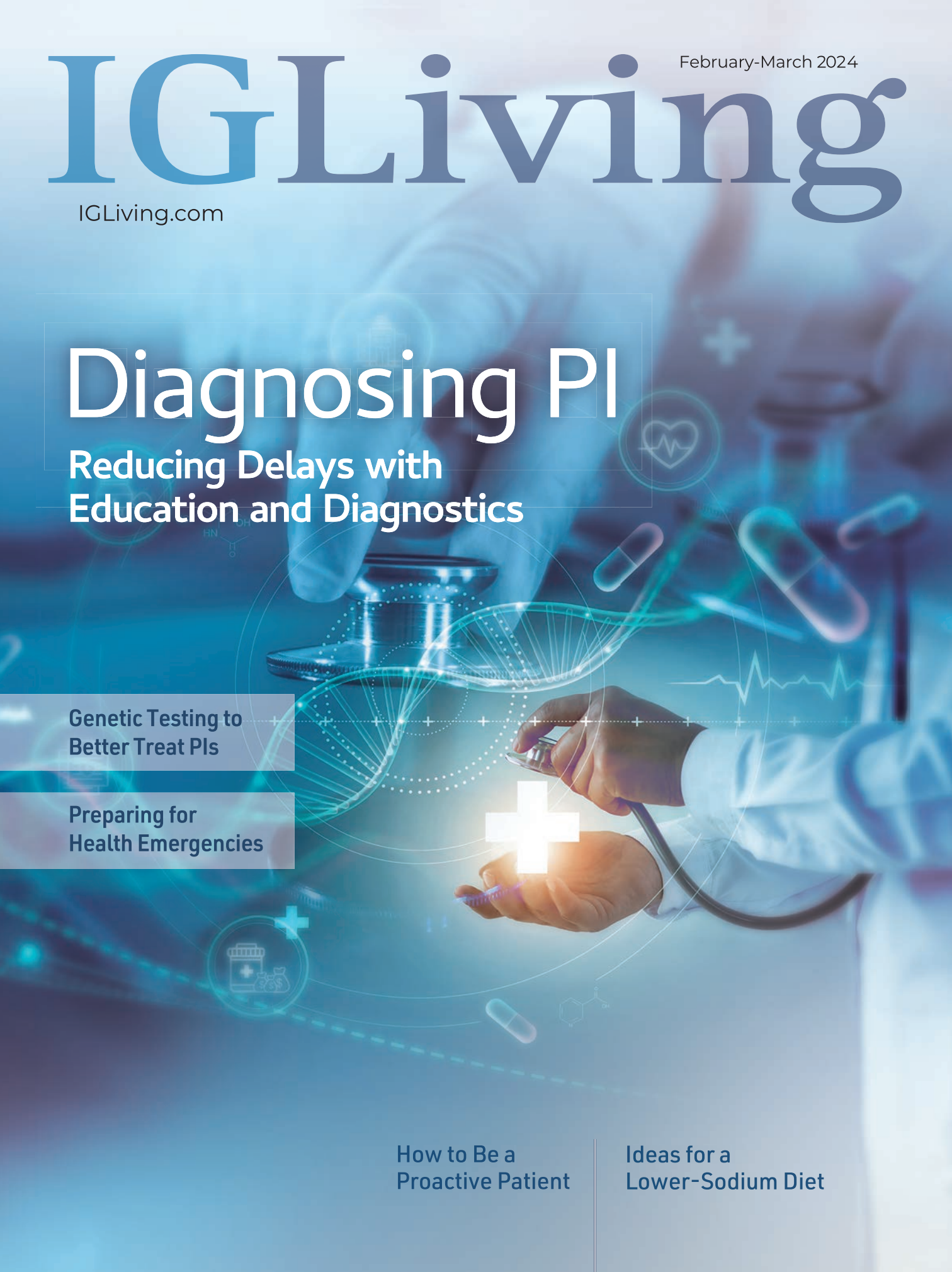
February-March 2024

# IGLiving

IGLiving.com



# Diagnosing PI

## Reducing Delays with Education and Diagnostics

Genetic Testing to Better Treat PIs

Preparing for Health Emergencies

How to Be a Proactive Patient

Ideas for a Lower-Sodium Diet

FOR PATIENTS WITH PRIMARY HUMORAL IMMUNODEFICIENCY (PI)

# IT'S WHAT'S INSIDE THAT COUNTS

ASCENIV™

IMMUNE GLOBULIN INTRAVENOUS (HUMAN) – slra 10% LIQUID

**DESIGNED TO DELIVER**

**Talk to your doctor about whether ASCENIV™ is right for you**

**asceniv.com**

Important Safety Information for ASCENIV™

**WARNING: RISK OF BLOOD CLOTS (THROMBOSIS), POOR KIDNEY FUNCTION, AND INABILITY TO FILTER WASTE FROM KIDNEYS. BLOOD CLOTS MAY OCCUR WITH INTRAVENOUS IMMUNE GLOBULIN PRODUCTS, INCLUDING ASCENIV.**

Before taking ASCENIV, talk to your doctor if you:

- Are of advanced age
- Are unusually sedentary (long periods of sitting down or inactive)
- Are taking estrogen-containing medicines (birth control pills, hormone replacement therapy)
- Have a permanent intravenous (IV) catheter
- Have hyperviscosity of the blood (diseases such as multiple myeloma or other causes of elevated proteins in the blood)
- Have cardiovascular (heart) problems or previous history of stroke

Thrombosis may occur even if you do not have any risk factors.

Serious kidney problems and death can also happen in certain patients who receive such products.

If you are at high risk of thrombosis or kidney problems, your doctor should adjust the dose of ASCENIV and will monitor you for signs and symptoms of thrombosis and viscosity, as well as kidney function.

**What is ASCENIV (immune globulin intravenous, human)?**
ASCENIV (immune globulin intravenous, human) is a prescription medicine to help adults and adolescents (12 to 17 years old) with primary immunodeficiency fight and prevent infections.

ASCENIV is for intravenous administration only. ASCENIV is made from healthy human blood/plasma.

**Who should not use ASCENIV?**
ASCENIV should not be used if you had a severe allergic reaction to human immune globulin or if you have been told by a doctor that you are immunoglobulin A (IgA)-deficient and have developed antibodies to IgA and hypersensitivity after exposure to a previous plasma product.

**What are possible warnings and precautions with taking ASCENIV?**
**Hypersensitivity.** Severe allergic reactions may occur with immune globulin products, including ASCENIV. If you have a severe allergic reaction, stop the infusion immediately and get medical attention. ASCENIV contains IgA. If you have known antibodies to IgA, you may have a greater risk of developing potentially severe allergic reactions.

If you take ASCENIV or a similar immune globulin product, you could experience a serious and life-threatening blood clot (thromboembolism). This may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, 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. If you are at risk, your doctor may decide to adjust the dose of ASCENIV. Your doctor will monitor you for any signs or symptoms of blood clots or poor blood flow in your arteries.

**Always tell your doctor immediately if your medical history is similar to what is described here, and especially if you experience any of these symptoms while taking ASCENIV.**

**Kidney problems or failure.** Kidney problems, kidney failure, and death may occur with use of human immune globulin products, especially those containing sucrose (sugar). ASCENIV does not contain sucrose.

If you have kidney disease or diseases with kidney involvement, your doctor should perform a blood test to assess your hydration level and kidney function before beginning immune globulin treatment and at appropriate intervals thereafter. If your doctor determines that kidney function is worsening, they may discontinue treatment. If your doctor determines you to be at risk, they may start your dose of ASCENIV at a safe level.

**People taking human immune globulin products, including ASCENIV, may experience hyperproteinemia (high levels of protein in the blood), hyponatremia (low levels of sodium in the blood), and hyperviscosity (poor blood flow). Your doctor may perform certain blood tests and monitor you to minimize any of the above risks.**

**Aseptic meningitis syndrome (AMS).** Aseptic meningitis is a non-infectious inflammation of the membranes that cover the brain. It causes a severe headache, which may occur with human immune globulin treatment, including ASCENIV. AMS usually happens within a few hours to 2 days after treatment. AMS is more commonly associated with higher doses of treatment and/or after rapid infusion. Your doctor may perform a neurological exam, including spinal tap (sampling fluid which surrounds the spinal cord) to evaluate your condition and to rule out other causes of meningitis.

**Hemolysis.** Hemolysis refers to the destruction of red blood cells. Immune globulin products, including ASCENIV, may contain certain antibodies that can result in the rupturing of red blood cells. Your doctor should monitor you for signs and symptoms of hemolysis, which may include additional confirmation tests.

Taking intravenous human immune globulin products may cause a build up of fluid in the lungs (pulmonary edema) that is unrelated to heart problems. Your doctor should monitor you for lung-related side effects and may conduct appropriate tests that can detect the presence of certain white blood cells (anti-neutrophils) in the drug or your blood. If needed, your doctor may decide to use oxygen or other respiratory methods to help your breathing.

**Transmissible infectious agents.** Because ASCENIV is made from human blood, it may carry a risk of transmitting infectious agents such as viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. Your doctor will report to the manufacturer any cases of suspected infections spread by the product.

**Interference with lab tests.** Because ASCENIV contains a variety of antibodies that are infused into your body, blood tests to determine antibody levels may provide misleading interpretations. Be sure to always tell your doctor, nurse, or lab technician of any medicines you are taking and that you are using ASCENIV.

**Interactions with medicines.** ASCENIV can make vaccines (like measles, mumps, rubella, and chicken pox vaccines) less effective in your body. Before you get any vaccines, tell your healthcare provider that you take ASCENIV.

**What are other possible side effects of ASCENIV?**
In clinical studies of ASCENIV, some patients experienced the following:

- Headache
- Sinus inflammation (sinusitis)
- Diarrhea
- Intestinal lining inflammation caused by virus (gastroenteritis)
- Common cold (nasopharyngitis)
- Upper respiratory tract infection
- Bronchitis
- Nausea

**These are not all the possible side effects of ASCENIV. Talk to your healthcare provider about any side effect that bothers you or that does not go away.**

**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.**

**For additional safety information about ASCENIV, please see full Prescribing Information at www.asceniv.com**

ADMA BIOLOGICS


10630-22-IGG-03292023_R00
Visit admabiologics.com

# Features



# Up Front

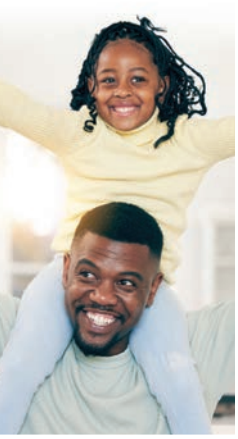


# Departments



# Columns






# Sources




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

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

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

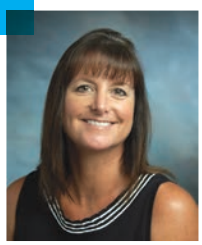
Subscriptions to IG Living are free, and readers may subscribe at IGLiving.com or by calling (800) 843-7477 x1461.





IG Living accepts article submissions. Submit manuscripts in MS Word format, or submit a query letter that covers the idea in a brief paragraph and how it will be presented, to editor@igliving.com. IG Living retains the right to edit submissions. The contents of each submission and their accuracy are the responsibility of the author(s) and must be original work that has not been, nor will be, published elsewhere, without the written permission of IG Living. A copyright agreement attesting to this and transferring copyright to FFF Enterprises will be required. Acceptance of advertising for products and services in IG Living in no way constitutes endorsement by FFF Enterprises.

# Rare Diseases: A Difficult Journey



**CHRONIC, RARE** diseases, which affect about 300 million patients worldwide, pose an extremely difficult journey. Many rare diseases are present from birth, with symptoms beginning in childhood and their impacts lasting a lifetime. There are challenges with diagnosis and treatment, but there are also challenges with employment, finances and, of course, family and social life. Fortunately, more is being learned about diagnosing and treating rare diseases and how patients can manage their lives.

While every rare disease journey is unique, perhaps the most common for primary immune deficiency (PI) patients is the excruciatingly long time to diagnosis. According to the Immune Deficiency Foundation, patients average nine to 15 years from symptom onset to diagnosis, with some experts estimating more than 70 percent of individuals with a PI remain undiagnosed. In our article, "Strategies to Reduce Diagnostic Delays in Primary Immune Deficiency" (p.22), we take a look at the factors that contribute to delayed diagnosis, including lack of awareness about PI in the medical community, lack of standardized testing and inadequate referral pathways to immunology specialists. With the high diagnostic cost, averaging almost $86,000 per patient, we provide some approaches to speed up the diagnosis of PI that, according to the National Institutes of Health, could save as much as $6,500 per patient.

Today, the preferred term for the approximately 500 types of PI is "inborn errors of immunity" (IEI) since they are caused by genetic variants. Each year, about 40 new genetic causes of PI are discovered that can lead to new treatments. In our article "Genetic Testing for Primary Immune Deficiencies" (p.26), we discuss what has been learned about IEIs, their genetic causes and how an understanding of them can impact treatment choices and family planning. Importantly, we also delve into the types of genetic tests available and their possible limitations so patients can make informed choices about which is most appropriate.

Indeed, discussing diagnostic options and treatment choices should be the foremost priority for patients. It's vital for patients to take an active role in their health. As we explain in our article "No More Nodding and Smiling: How to Become a Proactive Patient" (p.30), being proactive means being informed, engaged and assertive. To do so, we provide some practical tips such as expressing concerns, asking questions and sharing relevant information about symptoms or treatment with providers; seeking second opinions; taking advantage of technological tools; and staying motivated.

As always, we hope you enjoy these articles, as well as the many more educational and insightful topics presented in this issue of *IG Living*.

Ronale Tucker Rhodes, MS

IGLiving

Our mission is to support the IG community through education, communication and advocacy

A community service from FFF Enterprises, Inc.

Want to Learn About Topics Important to Chronic Illness Patients Living with Autoimmune and Immunodeficiency Disorders?

# LISTEN TO THE IG LIVING ADVOCATE AUDIO PODCAST!

**Sample Episode Topics:**

- The Increased Demand for Immune Globulin Products and Its Effects on Patient Access
- Planning for Retirement with Chronic Illness
- Changes in Medicare That Affect Patients Treated with Immune Globulin
- IG Infusions in the Home Setting
- The Road to Diagnosis

**The ONLY Podcast for Autoimmune and Immunodeficient Patients:**
**www.igliving.com/life-with-ig/ig-living-advocate-podcast.html**

Subscribe to IG Living Magazine to Receive Notifications About Upcoming Podcast Episodes

* Produced by IG Living magazine, written for patients treated with immune globulin therapy and their caregivers.

Abbie Cornett, MBA
IG Living Patient Advocate

# The Impact of Health Insurance Financial Rewards and Penalties

By Abbie Cornett, MBA

**HEALTH INSURANCE** had its origins in the 1930s, a period marked by the Great Depression.[1] It was set up as a vital safety net for individuals and families, offering protection against unforeseen medical expenses, with premiums established using conventional methods. However, in recent years, insurance companies have transformed how they structure and deliver their programs. Today, there's a notable shift toward tying lower or higher premiums to health behavior.[2]

Rewarding policyholders with lower premiums is a proactive approach that seeks to motivate policyholders to adopt and maintain healthier lifestyles by providing positive reinforcement and tangible incentives. Policyholders are encouraged to engage in activities such as regular exercise, healthy eating habits, preventive screenings and consistent medication adherence for those with chronic conditions. Rewards for engaging in these activities include reduced premiums, cash incentives, access to wellness programs and even discounts on health-related products and services.

While incentivizing people to adopt healthier lifestyles appears to be a win-win situation, it's not quite that straightforward. Financial incentives may inadvertently encroach upon individuals' autonomy and their ability to make personal decisions about their health.[3] The approach raises questions about whether financial rewards should be the driving force behind healthier choices or if people should be motivated by a genuine desire for well-being. In addition, there is a potential negative impact of using an incentive-based approach: While well-intentioned, it can have unintended consequences that disproportionately affect individuals with chronic illnesses. For instance, the challenges of managing their conditions are already substantial, and this may add an additional layer of complexity to their healthcare journey such as inadvertently creating disparities, financial stress and barriers to accessing essential care. The pressure to meet specific health goals to earn rewards can lead to stress, anxiety and feelings of exclusion that can further burden their physical and mental well-being.

On the flip side, imposing higher premiums based on lifestyle choices and health status presents a more punitive approach that can have significant implications for individuals dealing with chronic illnesses such as diabetes, heart disease or autoimmune disorders. The prospect of higher premiums due to factors beyond their control can generate substantial financial stress. Moreover, a punitive approach raises ethical concerns about fairness and equity. Penalizing individuals for their health choices assumes everyone has equal access to resources and opportunities to make healthier decisions. For individuals facing systemic barriers, socioeconomic disparities or limited access to healthcare resources, a punitive approach can exacerbate health inequalities.[4] It also places a considerable burden on those with chronic illnesses who may already be grappling with complex treatment regimens and medical expenses.

While the goal of attaching financial incentives for healthy lifestyle choices or imposing higher premiums based on health status is well-intentioned, careful consideration must be given to the potential disproportionate impact on the chronically ill population.

## References


1. Lichtenstein, E. The History of Health Insurance: Past, Present, and Future. AgentSync, Oct. 26, 2022. Accessed at agentsync.io/blog/loa/the-history-of-health-insurance-past-present-and-future.
2. Vlaev, I, King, D, Darzi, A, and Dolan, P. Changing Health Behaviors Using Financial Incentives: A Review from Behavioral Economics. *BMC Public Health*, 2019;19:1059. Accessed at bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-019-7407-8#citeas.
3. Halpern, SD, Madison, KM, and Volpp, KG. Patients as Mercenaries? The Ethics of Using Financial Incentives in the War on Unhealthy Behaviors. *Circulation: Cardiovascular, Quality and Outcomes*, 2009;Sept;2(5):514-516. Accessed at www.ncbi.nlm.nih.gov/pmc/articles/PMC2798138.
4. Artiga, S, Ubri, P, and Zur, J. The Effects of Premiums and Cost Sharing on Low-Income Populations: Updated Review of Research Findings. Kaiser Family Foundation, June 1, 2017. Accessed at www.kff.org/medicaid/issue-brief/the-effects-of-premiums-and-cost-sharing-on-low-income-populations-updated-review-of-research-findings/view/print.


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

## What Does It Mean to Be Immunocompromised?

*It means that one must be aware, trying to avoid people who are sick. But it also means that you can live a very full life! I prefer to focus on the positives in my life. I refuse to be defined by my cancer, immune deficiency or any of the chronic conditions I deal with each day. I am not a "woe is me" type of person. Pity parties don't look good on anyone. Everyone has challenges in their lives, but ultimately life is what we make it!*

*A lifetime of self-infused immunoglobulins, never-ending medical bills, continuous antibiotics, higher potential for cancer, fatigue (especially when there is a drug shortage of Ritalin), fear of infections, living with people who refuse to wear masks during a pandemic, unable to breathe and I could go on and on. My son has common variable immune deficiency and he continues to experience all of these and more (i.e., Rituxan every three months via mediport and, most recently, type 1 insulin dependent diabetes mellitus).*

## Do You Know How to Manage Medication Side Effects?

*I learned that if my body suffers side effects from a treatment or medication, it is time for a different therapy. Myasthenia gravis is hard enough. Adding other issues to that is not an option for me.*

*I have negative side effects of my intravenous immune globulin infusions. We have had to break it into three days first because it's such a big dose but also because I need so much Benadryl and zofran. It's a really rough time every four weeks. I wish there was a better way than having to have so many steroids and Benadryl pumped into my system.*

*I do subcutaneous immune globulin (SCIG) two times weekly, due to my need for a high dosage. The steroids caused too much anxiety and depression. Also, they lower your immune system, of which none of us need. So when SCIG came out well over 10 years ago, I got on board and have had minimal side effects. By doing it this way, I'm never so "depleted" of my immune response.*

## How Do You Manage Parenting with Your Illness? ?

*I was diagnosed at age 4 with "something wrong with her immune system" and treated with antibiotics only. My mom was my support system. By age 56, I was finally correctly diagnosed with IgG3 deficiency. Within those years, I was a parent and a grandparent. I found raising my daughter fairly easy (with my mom) as my immune system did not have severe issues until my 40s. But, babysitting daily for my grandchildren until they reached school age was difficult as I had no other support system. My mom had aged and passed by then. Many nights, my supper was cereal and bananas as I was too tired to cook.*

**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 you can weigh in on. These are some snapshots of what's being discussed.

## How Do You Balance Treatment for an Immune Deficiency with Treatment for Cancer?

What is the balance between treating lupus by calming down the immune system with methotrexate and stimulating the immune system with intravenous immune globulin (IVIG) treatments, especially for patients with combined immunodeficiency disorder and cancer (thymoma), leading to Good syndrome with thymoma, and lupus?

**Abbie:** I spoke with Terry O. Harville, MD, PhD, medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, and he said the concept of low immunity for immunodeficiency and high immunity for autoimmunity is not totally correct. We now know of approximately 500 genes that can cause immunodeficiency and autoimmunity or that may cause both in the same person. Therefore, we now consider this as dysfunctional or disordered immunity. Indeed, there are so-called gain-of-function disorders of immunity (what may be called high immunity) that result in immunodeficiency, which can be improved by prescribing medications that are typically considered immunosuppressive. Therefore, each patient and condition have to be considered and evaluated individually to provide the most appropriate therapy.

According to Dr. Harville, the use of immunosuppressive medications in someone who is immunodeficient can result in greater susceptibility to infections. Methotrexate at the typical dose of 10 mg to 15 mg a week is not truly immunosuppressive but rather anti-inflammatory.

Adding thymoma to the mixture does complicate the situation, he explains. In general, excess thymic tissue is surgically removed. Since B lymphocyte malignancy and antibody deficiency tend to be present, treatment of the B lymphocyte malignancy tends to be useful and not problematic since IVIG is typically used.

If a patient also has lupus, the therapies for that B lymphocyte malignancy (i.e., rituximab) is also very helpful. The strategy should be to maximize the use of a medication such as rituximab, along with a higher than the lowest typical dose of IVIG. This focuses the treatment against the removal of B lymphocytes, which can then be effectively treated with appropriate doses of IVIG.

## What Types of Medicare Policies Cover Hizentra in the Home for CIDP?

I was diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP) in 2015, and I am retiring at the end of this month (I am a primary care physician) and transitioning to Medicare. I am in the 10 percent of patients who still require "booster" infusions of intravenous immune globulin (IVIG) approximately every 10 weeks, even though I transitioned to self-administered weekly subcutaneous IG (Hizentra) in 2019.

I have worked with a consultant who states the IVIG infusions will be much better covered at an infusion center billed through Parts B and C rather than trying to have it covered as a home infusion through Part D. Additionally, Hizentra is also covered by Parts B and C, but are the associated supplies for this diagnosis covered as well?

**Abbie:** I spoke with Leslie Vaughan, RPh, CSP, IgCP, chief operations officer at Nufactor, a specialty infusion company, who said periodic IVIG would not be covered by Medicare Part B at home but would most likely be covered in an outpatient infusion center. Part B will pay 80 percent, and a supplemental policy will pick up the remaining 20 percent. Part D (with authorization) would cover Hizentra at home, but a Part D patient share of the cost would apply.

Hizentra is covered by Part B for CIDP at home. There is payment for supplies and the pump, as well as for nursing when supplied by a home infusion therapy provider when the nurse is in the home. Unfortunately, few specialists are accepting new Part B patients due to poor reimbursement, especially since sequestration has been reinstated.

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

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

# Breaking the Cycle of Chronic Pain

By Mairead McConnell, PhD

**MORE THAN** 20 percent of adults in the U.S. experience some form of chronic pain. If you live with chronic pain, you know the toll it can take on your daily activities, relationships and mental health. You've likely tried many interventions to get rid of pain, with little relief. Fortunately, there is a treatment for chronic pain that is noninvasive, based in neuroscience and effectively reduces pain. This method is called pain reprocessing therapy (PRT).

*The myth of chronic pain.* A key tenant of PRT is that most chronic pain is caused by neural pathways in the brain, *not* structural damage in the body. Read that sentence again.

As a chronic pain sufferer myself, I did not believe this concept at first, and you may be skeptical, too. But the evidence is clear; research shows that even for patients with medically diagnosed conditions and spinal abnormalities, the majority of their pain is not explained by those conditions. Rather, chronic pain is caused by the brain misinterpreting safe sensations in the body as dangerous. While this may be difficult to believe, it is excellent news. If the brain is making a mistake, it means that teaching your brain to accurately interpret these signals can minimize your pain.

*Neural pathway pain.* "So you're saying its all in my head?" you may be asking. No, I'm saying it's all in your *brain*. Your pain is 100 percent real. All pain is real; and all pain is caused by the brain. The brain's ability to process pain is necessary for survival. However, even the brain makes mistakes. When we experience acute pain (e.g., an injury such as a broken bone), this signal is accurate. Walking on a broken foot can create more damage. But long after injuries and bones heal, the brain may still experience pain; this danger signal is no longer accurate. In chronic pain, the brain receives a danger signal when, in fact, there is no immediate danger to your body.

*Breaking the cycle.* Pain is designed to tell us when something is wrong or dangerous. Therefore, pain puts the body on high alert, activating a fear response. This fear then sends a message back to the brain that the pain is in fact dangerous, and the pain-fear-pain cycle continues.

**The key to healing chronic pain is learning to observe sensations in your body without fear.**

The key to healing chronic pain is learning to observe sensations in your body without fear. This may sound simple, but learning to feel safe in your body, while you experience sensations that have previously felt unsafe, is a process that requires time, patience, practice and support. Regardless of how long you have been in pain or how intense your pain is, it is absolutely possible to heal.

*Where to begin.* It is impossible to explain all the features of PRT in a brief article, but if you are interested in trying it, there are a few simple ways to begin. Next time you are in pain (which may be right now), try one of these techniques:

1) Give yourself a gentle, kind reminder that there is no present danger or threat to your body. This may sound like "There is nothing wrong with [insert body part]" or "This is my brain misinterpreting sensations from my body; I am safe."

2) Turn to "my favorite things." Watch your favorite TV show, listen to your favorite song, recall a pleasant memory or call a good friend. Just like lyrics in the "Sound of Music" say, our favorite things can help us feel safe even in a difficult situation.

Note: These techniques are not designed to take your pain away. They are intended to help your brain realize you are safe. This sense of safety, practiced and revisited over time, is the key to turning down the fear and consequently reducing pain.

*Learn more.* If you think you might benefit from PRT, there's much more to learn, and many providers can help you on your journey. Check out Alan Gordon's book *The Way Out: A Revolutionary, Scientifically Proven Approach to Healing Chronic Pain*, or visit painreprocessingtherapy.com.

**MAIREAD MCCONNELL,** PhD, is a clinical psychologist and assistant professor at Banner University Medical Center in Tucson, Ariz. She specializes in health psychology and is passionate about helping patients live well while navigating the challenges of chronic illness.

# Reconnect with friends over dinner

People with primary immunodeficiency (PI) who infuse CUVITRU weekly or every other week may be able to experience more of these moments.

## What is CUVITRU®?

CUVITRU [Immune Globulin Subcutaneous (Human)] 20% Solution is a ready-to-use liquid medicine that is given under the skin (subcutaneously) to treat primary immunodeficiency (PI) in people 2 years and older.

## IMPORTANT SAFETY INFORMATION

**What is the most important information I need to know about CUVITRU?**

CUVITRU can cause the following serious reactions:

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

**Who should not use CUVITRU?**

Do not use CUVITRU if you:

- Have had a severe allergic reaction to immune globulin or other blood products.
- Have a condition called selective (or severe) immunoglobulin A (IgA) deficiency.

**What should I avoid while taking CUVITRU?**

- CUVITRU can make vaccines (like measles/mumps/rubella or chickenpox vaccines) not work as well for you. Before you get any vaccines, tell your healthcare provider (HCP) that you take CUVITRU.
- Tell your HCP if you are pregnant, or plan to become pregnant, or if you are nursing.

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

**CUVITRU can cause serious side effects. If any of the following problems occur after starting CUVITRU, stop the infusion immediately and contact your HCP or call emergency services:**

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of irritation and swelling of the lining around your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms. These could be signs of a blood clot.

Cuvitru
[Immune Globulin Subcutaneous (Human)] 20%

## Proven protection from infection

In the North American (NA) study, there were 0.012 acute serious bacterial infections (ASBIs) per patient-year.*† This exceeds the FDA standard for effectiveness, which is one serious ASBI per year.

## Nearly all infusions (99.8%) were completed without reduction, interruption or discontinuation due to tolerability

No patients discontinued due to local adverse reactions (ARs) and 0 serious ARs related to CUVITRU were reported.

The most common adverse reactions observed in clinical trials in ≥5% of patients were: local adverse reactions including mild or moderate pain, erythema, and pruritus, and systemic adverse reactions including headache, nausea, fatigue, diarrhea, and vomiting.

## Flexible administration that can be tailored to fit your lifestyle‡§

CUVITRU can be infused at the fastest rates and highest volumes with the fewest infusion sites of any subQ IG.§

In the NA clinical study, CUVITRU was studied in 77 people with PI ≥2 years of age. The main goal of the study was to measure how many acute serious bacterial infections (ASBIs) were experienced over the course of 1 year. ASBIs are short-term but serious infections that require immediate medical care. ASBIs were evaluated in 74 people taking CUVITRU for an average of 380.5 days (range, 30-629 days).

*One ASBI that occurred during the study was a case of pneumonia in a 78-year-old person.

†A patient-year is a patient experience in a clinical trial over the course of 1 year. One patient-year is equal to, for example, the experience of 2 patients for 6 months, or 12 patients for 1 month each.

‡In the NA study, the average infusion time was 0.95 hours (range 0.2-6.4 hours) and most (84.9%) used 1 to 2 needlesticks.

§You'll infuse your first 2 infusions at 10 to 20 mL/hr/site. After that, you'll be able to increase your rate up to 60 mL/hr/site as tolerated. Infuse at up to 4 sites simultaneously.

SubQ IG=subcutaneous immune globulin.

## IMPORTANT SAFETY INFORMATION (continued)

- Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver or blood problem.
- Chest pain or trouble breathing, or blue lips or extremities. These could be signs of a serious heart or lung problem.
- Fever over 100°F. This could be sign of an infection.

The following one or more possible side effects may occur at the site of infusion. These generally go away within a few hours, and are less likely after the first few infusions.

- Mild or moderate pain
- Redness
- Itching

The most common side effects that may occur are:

- Headache
- Nausea
- Fatigue
- Diarrhea
- Vomiting

**These are not all the possible side effects. Talk to your HCP about any side effect that bothers you or that does not go away.**

***Please see Important Facts about CUVITRU on the following 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.**

## Want to learn more about the effectiveness and safety of CUVITRU?

Scan the code to see the data and browse around the website.



Takeda

## IMPORTANT FACTS about CUVITRU (CUE-vih-troo) [Immune Globulin Subcutaneous (Human)] 20% Solution

### What is the most important information I need to know about CUVITRU?

CUVITRU can cause the following serious reactions:

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

### What is CUVITRU?

CUVITRU is a ready-to-use liquid medicine that contains immunoglobulin G (IgG) antibodies, which protect the body against infection. CUVITRU is used to treat patients with primary immunodeficiency diseases (PI).

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

### Who should not use CUVITRU?

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

### How should I use CUVITRU?

CUVITRU is given under the skin (subcutaneously). Most of the time, infusions under the skin are given at home by self-infusion or by caregivers. Instructions for giving CUVITRU under the skin (subcutaneously) are provided in the FDA-approved patient labeling (Information for Patients and Instructions for Use). Only use CUVITRU by yourself after you have been instructed by your HCP.

### What should I avoid while taking CUVITRU?

CUVITRU can make vaccines (like measles/mumps/rubella or chickenpox vaccines) not work as well for you. Before you get any vaccines, tell your HCP that you take CUVITRU.

Tell your HCP if you are pregnant, or plan to become pregnant, or if you are nursing.

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

The following are one or more possible reactions that may occur at the site of infusion. These generally go away within a few hours, and are less likely after the first few infusions.

- Mild or moderate pain
- Redness
- Itching

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

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

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

These are not all the possible side effects. You can ask your HCP for a physician's information leaflet. Tell your HCP about any side effect that bothers you or that does not go away.

Whenever giving yourself treatments at home, you should have another responsible person present to help treat side effects or get help if you have a serious adverse reaction occur. Ask your HCP whether you should have rescue medications, such as antihistamines or epinephrine.

### How do I store CUVITRU?

Store CUVITRU refrigerated or at room temperature.

- You can store CUVITRU in the refrigerator (36°F to 46°F [2°C to 8°C]) for up to 36 months or
- You can store CUVITRU at room temperature (up to 77°F [25°C]) for up to 24 months.
- Do not return CUVITRU to the refrigerator if you take it out to room temperature.
- Do not freeze.
- Do not shake.
- Check the expiration date on the carton and vial label. Do not use CUVITRU after the expiration date.
- Protect from light. You can use the original CUVITRU containers to protect it from light.

### How do I get more information about CUVITRU?

The risk information provided here is not comprehensive. To learn more, talk about CUVITRU with your HCP or pharmacist. The FDA-approved Full Prescribing Information, including Information for Patients, can be found at www.CUVITRU.com or by calling 1-877-TAKEDA7 (1-877-825-3327).



Takeda Pharmaceuticals U.S.A., Inc.
Lexington, MA 02421 USA
U.S. License No. 2020

US-CUV-0408v1.0 07/21

# Hyper IgE Syndrome (HIES): Final Summary

By Terry O. Harville, MD, PhD

**HYPER IGE** syndrome (HIES) is clinically characterized by the recurrence of non-inflamed boils and furuncles, so-called "cold abscesses," primarily due to staphylococcal and Candidal infections that can be severe, resulting in skin, lung and organ damage. HIES was initially called Job's syndrome due to its similarity to the description in the Bible of the boils and furuncles on the tormented Job. The major early laboratory finding of HIES was elevated serum IgE levels (commonly in the 5,000 to 10,000 IU/mL range). It was also noted that serum IgG levels and IgA levels may be low, suggesting the B lymphocytes had fully "class-switched" to produce IgE, therefore not allowing production of IgG and IgA. Thus, early treatment consisted of replacement immune globulin (IG) therapy; however since IG therapy still did not fully prevent infections, antibiotics were required. It was also believed early on that HIES could be caused by neutrophils failing to migrate appropriately to sites of infections.

After discovery of Th17 T lymphocytes and the role of interleukin 6 (IL-6) in activating these lymphocytes, it was found that the pathway of IL-6 activation was not working for those with HIES. This, then, led to the discovery of STAT3 mutations as the major cause of autosomal dominant HIES. The major function of Th17 T lymphocytes is to fight extracellular bacterial and fungal infections, so their dysfunction made logical sense for the infectious observations found in patients with HIES. Additionally, Th17 T lymphocytes have a role in attracting neutrophils to sites of infection, which may explain the early observation of dysfunctional attraction of neutrophils in patients with HIES. Ultimately, the autosomal dominant mutations of STAT3 with variable penetrance provided more clarity as to what was occurring in patients with HIES.

There are also rarer forms of HIES, some of which may be inherited in autosomal recessive patterns. Most of these still involve the signal-transduction associated with IL-6. Thus, mutations in the IL-6 receptor, the associated gp130 signal-transduction protein, JAK1 and Tyk2 can also produce the features of HIES since Th17 T lymphocytes will fail to appropriately activate via IL-6 and STAT3. DOCK8 and PGM3 mutations can also cause HIES, but through mechanisms other than direct IL-6 signaling.

At this point, there are no corrective gene therapies for HIES. Treatment consists of IG replacement and antibiotics. Treatment may also consist of anti-staphylococcal and anti-Candidal antibiotics to prevent infections, rather than waiting on infections to occur. This is determined by the extent of disease penetrance and on patient observation. Bone marrow transplantation may also be helpful, especially performed early before lung injury. A separate long-term consequence of HIES is osteopenia, which can result in bone fractures. Therefore, this must be carefully followed and treated early to prevent problems.

While technically not HIES (since IgE is not increased), STAT3 gain of function (GOF) mutations can produce some clinical features of HIES, and multiple autoimmune features may also be present. JAK and Tyk2 inhibitors may be useful treatments for STAT3 GOF, since they will reduce STAT3 activation, hopefully back to its normal range. A concern about trying to correct STAT3 mutations in HIES using gene therapy is the possibility of inadvertently causing STAT3 GOF disease, which would not improve the situation. A significant amount of further research is needed before gene therapy can be used to treat HIES.

In summary, patients with recurrent skin and/or tissue infections require investigation for inborn errors of immunity, including HIES. While measuring immunoglobulins is helpful to assess the underlying cause of disease, in our modern age, genetic evaluation, including gene sequencing (targeted, whole exome or, better, whole genome), should be performed for better assessment. Understanding which genes are involved in HIES and their specific mutations can allow for better personalized medicine treatment with expected better outcomes.

In the next issue, we will begin a discussion of a new topic.

**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.

# Understanding Vasculitis

By Michelle Greer, RN, IgCN

**VASCULITIS** (also called angiitis) refers to a group of nearly 20 rare autoimmune diseases that cause inflammation (swelling) of the blood vessels. This inflammation can affect small, medium or large blood vessels anywhere in the body, causing them to narrow, which can result in a blockage and damage to vital organs and tissues.

Vasculitis can be primary or secondary: Primary vasculitis does not have a known cause, while secondary vasculitis does have a known cause. Triggers of secondary vasculitis may include infection such as hepatitis or COVID-19, certain medications (hydralazine, allopurinol or tumor necrosis factor inhibitors), trauma or other inflammatory conditions such as other autoimmune disorders or cancer (lymphoma). Lastly, smoking or illegal drug use can increase the risk of developing vasculitis. Depending on the cause, symptoms can flare and remit.

Family history and genetics can play a role in the development of vasculitis. And, vasculitis affects some age groups more than others. Generally, it affects males, females and all ethnicities equally, although certain forms of vasculitis may affect one group more than another.

Symptoms of and treatment for vasculitis depend on the type, cause and the affected blood vessels. In some cases, diagnosis can take years due to presenting symptoms and whether any more common conditions are also present.

Vasculitis can occur in large, medium and small blood vessels. Following are two examples of each.

## Large Vessel Vasculitis

• *Behcet's disease*. Behcet's disease is a chronic condition without a clearly understood cause. It affects veins and arteries, including the largest vein in the body, the vena cava. Autoimmunity, certain genetic markers and infectious triggers may all play a role. There is an increased prevalence of this disease in Turkey, the Middle East and certain areas of the Mediterranean basin. It can occur at any age, but it usually starts between ages 20 and 30. Main symptoms include mouth and genital sores that either return or won't resolve; skin and joint pain; and inflammation of the eyes. Other areas of the body may be affected, but this tends to be rare. Diagnosis is largely based on the pattern of presentation and ruling out other conditions. Treatment includes corticosteroids and other immunosuppressants, biologics such as tumor necrosis factor drugs and other medications that help manage the symptoms, especially those for issues with eyes and sores in the mouth and on the genitals. Although there is no cure and symptoms may relapse and remit, most people with Behcet's disease can live a full life.

• *Giant cell arteritis (GCA)*. GCA is a type of vasculitis that mostly affects the arteries of the scalp and head, in particular the arteries over the temples. It typically affects adults over the age of 50, and it affects women more than men. It is also seen more frequently in patients who have polymyalgic rheumatica, another inflammatory disorder that affects various joints in the body. The most common symptom is a headache, usually over the temples. Pain in the jaw from chewing, loss of appetite with weight loss and fatigue can also occur. If the vessels of the eyes are affected, eyesight can be affected, and permanent vision loss can occur if not promptly treated. The first-line treatment for GCA is high-dose steroids that are then tapered with a lower dose used long-term. Actemra, a monoclonal antibody used to treat rheumatoid arthritis, was approved in 2017 to treat GCA. When GCA is treated properly, prognosis is good. Living with GCA is largely based on managing steroid dosing and its many unpleasant side effects. Treatment must be tailored to each individual case to address and avoid complications, especially related to vision.

## Medium Vessel Vasculitis

• *Kawasaki disease*. One of the most common forms of vasculitis in children, Kawasaki disease carries the risk of inflammation of the coronary arteries, which affects blood flow to the heart. Therefore, prompt treatment is essential, including a cardiac workup. Symptoms include prolonged high fever (for at least five days); dry or cracked lips, mouth and tongue; red eyes; redness and swelling of the hands and feet; and rash. Diagnosis is based on these symptoms and by ruling out any other possible cause. Kawasaki disease is treated with high-dose intravenous immune globulin (IVIG). Due to the potential for cardiac involvement, IVIG should be administered in the in-patient hospital setting. The goal is to reduce inflammation and the risk of developing coronary artery abnormalities. Just one dose of IVIG is needed in most cases, but occasionally a second dose and/or corticosteroids may be needed. Aspirin is also used, usually for a few months after diagnosis. The child will likely require cardiac follow-up care. Most children will recover completely.

• *Polyarteritis nodosa (PAN).* Also known as systemic necrotizing vasculitis, PAN affects the small and medium-sized arteries, resulting in damage to the affected vessels and the organs and tissues to which they supply blood. The cause is believed to be autoimmune and can occur more frequently in people with hepatitis B or C. PAN affects adults more than children. Because any organs or tissue can be affected, symptoms vary depending on the location and organs to which the vessels lead; skin, muscle, joints, the heart, gastrointestinal tract and kidneys may also be affected. Symptoms may include weakness and fatigue, fever, joint pain, achy muscles, abdominal pain and weight loss. If nerves are affected, the patient may have numbness, pain, burning and weakness. Damage to the nervous system may cause strokes or seizures.[1] Treatment involves medicines to suppress inflammation and the immune system. These may include steroids such as prednisone. Similar medicines such as azathioprine, methotrexate or mycophenolate that allow for reducing the dose of steroids are often used as well. Cyclophosphamide is used in severe cases.[1] With proper treatment, prognosis is good.

## Small Vessel Vasculitis

• *Eosinophilic granulomatosis with polyangiitis (EGPA).* Formerly known as Churg-Strauss syndrome, EGPA is a very rare form of vasculitis. It is believed to be autoimmune, affecting men and women equally at any age. The lungs are primarily affected but, depending on the person, other organs may be involved. It occurs in three phases:

Phase one: adult-onset asthmatic symptoms (chest tightness, shortness of breath, coughing and wheezing)

Phase two: a dramatic increase in eosinophils, a type of white blood cells that fight infection

Phase three: vasculitis that can include lung and other organ damage

Diagnosis may include assessment of the symptoms, blood and urine tests and biopsies. Treatment includes steroids, methotrexate and two monoclonal antibodies, Nucala and Dupixent, which are used to treat eosinophilic asthma. Nucala was the first medication to be approved by the U.S. Food and Drug Administration for treatment of EGPA. EGPA may relapse and remit; with remissions, treatment may be stopped. With proper intervention, including a healthy lifestyle, prognosis is good.

• *Immunoglobulin A (IgA) vasculitis.* IgA vasculitis is a rare, autoimmune form of vasculitis that may have a genetic predisposition. It causes IgA to collect in the blood vessels of the kidneys, intestines and joints. A red or purple rash is almost always seen. It can occur at any age, but it most commonly affects young children. Frequently, a respiratory infection precedes IgA vasculitis, although there can be other triggers. Symptoms usually completely resolve on their own with no treatment needed. At times, treatment involves symptoms management depending on the organs affected and the severity of the symptoms. They can reoccur but will resolve again without treatment. The most common and serious long-term health problem caused by IgA vasculitis is chronic kidney disease (CKD). Severe kidney damage is rare but, if it does occur, it may require aggressive treatment. Adults are much more likely than children to develop CKD.[2] Blood and urine tests, an abdominal ultrasound and biopsies may be used to diagnoses IgA vasculitis, depending on organs involved.

***Symptoms of and treatment for vasculitis depend on the type, cause and the affected blood vessels.***

## Living Well with Vasculitis

Pinpointing the form of vasculitis a patient has; understanding the severity of disease; receiving prompt diagnosis and treatment; identifying underlying conditions (if any); adhering to medical interventions; and maintaining medical care are all integral to enjoying the best possible quality of life when living with vasculitis. While there is no cure, patients with vasculitis can live full lives with a combination of proper treatment, social connection and support. For more information on vasculitis, including additional types, visit the Vasculitis Foundation at www.vasculitisfoundation.org.

### Sources


1. Mount Sinai. Polyarteritis Nodosa. Accessed at www.mountsinai.org/health-library/diseases-conditions/polyarteritis-nodosa.
2. National Institute of Diabetes and Digestive and Kidney Diseases. IgA Vasculitis. Accessed at www.niddk.nih.gov/health-information/kidney-disease/iga-vasculitis.


**MICHELLE GREER**, RN, IgCN, is senior vice president of sales at Nufactor, a specialty infusion company.

RESEARCH

# Clinical Trial to Explore Biologic Treatment for CVID Lung Condition

The Cincinnati Children's Hospital Medical Center is conducting a clinical trial to explore if a biologic medication already approved for other uses will benefit common variable immune deficiency (CVID) patients with granulomatous lymphocytic interstitial lung disease (GLILD), a potentially life-threatening noninfectious lung condition. Granulomas, or small masses of white blood cells, form in the lungs of patients with GLILD, causing long-term lung damage and impaired respiratory function. Between 10 and 20 percent of patients with CVID develop GLILD, which reduces life expectancy in adults by more than 50 percent after diagnosis.

The drug, abatacept, works by reducing the overactivation of T cells. It is a biologic medicine derived from two human proteins and is administered through infusion either subcutaneously or intravenously. Known by the trade name Orencia, it is already approved for use in patients with rheumatoid arthritis to relieve swelling, pain and stiffness caused by overactive T cells. Providers prescribe abatacept for GLILD, but it's considered an "off-label" use by the U.S. Food and Drug Administration, meaning it's an approved drug used for an unapproved purpose.

The multi-site Phase II study is enrolling 38 patients at the Cincinnati Children's Hospital Medical Center, the University of California, San Francisco, the Mayo Clinic in Rochester, Minn., and Duke University Health System in Durham, N.C. The study is accepting children age 4 years and older and adults. Patients must be on immune globulin replacement therapy for at least six months, have GLILD diagnosed by lung biopsy and persisting or worsening disease as shown on a CT scan. During the 26-week study, some study participants will receive abatacept and others a placebo.

The study's primary goal is to achieve a 30 percent or greater reduction in granulomas in a volume of lung tissue after six months. Researchers also aim to improve lung function and quality of life and reduce steroid use while avoiding new infections. If approved, abatacept would be administered regularly as a therapeutic instead of a one-time treatment.

Clinical Trial Explores Biologic Treatment for CVID Lung Condition. Immune Deficiency Foundation news release, Aug. 31, 2023. Accessed at primaryimmune.org/news/clinical-trial-explores-biologic-treatment-cvid-lung-condition.

MEDICINES

# KORU Enters Into a Subcutaneous Immune Globulin Prefilled Syringe Development Agreement

KORU Medical Systems has entered into a development agreement with a pharmaceutical manufacturer of subcutaneous immune globulin therapy (SCIG) to develop and seek regulatory approval of the Freedom Infusion System with an SCIG prefilled syringe. The agreement provides for KORU Medical to develop an adaptation to its Freedom Infusion System to enable an SCIG prefilled syringe to be usable by patients globally and to seek regulatory authorization for adaptation.

"As KORU Medical looks to simplify subcutaneous drug delivery for patients in the home, we are excited to partner with another major pharmaceutical company to further innovate our Freedom Infusion System for use with its prefilled syringes. Patients prefer prefilled syringes as they simplify the challenging task of transferring medication from vials," said Linda Tharby, KORU Medical's president and CEO. "The Freedom Infusion System is the only infusion system approved for prefilled syringes, and we are excited by the opportunity to expand the number of prefilled subcutaneous therapies that are FDA approved for our innovative infusion system."

KORU Medical Systems Announces Subcutaneous Immunoglobulin Prefilled Syringe Development Agreement. KORU Medical Systems press release, Jan. 25, 2023. Accessed at www.businesswire.com/news/home/20230125005261/en/KORU-Medical-Systems-Announces-Subcutaneous-Immunoglobulin-Prefilled-Syringe-Development-Agreement.

RESEARCH

# HSS Study Identifies Subtypes of Rheumatoid Arthritis

A new study published in *Nature*, conducted by the Accelerating Medicines Partnership (AMP), suggests rheumatoid arthritis (RA) can be characterized into at least four distinct subtypes. These distinctions may improve the efficacy of treatment by allowing doctors to personalize recommendations depending on the subtype of RA a patient has. Notably, the underlying biology of each corresponds to a different drug target. By comparing the targets in a patient's joint with the medications to which they respond, doctors may begin to tailor treatments, potentially leading to more rapidly effective treatment outcomes.

"We believe this work lays the foundation for a new era in the treatment of rheumatoid arthritis," said Laura Donlin, PhD, co-senior author and co-director of the Derfner Foundation Precision Medicine Laboratory at Hospital for Special Surgery (HSS). "While we have numerous medications available, the chance we'll choose the right one the first time is fairly low, around 40 percent. It's critical that we get patients the best medication possible as quickly as possible to slow the progression of disease. By understanding the unique features of a patient's condition, we can make more informed decisions and, hopefully, produce more successful outcomes for patients."

Dr. Donlin and her team at HSS are hopeful these results will lead to new standards of personalized care for RA.

HSS Researchers Enable Study Identifying Subtypes of Rheumatoid Arthritis. Cision PR Newswire press release, Nov. 15, 2023. Accessed at www.prnewswire.com/news-releases/hss-researchers-enable-study-identifying-subtypes-of-rheumatoid-arthritis-301989602.html.

VACCINES

# New Vaccine May Treat Autoimmunity and Prolong Transplant Survival

A team of researchers from the Department of Medicine and the Transplant Research Center at Brigham and Women's Hospital, in collaboration with researchers from the Dana-Farber Cancer Institute, have developed a new vaccine that shows promise for promoting immune regulation. The new vaccine utilizes synthetically modified natural peptides to stimulate CD8 T regulatory cells. T cells help the immune system fight infection and protect from disease; this vaccine stimulated and promoted regulatory T cells that in turn kept the harmful cells in check. These cells are central to the immune response and preventing inflammation.

Using a mouse model, the researchers discovered that self-peptides flag harmful immune cells for the body's own regulatory CD8 T cells to attack and eliminate. The researchers also found that the new vaccine prolongs allograft survival in mice and tested anti-allograft immunity on mismatched kidney transplants.

A comparable pathway in humans was also identified, suggesting this research could protect those with autoimmune disorders or organ transplant patients. According to the researchers, "Identification of human T cell receptors homologous to the mouse model tested may form the basis of a novel and effective treatment for disorders that reflect excessive or dysregulated immune responses."

According to Jamil R. Azzi, MD, PhD, and co-corresponding author of the study, "Our research identifies an analogous pathway in humans that we hope to target soon."

New Vaccine Promotes Immune Regulation That Treats Autoimmunity and Prolongs Transplant Survival. News Medical, Nov. 15, 2023. Accessed at www.news-medical.net/news/20231115/New-vaccine-promotes-immune-regulation-that-treats-autoimmunity-and-prolongs-transplant-survival.aspx.

RESEARCH

# FDA Clears Kyverna Therapeutics' IND Application for KYV-101 Trial for Myasthenia Gravis

The U.S. Food and Drug Administration (FDA) has given clearance for Kyverna Therapeutics' investigational new drug (IND) application to begin a Phase II clinical trial of KYV-101 for myasthenia gravis. The KYSA-6 trial will analyze KYV-101's ability to treat adults with the autoimmune disease. KYV-101 is a fully human CD19 chimeric antigen receptor (CAR) T-cell therapy that is designed to act on the CD19 protein. This protein is expressed on the B cell surface and is associated with myasthenia gravis and several other autoimmune diseases.

"We are grateful that the FDA's decision to clear the IND for our Phase II KYSA-6 trial will allow Kyverna to offer this potentially paradigm-shifting investigational treatment to patients who may benefit from a deep B cell depletion and possibly durable reset of their immune system," said Peter Maag, CEO of Kyverna Therapeutics.

KYV-101 is currently being analyzed for active lupus nephritis in the Phase I KYSA-1 trial in the U.S. and Phase I/II KYSA-3 trial in Germany. And, another Phase I/II KYSA-5 trial is evaluating the CAR-T cell therapy's efficacy in treating cutaneous systemic sclerosis in the United States.

Kyverna Therapeutics intends to evaluate KYV-101 for further indications and establish a pipeline of immunotherapies for autoimmune diseases.

"I welcome the FDA's decision and look forward to more clinical data to further our knowledge about CAR-T cell therapy in patients with severe neurological autoimmune diseases," said Otto-von-Guericke University Neurology department director Professor Aiden Haghikia.

Kyverna Therapeutics Given FDA Approval for KYV-101 Trial. Clinical Trials Arena, Nov. 14, 2023. Accessed at www.clinicaltrialsarena.com/news/kyverna-therapeutics-myasthenia-gravis/?cf-view.

RESEARCH

# Study Suggests Pregnant Women May Hold Key to Cure for Multiple Sclerosis and Arthritis

Researchers from Linköping University in Sweden have observed that women with multiple sclerosis (MS) experience significant improvement in their symptoms during pregnancy, but their condition often worsens postpartum. They have investigated this phenomenon, focusing on changes in the immune system during pregnancy, with the hope of paving the way for new treatments.

The study reveals that during pregnancy, the mother's immune system becomes more tolerant to prevent the rejection of the fetus, since half of the fetus' genetic material comes from the father; this tolerance is reflected in a 70 percent reduction in MS symptoms during the last trimester of pregnancy, a pattern also seen in other autoimmune conditions such as rheumatoid arthritis.

To understand the mechanisms behind this symptom reduction, the research team compared 11 women with MS to seven healthy women, analyzing blood samples taken before, during and after pregnancy. They focused on T cells, crucial components of the immune system that also drive MS and play significant roles during pregnancy. The study found networks of interacting genes within the T cells that change during pregnancy, many of which are linked to MS and key immune processes.

"What was possibly most striking is that we couldn't find any real differences between the groups during pregnancy, as it seems that the immune system of a pregnant woman with MS looks roughly like that of a healthy pregnant woman," said Sandra Hellberg, an assistant professor in the Department of Biomedical and Clinical Sciences at Linköping University. "We can see that the changes in the T cells mirror the amelioration in relapse frequency. The biggest changes happen in the last third of pregnancy, and this is where women with MS improve the most. These changes are then reversed after pregnancy at the point in time when there is a temporary increase in disease activity. It is important to stress that disease activity thereafter goes back to what it was prior to the pregnancy."

The affected gene networks during pregnancy also include those regulated by pregnancy hormones, especially progesterone. The researchers are now experimenting with these hormones in the lab to replicate the observed effects, aiming to develop potential treatment strategies.

Pregnant Women May Hold Key to Curing Multiple Sclerosis and Arthritis. Study Finds, Nov. 14, 2023. Accessed at studyfinds.org/pregnant-women-multiple-sclerosis.

RESEARCH

# Efgartigimod Found Effecacious and Safe to Treat ITP

The first-in-class novel human immunoglobulin G1 Fc fragment, efgartigimod, is efficacious and safe for patients with chronic or persistent primary immune thrombocytopenia (ITP), according to a study.

The Phase III 24-week study assessed the efficacy and safety of intravenous efgartigimod in adults aged 18 years or older with chronic or persistent primary immune thrombocytopenia who had an average platelet count of less than 30,000, had responded to at least one previous immune thrombocytopenia therapy and were on or had received at least a second previous immune thrombocytopenia therapy. A total of 131 patients were randomly assigned to efgartigimod or placebo (86 and 45, respectively).

The researchers found that 22 and five percent of those receiving efgartigimod and placebo, respectively, reached the primary end point of sustained platelet count response. The median number of weeks of disease control was 2.0 and 0.0 for patients with chronic immune thrombocytopenia receiving efgartigimod and placebo, respectively. Efgartigimod was well-tolerated, with adverse events mostly of mild-to-moderate severity. In both groups, the most common adverse events of interest were headache, hematuria and petechiae.

"The higher proportion of efgartigimod-treated patients with sustained platelet count responses and improved disease control compared with placebo in this population with chronic and persistent disease corroborates and extends the evidence of this novel mechanism for targeting the autoantibody-based pathophysiology of immune thrombocytopenia," said the researchers.

Several authors disclosed ties to biopharmaceutical companies, including argenx, which manufactures efgartigimod and funded the study. IG

Efgartigimod Efficacious, Safe for Primary Immune Thrombocytopenia. Health Day News, Oct. 6, 2023. Accessed at consumer.healthday.com/physician-s-briefing-thrombocytopenia-2665777355.html.

RESEARCH

# Experimental IVIG Treatment Appears to Safely Ease Many Symptoms of Systemic Sclerosis

A new Spanish study found that intravenous immune globulin (IVIG) may help to ease muscle, skin and digestive symptoms in people with systemic sclerosis (SSc).

In the study, researchers looked at the medical records of 78 adults (64 women, 14 men), all with an SSc diagnosis and a mean age of 58.5, from 18 hospitals across Spain. Forty six patients (59 percent) had diffuse SSc (the most severe form of the disease), and 32 (41 percent) had limited SSc. Half of these people also had another connective tissue disease. The most common was idiopathic inflammatory myopathy (41 percent), an inflammation of skeletal muscles due to unknown reasons, and Sjögren's syndrome (6 percent).

Patients were given IVIG in monthly cycles in combination with standard care. IVIG was given most often to treat myositis, or inflammation of the muscles (49 percent), followed by gastrointestinal (31 percent) and skin symptoms (22 percent). In seven (nine percent) patients, IVIG was used to treat more than one symptom. Patients were treated with IVIG at a median of five cycles each month. Most received IVIG in combination with corticosteroids (69 percent), immunosuppressants (67 percent) or biologics (18 percent). The most commonly used immunosuppressant was mycophenolate mofetil.

Muscle strength was evaluated before IVIG and three months after the last treatment cycle using a modified version of the Medical Research Council scale, which rates muscle strength from grade 5 (normal) to grade 0 (no visible muscle contraction or tightening). About 92 percent of treated patients had muscle strength grades of 3 to 5, suggesting IVIG may be easing muscle symptoms.

The levels of creatine kinase decreased significantly, falling from an average of 1,149 to 217 international units per milliliter of blood. Creatine kinase is an enzyme mostly found in skeletal muscles, and high levels in blood can indicate muscle damage. IVIG treatment also eased skin symptoms, as seen by a significant two-point decrease — from 15 to 13 points — in the average modified Rodnan skin score, a measure of skin thickness.

To assess the quality of life related to gastrointestinal symptoms, the University of California Los Angeles Scleroderma Clinical Trials Consortium gastrointestinal tract 2.0 questionnaire was used; higher scores indicate a poorer quality. Before IVIG, patients had an average score of 1.06 points in this questionnaire. Mean scores decreased significantly to 0.78 after treatment, suggesting IVIG also helps to ease gastrointestinal symptoms.

A total of 12 side effects were reported in 10 patients, the majority being mild or moderate in severity. Treatment was stopped in four patients, one due to a serious side effect.

According to the researchers, "Our findings suggest that IVIG should be a treatment option in cases of myositis, [skin] and gastrointestinal involvement in patients with SSc," as the treatment "has a good safety profile." IG

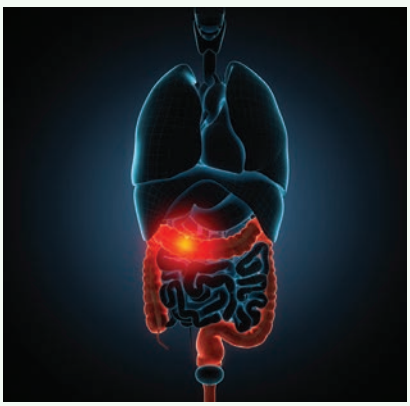
Maia, M. IVIG Treatment Appears to Be Safe, Able to Ease Range of SSc Symptoms. Scleroderma News, Oct. 31, 2023. Accessed at www.sclerodermanews.com/news/ivig-appear-safe-ease-range-scleroderma-symptoms-in-ssc.

MEDICINES

# FDA Approves Celltrion's Zymfentra to Treat Ulcerative Colitis and Crohn's Disease

The U.S. Food and Drug Administration (FDA) has approved Celltrion's Zymfentra, a subcutaneous injection formulation of its infliximab Remsima, for maintenance therapy in adults with moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) following treatment with infliximab administered intravenously. Zymfentra (infliximab-dyyb) is the world's first and only subcutaneous infliximab product. It is approved as a novel drug, and its development is based on Remicade (reference intravenous infliximab).

Approval was based on data from two



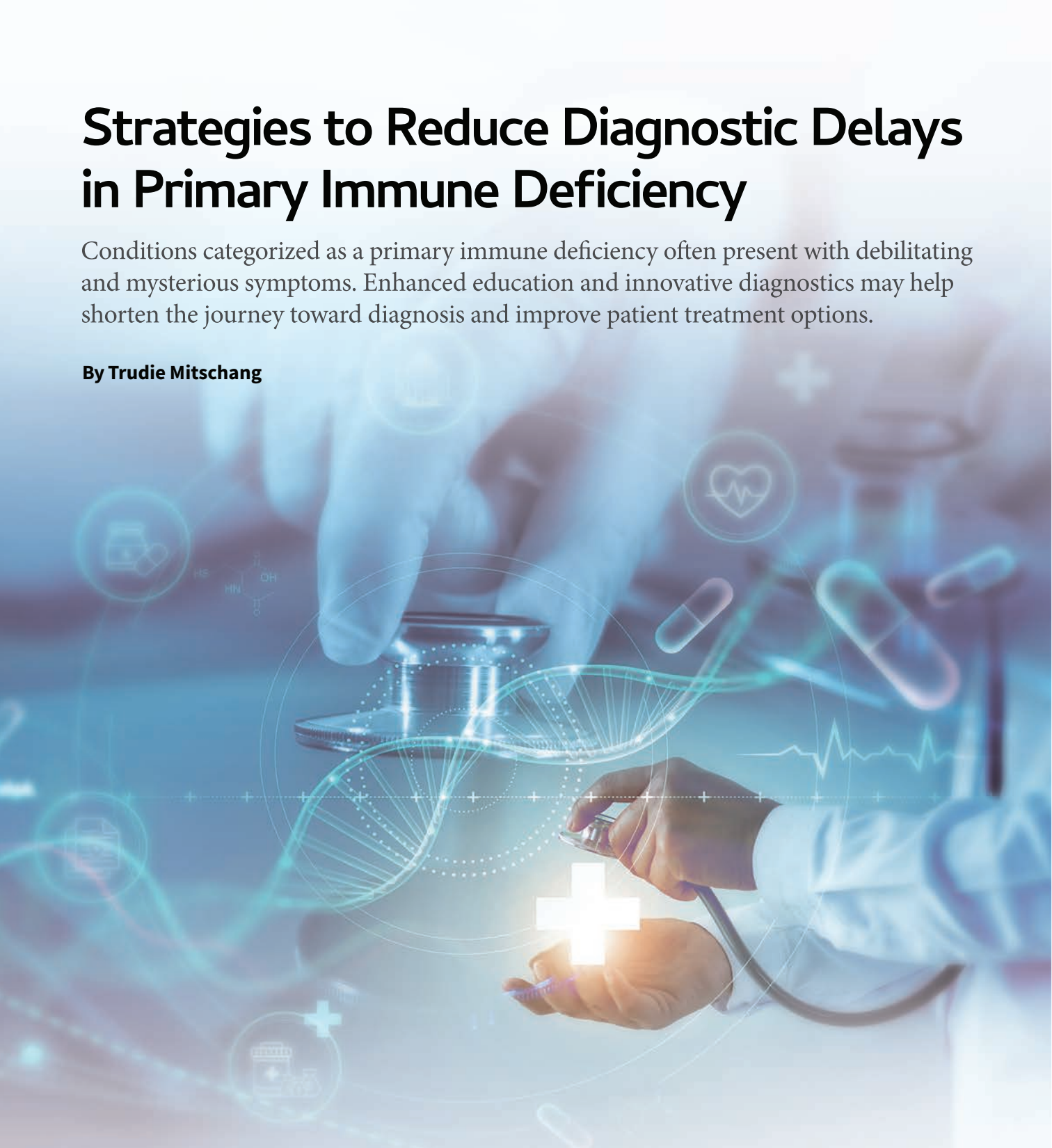
Phase III pivotal trials that assessed the efficacy of Zymfentra as maintenance therapy in patients with moderate to severe UC (LIBERTY-UC) and CD (LIBERTY-CD). Study results show Zymfentra had a superior response in achieving clinical remission (UC and CD) and endoscopic response (CD) compared to placebo as maintenance therapy after induction therapy of intravenous infliximab over a 54-week period. The overall safety profile of Zymfentra was similar to that of placebo during the maintenance period in both studies, and no new safety signals were identified.

Jeremias, S. FDA Approves First Subcutaneous Infliximab Product. AJMC, The Center for Biosimilars, Oct. 23, 2023. Accessed at www.centerforbiosimilars.com/view/fda-approves-first-subcutaneous-infliximab#.

# Strategies to Reduce Diagnostic Delays in Primary Immune Deficiency

Conditions categorized as a primary immune deficiency often present with debilitating and mysterious symptoms. Enhanced education and innovative diagnostics may help shorten the journey toward diagnosis and improve patient treatment options.

**By Trudie Mitschang**



**PRIMARY IMMUNE DEFICIENCY** (PI) disorders are a group of approximately 500 rare and often underdiagnosed conditions characterized by a weakened or dysfunctional immune system. Delayed diagnosis of PI can have serious consequences for patients, including recurrent infections, organ damage and an increased risk of complications. Despite advances in medical science, diagnostic delays for PI remain a common experience for those seeking definitive medical answers and treatment plans.

PI encompasses a wide range of disorders, each with its unique genetic, clinical and immunological characteristics. Common variable immunodeficiency (CVID), severe

combined immunodeficiency (SCID) and X-linked agammaglobulinemia are just a few examples. Despite their diversity, PIs share a common feature: a weakened or dysfunctional immune system, which hampers the body's ability to fight off infections. Early and accurate diagnosis is vital for managing these conditions effectively and improving patient quality-of-life.

Many factors contribute to the delayed diagnosis of PI, including:

- Lack of awareness about PI within the medical community. Healthcare providers, particularly primary care physicians (PCPs), may not be well-versed in recognizing the signs and symptoms of immune disease, and symptoms that commonly present along with PI such as recurrent infections, fatigue and growth delays often mimic other conditions and diseases.
- Lack of standardized testing. Accurate diagnosis of PI relies on specialized laboratory tests such as flow cytometry and genetic sequencing. Access to these tests may be limited in certain regions, further delaying diagnosis.
- Inadequate referral pathways. In some cases, patients with a suspected PI are not referred to immunologists, leading to unnecessary delays in diagnosis and appropriate care.

Despite these difficulties, reducing diagnostic delays for PI is crucial to improving the-long term prognosis and quality of life for affected individuals.

**PI diagnostic costs are calculated at $85,882 per patient and contribute $40 billion in costs to the U.S. healthcare system.**

### Counting the Cost of Diagnostic Delays

While there are many incentives for shortening diagnostic delays in PI, one of the most significant considerations is cost. According to a report cited by the National Institutes of Health (NIH), PI diagnostic costs are calculated at $85,882 per patient and contribute $40 billion in costs to the U.S. healthcare system. NIH also estimates that early diagnosis can save as much as $6,500 per patient.[1]

In one of the first studies of healthcare resource utilization and costs for patients with rare diseases, the EveryLife Foundation for Rare Diseases found that timely diagnosis and screening can shorten and possibly eliminate the diagnostic odyssey while significantly reducing the cost impact of rare disease for individuals, families and the healthcare system. In a September 2023 report titled "The Cost of Delayed Diagnosis in Rare Disease," the EveryLife Foundation offers an in-depth analysis of the avoidable costs associated with several rare diseases.

"The results of this study demonstrate the urgent need for faster and improved diagnostic strategies to help decrease the financial and personal impact of rare diseases on families and the healthcare system," said Annie Kennedy, chief of policy, advocacy and patient engagement at the EveryLife Foundation. "Timely diagnosis, using tools such as newborn screening and next-generation, evidence-based neonatal sequencing, is especially important when there are disease-altering or lifesaving treatments available that can prevent irreversible disease progression and change outcomes."[2]

A 2022 study titled "The National Economic Burden of Rare Disease" estimated the economic impact of 379 rare diseases in 2019 was nearly $1 trillion, with 60 percent of those costs being shouldered directly by families and society as a whole. The study also noted that from the first appearance of symptoms, it can take more than six years and as many as 17 clinical encounters before a person receives a definitive rare disease diagnosis. That finding was a major impetus for more recent studies that showed individuals whose diagnoses were delayed by an average of five years were approximately four times as likely to see three or more specialists than those with shorter diagnostic odysseys.

"Medical costs for rare diseases are inevitable, but avoidable costs from delayed diagnosis not only place financial strain on individuals and families but also divert crucial healthcare funds. These could be better used for treatments that enhance patient quality of life and boost workforce productivity," stated Amy Brower, PhD, director of the Newborn Screening Translational Research Network at the American College of Medical Genetics and Genomics. "Timely diagnosis can lead to targeted therapy, surveillance for complications and genetic counseling, which can positively affect health outcomes, survival and the overall healthcare system."[2]

In addition to care and cost concerns, more timely diagnosis of PI can help:

- Enable more appropriate preventive health measures such as personalized vaccination requirements for patients with PI.
- Uncover diagnoses of family members, since many PIs are inherited conditions.
- Empower and educate patients about chronic illness and enable them to connect with needed support systems.
- Address health disparities impacting minority patients, women and those with reduced access to healthcare.
- Minimize recurrent infections that can lead to complications, hospitalizations and increased healthcare costs.
- Avoid organ damage caused by chronic infections and inflammation, particularly in the lungs and digestive tract.
- Reduce the overuse of antibiotics, which can lead to other adverse effects.
- Minimize the psychological impact of living with an undiagnosed invisible illness.

**Awareness and Access: Keys to Timely Diagnosis**

The prospect of reducing the diagnosis timeline for PI patients is not a simple task, and in fact requires a multi-pronged approach involving the collaboration and commitment of many healthcare industry stakeholders. While not an exhaustive list, the following approaches may offer hope for those caught in the maze of PI misdiagnosis.

1) *Raising healthcare provider education and awareness.* One of the fundamental steps to reduce diagnostic delays is to enhance the awareness and education of healthcare providers. This includes PCPs, pediatricians and other specialists who may encounter patients with PI symptoms. Educational programs and resources can help healthcare professionals recognize potential signs of PI sooner and consider it as a diagnosis. In fact, one recent study reviewed a number of factors that contribute to diagnostic delays in rare disease patients and concluded that the failure to even suspect a rare disease was considered the first "factor to be of particular importance." The study went on to say that insufficient knowledge about rare diseases among physicians and medical professionals not partnering or communicating well with one another also contribute to rare diseases going undiagnosed, sometimes for years. "We found that one of the most important factors related to the prolonged undiagnosed period is the lack of suspicion of a rare disease by patients and their medical professionals," the researchers wrote. "Our results strongly suggest that measures are needed to facilitate patients and clinicians to become aware of rare diseases."[3]

The development and dissemination of clinical guidelines for the diagnosis of PI can also be instrumental in standardizing the diagnostic process. These guidelines should outline the key clinical features, laboratory tests and red flags that warrant referral to an immunologist.

The Immune Deficiency Foundation (IDF) is known for its efforts to educate the physician community about PI. From easily accessed online education series, on-demand videos and downloadable guides, IDF is committed to helping fast-track accurate diagnoses for PI patients.

In 2022, IDF launched a special effort to reach and educate clinicians across medical specialties. The organization's staff ran an exhibit at seven medical conferences outside of the field of immunology to share resources and raise awareness with healthcare professionals who may not be familiar with PI or IDF. "By spreading awareness among providers in a variety of specialties who may unknowingly see patients with undiagnosed PI, IDF hopes to reduce the time to diagnosis," IDF explained in a news release.[4]

2) *Improved access to diagnostic testing.* Another key way to shorten diagnostic delays in PI patients is to ensure that diagnostic tests such as flow cytometry and genetic sequencing are readily available in various healthcare settings. This includes not only major medical centers but also regional and community healthcare facilities. Expanding access to these tests can shorten the diagnostic journey for many patients. Some of the methods for accomplishing this include the use of decision support tools and electronic health record prompts to assist healthcare providers in considering PI as a potential diagnosis.

Additionally, ensuring individuals and families undergoing genetic testing for PIs have access to genetic counseling services to help them understand the implications of test results is vital. IDF has been instrumental in getting newborn screening for SCID implemented in all 50 states, and in 2022, the organization continued advocacy efforts to ensure federal programs remain in place to support these screening efforts.[5]

**From the first appearance of symptoms, it can take more than six years and as many as 17 clinical encounters before a person receives a definitive rare disease diagnosis.**

Another organization pioneering access to testing is the Jeffrey Model Foundation (JMF). In 2019, JMF introduced Jeffrey's Insights, a no-charge genetic sequencing pilot program for patients within the Jeffrey Modell Centers Network with an underlying PI, but without a genetic diagnosis. Building on the success of the pilot, JMF expanded the program globally to more than 400 centers by early 2020. A total of 1,398 patients were tested, with 20.3 percent receiving a molecular diagnosis and many more receiving helpful diagnostic leads. Results obtained from genetic sequencing led to an alteration of clinical diagnosis, disease management, treatment and genetic counseling in as many as 53 percent of patients. The global expansion of this program further underscores the crucial need for next-generation sequencing for PI, along with its efficiency and potential cost savings.[5]

In a study in *The Journal of Molecular Diagnostics*, investigators used next-generation sequencing technology to test a DNA panel of 130 different immune system genes from 22 study participants. They found that many patients had inherited a genetic defect that caused a disorder in their immune system. These findings will facilitate better treatment options and earlier diagnosis in family members who may have inherited the same genetic abnormality. "Genetic testing was costly to perform and was mostly targeted to DNA sequencing of a single or very small number of genes. Therefore, a genetic diagnosis was limited for many patients with [PIs]," explained lead investigator Lloyd J. D'Orsogna, MBBS, PhD, in the school of medicine at the University of Western Australia and department of clinical immunology at PathWest Laboratory Medicine, Fiona Stanley Hospital in Perth, Western Australia. "Recent advances in genetic technology allow affordable testing of multiple genes from the same individual. We can therefore identify a specific gene that may lead to frequent infections in patients. An earlier and more accurate diagnosis may improve the patient outcome and prevent complications."[7]

## A Hopeful Future

Reducing diagnostic delays in PI is a complex endeavor that requires the concerted efforts of healthcare providers, researchers, advocacy groups and the broader healthcare community. Early diagnosis can significantly improve the prognosis and quality of life for individuals with PI, preventing recurrent infections, organ damage and the psychological burden of undiagnosed disease. Ultimately, early diagnosis saves lives and reduces the healthcare burden associated with PI. By focusing on healthcare provider education, improved access to diagnostic testing and enhanced collaboration between specialists, we can see significant strides toward reducing diagnostic delays and ensuring that those with PI receive the care they need.

## References


1. Kumar, B, Zetumer, S, Swee, M, et al. Reducing Delays in Diagnosing Primary Immunodeficiency Through the Development and Implementation of a Clinical Decision Support Tool: Protocol for a Quality Improvement Project. *JMIR Research Protocols*, 2022 Jan 4;11(1):e32635. Accessed at www.ncbi.nlm.nih.gov/pmc/articles/PMC8767470.
2. New Study Measures Economic Impact of Delayed Diagnosis of Rare Diseases. EveryLife Foundation for Rare Diseases press release, Sept. 14, 2023. Accessed at www.everylifefoundation.org/new-study-measures-economic-impact-of-delayed-diagnosis-of-rare-diseases.
3. Inácio, P. Lack of Rare Disease Awareness Contributes to Diagnosis Delays. Angioedema News, May 12, 2022. Accessed at www.angioedemanews.com/news/hae-rare-disease-diagnosis-attributed-lack-of-awareness.
4. IDF Serves Thousands Through Education, Advocacy and Research Efforts. IDF news release, Jan. 24, 2023. Accessed at Accessed at www.primaryimmune.org/resources/news-articles/idf-serves-thousands-through-education-advocacy-and-research-efforts.
5. Ensuring Access to Care Tops IDF's Policy Priorities. IDF news release, Jan. 27, 2022. Accessed at Accessed at www.primaryimmune.org/resources/news-articles/ensuring-access-care-tops-idfs-policy-priorities.
6. Quinn, J, Modell, V, Johnson, B, et al. Global Expansion of Jeffrey's Insights: Jeffrey Modell Foundation's Genetic Sequencing Program for Primary Immunodeficiency. *Frontiers in Immunology*, 2022 Jun 10;13. Accessed at www.frontiersin.org/articles/10.3389/fimmu.2022.906540/full.
7. Targeted Next-Generation Sequencing Can Help to Diagnose Primary Immune Deficiency Disorders. Technology Network Diagnostics news release, May 25, 2022. Accessed at www.technologynetworks.com/diagnostics/news/targeted-next-generation-sequencing-can-help-to-diagnose-primary-immune-deficiency-disorders-361923.



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

# Genetic Testing
## for Primary Immune Deficiencies

Advances in understanding inherited disorders, along with a variety of tests that accurately diagnose them, are helping physicians point patients to the most effective treatments for their disease.

**By Cynthia Perry**

**DURING THE PAST** three decades, and especially since the onset of the COVID-19 pandemic, there has been a lot of research into the genetic causes of and treatments for various primary immune deficiency disorders (PIs). Nearly 500 unique immune disorders have been identified at this point, and a similar number of causative genetic mutations have been discovered. In fact, about 40 new genetic causes of immune disease are being found each year.[1]

As a result of these rapid discoveries, there are now treatments that go beyond the traditional use of antibiotics and immune globulin replacement therapy. The medical terminology is even changing, with "inborn errors of immunity" (IEI) now being preferred over the term "PI." This is in recognition of the fact that many patients have complex "immune dysregulation" issues, as opposed to just antibody, complement or cellular disorders.[2]

### Overview of the Immune System[2]

The immune system can be divided into two parts: 1) the innate immune system and 2) the adaptive immune system. In PIs, either or both of these systems can have mutations or polymorphisms, leading to various problems in detecting and fighting disease. PIs result from genetic variants; these variants can be from spontaneous genetic mutations or from inherited genetic variants. While there are some redundancies in the human immune system, both the innate and adaptive immune systems should be functioning properly to optimize health.

The innate immune system is the body's first line of defense against pathogens. It primarily includes phagocytes such as neutrophils, monocytes, macrophages, natural killer (NK) cells (all of these are types of white blood cells) and a set of proteins known as complement proteins (produced mostly in the liver). There are also other proteins found in the blood and tissues that may have some roles in immune protection.

The adaptive immune system "learns" to respond to specific pathogens. Typically, proteins from the invading organism are picked up by macrophages and dendritic cells, which in turn present them to the T and B lymphocytes (also known and T cells and B cells and are types of white blood cells) for activating them. Thus, the initial activation of innate immunity works in concert to activate adaptive immunity.

B cells are named because they were initially discovered in the Bursa of Fabricius in birds. Subsequently, it was

found that they derive from the bone marrow in mammals. B cells are responsible for producing and secreting immune globulins (antibodies), including IgA, IgG, IgM, IgD and IgE. It is important to note that IgD is rarely secreted and found normally on developing B cells. When found in substantial levels in the blood, a disease may be present. Each type of B cell can produce a specific class or subclass of immunoglobulin. Note that IgA has subclasses IgA1 and IgA2, while IgG has subclasses IgG1, IgG2, IgG3 and IgG4.

While T cells are derived from stem cells in the bone marrow, they migrate to the thymus to undergo maturation (hence the name T cells). The goal of the adaptive immune system is to provide memory, thus a longer-lasting protection against previously-encountered pathogens.

### Inborn Errors of Immunity (IEI)

IEIs are genetic disorders that can cause diverse symptoms, including recurrent infections, autoimmunity and cancer. Research shows that a specific genetic variant typically results in similar symptoms in affected patients, but the patterns can be variable. In addition, variants in a variety of genes can lead to similar clinical presentations. Researchers conclude that both genetic and environmental factors affect the presentation of symptoms in patients.[3]

Some IEIs cause broad malfunction of the immune system, while others involve a predisposition to a single type of infection.[4] In addition, some patients have a single genetic variant, while others may have multiple genetic variants that interact in as-yet unknown ways to cause the observed immune dysregulation symptoms.

Though IEIs are a diverse set of diseases, they all result from a mutation in at least one element of normal immune function such as T cells, B cells, natural killer cells, neutrophils, monocytes, antibodies, cytokines, the complement system or metabolic or other pathways, which can affect these immune system components. These mutations can result in any combination of:[2]

- Recurrent, unusually severe or unusual infections (infections from pathogens that don't cause disease in healthy individuals).
- Autoimmune disease in which the body attacks healthy tissue; in these cases the immune system believes the tissue to be a foreign pathogen.
- Allergies in which the body reacts to pollens and other molecules in the environment that aren't pathogenic.
- Cascade reactions (including cytokine storm and sepsis) from an overreaction to pathogens.
- Cancers, including blood cancers and solid-tumor cancers, as a result of the immune system failing to detect and eradicate malignant cells.

It's because researchers better understand this full spectrum of problems in immune regulation that IEI is now the preferred term over PI. All of these functional abnormalities can lead to fatal events, so correct diagnosis is crucial.

### Genetic Causes of IEIs

Most IEIs result from genetic anomalies in the protein-coding regions of DNA. DNA contains the genetic information needed to make proteins, and through a process called transcription, produces a molecule called messenger RNA (mRNA). mRNA tells cells how to synthesize proteins, including those necessary for a healthy immune system, in a process called translation. The proteins necessary for a healthy immune system include immunoglobulins, complement proteins, interferons, signal transduction proteins and white blood cells.[1]

**About 40 new genetic causes of immune disease are being found each year.**

Mutations in DNA can indeed lead to abnormal levels or function of these immune-related proteins, which can lead to an immune system that isn't fully functional. The body can produce too much, too little or dysfunctional immune-related proteins. Since a healthy immune system depends on many proteins working together, mutations in DNA can lead to a range of immune-related disorders as detailed above. It's not solely the abnormal levels or function of these specific proteins that can cause immune system dysfunction, but a broader range of interactions of the various parts within the immune system.[5]

Disease-causing genetic mutations can be inherited from parents in an autosomal dominant, autosomal recessive,

X-linked recessive or sporadic manner. For autosomal recessive and most sporadic patterns, both females and males have an equal chance of inheriting the disease. In the case of autosomal recessive inheritance, both parents must contribute the mutations in the same gene for a child to be affected, and each child has a 25 percent chance of inheriting the disease. However, children who inherit one mutated copy of a recessive genetic disease will be carriers of the disease and can pass it on to future generations. With dominant inheritance, only one parent needs to be affected, and each child has a 50 percent chance of inheriting the disease. Most IEIs are inherited in a sporadic or autosomal dominant pattern (which leads to the misconception of disease "skipping" generations).[4]

IEIs can also be inherited in an X-linked recessive fashion. Females have two X chromosomes and are generally less likely to express a full-blown X-linked recessive disease. During early development, one or the other X chromosome becomes inactivated. As long as the X chromosome with the normal functioning gene is active, disease does not occur. For some conditions such as X-linked chronic granulomatous disease, the female carrier can exhibit some disease manifestations, whereas in X-linked severe combined immunodeficiency (SCID), all of the T cells can be demonstrated to have the nonaffected X chromosome as the active X chromosome. Since males have one X and one Y chromosome, if a parent passes an X-linked mutated gene to them, they are not provided with the normal gene from a second X chromosome and will, therefore, be affected by the disease. Wiskott-Aldrich syndrome (WAS) is another example of an X-linked IEI.[5]

The International Union of Immunological Societies (IUIS) has defined 10 categories of IEI. These categories group known diseases by similar disease phenotypes, or symptoms. This type of classification system is commonly used in studying genetic diseases to facilitate the search for candidate genes in patient cohorts — patients with similar clusters of symptoms. The current IUIS classification is organized as follows:[5]

- Combined immunodeficiencies (including SCID)
- Combined immunodeficiencies with syndromic features (including WAS and ataxia-telangiectasia)
- Predominantly antibody deficiencies (including common variable immune deficiency and IgA deficiencies)
- Diseases of immune dysregulation (including autoimmune lymphoproliferative syndrome [ALPS])
- Congenital defects of phagocytes (including congenital neutropenias)
- Defects in intrinsic and innate immunity (including some interleukin deficiencies)
- Autoinflammatory diseases (including some forms of lupus and familial Mediterranean fever)
- Complement deficiencies
- Bone marrow failure (including Fanconi anemia)
- Phenocopies of IEI (including autoimmune lymphoproliferative syndrome [ALPS–SFAS] and severe COVID-19)

The prevalence of these rare diseases is difficult to know. However, according to a 2017 poll of IEI patients conducted by the Immune Deficiency Foundation, patients reported their diagnoses as:[6]

- 92 percent predominantly antibody deficiencies
- 4 percent combined immune deficiencies
- 4 percent other disorders

Selective IgA deficiency, one type of antibody deficiency, is the most common deficiency observed in about one in 500 individuals.

## Considerations in Genetic Diagnosis of IEI

With the rapid advances in researchers' understanding of the characteristics and genetics of IEIs, physicians now see the importance of finding a genetic cause of disease in patients. A clear genetic diagnosis can inform the best treatments for patients, or a "watch and wait" approach as appropriate, especially if the mutation is not known to be directly pathogenic.[7] In addition, a genetic diagnosis can provide the needed information for insurance companies to cover necessary treatments to reduce infections and other symptoms of patients with IEIs.[1]

Genetic diagnosis can also be helpful with regard to family planning, so patients understand the risk of passing their disease on to their children. In addition, patients may be able to participate in clinical trials related to their genetic diagnosis to help researchers understand symptoms and progression of disease, and to help them find effective treatments.[2]

On the other hand, genetic testing can be an emotional process for families; some people don't want to know they are carriers of a genetic disease. In addition, while the Affordable Care Act prevents health insurance discrimination due to genetic diagnosis, there are no laws against increased rates for life insurance due to genetic diagnosis.[1]

## Genetic Testing for IEIs

Before undergoing genetic testing for an IEI, patients should consult with a healthcare provider or genetic counselor to determine the most appropriate testing approach and to discuss the potential implications of genetic testing results. There are a number of approaches that can be taken to try to find a patient's genetic cause for disease:

- *Genetic panels.* Targeted genetic panels can offer a cost-effective way to find the genetic causes of IEI in patients. A number of companies offer these for patients with a suspected diagnosis of IEI. These include ARUP labs, BluePrint genetics, Centogene, Invitae and GeneDx. Some of these tests can be quite broad, looking at hundreds (now nearly 500) of candidate genes, and may be most appropriate when the patient's diagnosis isn't clear.[1]
- *Whole exome sequencing (WES).* WES looks at just two percent of the genome — the DNA regions that code for proteins. Mutations in the exomes are believed to account for up to 85 percent of genetic disease, but provide a genetic diagnosis in only about 30 percent of patients with IEI.[8] WES is commercially available; however, in the United States, insurance coverage varies.[7]
- *Whole genome sequencing (WGS).*[1] When WES fails to find a genetic cause of a patient's disease, the next step might be WGS. This testing analyzes a patient's entire genome and can include analysis of protein-coding DNA, non-coding DNA and mitochondrial DNA. Conventional thinking has been that the 98 percent of the DNA that doesn't code for proteins (non-exome DNA) wasn't important in human disease processes. But researchers have discovered these parts of the DNA play an important role in turning on and off the genes that code for proteins and are perhaps the most relevant items regarding diseases.
- *RNA sequencing.*[7] Another approach to genetic analysis is to look for abnormal RNA in patients. DNA codes for RNA, and in some patients the disease-causing mutation is in the resultant RNA, not the coding DNA. In some cases, for example in ADA-SCID, it has been shown that the transcribed mRNA is unstable and rapidly degrades, thus the ADA protein cannot be made. RNA analysis is also called transcriptome sequencing. This type of analysis is primarily limited to research settings, but may become commercially available in the future.
- *Chromosomal analysis.*[7] While targeted gene arrays, WES, WGS and RNA sequencing look at genes and gene products, chromosomal analysis looks at the bigger picture of the chromosomes. Humans have 46 chromosomes, 23 from each parent. This includes 22 pairs of autosomes (non-sex chromosomes) and one pair of sex chromosomes (XX in females and XY in males). Typically though, mere chromosome analysis is unable to detect a gene mutation due to the large size differences. However, for DiGeorge syndrome, fluorescence in situ hybridization studies of chromosomes can detect the hemizygosity or loss of some of chromosome 22 at position 22q11, which is diagnostic of this condition. Otherwise, chromosomal analyses have little use in diagnosing IEI.

## Final Considerations

It's important for patients considering genetic testing to know that WES, and even WGS, leave more than half of patients with a known IEI without a genetic diagnosis.[1]

In addition, one of the most frustrating outcomes of genetic testing can be findings of "variants of uncertain significance" (VUS). In this case, a genetic variant is discovered, but there isn't sufficient research to classify the variant as disease-causing (pathogenic) or benign. Sometimes when a VUS is found, patients can be enrolled in a clinical trial to help determine whether the variant is pathogenic.

It's also important to note that not all insurance covers genetic testing. The cost of testing is another important factor for patients to discuss with their doctors before embarking on this journey.

### References


1. Butte, M. Genetic Screening and Primary Immunodeficiency: Understanding the Whole Exome and Whole Genome. Immune Deficiency Foundation 2021 PI Conference Session, June 24, 2021. Accessed at www.youtube.com/watch?v=cI5a0NsPVy0.
2. The Immune System and Primary Immunodeficiency. Immune Deficiency Foundation, 2019. Accessed at primaryimmune.org/immune-system-and-primary-immunodeficiency.
3. Mauracher, AA, and Hendrickson, SE. Leveraging Systems Immunology to Optimize Diagnosis and Treatment of Inborn Errors of Immunity. *Frontiers in Systems Biology*, 2022 Jul;2. Accessed at www.frontiersin.org/articles/10.3389/fsysb.2022.910243/full.
4. Casanova, JL, and Abel, L. Inborn Errors of Immunity to Infection: The Rule Rather Than the Exception. *Journal of Experimental Medicine*, 2005 Jul;202(2):197-201. Accessed at pubmed.ncbi.nlm.nih.gov/16027233.
5. Tangye, SG, Al-Herz, W, Bousfiha, A, et al. Human Inborn Errors of Immunity: 2022 Update on the Classification from the International Union of Immunological Societies Expert Committee. *Journal of Clinical Immunology*, 2022 Oct; 42(7):1473–1507. Accessed at pubmed.ncbi.nlm.nih.gov/35748970/6.
6. IDF 2017 National Patient Survey. Immune Deficiency Foundation, 2017. Accessed at primaryimmune.org/sites/default/files/IDF%202017%20National%20Patient%20Survey%201.8.2020%20Patient.pdf.
7. Chinn, IK. Genetic Testing in Patients with a Suspected Primary Immunodeficiency or Auto Inflammatory Syndrome. UpToDate, updated May 14, 2021. Accessed at www.uptodate.com/contents/genetic-testing-in-patients-with-a-suspected-primary-immunodeficiency-or-autoinflammatory-syndrome.
8. Gilissen, C, Hoischen, A, Brunner, HG, and Veltman, JA. Disease Gene Identification Strategies for Exome Sequencing. *European Journal of Human Genetics*, 2012 May;20(5):490-7. Accessed at pubmed.ncbi.nlm.nih.gov/22258526.

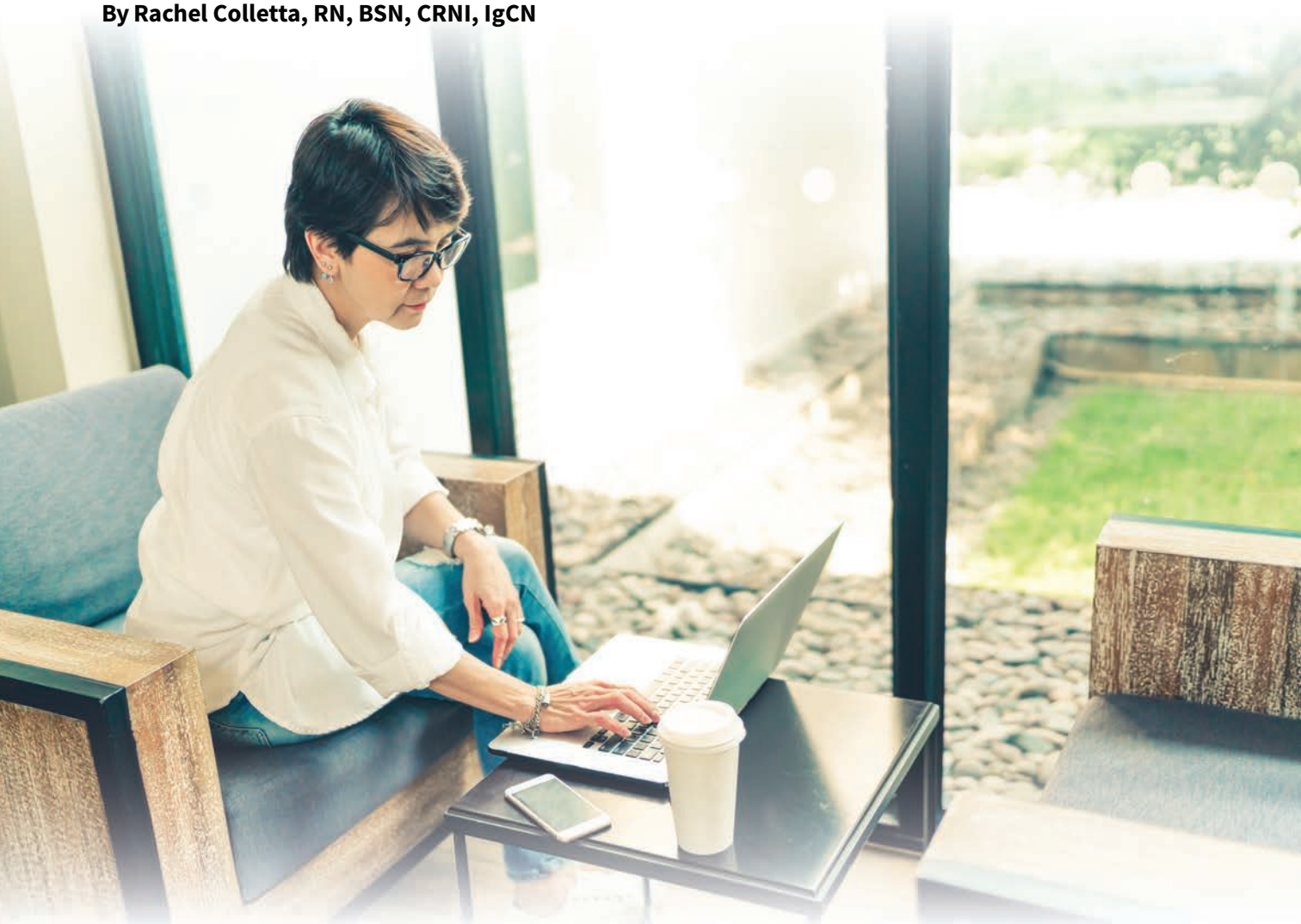


**CYNTHIA PERRY** worked in the medical device field for eight years, interviewing doctors, conducting market research and performing strategic planning work. She now writes articles, teaches classes focused on healthcare and volunteers her time to help patients obtain outstanding medical care. Cynthia has been diagnosed with multiple chronic conditions and is a breast cancer survivor.

# No More Nodding and Smiling: How to Become a Proactive Patient

Are you feeling like a passive participant in your healthcare? Now is the time to take control of your well-being and transform yourself into a proactive patient.

**By Rachel Colletta, RN, BSN, CRNI, IgCN**



**BEING A PROACTIVE** patient means you are informed, engaged and assertive. It involves asking questions, seeking second opinions and participating in treatment decisions. Instead of passively accepting whatever treatment the doctor recommends, proactive patients seek out additional information and options and speak up on their own behalf. Proactive patients move from quiet participant to vocal advocate.

Are you ready to champion your health, too? This shift in mindset can profoundly impact your well-being, allowing you to make more informed decisions and take actions that align with your values and preferences. By taking an active role in your healthcare, you can improve the quality of your care and enhance your overall well-being.

## Understanding the Role of a Proactive Patient

Passive patients attend appointments and follow doctors' orders, but proactive patients take it upon themselves to get involved in decision-making. They educate themselves about their condition, explore alternative treatment options, actively engage with their healthcare team, voicing their questions and concerns. They anticipate their own needs and don't wait for someone else to get them met.

They make it a priority to research and educate themselves, their caregivers and their family about their condition. In doing this, they help themselves and their support systems to better understand the diagnosis and treatment options, enabling them to ask informed questions and actively participate in care. Arming themselves with knowledge allows them to have more productive conversations with healthcare providers and make decisions that align with their healthcare goals.

## Let's Get Proactive!

Becoming a proactive patient is a journey that requires commitment and effort. Here are some practical steps to help you take a more active role:

1) *Educate yourself about your condition.* This is the first step toward becoming proactive. Take the time to research and understand the causes, symptoms and available treatment options. This will help empower you to ask relevant questions during your appointments and make more informed decisions.

Start by gathering information from reliable sources such as reputable medical websites, books and support groups. However, remember that not all online information may be accurate or applicable to your specific situation. Always consult with your healthcare provider for personalized advice and guidance.

2) *Establish effective communication with your healthcare provider.* Ensure you clearly express your concerns, ask questions and share relevant information about your symptoms or treatment preferences. Remember that communication is a two-way street. Listen attentively to your healthcare provider's explanations and instructions, and ask for clarification if something is unclear. Building a solid and trusting relationship with your healthcare provider not only helps meet your needs, but it can also significantly enhance your overall healthcare experience.

3) *Seek a second opinion, and explore alternative treatments.* If you have doubts about your diagnosis or treatment plan, don't hesitate to consult with another healthcare provider. A fresh perspective can provide valuable insights and help you make more informed decisions.

In addition to seeking a second opinion, consider exploring alternative treatments that align with your values and preferences. This may include complementary therapies, lifestyle changes or integrative medicine approaches. However, it's essential to consult your healthcare provider before changing your treatment plan.

4) *Keep track of your medical history and records.* This includes maintaining copies of your test results, prescriptions and other relevant documentation. Access to your medical records can help you stay informed about your past treatments, monitor your progress and share important information with your healthcare team.

Consider creating a dedicated folder or digital file to organize your medical records. This will make it easier for you to retrieve and review them whenever needed. Also, log your symptoms, treatments and any questions or concerns, which will help you stay organized and ensure no vital information slips through the cracks.

**If you have doubts about your diagnosis or treatment plan, don't hesitate to consult with another healthcare provider.**

5) *Take charge of your healthcare appointments.* This involves preparing for your visits, asking relevant questions and actively participating in the discussions. Here are some tips to help you make the most of your appointments:

- Write your questions and concerns beforehand to ensure you don't forget anything important.
- Be prepared to share any changes in your symptoms or side effects.
- Take notes during your appointments to help you remember important information.
- Don't be afraid to ask for clarification or more detailed explanations if something is unclear.

For the treatment of primary immunodeficiency in patients 2 years of age and older

# XEMBIFY offers steady protection from infection with the convenience of subcutaneous administration[1,2]

**Learn more at XEMBIFY.com**

Xembify®
(immune globulin subcutaneous human-klhw) 20%

XEMBIFY® (immune globulin subcutaneous human–klhw) is a 20% immune globulin indicated for treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older. XEMBIFY is for subcutaneous administration only.

XEMBIFY should not be used if you have had a severe allergic reaction to human immune globulin, or if you have been told by a doctor that you are IgA deficient and have developed antibodies to IgA and hypersensitivity after exposure to a previous plasma product.

## XEMBIFY Patient Speaker Programs

Join a virtual education session led by a healthcare professional to learn about PI, IG therapy, and XEMBIFY.

**Scan the code or visit XembifyPatientProgram.com to learn more and register.**

GRIFOLS

**Please see Important Safety Information for XEMBIFY on the following page.**

Xembify®
(immune globulin subcutaneous human-klhw) 20%

# Important Safety Information

**What is XEMBIFY®?**

XEMBIFY® (immune globulin subcutaneous human–klhw) is a 20% immune globulin used in the treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older. XEMBIFY is for subcutaneous administration only.

**IMPORTANT SAFETY INFORMATION**

**WARNING: THROMBOSIS**

- **Thrombosis (formation of blood clots within blood vessels) may occur with immune globulin products, including XEMBIFY. Before you take XEMBIFY, talk to your doctor if you:**
  - **Are older**
  - **Are sedentary (need to lie down or sit down) for long periods of time**
  - **Are taking estrogen-containing medicines (birth control pills, hormone replacement therapy)**
  - **Have a permanent intravenous (IV) catheter**
  - **Have hyperviscosity of the blood (diseases such as multiple myeloma or other causes of elevated proteins in the blood)**
  - **Have cardiovascular (heart) problems or previous history of stroke**
- **Thrombosis may occur even if you don't have any risk factors**
- **If you are at risk of thrombosis, your doctor may prescribe XEMBIFY at the minimum dose and infusion rate. Make sure you drink plenty of fluid before taking XEMBIFY. Make sure your doctor is checking you regularly for signs and symptoms of thrombosis and is checking your blood viscosity if you are at risk of hyperviscosity**

**Who should not use XEMBIFY?**

- XEMBIFY should not be used if you have had a severe allergic reaction to human immune globulin, or if you have been told by a doctor that you are IgA deficient and have developed antibodies to IgA and hypersensitivity after exposure to a previous plasma product

**What are possible serious side effects of XEMBIFY?**

- **Hypersensitivity.** Severe allergic reactions may occur with immune globulin products, including XEMBIFY. If you have a severe allergic reaction, stop the infusion immediately and get medical attention. XEMBIFY contains IgA. If you have known antibodies to IgA, you may have a greater risk of developing potentially severe allergic reactions
- **Aseptic meningitis syndrome (AMS).** Aseptic meningitis is a non-infectious inflammation of the membranes that cover the brain. It causes a severe headache syndrome, which may occur with human immune globulin treatment, including XEMBIFY. If you are showing signs and symptoms of AMS, your doctor may conduct a thorough neurological evaluation including spinal tap (sampling fluid which surrounds the spinal cord) to rule out other causes of meningitis. Stopping human immune globulin treatment has resulted in the end of signs and symptoms within several days. Treatment may include analgesics (pain medicines) and/or a special procedure known as a "blood patch" to stop headache
- **Kidney problems or failure.** Kidney problems or failure may occur with use of human immune globulin products, especially those containing sucrose (sugar). XEMBIFY does not contain sucrose. If you have kidney disease or diabetes with kidney involvement, your doctor should perform a blood test to assess your hydration level and kidney function before beginning immune globulin treatment and at appropriate intervals thereafter. If your doctor determines that kidney function is worsening, they may discontinue treatment
- **Hemolysis.** Your doctor should monitor you for symptoms of hemolysis (destruction of red blood cells causing anemia, or low red blood cell count). If your doctor suspects hemolysis, they should perform additional tests to confirm
- **Transfusion-related acute lung injury (TRALI).** TRALI is a rare but serious syndrome characterized by sudden acute respiratory distress following transfusion. If your doctor suspects TRALI, they will monitor you for any other lung issues. TRALI may be managed with oxygen therapy
- **Transmissible infectious agents.** Because XEMBIFY is made from human blood, it may carry a risk of transmitting infectious agents such as viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. No cases of transmission of viral diseases or CJD have been associated with the use of XEMBIFY
- **Interference with lab tests.** Because XEMBIFY contains a variety of antibodies, blood tests to determine antibody levels may be falsely elevated. Be sure to tell your doctor or lab technician that you are using XEMBIFY

**What are other possible side effects of XEMBIFY?**

- In clinical studies of XEMBIFY, some patients experienced local side effects (at the injection site) including pain, redness, puffiness, bruising, nodules, itching, firmness, scabbing and swelling at the site on the skin where the injection occurred. Some patients experienced non-injection-site side effects including cough and diarrhea.
- Use of XEMBIFY may interfere with the immune response to virus vaccines, such as vaccines for measles, mumps, rubella and varicella. Tell your doctor you are taking XEMBIFY before getting vaccinations

**Please see the full Prescribing Information for XEMBIFY at XEMBIFY.com.**

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.**

**References: 1.** Sleasman JW, Lumry WR, Hussain I, et al. Immune globulin subcutaneous, human - klhw 20% for primary humoral immunodeficiency: an open-label, Phase III study. *Immunotherapy*. 2019;11(16):1371-1386.
**2.** XEMBIFY® (immune globulin subcutaneous human-klhw) 20% Prescribing Information. Grifols.

GRIFOLS

# XEMBIFY®

## XEMBIFY (immune globulin subcutaneous, human – klhw) 20% solution

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

**XEMBIFY (immune globulin subcutaneous, human – klhw) 20% solution**

**Initial U.S. Approval: 2019**

**WARNING: THROMBOSIS**

***See full prescribing information for complete boxed warning.***

- **Thrombosis may occur with immune globulin products, including XEMBIFY. 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. Thrombosis may occur in the absence of known risk factors.**
- **For patients at risk of thrombosis, administer XEMBIFY 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 ----------**

XEMBIFY® (immune globulin subcutaneous, human- klhw) is a 20% immune globulin solution for subcutaneous injection indicated for treatment of Primary Humoral Immunodeficiency (PI) in patients 2 years of age and older.

**----------DOSAGE AND ADMINISTRATION ----------**

**For subcutaneous infusion only.**

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

**Dose**

- Switching from immune globulin intravenous (human), 10% (IVIG) to XEMBIFY: calculate the dose by using a dose adjustment factor (1.37)
- Weekly: Begin XEMBIFY one week after last IVIG infusion.
- Establish initial weekly dose by converting the monthly (or every 3 weeks) IVIG dose into an equivalent weekly dose and increasing it using a dose adjustment factor (1.37).

$$\text{Initial weekly dose (grams)} = \frac{\text{Prior IVIG dose (in grams)}}{\text{Number of weeks between IVIG doses}} \times 1.37$$

- Frequent dosing (2-7 times per week): Divide the calculated weekly dose by the desired number of times per week.
- Switching from immune globulin subcutaneous (human) treatment (IGSC): Weekly dose (grams) should be the same as the weekly dose of prior IGSC treatment (grams).

**Administration**

Infusion sites: up to 6 infusion sites simultaneously, with at least 2 inches (5 cm) between sites avoiding bony prominences. Rotate sites for each administration.

**---------- DOSAGE FORMS AND STRENGTHS ----------**

XEMBIFY is a solution containing 0.2 g/mL (200 mg/mL; 20%) protein solution for subcutaneous infusion.

**---------- CONTRAINDICATIONS----------**

- Anaphylactic or severe systemic reactions to human immunoglobulin or inactive ingredients of XEMBIFY such as polysorbate 80.
- IgA deficient patients with antibodies against IgA and a history of hypersensitivity.

**---------- WARNINGS AND PRECAUTIONS----------**

- Hypersensitivity and anaphylactic reactions may occur. IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity or anaphylactic reactions.
- Aseptic Meningitis Syndrome (AMS) may occur within two days of treatment.
- Monitor for renal function in patients at risk for renal failure.
- Hemolysis can develop. Risk factors include high doses and non-O blood group. Closely monitor for hemolysis and hemolytic anemia.
- Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
- XEMBIFY is made from human plasma and 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.
- Passive transfer of antibodies may confound serologic testing.

**---------- ADVERSE REACTIONS ----------**

The most common adverse reactions in ≥ 5% of subjects in the clinical trial were local adverse reactions including infusion site erythema (redness), infusion site pain, infusion site swelling (puffiness), infusion site bruising, infusion site nodule, infusion site pruritus (itching), infusion site induration (firmness), infusion site scab, infusion site edema, and systemic reactions including cough and diarrhea.

**To report SUSPECTED ADVERSE REACTIONS, contact Grifols Therapeutics LLC at 1-800-520-2807 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**---------- DRUG INTERACTIONS----------**

The passive transfer of antibodies may transiently interfere with the response to live virus vaccines, such as measles, mumps, rubella, and varicella.

**----------USE IN SPECIFIC POPULATIONS ----------**

Geriatric: In patients over 65 years, do not exceed the recommended dose and infuse XEMBIFY at the minimum rate practicable.

Manufactured by:
GRIFOLS
**Grifols Therapeutics LLC**
Research Triangle Park, NC 27709 USA
U.S. License No. 1871
3056462
Revised 8/2020

• Request copies of your visit summaries or treatment plans for your records.

6) *Advocate for yourself, and ask questions.* This is a crucial aspect of being a proactive patient. Don't be afraid to speak up and ask questions when something doesn't feel right or you need more information. Remember, you oversee your healthcare, and your voice matters.

If you feel your concerns are not being taken seriously or you are not receiving the care you desire, consider seeking a second opinion or discussing your concerns with a patient advocate. It's important to advocate for yourself and ensure your needs are met.

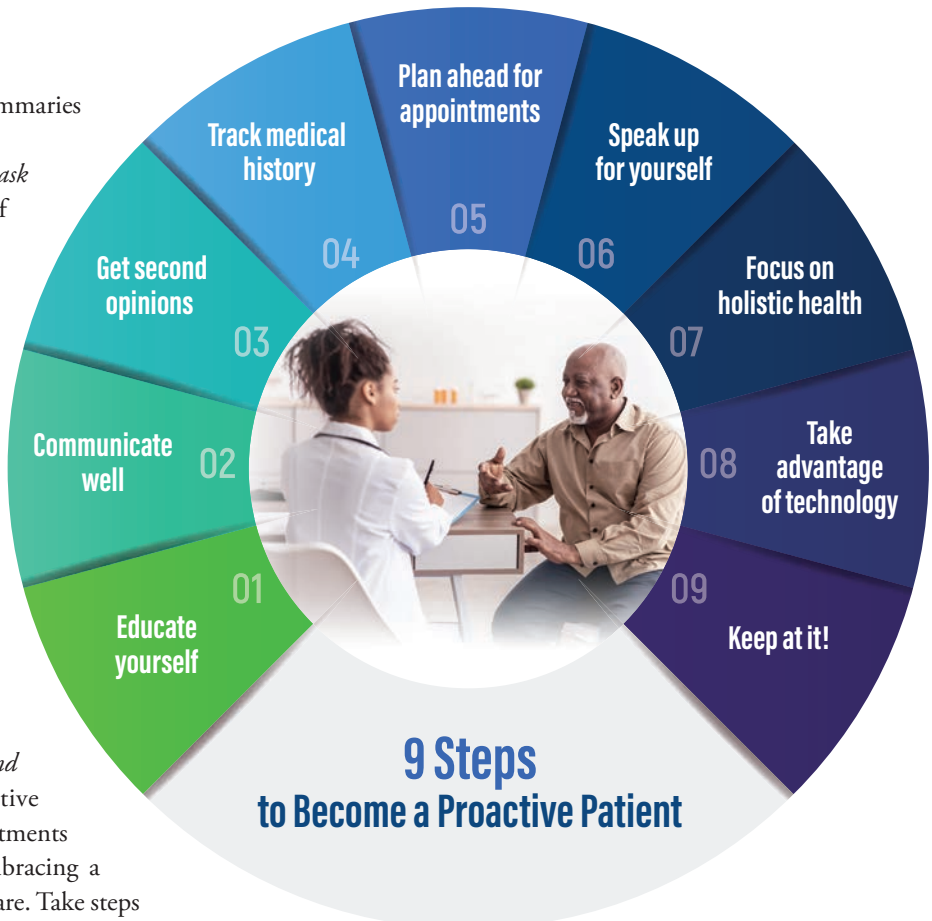
7) *Embrace a healthy lifestyle and practice self-care.* Being a proactive patient goes beyond medical appointments and treatments. It also involves embracing a healthy lifestyle and practicing self-care. Take steps to prioritize your physical and mental well-being by:

- Eating a balanced diet and staying physically active
- Getting enough sleep and managing stress
- Engaging in activities that bring you joy and relaxation
- Seeking support from friends, family or support groups
- Taking time for self-reflection and self-care activities

Remember, your overall well-being is interconnected with your healthcare journey. By focusing on your holistic health, you can support your body's natural healing processes and enhance the effectiveness of your treatments.

8) *Utilize technological resources*. In this digital age, numerous tools and resources are available to help you be a proactive patient. Utilizing these resources lets you stay informed, connected and engaged in your healthcare journey. Take advantage of them to help you manage your health more effectively. Here are a few examples:

- Use smartphone apps or wearable devices to track your symptoms, medications or vital signs.
- Explore online patient communities or forums to connect with others with similar conditions.
- Utilize telemedicine or online platforms for virtual consultations or follow-up appointments.




- Subscribe to reputable health websites or newsletters to stay updated on the latest research and treatments.

9) *Overcome challenges and stay motivated.* Becoming a proactive patient is not always easy. It can be challenging to navigate the complex healthcare system, understand medical jargon or speak up for yourself. However, you can overcome these challenges with determination, education and proper support.

**You Can Do It!**

Remember, being a proactive patient is a continuous learning process. Don't be too hard on yourself if you make mistakes or sometimes feel overwhelmed. Contact your healthcare team, support groups or patient advocacy organizations for guidance and assistance. Surround yourself with a supportive network to help you stay motivated.

**RACHEL COLLETTA**, BSN, CRNI, IgCN, is director of educational resources at the Immunoglobulin National Society.


# Preparing for Health Emergencies: A Comprehensive Guide

Unforeseen crises can arise anywhere, anytime. Are you ready to respond if they happen to you?

**By Surayyah Morris, PharmD**

**EMERGENCIES** can strike at any time, and being prepared to deal with them is essential for safeguarding your own health and well-being, that of your loved ones and even the community at large. Whether it's a sudden injury, a natural disaster, a pandemic or any other unforeseen event, having a plan in place can make all the difference. Let's explore the importance of preparing for health emergencies and provide you with a comprehensive guide on how to do so effectively.

## Reasons to Prepare

The importance of preparing in advance for emergencies cannot be overstated. It is a multi-faceted strategy that protects lives, property and communities while promoting self-reliance and resilience. Emergency preparedness:

1) *Safeguards lives and well-being*. The primary goal of emergency preparedness is to protect lives during dangerous situations. When health crises occur, prepared individuals and communities are more likely to have the knowledge, resources and infrastructure in place to respond effectively. This can mean the difference between life and death for those affected.

2) *Enables rapid response*. Health emergencies often require quick decision-making and immediate action. Being prepared in advance ensures you can respond promptly, which can be critical in life-threatening situations.

3) *Reduces stress*. Knowing what to do during an emergency — and having the means to do it — reduces stress and anxiety. People who have taken the time to develop

emergency plans and gather supplies ahead of time are better equipped to cope with the chaos and uncertainty that often accompany disasters. They are more likely to stay calm and make rational decisions, which can be crucial for personal and community safety.

4) *Conserves resources and ensures adequate supplies.* Proper preparation ensures access to essential resources such as medical supplies, food and water, enabling you to sustain yourself until you receive the help you need. It also helps alleviate the burden on community disaster relief by making more resources available to others who need it.

Health emergencies can disrupt the supply chains for essential medical equipment and medications. Preparedness efforts by hospitals and community officials, including diversifying suppliers and maintaining strategic stockpiles, can prevent shortages and ensure critical supplies are available when they are most needed.

5) *Alleviates burden on healthcare systems.* Widespread health emergencies often place an immense burden on healthcare systems. Hospitals and medical facilities may become overwhelmed with patients, which can lead to critical shortages of personnel, equipment and beds. Preparedness measures such as expanding healthcare capacity, stockpiling medical supplies and developing surge plans help alleviate this strain and ensure medical care remains available to those in need.

6) *Builds community resilience.* Emergency preparedness is not limited to individuals and families; it also extends to businesses, government agencies and essential service providers. Hospitals, utilities and emergency services must have plans in place to ensure the continuity of critical services during and after emergencies. Without proper preparedness, the functioning of these essential services can be compromised, leading to more significant challenges during the disaster and its aftermath. When neighbors, businesses and local authorities work together to prepare for emergencies, they can respond effectively and recover more quickly. This collaborative effort can save lives and resources while helping communities bounce back from the impact of disasters faster.

**Key Steps to Take**

Taking these 10 steps will ensure you are properly prepared for emergencies:

1) *Develop an emergency plan.* Create a personal/family emergency plan that outlines how you will communicate, where you will meet and what to do in different scenarios (personal health crisis, natural disaster, house fire, etc.). Establish a communication network with family members, friends and neighbors. Make sure everyone knows how to contact each other in case of separation during an emergency. Identify evacuation routes; gather and safeguard important documents such as passports, birth certificates and medical records; prepare an emergency kit; and identify local emergency resources such as hospitals, clinics and shelters, and include their contact information in your plan.

2) *Assemble an emergency kit.* Prepare a well-stocked emergency kit that includes essential items like nonperishable food, water, flashlight(s), batteries, hand-crank radio, chargers, first aid kit, medications, sanitation items, personal hygiene items and important documents (e.g., identification, insurance, medical records).

3) *Stay informed.* Set yourself up to keep abreast of potential health risks in your area, including weather-related issues, disease outbreaks, vaccination campaigns, health advisories and any threats specific to your area. Sign up for local alerts and notifications through your smartphone, community websites or news outlets. Reliable sources such as the World Health Organization, Centers for Disease Control and Prevention and the local health department can also provide valuable information.

4) *Prepare for specific threats.* Tailor your preparations to the most likely emergencies in your area. For example, if you live in a flood-prone region, purchase water pumps, tarps and sandbags.

5) *Ensure financial stability.* Health emergencies can have far-reaching consequences, not only for your physical well-being but also for your financial stability. Unexpected medical expenses, lost income and other financial challenges can quickly become overwhelming during a health crisis. To protect your financial well-being, it's essential to take steps to set aside an emergency fund to cover unexpected medical expenses. Also consider purchasing additional insurance that covers various emergency scenarios (disability, flood, earthquake, etc.).

6) *Learn essential lifesaving skills.* Brush up on basic first-aid techniques, and consider getting certified in cardiopulmonary resuscitation (CPR). CPR is a lifesaving technique used to maintain blood flow and oxygenation in a person experiencing cardiac arrest. Many health emergencies such as heart attacks or drowning incidents may require CPR. Additionally, understanding how to use an automated external defibrillator can further increase the chances of survival, as it can help restart the heart's normal rhythm in some cases.

During a health emergency, especially when someone experiences a sudden cardiac arrest or severe injury, the first few minutes are critical. Rapid intervention can make a significant impact on the individual's chances of survival. Knowing how to assess the situation, provide basic first aid and perform CPR can bridge the gap until professional medical help arrives. You can step in and take action when needed, improving the chances of a positive outcome. Check out www.redcross.org/take-a-class for some great training options.

7) *Prioritize health and hygiene.* Remember that a strong immune system and overall good health are essential. Focus on maintaining a balanced diet, exercising regularly and getting enough rest so you are in good health and able to respond if an emergency does strike.

Maintaining good hygiene is challenging during an emergency, so ensure you have access to clean water for drinking and sanitation. Make sure your emergency kit contains personal hygiene items, including feminine hygiene items, wipes, soap, hand sanitizer and disinfectant. In the event of a widespread emergency, follow recommended hygiene practices to reduce the risk of infection such as regular handwashing and wearing masks.

8) *Review and update your plan regularly.* Emergency plans should not be static. Emergency plans and kits should be periodically reviewed and updated to account for changing family needs and any new potential threats. Make changes as your family's needs evolve or as new information becomes available to ensure it remains relevant and effective.

9) *Protect vulnerable populations.* Health emergencies disproportionately affect vulnerable populations such as the elderly, the immunocompromised and those with limited access to healthcare. Preparedness measures should also include identifying and protecting these groups by providing targeted support and ensuring equitable access to resources.

10) *Support your community.* Preparing for health emergencies goes beyond the immediate response. Engage with local community groups and emergency services to contribute to community resilience efforts. Connect with local organizations to establish a support network to provide assistance, share resources and offer emotional support when needed. Volunteer if you can. It involves building resilience within communities and healthcare systems to withstand future crises. This resilience can prevent the same vulnerabilities from being exploited again.

## Be Ready to Respond

Preparation for health emergencies is an ongoing process that requires time and commitment. While we cannot predict the exact nature of future emergencies, we can control how we respond to them. By following the steps outlined in this guide, you can increase your readiness, reduce stress and help protect yourself and your loved ones when health emergencies strike. Remember, being prepared is not just a personal responsibility; it contributes to the overall resilience of your community and society as a whole.

From individuals and families to businesses and governments, everyone has a role to play in preparing for the unexpected. By making preparedness a top priority, we can minimize the impact of emergencies and ensure a safer, more secure future for ourselves and our communities. IG

**SURAYYAH MORRIS**, PharmD, is an IG patient from Central Florida. As a medication therapy management and pain management specialty pharmacist, she enjoys supporting patients with chronic pain and chronic conditions to help find balance and improve quality of life.

nufactor®
A SPECIALTY INFUSION COMPANY

# Making a difference one patient at a time

## Specialty Solutions in Chronic Care

*Immune Globulin | Factor | Infliximab*

Nufactor Specialty Pharmacy has earned The Joint Commission Gold Seal of Approval

URAC ACCREDITED Specialty Pharmacy Expires 03/01/2024

URAC Specialty Pharmacy

**For more information**

**Phone: (800) 323-6832**
**Referral Fax: (855) 270-7347**
**www.nufactor.com**

# Tips to Reduce Sodium Without Sacrificing Flavor

Here are six ideas for making a lower-sodium diet delicious.

**By Emily Cooper, RDN**

**WHETHER YOU** are looking to cut back on sodium for a specific health condition or simply for the sake of your overall health, consuming less salt doesn't have to mean eating boring and bland foods from here on out.

The American Heart Association (AHA) recommends adults consume between 1,500 mg and 2,300 mg of sodium per day.[1] For perspective, one teaspoon of table salt contains 2,325 mg of sodium! AHA recommends that those with high blood pressure stick to the lower limit of 1,500 mg of sodium per day. A diet high in sodium can increase the risk of high blood pressure, heart attack and stroke.[1] With that in mind, everyone should pay attention to how much salt they consume!

Cutting back on sodium can be a little challenging at first, but it doesn't have to be for the long run. With the right tips and tools, enjoying a lower-sodium diet can easily fit into most any lifestyle. Here are six simple ways to reduce your salt intake, but still enjoy flavorful, delicious meals.

### 1) Skip the Salt Shaker

The first step to cutting back on sodium is to take the salt shaker off of the kitchen table. A study from the *European Heart Journal* found that a higher frequency of adding salt to foods was associated with premature death and lower life expectancy.[2]

If you are used to adding salt to most of your meals, skipping an extra dash of salt may be easier said than done, since it can be an automatic habit. But remember: Sprinkling table salt on top of your food adds extra sodium to meals or dishes that don't necessarily need it. As you consistently skip that extra dash of salt, your tastes will change and get used to lower amounts of salt in the things you eat.

If you really struggle to kick the salt shaker habit, some low-sodium salt substitutes can be used instead. However, be aware that some of these seasoning blends are high in potassium, which can be a problem for those with kidney-related health issues. It is best to check with your healthcare provider before trying a salt substitute to make sure it is right for you.

Tip: When sitting down to eat, make it a new habit to taste your food first, and then decide if it needs a little bit more flavor. Add additional table salt sparingly.

### 2) Swap Herbs and Spices for Salt

One of the best ways to bump up the flavor of your food is by cooking with herbs and spices. Most of them are naturally sodium-free and are an easy way to add tons of flavor without also adding extra fat or calories. If you're new to cooking or seasoning your food with herbs and spices, try some dry seasoning blends (available at major grocery stores) before experimenting with your own. Make sure to read the label to double check it doesn't contain any added salt.

Tip: Herbs and spices are delicate and must be handled with care for best flavor results.

• Keep dried herbs and spices away from heat. Store them in a cool, dry place to help their flavor last longer.

• Fresh herbs are best added when cooking is nearly done or ready to serve, since prolonged cooking can destroy their flavor.

• Dried herbs are more powerful than fresh herbs. If using dry herbs instead of fresh herbs (when following a recipe that calls for fresh), cut back on the amount you use. (Rule of thumb: Use 1 teaspoon of dried herbs for every 1 tablespoon of fresh herbs.) Unlike fresh herbs, you can add dried herbs earlier on when cooking, unless your recipe states otherwise.

• Start with small amounts, especially if the herb you are using is a new flavor for you. It is always possible to add more later, but you can't take it out if you add too much.

• Read labels. Some dried herbs and spices may contain salt. Some examples to be on the lookout for are chili seasoning, lemon pepper and taco seasoning.

### 3) Add Aromatics

What exactly are aromatics? Like their name implies, aromatics are ingredients that emit a wonderful aroma when cooked. Not only do they make your kitchen smell delicious, but they can add a wonderful flavor to your dish without the need for extra salt. Some common aromatics include onions, garlic, celery, carrots, bell peppers and ginger.

Tip: Try these classic aromatic combinations:

• Cajun/Creole holy trinity: onions, green bell peppers and celery. This is most commonly used in gumbo and jambalaya.

• Chinese holy trinity: garlic, scallions and ginger. This is often used in stir-fries.

• French mirepoix: onions, leeks, carrots and celery. This is often used in soups or roasts.

• Spanish sofrito: onions, garlic, tomato and bell peppers. This can be used in paella, rice dishes, black beans, stews and sauces.

### 4) Experiment with Acidity

Another way to add a layer of flavor without salt is with acidity. Adding something acidic to a dish tends to brighten its flavor. This can come in the form of a splash of vinegar or a squeeze of citrus. Different vinegars or citrus fruits also bring a different flavor profile with them: Apple cider vinegar tastes different than balsamic or red wine vinegar, and limes taste different than lemons. Play with which acid pairs best with the dishes you cook.

Tip: Here's how to use acid:

• Add a splash of your favorite vinegar toward the end of cooking soups, stews or tomato sauce.

• Use vinegar to make a quick salad dressing or sauce, or to pickle your favorite vegetable.

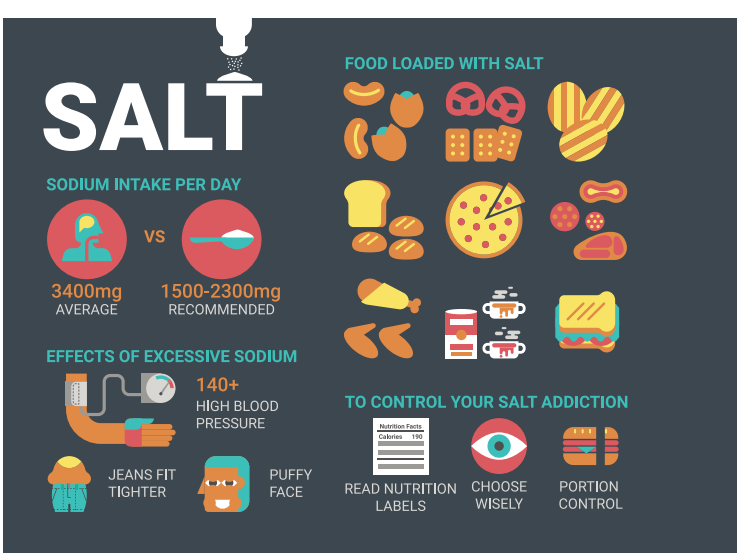
• A squeeze of fresh citrus is a perfect finishing touch for tacos, pasta or seafood, and it brightens up a homemade salad dressing.

• Add some zest from a citrus fruit to really pump up the flavor.

### 5) Cook in New Ways

If you tend to cook your veggies, meats and grains in the same exact way, changing up your cooking method can add another layer of flavor you haven't experienced before. For example, if you usually steam asparagus or poach fish, try roasting them instead. Simple cooking swaps can boost the flavor of almost any meal.

Tip: Here are three ideas for changing up your cooking method:



HyQvia

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


## What is HyQvia®?

HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] is a liquid medicine that is given under the skin (subcutaneously) to treat primary immunodeficiency (PI) in people 2 years and older.

## IMPORTANT SAFETY INFORMATION

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

- HyQvia can cause blood clots.
- Call your healthcare professional (HCP) 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 HCP may perform blood tests regularly to check your IgG level.
- Do not infuse HyQvia into or around an infected or red swollen area because it can cause infection to spread.

### Who should not take HyQvia?

Do not take HyQvia if you:

- Are allergic to IgG, hyaluronidase, other blood products, or any ingredient in HyQvia.

### What should I avoid while taking HyQvia?

- HyQvia can make vaccines (like measles/mumps/rubella or chickenpox vaccines) not work as well for you. Before you get any vaccines, tell your HCP that you take HyQvia.

### What should I tell my HCP before I start using or while using HyQvia?

Tell your HCP 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. It is not known whether HyQvia can harm the unborn baby or breastfed infant.

### What are the possible or reasonably likely side effects of HyQvia?

**HyQvia can cause serious side effects. If any of the following problems occur after starting HyQvia, stop the infusion immediately and contact your HCP or call emergency services:**

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of irritation and swelling of the lining around your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms, 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.

# Meet the only monthly* subQ IG treatment and say hy to more of what you love.

## **0.025 infections** per year

This is equivalent to 25 acute serious bacterial infections (ASBIs) out of 1,000 patients over the course of the 12-month study period.

The FDA standard for efficacy—that is, if an immunoglobulin works—is less than 1 ASBI per year. In the clinical trial, people taking HyQvia experienced significantly less than that.

## **0 days** in the hospital per year

There was a mean of 0.037 days spent in the hospital due to infection during the study.

## **<4 days** off work or school per year

On average, patients taking HyQvia missed 3.31 days of work or school due to an infection.

- HyQvia was studied in a clinical trial of 83 people with PI, with the main goal of measuring how many acute serious bacterial infections (ASBIs) they experienced over the course of 1 year
- ASBIs are short-term but serious infections caused by bacteria that require immediate medical care
- ASBIs included 2 episodes of pneumonia, both treated as outpatients with oral antibiotics. An additional episode of pneumonia requiring hospitalization occurred during the ramp-up
- The most common general (systemic) side effects were headache, antibody formation against hyaluronidase (Hy), fatigue, nausea, fever, and vomiting. The most common side effects at the infusion site (local) were pain, redness, swelling, and itching

*Between infusions, based on administration every 3 or 4 weeks.
subQ IG=subcutaneous immune globulin.

## IMPORTANT SAFETY INFORMATION (continued)

- Chest pain or trouble breathing, blue lips or extremities. These could be signs of a serious heart or lung problem.
- Fever over 100°F. This could be a sign of an infection.

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 possible side effects may occur at the site of infusion and generally go away within a few hours, and are less likely after the first few infusions.

- Mild or moderate pain
- Redness
- Swelling
- Itching

The most common side effects of HyQvia are:

- Headache
- Fatigue
- Nausea
- Fever
- 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 hyaluronidase (PH20). PH20 is present in the male reproductive tract. So far, these antibodies have not been associated with increased or new side-effects.

**These are not all the possible side effects. Talk to your HCP about any side effect that bothers you or that does not go away.**

***Please see Important Facts about HyQvia on the following 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.**

## Up to 100% of out-of-pocket co-pay costs could be covered.

Scan the QR code to learn more about HyQvia, including co-pay costs.



Takeda

# IMPORTANT FACTS about HYQVIA (Hi-Q-via) [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] Solution, for subcutaneous administration

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

- HYQVIA can cause blood clots.
- Call your healthcare provider (HCP) 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 HCP may perform blood tests regularly to check your IgG level.
- Do not infuse HYQVIA into or around an infected or swollen area because it can cause infection to spread.

## What is HYQVIA?

HYQVIA is a liquid medicine containing immune globulin and Recombinant Human Hyaluronidase. HYQVIA is given under the skin (subcutaneously) to treat primary immunodeficiency (PI) in people 2 years of age and older. 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.

## What should I tell my HCP before I start using or while using HYQVIA?

Tell your HCP 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 breastfeeding. It is not known whether HYQVIA can harm the unborn baby or breastfed infant.

## Who should not take HYQVIA?

- Do not take HYQVIA if you are allergic to IgG, hyaluronidase, other blood products, or any ingredient in HYQVIA.

## How should I take HYQVIA?

- HYQVIA is infused under the skin (subcutaneously) up to once every 4 weeks.
- You can get HYQVIA at your HCP's office, clinic, or hospital.
- You can use HYQVIA at home. You and your HCP 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
- Itching

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

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 HCP 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 irritation and swelling of the lining around your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.
- Pain, swelling, warmth, redness, or a lump in your legs or arms, 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 serious heart or lung problem.

These are not all of the possible side effects for HYQVIA. You can ask your HCP for information that is provided to HCPs. Talk to your HCP about any side effects that bother you or that don't go away.

## How do I store HYQVIA?

Store HYQVIA refrigerated or at room temperature.

- You can store HYQVIA in the refrigerator (36°F to 46°F [2°C to 8°C]) for up to 36 months.
- You can store HYQVIA at room temperature (up to 77°F [25°C]) for up to 3 months during the first 24 months from the date of manufacturing (Mfg Date) printed on the carton.
- Do not return HYQVIA to the refrigerator if you take it out to room temperature.

Check the expiration date on the carton and vial label. Do not use HYQVIA after the expiration date.

Do not freeze.

Protect from light. You can use the original HYQVIA containers to protect it from light.

## How do I get more information about HYQVIA?

The risk information provided here is not comprehensive. To learn more, talk about HYQVIA with your HCP or pharmacist. The FDA-approved Full Prescribing Information, including Information for Patients, can be found at www.HYQVIA.com or by calling 1-877-TAKEDA7 (1-877-825-3327).



US-HYQ-0299v4.0 06/23

• *Grilling*. Firing up the grill, no matter what season, can bring on the flavor. Grilling adds a smoky flavor and crispy texture to just about anything. The usual meats such as chicken or beef are great for the grill, but so are other foods such as fresh fruits and vegetables and even pizza!

• *Roasting*. Roasting gives food a crispy golden texture and brings out its natural sweetness. If you're used to steaming or boiling your vegetables, try roasting them in the oven instead. This helps make them crispy on the outside and gives them a sweet, caramelized flavor throughout. Roasting meats such as chicken, pork or fish leaves them juicy on the inside, but crispy and delicious on the outside.

• *Use broth*. While using a low-sodium broth for cooking may add some sodium initially, it will save you from adding a lot more later on. Cooking grains such as rice, quinoa or barley in low-sodium chicken or vegetable broth instantly adds more flavor to them. You can even throw in some fresh or dried herbs or a squeeze of lemon juice at the end of cooking.

### 6) Beware of Hidden Sodium

Certain foods are notorious for being high in sodium such as frozen, prepared meals, canned soups, deli meats, chips and pretzels. Buying lower-sodium varieties of these foods, or limiting how often you eat them, can be a way to cut back on salt. But some foods with high sodium content are surprising. While they may not taste salty, their high sodium content is cause for caution.

Tip: Read nutrition labels before purchasing or consuming processed foods, paying close attention to sodium content per serving. Twenty percent of the daily value is considered high.[3] Here are some common culprits to pay attention to:

• *Bread*. On average, one slice of prepackaged bread contains 200 mg of sodium, about nine percent of the daily limit. That may not seem like a lot, but adding an additional slice doubles that amount. If you make a sandwich with deli meats and cheese and serve it with a side of chips, your lunch is easily turned into a high-sodium meal. Shop for a bread that has around 100 mg, or five percent of the daily limit for sodium instead.

• *Poultry*. Chicken is a popular lean protein, but it can be a hidden source of sodium. Raw chicken is sometimes injected with a salt water solution to keep it juicy when cooked. Check the label on your chicken, and look for options that contain 70 mg of sodium per serving or less.

• *Condiments*. Soy sauce may be the first condiment to come to mind when thinking of high-sodium sauces, but many other common sauces are sources of hidden sodium, too. Pasta sauce can have upwards of 20 percent of the daily limit of sodium per one-half cup serving. Other salty condiments include bottled salad dressings, ketchup, barbecue sauce, teriyaki sauce and salsa. Read the labels to choose options with less sodium.

• *Dairy products*. Dairy foods are natural sources of protein and calcium, but some can also contain more salt than you might expect. Cottage cheese has an average of 300 mg, or 13 percent of the daily sodium limit, per one-half cup serving. Certain varieties of cheese such as feta and parmesan are also higher in sodium, while lower-sodium cheese options include mozzarella, swiss and ricotta.

• *Sports drinks and sodas*. These beverages are known for their high amounts of sugar, but they are also secretly a source of sodium. Sports drinks are designed to replace electrolytes lost during exercise or activity, which is why they contain sodium. If you're drinking these when not exercising, remember: The average bottled sports drink has 380 mg of sodium, or about 17 percent of the daily limit! Sodas don't contain as much sodium (about 40 mg or 2 percent of the daily limit in one can), but this amount can easily add up if drinking multiple servings in a day.

### Less Sodium, Lots of Flavor

If you are looking to cut back on sodium in your daily diet, rest assured there are plenty of ways to add flavor to just about any meal or dish. Experiment with new flavors, embrace aromatics and acidity and give a different cooking technique a try. Start slowly so you don't get overwhelmed; try one new idea per week. That, along with being aware of what foods and drinks may contain hidden sources of sodium, are small, helpful ways to make different choices that will help you reach your goals. Remember, habits are hard to break! Take this lower-sodium journey one step (or shake) at a time.


### References

1. American Heart Association. Why Should I Limit Sodium? Accessed at www.heart.org/-/media/files/health-topics/answers-by-heart/why-should-i-limit-sodium.pdf.
2. Rosengren, A. Salt: The Sweet Spot? *European Heart Journal*, 2022 Aug;43(30):2889-2891. Accessed at academic.oup.com/eurheartj/article/43/30/2889/6623279.
3. U.S. Food and Drug Administration. Sodium on the Nutrition Facts Label. Accessed at www.fda.gov/food/nutrition-education-resources-materials/sodium-nutrition-facts-label.



**EMILY COOPER**, RDN, is a nationally recognized registered dietitian, health writer and recipe developer based in New Jersey. She is the author of *Mediterranean Diet on a Budget* and the website sinfulnutrition.com

# *Profile:* Vanda Vanover Kercher

By Trudie Mitschang

*After suffering sinus, stomach, lung and urinary tract infections, as well as gastrointestinal issues, since childhood before finally being diagnosed with CVID at 60 years old, Vanda wishes she had pushed harder for an earlier diagnosis and encourages others to do so.*

**AS A CHILD**, Vanda Vanover Kercher was often sick, frequently missing school. Later as an adult, her poor health caused her to miss work and social functions. Thankfully, Vanda's recent diagnosis of common variable immune deficiency (CVID) has finally given her answers to questions that years of doctor visits could not seem to provide. Today, this resilient 60-year-old is optimistic that her new infusion regimen will begin to restore her energy and quality of life.

**Trudie:** What were your symptoms leading up to your diagnosis?

**Vanda:** Since childhood, I remember always being sick. I was sent home frequently from school with a cold, chronic cough and runny nose. Unfortunately, I was never taken to the doctor. I think my mom, a single parent of six and living on a very limited income, believed my symptoms were caused by allergies and did not warrant a trip to the doctor. As an adult, I was able to afford medical care; however, looking back, I was always at the doctor's office. I was prescribed course after course of antibiotics for what was believed to be sinus, stomach, lung and/or urinary tract infections. I recognized I was always sick. I accepted chronic sickness as the result of pushing my way through 12- to 14-hour workdays in a very stressful career. Allergies was another common self-diagnosis. I missed work frequently but my bosses, pleased with my work and my long-term employment, found ways to accommodate me.

**Trudie:** Tell us about your diagnostic journey.

**Vanda:** I was finally diagnosed in September 2023 at age 60. I was initially referred to an immunologist in 2020 by my primary care physician based on my blood work and history of chronic infection. At this point, I was unable to even control my bowels when I coughed or sneezed. The immunologist had my blood drawn and recognized I was severely vitamin D- and B12-deficient, and before he could help me, I would need a gastroenterologist. The gastroenterologist diagnosed me with pernicious anemia and autoimmune gastritis (AIG). The good news was that in the process, they found a hernia and surgically repaired it, correcting my inability to control my bowels. That was a relief. Once my anemia and AIG were stabilized, I was referred to a new immunologist. I waited six weeks for his next available appointment only to learn on my first visit that he was leaving this practice for another one. Argh!! He drew my blood and referred me to another immunologist.

**Trudie:** What happened next?

**Vanda:** I was able to review my blood work online and could see that my IgA, IgG and IgM levels were extremely low, with a note that said "no surprises here." They suggested I get another pneumonia vaccine and another round of blood work in six weeks. I was frustrated with this response, especially since it was a surprise to me! I could tell this doctor was not vested in my health since he was leaving. Expecting another six-week delay, I immediately made an appointment with a new immunologist.

**Trudie:** How did you learn it was CVID?

**Vanda:** While I was waiting to see the new doctor, I began researching what my blood results meant, associated diseases and why I needed another pneumonia vaccine. I learned the purpose of the titer blood test and, in the process, I found out about CVID and if that is what I have, everything lined up. When the titer blood test showed I was still not protected from pneumonia even after two vaccines, it confirmed this diagnosis.

**Trudie:** Did you click with your new doctor?

**Vanda:** My new immunologist is wonderful! Within a week of diagnosis, nurses were being lined up to begin

the subcutaneous immune globulin (SCIG) infusions. The diagnosis process was long and frustrating for me and, at times, very discouraging. I had self-doubt about my own symptoms. Autoimmune and immunodeficiency are diseases that, unless you have them, you can't understand. I have had two infusions so far. My fingers are crossed that I will at least be able to build up my immune system to be around family and friends or attend a special occasion. I am truly grateful for those who donate their plasma; there are many people who are dependent on their time and commitment.

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

**Vanda:** I will use inhalers, take an every-other-day antibiotic and have a weekly SCIG infusion for the rest of my life. I also take a handful of other medications throughout the day and evening.

**Trudie:** How has living with chronic illness impacted your personal life and career?

**Vanda:** I can no longer sustain my 42-year career of leading people and building teams because any exposure to sickness could land me (and has landed me) in the emergency room with pneumonia. My autoimmune gastritis, besides digestive concerns, prevents me from absorbing vitamins B12 and D, causing me to struggle with fatigue, weakness and anemia. On top of that, Hashimoto's disease taps into my energy level. I have become a prisoner in my own home. I have had the opportunity to take some amazing vacations but would always become sick while traveling or paid the price when I got home. I just can't take those chances anymore. Every time I hear about someone's travels, they end up with COVID. I have been unable to attend family events, parties, anything that involves a crowd. My social interactions have depended on friends coming to visit me at my house and, I can tell you, those visits really mean a lot to me.

**Trudie:** Are you part of any support groups?

**Vanda:** I recently joined two CVID Facebook groups. I did this so I can learn about CVID from others. From reading their comments, I feel I have found "my people." It's encouraging to interact with others who have health challenges similar to mine.

**Trudie:** How is your health today?

**Vanda:** I like to think of myself as healthy but, in reality, I am not. I must accept the cards I have been dealt. Sometimes life has a way of slowing you down, and I am learning to listen to what my body is telling me. I have been humbled just learning to depend on or even accept help from others. Perhaps my life is just being redirected. I am hoping the SCIG will build my immune system strong enough to at least allow me to interact socially again with family and friends, maybe attend church, watch my nephew's football game — the normal things in life.

**Trudie:** What has this experience taught you about yourself?

**Vanda:** I realize that I was overly hard on myself when I would miss work or let someone down because I was sick. I pushed through the fog of being constantly sick and weak because I knew people were counting on me. I should have realized that how I was feeling was not normal, put myself first and pushed my doctors for more answers instead of just accepting another antibiotic.

**Trudie:** How important is it to be your own healthcare advocate?

**Vanda:** It is critical that you be an advocate for yourself instead of just accepting another round of antibiotics. I wish I would have pushed my doctors for better answers to my chronic health problems. I could have been diagnosed much sooner.

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

**Vanda:** I try to be as independent as I can because this helps me feel better about myself. I like to find the strengths in myself and focus on those.

**Trudie:** What do you wish family and friends understood about your condition?

**Vanda:** I don't want them to be afraid to come see me because they are afraid they may get me sick. I spend much of my time in isolation and enjoy a planned visit provided they are not sick themselves. I am hoping that with a few months of the SCIG infusions, I will have a strong enough immune system and will be able to go see them. I want my friends and family to know I appreciate them, especially those who have checked up on me.

**Trudie:** What advice do you have for others newly diagnosed or living with chronic illness?

**Vanda:** Stay as positive and optimistic as possible. Focus on the things you *can* do. Push yourself, but don't be *too* hard on yourself if you come up short.

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

# Should You Live Alone?

By Michelle Searle

**FOR SOME,** living alone might sound like an absolute dream. For others, it sounds like a nightmare. Maybe you've spent your whole life sharing your room with siblings and can't wait to have your own space where you can make all the decisions. Or maybe you've spent your entire life living with others, and the thought of living alone scares you.

Everyone has their preference about living alone, and if you haven't figured out yours yet, I'm sure you will in your 20s. And, even if you already have a preference, it might change over the years. When I first went away to college, I loved living with my roommates! I wouldn't have had it any other way. I was one of the fortunate ones who went to a college that didn't have shared bedrooms, only shared apartments, which made the experience more enjoyable. But, over the years, I had my fair share of terrible roommates who made me want nothing more than to live by myself. So, after nine years of living with roommates, I finally rented a one-bedroom apartment for eight months and lived alone. It was incredible!

I'm a very clean and organized person who likes to go to bed early and wake up early. But for years, I lived with roommates who wouldn't clean, but who would throw parties, smoke in the house, ruin my kitchenware, steal my stuff — you name it, they did it! For example, one day, I walked into my room and found dog poop on my bedroom carpet. I didn't even own a dog! I had experienced so much stress, anxiety and anger living with bad roommates over the years that once I finally lived alone, the loneliness didn't bother me. Even when I lived with other people, I often felt lonely because I didn't like the people I was living with. At least once I lived alone, I no longer felt the stress, anxiety, awkwardness and anger I used to feel.

I recently moved to New York from Italy, and my fiancé and I got an apartment together. I enjoyed the last eight months of living alone, but now I'm enjoying living with my partner. It's been a lot of fun to live with one of my best friends, but it hasn't come without its challenges. I've had to get used to the apartment not looking exactly how I leave it or exactly how I want it. For the first time in my life, I'm sharing a bedroom with someone and can no longer call a space completely mine. Once again, I must be considerate of when I want to listen to music or a podcast or watch TV in the living room. I'm just thankful we're not living in a studio apartment!

But living alone comes with its own set of necessary adjustments, too. For instance, when living with others, you may have had help bringing your groceries home, and now that's a task you have to figure out how to do by yourself. If you're like me and have a huge fear of bugs, living by yourself means you're left alone to deal with the bugs instead of turning to roommates to kill them for you. Having a good relationship with your neighbors and landlord can help in this situation. Luckily for me, while I was living alone, my landlord lived below me and we had a good relationship, so he would come to pick up a dead cockroach that I didn't have the stomach to get on my own.

Another consideration if you're contemplating living alone is how it will affect your chronic illness. I've talked to some people who self-infuse and are afraid to live alone or infuse when their partner isn't home in case something happens. I've also been in situations in which I was too sick to go to the grocery store to buy food and drinks. If I didn't have good roommates, I would call friends who lived nearby to help. I've learned to prepare for these moments by making sure I have what I might need if I get a migraine or fever after an infusion or if I suddenly don't feel well enough to cook or go grocery shopping. Even today, I try to always make sure I have food or premade meals in the freezer such as a frozen pizza that can easily be warmed up in case I'm suddenly not feeling well enough to cook.

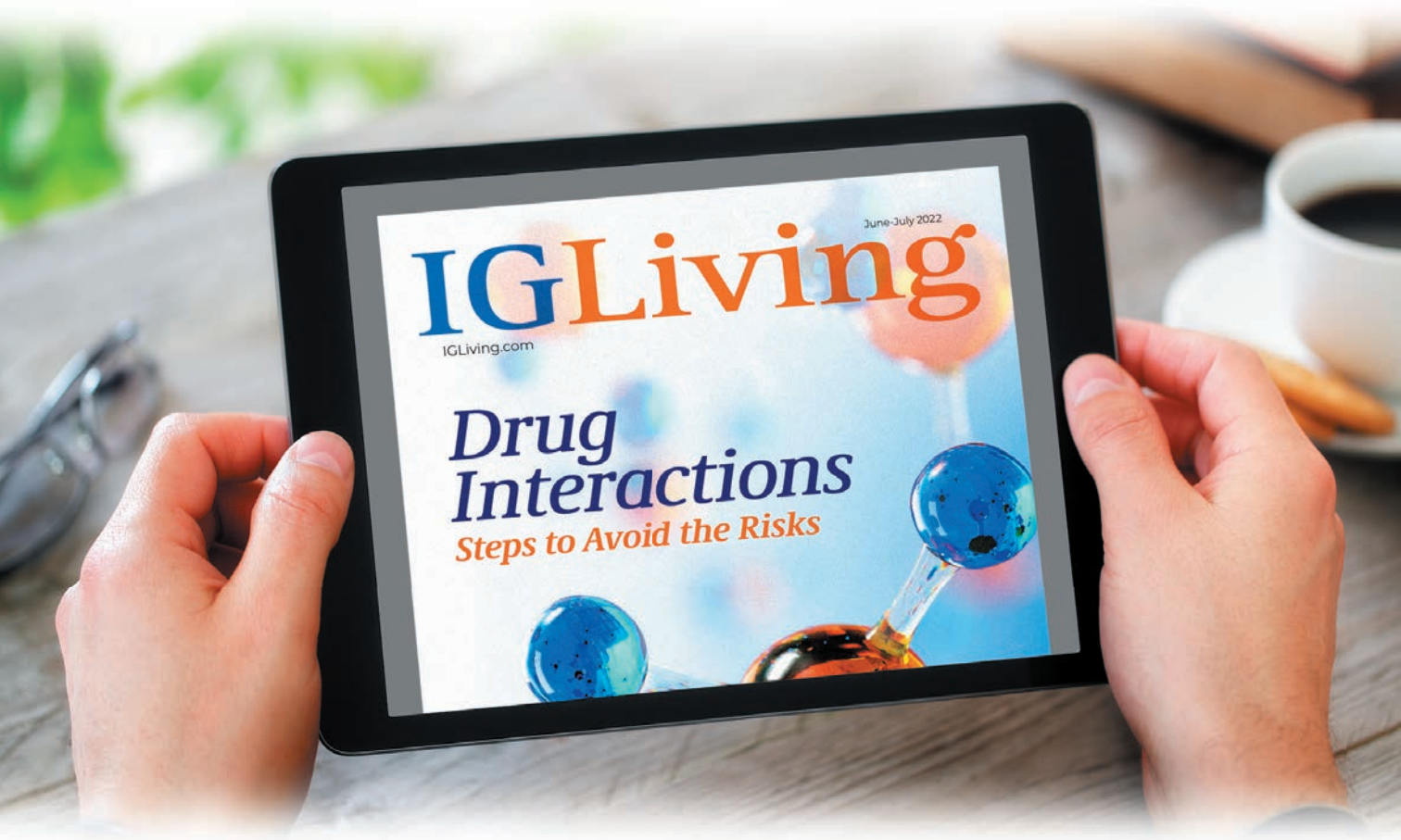
Everyone has their preference about whether or not to live alone, because everyone's situation is different. Whether you're debating about whether to move out of your parents' house to become more independent or you're sick of living with roommates and want to get your own apartment, there are a lot of issues to consider, especially if you have special needs because of your health.

**MICHELLE SEARLE** is a teacher from South Florida who was diagnosed with common variable immunodeficiency at 11 years old. She is currently living in New York where you will most likely find her eating pizza or trying to make friends with the local cats.

# Help IG Living Magazine *Go Green*

## Join our campaign to reduce unnecessary paper consumption!

**Here's how you can help:** If you can forgo receiving a hard copy of the magazine and utilize the digital version instead, go to **www.IGLiving.com** to select the Go Green tab to sign up for the electronic version and opt out of the print version.




### The Benefits of Going Digital for You!

- Enjoy earlier access to every new issue weeks ahead of receiving the print version by mail
- Print copies of individual articles easily to keep or hand out to friends, family and care providers
- Share articles instantly on Facebook
- Read the issues anywhere at any time on all of your digital devices (smartphone, computer, iPad, tablet)
- Quickly access all published articles in IG Living's Archives
- Receive an email reminder when every new digital issue is available

# For I Know the Plans I Have for You

By Whitney L. Ward

**WHEN PEOPLE** think of miracles, sunshine, daisies and rainbows most often come to mind. But sometimes miracles don't come in perfectly wrapped packages with beautiful bows on top. Many times, a miracle comes with pain, trauma and a messed-up plan. So how do we still believe in Jeremiah 29:11 ("For I know the plans I have for you...") — one of the most quoted Bible verses in the world? How do we still trust the plans God has for us are good?

It can be difficult to believe what the good book says, and I for one learned that when I spent three weeks in the hospital at the National Institutes of Health (NIH). But, thankfully, I have also learned that it's OK to question God's plan because he has the answer. During the three weeks I was at NIH, I clung to the signs and confirmations I saw that reminded me to keep going to find the plans that would prosper me and would give me hope for the future.

*1) Keep divine appointments close to your heart.* The first week I was admitted at NIH, I received an email message from a woman I had never met. Her son was also a rare disease patient at NIH and he had just surpassed his 100th day posttransplant. One day after her son's appointments, she went to the NIH bookstore, and her eyes happened to connect with my book, *MORE Than My Mountains*. After reading the first few pages, she decided to buy it. And after reading it, she emailed me and found me on Facebook, where she discovered we were both at NIH! She asked if we could meet, and we did; it was the most precious meeting I have ever been a part of. I asked her how she heard about my book. Since we had the same NIH team, I thought maybe one of my nurses or doctors told her about it. But I was in for a surprise: "Oh, I was just browsing the bookstore. I had no intention of buying anything because I had brought a book with me from home, and I have been too antsy to read it. But, somehow, my eyes connected with your book, and I started reading the first few pages. I knew I had to buy it, and I read it in two days. It has helped me so much through this journey with my son."

Wow! It was in that moment that God reminded me that even in the seasons when we feel stuck and isolated, he is still using us for his greater good.

*2) Take the time to grieve, and know it's OK to say, "This setback affects me."* When I went to NIH on August 11, I knew there was a chance I would be there until August 26. But I also knew I needed to be home by August 26 at the latest because on August 27, I was hostingg a party for the Sunday School class I taught, honoring the kids who were moving up to the next class. So, when my NIH team came into my room to brief me on the plan, they gave me the sad news that I would be staying in the hospital past August 26 so they could conduct the necessary tests to figure out what type of infection my body was battling.

This news hit me hard, and my tears began to flow. I looked at my team who had tears in their eyes from watching me get so upset, and explained why I was crying: "I'm OK," I told them, "It's just hard because it's one more thing I have to miss. I handle it all so well, so people don't think it affects me, but it does. But I'll adapt, like I always do."

I cried the whole afternoon, grieving for the trauma my body was going through and the trauma of yet again missing out on a memory because of my chronic illness. I grew up during a time when emotion and grieving were looked at by the church as complaining and not "joyfully" facing trials as Apostle Paul said to do. But I learned that's not what Paul meant at all. Paul meant that we should not focus on our trials so much that we quit. Admitting we're hurting and crying aren't weaknesses or a plea for attention or pity. Look at how many times King David cried out to God, and he was known as a man after God's own heart! Crying out our hurt isn't only healthy, it heals our souls.

So, the next time your plan gets messy and totally off course, look for the miracle and remember these truths, because even when the climb gets difficult, you'll find the strength to keep going by crying out and clinging to God, whose plans for you are good. IG

**WHITNEY L. WARD** was not only the first person in the world diagnosed with MAGIS syndrome, but she also had the honor of naming the new primary immune deficiency. MAGIS means "more" in Latin, and Whitney hopes to instill in her readers the message they are more than their disease. Find out more about Whitney's journey at www.whitneylaneward.com.

Want to Learn About Topics Important to Chronic Illness Patients Living with Autoimmune and Immunodeficiency Disorders?

# LISTEN TO THE IG LIVING ADVOCATE AUDIO PODCAST!


Abbie Cornett, MBA
IG Living Patient Advocate

**Sample Episode Topics:**

- The Increased Demand for Immune Globulin Products and Its Effects on Patient Access
- Planning for Retirement with Chronic Illness
- Changes in Medicare That Affect Patients Treated with Immune Globulin
- IG Infusions in the Home Setting
- The Road to Diagnosis

The ONLY Podcast for Autoimmune and Immunodeficient Patients:
**www.igliving.com/life-with-ig/ig-living-advocate-podcast.html**

Subscribe to IG Living Magazine to Receive Notifications About Upcoming Podcast Episodes

Produced by IG Living magazine, written for patients treated with immune globulin therapy and their caregivers

# Diagnosed But Not Defeated: Tips for Raising Resilient Kids

By Jessica Leigh Johnson

**IT GOES** without saying that kids with a primary immunodeficiency disease (PI) or other chronic conditions face adversity on a regular basis. They may miss more school than the average kid and have to work harder to keep up with assignments. They may have physical manifestations of their illness such as a chronic cough or frequent pink eye, and face bullying or rude comments from other children as a result. What helps kids to navigate these kinds of challenges is resilience. Kids who are resilient have an easier time dealing with adversity. They may fall down, but they don't stay down. They know how to ask for help when they need it, and they can use problem-solving skills to figure out their next steps.[1]

Lynn Lyons, a licensed social worker and psychotherapist in Concord, N.H., says that when resilient kids face a challenging situation, "they have a sense they can figure out what they need to do and can handle what is thrown at them with a sense of confidence."[1] But what if a child just isn't resilient? Some kids are simply born resilient, and others aren't, right? It's not a skill that can be taught — or is it?

## Fostering Resilience

Is resilience something parents can teach their kids, just as they'd teach them personal hygiene or good manners? Not exactly. Every child is born with a certain degree of resilience, which can be encouraged or hindered by life situations.[2] Some kids seem to come by the trait more naturally, while others must develop resilience over time and through trials. Resilience essentially includes two factors: risk or adversity, and positive adaptation or competence. So in very basic terms, fostering resilience means letting kids go through tough experiences, and allowing them space to figure out how to make it not so tough the next time.[2]

Resilience is not a one-size-fits-all concept. When parents are trying to raise more "resilient kids," resilience is not necessarily the end goal, because it means different things to different people. Most importantly, parents should be teaching their kids specific tools and coping strategies to cultivate things such as self-esteem, self-efficacy, trust, emotional regulation skills, adaptability and relationship skills.[1]

## Allowing Children to Face Adversity

Most parents would agree they want their children to be able to adapt to changing circumstances and make good decisions when facing challenges. Those same parents are probably somewhat less comfortable with the idea of exposing their kids to the uncertain, adverse situations that build these traits.[2] Naturally, many parents feel their role is to protect their kids from such things. This is especially true for parents of chronically ill children. If we can shield them from as many hardships as possible, we're being good parents. Or are we?

Obviously, we should steer our kids away from any situation that puts them in harm's way. The younger children are, the more they need their parents' guidance. But as they grow, it doesn't hurt to give them room to navigate certain situations on their own while they're still under the protection of our watchful eye. Childhood offers an excellent "training ground" for kids, offering small, age-appropriate challenges every day to grow resilience in them.[2]

## Raising Problem-Solvers

The ability to encounter a problem and find a solution is a key component of resilience. Parents can help develop this trait in their children by encouraging them to participate in solving the small problems that occur throughout their day. A large part of the role of parents is to help their children understand that they must gradually take responsibility for their own problems.[2]

When children face a problem, parents should ask them to think about what it would take to solve it, whether it's a spilled drink, a lost toy or a broken vase. Questions such as "What do you think we should do about that?" or "How would you find it?" are very helpful in directing children toward finding their own solution.[2]

Parents could also ask themselves what they are doing for their kids that their kids could do for themselves. Rather than providing kids with every answer to every question they have, parents can start using the phrase "I don't know" as a response, followed by a suggestion that promotes problem-solving. Using these phrases gives kids the opportunity to learn how to handle uncertainty and think about solutions to potential challenges.[1]

Also, exposing kids to small adverse situations when they're young helps prepare them to handle bigger trials when they're older. Older kids and teens can have personal responsibilities such as setting their own alarm clock on school days and getting out of bed on time, and then dealing with the consequences if they sleep in, and freedom to make choices such as whether to study for the big biology exam or attend a sporting event instead and study after — or not. Parents are always there as a sounding board, but our first priority should be to help them come up with a solution on their own.

Solving small problems when they're young helps children grow to be resilient problem-solvers as teens and adults. "When they're young, the stakes may not be as high and the consequences for mistakes may not be so severe," says Vicki Caruana, an international speaker and author with a PhD in education. "Now is the time to help them learn to think for themselves and embrace the problems of life as opportunities to learn."[2]

## Let Children Make Mistakes

Allowing kids to mess up can be difficult and painful for parents. Parents of chronically ill children can be especially sensitive to their children's successes and failures. It may seem like sometimes they just can't catch a break, and all we want is for them to have as many "wins" as possible. We might even hover and become "helicopter parents," jumping in to save the day and heading off danger at every turn — but even though we are doing it all out of love, in actuality, we may be doing our kids more harm than good. Making mistakes helps them learn how to fix errors in behavior and judgment, as well as make informed decisions to avoid those same pitfalls the next time. If a child has a school assignment, an anxious or overprotective parent may try to ensure the project is done perfectly. These parents may even step in and try to complete part of the project themselves! But it's far more helpful in the long run for parents to let their kids do their own work, whether good or bad, and see the consequences of their decisions and actions as they play out.

In the same way, if a child doesn't want to go to basketball practice, parents who want to teach resilience might let the child stay home. But, if that child ends up sitting on the bench during the next game, he or she will at least have plenty of time to think about that decision.[1]

## What Resilience Is *Not*

It's important to note that despite all of the ways listed here to help foster resilience in children, resilience is not 100 percent a choice. All children adapt to situations differently and process adverse events in their own unique way. Children should not be blamed for *not* being resilient according to a certain standard or whatever the latest definition of "resilience" is.[3] When a child seems to be struggling with a particular event or coping with an ongoing health issue, parents should not mistake these behaviors for resilience: numbing, ignoring, being in denial, avoidance or harmful coping mechanisms such as alcohol or substance abuse. Resilience is *not* shutting down and going numb.[3] If a child exhibits any of these negative behaviors, it may be time to get in touch with a professional who can help the child navigate the more challenging aspects of life.

### References


1. Tartakovsky, M. 10 Tips for Raising Resilient Kids. Psych Central, updated July 18, 2022. Accessed at psychcentral.com/health/tips-for-raising-resilient-kids#defining-resilience-for-parents.
2. Fry, V. Raising Resilient Kids. Focus on the Family. Accessed at www.focusonthefamily.com/parenting/raising-resilient-kids.
3. Rice, A. What Resilience Is and Isn't. Psych Central, updated Jan. 6, 2022. Accessed at psychcentral.com/lib/what-is-resilience.


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

# Emergency Preparedness

By Rachel Maier, MS


*HOPE FOR the best; plan for the worst. Those who fail to plan, plan to fail. Expect the unexpected.* This list of clichés could go on and on. When it comes to emergencies, I bet you know you should be prepared, but are you?

A few years ago, my father-in-law came to my house to check on me and the kids while my husband was out of town. A severe thunderstorm was brewing and he wanted to make sure I was ready for it. "Do you have a flashlight with new batteries?" I did. "And a hand-crank radio?" Had that too. I signed up for the county emergency notification system, designated a safe room in the basement and remembered to stock it with flashlights and bottled water. "What about an old mattress?" he asked. I shook my head, clearly confused. "It's helpful to have one in your safe room to hide behind during a tornado," he explained, realizing this California girl had no idea what he was talking about. (Turns out, an old mattress makes a good buffer between people and falling debris.)

The wind howled, rain poured and trees lost branches, but we didn't have to use that old mattress to hide from falling debris. I quickly realized, though, that while I was prepared to take shelter from a tornado, I wasn't really prepared to deal with the aftermath of one — or any real emergency, for that matter.

## Are You Ready?

What about you? Are you ready to deal with emergencies? If you're like me, the answer is probably no.

The way I see it, there are three major roadblocks to emergency preparedness: inconvenience, expense and expectation. It takes a lot of time and money, and if we're being honest, it doesn't feel like disaster will strike *us*. Is it really worth the trouble? In short: *yes, it's worth it.* Let's not forget: Disasters can strike anywhere, anytime and often without much warning. Those who have the best shot at surviving them are the ones who prepare in advance.

Emergency preparedness starts with providing for basic needs — food, water, shelter — but it also extends to things like knowing what to do during an emergency and after it is over. You've got to think about storing things such as a wrench to turn off utilities, a fire extinguisher to put out fires and even a can opener to open canned foods. It also involves securing access to vital health records in advance; considering methods for communicating health history to emergency medical personnel; preserving important legal documents such as birth certificates, social security numbers, mortgage information or a copy of a family trust.

I'm still working on my emergency preparedness — there's just so much to do! — but little by little, I'm getting our family well-positioned to handle whatever emergency may come our way. Today is a good day for you to get started, too.

## 5 Tips for Getting Started

1) *Start small, but start somewhere.* Pick one thing you can reasonably accomplish, then do it. For example, print a checklist of items to include in your emergency kit, replace batteries in your flashlights or buy a fire extinguisher and learn how to use it.

2) *Make a list.* Use a free printable checklist (www.ready.gov/kit) so you know what you need to gather or purchase.

3) *Use what you have.* Use your kids' old backpacks to create their own personal "go" bag with a change of clothes, extra shoes and any other personal items they may need. Collect sample-size toothpastes and toothbrushes from dental visits or shampoos, conditioners and soaps from hotel stays, and use them to build personal hygiene kits.

4) *Collect items over time.* Pick up one thing to add to your kit every time you go shopping: bottles of water, a box of granola bars, a book of matches, a pack of batteries, etc. Little by little, your stash will grow.

5) *Shop sales.* Emergency prep sites like mypatriotsupply.com and beprepared.com often run specials, and garage sales, OfferUp and Facebook Marketplace are great places to find deals on pre-owned equipment. IG

**RACHEL MAIER,** MS, is the associate editor of *IG Living* magazine.

### Jase Medical

The Jase Base Case gives you peace of mind with five emergency antibiotics (amoxicillin, azithromycin, ciprofloxacin, doxycycline and metronidazole) and the option to add on popular medications such as albuterol, epinephrine, ivermetin, ibuprophen, acetaminophen, celecoxib and more. Or, with Jase Daily, you can get up to a 12-month backup supply of your current daily prescription medications for high blood pressure, diabetes, high cholesterol, thyroid disease or other chronic health conditions. Jase Medical uses licensed pharmacies, so you can have peace of mind that your medications are safe. *Starts at $269.95; jasemedical.com*

### Be Smart Get Prepared First Aid Kit

Manufactured by the number one leading manufacturer of first aid kits in the U.S., the Be Smart Get Prepared 201 piece first aid kit meets the U.S. Food and Drug Administration regulatory standards as a medical device. The case is compact, durable, waterproof and adjustable, making it easy to grab and go when needed. It includes gloves, scissors, bandages, alcohol wipes, instant cold pack, pain relievers, emergency bright stick, whistle and much more.

*$20 for a 201 piece kit; www.amazon.com/Be-Smart-Get-Prepared-First/dp/B001GRSI3C?ref_=ast_sto_dp*

## Shopping Guide for Emergency Preparedness

### Medical ID USB Drives

Universal Medical Data provides medical ID USB drives to hold 2 GB worth of your medical information, no matter where you are. You can wear this device in the form of a medical USB bracelet or purchase engraved dog tags that are equipped to store flash drives securely. The USB medical ID wearable products are waterproof and biohazard safe, so you will never have to worry about your data becoming unreadable or unusable. A medical ID USB drive is also an excellent tool for doctors, as they can download your full medical history. *Starts at $29.95; www.universalmedicaldata.com/product-category/usb-products*

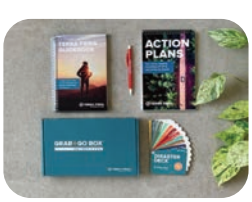
### GE 4-in-1 Emergency Light

This 4-in-1 emergency LED light includes a light-sensing night light, power failure light, task light and emergency flashlight all in one. It provides 40 lumens of soft white light when used as a portable emergency flashlight and 5 lumens when used as night light/table top light. The built-in light sensor automatically turns the LED night light on at dusk and off at dawn and comes on instantly when power goes off. There is a manual Hi/Low/Off switch to easily switch between lighting. *$9; www.amazon.com/GE-37373-Foldable-Emergency-Flashlight/dp/B077Y4STKD*

### Fireproof, Water-Resistant Document Organizer

The IronClad keeps your important papers safeguarded in this durable and reliable fireproof document holder. Withstanding temperatures up to 2,000 Fahrenheit, this document organizer is fireproof and water-resistant, providing unmatched security and peace of mind for your most important papers. *$34.99; shop.ironcladfamily.com/products/fireproof-waterproof-important-documents-organizer*

### GRAB + GO BOX

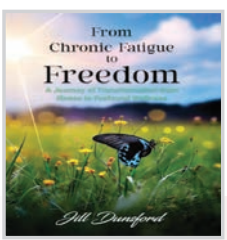



This disaster preparedness kit includes a simple, step-by-step guidebook that takes you through the process of preparation and recovery in a disaster; action plans for teaching your family how to stay safe adapting, evacuating and being well during and after any disaster; a pocket-sized disaster deck of color-coded instructional cards that include steps to take for any natural disaster; and supplies such as a cash bag, wristbands, emergency stickers, emergency contact cards, wax pencil, bin labels and much more. *$54.99; www.terrafrma.com/products/grab-go-box*

## *From Chronic Fatigue to Freedom: Healing the Mind to Heal the Body, Healing the Body to Heal the Mind: A Journey of Transformation from Illness to Profound Wellness*

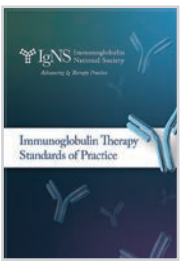
*Author: Jill Dunsford*
*Publisher: Self-Published*

This book is a story of transformation from profound and debilitating fatigue to freedom and wellness, written by a chartered physiotherapist. The author's unique experiences as a qualified professional, a sufferer and someone who has recovered thanks to her own determination to do so, give her insights that can help others. While most books provide guidance on how to live with fatigue, Jill shows readers how to take control and transcend the current narrative, to return to living a happy and joyful life and to free oneself from the limitations of chronic fatigue by addressing and healing all parts of what makes people who they are, body, mind and spirit.



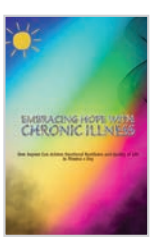

## *IgNS Standards of Practice Version 3.1*

*Author: Immunoglobulin National Society (IgNS)*
*Publisher: IgNS*




This initiative delivers the national standards of practice for immune globulin (IG) therapy, providing the standards and practice guidelines across a wide range of therapeutic areas and practice settings. This edition contains new guidelines for vital sign assessment and infusion management; oral hydration guidelines; adverse drug reaction management; risk factor mitigation strategies; subcutaneous IG assessment intervals; infusion pump utilization; and USP 797. Also included are major practice updates for vaccine/biologics interactions and dosing intervals; pregnancy/lactation and appropriate premedications; and dialysis and plasmapheresis. Finally, there are updated competency requirements, including a new staff competency section; laboratory, clinical and risk factor monitoring; clinical diagnosis and product-specific factors; and infusion pump management per patient assessment and tolerability.

# New and Useful Reading



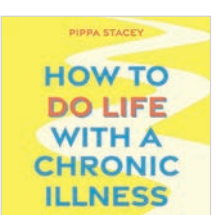

## *Embracing Hope with Chronic Illness: How Anyone Can Achieve Emotional Resilience and Quality of Life in Minutes a Day*

*Author: Sasha Kelly*
*Publisher: Self-Published*

Through personal narratives and expert insights, *Embracing Hope with Chronic Illness* explores the emotional challenges individuals face, the profound impact of grief and loss and the importance of emotional self-care. It delves into the concept of emotional resilience, providing practical tools to strengthen one's ability to cope with the emotional toll of chronic illness. Readers will discover strategies for finding joy and meaning in their lives, even amid pain and limitations, and will learn how to nurture supportive relationships and effective communication. This book equips individuals with the tools they need to become their own advocates in the healthcare system, helping them achieve a balanced life that combines self-care and advocacy effectively.

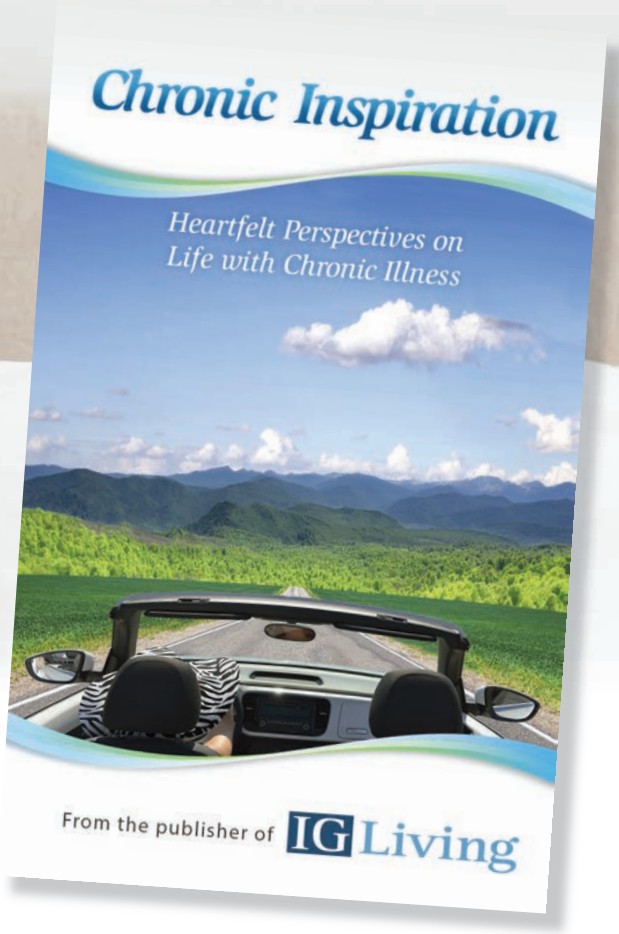
## *How to Do Life with a Chronic Illness: Reclaim Your Identity, Create Independence, and Find Your Way Forward*

*Author: Pippa Stacey*
*Publisher: John Murray*




Rather than focusing on the medical side of long-term conditions, this book contains advice for the parts of everyday living that often go unspoken — from practical advice on friendships, dating and independent living, to more reflective guidance on rediscovering one's identity and learning to self-advocate. As well as useful advice, readers will also find real-life experiences from diverse contributors, journal prompts and interactive features, and words of comfort and reassurance that chronic illness sufferers don't hear enough.

# Download the *IG Living* eBook today—now available for iPad, Nook and Kindle!




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

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

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

*— Jenny Gardner*

IG Living

*Chronic Inspiration* can be purchased on iTunes, Amazon and Barnes and Noble.com

### Ataxia Telangiectasia (A-T)

**Websites**

- A-T Children's Project: www.atcp.org

### Chronic Inflammatory Demyelinating-Polyneuropathy (CIDP)

**Websites**

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

### Evans Syndrome

**Online Peer Support**

- Rare Connect Evans Syndrome Community Group: www.rareconnect.org/en/community/evans-syndrome/faqs

### Guillain-Barré Syndrome (GBS)

**Websites**

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

**Online Peer Support**

- GBS Support Group: www.gaincharity.org.uk
- GBS/CIDP Foundation International Community Forums: forum.gbs-cidp.org

### Immune Thrombocytopenia (ITP)

**Websites**

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

### Kawasaki Disease

**Websites**

- American Heart Association: www.heart.org/en/health-topics/kawasaki-disease
- American Academy of Family Physicians: www.aafp.org/afp/2006/1001/p1141.html
- Kawasaki Disease Foundation: www.kdfoundation.org
- KidsHealth: www.kidshealth.org/parent/medical/heart/kawasaki.html

### Mitochondrial Disease

**Websites**

- United Mitochondrial Disease Foundation: www.umdf.org
- MitoAction: www.mitoaction.org

### Multifocal Motor Neuropathy (MMN)

**Websites**

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

### Multiple Sclerosis (MS)

**Websites**

- Multiple Sclerosis Association of America: www.mymsaa.org
- Multiple Sclerosis Foundation: www.msfocus.org
- National Multiple Sclerosis Society: www.nationalmssociety.org

**Online Peer Support**

- Friends with MS: www.FriendsWithMS.com
- MSWorld's Chat and Message Board: www.msworld.org
- Overcoming Multiple Sclerosis: www.overcomingms.org/community

### Myasthenia Gravis (MG)

**Websites and Chat Rooms**

- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org
- Myasthenia Gravis Association: mgakc.org

**Online Peer Support**

- Genetic Alliance: www.geneticalliance.org

### Myositis

**Websites**

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

**Online Peer Support**

- Juvenile Myositis Family Support Network: www.curejm.org/fsn/index.php
- The Cure JM Foundation: www.curejm.org
- Myositis Association Support Group: www.myositis.org/patient-support/support-groups
- Myositis Support Group – UK: www.myositis.org.uk

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

**Websites**

- PANS/PANDAS UK: www.panspandasuk.org
- PANDAS Network: www.pandasnetwork.org
- PANDAS Physician Network Family Resources: www.pandasppn.org/parent-information
- National Institute of Mental Health: www.nimh.nih.gov/health/publications/pandas/index.shtml

### Pemphigus and Pemphigoid

**Websites**

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

### Peripheral Neuropathy (PN)

**Websites**

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

### Primary Immune Deficiency Disease (PI)

**Websites**

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

**Online Peer Support**

- IDF Friends: www.idffriends.com
- Jeffrey Modell Foundation Facebook Page: www.facebook.com/JMFworld
- IDF Peer Support Program: www.primaryimmune.org/idf-peer-support-program

### Scleroderma

**Websites**

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

**Online Peer Support**

- Scleroderma Support Forum: www.curezone.com/forums/f.asp?=404

### Stiff Person Syndrome (SPS)

**Websites**

- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- Living with Stiff Person Syndrome (personal account): www.livingwithsps.com

# Get Connected

*Your Complete Resource for Advocacy, Education and Support*

## On IGLiving.com


Features an easy-to-navigate design

Indepth content on IG-treated diseases and treatment

Connect with our Patient Advocate, Abbie Cornett

Read weekly blogs about issues related to living with chronic illness

Valuable Resources and more

IG LIVING
44000 Winchester Road
Temecula, CA 92590-9760

PRSRT STD
US POSTAGE PAID
LEBANON JUNCION, KY
PERMIT NO. 714

## PREPARE TO
# #FightFlu

With **MyFluVaccine.com** easy online ordering

Don't give flu a fighting chance to be the co-respiratory disease we confront next season. Together, let's **#fightflu.** Visit MyFluVaccine.com and place your order today to help minimize the impact of the 2023-24 flu season.

MyFluVaccine®

**YOU PICK THE DELIVERY DATE(S) –** Conveniently secure YOUR best delivery date(s)

**YOU PICK THE QUANTITY** – Choose from a broad portfolio of products

**WE SAFELY DELIVER –** Count on FFF's secure supply channel with Guaranteed Channel Integrity™

**MyFluVaccine.com | 800-843-7477 | FFFenterprises.com**