Mobile Health
Apps that Track and Communicate

Orphan Diseases: Overcoming the Obstacles
Home Infusion Monitoring for Safety
SCIG Therapy: An Investigational Frontier

Increasing Awareness about Sjögren’s Syndrome
8 Critical Steps

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Covering Your Concerns

THANKS TO ALL of you who responded to our reader survey that was included in both the last issue of IG Living and on our newly redesigned website. Your responses are helping us to get to know you better and, thus, tailor our content in the magazine and on our Facebook page and blog. You gave us a tremendous amount of praise for the information we provide in each issue of IG Living, and now, after tallying the survey results, I feel even more strongly that this edition’s articles are extremely timely and pertinent to your issues and concerns.

Of course, we don’t need survey results to know that your diseases are rare. Only a small portion of the population is diagnosed with a primary immunodeficiency (PI) and/or an autoimmune or neuropathic issue. These rare diseases, known as orphan diseases, come with a separate set of hurdles than the diseases themselves. Not only do you struggle to make others understand your illnesses that are rarely transparent and often never heard of, but many of you battle to get treatment. Oftentimes, there are very few treatment options, and those that are in development are slow to come to market. In our article “Orphan Diseases: Hurdling the Obstacles,” we shed some light on why that’s true and what’s being done to overcome that.

Many autoimmune conditions fall under the orphan disease designation, and approximately 70 percent of common variable immunodeficiency (CVID) patients, the most common PI, present with autoimmune disorders as well. In our article “The CVID-Autoimmunity Connection,” we examine how autoimmunity affects CVID diagnosis, the types of autoimmune conditions that most likely come into play and what that means for long-term prognosis.

Since immune globulin (IG) is the primary and, in many cases, the only lifesaving therapy for PI and other autoimmune and neurological diseases, we thought it would be helpful for you to understand how physicians determine which IG product to prescribe. Our article “Meeting Your IG Match” looks at the contraindications, age considerations, product features, patient tolerability and cost — all of which factor into IG choice.

In 2006, the first subcutaneous IG (SCIG) product made its debut. Our PI Parody columnist Cheryl Haggard takes a very comical look at its introduction at one of the Immune Deficiency Foundation conferences in “Sub-Q and the Mouse”; it is testament to the many benefits that the subcutaneous route of administration offers over the intravenous route. While our survey results show that the majority of our readers still infuse IG intravenously, recent studies show that the subcutaneous route is both as effective and preferred by patients. Our article “SCIG: New Therapeutic Uses Beyond PI?” looks at the advantages of SCIG in terms of systemic reactions, dosing schedules, tolerability, costs and health-related quality of life, as well as reports on a host of studies and case reports that highlight how SCIG may soon be the route of preference for not only PI, but also other autoimmune neuromuscular disorders.

An interesting finding in our survey is that the majority of you infuse at home. The shift away from center-based infusion therapy has brought safety to the forefront due to decreased direct contact between patients and their healthcare providers. Therefore, in our article “Home Infusions: Monitoring for Safety,” we look at the importance of clinical monitoring in the home and the types of data that should be collected whether infusions are subcutaneous or intravenous.

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

Ronale Tucker Rhodes, MS
ABBIE’S CORNER

Introducing Abbie’s Corner for Advocacy

By Abbie Cornett

WELCOME TO OUR new patient advocacy column. As a patient myself who has transitioned into a career of advocating for chronically ill patients, I am excited to introduce this column through which I will look out for your best interests. In this column, I’ll help you navigate the healthcare system by exploring current issues that affect us as patients, including trends in insurance issues (appeals, fail-first policies, payment tiers, etc.), medical breakthroughs, support groups, legislative news and stories — both triumphant and sorrowful — about patients I meet.

But first, let me tell you about myself. After being diagnosed with common variable immunodeficiency (CVID) in 2004, my whole world changed. That was a good thing. Being diagnosed was nothing short of life-saving, or at least sanity-saving, for me. Prior to being diagnosed, I had spent my entire life sick with one illness after another, spending weeks in the hospital. For periods of time, I was in denial that something was actually wrong with me. I had tried for years to hide that I was sick, but the older I got, the worse I got. When I was in my early 30s, my illness hit a crisis point that left me in the hospital for weeks, out of work for months and in financial ruin. Not only was my work suffering, but so was my marriage. No doctor could tell me what was wrong, and I was taking so many medicines that I had to write out a schedule so I knew what to take and when. Illness became my life, and for the first time in my life, I started to question myself.

That all changed after being referred to an amazing immunologist who was not only able to diagnose what was wrong but was also able to treat me. I started intravenous immune globulin (IVIG) therapy in the summer of 2004 and was immediately on the road to getting better. With my diagnosis and treatment came health and a new direction in my life. I became active in issues that affect patients. I started by attending Hill Day for the Immune Deficiency Foundation, and then in 2006, I helped form a nonprofit organization that dealt with policy issues that affected patients’ access to care.

In the spring of 2014, I was fortunate enough to be hired by IG Living magazine as its patient advocate. Since then, I have been given the opportunity to help patients and their families in a number of ways. I have become directly involved with patients, meeting them and their families and helping them with their issues on a one-on-one basis. I am attending meetings and am involved in the start-up of patient groups.

In September, I attended the annual conference of The Myositis Association in Reno, Nev., where I met with people from all over the country. While there, I met a wonderful woman named Brenda Enger-Abernathy, who invited me to speak at the TMA Keep In Touch support group meeting held in October in Pasadena, Calif. While there, I was able to speak directly with patients and their families regarding their disease and their personal issues related to their illness — most notably, insurance, medication and coordination of care.

I also helped organize a support group in the Midwest for families of children diagnosed with pediatric acute onset neuropsychiatric syndrome and pediatric autoimmune neuropsychiatric disorder associated with strep (PANS/PANDAS). The first meeting, held Oct. 19 in Omaha, Neb., was attended by more than 75 people, including patients, family members and physicians. It was a wonderful opportunity for me to learn how important to the families and patients a forum is to learn about their disease and to share their experiences.

As IG Living’s patient advocate, I am here for you. In addition to the information I will share with you in this column, you can reach out to me with specific questions by posting a question on IG Living’s Ask the Experts page (www.IGLiving.com/AskTheExperts.aspx) or by emailing me at patientadvocate@IGLiving.com.

ABBIE CORNETT is the patient advocate for IG Living magazine.
FACES OF IG

Join the conversation! Connect with other immune globulin patients through IG Living’s Facebook page at www.facebook.com/IGLivingMagazine. Each day, we post interesting articles and facts, as well as thought-provoking questions that you can weigh in on. These are some snapshots of what’s being discussed.

How do you juggle medical expenses?

We are close to losing our home. Any agency we have sought for help only considers monies coming into the household, not monies being paid out for exorbitant medical expenses.

— Kay P.B.

It’s definitely a financial struggle, especially after a major life change, like my divorce and being a single parent and being expected to make the mortgage payment alone, which was more than my paycheck. We lost our home due to foreclosure; now, I have bad credit as a result, and I will never own a home again. I’ll need to file bankruptcy, but I need to talk to someone first because even with my insurance and [my daughter’s] infusions, my copay portion is over $900 a month. It’s an ongoing debt that will never end and will get worse. The big worry looming over our heads now is that she will turn 26 this September and will have to come off my insurance. Then what? She has been denied four times for disability, once with a lawyer; they said her CVID is not “severe enough”!

— Cheryl B.S.

[I] just received a letter stating that the insurance company has denied my second appeal for a certain blood test my oncologist ordered. [I] love the way they are spending way more money to pay outside “experts” to review things, and they say they don’t stand in the way of the decisions made by my doctors and me regarding treatment. [It’s] such B.S. When they won’t cover a test or procedure, and I can’t afford to pay more out of pocket, then they certainly are.

— Debbie K.

How do you juggle medical expenses?

I’m from Oregon and can say I am so proud of my state for allowing the patient to have at least a tiny glimpse of control. I can’t speak for others, but when I was diagnosed with a chronic illness, I felt robbed. I felt like all the plans I had for my future were stripped from me. I had to alter my dreams and goals to fit what I could physically do. I was angry, hurt and depressed … sometimes I still am. Having a terminal disease is something I couldn’t imagine dealing with, and the fact that [Brittany] was strong enough to take that control back and say “I will die but it will be on my own timing!” Wow! I support her and her decision 100 percent.

— Jessica K.G.

Around the country today, there are several ballot measures impacting patients’ rights. Brittany Maynard’s story put a spotlight on “right to die” legislation.

Where do you stand?

We don’t have a “right to die.” Our lives aren’t just ours to throw away. Dying affects more than just ourselves; it affects everyone around us. I’m not downplaying the gravity of [Brittany’s] situation at all; but I am saying that we should be able to accept everything life throws at us with dignity and not take the easy way out. We should take every bad circumstance as an opportunity to encourage and support those in similar situations. Our lives are short enough without shortening them ourselves. Also, this issue can open up other cans of worms like it has in other countries where the right to die becomes something we feel more obligated to do because we feel like burdens. This could especially apply to all us zebras since we usually have so many ridiculous concoctions of health issues.

— Eileen T.
Michelle » Meningitis is inflammation of the lining of the brain caused by several things. Aseptic meningitis is considered drug-induced and is not contagious. Viral meningitis is caused by a virus, and it is contagious. The type of virus dictates the treatment, but normally there is no treatment for either other than rest, etc. I don’t think they can cause brain damage, but viral meningitis can be fatal if a person has a weakened immune system and other pre-existing conditions that put them at higher risk for complications during an illness.

Precautions for viral meningitis include the routine things that one would do to prevent spread of any infection: handwashing and keeping surfaces clean, for which bleach can be effective. Nothing can prevent aseptic meningitis occurring due to intravenous immune globulin (IVIG) therapy; there are no germs or viruses spread with the use of IVIG. Some people will get it and others won’t, but it is very rare. ✗

Michelle » Aseptic vs. Viral Meningitis

What is the difference between aseptic and viral meningitis? Is either one contagious, and can they cause brain damage, neurological damage or changes in personality and memory? If so, what precautions should be taken to make certain family members don’t contract it? Is using bleach effective in killing all germs from meningitis and any germs and viruses that could be contracted from immune globulin therapy?

Michelle » IG and Side Effects

I have polymyositis, and for the past year-and-a-half have been receiving intravenous immune globulin (IVIG). Most of the time, I am side effect-free. But then, suddenly, I’ll experience horrible side effects after a treatment, even though I followed the same regimen (extra hydration, premeds, rate of infusion, etc.). Is it possible that this could occur due to a bad batch of plasma caused, for example, by a drug addict or sick donor?

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

Michelle Greer, RN, is senior vice president of sales at NuFACTOR Specialty Pharmacy.

Abbie Cornett is the patient advocate for IG Living magazine.
WE CONTINUE with the discussion of a 2-year-old boy with chronic respiratory infections whose family members had been similarly ill during early childhood but had outgrown the problems later in childhood. An immune evaluation revealed this child had a functional deficiency in the ability to make antibodies to the pneumococcal polysaccharide vaccine, even with the presence of normal serum levels of IgG, IgA, IgM and IgE.

Several questions have been discussed with regard to initiating the most correct therapy. The next questions are: Should the boy be started on immune globulin (IG) replacement therapy (and/or should other therapies be used)? And, is there only one correct treatment approach? The decision to begin IG therapy can be difficult, and the therapy is expensive. Yet, much like the diabetic who needs insulin replacement, those who are antibody deficient need IG replacement.

In this situation, there are at least two reasonable approaches. The least invasive approach is to continue to treat infections as they occur with appropriate antibiotics, and to maximize the therapies for asthma and allergy symptoms. With this approach, there would be a plan to periodically re-evaluate the immune system such as once a year. Quantitative IgG levels would be measured and the pneumococcal titers would be spot-checked (i.e., not performing a pre-/post-immunization challenge, but looking for natural declines or improvements in the levels). Should a clear clinical and laboratory worsening occur, that would indicate IG replacement therapy should begin. Otherwise, a lessening of the severity of the infections and continued overall improvement in the laboratory findings could be considered a good sign for him to eventually outgrow the problems as his immune system matures, as was the case for other family members.

An important separate consideration is the overall effect of the illnesses on this child and the family. If the child requires hospitalizations for illnesses and there is a great disruption in the overall family well-being, it may be prudent to consider initiating IG replacement therapy. With this approach, the boy would be treated with either subcutaneous or intravenous IG throughout the fall, winter and spring months (approximately nine months of the year), but IG therapy would be discontinued during the summer. The time off during the summer can be clinically very telling. An obviously good sign is if the child remains free from infections. A further good sign would be an improvement in the immune system (by measuring quantitative IgG levels and spot-checking the pneumococcal titers), which would indicate that additional IG treatment may not be necessary. (A person needs to be off of IG replacement therapy for three to six months for the testing to be valid.) Alternatively, if infections resume after discontinuing IG replacement, this may indicate that the immune system is not appropriately maturing. And, if the laboratory testing does not improve, or actually worsens, this would indicate that IG replacement should be restarted in the fall, before the winter viral season commences. The pattern of coming off of therapy for the summer and retesting could be continued until the immune system either demonstrates maturation and normalization, or it is clear that an antibody deficiency is truly present and permanent replacement therapy is required.

We will begin a new discussion in the next issue. 

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

Disclaimer: This case report is intended as an illustration for education purposes only. It does not necessarily represent an individual or precise information from patient files.
COMMON VARIABLE IMMUNODEFICIENCY (CVID) is considered one of the more common immune deficiencies, with a prevalence of between one in 25,000 and one in 50,000 people in the U.S.¹ It is categorized by low IgG antibody levels (usually less than 400 mg/dL), and low levels of IgM or IgA antibodies may also be present. Presentation of CVID can vary widely from patient to patient. Seventy percent to 80 percent of CVID patients present with sinopulmonary infections that are indicative of an immunodeficiency, but approximately 20 percent of CVID patients present with signs of autoimmunity instead, resulting in diagnostic delay.² The “variable” in CVID is what contributes to diagnostic delay, which can result in years of delay in proper treatment. For instance, patients may be seen by their gastroenterologist for gastrointestinal issues, their pulmonologist for respiratory manifestations or their oncologist for cancer without a physician ever thinking to check for low IgG levels. And, while serum antibodies may be detected in autoimmune conditions,³ a diagnosis of autoimmunity will not preclude a diagnosis of CVID in a patient with an accompanying immune deficiency.

Autoimmunity occurs when the immune system fails to distinguish self from non-self. When this happens, the immune system attacks specific tissues through the production of auto-antibodies, thus causing autoimmunity.³ Paradoxically, autoimmunity is common in diseases of antibody deficiency, but how antibodies are produced against a patient’s own tissues when overall antibody production is impaired is unclear.² It has been suggested that both conditions may be related to genetic immune dysregulation.¹

Types of Autoimmunity in CVID
Charlotte Cunningham-Rundles, MD, David S. Gottesman professor of immunology at the Mount Sinai School of Medicine in New York, says that CVID patients can be categorized into two groups: those who present with infections and those who present with inflammatory or autoimmune conditions in addition to infections.¹ However, approximately 20 percent of CVID patients have some manifestation of autoimmunity in the absence of infection.² Inflammatory and autoimmune conditions can range from gastrointestinal disease to inflammatory lung diseases and even cancer. In a large European study of 334 patients, 71 percent presented with one or more of these inflammatory and/or autoimmune manifestations, as well as infections, while the remainder presented with infections only.¹ In patients who present with both autoimmune manifestations and infections, the autoimmune manifestations are often the first to appear, thus contributing to diagnostic delay.²

The presentation of autoimmune manifestations in CVID patients may be just as variable as the presentation of CVID itself. Although autoimmune conditions that affect solid organs do occur in CVID patients, most studies recognize the blood conditions idiopathic thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA) as the most common concomitant autoimmune manifestations.
in CVID.\textsuperscript{1,2} It is estimated that 5 percent to 8 percent of CVID patients also have ITP and/or AIHA.\textsuperscript{2} Rheumatologic conditions have been known to occur in up to 10 percent of CVID patients and may include the involvement and destruction of one or many joints.\textsuperscript{2} Autoimmune or inflammatory gastrointestinal disease may be present in between 6 percent to 10 percent of CVID patients, and is particularly difficult to treat.\textsuperscript{2} Lymphoma and other cancers are also recognized as a complication of CVID. In an Australian study of 416 CVID patients, the incidence of malignancies was four times as common as in the general population.\textsuperscript{1}

The CVID-Autoimmunity Prognosis

Patients who present with autoimmune complications in addition to infections usually have a poorer prognosis than patients who present with infections alone. In fact, inflammatory and autoimmune conditions are recognized as being responsible for most of the morbidity and mortality in CVID.\textsuperscript{1} In a U.S. study of 473 CVID patients, those who had one or more inflammatory or autoimmune complications were 11 times more likely to die during the 40-year follow-up period than patients who had infections only.\textsuperscript{4} This number is still less than what is seen among the general population, and survival in CVID has improved significantly over time. The majority of patients in this study were able to live normal, active lives with appropriate treatment. And, improved diagnosis and treatment options are likely to continue this positive trend.\textsuperscript{4}

Due to the variability in the presentation of CVID and the resulting morbidity and mortality from the inflammatory and autoimmune complications that can accompany it, CVID patients must be carefully monitored for signs and symptoms of autoimmune or inflammatory conditions to ensure the best possible prognosis. Unfortunately, other than monitoring IgG levels, there is not much consensus on the best way to follow up with CVID patients. It is suggested that periodic blood panels, examinations of lung function, monitoring of gastrointestinal symptoms and investigation of any general health complaints will be helpful in the diagnosis of problems that can arise in CVID patients due to autoimmunity.\textsuperscript{1} It is also hoped that disease management will help reduce the serious complications that can lead to CVID morbidity and mortality.\textsuperscript{4}

ELISSA RITT, RN, is medical science liaison for NuFACTOR Specialty Pharmacy.

References
IN THE NEWS

Safety

PPTA Implements Voluntary Deferral of Plasma Donors of Ebola-Affected Areas

Due to concerns about the Ebola virus outbreak, especially among persons with immunodeficiencies who are more vulnerable to infections, the Plasma Protein Therapeutics Association (PPTA) has 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. According to PPTA, it is unlikely that the Ebola virus would ever be introduced into a plasma pool for fractionation because individuals are rejected for donation if they have symptoms of viral infection (e.g., fever). However, PPTA says its voluntary inventory hold of all incoming plasma for fractionation of 60 days would be adequate to allow for removal of a unit in question if necessary.

This measure is an additional safeguard to protect the plasma pool. Over the years, PPTA member companies have implemented at least two effective virus inactivation/removal steps for the manufacturing of plasma-derived products such as immune globulin. And, regardless of taxonomical differences of the Ebola virus with other enveloped RNA or DNA viruses against which the inactivation/removal steps protect, data support protection against the Ebola virus as well. For more information about the Ebola virus and plasma protein therapies, go to www.pptaglobal.org/28-news/ppta-news/922-ebola-virus-and-plasma-protein-therapies.

Medicines

Grifols Introduces New 40g IVIG Vial Size for Gamunex-C

A 40-gram vial size for Gamunex-C (immune globulin injection [human] 10%) became available on Nov. 3 in the U.S. With this addition, Gamunex-C is now available in six different vial sizes, including 1 gram (10 mL), 2.5 grams (25 mL), 5 grams (50 mL), 10 grams (100 mL) and 20 grams (200 mL). The wide range of vial sizes is intended to help avoid unnecessary waste and provides an easier, more convenient way of dosing according to prescription.

Gamunex-C is approved by the U.S. Food and Drug Administration to treat chronic inflammatory demyelinating polyneuropathy, primary humoral immunodeficiency disease and idiopathic thrombocytopenic purpura.

Insurance

Kaiser’s Healthcare Marketplace Calculator Adds 2015 Specific Data

The Kaiser Family Foundation’s Health Insurance Marketplace Calculator now includes ZIP code-specific data on 2015 health plans that are being sold through the Affordable Care Act’s insurance marketplaces during the open enrollment period that began Nov. 15. With the new tool, consumers can generate estimates of their health insurance premiums and government subsidies for 2015 plans. Estimates are based on ZIP code, household income, family size and ages of family members. The calculator also helps consumers determine whether they could be eligible for Medicaid. It can be accessed at kff.org/interactive/subsidy-calculator.

The calculator is part of a series of new and updated foundation resources to help consumers understand health insurance and navigate open enrollment. Other tools include Understanding Health Insurance, an updated collection of nearly 300 frequently asked questions about the Affordable Care Act (kff.org/understanding-health-insurance), and a new animated video titled Health Insurance Explained — The YouToons Have It Covered (kff.org/health-reform/video/health-insurance-explained-youtoons).
**Medicines**

**Baxter’s Investigational 20% SCIG Therapy Meets Study Endpoint**

Baxter International’s 20% subcutaneous immune globulin (IG) therapy has met its primary endpoint during a Phase II/III clinical study, which measured the rate of validated acute serious bacterial infections (VASBIs). In the study, 48 European primary immunodeficiency disease (PI) patients at least 2 years old received an SCIG 16% therapy for three months, followed by weekly doses of SCIG 20% for up to 12 months (median of two sites per infusion). A single event was reported during treatment with SCIG 20% (pneumonia of moderate severity), which equated to a low VASBI rate of 0.022 percent per patient-year compared with the specified threshold of one VASBI per patient-year. The rate of infections with SCIG 20% (without dose adjustment) was 4.38 per patient-year, and mean serum IgG trough levels were comparable to intravenous IG 10%.

There were no serious adverse events related to treatment. The rate of local adverse events considered related to SCIG 20% treatment was 0.052 per infusion (17 of 48 patients), the majority of which were mild in severity. The most common were erythema, swelling, pruritus and pain/discomfort. There were no reports of severe local or systemic adverse events related to treatment. And, importantly, nearly all infusions (99.8 percent) were completed without any interruption, slowing or stopping of the infusion.

Results of a separate study of SCIG 20% among PI patients in North America are expected to be available next year.

**Grants**

**Jeffrey Modell Foundation Awards $1 Million for PI Research**

In September, the Jeffrey Modell Foundation (JMF) awarded $1 million for translational research for primary immunodeficiency disease (PI). As part of its Translational Research Program to support research contributing to the advancement of knowledge, understanding and treatment of PI and, ultimately, cures, JMF awards physicians and scientists who are prominent in their field with vast expertise in PI from countries all over the world. This year, the program received 42 high-level applications from investigators in 15 countries.

Special emphasis focused on novel PI defects, innovative approaches for early diagnosis, treatment advances to a cure and overall impact on patient health. Five grants were awarded to leading centers in Boston, Washington, D.C., France, Israel and Italy. “We are fully committed to support physicians involved in groundbreaking and state-of-the-art research,” said Vicki Modell, co-founder of JMF. “We are passionately committed to advance our understanding of these defects. JMF supports these experts so that we can advance clinical progress and help families affected by primary immunodeficiency receive optimal care.”
IN THE NEWS

Patient Advocacy

Family Promotes Local Awareness for PI

Increasing awareness about primary immunodeficiency disease (PI) can happen at all levels, and a group of middle school kids supported by two of their mothers recently set a prime example of how to promote PI at the local level. In October, Dona Darr, a blogger and contributing writer for IG Living, her friend Fay Mayes, along with their daughters, Emily and Addison (Emily’s “bestest” friend), and Emily’s friend Veronica Whiteside, sponsored a booth to spread awareness about PI at their annual Elsberry Classics on Wheels Car Show and Fall Festival, which is sponsored by the Kiwanis Club and the Elsberry, Mo., R2 school district. Emily was diagnosed with IgG subclass deficiency and complement deficiency in 2004, and there are two other kids in her school who also have a PI. For the booth, they passed out educational materials from the Immune Deficiency Foundation, the Jeffrey Modell Foundation, IG Living and their local Elsberry Pharmacy. And, as Dona explained, “Emily and two of her friends even walked through the crowd handing out information. It was a beautiful day filled with fun, music and many friends and neighbors.”

Patient Support

New Website Launched for Kids with Childhood Diseases and Their Families

The I Give for Kids website has launched to support communities and families impacted by childhood diseases such as PANS/PANDAS, Kawasaki disease and primary immunodeficiencies through education, communication and advocacy. The site, which is dedicated to improving the quality of life for those diagnosed or yet-to-be diagnosed and their families, offers a wide range of programs for the public, patients and healthcare professionals. Included are links to support groups and resources, event listings, recent news and a patient advocate forum. The site can be accessed at www.IGiveforKids.com.

Partnership

IDF Transforms Medical Mobile Portal for Patients

The Immune Deficiency Foundation (IDF) has partnered with Get Real Health to provide its patient community with a new web and mobile portal to electronically track their symptoms, medications and other health-related information. It also provides patients the opportunity to participate in research and to consent to have their data shared with the U.S. Immunodeficiency Network (USIDNET) registry. Using the new InstantPHR-powered portal, patients can enter their information anywhere, anytime from their mobile devices, including smart phones and tablets. The portal also includes a sync to Microsoft HealthVault’s ecosystem of devices, pharmacies and labs, as well as provider-to-provider emailing and access to additional health records through Blue Button Plus. The new portal is the result of an award granted to IDF by the Patient-Centered Outcomes Research Institute to create a Patient Powered Research Network, called PI Connect, to link patient-entered data and experiences with clinical information in the USIDNET patient-consented registry.
Autoimmune Corner

Research

High IgG Levels Signal Autoimmunity in Kids

A recent study shows that high levels of immunoglobulin G (IgG) in children — and particularly in girls — are associated with the development of autoimmune disease. Conducted at Harvard University and published online in Pediatric Rheumatology, the retrospective study identified patients at Boston Children’s Hospital who had IgG measurements of 2,000 mg/dL or higher between January 2000 and December 2009. The average age of patients was 14.3, and mean follow-up was 3.48 years. Almost two-thirds of the patients were female, and 58 percent were white.

Of the 442 patients, 50 percent were ultimately diagnosed with an autoimmune or autoinflammatory disease. Girls with elevated IgG levels were three times as likely as boys to develop autoimmunity. Diagnoses in the autoimmune group included systemic lupus erythematosus in 48 and mixed connective tissue disease in 29. Arthritic-type autoimmune diseases were less common than lupus. Polyarticular juvenile idiopathic arthritis was diagnosed in 29, systemic-onset juvenile idiopathic arthritis in 15 and spondyloarthritis in 11. Other types of autoimmune diseases included Crohn’s disease (10), ulcerative colitis (14) and autoimmune hepatitis (10), as well as several types of vasculitis. Infections comprised 37 percent of diagnoses among children with high IgG levels, primarily recurrent bacterial infections in those with cystic fibrosis. Streptococcal and post-streptococcal infections also were prevalent. In addition, there were small numbers of patients with malignancies, primary immunodeficiencies, drug reactions and other diagnoses such as trisomy 21. A total of 10 percent of the children died during follow-up, with deaths being caused most often by malignancy (30 percent) and infection (18 percent).

Research

Potential Cure for MS Developed in Japan

Japanese researchers have developed a drug they claim could cure multiple sclerosis (MS). Developed by Takashi Yamamura, the head of the National Center of Neurology and Psychiatry at Kodaira’s immunology department, the drug stimulates a type of immune cell that softens the attacks by lymphocytes and creates a protein that suppresses inflammation. A three-month clinical trial began in March with nine patients. In the trial, the drug will be consumed in powder form dissolved in water. If the drug’s efficacy is confirmed, it will be moved into a large-scale trial.

Research

New Study Links Autism and Autoimmunity

A new large-scale study of more than 2,700 mothers of children with autism shows that about one in 10 mothers have antibodies in their bloodstream that react with proteins in the brain of the babies. The study, led by Dr. Betty Diamond, head of the Center for Autoimmune and Musculoskeletal Disorders at The Feinstein Institute for Medical Research in Long Island, N.Y., shows that while the blood-brain barrier in adult women prevents them from being harmed by the antibodies, that same filter in the fetuses is not developed well enough and may allow the anti-brain antibodies to pass through the babies’ brains, possibly causing autism. According to Dr. Diamond, the large sample size in the study “gives a clearer impression of the prevalence of these antibodies.”

Approximately 50 million Americans live and cope with autoimmune disease, 75 percent of whom are women. The study was published in the Aug. 20 edition of Molecular Psychology.
An increasing number of healthcare apps provide a range of functionality, and as they grow in popularity, safety is becoming an issue.

By Amy Scanlin, MS

**MANY COMPANIES ARE** creating interesting options in healthcare apps to make the population a little healthier. In fact, the market for these handy readers and trackers is expected to reach more than $26 billion by 2017, according to a report by Research2Guidance, with more than 500 million smartphone users worldwide using them. Some mobile apps, which are really just a software platform designed to run on a smartphone, are “just-for-fun” fitness-type trackers; others can take that fitness log and tap into personal health records and even report the data to an individual’s trainer and physician. Still other apps have the capability, with an attachment or two, to become a blood pressure cuff, an ECG and any number of other devices that can move the app from merely a consumer application to a patient’s medical device. Some apps even require a doctor’s prescription.

Healthcare apps allow for greater functionality, better tracking of data and, with cameras and microphones, even allow the user’s phone to be a two-way communication tool for health communication. The World Health Organization’s Global Observatory for eHealth says this phenomenon of mobile health, or mHealth, has the possibility to take things to a whole new level. Think wellness management and healthcare to go!

Most apps are available for iPhones and Androids, with a few exceptions. Some are designed for physician use and are not available for consumers to purchase. Others are available by prescription only and, again, are not available for purchase in general app stores. However, about 50 percent of the nearly 100,000 wellness apps are available to download free, and most of those have the capability to provide information, fitness tips, guided meditation and the like.
Mobile Prescription Therapy

A well-respected app with great functionality is the diabetes management app from WellDoc called BlueStar. This U.S. Food and Drug Administration (FDA)-approved, prescription-only app aims to assist diabetic patients through improved self-care via personalized advice and enhanced two-way communication with providers, as well as better tracking of their own condition through real-time information. A study of type 2 diabetics showed that patients who used the WellDoc app for glucose monitoring lowered their A1c levels by approximately 2.03 percent compared with a control group that saw a reduction of just 0.68 percent. Eighty-four percent of those patients had their medications adjusted compared with just 23 percent of the control group that saw a change. The app’s GuidedComplianceTool, which tells patients when it’s time to check their glucose levels and provides lifestyle change tips, was credited in part with these and other positive changes. (It should be noted that the control group also received the same lifestyle change suggestions.) Long-term success rates with the app are proving to be equally effective.

With numerous fitness and nutrition trackers, these apps provide motivation and fitness tips, and some even offer guided meditation.

This type of compliance enhancement capability holds such promise that the Maryland Chapter of the American Diabetes Association has partnered with WellDoc, and has hinted about more expanded collaboration in the future. “BlueStar falls into the category of mobile prescription therapy (MPT), according to the FDA,” explains Ali Tighe, associate director of corporate development at the association. “This is not a drug therapy, but rather a way to provide important data that a healthcare provider can use to develop the best therapy for their patient and for the patient themselves to better understand what they need to do to control their type 2 diabetes.”
Another type of mobile prescription can be found in the many pharmacy apps that allow patients to do things like refill prescriptions, identify pills by color and imprints, check medication interactions and schedule vaccinations in the store. Walgreens, Rite Aid, CVS, Walmart and many others offer similar services. Walgreens has even partnered with WebMD for virtual wellness coaching through its Balance Rewards healthy choices programs, and it has plans to integrate those programs into WebMD’s Healthy Target mobile health improvement program. Healthy Target allows for uploading data from activity trackers, wireless scales and glucometers and allows users to receive tailored, physician-reviewed content, as well as motivational tips.

**Fitness and Wellness Apps**

Fitness and wellness apps are probably the most common introduction individuals have into the world of health-enhancing mobile apps. With numerous fitness and nutrition trackers, these apps provide motivation and fitness tips, and some even offer guided meditation. There are any number of easy ways for people to get their start in the mobile world of wellness.

Debbie Ruth of Arlington, Va., uses a Fitbit and its app to track and communicate her exercise program with her personal trainer. “(My) trainer recommended the Fitbit,” she said, and “once I ‘friended’ her, she could see my activity level and use the information to make adjustments to my activities. Because I know she can see my steps, I work harder to meet my daily goals. This really has impacted my behavior! My trainer is very supportive. After reviewing the data, we use the information to plan our [personal training] sessions. For example, I have no problem walking a certain number of steps, but I lack aerobic fitness and weight training, so that is what we concentrate on during our sessions. It’s nice to see the progress during the day. If I only have 4,000 steps by late afternoon, I can plan to use the treadmill or arc trainer to reach my goal. I also like that the device sends messages about how close to my goal I am during the day; this is very encouraging.”

The promise of improving health outcomes by using mobile apps led the National Cancer Institute to award $365,000 to a University of Arizona study, a first of its kind that looks at how mobile apps can help women quit smoking while incorporating exercise and healthy eating to avoid weight gain. With prerecorded positive affirmations and meditations of empowerment and, eventually, the woman’s own recorded mes-
sages for playback, the hope is that the mobile app will help to incorporate the three behaviors together for better health.

Numerous studies show the benefits of mindful meditation — reduced stress, reduced blood pressure and heart rate, improved focus, and the list goes on. A mobile app of guided meditations and affirmations can help to quiet the mind and calm the nervous system. As Lysa Volpe, one of the meditation specialists at Miraval Arizona Resort and Spa in Tucson, Ariz., explains: “When we are able to bring our attention to one pointed focus as we do in meditation (for example an image, the breath or a mantra) without getting carried away into a story, we are able to calm the nervous system. What this means is that we can quickly go from a stressful state to moving to a more relaxed state. As we reduce the stress hormones of the body, like adrenaline and cortisol, we then reduce our heart rate and improve the efficiency of our immune system, which can be incredibly helpful with managing chronic conditions such as anxiety, pain and other illnesses.

“Likewise, with chronic pain, the body becomes fatigued and often reverts into a habit of functioning in a state of ‘fight or flight,’ which then means we become hyper aware of the constant subtleties of nerve endings being aggravated. With meditation, the sufferer will still experience the pain but will be far more apt to redirect their focus to maybe their breath or a neutral sensation of the body, therefore again calming their nervous system and diminishing the intensity of the pain. Overall, meditation is indeed a highly useful tool for chronic illness management.”

Safety

FDA recently issued a guidance document regarding oversight of medical-related mobile apps that turn smartphone and tablet devices into medical devices such as those that, with attachments, can take blood pressure readings, ECG measurements, etc. The oversight will not apply to apps that track items like activity levels or food consumption because those types of apps do not have the potential to cause harm.

With FDA oversight of medical device products, the extension of that oversight to medical apps makes sense. According to Dr. Jeffrey Shuren, director for FDA’s Devices and Radiological Health, the arm that oversees medical devices, it’s not the platform in which FDA has interest, it’s the functionality of the platform. In other words, an ECG is an ECG no matter how it is taken. So far, FDA has already cleared more than 100 medical-related apps. That oversight is important because as the apps market grows, there will surely be those that provide incorrect or misleading information, which has the potential to cause medical errors.

An option for people who are looking to vet information on an app’s usability and content is a rating system called AppRx, which was designed by HealthTap. With AppRx, doctors can rate apps on their usability, usefulness and whether they are medically sound. Once 30 doctors have rated an app, and those ratings have been reviewed by HealthTap’s review board, the ratings are made available to the company’s non-doctor customers, who can “applaud” an app they like as well.

No matter what type of mobile app is being used, data safety is always an issue. It’s one thing for a fitness tracking device to lack secure password encryption, but the risk becomes exponential when the encryption issue pertains to a patient’s medical and personal information. While patient information in an electronic health record must meet the security criteria of the Health Insurance Portability and Accountability Act (HIPAA), this requirement is somewhat fuzzy in the mobile app world because there is no standard that shows an app is HIPAA-compliant. According to the IMS Institute for Healthcare Informatics, apps that collect, store or transmit data that is considered to be protected health information must do so in a HIPAA-compliant manner, and those that connect to personal health records must transmit the data in a secure manner. In addition, all stakeholders must agree to and maintain in good faith their role in that protection.

Popular and Here to Stay

The portability, utility and popularity of health and wellness apps clearly indicate they are here to stay. With this simple-to-use technology, improved well-being can be just a click away. But, finding the right app to fit one’s interests and style may be the hardest part with so many popular choices on the market.

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

Sources
It is still unknown what causes this chronic autoimmune disease that affects so many people, but with growing awareness surrounding the disease, increased research is revealing new clues and more effective treatment options.

DESPITE THE HIGH incidence of Sjögren’s syndrome, the disease was not well known until 2011, when world champion tennis player Venus Williams revealed she had been diagnosed with it, forcing her to withdraw from the U.S. Open. Suddenly, Sjögren’s went from obscurity to limelight, creating awareness not only on this particular autoimmune disease but on the growing prevalence of autoimmunity in general.

The symptoms of Sjögren’s were first observed in 1930 by Dr. Henrik Sjögren, an ophthalmologist in Jönköping, Sweden, after a patient presented with low secretions from the lacrimal and salivary glands.

Dr. Sjögren published his doctoral thesis in 1933 describing 19 females with these symptoms, which caused
dry eyes (keratoconjunctivitis), for which he coined the term keratoconjunctivitis sicca. But, his thesis was not well-received until he published a paper in 1951 that described 80 patients with keratoconjunctivitis sicca, 50 of whom also had arthritis. This led to an international interest in the condition, which began to be identified as Sjögren’s syndrome.¹

Today, Sjögren’s affects approximately four million people in the U.S., 90 percent of whom are women.² And, while anyone can develop Sjögren’s at any age, it is extremely rare in children, and most people are older than 40 at the time of diagnosis.³,⁴

What Is Sjögren’s?
Sjögren’s is a chronic autoimmune disease that occurs when the white blood cells attack the saliva and tear glands, leading to dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca). In some women, the gland responsible for keeping the vagina moist is also affected, resulting in vaginal dryness. The attack on the glands takes place in association with lymphocytic infiltration of the glands, an inflammatory process that eventually severely damages or destroys the glands.¹,⁵

The syndrome is characterized as either primary or secondary Sjögren’s. In primary Sjögren’s, the disease doesn’t develop as a result of another condition, while with secondary Sjögren’s, it results because of or alongside another connective tissue disease such as lupus or rheumatoid arthritis.⁵

Symptoms of Sjögren’s
Sjögren’s is a systemic disease that affects the entire body. In addition to dry eyes and dry mouth, there are many other symptoms that may occur. Symptoms associated with dry mouth include tooth decay (and eventual loss of teeth), persistent dry cough, problems chewing, loss of sense of taste, mouth sores or pain, problems swallowing, hoarseness, difficulty speaking, swollen salivary glands and recurring oral thrush. Symptoms associated with dry eye include a sensation that there is something in the eye, tired eyes, itchy eyes, mucus discharge from the eyes, photophobia, stinging or burning eyes, and swollen and/or irritated eyelids.⁴,⁵

There also are symptoms that occur when other glands are inflamed, although these are less common. For instance, the lining of the breathing passages can become inflamed causing lung infections, and the vaginal glands can become inflamed causing pain during intercourse or recurrent vaginal dryness.⁶

In individuals whose immune system also attacks other parts of the body, symptoms can include general tiredness; aching muscles; inflammation, stiffness and pain in the joints; peripheral neuropathy; Raynaud’s phenomenon; and vasculitis.⁴,⁵

Symptoms vary among individuals; they can remain steady, worsen or, uncommonly, go into remission. Some people experience mild discomfort, while others suffer debilitating symptoms that impair their functioning.²

Causes of Sjögren’s
It’s unknown what causes Sjögren’s, but it’s believed that primary Sjögren’s occurs due to a combination of environmental and genetic factors. For instance, genes can make some people more susceptible to having an abnormal immune system. And, an environmental factor such as hepatitis C viral infection or Epstein-Barr virus can trigger the immune system to not work properly. Since Sjögren’s is diagnosed most commonly during
the age when menopause occurs, some experts believe that falling levels of estrogen might disrupt the immune system. Secondary Sjögren’s, on the other hand, develops when another autoimmune condition progresses.5

**Diagnosing Sjögren’s**

Because symptoms of Sjögren’s often mimic other conditions or occur as a result of some medications, the disease is often overlooked or misdiagnosed, which is why it takes, on average, 3.9 years to diagnose.6,7 This lengthy delay can impede early treatment for Sjögren’s and result in years of needless discomfort and even irreversible organ damage.

Ophthalmologists typically administer two tests to diagnose Sjögren’s: the Rose Bengal test in which a nontoxic dye is dropped onto the surface of the eyes to measure the state and function of tear glands; and the Schirmer test in which strips of blotting paper are placed under the eyelid to analyze how much liquid the eye is producing.

Other tests include a lip biopsy, blood tests to determine if there are SSA and SSB (anti-Ro and anti-La, respectively) antibodies that show up in about 60 percent of Sjögren’s patients, salivary flow rate to determine if the salivary glands are working properly, sialogram X-ray to determine how much saliva flows into a patient’s mouth, salivary scintigraphy to measure salivary gland function, chest X-ray to determine if there is lung inflammation, and a urine sample to determine whether the kidneys have been affected.8

In 2013, the U.S. Food and Drug Administration approved a new lab test for early detection of Sjögren’s. Developed by Immco Diagnostics and marketed by its partner, Nicox, Sjö combines three proprietary biomarkers — SP-1 (salivary gland protein-1), CA-6 (carbonic anhydrase-6) and PSP (parotid secretory protein) — with traditional markers (antineutal antibodies [ANA], Ro, La and Rf [rheumatoid factor]). The proprietary markers — discovered by researchers at the University of Buffalo and Immco Diagnostics — are likely to be present early in the disease, allowing for faster and more accurate diagnosis. “The practitioner will be able to write the order for the patient to go to a local lab,” said Nicox Director of Marketing Jason Menzo. “Forty-eight hours later, the practitioner will receive the results. Alternatively, the practitioner may use a lancet to take a sample, then overnight the sample to the Immco laboratory to avoid sending the patient out.”6,8

Most Sjögren’s centers around the world diagnose Sjögren’s based on the American-European criteria published in 2002 in the Annals of Rheumatic Diseases (Table 1). Originally designed to define patients for research studies, the criteria outline several different parameters, including key symptoms, objective tests for dry eyes and dry mouth and tests for autoimmunity. Based on these criteria, the diagnosis of primary Sjögren’s (dry eyes and dry mouth in a patient with no pre-existing history of connective tissue disease) requires the fulfillment of four out of six criteria. One of those criteria must be either anti-SSA/SSB positivity or a positive lip biopsy. Diagnosis of secondary Sjögren’s (dry eyes and dry mouth in a patient with another pre-existing connective tissue disease) requires one dryness symptom plus two out of three objectives (numbers 3 through 5). Diagnosis of Sjögren’s in a patient with no sicca symptoms (dryness of the eyes, mouth or other body parts) can be made if three of four objective criteria are fulfilled (numbers 3 through 6).9

In 2012, the Sjögren’s International Collaborative Clinical Alliance (SICCA) released new classification criteria, the first that are based solely on objective clinical tests. The SICCA criteria stipulate that to be classified as Sjögren’s, research participants must be positive for at least two of three objective diagnostic tests: anti-SSA/SSB blood test that results in 1) positive serum levels of either the SSA and/or SSB antibody and/or 2) positive serum levels of the rheumatoid factor antibody and elevated antinuclear antibody titers; a score of three or more on the ocular surface staining test, which measures the dissipation rate of a specialized dye that is applied to the tear film that bathes the surface of the eye; and a positive salivary gland biopsy.10

**Complications of Sjögren’s**

Sjögren’s is often associated with other complications. Some less serious complications are dental cavities and eye damage. More common associations are autoimmune thyroiditis (Hashimoto’s), which can lead to abnormal thyroid levels, gastroesophageal reflux disease, which can cause difficulty swallowing and heartburn, and pulmonary infections. Biliary cirrhosis, an autoimmune disease of the liver that leads to scarring of the liver tissue, is a rare and serious disease association with Sjogren’s, as are kidney failure and vasculitis. Last, a small percentage of Sjögren’s patients develop lymphoma; however, this normally occurs only after many years with the illness.4,6

**Treating Sjögren’s**

There is no one specific medication to treat Sjögren’s. Instead, the goal is to relieve symptoms mostly through topical therapy. However, physicians do prescribe some medications, including pilocarpine (Salagen) and cevimeline (Evoxac) to increase the production of saliva and, sometimes, tears. These are typically used when systemic therapy is needed or local therapy isn’t successful.11 Other drugs may include hydroxychloroquine (Plaquenil), a drug designed to treat malaria, and methotrexate, which suppresses the
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Table 1. American-European Summary of Sjögren’s Syndrome Classification Criteria

<table>
<thead>
<tr>
<th>1. Ocular symptoms (any 1 of 3)</th>
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<tbody>
<tr>
<td>Dry eyes &gt;3 months</td>
</tr>
<tr>
<td>Tear use &gt;3x/day</td>
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<tr>
<td>Foreign body sensation in eyes</td>
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<tr>
<th>2. Oral symptoms (1 of 3)</th>
</tr>
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<tbody>
<tr>
<td>Dry mouth &gt;3 months</td>
</tr>
<tr>
<td>Swollen salivary glands</td>
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<tr>
<td>Need liquids to swallow</td>
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<tr>
<th>3. Ocular signs (1 of 2)</th>
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<tbody>
<tr>
<td>Unanesthetized Schirmer’s &lt;5mm/5min (both eyes)</td>
</tr>
<tr>
<td>Positive vital dye staining (rose bengal fluorescein, lissamine green)</td>
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<th>4. Oral signs (1 of 3)</th>
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<tr>
<td>Abnormal salivary gland scan</td>
</tr>
<tr>
<td>Abnormal parotid sialography</td>
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<tr>
<td>Abnormal unstimulated salivary flow (&lt;0.1ml/min)</td>
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<th>5. Positive lip biopsy</th>
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<tr>
<td>Focal lymphatic sialadenitis (focus score &gt;1/4mm)</td>
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<tr>
<th>6. Positive anti-SSA and/or SSB antibodies</th>
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<tbody>
<tr>
<td>Exclusions: hepatitis C, graft vs. host disease, use of drying medications, etc.</td>
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Living with Sjögren’s

Sjögren’s is not usually life-threatening, but it can be very life-altering. Individuals can ease their symptoms of Sjögren’s by sipping water throughout the day, chewing sugarless gum, avoiding medicines that cause mouth dryness, avoiding alcohol and using mouth rinses to replace minerals in their teeth. Other over-the-counter remedies include non-steroidal anti-inflammatory drugs such as ibuprofen to ease joint and muscle pains, saliva substitutes, drugs to help their salivary glands make more saliva, skin creams to ease dry skin, vaginal lubricants and moisture chamber spectacles (special glasses that wrap around the eyes to keep moisture in). Patients newly diagnosed with Sjögren’s may find it helpful to view a video titled “Sjögren’s Syndrome: A Place to Begin” produced by the Sjögren’s Syndrome Foundation.

Improving Sjögren’s Outcomes

A good deal of research is being conducted to improve the outcomes for Sjögren’s patients by identifying its possible causes for earlier diagnosis and developing new and more effective treatments. In 2010, a group of Swedish researchers discovered that individuals with Sjögren’s have “skewed B cell maturation after receiving the H1N1 flu vaccine, resulting in higher amounts of vaccine-specific antibodies that may be related to inflammation … [and] may reveal some links between B cells and autoimmune problems in Sjögren’s syndrome.”

Researchers at the National Institutes of Health are studying ways to diagnose Sjögren’s earlier by biopsying salivary glands of Sjögren’s patients to identify microRNAs (genes) that may be related to the disease. In fact, gene therapy is one of the more promising areas of research. A group of Dutch researchers have found that using B cell-targeting gene therapy to treat the salivary glands of mice reduced autoimmune-related inflammation, suggesting that gene therapy may help people with Sjögren’s.

Most of the new drug development is coming from Asia. Mizoribine (Bredinin) is an immunosuppressant drug designed to quiet an overactive immune system, although it is only available in Japan and China at this time. Mycophenolate sodium (Myfortic) is another immunosuppressant already in use as a treatment to prevent organ rejection in transplant recipients, but...
it is being studied in a number of autoimmune, arthritis-related diseases, including Sjögren’s. Nizatidine (Tazac, Axid) is an oral H2 blocker drug used commonly to treat excess stomach acid and is also being studied in Sjögren’s as a way to treat oral dryness. Rebamipide (Mucosta) is a mucosal protective agent in Phase II trials in the U.S. for treating dry eye and mouth.

Researchers also are trying to develop artificial or regenerated salivary glands using tissue engineering, gene therapy-like techniques and stem cell methods.15

Awareness about Sjögren’s syndrome has increased significantly since tennis star Venus Williams brought the disease to the public eye in 2011. But, much more needs to be learned. The Sjögren’s Syndrome Foundation has taken a leading role in moving the field of Sjögren’s forward by raising millions of dollars to fund research. Recently, it launched an initiative to improve the quality of care for Sjögren’s patients by developing clinical practice guidelines for assessment and management of the systemic manifestations, dry eye and dry mouth that occur due to the disease.16

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

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

For adults with primary immunodeficiency

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

Limitation of Use:
Safety and efficacy of chronic use of recombinant human hyaluronidase in HYQVIA have not been established in conditions other than PI.
HYQVIA is infused under the skin into the fatty subcutaneous (subQ) tissue, in 1 infusion site, up to once every 4 weeks. A second infusion site may be used if needed.

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

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

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a 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 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).

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 move the immune globulin get absorbed into the body to fight infection.

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

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

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

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

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

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

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

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

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

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

Before starting HYQVIA, tell your healthcare professional if you:

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

What is HYQVIA?

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

Who should not take HYQVIA?

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

How should I take HYQVIA?

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

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

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

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

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

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

Call your healthcare professional or go to your emergency department right away if you get:

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

These are not all of the possible side effects for HYQVIA. For more information about HYQVIA, go to www.HYQVIA.com. For more information on patient resources and education, please visit www.immunedisease.com.
While the intravenous route has been the standard method of IG therapy for autoimmune and other neuromuscular disorders, recent studies show that the subcutaneous route is both as effective and more preferred by patients.

By Keith Berman, MPH, MBA

WHILE THEY HAVE been available and increasingly popular in Europe over the last 25 years as replacement therapy for persons with primary immunodeficiency disorders (PIs),1 the first subcutaneous immune globulin (SCIG) product wasn’t approved for marketing in the U.S. until 2006. As recently as 2011, there was but a single SCIG brand — rather inconveniently formulated at the same 16 percent concentration as intramuscular immune globulin. Early on, some physicians recommended SCIG for carefully selected PI patients, but the vast majority continued to receive intravenous immune globulin (IVIG) every three to four weeks in a hospital outpatient clinic or physician office setting.

Thanks in part to a wave of published comparative studies, reviews and commentaries over the last several years, more U.S. immunologists and infectious disease specialists have become aware of specific advantages of SCIG in relation to IVIG for qualifying and motivated PI patients. Today, physicians can select from among five approved SCIG product options for their patients (Table 1), with at least two others reported to be in development. A steadily growing proportion of PI patients who require lifelong IG replacement therapy are newly
initiating or switching to SCIG therapy, drawn in part by the obvious appeal of self-administering their therapy at home in lieu of hospital, office clinic or home nursing visits to receive IVIG therapy.

With the benefit of years of experience with these products, investigators across Europe more recently have reported that SCIG may represent a better treatment option for patients chronically managed with IVIG for certain autoimmune neuromuscular diseases and secondary immunodeficiency disorders at risk for serious bacterial infections. Could self-administered SCIG represent a better option than IVIG for some patients with these disorders as well as patients with PIs?

What Makes SCIG a Better Option for Some PI Patients?

To answer this question, it is important to consider why SCIG self-administration — typically using a programmable syringe infusion pump — continues to attract a growing following among PI treatment specialists and patients.

Non-serious systemic adverse reactions are much less frequent with SCIG than IVIG therapy. Typically, smaller, more frequent doses of SCIG act to moderate spikes and troughs in IgG serum concentration. The high supra-physiologic serum IgG peak that occurs immediately following IVIG infusion likely contributes to a two- to three-fold higher incidence of non-serious systemic adverse reactions — mainly headache, fatigue, pyrexia, chills, nausea and vomiting — than is seen following SCIG infusion. Roughly one-half of patients newly starting SCIG experience generally minor local infusion site reactions — far more often than occurs with IVIG administration — but typical redness and swelling is transient and usually declines over time.

Risk of serious systemic adverse reactions is exceedingly low for currently licensed SCIG preparations. While serious systemic adverse events associated with IVIG therapy — primarily aseptic meningitis, thrombosis and hemolysis — are
very uncommon (and often preventable with premedication and slowing of the infusion rate), they do occur and have been reported both in published clinical studies and retrospective chart reviews. By contrast, no serious systemic adverse reactions have occurred to date in licensing trials conducted for any currently available SCIG product. These findings are consistent with a number of published case series. Recent U.S. and Swedish studies in 47 and 60 PI patients, respectively, reported a combined total of more than 4,000 home-based SCIG infusions with no serious systemic adverse events.6,7 An earlier large Scandinavian study documented just six moderate adverse systemic reactions and no severe or anaphylactoid reactions in 165 patients who received a total of 33,168 SCIG infusions.8 Simply put, opting for SCIG therapy reduces a very low risk of serious systemic adverse events to an extremely remote risk.

SCIG offers an equally effective treatment option for patients with IVIG tolerability or venous access problems. A very small but significant proportion of patients repeatedly experience very unpleasant or debilitating adverse reactions to IVIG that cannot be managed with premedication, a reduction in infusion rate or a change of product brand. Patients occasionally present with veins that are very difficult to access, necessitating surgical implantation of indwelling catheters that introduces its own potential infection risks. For these patients who are willing and capable of self-infusing at home, SCIG represents a safe and simple option to resolve these issues and continue to receive the full protective benefit of IG therapy.

SCIG self-administration permits dosing schedule flexibility and results in fewer lost work and school days. IVIG therapy generally necessitates a clinic visit every three to four weeks. For non-elderly patients, those scheduled visits — including the infusion itself and post-infusion recovery and observation time — translate into lost work and school days. Self-administration of SCIG, by contrast, can be flexibly scheduled after school or work, during evenings or on weekends. Multiple studies have quantified important reductions in lost school and work days after switching from IVIG to SCIG.9

Patients who experience SCIG therapy consistently prefer it over IVIG. IVIG may be a better option for PI patients with good venous access who tolerate the product well, and who variably have poor manual dexterity, lack of motivation to take responsibility for self-treatment, or have expressed reluctance to deal with needles or the mechanics of self-infusion. But surveys of other patients who were able to switch to SCIG consistently document a strong preference for SCIG therapy (Table 2), as well as improved health-related quality of life (HRQL) measures.

An additional consideration when choosing between these two options is, of course, cost. Consistent with several European reports, two recent Canadian studies identified significant annual cost savings associated with home self-infusion of SCIG, driven by near-elimination of the need for infusion nursing and ancillary personnel.10,11 These analyses are predicated on dosing SCIG equivalently to IVIG, a practice that also prevails in Europe. In the U.S., initial dosing instructions for four of the five available SCIG products* recommend boosting the total SCIG dose either by 37 percent (Gammagard Liquid, Gamunex-C and Gammaked) or by 53 percent (Hizentra) — with the objective of equalizing the estimated “area under the curve” (AUC) that corresponds with total circulating IgG over a specified period of time. However, available evidence, including a recent crossover study, suggests that dose-equivalent therapy with SCIG is as effective as IVIG for protection of PI patients against serious infections.12 Possibly, the pharmacokinetics of SCIG — characterized by much less fluctuation in serum IgG and a significantly higher mean serum IgG trough level than IVIG — may help to offset the lower AUC profile of a dose-equivalent SCIG regimen.

Table 1. Licensed Subcutaneous Immunoglobulin Products

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>HIZENTRA</th>
<th>HYQVIA</th>
<th>GAMMAGARD LIQUID</th>
<th>GAMUNEX-C</th>
<th>GAMMAKED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>CSL Behring</td>
<td>Baxter</td>
<td>Baxter</td>
<td>Grifols</td>
<td>Kedrion Biopharma</td>
</tr>
<tr>
<td>IgG concentration</td>
<td>20%</td>
<td>10%*</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

*Co-administered following initial infusion of recombinant human hyaluronidase

* HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] full prescribing information recommends administering the product at the same dose and frequency as the previous intravenous treatment, after the initial dose ramp-up.
SCIG for Autoimmune Neuromuscular Disorders and More

The multiple demonstrated advantages of SCIG therapy for qualified PI patients have not been lost on specialists who often prescribe IVIG as long-term maintenance therapy to manage certain autoimmune inflammatory neuromuscular disorders. Again, the Europeans have been out in front in investigating the feasibility of SCIG for a number of important conditions for which IVIG is already an established first-line therapy.

**Chronic inflammatory demyelinating polyneuropathy (CIDP).** Interest in SCIG as a treatment option for this disorder was signaled in 2008 with publication of case reports describing its effectiveness and good tolerability in CIDP patients already successfully managed with IVIG.13,14 In 2013, Danish investigators reported on a study that randomized 30 adult patients successfully managed on maintenance therapy with IVIG to either SCIG at a total dose corresponding to their pre-study IVIG dose or to subcutaneous saline.15 The SCIG group actually experienced a modest increase in isokinetic muscle strength of 5.5 ± 9.5 percent (P < 0.05) as compared with an expected decline of 14.4 ± 20.3 percent (P < 0.05) in the saline placebo group. Various other key functional measures similarly improved following SCIG in relation to saline placebo.

This same Danish group then followed 17 CIDP patients, all of whom had previously responded to IVIG, for one year on SCIG maintenance therapy. SCIG preserved muscle strength and functional abilities.16 “SCIG should be considered as an alternative in long-term treatment of CIDP patients,” they concluded.

Very recently, an Italian research team reported sustained clinical efficacy, as measured by the Overall Neuropathy Limitation Scale (ONLS), with SCIG therapy in a group of 66 CIDP patients previously managed with IVIG (P= 0.018). Just one subject experienced a worsening of symptoms over the four-month study period. Patients additionally reported an improvement in relation to IVIG therapy in their perception of the therapeutic setting.17

With support from CSL Behring, an ambitious 350-subject multicenter, prospective, randomized, double-blind, placebo-controlled trial now in progress will not only try to affirm the therapeutic equivalence of its 20 percent SCIG product, Hizentra, to IVIG, but will attempt to answer whether more aggressive maintenance dosing provides additional clinical benefit. Participating study sites in 15 countries are randomizing subjects with IVIG-dependent CIDP to receive “low dose” or “high dose” weekly SCIG infusions of 0.2 g/kg or 0.4 g/kg body weight, or to receive placebo infusions. This study is expected to be completed in November 2015.

**Multifocal motor neuropathy (MMN).** Hypothesizing that an equivalent dosage of SCIG is as effective as IVIG in patients with IVIG-responsive MMN, Danish investigators completed a randomized crossover study in nine subjects.18 The two treatments were equally effective, with SCIG use additionally sparing subjects from “end-of-dose weakness” episodes that some experienced with IVIG therapy. Patient preference findings, however, were not in line with those expressed by PI patients, who strongly favor SCIG. Four of the nine subjects in this small MMN study preferred SCIG, three had no preference and two preferred IVIG. The reason could be traced at least in part to the study protocol: subjects had to self-infuse two to three times weekly.

A UK study of seven MMN patients on stable IVIG dosing who completed six months of once-weekly SCIG treatment again documented no change in muscle strength, disability, motor function or health status. With respect to HRQL, all seven rated SCIG home treatment as “extremely good.” The investigators concluded that “MMN patients with stable clinical course on regular IVIG can be switched to SCIG at the same monthly dose without deterioration and with a sustained overall improvement in HRQL.”19 Sustained clinical efficacy with a stable ONLS score was very recently reported in a series of 21 MMN patients, just one experiencing worsening symptoms.17

**Other neuromuscular disorders.** At present, IVIG is first-line therapy for patients with steroid-resistant dermatomyositis (DM) and polymyositis (PM). Italian investigators recently reported that no relapse of disease occurred during weekly SCIG treatment of seven patients with severe idiopathic DM or PM previously on maintenance IVIG therapy over a median follow-up period of 14 ± 4 months.20 Three of the seven patients were able to discontinue immunosuppressive drug therapy, and all were able to reduce their daily maintenance prednisone dose. A U.S.

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### Table 2. Patient-Reported Preferences Following Experience with Both Hospital-Based IVIG Therapy and Home-Based SCIG Therapy

<table>
<thead>
<tr>
<th>YEAR</th>
<th>COUNTRY</th>
<th>SUBJECTS</th>
<th>PREFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>U.S./Canada</td>
<td>28</td>
<td>81% of patients preferred home-based SCIG</td>
</tr>
<tr>
<td>2008</td>
<td>Sweden</td>
<td>12</td>
<td>100% of patients preferred home-based SCIG</td>
</tr>
<tr>
<td>2010</td>
<td>Europe (multicenter)</td>
<td>82*</td>
<td>92% of patients preferred home-based SCIG</td>
</tr>
</tbody>
</table>

*Includes patients with both primary and secondary immunodeficiency disorders

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**IG Living** | February-March 2015 | IGLiving.com
prospect of study is set to enroll 10 IVIG-naïve adult subjects with DM this year to evaluate both changes in strength from baseline and participant preference for SCIG in relation to IVIG.\textsuperscript{21}

Another newly organized single-center Phase 2 study at the University of Kansas will assess the safety and efficacy of SCIG in 25 subjects with myasthenia gravis who require maintenance IVIG therapy.

Wherever there is an autoimmune neuromuscular disorder or a disease commonly associated with secondary antibody immunodeficiency requiring chronic IVIG therapy, expect to see new case reports and small patient studies going forward. A prime example is the very recently published Italian single-center experience comparing IVIG and SCIG use in 61 patients with hypogammaglobulinemia secondary to chronic lymphocytic leukemia (CLL) and non-Hodgkins lymphoma (NHL). Unsurprisingly, their results closely mirrored findings in PI patient studies: fewer systemic adverse events, significantly higher IgG trough levels, similar effectiveness in reducing infectious events and need for antibiotic coverage, and a decided improvement in quality of life-related parameters after the switch to SCIG.\textsuperscript{22}

### Older Age, Higher Dosage May Mean More SCIG Benefit

While SCIG therapy was originally tested in PI patients and has since become well accepted as a similarly effective alternative to IVIG with fewer adverse systemic effects, arguably the benefits of SCIG are even more important for patients with autoimmune neuromuscular disorders who require IG therapy. The PI IG-treated population includes all ages butskews heavily toward children and younger adults. Patients with inflammatory neuromuscular conditions that require IVIG therapy, most prominently CIDP and MMN, are largely at the other end of the age spectrum. Most CIDP patients are over age 50 years, with many in their 60s, 70s and even 80s.\textsuperscript{23} The mean age of onset of MMN is 40 years.\textsuperscript{24} Of course, CLL and NHL patients on IVIG replacement therapy also comprise an older age demographic.

We know that older age and, in all likelihood, higher dose are among important risk factors for rare but well-documented thrombosis events following IG infusions. Persons whose neuromuscular disorders are managed with IVIG are generally older, and their average monthly dosage is at least two-fold higher than the average for persons with PI. In crossover studies, weekly SCIG self-infusions have been consistently preferred by patients and have a sharply lower serious adverse event risk profile than IVIG therapy. The convenience of SCIG for home infusion has taken an important leap forward with the recent approvals of every-two-week dosing for Hizentra and every-three-to-four-week dosing with HYQVIA.

As with PI, adoption of SCIG therapy will take time, but there now seems little doubt that it is an advantageous IG delivery option for properly selected patients with neuromuscular and secondary immunodeficiency disorders now chronically managed with IVIG.

### KEITH BERMAN, MPH, MBA, is the founder of Health Research Associates, providing reimbursement consulting, business development and market research services to biopharmaceutical, blood product and medical device manufacturers and suppliers. Since 1989, he has also served as editor of International Blood/Plasma News, a blood products industry newsletter.

### References

OVER THE PAST two decades, immune globulin (IG) therapy has undergone dramatic transformations. One of the most significant is the shift from center-based infusion therapy to home infusions. This shift away from the hospital/clinic setting to patients’ homes is a positive trend leading to greater convenience, lower cost, less exposure to high infection-risk settings and less disruption of patients’ lives. However, this change also has led to decreased direct contact between patients and their healthcare providers, which could potentially compromise adequate communication and monitoring of patients’ ongoing medical conditions. As such, there is a need to find a way to better regularly monitor patients’ status in the home setting. A system of remote collection and monitoring of patients’ clinical data would enable patients to have all the advantages of home infusions, as well as improved communication and quality of care.

The Importance of Clinical Monitoring

There are many reasons why it is important to monitor the clinical status of patients. First, while there are dosing guidelines, each patient is different, and the right dose needs to be tailored to both laboratory values and patients’ clinical status. Second, IG infusions can be associated with a constellation of adverse events, which need to be monitored and addressed in a timely manner. Most importantly, because many of the conditions that are treated with IG therapy can progress over time and predispose individuals to develop new complications, it’s crucial to be vigilant about the development of new symptoms.

For primary immunodeficiency disease (PI) patients, the main goal of IG therapy is to decrease frequency of infections. While it is conventional to start patients on an IG dose of 300 to 600 mg/kg per month, the exact dose will depend on whether it is reducing the frequency of infections in a clinically meaningful manner. Therefore, to arrive at the optimal dose for a patient, all the infectious complications need to be documented to provide adequate information for proper titration of dose or adjustment of administration frequency.

IG therapy has greatly decreased the infectious mortality and morbidity of one of the more common PI diagnoses: common variable immunodeficiency (CVID). However, CVID has to be understood as not simply a deficiency of the immune system, but as a syndrome of immune dysregulation, which is what predisposes individuals to develop autoimmune, gastrointestinal and malignant complications — none of which IG replacement treats. Early signs of many of the autoimmune and malignant complications can be subtle and nonspecific such as fatigue, malaise, unintentional weight loss, easy bruising, decreased exercise tolerance, etc. And, because it’s not easy to diagnose autoimmune disorders or the early stages of malignancies, frequent and accurate collection of clinical data is extremely important to enable physicians to determine whether action needs to be taken.

As an example, one CVID patient in our clinic who suffered no infectious complications while on home infusion IG therapy developed massive enlargement of her spleen and liver due to formation of granulomas in the liver (autoimmune disease) over a period of six months. Unfortunately, she only came to clinic every four months. So, while we were able to proceed immediately to a thorough evaluation once we saw her, she could have been evaluated sooner if there was a better way to monitor her clinical status at home on a monthly or even weekly basis.
Collecting the Clinical Data

Clinical data monitoring for home infusions can be performed in several ways depending on who is entering the information and how it is transmitted and presented to providers.

Since patients administer their own subcutaneous infusions, they would need to enter their clinical data and subsequently deliver it to either their physician or infusion agency. The advantage to patients tracking their own data is that they know their bodies best, and it is the most direct way of collecting information. However, the disadvantage is that patients are not trained in clinical care, and they may focus on certain benign symptoms while overlooking more ominous ones. Furthermore, without the vigilance of a healthcare provider, patients may forget to document clinical information leading to incomplete collection of crucial data.

There are greater advantages to infusion nurses collecting clinical information. Because they are at patients’ homes for several hours during each infusion, they have ample opportunity to ask patients questions about their clinical status and perform necessary diagnostic procedures. Furthermore, infusion nurses are already charting nursing notes, and the additional clinical information can be collected using the same or similar platform. However, while nurses are trained to assess clinical status, they come to patients’ homes only once every three to four weeks. During the interim, symptoms may have developed that patients may forget to mention. Therefore, collection of clinical information by infusion nurses may improve efficiency, but it would not be collected as frequently or in real time as it would with patients collecting the data.

Whether nurses or patients enter the data, comprehensive clinical data monitoring software is needed. The ideal software program should allow for both breadth and depth of clinical information collection. It has to be broad enough to cover all the possible organ systems that the disease may affect and the myriad of symptoms that commonly present in those conditions. It also has to be flexible enough that it can be adaptable across disease states and groups of disorders. However, within each symptom or assessment of organ dysfunction, there needs to be considerable depth of data collection to account for nuances of symptom presentation and severity of disease.

For instance, data could be collected in the following fields: efficacy, adverse effects, disease-related symptoms, dose/medication, healthcare usage and general well-being. Efficacy of treatment is examined by evaluating disease-specific outcome measures that should improve with IG replacement. For example, for PI, the IG-related outcomes are number/frequency of infections, severity of infections, frequency of fevers and lung function as measured by spirometry. Disease-related symptoms for PI can include symptoms related to gastrointestinal complications (i.e., diarrhea, abdominal pain, nausea/vomiting, etc.), hematologic complications (i.e., easy bruising, bleeding, anemia manifested by chronic fatigue, etc.), musculoskeletal complications (i.e., muscle aches, joint pains, immobilizations, etc.) and dermatologic complications (i.e., rash, hives, etc.). Adverse event monitoring includes IG administration-specific issues such as fever, diffuse body aches, blood clots, headache, etc. Dose medication tracking specifically monitors the patient’s administered dose and any changes in the dose, frequency, administration sites, brand of IG or route of administration. Healthcare usage would note the amount of additional doctor office visits, urgent/emergency care visits, hospitalizations and antibiotics used. Lastly, general well-being would track the patient’s overall activity level, energy level, mood, weight gain/loss and satisfaction with treatment.

While the program needs to be comprehensive, it also should be user-friendly and not overwhelming or time-consuming. Finally, this information needs to be transmitted to providers in a timely manner to help them make clinical decisions. This can be done by patients uploading it and making it electronically accessible by the physician as data is entered, or by the specialty pharmacy (possibly with pharmacist involvement) that sends a summary report on a quarterly or monthly basis.

Better Data Equals Better Care

Development of clinical data monitoring systems for home infusion patients is crucial to achieving better care and more optimal outcomes. In addition, these systems have enormous potential for developing a better understanding of and guidelines for IG therapy. While there are some programs in use today by specialty pharmacies, the best method of collecting and transmitting data will be determined as more of them are developed.

BOB GENG, MD, MA, studied medicine at Washington University School of Medicine in St. Louis, where he also completed his residency training in internal medicine. He is currently a third-year fellow in allergy and immunology at UCLA Medical Center. Dr. Geng received his bachelor and master of arts in Georgetown University’s School of Foreign Service.
Hizentra treats various forms of primary immunodeficiency (PI) in patients age 2 and over.

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

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

Please see additional Important Safety Information on reverse side and brief summary of full prescribing information for Hizentra, including boxed warning, on adjacent page.
**Steady State / Low Volume:**
Hizentra delivers steady-state levels in half the volume of 10% solutions*

**Confidence:**
More than 10,000 patients and providers put their confidence in Hizentra 20%. Hizentra has demonstrated safety & tolerability in pediatric (2 years and older) through geriatric patients

**Individualized Dosing:**
With the option of weekly or biweekly (every 2 weeks) dosing, Hizentra allows patients to work with their providers on a dosing schedule that works for them

**Tolerated in Children:**
In a study with children and adolescents, patients & guardians evaluated the local tolerability of Hizentra therapy as very good or good for 98.5% of the infusions.

*Based on an equivalent dose in grams.

**Important Safety Information (continued)**

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

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

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

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

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

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

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

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

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
HIZENTRA®, Immune Globulin Subcutaneous (Human), 20% Liquid  
Initial U.S. Approval: 2010

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

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

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

DOSAGE AND ADMINISTRATION  
For subcutaneous infusion only. Do not inject into a blood vessel. Administer weekly or biweekly (every two weeks).

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

Weekly: Start Hizentra 1 week after last IGIV infusion
  Initial weekly dose = Previous IGIV dose (in grams)  x 1.53  
  No. of weeks between IGIV doses

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

• Adjust the dose based on clinical response and serum IgG trough levels (see Dose Adjustment).

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

DOSAGE FORMS AND STRENGTHS  
0.2 g per mL (20%) protein solution for subcutaneous injection

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

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

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

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

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

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

Based on September 2013 version
Orphan Diseases: where are we now

By Heather Claverie

IT’S 1980 AND Adam Seligman has just hit a wall. At the time, the drugs necessary to treat the teen’s Tourette’s syndrome were unavailable in the United States. So Seligman turned to our neighbors to the North, ordering the medication from a Canadian doctor. When the drugs were seized at the border, Seligman’s mother contacted her congressman, Rep. Henry Waxman, D-Calif., and relayed her son’s story.¹ Soon, the cause of rare diseases, or so-called orphan diseases, made its way from California to Capitol Hill, and a mother’s crusade to help her son receive some much-needed medicine morphed into quite the Hollywood story.

Before awareness-raising events like the Ice Bucket Challenge and social media, many of the diseases Americans are now familiar with were completely foreign. These so-called orphan diseases — primary immunodeficiency, chronic inflammatory demyelinating polyneuropathy (CIDP), polymyositis, Sjögren’s syndrome, Lou Gehrig’s disease and many more — were, and still are, so rare that few companies were willing to dedicate resources to develop these pricey prescriptions, which can cost hundreds of thousands of dollars per year. Still, the obscure topic wasn’t exactly a hot-button issue. Enter Seligman and Rep. Waxman. Seligman’s story tugged at the congressman’s heartstrings, so Rep. Waxman convened a hearing to learn more about the issue.

A reporter from the Los Angeles Times was the only media presence at the hearing. After his story ran, it caught the eye of Jack Klugman, star of the 1980s crime drama “Quincy, M.E.” and co-star of “The Odd Couple.” Klugman and his brother, Maurice, a writer and producer who suffered from a rare form of cancer, decided to use their show as a platform for awareness, writing Tourette’s syndrome and the orphan drug problem into an episode of Quincy.² Klugman then headed to Washington, D.C., to testify before Congress, where his prowess shined a spotlight on the issue and The New York Times ran a front-page article on orphan drugs, turning the previously little-known topic into national news.

Orphan diseases are defined as any disorder affecting fewer than 200,000 Americans. An orphan drug is one that is intended to treat fewer than 200,000 Americans or one that treats a disease that affects more than 200,000 people but the company developing and marketing the drug doesn’t expect to recoup the costs of research and development.³ There are currently between 6,000 and 7,000 orphan diseases affecting nearly 30 million Americans, or less than 1 percent of the population.⁴ And, half of the diseases affect children.⁵

The Orphan Drug Act of 1983

Before 1983, individuals suffering from rare diseases stood at a dead-end road. Because such a small percentage of the population suffers from these diseases — some affect as few as 150 Americans — pharmaceutical companies before 1983 were reluctant to invest time and resources to develop these pricey prescriptions, which can cost hundreds of thousands of dollars per year. Still, the obscure topic wasn’t exactly a hot-button issue. Enter Seligman and Rep. Waxman. Seligman’s story tugged at the congress-
During the hearings, at which witnesses from FDA, National Cancer Institute, Pharmaceutical Research and Manufacturers of America and many drug companies testified, it was discovered that there were 134 drugs developed for rare diseases, yet only 47 were approved for use by FDA, and only 10 had been developed and marketed solely by pharmaceutical companies. One witness in particular, Dr. J. Richard Crout, then director of the U.S. Bureau of Drugs, testified that the major problems with orphan drugs were patentability and liability. In essence, because the drugs were designated for such a small population, developing them was a risk for companies since so few individuals were available for clinical trials.6

Eventually signed into law by President Reagan on Jan. 4, 1983, the Orphan Drug Act of 1983 provides financial incentives to drug companies willing to develop treatments for rare diseases or conditions. If a drug is granted orphan status, the act provides the following: federal funding of grants and contracts for clinical trials, a tax credit of 50 percent of clinical testing expenses paid or incurred during the year, and 50 percent of clinical testing expenses paid or incurred during the year, and exclusive marketing rights for seven years from the date of FDA approval.7

Today, more than 3,000 products are designated as possible treatments for orphan diseases, with more than 450 approved by FDA for clinical use, according to the National Organization of Rare Disorders (NORD), a nonprofit dedicated to assisting individuals with rare diseases through advocacy, education and research.

Orphan Disease Obstacles
More than three decades have passed since the signing of the Orphan Drug Act, yet many obstacles remain for individuals suffering from orphan diseases. "I think the challenge for all of us in the community now is to figure out how we translate this great research into safe, effective treatment for patients," said Mary Dunkle, vice president of communications for NORD. "There’s a great sense of urgency in the community. In many cases, the patients are children, so there’s always this feeling that the clock is ticking.”

Spending years hopping from physician to physician is the hallmark of patients suffering from rare diseases. Many are misdiagnosed, and some, like Barbara Fowkes, are even told it’s a mental, not a physical, issue. "They diagnosed me with rheumatoid arthritis, Sjögren’s and fibromyalgia, and ‘it’s all in your head,’” said Fowkes.

When the Pennsylvania resident one day found herself so weak she was unable to open her car door, she knew it had to be something else. Fowkes was eventually diagnosed with CIDP. “You have to be your own advocate throughout the whole process,” she said. "Even after your diagnosis, I tell people ‘never stop being your own advocate.’”

Fowkes, who serves as a liaison for the GBS/CIDP Foundation International, said that since there are so few individuals suffering from these orphan diseases, it’s paramount to seek out an organization that specifically serves the communities associated with these rare diseases. And, she encourages anyone having a difficult time receiving a diagnosis to head to a teaching hospital in an urban area. Since teaching hospitals are affiliated with a university, physicians tend to be more open to possibilities and have more experience with rare diseases.

The Future of Orphan Diseases
It’s still too early to say exactly how the Affordable Care Act will impact those suffering from orphan diseases. Eliminating discrimination of those with pre-existing conditions is one aspect of the law that helps those with orphan diseases. But, there are many concerns as to how the Act will affect the research and development of these pricey drugs. Still, there is some good news. The plummeting cost of sequencing DNA could lead to the development of more drugs and help drop prices. In addition, some companies have found a way to turn major profits from the development of orphan drugs, which is likely to entice more pharmaceutical companies.8 And, because the pool of insured individuals has increased under the new law, these niche drugs are bound to become more commercially viable, enticing current and future developers of orphan drugs.

In the meantime, organizations like NORD will continue to promote awareness through a variety of outlets. The nonprofit funds between five and 10 research grants a year. On the last day of February, Rare Disease Day is staged.

On the legislative front, Congress launched the initiative 21st Century Cures in April, with the goal of accelerating the pace of cures and medical breakthroughs in America. NORD has provided personal testimony for the initiative, bringing the issues of orphan diseases to the congressional table. ■

HEATHER CLAVERIE is a staff writer for IG Living magazine.

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LEANN RUDESEAL GREW up as the baby in her family and was always the one who was sick, weak or hospitalized. As an adult, chronic sinus infections led to multiple (unsuccessful) surgeries, and finally, a diagnosis of common variable immunodeficiency (CVID). Although initially devastated by her “new normal,” LeAnn has discovered an inspiring way to pursue her dreams and encourage others in the process.

**Trudie:** When did you suspect you were chronically ill?

**LeAnn:** Growing up, I was always the one who was either sick or had more of a severe case of all the childhood illnesses. By the time I was a young adult, I would joke and say that my brother got all the good genes, and in the back of my mind, I would wonder what was wrong with me. Eight years ago, the sinus infections started. I was on and off of heavy antibiotics and steroids to no avail. In 2013, I had my first sinus surgery and was hopeful that I was finally going to get well. Almost a year to the date of my first sinus surgery, I had my second sinus surgery. Three weeks post-op, all my sinus infection symptoms came back, stronger than ever. At this point, I was desperate and made an appointment to see an allergist/immunologist.

**Trudie:** How were you finally diagnosed?

**LeAnn:** My doctor first tested me for allergies, and I tested negative to everything. That is when I first heard the words “common variable immunodeficiency.” I went through the proper testing and was diagnosed July 22 of 2014. I finally had the piece of the puzzle and a name to put with it. I had no idea of the complexity of this illness or how my life was about to change.

**Trudie:** How has your life changed?

**LeAnn:** I started doing research on CVID, and it was not long before I was totally overwhelmed. Then, the grieving process began. My body, mind and soul had become so weary of never feeling good or having a good day or even a good time. I had forgotten how to have fun. I landed in a place where I felt I had no purpose. Everything came to a screeching halt. I did not like myself and really didn’t want to deal with all that goes with CVID. I felt as though my dreams and ambitions had come to an end. I had hit rock bottom.

**Trudie:** How did you overcome that challenge?

**LeAnn:** They say that when you are at the bottom, the only thing to do is look up, so I did. I submerged myself...
in my faith and the love of my husband, family and friends. We all have things that we go through, regardless of our health. I have people in my life who have their health and have had to go through far worse things than me. Really, no one gets a free ride. The words “new normal” mean more to me now. My dreams have taken on a new direction; I do have purpose, and I am a good wife, mother, daughter and friend because I do things differently now. Overall, I am kinder, more honest and more authentic as a human being than I ever was before.

Trudie: What is your treatment plan?
LeAnn: I am on intravenous immune globulin infusion treatments once a month, and I am currently building my dream team of doctors for all the “cherry on the top” issues that go along with CVID.

Trudie: What has been the biggest obstacle for you?
LeAnn: Probably trying to help people understand the illness. It is so hard for people to grasp what your immune system has to do with your sinuses or lungs. Or to get them to understand that my level of activity truly depends on how I wake up each morning. I now have a daily goal of doing one thing that is productive, and we celebrate that little thing. I am now finding that the one thing is turning into three or more things. So I am rid of the pressure to perform. We celebrate the productive things and give grace to the rest of the day.

Trudie: Tell us about your jewelry.
LeAnn: I have been designing jewelry for over 10 years, but these past seven years, the total structure of my business has changed. My faith is the driving force for this new adventure; even the new name of my company is connected to that faith. The line is called For Such A Time As This Handmade Jewelry. I am working on designs that will bring awareness to those of us who live with chronic illness. I want to bridge the gap between patients and their friends and family members. The symbols and designs will speak quietly to those who wear them, and provide the opportunity to explain the meaning of the piece, and create an opportunity to bring awareness to chronic illness. For the family member who wears a piece in support of a patient, it will remind them to be loving and encouraging. I know now that I was born “for such a time as this,” like it says in the Bible, and my new dream is better than any I had before CVID. I count it a joy to live with CVID if this line of jewelry brings healing to just one person and family.

Trudie: What is your advice to others?
LeAnn: Extend grace to yourself. Practice courage. Take the very best care of yourself, and do your best to live as healthy as you can. Continue to dream, know that you have a purpose and that you still can make a difference in someone’s life. CVID is not a prison; in fact, it is freeing to love yourself, respect yourself and to get to know yourself in ways that you would not have before living with a chronic illness like this. My body is going to fail me, but my heart, soul and spirit will not. As our illness is rare, we have to find the rare ways to give back — that’s what motivates me.

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.
AS I WRITE this, I am sitting in the midst of a mountain of boxes, bare walls and floors, and am clutching a to-do list that rivals the length of Santa’s list right before the holidays. My husband and I are moving into our first (and hopefully forever) home. It’s exciting, scary, thrilling and nerve-racking. We can’t wait for our dog to run around in her own yard, but dealing with contractors is a new experience worthy of being a sitcom on television. We are blessed to be in a situation to finally see this dream come true. However, there’s a twinge of fear and anxiety for me with this particular move. I’m packing up not only my possessions, but my feelings and health issues as well. I’m leaving the place we lived when I first became ill and was diagnosed, and where I have spent the last seven years dealing with the challenges of multifocal motor neuropathy, lupus and Sjögren’s syndrome and getting monthly infusions of intravenous immune globulin (IVIG).

When I moved in my 20s and 30s, it was a breeze. I was young, everything I owned fit in a van, and I zipped about living where I wanted. As I got older and married, our “stuff” grew, in a good way, but it was time to hire movers. (Friends don’t find beer and pizza a reward for back problems after helping you lift heavy objects.) Even through those decades, I was a moving machine. I could unpack the house in an entire weekend after moving in. I had energy without end. Then, like a needle scratching across a record as it was playing, it all stopped.

All my autoimmune and neurological illnesses make me feel like I have a leash on my energy. I’m yanked into submission by fatigue or neuropathic problems with my hands and legs. I am now in my mid-40s, but I don’t even think about the age problems I’m supposed to be obsessing about: bad back, gaining weight with a slowed metabolism, slowing down, etc. All of these issues have been overshadowed by my bigger health problems. At one point, before I was diagnosed and started receiving my IG infusions, I couldn’t walk half a block. I was hunched over, and lifting a fork to eat felt like I was holding a lead paperweight. So once I started receiving IG (which I refer to as magic juice, because it truly is!), I felt like a new person. Not like my old self, but a perkier, more functional version.

As I age and deal with my health conditions, I’m different from how my mind’s eye sees me. Part of me still feels like a teenager, even though I am well aware I’ll never be that agile again. In fact, choosing our home meant getting one that didn’t have an upper level because I can’t handle the stairs. My neurological issues are a determining factor regarding where we live. That was a startling realization. Right now, my health is remaining steady with medications and IG infusions, but I have to think about the future — not only the factors involved with nature taking its course as I become older, but those involving my special medical needs.

There’s a song by Soul II Soul I haven’t thought of in ages: “Keep on moving, don’t stop, keep on moving, don’t stop.” Whether it’s due to time, age or illness, there are going to be changes. I’m putting the welcome mat out for the new chapter in my life and walking through the door.

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.
Using Your Time Wisely: Everything You Could Do During Your Infusion

By Ilana Jaqueline

GETTING YOUR REGULAR intravenous immune globulin (IVIG) infusion can take hours, often with you stuck in a recliner, bored, with nothing to do. Even subcutaneous (SCIG) infusions at home can be boring. And all that waiting and staring at needles and tubing — well, it can get kind of depressing. Keep yourself occupied this week by following some of these simple dos and don’ts to using your infusion time effectively.

Do: Catch up on your social media. There’s never a better time to scroll through your Twitter feed (and maybe unfollow some lame accounts) than when you’re stuck in a chair for an hour (or six). I like to use the search function to find other people with similar diseases or jobs or even just users who live in my town. You can even live-tweet your infusion and spread a little awareness about primary immunodeficiency disease. Make sure to hit up @IlanaJacqueline!

Don’t: Try to take a Twitpic while actually inserting your sub-q needles. Not a great time to divide your attention.

Do: Catch up on work. You’re going to be here for a while anyway, so you might as well pump out that last term paper or finish up your paperwork. It actually works out great if you plan for this to be your dedicated working hour. As long as you’ve got your laptop in front of you, you can research, take notes or sign in to any programs you might use on the job. Now is a great time to respond to all those emails, figure out that new program your company started working with and put yourself ahead of the game for upcoming projects.

Don’t: Try to catch up on your work if you are a professional gymnast or rugby player. Pretty sure there’s no tackling or headstands allowed during this process.

Do: Spend time with your friends or family. There’s nothing wrong with getting your IVIG while watching a movie with your friends or playing an intense game of Bananagrams with your sister. A game of cards is easy to carry along to your infusion center and will help the time pass even more quickly.

Don’t: Start a game of Twister with your notoriously clumsy cousins.

Do: Binge-watch a new show on Netflix. “Gilmore Girls”? “Jericho”? “Once Upon a Time”? These are all great series, perfect for binge-watching while stuck in your chair for a while. Check out your top recommendations, or see what shows your friends are addicted to lately.

Don’t: Get so caught up in your show that you forget to check when your infusion is done.

Do: Organize your life. Whether you use an old school paper agenda or Google Calendar, now is the perfect time to fill in all the blanks: birthdays, holidays and your SCIG or IVIG schedule. Set up your plans for the week. You’re getting gas in the tank — might as well start looking at the road map.

Don’t: Worry so much about missing your great aunt’s birthday; just don’t forget to give the dog his flea medication on the right date and come up with a covert code word for scheduled naps.

ILANA JACQUELINE is a 24-year-old dysautonomia and primary immune deficiency disease patient from South Florida. She’s been writing professionally since 2004 on everything from health and wellness to celebrities and beauty. Her blog www.letsfeelbetter.com is both a personal collection of anecdotes about life with chronic illness, as well as a resource for patients of all ages.
THE CROWD AROUND the mysterious woman grew slowly. Curiosity drew folks from every corner of the room like kids to Nana’s fresh-from-the-oven chocolate chunk cookies. Despite being at the “happiest place on earth” for our first Immune Deficiency Foundation (IDF) conference, where we had access to world-renowned immunologists during the day and played with a world-renowned mouse at night, this mysterious woman — more specifically what she was doing to herself — had us captivated. Mesmerized. Awestruck. Eyes wide open. I inched myself closer to the zombified crowd, hoping to catch a glimpse of what had turned patients, a few medical professionals, one keynote speaker and the omelet chef from the morning’s breakfast buffet completely dumbstruck.

“Then, all I do is place the syringe in the pump, release this lever, and — 5, 4, 3, 2, 1 — I’m in business!” the mysterious woman demonstrated. A hush spread through the crowd like tule fog in California’s Central Valley; it was so quiet, you could hear a bifurcated needle drop.

Deep silence was (thankfully) interrupted by a mop-headed teenager: “Nooo waaaay, Dude! I gotta get me one of those!”

What, pray tell, could possibly unite this span of humanity, hold them hostage of their own free will, during an immune deficiency conference no less, in oppressive heat and humidity, all while at the mouse’s house? Three little words: subcutaneous gamma globulin.

I’ll never forget my first time watching this mystery woman demonstrating the latest and greatest offering from the scientific community that (gasp!) dared to create a product that would make the chronically ill’s lives better. “It’s a miracle!” a middle-aged gentleman whispered just loud enough to break the bond of the audience’s shock and awe.

Then another: “Who do I, well, we talk to if we are interested in starting subcutaneous infusions?”

And yet another: “Where is their booth?”

The mystery woman, within the 15 minutes of her demo, answered as many questions from the curious crowd as she could. Despite deep satisfaction with the way our primary immunodeficiency disease (PI) kids, Caleb and Molly, were receiving their gamma globulin — via their port-a-catheters every four weeks monitored by our most wonderful homecare nurse, Nancy — I had to admit my curiosity was spiked. Caleb could take his gamma like a horse; Molly, on the other hand, became wretchedly ill exactly 48 hours after an infusion (migraine, body aches, chills, aseptic meningitis).

We could count down the minutes until the first “Mommy, I’ve got the headache starting.” Cue: her favorite fluffy (falling apart from every seam due to a thousand washes), comforter, cold compresses and Miss Ellie, her stuffed elephant.

Molly endured these every-four-weeks’ infusion reactions throughout most of her primary years until, drumroll please,
subcutaneous gamma globulin was gloriously approved for children!

“Can you believe it?” our most wonderful immunologist beamed. “Do you know how this is going to change Molly’s and Caleb’s lives?” Dr. Smith gushed.

“Molly is going to start sub-q?” I asked, adjusting myself in the hard plastic seat that protected me from falling through the hospital’s floor in shock.

“And so is Caleb!”

“I’m doing what?” Caleb asked with great disdain (read: with great fear). “One needle once every four weeks versus two needles twice a week? I may not be the ‘phat’ist cat in the alley, but…” Caleb closed his eyes and began counting with his fingers. He squinted hard, looked up to the ceiling and muttered: “You carry the one, then times it by 12 and you get (big pause) 96!” And, when we didn’t argue with his mathematics, Caleb’s ire got lit. “That’s 12 needle pokes in a year with IV versus 96 — 96! — with sub-q! Is anybody listening. To. Me?”

And just when I thought I was going to throw in the towel, Dr. Smith threw us a bone.

“But, Caleb,” she cooed, “when you do sub-q, you can infuse anywhere and anytime you want.”

“I’m listening,” Caleb said, now sitting at attention on the examining table.

“Even while fishing,” Dr. Smith said, flashing her comforting smile. She hooked him with fishing. “And for you, Cheryl, sub-q has proven to completely relieve patients of aseptic meningitis-type reactions.”

“No more headaches?” I asked. No more endless movies about pink princesses and their uptight princes completely inappropriately animated?

“Nope, nope and nope! Molly’s chances are extremely favorable on sub-q!” Dr. Smith said while writing down some thoughts on her computer.

Four years later, my PI kids haven’t had any remarkable infections to report, and Molly hasn’t had a reaction since starting subcutaneous gamma globulin. The only big changes have been not getting to be with our wonderful homecare nurse every four weeks. And for Caleb, he’s lost his big excuse for a legit day off from school, poor kid.

But we don’t “poor kid” Caleb too much, as he has been on a fishing trip or two hooked to his gamma globulin. In fact, we’ve kind of made a game of it. With each infusion, we try to one-up the mystery woman from the IDF conference. For example, last week, we infused Caleb on the sideline of his JV football game, then one-upped by infusing Molly while on a family bike ride (her bike basket made for a perfect place to keep her pump and puppy dog safe, while keeping the sharps container well-hidden). One of our most memorable spots was this past summer behind a Dollar Store connected to a strip mall on our way home from a fishing trip in the middle of Utahiannowhere. I was quite sure we were going to get arrested for “shooting up” our kids. Of course, we’ve infused the kids at the movies, basketball games, hunting and family bowling night, but the thrill of one-upmanship isn’t there. Anywhere gutsier than infusing in public is the goal. We all agreed that the mystery woman had some pretty big mouse ears to pull that off, but Haggard mouse ears are much bigger. And, they have superpowers.

Whether at the mouse’s house or at the movie house, there are two things we can all agree upon: Sub-q may not be for everyone, but it is a wonderful alternative to IV. And, finally, when it comes to where we choose to infuse, there really is no place like home — wearing our supercharged, superpower mouse ears, of course!

CHERYL L. HAGGARD is a stay-at-home mom and has three children with PI, two of whom have CVID.
WHEN YOUR CHILDREN have a cold or an upset stomach, it’s easy to encourage them by saying: “Don’t worry, you’ll feel better in a few days.” You may pop in their favorite movie, give them dinner in bed and pamper them with extra hugs and kisses. If they’re lucky, they may even miss school. With this kind of special treatment, children might enjoy being sick — for a few days. But, what if your children are diagnosed with a condition that isn’t short-term? After a few months of watching “Frozen” every Friday night during medical treatments, or missing school so often it’s hard to keep up with assignments, being sick gets old. Fast. How do you explain to your children that their illness isn’t going away “in a few days” and that a bowl of chicken soup might not be enough to make them feel better?

Share the Truth in Age-Appropriate Ways

Doctors at the University of Michigan define chronic, or long-term, illness as any health problem that lasts longer than three months, affects a child’s normal activities and requires hospital stays, home healthcare and/or extensive medical care by (often numerous) specialists. While the occurrence of acute illness may be frequent or occasional, the child with a chronic illness is always living with his or her condition.1

Since we’ve been dealing with our children’s long-term illness (primary immunodeficiency disease) for eight years, I feel I have a pretty good understanding of the disease and how it will affect them. I can rattle off 18-letter words without batting an eye (can you say agammaglobulinemia three times fast?), and I’m pretty proud of how smart it makes me sound. But, when the kids ask questions about their condition, I try not to talk to them like I would another adult. The key to explaining a chronic condition to affected children lies in giving them information in age-appropriate language.

For toddlers. Young children only know that they don’t feel well; they don’t understand the reasons why. Some preschool-aged children may believe that their chronic illness is a result of something they’ve done, or a punishment for being bad.2 Explain to your children that you don’t know the reason they have the disease, but it is in no way a consequence of their actions.

Be honest about the realities of your children’s treatment. For example, if the treatment for your children’s illness includes needle pokes, it’s almost a parental reflex to say: “Don’t worry. This won’t hurt.” We may wish that were true, but if it were, then my 5-year-old wouldn’t scream and run away from me when it’s time for his subcutaneous immune globulin infusion. As much as I’d like to imagine that his needle poke feels like fluffy kitten fur tickling his leg, it probably feels more like a bee sting — and that hurts. While you can’t avoid all unpleasant treatments, you can help your children through scary or painful procedures by reassuring them...
that the discomfort is only temporary, and giving extra hugs and support.1

For school-aged children. Kids are curious. They love to ask questions. Children with a chronic illness may have plenty of questions about their condition, and it’s important to give clear and honest answers whenever possible. Parents often assume that withholding information is better for their children and that honesty would only lead to unnecessary worry.2 Unfortunately, this approach may actually cause their children to imagine the worst. Instead, discuss the condition with your children truthfully, using words they can understand. Tell them what their illness is all about and what will happen to them in the hospital or during treatments should the need arise.

Sometimes there are questions that have no easy answers, and that’s OK. Children should be encouraged to express their concerns and reassured that their feelings and emotions are totally normal. It’s not unusual for chronically ill children to ask: “Why me?” Don’t feel bad when all you can say is: “I don’t know.” That’s usually the case. My sons often say: “I wish I didn’t have XLA.” I tell them I feel the same way, and that I’m doing everything I can to keep them as healthy as possible. Keeping kids informed about their disease, prognosis and the importance of treatments is crucial to minimizing the severity of symptoms and controlling the advancement of the disease.2

For teenagers. Being diagnosed with a chronic illness can be especially difficult during the teen years. Unlike younger children, adolescents possess a better ability to understand their condition, but they may have more trouble adjusting to the lifestyle changes it will cause. They value their freedom and may resent being home-bound for treatments or frequent sick days.

When explaining a long-term illness to teens, keep in mind that as soon-to-be adults, teens are trying to establish their own identity. Teens are also beginning to develop a real independence from their families.1 The diagnosis of a chronic illness can pose a threat to this newfound independence by creating the need for teens to rely on parents like they did as young children. This can cause teens to rebel, become defiant and refuse necessary treatment.

It may also be difficult for the parents, who have been gradually relinquishing their role as primary caregiver1 and handing the responsibility over to their children, to trust them with their own healthcare in light of the diagnosis.

The role of parents of teens with chronic health conditions is to educate them about their illness, teach them how to self-administer treatment, and help them to gain control of their disease management1 while maintaining appropriate boundaries. Be available to talk and listen often — not just about the disease, but about all other issues facing teens today.1

You Don’t Have to Go It Alone

Raising children with a long-term illness is a challenge, and explaining a disease that you, as parents, don’t have and don’t always understand can be difficult. Fortunately, it’s not something we have to face on our own. Your doctor or other medical professional can offer advice on how to talk to your children about the illness. Most hospitals have a child and adolescent psychiatrist on staff who can help children and their parents understand the impact of chronic disease on families. This specialist can also suggest strategies for coping with the various lifestyle changes created by the illness.2 Support groups, social media groups that focus on your child’s particular disease, social workers, family and friends can all lend support and a

The key to explaining a chronic condition to affected children lies in giving them information in age-appropriate language.

References
Meeting Your IG Match

Even though the U.S. Food and Drug Administration considers all immune globulin (IG) replacement products to be equivalent, just as patients and disease states differ, there are differences in the manufacturing and additives that result in some differences in IG products. With careful consideration of these differences, certain products may be better matched for patients with specific issues.

**WHEN AN INDIVIDUAL** is diagnosed with an illness, many factors go into determining which medications will produce the best outcomes. For patients who are prescribed immune globulin (IG) replacement therapy, there are currently 14 different brands to choose from. Physicians will prescribe one of these on several factors, including method of infusion, potential comorbidities, the patient’s third party reimbursement plan and, in particular, the familiarity and comfort the physician has with a particular product.

**Age and Comorbidity Considerations and Potential Contraindications**

Medical history, patient age and comorbidities must be carefully considered regarding an appropriate product for infusion.

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**Bivigam 10%**
Indication: primary immunodeficiency
(800) 458-4244; www.bivigam.com

**Carimune NF**
Indications: primary immunodeficiency and acute and chronic idiopathic thrombocytopenic purpura
(800) 504-5434; www.cslbehring-us.com

IG replacement products vary when it comes to osmolality, sodium and sugar levels, pH and IgA content due to the differing manufacturing processes. As a result, comorbidities (the presence of one or more additional disorders co-occurring with a primary disease) are a concern. For example, while some IG preparations contain sugar as a stabilizer, others contain glucose, sucrose, D-sorbitol or L-proline. Sorbitol does not increase glucose levels in the blood, but it is metabolized to fructose, and patients who are known to have fructose intolerance should be cautious. Patients with hyperprolinemia should probably not receive products stabilized with L-proline.

Most liquid IG products come pre-formulated at 10% solution. Some products are higher in sodium, and some products contain sucrose. There are also proprietary ingredients added such as

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**Gamunex-C 10%**
Indications: primary immunodeficiency, idiopathic thrombocytopenic purpura and chronic inflammatory demyelinating polyneuropathy
(888) 474-3657; www.gamunex-c.com

**Gammaked 10%**
Indications: primary immunodeficiency, idiopathic thrombocytopenic purpura and chronic inflammatory demyelinating polyneuropathy
(855) 353-7466; www.gammaked.com

**Octagam 5%/Octagam 10%**
Indication: primary immunodeficiency/Indication: idiopathic thrombocytopenic purpura
(800) 826-6905; www.octapharma.com

Meeting Your IG Match

By Trudie Mitschang
“solvent/detergent” for viral inactivation and chemical components used as stabilizers. Previously, it has been reported that elderly patients receiving 10% solution of intravenous IG (IVIG), especially with a more rapid infusion rate, may develop increased viscosity of their blood, with the risk for cerebral stroke. Using a 5% solution, infusing more slowly or infusing additional fluids may help to reduce or prevent this. Many older patients or those with cardiac conditions may have sodium intake restrictions so that a low sodium product may be better to use.

There is concern regarding patients with diabetes with products containing sucrose, and there have been reports of acute renal failure in patients who have or who are at risk for kidney disease with products containing sucrose. Therefore, for these patients, non-sucrose containing products may be more suitable.

Some patients at any age develop idiosyncratic reactions (unexpected reactions without obvious explanations) with IVIG or subcutaneous IG (SCIG) replacement products. It is not uncommon for these to be rashes and/or hives. While responsibility for most of these mechanism(s) cannot be ascertained, many patients respond well to an infusion of an alternative product. Some patients may require trying several brands until one is found that can be infused without significant reactions.

The pH in the IG replacement product may also require consideration, since lower pH may be more irritating to blood vessels, especially in small infants.

One important area of confusion has been the relative contraindication of infusing IG replacement products into patients with IgA deficiency. This stems from very old literature about reactions occurring in patients receiving blood products. It is thought that in rare circumstances that a person who lacks IgA may produce IgE antibodies directed against IgA, and upon exposure to infusion of a plasma or blood product containing IgA, anaphylaxis may occur. This has been found to occur in only a very small number of patients with immunodeficiency. Most laboratory tests can only detect IgA levels at 7 mg/dL or more. Therefore, some IgA may still be present, but not detectable, in many patients. Thus, lack of detection of IgA in a patient is helpful for making a diagnosis of immunodeficiency, but should not be used as a relative contraindication to infusion of IG replacement. If concern is present, an IG replacement product with the lowest detectable levels of IgA may be of benefit. Yet, other components in such a product could result in unintended problems, so all the issues need to be considered.

**Tolerability and Rate of Infusion**

As mentioned, rate of infusion is a factor when it comes to tolerability, and trial and error may be needed to determine the best infusion rate for each patient. Keep in mind that each product has a recommended rate of infusion that should be followed. That rate should be incrementally increased to determine a patient’s maximum tolerated rate. Adverse reactions can occur at any time, so stopping the infusion should always be the first consideration. When the reaction subsides, restarting at a slower rate, not exceeding the previous rate where a reaction occurred, may be tolerated.

Finally, methods of infusion are a factor. There are currently nine U.S. Food and Drug Administration-approved products for IVIG administration and five for SCIG administration. Physicians typically select the brand for patients. If adverse reactions occur with IVIG, infusion nurses can slow the rate of infusion, or physicians may switch brands. If site reactions occur with SCIG, different sites and/or concentrations can be tried.

*Editor’s note: We would like to thank Dr. Terry O. Harville, MD, PhD, for his input on this article.*
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hands-on

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