srfcure.org)
  - Scleroderma Center: [www.hopkinsmedicine.org/rheumatology/clinics/scleroderma_center.html](http://www.hopkinsmedicine.org/rheumatology/clinics/scleroderma_center.html)
  - **ONLINE PEER SUPPORT**
    - International Scleroderma Network: [www.sclero.org/support/forums/a-to-z.html](http://www.sclero.org/support/forums/a-to-z.html)

**Stiff Person Syndrome (SPS)**
- **WEBSITES**
  - American Autoimmune Related Diseases Association Inc.: [www.aarda.org](http://www.aarda.org)
  - Genetic Alliance: [www.geneticalliance.org](http://www.geneticalliance.org)
  - Living with Stiff Person Syndrome (personal account): [www.livingwithsp.com](http://www.livingwithsp.com)
  - Stiff Person Syndrome: [www.stiffpersonsindrome.net](http://www.stiffpersonsindrome.net)
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