Post-Diagnosis Relationships
Coping with the Loss of Friendships

Using Mindfulness to Ease Symptoms of Chronic Illness

Managing the Impacts of Stress

Immunodeficiency in Newborns
Diets to Reduce Inflammation
How to Qualify for SSDI
Important Safety Information

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

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

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

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

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

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

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

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

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

Before being treated with Hizentra, inform your doctor if you are pregnant, nursing or plan to become pregnant. Vaccines (such as measles, mumps and rubella) might
Getting started

1. Contact your Specialty Pharmacy and express a financial need for Hizentra Co-Pay Assistance

2. Your Specialty Pharmacy will verify your eligibility and process your request through Medmonk, the company that administers the co-pay program on behalf of CSL Behring

3. Access your account anytime at the secure online patient portal: Hizentra.medmonk.com

If you have any questions, call the IgIQ resource hotline:

IgIQ®
Your single source for Ig solutions

1-877-355-IGIQ (4447)
Monday–Friday,
8 AM–8 PM ET

not work well if you are using Hizentra. Before receiving any vaccine, tell the healthcare professional you are being treated with Hizentra.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
Hizentra Co-Pay Relief Program
Increases Financial Assistance to Patients

Enhancements to the Hizentra Co-Pay Relief Program mean new and current patients who express financial need can receive up to $5,000 per year in out-of-pocket cost assistance. See inside for more details.

Hizentra®, Immune Globulin Subcutaneous (Human), 20% Liquid
Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

WARNING: THROMBOSIS

See full prescribing information for complete boxed warning.

1. Thrombosis may occur with immune globulin products, including Hizentra.
2. 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.
3. For patients at risk of thrombosis, administer Hizentra at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

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**INDICATIONS AND USAGE**

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

**DOSE AND ADMINISTRATION**

For subcutaneous infusion only. Do not inject into a blood vessel. Administer at regular intervals from daily up to every two weeks (biweekly).

**Dosage**

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

- **Weekly**: Start Hizentra 1 week after last IGIV infusion
  
  Initial weekly dose = Previous IGIV dose (in grams) x 1.37
  
  No. of weeks between IGIV doses

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

- **Frequent dosing (2 to 7 times per week)**: Start Hizentra 1 week after the last IGIV or Hizentra/IGSC infusion. Divide the calculated weekly dose by the desired number of times per week.

- **Adjust the dose** based on clinical response and serum IgG trough levels.

**Administration**

- Infusion sites – 1 to 4 injection sites simultaneously, with at least 2 inches between sites.

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**DOSAGE FORMS AND STRENGTHS**

0.2 g per mL (20%) protein solution for subcutaneous injection

**CONTRAINDICATIONS**

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

**WARNINGS AND PRECAUTIONS**

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

**ADVERSE REACTIONS**

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

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

**DRUG INTERACTIONS**

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

**USE IN SPECIFIC POPULATIONS**

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

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**Infusion Parameters**

<table>
<thead>
<tr>
<th>Infusion Number</th>
<th>1st</th>
<th>2nd to 4th</th>
<th>5th</th>
<th>6th and above</th>
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<tr>
<td>Volume (mL/site)</td>
<td>≤ 15</td>
<td>≤ 20</td>
<td>≤ 25</td>
<td></td>
</tr>
<tr>
<td>Rate (mL/hr/site)</td>
<td>15</td>
<td>≤ 25</td>
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As tolerated

Based on January 2015 revision
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Join our campaign to reduce unnecessary paper consumption!

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# Up Front

**5 Editorial**  
Managing the Complications  
By Ronale Tucker Rhodes, MS

**6 Abbie’s Corner**  
The Doctor-Delayed Diagnosis  
By Abbie Cornett

**7 Faces of IG**  
From our Facebook page  
By Abbie Cornett

---

# Features

**16 Where Did Everyone Go? Coping with the Loss of Friendships Post-Diagnosis**  
By Trudie Mitschang

**20 How Mindfulness Can Ease the Symptoms of Chronic Illness**  
By Dana Henry

**24 The Impact of Stress on Chronic Illness**  
By Amy Scanlin, MS

**32 Immunodeficiency in Newborn Infants**  
By E. Richard Stiehm, MD

**41 Qualifying for Social Security Disability Benefits**  
By the Outreach Team at Disability Benefits Help

**42 Diets for Inflammation Reduction and Chronic Illness Treatment**  
By Meredith Whitm ore

---

# Departments

**8 Ask the Experts**  
Healthcare professionals’ responses to patient questions

**9 Immunology 101**  
DiGeorge Syndrome: Genetics, Chromosome 22q11.2 Hemizygosity  
By Terry O. Harville, MD, PhD

**10 In the News**  
Research, science, product and insurance updates

---

# Columns

**46 Let’s Talk! — Kelly Bruski**  
By Trudie Mitschang

**48 Patient Perspective — Let’s Not Talk About ‘It’**  
By Stacy Oliver

**49 Life as a 20-Something — Too Sick to Go Out? Check Out These Apps for Independence**  
By Ilana Jacqueline

**50 Parenting — Dealing with Teen Anxiety**  
By Jessica Leigh Johnson

**52 Product Guide**  
Healthy Hydration to Minimize IVIG Side Effects  
By Trudie Mitschang

**54 Resource Center**  
Community foundations, associations, forums and other resources

---

**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.aspx. Or contact advertising@igliving.com.

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IG Living, ISSN 1949-4548, published bimonthly, is a community service provided by FFF Enterprises, 41093 County Center Drive, Temecula, CA 92591, (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 x1351.

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Managing the Complications

WE DEVOTE A good deal of space in each issue of *IG Living* magazine to the topic of coping with chronic illness. And, for good reason. While chronic illnesses cannot be cured, many of the complications arising from them can be controlled or managed.

One such complication can be friends. While friendships come and go in everyone’s life, individuals diagnosed with a chronic illness often discover friendships disappear at a much higher rate, causing feelings of confusion, guilt, hurt and, even, betrayal. Undoubtedly, there are many reasons friendships end, as we explain in our article “Where Did Everyone Go? Coping with the Loss of Friendships Post-Diagnosis.” The important thing to understand is that a diagnosis can be just as difficult for friends as it is for patients. Friends, too, can experience feelings of grief, but also feel intimidated due to an inability to know how to help. And, while it may be hard to let go of friendships, the needs of persons with chronic illness can sometimes be better served by friendships made post-diagnosis.

One of the most common complications of chronic illness is negative stress, which can have biological repercussions on the body that can actually exacerbate a chronic illness. If individuals can learn to deal with the stress of an illness and its effects, however, they can help to reduce its damage. In our article “The Impact of Stress on Chronic Illness,” we explain the physiological effects of stress, and provide suggestions for how to manage it “like a risk factor.”

One way of dealing with stress, as well as depression, is mindfulness. This Buddhist practice seems to be ever-present today, and is especially recommended for those with chronic illness. As explained in our article “How Mindfulness Can Ease the Symptoms of Chronic Illness,” the term means to keep one’s mind in the present. It can come in different forms, one of which is mindfulness meditation, credited with reducing chronic pain by anywhere from 57 percent to 90 percent for those who are very accomplished in its practice. There are also mindfulness-based stress reduction programs offered at colleges and other locations, as well as therapeutic offerings such as mindfulness-based cognitive therapy, dialectical behavior therapy, and acceptance and commitment therapy.

Modifying diet can be a very beneficial part of managing the effects of chronic illness, especially in reducing inflammation that so often accompanies these illnesses. In our article “Diets for Inflammation Reduction and Chronic Illness Treatment,” we explain how two popular dietary approaches could be used to either reduce or replace medications prescribed to reduce inflammation. Though they are “on opposite ends of the spectrum,” research shows that low-fat, plant-based diets and low-carbohydrate, high-fat diets both achieve beneficial results. The key is discovering which works best for each person.

As always, I hope you gain insight from the information presented and enjoy this edition of *IG Living.*
The Doctor-Delayed Diagnosis

By Abbie Cornett

**AS A PATIENT** advocate for people with rare and chronic diseases, I frequently hear about the long diagnostic process most patients go through. In fact, the average time to diagnosis for patients with rare diseases is 7.6 years in the United States, and the average number of doctors they see before being correctly diagnosed is eight.¹ And, these statistics don’t even begin to cover the number of patients who go undiagnosed or misdiagnosed. According to the *Orphanet Journal of Rare Diseases*, a United Kingdom survey found that 30 percent of patients reported three or more misdiagnoses.

Contrary to logic, doctors may be the biggest barrier to patients receiving the correct medical treatment for their illness.

While awaiting a correct diagnosis, patients frequently experience worsening symptoms, a decline in overall health and even death. These delays not only have physical health implications, but also cause mental health issues such as anxiety, stress, feelings of isolation, worry and depression. What’s worse, they can significantly lower patients’ quality of life compared with patients who have been correctly diagnosed and are receiving proper treatment.

The question is: Why does it take so long for patients to be correctly diagnosed? Contrary to logic, doctors may be the biggest barrier to patients receiving the correct medical treatment for their rare disease. Many factors contribute to this. First, doctors are taught in medical school to look for the most obvious diagnosis to fit the symptoms a patient is experiencing. Theodore Woodard, MD, a professor at the University of Maryland School of Medicine in Baltimore, coined this phrase in the 1940s: “If you hear hoofbeats, think of horses, not zebras.” This aphorism has resulted in many patients not receiving the correct diagnosis for years. Indeed, it is so well-established that rare disease groups have adopted the zebra as their mascot, and have revised the phrase: “When you hear hoofbeats, sometimes it’s a zebra.”²

Neglecting to look outside the box is part of the proverbial problem of many reporting high levels of burnout and fatigue associated with stress. Physicians report they frequently don’t have the necessary time to spend with patients, or the resources available to adequately treat them. Patients with rare diseases require longer and more frequent visits, making it difficult for physicians to provide the needed care in the allotted appointment time.¹ And, patients with rare diseases require a higher level of time-consuming collaboration with other specialists.

Further, information on rare diseases is difficult to find. Doctors report not having access to the information they need.³ According to them, opportunities to network with other specialists are limited, and information provided by professional organizations on rare diseases needs to be improved.

By virtue of their title, doctors enjoy a higher level of trust than most other professionals. While trust is an important part of the doctor-patient relationship, it can also lead to a delay in diagnoses if patients blindly accept what they are told. It is important to remember that doctors are human, and they don’t always have the answers. And while it is rare, some are not motivated to look. As a matter of fact, doctors are under increased pressure themselves today, with many reporting high levels of burnout and fatigue associated with stress.

When receiving inadequate treatment and attention, patients need to ask themselves: Is it time to look for a new doctor? There are many reasons patients should take this step. First and foremost is if they are not getting better! Patients who are receiving treatment, yet their symptoms have not improved or have worsened, should also consider finding a new doctor. And, if patients feel their physician is not actively seeking answers, or is not engaged in their treatment, they should look for a doctor better suited to their needs.

As a patient advocate, I am frequently asked to help patients find a specialist. If you are having trouble locating a doctor in your area, please contact me and I may be able to suggest options for you.

**References**


**ABBIE CORNETT** is the patient advocate for *IG Living* magazine. She can be reached at patient advocate@igliving.com or (800) 843-7477 x1366.
How do you manage stress?

It depends on what situation is causing the stress, and if I am able to, I remove myself from the cause of the stress. I try to walk 25 minutes a day without any distractions. I have learned to say no to invites if I know the environment will be stressful. Sometimes, it is just impossible to escape stress, and I suffer the consequences.

— Judy S

Writing, reading, playing with my dogs and, now, planning dates with my boyfriend! Talking to him about anything is helpful. He has a calming, soothing way about him.

— Mikki C

While we can’t always avoid stressful situations, we can control our response to them. I try to avoid as much drama in life as possible by limiting interaction with people who thrive on it.

— Debbie K

Do you know the difference between the cold and flu?

Apparently, my body didn’t get the memo! I ache like I always have the flu. [I] run temperatures and the like. Because of my vocal cord paralysis, I am often congested and coughing. So, it is always a circus with my immune system trying to catch up.

— Janet S-D

Not always. I think it can be very hard to determine for most. I’m well aware of my body. [As] a paramedic, I usually can determine if I’m flush. Either way, at my six-month specialist checkup, I ask for Tamiflu to have on hand. Because, obviously, time is of the essence, and if I wake up with the flu, the last thing I want to do is drive 56 miles each way to my primary care doctor to see if I can get in.

— Dave S

Does your treatment ever seem worse than the disease?

Yes. I am treated with intravenous immune globulin (IVIG) for myasthenia gravis approximately every four to six weeks. The side effects are extreme fatigue, nausea and flu-like symptoms. These symptoms last for several days after the IVIG is over. I have, on a few occasions, gotten aseptic meningitis. Turns out I was allergic to a particular brand of IVIG. Sometimes I wonder if it’s worth it. Then, when I’m better, I realize it is worth it.

— Judy S

[My treatment] nearly kills me if it is infused at a fast rate. I can only tolerate a four- to six-hour infusion. [With] a six-hour infusion, I have no side effects. [With] a four-hour infusion, I have extreme fatigue. [I’m] not complaining. Life could be worse! [I’m] very grateful for blood donors!

— Andrea B
Abbie» I spoke with immunologist Terry O. Harville, MD, regarding your question. He states that IVIG infusions, on rare occasions, have resulted in thrombotic events in various parts of the body such as PE. These events tend to occur in older patients who are receiving high doses of concentrated IVIG over short time frames, which are typically used to treat autoimmune disorders such as CIDP.

Generally, PE and other thrombotic events and adverse reactions to IVIG can be prevented with relatively simple measures:

1) The concentration of the dose of IVIG can be decreased from 10% to 5%. For powdered forms of IVIG in which twice as much buffer is used for reconstitution, this can be done by the dispensing pharmacy.

   For liquid forms of IVIG, which are 10% solutions, one liter of normal saline (NS) or half NS can be infused immediately before the IVIG infusion to expand blood volume. Or, one liter of NS or half NS can be infused simultaneously with the IVIG (this is often better, but some pharmacies and nurses will not infuse simultaneously).

2) The infusion time can be increased to between six and eight hours. This is accomplished by slowing down the maximum infusion rate so the infusion takes two to three times as long.

   Even though thrombotic events such as PE have been reported in patients infused with IVIG, it is important to determine if there are risk factors for thrombosis. It has not been studied whether persons experiencing thrombosis had specific inherited or acquired risk factors for it. Dr. Harville believes experiencing thrombotic events with IVIG is a result of predisposing, underlying conditions that may make patients susceptible. These include mutations in factor V Leiden, protein C, protein S, antiphospholipids, antithrombin deficiency, prothrombin mutations, increased homocysteine, diabetes, obesity, smoking, oral contraceptive use, corticosteroid use, etc. For example, protein C deficiency occurs in approximately one in 300 persons, and is not routinely screened for, but could have fatal consequences if not recognized and treated. Therefore, a complete workup should be performed to determine if there are inherited, acquired or other risks for thrombosis.

Question >> Can IVIG Infusions Result in a Pulmonary Embolism?

For the past year, I have been treated for chronic inflammatory demyelinating polyneuropathy (CIDP) with Gammagard intravenous immune globulin (IVIG) infusions every four weeks. Last month, I developed a pulmonary embolism (PE). Are there any reports of this as an adverse reaction to IVIG, and if so, could it be dose- or concentration-related?

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

ABBIE CORNETT is the patient advocate for IG Living magazine.

Question >> Is a Rash a Known Side Effect of IVIG?

I receive intravenous immune globulin (IVIG) infusions for chronic inflammatory demyelinating polyneuropathy (CIDP). Specifically, I am treated with 85 grams of Gammagard liquid infused over two days every three weeks. I have had no problems with these infusions until recently, when I developed red welts (bumps) on my chest, back, arms and neck, which itch, especially at night. Have you heard of this as a symptom of IVIG? If so, what can I do to relieve it?

Abbie » A rash and/or allergic reaction is a known side effect of IVIG, and can occur at any time during therapy. Some options to try are switching brands and using topical or oral steroids to treat the rash. Contact your treating physician, and let him or her know about the side effects you are experiencing so you can determine what options are best for you.
DiGeorge Syndrome: Genetics, Chromosome 22q11.2 Hemizygosity

By Terry O. Harville, MD, PhD

IN PREVIOUS issues, we discussed features of DiGeorge syndrome (DGS) and partial DGS (PDGS) resulting from the consequences of improper timing of the sequence of events during early phases of embryonic development. To better understand this disease, this column will begin a discussion of genetics involved in these miscues.

It is now thought that more than 90 percent of patients with DGS/PDGS have lost some DNA from chromosome 22. (Mutations on chromosomes 4, 10 and 18 have also been ascribed to causing DGS/PDGS, but these have generally been isolated occurrences, and may account for only a small percentage of overall cases.) Only one of the two chromosomes 22 that individuals inherit needs to be involved. Therefore, terms such as hemizygosity, hemideletion or microdeletion of chromosome 22 are used. Some refer to deletions that occur in a specific region of the long arm of chromosome 22 as a 22q11.2 deletion syndrome. Also, there are additional conditions associated with DNA deletions in this region that can overlap the clinical features of DGS/PDGS. These are known as “CATCH 22” (Cardiac abnormalities, Abnormal facies, Thymic hypoplasia, Cleft palate, Hypocalcemia); CHARGE syndrome (Coloboma/ Cranial nerve palsy, Heart abnormalities, Atresia of the choanae, Retardation of growth and development, Genital and urinary abnormalities, Ear abnormalities or hearing loss); Velocardiofacial syndrome; and Shprintzen syndrome. While these conditions have similar chromosomal deletions as DGS/PDGS, their different names may be used when additional features are found that may be more commonly associated with that particular disorder.

The deletion of DNA from the chromosome 22q11.2 region is thought to primarily occur during the DNA replication process, when sperm or eggs are produced. About 45 genes are reported to be in the region of 22q11.2 where DNA is lost in DGS/PDGS. It remains unclear how, specifically, these deletions result in DGS/PDGS, but some of the DNA sequences appear to have similarity to the fruit fly (drosophila) DNA sequences, which play roles in timing developmental events. This would be consistent with the improper timing of the sequence of events during development observed in DGS/PDGS. Some genes have also been noted to have roles in the development of specific tissues and organs, including the heart, kidneys, brain and thymus. Therefore, correlation between the affected genes in the region of chromosome 22q11.2 appears to be congruous with the disrupted developmental features of these organs in DGS/PDGS.

We will continue in the next issue with discussion of genetic issues and how they cause problems in DGS/PDGS.

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.
**Medicines**

**FDA Approves Gammaplex 10% to Treat Adult PI and ITP Patients**

The U.S. Food and Drug Administration (FDA) has approved Bio Products Laboratory’s (BPL) Gammaplex 10% (immune globulin intravenous [human] 10% liquid) for the treatment of primary immunodeficiency (PI) and chronic immune thrombocytopenic purpura (ITP) in adults. Gammaplex 10% is made with the same process as BPL’s previously approved intravenous immune globulin, Gammaplex 5%, but is more concentrated with an IgG concentration of 100 g/L and is stabilized with glycine.

Approval was based on a two-phase, crossover bioequivalence study comparing Gammaplex 10% and Gammaplex 5% in 33 adult patients with PI. In the study, both Gammaplex 10% and Gammaplex 5% infusion rates were increased incrementally at 15-minute intervals if tolerated. No notable differences were observed in the safety and tolerability between the products, and the Gammaplex 10% infusion rate was increased per the prescribed infusion schedule to maximum infusion rate in 96 percent of infusions. The mean infusion time for Gammaplex 10% was one hour and 51 minutes, which was 57 minutes faster than Gammaplex 5%. The most common adverse reactions were headache (12.5 percent), migraine (6.3 percent) and pyrexia (6.3 percent). No serious product-related adverse effects occurred.

While the safety of Gammaplex 10% has not yet been established in ITP patients, Gammaplex 5% has been studied, and it is anticipated that the safety profile for both formulations are comparable.

**Research**

**Study to Test Gene Therapy in SCID Patients**

A new study will test gene therapy in patients with severe combined immunodeficiency (SCID) as an alternative to stem cell transplants using donor cells that can result in serious infection. The study expects to treat up to 15 children over the next five years and is open to patients with X-linked SCID, a rare disorder that affects one in every 60,000 newborn males.

Funded by a five-year, $11.9-million grant from the California Institute for Regenerative Medicine (CIRM), the study will use technology developed by St. Jude Children’s Research Hospital. The lentiviral gene therapy vector will deliver a functional gene into the patient’s blood-producing stem cells. It is a transduction process in which genetic material is transferred via vector, which freezes the transduced cells and returns them to the University of California San Francisco (UCSF) for infusion into the patient. “What is unique about this trial is that the patient’s own bone marrow stem cells are collected and corrected with the gene therapy, and the corrected cells are then reinfused into the patient,” said Morton Cowan, MD, of the UCSF Division of Allergy, Immunology and Blood and Marrow Transplant, and principal investigator at the trial at UCSF. “In stem cell transplants from a donor other than the patient, up to 20 percent of patients with SCID will develop graft-versus-host disease, in which the donor cells attack the recipient’s tissues. In addition, there is always a risk of the recipient rejecting the donor cells. Using the patient’s own stem cells means no rejection and no graft-versus-host disease.”

The bone marrow transplant program at UCSF is among the largest SCID transplant centers in North America. UCSF also played an instrumental role in the St. Jude treatment protocol by including a targeted chemotherapy agent, busulfan, along with the gene therapy, which is expected to optimize immune correction. Previous trials have tested gene therapy for SCID, but they didn’t combine it with chemotherapy and had only partial immune correction. Three patients have already been treated with this lentiviral gene therapy vector, two at St. Jude and one at UCSF.

IGNS 2017 Conference Scheduled for Oct. 5-8

The IGNS 2017 6th National Conference will be held Oct. 5-8 at the Red Rock Casino Resort and Spa in Las Vegas, Nev. The conference is a comprehensive, advanced educational program critical to healthcare professionals in the immune globulin (IG) therapy field that will be attended by more than 500 attendees, including nurses, pharmacists and physicians.

IGNS 2017 begins with the Ig Academy, an annual one-day IG therapy review course, followed by advanced IGNS plenary sessions, concurrent breakouts, round tables, poster session and exposition hall. The conference features renowned speakers and leading clinicians who will share updates on practice standards, disease states, research and product developments, legislation and reimbursement. Attendees will receive nursing and pharmacy continuing education, American Medical Association Physician’s Recognition Award credit and IG certification nurse recertification units.

To register for the event, go to www.ignsconference.com.

Rigel Announces Results from the Second FIT Phase 3 Study and the Long-Term Open-Label Extension Study for Fostamatinib in ITP.

Phase III Studies of Treatment for ITP Show Positive Results

Rigel Pharmaceutical’s fostamatinib, an oral spleen tyrosine kinase inhibitor, met the primary endpoint in the first (047) of two double-blind studies in the FIT Phase III clinical program for the treatment of chronic/persistent immune thrombocytopenia (ITP). Yet, the second FIT Phase III study (048) did not meet its primary endpoint. However, when data from both studies were combined, the difference was statistically significant, demonstrating the consistent benefit of fostamatinib in ITP.

The two studies are identical multicenter, randomized, double-blind, placebo-controlled studies of approximately 75 adult patients who have been diagnosed with persistent or chronic ITP, have blood platelet counts consistently below 30,000/uL of blood and have had at least one other treatment such as steroids, Rituxan, splenectomy and/or TPO membrane. Patients were randomized in a two-to-one ratio to receive either fostamatinib or placebo twice a day to be taken for up to six months, with study subjects remaining on treatment for up to 24 weeks. The primary efficacy endpoint is a stable platelet response defined as achieving platelet counts at or above 50,000/uL of blood for at least four of the last six clinic visits of the study. Both studies showed that 18 percent of patients receiving fostamatinib achieved a stable platelet response. However, in the first study, none of the patients receiving a placebo achieved a stable platelet response, whereas one did in the second study, which was why that study didn’t meet its primary endpoint.

Patients from both studies were given the option to enroll in a long-term open-label extension study (049) to receive treatment with fostamatinib. As of June 2016, 118 patients have been enrolled. All patients who responded to fostamatinib in the parent studies enrolled in study 049 and had a median platelet count of 96,000/uL of blood. As of October, these patients had been exposed to fostamatinib for a median of 13 months through the combined parent and 049 trials. In addition, there were 43 placebo nonresponders from the 047 and 048 studies who enrolled in the 049 study, 36 of whom had at least 12 weeks of follow-up. Of these, six patients (17 percent) achieved a prospectively defined platelet response in the 049 study.

“This heterogeneity means that treatments that work by different mechanisms can make important contributions in certain patients such as those who might be especially responsive to fostamatinib because of its unique mechanism of action,” said James B. Bussel, MD, professor of pediatrics, pediatric hematology oncology and gastroenterology at Weill Cornell Medicine, and the principal study investigator of the FIT Phase III program. “The FIT Phase III studies have both demonstrated that fostamatinib provided a robust and enduring benefit of those patients who responded to the drug.”

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— Marcia Boyle
President and Founder, Immune Deficiency Foundation

*Certain limitations apply—see program Terms and Conditions at www.cslbehringassurance.com.
Autoimmune Corner

Conference
11th Annual Neuropathy Action Awareness Day Is June 23

The 11th Annual Neuropathy Action Awareness Day will be held Friday, June 23, at the InterContinental Hotel in Los Angeles. This largest neuropathy awareness and education event in the U.S. provides an opportunity for patients to interact with other patients, providers and exhibitors, as well as to learn about neuropathy and how to cope with the disease, policy issues and patient advocacy. The day begins with an exhibit area and educational sessions in the morning, followed by a luncheon and additional educational sessions and exhibit area with refreshments in the afternoon. Additional features include a celebrity speaker, elected officials and a silent auction that includes trips, activities and other fun items.

To ensure as many patients can participate as possible, the Neuropathy Action Foundation (NAF) has booked a block of rooms at the hotel for a special, reduced rate. For those with a financial hardship, NAF will pay for up to 10 flights and hotel room for the night of the event or the night before the event for patients from outside the Los Angeles area. In addition, those unable to attend in person can listen free of charge via Livestream technology using a computer with an Internet connection. Those individuals will also be able to ask speakers questions and receive answers in real time. The event will be recorded, so individuals can watch the event even after it has ended.

To register, go to the NAF website (neuropathyaction.org) and click on “register today” on the right side of the homepage. Once registered, those watching via Livestream will receive a link to view the event. Registration is $25 for patients and caretakers for the event and luncheon. For nonpatients and noncaretakers, the event is $125 per person. The event is free for Livestream participants. Registration after June 9 is an additional $50.

Research
Study Finds IVIG Eases Symptoms of Small Fiber Neuropathy

A new study shows that intravenous immune globulin (IVIG) alone or in combination with infliximab may significantly ease symptoms of sarcoidosis-associated small fiber neuropathy (SSFN). In the retrospective analysis, 115 sarcoidosis patients with SSFN were followed for an average of 31 months after starting IVIG and anti-tumor necrosis factor-alpha (anti-TNF) therapy to assess their response to treatment. Among patients treated with IVIG, anti-TNF or both, 74 percent reported subjective improvement described as reduced pain, paresthesias and symptoms of dysautonomia usually within the first month of treatment. The largest number of patients reporting improvements was in the IVIG group (75 percent) and the combination therapy group (71 percent), while 66 percent of those given only anti-TNF also reported improvement. Fewer than 15 percent of those untreated reported improvement, and 81 percent experienced worse symptoms.

Small fiber neuropathy is a common complication of sarcoidosis that affects nerve fibers, specifically those of the peripheral nervous system, and causes weakness, numbness and pain, most frequently in the hands and feet. Treatment with standard immunosuppressants, including corticosteroids and methotrexate, has largely failed to improve clinical outcomes in patients. These findings suggest that SSFN may progress to chronic pain syndrome if left untreated.
VARIZIG®
[Varicella Zoster Immune Globulin (Human)]
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FOR HIGH-RISK PATIENTS FACING THE THREAT OF VARICELLA:

• Consider VARIZIG for postexposure prophylaxis¹
• Administer as soon as possible after exposure¹
• Ensure VARIZIG is in stock when it’s needed

INDICATION
VARIZIG is a Varicella Zoster Immune Globulin (Human) indicated for postexposure prophylaxis in high-risk individuals. High-risk groups include:
• Immunocompromised children and adults
• Newborns of mothers with varicella shortly before or after delivery
• Premature infants
• Infants less than one year of age
• Adults without evidence of immunity
• Pregnant women
VARIZIG administration is intended to reduce the severity of varicella.

SELECTED IMPORTANT SAFETY INFORMATION
Individuals known to have severe, potentially life-threatening reactions to human globulin should not receive VARIZIG or any other immune globulin (Human). Individuals who are deficient in IgA may have the potential for developing IgA antibodies and have severe, potentially life-threatening allergic reactions.


Aptevo BioTherapeutics LLC, Berwyn, PA 19312

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Please see VARIZIG Important Safety Information and full Prescribing Information at www.varizig.com.
VARIZIG® [Varicella Zoster Immune Globulin (Human)]

for intramuscular administration only.

Sterile Solution for Injection

**Brief Summary of Prescribing Information:** Please see full prescribing information for details.

**INDICATIONS AND USAGE**

VARIZIG® [Varicella Zoster Immune Globulin (Human)] is indicated for post-exposure prophylaxis of varicella in high risk individuals. High risk groups include:

- Immunocompromised children and adults,
- Newborns of mothers with varicella shortly before or after delivery,
- Premature infants,
- Neonates and infants less than one year of age,
- Adults without evidence of immunity,
- Pregnant women.

VARIZIG administration is intended to reduce the severity of varicella. Administer VARIZIG as soon as possible following varicella zoster virus (VZV) exposure, ideally within 96 hours for greatest effectiveness.

- There is no convincing evidence that VARIZIG reduces the incidence of chickenpox infection after exposure to VZV.
- There is no convincing evidence that established infections with VZV can be modified by VARIZIG administration.
- There is no indication for the prophylactic use of VARIZIG in immunodeficient children or adults when there is a past history of varicella, unless the patient is undergoing bone marrow transplantation.

**CONTRAINDICATIONS**

- Individuals known to have anaphylactic or severe systemic (hypersensitivity) reactions to human immune globulin preparations should not receive VARIZIG.
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity may have an anaphylactoid reaction.
- VARIZIG contains less than 40 micrograms per milliliter of IgA.

**WARNINGS AND PRECAUTIONS**

**Thrombotic Events**

Thrombotic events may occur during or following treatment with immune globulin products (1, 2, 3). Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known/suspected hyperviscosity. Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies.

**Coagulation Disorders**

Administer VARIZIG intramuscularly only. In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer VARIZIG if the expected benefits outweigh the potential risks.

**Hypersensitivity**

Severe hypersensitivity reactions may occur following VARIZIG administration. Administer VARIZIG in a setting with appropriate equipment, medication and personnel trained in the management of hypersensitivity, anaphylaxis and shock. In the case of hypersensitivity, discontinue administration of VARIZIG immediately and provide appropriate treatment.

VARIZIG contains trace amounts of IgA (less than 40 micrograms per milliliter). Patients with known antibodies to IgA have a greater risk of severe hypersensitivity and anaphylactic reactions. VARIZIG is contraindicated in IgA-deficient patients with antibodies against IgA and history of hypersensitivity reactions (see CONTRAINDICATIONS).

**Transmissible Infectious Agents**

Because VARIZIG is made from human plasma, it 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. The plasma donors are screened for the presence of certain infectious agents and the manufacturing process for VARIZIG includes measures to inactivate and remove certain viruses. Despite these measures, products derived from human plasma can still potentially transmit diseases. No cases of transmission of viral diseases, vCJD or CJD have been associated with the use of VARIZIG.

Report all infections thought by a physician to have been transmitted by VARIZIG to Cangene Corporation at 1-800-768-2304. Discuss the risks and benefits of this product with the patient before administering it to the patient.

**ADVERSE REACTIONS**

The most serious adverse drug reactions observed in clinical trials for all subjects and patients (n=601) include pyrexia, nausea, and vomiting.

The most common adverse drug reactions (reported by ≥ 1% of subjects) observed in clinical trials for all subjects and patients (n=601) are the following:

- Injection site pain (3%),
- Headache (2%),
- Rash (including terms pruritus, rash, erythematous, vesicular, and urticaria) (1%),
- Fatigue (1%),
- Chills (1%),
- Nausea (1%).

All other adverse drug reactions occurred in less than 1%.

**Clinical Trial Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Six hundred and one (n=601) high risk individuals received VARIZIG intramuscularly in two clinical trials which included pregnant women, infants and immunocompromised pediatric and adult patients. The highest incidence of adverse reactions occurred in pregnant women (n=166), including injection site pain (7%), rash (including terms pruritus, rash, erythematous, and rash vesicular) (4%), headache (3%), and fatigue (2%). All other adverse reactions occurred in 1% or less of clinical trial subjects within each high risk group. A single incidence of serum sickness (approximately one in 600 patients treated with VARIZIG) was observed in an immunocompromised adolescent patient.

There were eight reported adverse events associated with the coagulation system including, deep vein thrombosis (n=1), disseminated intravascular coagulation (n=1), intracranial hemorrhage (n=2), coagulopathy (n=2), intraventricular hemorrhage (n=1), and pulmonary hemorrhage (n=1) in 621 subjects in the open-label, Expanded Access Protocol (EAP); the study was not designed to differentiate between adverse events attributed to the underlying medical condition and adverse reactions to VARIZIG.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Pregnancy category C. Animal reproduction studies have not been conducted with VARIZIG. It also is not known whether VARIZIG can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. VARIZIG should be given to a pregnant woman only if clearly needed.

The safety and effectiveness of VARIZIG have been evaluated for post-exposure prophylaxis in clinical trials in 166 pregnant women (see ADVERSE REACTIONS and CLINICAL STUDIES).

**Nursing Mothers**

It is not known whether VARIZIG is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VARIZIG is administered to a nursing mother.

**Pediatric Use**

The dosing recommendations in the treatment of pediatric patients are by body weight. The safety and effectiveness of VARIZIG have been evaluated for post-exposure prophylaxis in the VARIZIG expanded access clinical trial in 374 pediatric patients, including immunocompromised pediatric patients.
- 94 preterm newborns and infants,
- 53 term newborns,
- 45 infants and toddlers,
- 176 children and,
- 43 adolescents.

In the EAP, follow up data were available for 110 VARIZIG treatments in infants (including newborns, pre-term infants, and infants <1 year old). Three severe infections were reported, all three with pox count >100, one of which also had pneumonia and another one also developed probable varicella encephalitis.

**Geriatric Use**

Clinical studies of VARIZIG administered intramuscularly for post-exposure prophylaxis did not include sufficient numbers of geriatric subjects (aged 65 and over) to determine whether they respond differently from younger subjects.

Use caution when administering VARIZIG to patients age 65 and over who are judged to be at increased risk of thrombotic events [see WARNINGS AND PRECAUTIONS]. Do not exceed recommended doses and administer VARIZIG intramuscularly only.

**Immunocompromised Patients**

In the EAP, both adult (n=37) and pediatric immunocompromised subjects (n=235) were treated. Twelve immunocompromised subjects developed clinical varicella and none developed varicella pneumonia; however at least five are reported to have received concomitant acyclovir and due to incomplete reporting, it is not known if others also received acyclovir.

**CLINICAL STUDIES**

**Pregnant Women Exposed to Varicella Zoster Virus**

A randomized, open-label, multicenter, active controlled clinical trial was conducted in 60 pregnant women without immunity to VZV as confirmed by a latex agglutination test. Patients were stratified on the basis of time from first exposure to varicella as follows:

- one to four days post-exposure and,
- five to 14 days post-exposure.

The women were randomized into one of three study arms as follows:

- a single intramuscular dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of VARIZIG, or,
- a single intravenous dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of VARIZIG, and
- a single intramuscular dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of VZIG (licensed comparator product).

Patients were followed for 42 days.

Incidence of clinical varicella was similar across all treatment groups with an overall incidence of 33%; however, in the subset of 28 subjects with more than 24 hours exposure to varicella, the incidence of varicella in the combined treatment groups was 64%.

Mean weighted constitutional illness scores (CIS) (4) were similar across all groups and none of the subjects had serious complications of varicella. The small number of subjects in each treatment stratum and the lack of agreed upon pre-specified hypothesis testing precluded formal statistical comparisons between groups.

**High Risk Patients Exposed to Varicella Zoster Virus**

An open-label, Expanded Access Protocol (EAP) conducted in the United States of America was designed to provide VARIZIG to high risk individuals who were exposed to varicella zoster virus (VZV). Although the study was not designed to evaluate efficacy, the objective of the study was to further assess and confirm the safety and efficacy of intramuscular injection of VARIZIG in the prevention or reduction of severity of complications from varicella infections in the indicated high risk populations. Initially, enrolment was limited to allow treatment with VARIZIG only within 96 hours of exposure, but the protocol was amended to expand the treatment window to 10 days post-exposure.

The incidence of clinical varicella (chickenpox lesions), was compared to predefined historical reference rates. The incidence of severe varicella complications, including pneumonia, encephalitis, severe varicella with pox counts >100 pox, mortality and all complications was also evaluated. The overall incidence of clinical varicella was evaluated in an interim analysis, where 10% (31/311) of high risk individuals exposed to VZV and treated with VARIZIG for all combined populations, for whom complete or partial efficacy data was available. Clinical varicella was observed in 8.4% (13/154) of immunocompromised pediatric and adult patients, in 6.8 % (5/74) of pregnant women, in 14.8% (12/81) of infants and one healthy adult (Table 1). Clinical varicella was more common after prolonged VZV exposure. The final report confirmed the efficacy results in the interim analysis (Table 2). In addition, a comparison of the incidence of varicella based on treatment window revealed that treatment between 5 and 10 days post-exposure was no different from treatment within 96 hours.

**Table 1 Comparison of Varicella Incidence in Subjects Treated with VARIZIG to Historical Incidence of Varicella in Untreated Individuals – Interim analysis**

<table>
<thead>
<tr>
<th>High Risk Population</th>
<th>Historical Incidence of Varicella in Untreated Individuals</th>
<th>VARIZIG-treated Subjects</th>
<th>95% Confidence Interval</th>
<th>p-value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant Women</td>
<td>70%</td>
<td>6.8% (n=5)</td>
<td>(2.2-15.1%)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>88%</td>
<td>8.4% (n=13)</td>
<td>(4.6-14.0%)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Infants</td>
<td>50%</td>
<td>14.8% (n=12)</td>
<td>(7.9-24.5%)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

¹ n = number of VARIZIG doses for post-exposure prophylaxis of varicella in efficacy population.
² One sample two-sided exact binomial test.
*Statistically significant (α=0.05).

**Table 2 Updated Summary of Incidence of Varicella in Subjects Treated with VARIZIG - Final Report**

<table>
<thead>
<tr>
<th>High Risk Population</th>
<th>Incidence of Varicella in VARIZIG-treated Subjects</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant Women</td>
<td>7.3% (n=10)</td>
<td>(3.6%-13.0%)</td>
</tr>
<tr>
<td>Immuno-compromised</td>
<td>4.5% (n=12)</td>
<td>(2.3%-7.7%)</td>
</tr>
<tr>
<td>Infants including</td>
<td>11.4% (n=12)</td>
<td>(6.1%-19.1%)</td>
</tr>
<tr>
<td>newborns, pre-term</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infants and infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ n = number of VARIZIG doses for post-exposure prophylaxis of varicella in efficacy population

**REFERENCES**

Where Did Everyone Go?

Coping with the Loss of Friendships Post-Diagnosis

There are many reasons friendships fall by the wayside after a chronic illness diagnosis, but there are methods of coping, including letting go and discovering new friendships.

By Trudie Mitschang
THE LOSS OF a friendship is rarely a clean break. Unlike the end of a romance, there are no screaming matches, slammed doors or even break-up texts. Often, there is more of a drifting away, a slow disconnect that can be more painful than a harsh goodbye. And, for a patient with chronic illness, this type of relationship unraveling tends to play itself out repeatedly, as one friend after another gradually seems to simply disappear. The fact that this occurrence is common and shared by so many does not make the pill any easier to swallow. “One of my friends — a friend I had been close with for 10 years — failed to visit, call, text or even message me on social media when I was going through several weeks of long hospital stays,” says Ilana Jacqueline, a 27-year-old dysautonomia and primary immune deficiency disease patient from South Florida. “I was stunned, but told myself: I’m OK. I don’t need her support. She has a busy life. It’s a busy week. I can’t just expect her to drop everything and acknowledge that I’m struggling a little bit here. Can I?”

Jacqueline, like many patients, initially blamed herself for the unexplained distance in her friendship. Over time, she began to see things from a different perspective. “I tried for a long time to convince myself that it was my fault. That I was boring. That I couldn’t go out. That it was my fault I fell off her radar,” she explains. “Finally, I was just like, you know what? Even when I can’t go out and make plans, I still reach out and check in on my friends. I still offer support and comfort. I deserve people who will do the same.”

Jenni Prokopy, a Chicago-based writer and motivational speaker who was diagnosed with fibromyalgia at the age of 25, agrees: “Plenty of my friendships have changed since I was diagnosed with chronic illness, but that was nearly 20 years ago, so I have to say that most of my friendships today are with people who I’ve known since I got sick.”

It’s Not You, It’s Me

The tendency to blame oneself for relationship conflicts that arise post-diagnosis is a normal reaction, and is often coupled with feelings of grief and loss. The truth is, most people pull away during times of crises because of their own shortcomings and inability to handle the stress and limitations brought on by chronic illness and pain. In such instances, a person may hear common sentiments such as: “It was hard to see you in so much pain,” or “I didn’t know what to say, so I didn’t call you.” These excuses undoubtedly fall flat when compared to the insurmountable challenges faced by a patient with an incurable disease.

More often than not, the friend who pulls away offers no explanation at all. “I had a friend who I lost a few years ago, for reasons unknown,” recalls Prokopy. “I was going through a really intense flare-up, and I wasn’t able to hang out as often or go on trips with her like we had in the past. I realized one day that she had just stopped reaching out. I tried to reconnect with her, but she just faded away. That was really hard to take because to this day, I do not know what precipitated that friendship breakup.”

Friends and family can be incredibly supportive, yet in many instances, they can also be extremely intimidated when it comes to helping a loved one, and may feel so overwhelmed themselves that they don’t have the strength to do so, says Beth Kane, LCSW, a private practitioner in Toms River, N.J., who specializes in working with patients coping with illness. “Very often, close family and friends can find themselves thrown into this ongoing grief process and are constantly reminded of how their own lives were before, how their own lives have changed and how the person used to be,” she explains. “They are as much in need of support and help as the individual who has the illness, sometimes more so, especially if they are the primary caregivers.”

The tendency to blame oneself for relationship conflicts that arise post-diagnosis is a normal reaction, and is often coupled with feelings of grief and loss.

Well-meaning individuals may also make things worse in an effort to provide support by continually saying the wrong things. Some, for example, may try to be encouraging by saying things like, “It could be worse” or “You look fine” — statements that seem innocent enough but only serve to invalidate a person’s physical and emotional suffering, especially for those with invisible illness. “The notion of ‘it could be worse’ translated into ‘you could be dead’ is a big roadblock,” says Kane. “There is a lot of material out there about positive thinking, which in its own right has its own merits and can be useful. But, when statements like this are used as a viewpoint, it is very dismissive of the pain the person experiencing this type of grief is trying to manage.”
Finding a New Normal

Psychologically, an illness diagnosis can stir up tremendous feelings of loss. A newly diagnosed individual may struggle to accept everything from the loss of health, career, income and freedom to the loss of cognitive function, independence and certainty. Later, unexpected losses such as the dwindling circle of close personal friends can really take their toll. When it comes to developing coping skills, mental health experts suggest patients make an attempt to see things from the healthy friend’s perspective. “People really don’t want to be around sick people,” says Steven Feinberg, MD, a past president of the American Academy of Pain Medicine. “When someone is ill, you feel sorry for them. But we’re all busy. We say we care and things like that, but the reality is, except for our immediate family, we don’t want to be reminded of our own mortality.”

The dilemma is often compounded when, at the same time friends may be pulling away, the person who is ill may not have the energy to invest in the friendship either. “If you’re in chronic pain, you don’t have the physical strength,” explains Dr. Feinberg. “You’re irritable, and people don’t want to be around you. So you start losing relationships.”

In her book, *A Delicate Balance: Living Successfully with Chronic Illness*, author Susan Milstrey Wells explores the myriad ways a diagnosis can negatively impact relationship dynamics. “Chronic illness throws a monkey wrench into our relationships. We may seem as foreign to the people who love us as if we had begun speaking a different language,” she explains. “Our family and friends still want us to be the mom who works, the dad who plays baseball in the backyard and the friend who meets them for lunch. In turn, we want to be treated as the same loving spouse, parent and friend we always have been. A large part of the responsibility for making those relationships work falls to us. We have to educate our family and friends about our disease, allow them to express their emotions openly, and clearly state our limits and our needs. Also, we have to expect these changes to be unsettling.”

In fact, it is that sense of feeling misunderstood that can drive a wedge between current and even potential new friendships. “I don’t think other parents understand my child’s diagnosis,” says Jessica Leigh Johnson, a mother of three sons with X-linked agammaglobulinemia (XLA) and one who passed away from XLA. “A lot of times people will say, ‘Well, if you expose him to more kids, he can build up an immunity by being around more sickness.’ And that’s exactly what he can’t do. I also don’t think they understand why I am so afraid of my kids catching something like influenza that could further damage their already damaged lungs. It’s a big deal, but I feel like other parents think I’m making a big deal out of nothing.”

Feeling misunderstood and judged is a big reason many patients and parents of children with chronic illness tend to withdraw socially, finding it easier to spend time with close family members or others who are facing a similar diagnosis. “I don’t cope very well with this challenge at all,” explains Johnson. “I find myself withdrawing from other moms my age. I figure they won’t understand me so I don’t put myself out there, and I don’t try very hard. Actually, my closest friends are my sisters-in-law. Members of our family understand because they’ve been with us from the beginning.”

Jacqueline agrees, and says she has also relied on the support of close family members when friendships fell by the wayside: “I turned to my sister who’d recently gone through something similar after her fiancé was diagnosed with pancreatic cancer. Some of their friends just seemed to disappear in the moment. They didn’t reach out at all. It was baffling.”

It’s important to consider that during the various stages and cycles of an illness, family and friends are also profoundly affected and may end up needing their own support. For some, there are significant changes in roles and responsibilities that can overwhelm the well person and contribute to feelings of powerlessness. For many, relationship dynamics are dramatically altered, leading to sadness and even anger over the loss of the person they knew before illness. Intimacy issues and learning how to maintain friendships as one pursues “a new normal” is possible, although it may require some ingenuity.

Some patients have coped by striving to reinvent their social time with friends and family. In an article that appeared in Health online, Shelley Kirkpatrick, 32, of Bellefontaine, Ohio, described how family and friends stuck by her once she helped them understand how fibromyalgia limited her social life. “I can’t go with a group of friends to the mall and shop all day
anymore,” she says. “I can’t spend an entire day out in the sunshine on the beach; I get fatigued.” Instead, Kirkpatrick and her friends have started planning activities around her energy levels. “I may be able to go shopping for half a day instead of a whole day. So we may plan to do shopping in the morning and see a movie in the afternoon, instead of trying to cram everything into one day. We all just kind of work together to get things done.”

**Learning to Cope and Move On**

There’s no question that living with a chronic illness can be difficult and lonely. While it’s not possible to control another person’s reaction to someone’s diagnosis, there are some practical steps patients can take to begin addressing their need for friendship and support:

*Educate loved ones about the illness.* Friends and family are able to be more supportive when they understand what the patient is going through. Share websites, books or other resources that explain the illness.

*Invite a close friend to a doctor’s appointment.* Getting more information about the condition can give both the patient and the friend peace of mind. Suggest the friend come along to learn more about the illness and how he or she can help.

*Ask friends for what is needed, and be specific.* Oftentimes, friends want to provide support but don’t know how. A patient should consider asking for help running an errand, completing chores or watching kids. Make a list of things needing to be done, and the next time someone asks if there’s anything they can do to help, tell them.

*Pursue the ones who disappear.* If certain friends go MIA, it’s possible they just don’t know what to say. Reaching out in a lighthearted way may take the pressure off and break the ice. Say something like: “Hey, John, I was diagnosed with primary immune deficiency not leprosy — it’s not contagious! I miss getting together.”

*Reach out to new people.* To extend one’s social circle, a patient might have to get out of his or her comfort zone. Try striking up a conversation with a classmate, neighbor or coworker. Join a support group either online or close to home. Getting involved in a cause related to the person’s illness can help to meet people with similar struggles.

*See a therapist.* A mental health professional can provide a supportive and understanding ear when a patient is feeling down. The professional can also help the patient cope with relational changes. Ask a doctor for recommendations, or run an online search for therapists who have knowledge about the condition.

**Letting Go When Needed**

Seeing a friend diagnosed with a chronic illness is hard for many people because it reminds them that anybody can get sick. They may disappear from their friend’s life because it makes them feel uncomfortable to think about their own health and mortality. Others may feel they have less in common with their friend now that their range of activities and interests has changed. And still others may simply be fair-weather friends who have decided to move on, requiring the patient to do the same. The bottom line is, if a friend repeatedly abandons someone when they’re needed most, perhaps the relationship isn’t worth pursuing. Letting go of a friendship is difficult, but it is sometimes the best thing to do for one’s emotional well-being.

**SEEING A FRIEND DIAGNOSED WITH A CHRONIC ILLNESS IS HARD FOR MANY PEOPLE BECAUSE IT REMINDS THEM THAT ANYBODY CAN GET SICK.**

“I really encourage newly diagnosed people to remember that not every friend is going to be your BFF. It’s natural for friendships to change over time, and that’s not always a negative,” says Prokopy. “When it comes to making new friends, I say keep your mind open about what kinds of people might become your friends. You may not be used to thinking about meeting people in different places besides your regular social circle and work life, but there are a lot of different places for you to meet friends, and it’s important to keep your mind and heart open to possibilities.”

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

**References**


How Mindfulness Can Ease the Symptoms of Chronic Illness

The term mindfulness has become ubiquitous in recent years, but it holds promise for those living with chronic illnesses.

By Dana Henry

SINGER/SONGWRITER Julianna Raye discovered mindfulness after her 1990s record deal with Warner Bros. Records ended and she experienced depression. Her therapist encouraged her to try meditation. She says she was just desperate enough to give it a shot. She went into it with no expectations, an attitude that served her well. To her surprise, meditating worked. Slowly. “Two years later, I was still doing it,” she says. That’s when she knew she was onto something. She says she felt more grounded and experienced positive physical changes.

Since then, Raye has become a mindfulness meditation trainer and has helped many clients deal with their own debilitating health issues, including chronic illnesses, through mindfulness. Her own mindfulness work proved that her body and mind were far more resilient than she had been giving them credit for. As a trainer, she knows that same realization is important for anyone facing a chronic illness.

For those living with chronic conditions, Raye says mindfulness is ultimately about learning how to use their illness to deepen who they are as human beings and, ultimately, to experience more fulfillment and well-being. “You can, over time, rewire yourself,” she says. “You can have a new permanent baseline of well-being and tranquility and energy.”
What Is Mindfulness?

Mindfulness, simply put, means keeping one’s attention trained on the present. It may seem like people do that naturally, but more often than we realize, our minds skitter away from the present and instead replay the past or anticipate the future. That can happen even while carrying out physical tasks in the here and now, such as driving, doing chores or performing routine duties at work. This split between acting in the present and thinking in the past or future can lead to disharmony, especially when chronic illness is involved. It’s easy to ruminate on negative health issues or worry about what the future may hold in terms of prognosis or treatment.

One of the most-common forms of mindfulness is mindfulness meditation, which has its origins in ancient Eastern religion and philosophy. In the West, this form of meditation is used to address symptoms associated with issues such as anxiety and depression. Meditation has also been shown to reduce chronic pain by 57 percent, with accomplished meditators achieving pain-reduction rates of more than 90 percent. Mindfulness meditation is prescribed for a range of illnesses, including arthritis, back pain, cancer, celiac disease, chronic fatigue, diabetes, fibromyalgia, heart disease, irritable bowel syndrome, migraines and multiple sclerosis.

“Mindfulness meditation is unique in that it is not directed toward getting us to be different from how we already are,” says Karen Kissel Wegela, professor at Naropa University, where she focuses on integrating psychotherapy and Buddhist psychological principles. Instead, meditation teaches people to be present with whatever is happening, no matter what it is, she explains. This can be incredibly beneficial mental training for people with chronic health issues. The way to alleviate suffering, Wegela states, is to go more deeply into the present moment and into ourselves rather than changing the situation or ourselves.

Founded in 1979, the Mindfulness-Based Stress Reduction Program (MBSR) at the University of Massachusetts focuses on intensive training in mindfulness meditation. Now taught widely in medical settings, this form of mindfulness has been researched using rigorous scientific methods. MBSR focuses on the mental and physical effects that can be produced through mindfulness. Research has shown that MBSR contributes to pain management in people living with chronic pain. And, it has been shown to help alleviate depression, anxiety and stress in breast cancer patients.

Other forms of mindfulness practiced in therapeutic settings include mindfulness-based cognitive therapy, dialectical behavior therapy, and acceptance and commitment therapy. Each has its own characteristics, but the common denominator is staying in the present.

The Physical Effects of Mindfulness

Mindfulness goes beyond treating psychological issues related to chronic illness. A study of people with chronic heart disease demonstrated that MBSR had a positive effect on blood pressure and body mass index, two biomarkers that are strongly correlated with health and disease.

Brain imaging reveals that mindfulness practice leads to alterations in the brain’s structure, which means the concept of mindfulness “rewiring” the brain isn’t just metaphorical. There’s an actual neurological process at work. Regions involved in body awareness consistently change with mindfulness. These include changes in the way people experience their bodies in relation to the outside world, as well as the ways in which they perceive the internal world of the body. One example of perceiving the body differently is that people who practice mindfulness tend to experience less pain. Raye says it is this reshaping of the relationship with pain that allows pain to be released.

Another area of the brain that mindfulness alters is the prefrontal cortex. This is the part of the brain involved in personality, impulse control, complex planning and, not surprisingly, attention. Six additional regions of the brain also change with meditation.

Meditation has been shown to reduce chronic pain by 57 percent, with accomplished meditators achieving pain-reduction rates of more than 90 percent.

Neuroimaging studies also show that mindfulness meditation improves cognitive performance. One study determined that even brief meditation training (totaling four sessions) improved visuospatial processing, working memory and executive functioning — changes formerly associated only with long-term meditation.
Tips for Starting a Mindfulness Meditation Practice

Be patient. Raye says people’s expectations about meditation can hinder their experience of the process. Rather than expecting huge changes immediately, be receptive to what is happening, even if it doesn’t feel like much. Keep at it, and the benefits will accumulate over time.

Go easy on yourself. Raye encourages people to avoid being too hard on themselves if they aren’t having what they perceive as the ultimate meditation experience. Mindfulness meditation isn’t about being distraction-free. It’s about learning to come back to the present when distractions happen, while cultivating internal kindness toward the mind and its tendency to meander.

Drop expectations. Being with “what is” can be liberating, unless “what is” is replaced with “what should be.” Developing a concept about what should be is a way of avoiding the present entirely, not unlike the way the mind already attempts to dodge the moment and find harborage in what was (e.g., the past) and what might be (e.g., the future).

Expectations are another way of rejecting what’s happening in the present moment. “Mindfulness, paying precise, nonjudgmental attention to the details of our experience as it arises and subsides, doesn’t reject anything,” Wegela says. “Instead of struggling to get away from experiences we find difficult, we practice being able to be with them.”

Go deeper. About two years into her practice, Raye realized she needed guidance to better understand the effect meditation was having on her health and well-being. For her, the next step involved learning from an expert. This is a common route meditators take. Teachers come in all shapes and sizes. They can be found at universities, in local meditation centers and even in healthcare settings in the form of trained therapists and psychiatrists. Indirect teaching is available through books and online. Teaching can also be found through retreats that can be as short as a day or two.

Putting It into Practice: A Simple Mindfulness Skill

Observing and describing is an essential mindfulness skill that can be used throughout the day, not just during meditation. Observing means paying attention to whatever is going on. All the senses are involved in observing, including sights, sounds, scents and textures.17

Describing means labeling whatever is observed, but without judgment or evaluation. Describing pays attention to what is observed, not thoughts and ideas about what is observed. “The waiting room is busy” is an example of describing. “The waiting room is stressful” is an example of adding an evaluation to the description.

Observing and describing are central to meditation as well. As thoughts enter the mind, they can be noted, labeled without judgment and dismissed. It can be helpful to envision the thoughts floating away in helium-filled balloons or being placed into a box where they can be revisited later.

Being mindful means being present, not just in the present. The benefit of this orientation is that, over time, it can bring the mind into sharper focus and make distractions — including inner distractions such as worrying — less

Resources

- ACLU Mindful Awareness Research Center: marc.ucla.edu/default.cfm
  ACLU offers free guided meditations in English and Spanish. Some are as short as five minutes.

- Center for Mindfulness: www.umassmed.edu/cfm
  The Center for Mindfulness at the University of Massachusetts maintains a mindfulness-based stress reduction teacher directory on its website, in addition to videos, mindfulness chatrooms and a virtual meditation room.

- Mindful: www.mindful.org/meditation/mindfulness-getting-started
  This website defines mindfulness and describes the basics of mindfulness practice. It includes short audio and video clips that facilitate the process.

- MIT Medical: medical.mit.edu/community/sleep/resources
  For sleep problems, MIT offers several mindfulness meditation audio downloads, including one on mindful breathing.

- Palouse Mindfulness: palousemindfulness.com/resources.html
  This site offers free self-paced online training in mindfulness-based stress reduction, as well as a number of resources, including audio recordings, book recommendations and retreats.

- Tara Brach: www.tarabrach.com
  Brach blends Western psychology and Eastern spiritual practices and has written extensively about working through difficult issues and experiences through meditation. Her website includes a free library of guided meditations.
powerful.  “When we are mindful, we show up for our lives,” Wegela says.

From research and people’s direct experiences, we know mindfulness can have profound physical and psychological effects. It can help people experience the symptoms of their illness differently, it can change important health biomarkers and it can reshape the brain. At the same time, mindfulness is not the one and only answer where chronic illnesses are concerned. As Raye says, it’s important to find the healing modalities that work for each person and his or her condition — and that complement each other. Mindfulness is one tool among many that, in combination, can produce lasting benefits.  

DANA HENRY is a writer and editor in the Kansas City area who specializes in science, medicine and health.

References

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A CHRONIC ILLNESS diagnosis begins not only with the physical and pharmacologic journey of stabilization, but also with the mental journey of coming to terms with it. Questions such as “Why me?” “What could I have done?” and “How will I and my family manage this financially and emotionally?” are coupled with the stressors of anger, denial and, often, depression.

A main concern about stress is its effect on the immune system, which can ultimately lead to further complicating an illness. It is well-accepted that chronic, negative stress can have an immuno-suppressive effect. Stress leads to increasing levels of catecholamine and T suppressor cells that can lead to viral infections due to an out-of-balance immune system. And, while there is no direct link between stress and cancer, certain studies have found links between stress, tumor development and suppression of natural killer cells.

The Centers for Disease Control and Prevention estimates that stress accounts for 75 percent of all doctor visits. The longer a person is negatively impacted by stress, the higher the risk of it having an effect on his or her body. Likewise, the negative effects of long-term stress can have an even greater impact on those who are older and who are already ill.

In some cases, the biology of an illness can cause stress and result in depression, which has been seen in some patients with Parkinson’s disease, cerebrovascular disease, multiple sclerosis and certain endocrine diseases. In other cases, a chronic illness may mimic symptoms of depression such as sleep apnea and Cushing’s syndrome, leading to confusion for both the patient and practitioner. And, the severity of an illness coupled with complicated treatment plans may reduce the likelihood that depression will be recognized or treated at all. Instead, the condition may trump any available time with a provider, or a provider may not look beyond the illness for answers to symptoms such as loss of appetite or fatigue.

Stress Simplified
According to Mary Wingo, PhD, author of The Impact of the Human Stress Response, “It is important to realize that a … stress response is not just psychological. Physical parts of us can get

THE IMPACT OF STRESS ON CHRONIC ILLNESS

While stress is common for those with a chronic illness diagnosis, there are effective approaches to managing it.

By Amy Scanlin, MS
mechanically or chemically stressed as well. Too much sun will burn us, and too much cold will freeze us, but we can cope with a considerable amount of physical stress before it overpowers us.” However, she explains, an overexposure and inability to cope can cause a body to break down. Simplistically, cells fluctuate between an open and closed state, reorganizing for just the right amount of plasticity and rigidity as needed. When a stressor or inflammation occurs, the body becomes more rigid, but only temporarily. The stress of a sprained ankle is a good example of this, says Dr. Wingo. Fluid rushes to protect the injury, and the area is sealed off while it heals. Once healed, the swelling goes down, and the tissues return to normal.

When a stressor becomes too great and an individual is ill-prepared to handle it, he or she will begin to have trouble returning to a normal state, a concept known as maladaptive adaptation. The need to return to the normal state is so important that the body will spend a great amount of energy on it, but that available energy is finite. Dr. Wingo offers an analogy: Imagine “you have taken out a huge biological emergency credit card loan with a 40 percent loan shark interest and henchmen ready to collect on the balance. As time progresses (the length of which is related to the intensity of the stressor), there is a limited amount of ‘adaptation energy’ available for adjusting to the environmental demands.” Essentially, the credit card gets “maxed out.”

Just living in today’s world with its near-constant stress (traffic, money, social media, news media, family, friends, illness) is stressful enough, but “major activation of our biological stress response is only designed to operate at irregular intervals,” explains Dr. Wingo. “You see the lion chasing you, you flee or fight. Then, if you are not eaten, you shake it off and get on with life. Hopefully, the times that you get chased by a lion are rare.” The constant need to readjust and reorient oneself is the real cause of breakdown in response to stress. Individuals must find better ways of managing stress, particularly in the context of a chronic illness and adapting to physical limitations.

Impact on Caregivers

The stressful effects of caring for a person with a chronic condition cannot go overlooked. Some studies show stress can shorten a caregiver’s life by as many as four years to eight years due to changes in chromosomes that can effectively amount to increased aging.

It is estimated that 15 percent of families have a chronically ill child who requires special care, and those demands can be more stressful than the illness itself. Trying to balance doctor visits and specialty at-home care with the usual requirements of parenting can be exhausting. Add to that the stress of seeing one’s child in pain with concerns for how the child will navigate the world as they grow up, and it can all become overwhelming.

“You have to have a good friendship team,” explains Amy Wyrick, referring to the partnership she and her husband Ted have in the care of their 15-year-old daughter who was diagnosed at age 2 with cerebral palsy just before the birth of their now 13-year-old son. “Score keeping has to go out the window.” Wyrick explains that friendship is the starting point for everything they do as parents. “We are doing this together, and it’s never going to be 50-50. Sometimes, she’ll need her mom more, and sometimes she’ll need her dad. Certainly, over the years, we have looked at each other and said, ‘This is very, very hard.’ Everything about it takes a toll, even just trying to find a solution that is right for you. When we reach a bump, we buckle down and see what we need to do.”

Managing Stress

According to the American Psychological Association, distress is common following a chronic disease diagnosis. Further, no matter the chronic illness, depression is one of the most common complications, with up to one-third of patients experiencing symptoms. Patients must learn to quickly deal with the intense emotions their diagnosis causes; they have to adjust behaviors to deal with their condition, maximize treatment protocols and navigate the disruptions to their work, family and personal life.

A MAIN CONCERN ABOUT STRESS IS ITS EFFECT ON THE IMMUNE SYSTEM, WHICH CAN ULTIMATELY LEAD TO FURTHER COMPLICATING AN ILLNESS.

Confronting the condition head-on is the best way to deal effectively with the physiological and emotional implications. Developing a plan of action and seeking social support engenders a feeling of satisfaction versus choosing to avoid a diagnosis. The difference between “healthy coping” and “avoidance” is key.

The Wyricks didn’t know anything about cerebral palsy when their daughter was diagnosed, but their first question was “What do we do?” rather than “What is wrong?” They connected with
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CUVITRU [Immune Globulin Subcutaneous (Human)] 20% Solution

Indication and Important Safety Information

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 indicated for the treatment of primary humoral immunodeficiency (PI) in adult and pediatric patients two years of age and older.
- 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.
- 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. Only use CUVITRU by yourself after you have been instructed by your healthcare provider.

Important Safety Information

What is the most important information that I should 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:

- Are allergic to immune globulin or other blood products.
- Have selective (or severe) immunoglobulin A (IgA) deficiency with antibodies to IgA.

CUVITRU can cause serious side effects. Call your healthcare professional or go to the 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 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 sign of an infection.

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

The following one or more possible side effects may occur at the site of infusion: mild or moderate pain, redness, and itching. These generally go away within a few hours, and are less likely after the first few infusions. The most common side effects that may occur are: headache, nausea, fatigue, diarrhea, and vomiting.

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

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire at 1-800-999-1785.

The risk information provided here is not comprehensive. To learn more, talk about CUVITRU with your healthcare provider or pharmacist. The Brief Summary of the FDA-approved patient labeling can be found on the reverse side.


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- The most common side effects that may occur are headache, nausea, fatigue, diarrhea, and vomiting

To learn more about CUVITRU, visit ListenPI.com and talk to your doctor to find out if CUVITRU is right for you.

Important Safety Information

CUVITRU can cause blood clots in the heart, brain, lung, and elsewhere in the body. Call your healthcare professional or go to your emergency department right away if you have pain, swelling, warmth, redness, a lump in your legs or arms, chest pain, trouble breathing, or blue lips or extremities. These could be signs of a blood clot.

Do not take CUVITRU if you are allergic to immune globulin or other blood products, or have selective (or severe) immunoglobulin A (IgA) deficiency with antibodies to IgA.

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IMPORTANT INFORMATION ABOUT CUVITRU [Immune Globulin Subcutaneous (Human)], 20% Solution

The following summarizes important information about CUVITRU. Please read it carefully before using this medicine. This information does not take the place of talking with your healthcare provider, and it does not include all of the important information about CUVITRU. If you have any questions after reading this, ask your healthcare provider.

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 adult and pediatric patients two years of age and older 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.

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 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 to determine if CUVITRU can be given to you. Tell your healthcare provider if you 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 that you take CUVITRU.

• Tell your healthcare provider 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 one or more possible reactions may occur at the site of infusion: mild or moderate pain, redness, and itching. These generally go away within a few hours, and are less likely after the first few infusions.

The most common side effects with 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 healthcare provider 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 problem or a 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 of the possible side effects with CUVITRU. You can ask your healthcare provider for physician's information leaflet. Tell your healthcare provider about any side effect that bothers you or that does not go away.

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire at 1-800-999-1785.

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Issue Date: 09/2016
16D028-CUV-US
S28017 01/17
physical therapists, became educated both formally and informally and began developing a plan. When their daughter wanted to put her own hair in a ponytail, she learned to do so in six weeks. When she wanted to learn to ride a bike, they started searching for a bike that would work for her. It’s all about empowerment and helping her to succeed. “We both want to be there for her successes,” Wyrick explains, but they also knew a support system was crucial.

As important as it is to confront the situation head-on, it is equally important for both patient and caregiver to stop and take a break. Parents need to get away, and frankly, sometimes so does the patient. “It is important for her to sometimes have a breather from all the treatments,” explains Wyrick. “You can occupational and physical therapy to death, both logistically and emotionally. Your intensity cannot always be at 100 percent.”

Managing stress is not merely a matter of managing the emotional environment, says Dr. Wingo. Managing the physical environment is also effective in improving one’s ability to handle stress and prevent stress-related illnesses.

Following are a few simple steps to reduce stress levels:

1. **Simplify where you can.** Dr. Wingo suggests identifying which of the top stressors take up the most energy and then trying to eliminate as many as possible. Of those, eliminate the smaller energy wasters, which she describes as dripping faucets, with small drains adding up to huge amounts of energy for the body and mind.

2. **Eat nutritious foods.** While there are many ideas about what constitutes the “healthiest” diet, one thing is certain: Nearly everyone has room for improvement. Talk with a doctor, ask for a referral to a nutritionist and get the best information possible to maximize health and wellbeing and reduce stress. Many people choose certain foods in response to stress. The decision about what to eat and how much is, in most cases, within one’s control, and managing stress can help individuals make better food choices that can have a positive effect on stress. The two go hand in hand. “Perhaps the most potent chemical stressor is actually the food we eat,” explains Dr. Wingo, and a “major toxic stressor is sugar.”

3. **Get plenty of sleep.** An American Psychological Association sleep survey shows that Americans are getting neither the quantity nor quality of sleep needed, and many report their stress levels increase as their sleep decreases. To reverse this, go back to tip number one, and simplify where possible. Then, put that time to good use such as adding sleep. Individuals’ bodies and minds recharge and repair while sleeping.

4. **Reduce screen time.** Turn off the phone, TV and computer, if only for a little while, to reap the benefits of quiet. Do you really need to know what your friend had for breakfast? Unsubscribe from some of those email lists, and get back to the basics: Have a real conversation, take a walk, break bread with family or friends, and get some sleep.

5. **Ask for help.** Whether it’s logistical, physical or emotional support, ask for help from the many people in your life who are more than willing to give it. So often, people shy away from asking because they don’t want to trouble anyone. But friends want to be troubled and want to know how they can help. When the need for assistance is greater than a friendly ear or arm, seek professional support from the many community and medical resources available.

### Approaching Stress Usefully

People have a lot of stress-related mortality and disability, explains Dr. Wingo. We have created an epidemic of unsustainable stress, including its impact on our health. “The hard reality is a lot of people are dying in their 50s and 60s,” she says. “What used to be easy has now become impossibly hard as those individual stressful events become cumulative and our episodic stress becomes chronic.”

Dr. Wingo recommends treating stress like a risk factor. And, she says, “be honest; you may not realize how much stress you are under. Anything you can take off the table, do.” There is a lot of “woo-woo” around stress, she says. “But, it’s not all just bad traffic or kids [who] won’t obey. We need to create a user-friendly system of being able to identify our stressors” and approach them in an intelligent and useful way.

Whether seeking information or eliminating a stressor from life, each situation should be approached with intention and clarity. Sustainable steps can be taken, and help can be asked for. “Ted and I did some serious talking and serious praying,” says Wyrick, including their decision about whether their daughter would have the risky selective dorsal rhizotomy spinal cord surgery. Utilizing all of the support at their disposal, they came to a decision. “I can’t change her situation,” says Wyrick, “but what can I do to make it better?”

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

### References

Immunodeficiency in Newborn Infants

By E. Richard Stiehm, MD

Four vignettes describe risk factors for immunodeficiency in newborns, as well as diagnoses and treatments.

The Newborn Emerges from the womb into an environment swarming with microbes, which quickly colonize the infant’s upper airway, skin and gastrointestinal tract. Most newborns survive this invasion because of anatomic barriers, innate immunity and maternal transplacental antibodies. In addition, most U.S. newborns are cared for in clean environments, away from unwell persons and fed breast milk or sterile nutrition.

Newborns have an immune system that is anatomically intact, antigenically naïve and functionally compromised. Their B cells have a reduced capacity to make antibodies, their T cells are functionally weak and their phagocytic cells have poor mobility and a diminished marrow reserve. All of these weakened responses make infection a significant hazard. But, if an infant has additional immune defects as a result of prematurity, maternal illness or medication, or heredity, the risk for infection is greatly enhanced. Thus, recognizing an immunodeficiency in newborns is crucial before infections ensue.

Factors that predispose newborns to an immunodeficiency are listed in Table 1. The most common risk factor is prematurity, in proportion to their degree of immaturity. Some of these are illustrated in the following vignettes.

Case 1: Tommy is a 32-week-old preemie with fever and poor feeding on day three

Tommy was born with a birth weight of 1,470 grams (3 pounds, 2 ounces) to a 35-year-old woman. Her fourth pregnancy was complicated by preeclampsia with hypertension and proteinuria (urine containing abnormal amount of protein), requiring antihypertensives during the last months of pregnancy. After a two-hour labor, Tommy was born vaginally with an Apgar score of 7. On the third day of life, he developed a fever and poor feeding. Physical exam showed tachypnea (rapid breathing) and abdominal distention.

Tommy’s hemoglobin (Hb) was 14.7 g/dL, and white blood cell count (WBC) was 4,250/uL with 10 percent neutrophils, 80 percent lymphocytes, 6 percent monocytes and 4 percent eosinophils. His platelet count was 53,000/uL. Blood and urine cultures were positive for E. coli. Tommy was started on intravenous ampicillin and cefotaxime. He became afebrile after three days, but the neutropenia (low concentration of a kind of white blood cells) continued for a week with WBCs less than 1,000/uL. A bone marrow showed a maturation arrest. Genetic tests for congenital neutropenias were negative, as were tests for
neutrophil antibodies in the mother’s and infant’s serum.

Diagnosis: Neutropenia of infancy with sepsis secondary to maternal hypertension

Comment: Variable neutropenia occurs in 40 percent to 50 percent of babies born to hypertensive mothers. Usually, the neutrophil count is less than 3,000 cells/uL but greater than 500 cells/uL. Neutropenia is more likely in low-birth weight infants and those with a fever or other evidence of infection. Most neutropenic infants remain well, and their neutrophil count normalizes in a few weeks. Antibiotic treatment is indicated if there is fever, chorioamnionitis (bacterial infection that occurs before or during labor) or prolonged rupture of membranes.

Other causes of neutropenia in infancy include drug reactions, isoimmune or autoimmune neutropenia, severe congenital neutropenia (Kostmann syndrome), viral infections, cyclic neutropenia and several primary immunodeficiencies, including reticular dysgenesis (rare and severe form of combined immunodeficiency) and the hyper IgM syndromes.2,3

Case 2: Sally is a 3-month-old infant with a heart murmur and cyanosis (bluish discoloration of the skin due to lack of oxygen)

Sally was the first child for an unrelated couple. The 29-year-old mother has diabetes and an alcohol problem. The infant weighed 3,500 grams (7 pounds, 7 ounces) after a 38-week pregnancy. The infant was slightly cyanotic and tachypneic with crying and feeding. A faint heart murmur was noted. A chest X-ray disclosed a boot-shaped heart, absent thymus and diminished lung markings. An echocardiogram disclosed Tetralogy of Fallot (congenital heart defect).

The Hb was 15.2 g/dL and WBC was 8,500/uL with 65 percent neutrophils, 15 percent lymphocytes, 15 percent monocytes and 5 percent eosinophils. Platelets were 26,000/uL, and electrolytes, calcium and phosphorus levels were normal.

An immunologic consultant noted tapered fingers, low-set ears and slight microcephaly (smaller than normal head). Flow cytometry showed CD3 total T cells of 820/uL, CD4 helper T cells of 620/uL, CD8 cytotoxic T cells of 130/uL, CD19 B cells of 250/uL and CD16/56 natural killer (NK) cells of 140/uL. A lymphoproliferative assay with the mitogen phytohemagglutinin (PHA) showed a stimulation index of 35 compared to a control of 80 (a low normal response). Chromosome fluorescent in situ hybridization analysis identified a 22q11 deletion in the patient but not in either parent.

Diagnosis: Partial DiGeorge syndrome with low but not absent T cells

Table 1. Prenatal Factors That Increase the Risk of Newborn Immunodeficiency

- Family history of immunodeficiency or early death
- Consanguinity (common blood ancestry)
- Ethnicity with a high incidence of primary immunodeficiency (e.g., severe combined immunodeficiency in Navajos, ataxia-telangiectasia in Amish and Bloom syndrome in Ashkenazi Jews)
- Maternal infection (chronic, acute, perinatal)
- Maternal hypertension
- Maternal autoimmune disease
- Maternal immunodeficiency
- Maternal immunosuppressive medications
- Maternal malnutrition or obesity
- Maternal use of alcohol, tobacco, opioids or street drugs

Comment: DiGeorge syndrome, sometimes called the CATCH-22 syndrome (Cardiac defects, Abnormal facies, Thymic aplasia, Cleft palate, Hypocalcemia/Hypoparathyroidism and deletions of Chromosome 22) is the second most common chromosome abnormality (after Down syndrome) with an incidence of one in 3,000 births. Diabetes and alcohol abuse during pregnancy may be risk factors. Only a small percentage (5 percent) have a profound combined immunodeficiency — the complete DiGeorge syndrome. Sally was scheduled for corrective heart surgery after she had grown to 8 kg (17.6 pounds). Because of her low CD4 count, she was started on Bactrim prophylaxis, and given palizumab (Synagis) in the winter months. Serial immune studies were recommended after inactivated vaccines to measure her antibody function.

DiGeorge syndrome patients may develop autoimmunity, endocrinopathies, palatal and swallowing problems, and slow mental and physical development. Selective IgA deficiency and specific antibody deficiency are not uncommon. All patients with cardiac outflow tract abnormalities should be studied for DiGeorge syndrome.

Case 3: Jorge is a 2-month-old ex-premature infant with fever and tachypnea

Jorge is a 2-month-old male born at 31 weeks with a birth weight of 1,460 grams (3.2 pounds). He was the first child for the 24-year-old mother who had two prior miscarriages associated with severe obesity and tobacco use. The infant
Jorge’s WBC was 18,000/uL with 72 percent neutrophils, 10 percent monocytes and 18 percent lymphocytes. Blood, throat and urine cultures were obtained. A chest X-ray showed a few streaky densities. IgG was 120 mg/dL (very low), IgM was 35 mg/dL, IgA was less than 5 mg/dL and ESR was 45 mm/hr. T and B subsets were low normal. The mother’s IgG was 502 mg/dL (low normal), IgM was 102 mg/dL and IgA 30 was mg/dL. Complement activity (CH 50) was 75 units (normal for age).

Because of the fever, low IgG and suggestive evidence of pneumonia, Jorge was started on antibiotics and intravenous immune globulin (IVIG) to maintain his IgG near 600 mg/dL. Bacterial and viral cultures were negative. He became afebrile after three days, and the chest X-ray infiltrates were resolving.

Diagnosis: Pneumonitis in a hypogammaglobulinemic premature

Comment: Jorge’s low IgG was a result of four factors: 1) low maternal IgG with diminished transplacental IgG passage, 2) prematurity further reducing the IgG transplacental passage, 3) frequent blood draws and 4) presence of infection, which accelerates IgG catabolism. A primary antibody deficiency such as X-linked agammaglobulinemia was excluded by the presence of normal B cells. Prophylactic use of IVIG in prematures is not recommended unless the child is infected and/or profoundly neutropenic.

Case 4: Jason is a 3-month-old boy with sudden onset of diarrhea and vomiting

Jason was the first child of unrelated parents. He was born at term with a birth weight of 4,250 grams (9.37 pounds) and did well for the first months of life on breast feedings. He received all recommended vaccines starting at 2 months of age (hepatitis B, measles-mumps-rubella, Haemophilus influenzae, pneumococcal conjugate and oral rotavirus vaccines). Three weeks after these vaccines, he developed fever and diarrhea requiring hospitalization for dehydration. Physical exam disclosed oral thrush, dehydration and a distended abdomen.

Jason’s hemoglobin was 14 g/dL and WBC was 9,300/uL with 72 percent granulocytes, 1 percent lymphocytes, 8 percent monocytes and 7 percent eosinophils. His platelet count was 152,000/uL, and his absolute lymphocyte count was 1,540/uL. Blood chemistries showed a mild acidosis. Jason’s IgG was 205 mg/dL, IgM was 15 mg/dL and IgA was less than 3 mg/dL. Lymphocyte phenotyping showed CD3 T cells of 95/uL, CD4 of 52 /uL, CD8 of 32/uL, CD19 of 600/uL and CD 16/56 of 24/uL. Thus, he had a T-B+NK-severe combined immunodeficiency. 2,3 A stool culture was positive for rotavirus.

Diagnosis: Rotavirus vaccine-induced diarrhea in severe combined immunodeficiency (SCID)

Comment: Jason was born in one of the few states that did not have newborn heel stick SCID screening. Thus, he received the live attenuated rotavirus vaccine. Because he could not develop an immune response to the vaccine, the virus proliferated in his gastrointestinal tract to cause diarrhea. 5

Genetic analysis indicated that he had a new mutation of the IL-2 receptor gene on the X chromosome. This receptor is also termed the common gamma gene receptor since it is also the receptor for five other cytokines (IL-4, IL-7, IL-9, IL-15 and IL-21). The mother was not a carrier, so this was a new mutation. This is the most common mutation resulting in SCID.

One advantage of SCID testing and early diagnosis in infants is to avoid live virus and bacterial vaccines. There are several reports of post-vaccine diarrhea following rotavirus vaccine in SCID children but no fatalities. 5,6 Newborn screening also identifies severe lymphopenia in other disorders, including ataxia-telangiectasia, extreme prematurity, maternal immunosuppres-
sive therapy or in utero fluid extravasation into the chest or peritoneum. 7

Discussion

Prebirth risk factors that increase the likelihood an infant will be immunodeficient are listed in Table 1. In the cases above, one woman had hypertension during pregnancy, another had diabetes and alcohol use and another had risk factors for premature delivery (smoking, obesity). One infant was at risk because he had a genetic defect and was born in a state where newborn SCID testing was not yet in place. These factors emphasize the importance of vigilance during pregnancy and good prenatal care.

Several clinical or laboratory features suggest immunodeficiency (Table 2). The most common is low birth weight and/or prematurity, particularly those with birth weight less than 1,500 grams (3.3 pounds). These infants have diminished opsonic activity (process by which bacteria are altered so that they are more readily and efficiently engulfed by phagocytes) due to low IgG and complement levels, and more compromised antibody and T cell immunity than term infants. Some of these infants have characteristic clinical features that warrant an immunologic evaluation. Others are recognized by newborn SCID screening or an abnormal routine laboratory test.

Initial laboratory studies begin with a complete blood count with differential. The presence of leukocytosis (a WBC less than 12,000 cells/µL) or leukopenia (a WBC less than 4,000 cells/µL) may be a primary or indicate infection or a hematologic illness. The absolute lymphocyte count (as determined by the differential and a WBC less than 2,500 cells/µL) suggests a T or B cell defect. Thrombocytopenia (platelets less than 100,000 cells/µL) occurs in certain immunodeficiencies (e.g., Wiskott-Aldrich syndrome) or viral infections. If lymphopenia is present, a chest X-ray should be done to look for the presence of a thymic gland; its absence suggests SCID or DiGeorge syndrome.

IgG determination is also recommended. A term infant’s IgG level reflects the maternal IgG level, but the premature’s IgG level is lower than that of the mother in proportion to the degree of immaturity. An elevated IgM (greater than 20 mg/dL) suggests congenital infection, and an elevated IgA suggests maternal-fetal bleed. A very low IgG level may result from extreme prematurity, IgG loss, maternal hypogammaglobulinemia or medication such as rituximab.

Additional screening tests may include a chemistry panel (electrolytes, blood urea nitrogen, creatinine, liver function, albumin, calcium and phosphorus), urinalysis and acute phase reactants (erythrocyte sedimentation rate and/or C-reactive protein). Infection evaluation includes imaging of suspected sites of infection, and cultures or polymerase chain reaction tests to identify an infectious agent.

The first intermediate test recommended is lymphocyte subset enumeration by flow cytometry. This procedure measures the number of total T (CD3) cells, helper T (CD4) cells, cytotoxic T (CD8) cells, NK (CD8/CD16) cells and B (CD19) cells, and will identify most patients with SCID or complete DiGeorge syndrome. If a T cell defect is suspected, their function is assessed by their ability to proliferate following activation by the mitogen PHA.

Infants suspected of a primary immunodeficiency should be kept in protective isolation, or if at home, away from individuals (including siblings) who may transmit infection to them. Advanced diagnostic tests should be done in conjunction with an immunologist.

If blood products are given, they should be irradiated, cytomegalovirus-negative and leukodepleted. Formulae should be sterile. Breast milk feedings are allowed unless there is a suspicion of maternal HIV infection. If IVIG infusions are planned, blood for IgG levels and antibody titers should be drawn prior to its administration.

If infants are suspected of immunodeficiency, live vaccines (e.g., rotavirus, BCG) should be avoided. Prophylactic antibiotics to prevent Pneumocystis are given to infants with severe T cell deficiency. In addition to IVIG therapy, palivizumab (Synagis) is given monthly in the winter to prevent respiratory

Table 2. Clinical Features Suggestive of Newborn Immunodeficiency

- Infection at any site
- Failure to thrive
- Chronic diarrhea
- Heart or lung disease
- Mucosal abnormalities: thrush, mouth sores, ulcerations
- Rashes, pigmented abnormalities, alopecia
- Petechiae, melena, bleeding
- Lymphadenopathy and/or hepatosplenomegaly
- Syndromic appearance (abnormal facies or habitus)
- Abdominal distention
- Neonatal surgery
- Delayed umbilical cord separation
- Infection following live vaccine
Table 3. Most Common Causes of Immunodeficiency Presenting at Birth or in Early Infancy

<table>
<thead>
<tr>
<th>Humoral (antibody) deficiencies (IgG &lt;400 mg/dL, severe &lt;200 mg/dL)</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Prematurity</td>
<td>Severe infection in infants less than 1,500 grams</td>
</tr>
<tr>
<td>Physiologic hypogammaglobulinemia of infancy</td>
<td>Usually asymptomatic</td>
</tr>
<tr>
<td>Maternal hypogammaglobulinemia</td>
<td>Mother has untreated hypogammaglobulinemia or on immunosuppression causing low B cells</td>
</tr>
<tr>
<td>Immunoglobulin loss</td>
<td>Surgery, blood drawing, diarrhea, exudative skin lesions</td>
</tr>
<tr>
<td>Congenital agammaglobulinemias</td>
<td>Usually asymptomatic, IgG low after several months</td>
</tr>
<tr>
<td>Combined immunodeficiencies</td>
<td>Severe infection, IgG low after several months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cellular (T cell) immunodeficiencies (CD3 T cells &lt;500/microL, severe &lt;200 cells/microL)</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Severe combined immunodeficiencies</td>
<td>Thrush, diarrhea, failure to thrive, Pneumocystis jirovecii pneumonia</td>
</tr>
<tr>
<td>DiGeorge syndrome</td>
<td>Outflow cardiac defects, typical facies, hypocalcemia, absent thymic shadow</td>
</tr>
<tr>
<td>Wiskott-Aldrich syndrome</td>
<td>Boys with thrombocytopenia, bleeding, eczema, respiratory infections</td>
</tr>
<tr>
<td>Hyperimmunoglobulin M syndromes</td>
<td>Respiratory infection (e.g., P. jirovecii pneumonia), neutropenia, elevated IgM hemolytic anemia</td>
</tr>
<tr>
<td>Mucocutaneous candidiasis</td>
<td>Early onset of thrush, esophagitis, skin infections, endocrinopathies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neutropenia (granulocytes &lt;500/microL, severe &lt;200 cells/L)</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Neutropenia due to maternal hypertension mild</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>Drug-induced neutropenia</td>
<td>Various drugs, usually reversible, asymptomatic</td>
</tr>
<tr>
<td>Benign neutropenia</td>
<td>Moderate, asymptomatic, normalizes with infection</td>
</tr>
<tr>
<td>Severe congenital neutropenia</td>
<td>Early onset of refractory infection</td>
</tr>
<tr>
<td>Cyclic neutropenia</td>
<td>Moderate or severe infections, often asymptomatic</td>
</tr>
<tr>
<td>Autoimmune or isoinmune neutropenia</td>
<td>Maternal neutropenia, neutrophil antibodies, familial</td>
</tr>
<tr>
<td>Neutropenia of infection</td>
<td>Develops during severe infection of the newborn, poor prognostic sign</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other phagocytic immunodeficiencies (T and B cell function normal, no neutropenia)</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Chronic granulomatous disease</td>
<td>Deep-seated infections, abscesses, pneumonia, moderate leukocytosis</td>
</tr>
<tr>
<td>Leukocyte adhesion deficiency</td>
<td>Marked leukocytosis, poor wound healing, delayed umbilical cord separation (&gt;30 days)</td>
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<tr>
<th>Immunoregulatory disorders</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Mendelian susceptibility to mycobacterial diseases</td>
<td>Chronic Bacillus Calmette-Guérin (BCG) infection, environmental nontuberculous mycobacteria</td>
</tr>
<tr>
<td>Hemophagocytic lymphohistiocytosis (HLH)</td>
<td>Fever, vomiting, hepatosplenomegaly, seizures, liver failures</td>
</tr>
<tr>
<td>Immunodysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome</td>
<td>Boys with enteropathy/colitis, diabetes, dermatitis</td>
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</tbody>
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<table>
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<tr>
<th>Innate immune defects</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>NF-kappa-B essential modulator (NEMO) defects</td>
<td>Severe infections, sparse hair</td>
</tr>
<tr>
<td>Toll-like receptor (TLR) defects</td>
<td>Severe bacterial infections (especially Staphylococcus and pneumococcus) with little or no fever or elevation of inflammatory markers</td>
</tr>
<tr>
<td>Congenital asplenia</td>
<td>Overwhelming sepsis, other abnormalities</td>
</tr>
<tr>
<td>Natural killer cell deficiencies</td>
<td>Severe herpes infections</td>
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<table>
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<tr>
<th>Complement deficiencies</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cause</strong></td>
<td><strong>Features</strong></td>
</tr>
<tr>
<td>Prematurity with opsonic defects</td>
<td>Neonatal sepsis in infants &lt;1,500 grams</td>
</tr>
<tr>
<td>Regulatory protein deficiencies</td>
<td>Hemolytic-uremic syndrome, renal failure, thrombocytopenia</td>
</tr>
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</table>
syncytial virus infections. Referral to a medical center for a definitive diagnosis, genetic testing and advanced therapy should be considered.

Some of the most common immunodeficiencies of the young infant are presented in Table 3.

Summary
The newborn immune system is anatomically intact, antigenically naïve and functionally deficient. Most newborns survive their entry into the external world thanks to innate immunity, passive maternal antibody, a clean environment and sterile feedings. Just a few infants have early onset of a primary or secondary immunodeficiency.

Factors predisposing immunodeficiency include maternal illness, infections and inherited factors. These infants may present with low birth weight, infection, hepatosplenomegaly (enlargement of both liver and spleen), skin abnormalities, failure to thrive or syndromic appearance. The most common causes of immuno-
deficiency are prematurity, neutropenia and DiGeorge syndrome. Less common disorders include variable T-cell defects, phagocytic disorders and innate immune defects.

Blood tests, cultures and genetic tests are available to pinpoint an exact diagnosis. Consultation with an immunologist for diagnosis and treatment is recommended.

E. RICHARD STIEHM, MD, is professor of pediatrics at the David Geffen School of Medicine at the University of California, Los Angeles.

References

HlgH-Flo needles were designed with safety & comfort in mind.

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HlgH-Flo Subcutaneous Safety Needle Sets
Important Safety Information

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

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

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

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

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

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

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

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

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

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

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

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

Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

WARNING: THROMBOSIS
See full prescribing information for complete boxed warning.

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

• For patients at risk of thrombosis, administer Hizentra at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

For subcutaneous infusion only.

Administer at regular intervals from daily up to every two weeks (biweekly).

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

Weekly: Start Hizentra 1 week after last IGIV infusion
  Initial weekly dose = \[
  \frac{\text{Previous IGIV dose (in grams)}}{\text{No. of weeks between IGIV doses}} \times 1.37
  \]

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

Frequent dosing (2 to 7 times per week): Start Hizentra 1 week after the last IGIV or Hizentra/IGSC infusion. Divide the calculated weekly dose by the desired number of times per week.

Adjust the dose based on clinical response and serum IgG trough levels.

Dosage

Administer at regular intervals from daily up to every two weeks (biweekly).

For subcutaneous infusion only.

 Dosage (2.2)

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

Weekly: Start Hizentra 1 week after last IGIV infusion
  Initial weekly dose = \[
  \frac{\text{Previous IGIV dose (in grams)}}{\text{No. of weeks between IGIV doses}} \times 1.37
  \]

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

Frequent dosing (2 to 7 times per week): Start Hizentra 1 week after the last IGIV or Hizentra/IGSC infusion. Divide the calculated weekly dose by the desired number of times per week.

Adjust the dose based on clinical response and serum IgG trough levels.

Administration

• Infusion sites – 1 to 4 injection sites simultaneously, with at least 2 inches between sites.

<table>
<thead>
<tr>
<th>Infusion Parameters*</th>
<th>Infusion Number</th>
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<td></td>
<td>1st</td>
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<tr>
<td>Volume (mL/site)</td>
<td>≤ 15</td>
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<tr>
<td>Rate (mL/hr/site)</td>
<td>15</td>
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As tolerated

DOSAGE FORMS AND STRENGTHS

0.2 g per mL (20%) protein solution for subcutaneous injection

CONTRAINDICATIONS

• Anaphylactic or severe systemic reaction to human immune globulin or components of Hizentra, such as polysorbate 80

• Hyperprolinemia (type I or II) (Hizentra contains the stabilizer L-proline)

• IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

WARNINGS AND PRECAUTIONS

• IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions.

• Thrombosis may occur following treatment with immune globulin products, including Hizentra.

• Aseptic meningitis syndrome has been reported with IGIV or IGSC treatment.

• Monitor for clinical signs and symptoms of hemolysis.

• Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])

• Hizentra is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

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

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

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

• Pediatric: No specific dose requirements are necessary to achieve the desired serum IgG levels.
Qualifying for Social Security Disability Benefits

This helpful guide explains how to qualify for disability entitlements due to chronic illness.

By the Outreach Team at Disability Benefits Help

THOUSANDS OF Americans live with immune and autoimmune disorders every day. While it is entirely possible to live a normal life with such a disorder, some find their severe symptoms prevent them from working or providing for themselves.

For those experiencing daily difficulty because of their disorder, disability benefits may be an option. Social Security disability insurance (SSDI) is a government-run program that provides monthly benefits to people and families in need.

Technical Requirements

To qualify for SSDI benefits, certain financial and work-related requirements must be met. An applicant must have enough history of contributing taxes to Social Security. These contributions are called “credits” and can be earned up to four times per year (once per work quarter).

The amount of credits and work years an applicant needs depends on his or her age. For example, someone who became disabled at age 22 would need one-and-a-half years of prior work with six credits required to qualify for SSDI. However, a 40-year-old would need at least five years of recent work and 20 credits to qualify. These numbers rise until they cap out at age 62 (retirement age), when most people begin to qualify for retirement benefits. To understand the requirements, individuals can reference the Social Security Administration’s (SSA) credit requirement chart and credit calculator online (www.ssa.gov/planners/credits.html).

If an individual is under 18 or does not have enough work history or credits to qualify for SSDI, he or she may choose to apply for Supplemental Security Income (SSI) instead. This Social Security program does not require income or work history, but is reserved for disabled Americans who demonstrate severe financial need.

Medical Requirements

If the technical requirements are met, the next important piece of the application is the medical qualifications section. When SSA reviews an application, it looks to confirm that an applicant is “totally and permanently disabled.” This means the applicant must have a severe physical or mental disorder that is expected to last longer than one year or result in death. SSA determines this by referring to the “Blue Book” (www.ssa.gov/disability/professionals/bluebook), which lists all SSA-approved disorders and the requirements needed to qualify.

Because there are so many variants, the Blue Book has a section entirely devoted to qualifying immune system disorders (Section 14.00). This section describes exactly how SSA defines an immune system disorder, the differences between various diagnoses and the symptoms/test results required to prove the severity of each case. To determine if one is qualified, an individual needs to find his or her diagnosis in the list of immune disorders and prepare the necessary paperwork.

For example, if an individual is interested in applying for benefits for his or her immune deficiency disorder, he or she would reference Section 14.07 in the Blue Book. This section states that, to qualify, an applicant must have infections that are either resistant to treatment or require hospitalization or intravenous treatment three or more times in a 12-month period. An individual can also qualify if he or she has had a stem cell transplantation, or if the condition limits activities of daily living, maintaining social function or completing tasks in a timely manner due to deficiencies in concentration, persistence or pace.

If a precise diagnosis is not listed in the Blue Book, an individual may still qualify. If symptoms are severe enough to qualify under another listing, SSA still may approve an individual’s case. For example, someone with an immune disorder that isn’t an immune deficiency disorder may still qualify under this listing if multiple organs have been affected by the disorder. Those without qualifying listings may also still receive benefits under a medical vocational allowance (MVA). An MVA is provided to unlisted disorders that are still severe enough to prevent the applicant from working or living normally.

Applying for Benefits

Applications for SSDI can be found on SSA’s main website (www.ssa.gov/applyfordisability). Aside from the application, the website also contains application preparation lists, questionnaires and FAQs about the application, should individuals need help during the process. If it is preferred to apply elsewhere, individuals can call their local Social Security office to either schedule an appointment or fill out their application over the phone.

Disability Benefits Help provides information about disability benefits and the application process. To learn more, visit the organization’s website at www.disabilitybenefitscenter.org or contact them at help@ssd-help.org.
FOR AVERAGE AMERICANS striving to improve their overall health, studying various nutritional regimens can at times feel like studying dogmas. Vegans, vegetarians, pescatarians and their more carnivorous challengers, including Paleolithic (paleo) and ketogenic diet supporters, flock to publishers to “duke out” their beliefs, trying to refute one another’s research and prove which diet is best.

Look to Amazon or a local bookstore for proof. Book and video titles such as The Low-Carb Myth, The Vegetarian Myth, Proteinaholic, The Starch Solution, Cereal Killers, The Case Against Sugar and the ever-witty Eat Bacon, Don’t Jog represent warring viewpoints. Look also to YouTube, which is full of dietary debates, including impressive exchanges between lifestyle leaders such as epidemiologist T. Colin Campbell, PhD, author of Forks Over Knives, and Duke University researcher and obesity expert Eric Westman, MD.

Increasingly, however, experts have one belief in common no matter the “flavor” of their dietary choices: Chronic systemic inflammation is a key enemy to people’s overall health.1

While acute inflammation is brief, beginning after a wound or the onset of illness, and is a sign that the body is healing itself, chronic inflammation can be a sign that the body is turning against itself. Caused by a prolonged activation of the immune system (often the result of a poor diet or genetics), chronic inflammation can contribute to or even cause illnesses such as heart disease, diabetes, Alzheimer’s and cancer. It can also exacerbate chronic illnesses such as rheumatoid arthritis, multiple sclerosis and other diseases. When a person decreases their inflammation, overall health often improves, regardless of any underlying chronic illness that remains.1,2

So, how does one reduce inflammation beyond using medication such as statins? For those wanting to forego pills, diet and weight loss are key.3 Two of the most popular dietary approaches eliminate refined carbohydrates such as sugars and white flour, which are known to increase inflammation. These approaches are a low-fat, whole-food, plant-based diet (including vegetarianism), and a high-fat, moderate protein, low-carbohydrate lifestyle often known as a ketogenic lifestyle. While they are on opposite ends of the spectrum, both may offer benefits.
**Low-Fat, Plant-Based Diets**

Charles Ross, MD, an osteopathic physician and professor at Western University of Health Sciences, is a passionate proponent of the whole-food, plant-based diet. He has studied diet for 40 years and happily landed in the vegetarian camp, basing his beliefs largely on research by Michael Greger, MD, who has an extensive online presence. “It’s been known for some time that the break-down products of meat and dairy produce inflammatory products. But the fiber in one’s diet can reduce inflammation,” says Dr. Ross. “Fiber produces compounds such as butyrate, and butyrate is an anti-inflammatory hormone that signals to the brain that you have enough healthy bacteria in your body. If your butyrate levels go down, though, that can mean that there aren’t good bacteria, and that can mean areas of inflammation throughout the body. You get butyrate from the fiber in your diet. And where do you get fiber? Plants. Fiber is not found in any animal product. Zero.”

In fact, Ross says fiber is extremely important for health. “We were eating 60, 80, 100 grams of fiber per day back in the 1900s, and the average American is down to 14 grams of fiber today,” explains Dr. Ross. “For every 10 grams of fiber you add to your diet, you decrease your colon cancer risk by 10 percent, your breast cancer risk by 8 percent and your heart attack risk by 9 to 10 percent. And if you add 14 grams of fiber into your diet, you reduce your desire for calories by about 10 percent.” That, says Dr. Ross, translates to weight loss and lowered inflammation.

“The only diet that’s ever been shown to reverse heart disease — not just prevent it, but reverse it — is a whole food, plant-based diet, without refined carbohydrates. No refined oil, no refined sugar. If we want oil or fat in our diet, then we eat the olive or the nuts or an avocado. And we eat only about 10 percent fat. We get our protein and other nutrients from beans, lentils, rice, quinoa, potatoes, soy, fruit,” adds Dr. Ross.

“Dr. Dean Ornish and Caldwell Esselstyn showed in their research that people can reverse clogging in arteries in one to three years of eating a whole-food, plant-based diet. You don’t need a stent. You don’t need a bypass. For two years, I did this. No olives, no nuts and seeds, no avocado, nothing with any refined oil in it, actually. I got my only oil from beans, lentils and other plants. My protein was about 8 to 10 percent also, which is more than adequate for health, and much less than what the SAD [standard American diet] follows. In one month after following [John McDougall, MD] as well as [Drs.] Esselstyn, Ornish and Greger, my cholesterol was down from 230 to 148. Now, it’s down to 135. My weight is down 20 pounds, too. I feel great. And so do the 500 or so students who have been through my program and switched to a whole-plant, low-fat diet. Their testimonials of health improvements are inspiring.”

**Low-Carbohydrate, High-Fat Diets**

On the other side is a high-fat, low-carb diet, known as a ketogenic lifestyle. A growing number of studies show that dietary fat is not the dreaded enemy it was once considered after the release of a 1958 study on its effect on heart disease conducted by Ancel Keys, PhD. Many experts, in fact, now believe that Dr. Keys got his data entirely wrong, and the flawed research has led to the low-fat, high-carbohydrate lifestyles believed to have caused the obesity epidemic in this country. Instead, doctors who promote a ketogenic lifestyle say fat intake can reduce one’s weight and help to reduce pain and chronic inflammation.

Sean Bourke, MD, co-founder and chief medical officer of JumpStart, a San Francisco-based nutrition education and lifestyle change program, sees things much differently from Dr. Ross. In referring to *The China Study*, a book by T. Colin Campbell that examines the relationship between consuming animal products and chronic illnesses, Dr. Bourke says: “Dr. Campbell is a statistician/epidemiologist, not a physician. *The China Study* is the largest epidemiological study ever done. But the problem with observational epidemiological studies is that you can create associations but not necessarily causality. And he’s done the opposite. He has this great epidemiological study, but of course we can’t show causality. Then, however, he goes to say that everybody should be a vegetarian.”

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**A growing number of studies show that dietary fat is not the dreaded enemy it was once considered.**

One of the problems with that, says Dr. Bourke, is that carbohydrates of any kind have been shown to increase inflammation in many people: “One of the biggest predictors of creating diabetes, for example, is an inflammatory state. So then you have your smoking gun in that the number-one macronutrient change that we’ve made over the last 50 or so years in a low-fat phobic state was a reduction in fat and an increase in carbohydrate consump-
“Vegetarianism might work for some people but it certainly doesn’t work for everyone. We see plenty of vegetarians who come into JumpStart, and they’re sick. That said, we can also do JumpStart in a vegetarian state. It’s all a matter of trying to properly engineer macronutrients [protein, carbohydrate, fat] to minimize inflammation and create a low-insulin state. Such a state also lowers inflammation.”

Dr. Bourke also refers to the A to Z Trial, a research study conducted by Christopher Gardener, PhD, at Stanford University in 2007 and published in the Journal of the American Medical Association. Participants in the study followed high-, medium- or low-carbohydrate diets. After one year, results showed the low-carbohydrate group had the best overall, both in terms of weight loss and risk reduction. The insulin-resistant subjects did particularly poorly on a high-carbohydrate diet and particularly well on a low-carbohydrate diet.

Besides lowering health risks, including inflammation, people feel better and have steady fuel flow in a consistently low-carb, low-insulin [ketosis] state, says Dr. Bourke: “You’re not hungry because you’re tapping, or liberating, your fat reserves constantly. That’s part of the battle and the benefit of a low-carb state. There’s less craving, there’s less hunger despite a lower calorie count, and there’s a steadier energy level with fewer highs or lows.

“If you want proof that ketogenic lifestyle works, go to presentations. There are presentations galore around the country where panels show definitively that high-fat, low-carb works. The evidence crushes the low-fat, DASH [Dietary Approaches to Stop Hypertension] fruit and vegetable diet argument. I mean, the low-fat arguments simply don’t win.”

Diets Are Individual

Though it would be more convenient, there’s no one diet that helps everyone. Both plant-based and ketogenic diets have benefits, depending on a person’s needs and genetics. No matter which lifestyle is of interest or seems to fit better, individuals should not undertake any new dietary plan without medical guidance. They should seek a doctor who specializes in ketogenic or plant-based diets for advisement.

MEREDITH WHITMORE is an English professor and freelance journalist in the Northwest.

References
4. Personal interview with Dr. Charles Ross.
9. Personal interview with Dr. Sean Bourke.
“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

*Chronic Inspiration* can be purchased on iTunes, Amazon and Barnes and Noble.com
LET’S TALK

Kelly and Kyle Bruski, whose sons were born with Bruton’s agammaglobulinemia, raised $1,000 to purchase Cuddle Bear books and their accompanying plush toys for the kids at the infusion clinic where their sons are treated.

PROFILE:  Kelly Bruski

By Trudie Mitschang

WHEN YOUR CHILDREN have a rare disease, you will do whatever is necessary to make sure they get the care they need to survive. For Kelly and Kyle Bruski, that means traveling nearly 500 miles round trip each month from their farm in Baker, Mont., to an infusion clinic in Billings. The Bruski’s two young sons 7-year-old Taylor and 3-year-old Colton have an inherited immune disorder that requires monthly infusions of immune globulin (IG). And, although the family could get treatments closer to home, they have bonded with the staff and doctors at the Billings Clinic pediatric infusion room. Touched by the outpouring of support they have received, Kelly was recently inspired to give back by launching a fundraising project to support other families with sick children.

Trudie: Tell us about your children’s diagnosis.
Kelly: Both of my sons have Bruton’s agammaglobulinemia, an inherited disorder affecting only males (females can be carriers of the disease) and characterized by very low levels of protective immune system proteins called immunoglobulins that make it more likely for them to acquire infections. The disease my kids have is extremely rare; only one child in every 200,000 live births is born with this condition. I’ve been told there are less than half a dozen cases of Bruton’s in the entire state.

Trudie: Were you aware of risk factors in your family?
Kelly: Yes, I knew that it runs in my family. My brother has it and so does my uncle (my mom’s brother). My mom is a carrier and so is my grandma, and as far as we know, it may date back to the 1930s because there is some history of baby sons dying, and they could never figure out why.

Trudie: When were you and your sons tested for Bruton’s agammaglobulinemia?
Kelly: I got tested when I found out I was pregnant. My oldest son, Taylor, got tested when he turned 1 year old (we waited a year because it took nine vials of blood to test for the gene at that time). By the time my younger son, Colton, was born, he could be tested as an infant. That was amazing, especially since the first year of Taylor’s life he was constantly getting sick every month; Colton didn’t have to go through that.

Trudie: Tell us about your treatment plan for the boys.
Kelly: We drive about eight hours round trip every month to Billings for intravenous IG (IVIG) treatment. Their infusions last about three hours so it is an all-day thing for us one day each month. Unless a cure is found, they will need these infusions for the rest of their lives.

Trudie: How has their health improved since being treated with IVIG?
Kelly: They are doing wonderful, and we haven’t really had any major health issues, probably because they started the infusions at a really young age. Treatment options have really improved since my uncle and brother faced this diagnosis. We are very thankful.

Trudie: When your children are older, will you consider subcutaneous IG (SCIG) infusions at home?

Kelly: Yes, when my youngest is about 5 or 6 years old, we will consider SCIG at home for both boys.

Trudie: Has spending so much time at the clinic helped you connect with other families?

Kelly: We don’t see any other families since it’s like going to a doctor appointment. Maybe we would if we went to some of the annual events. Every year, the clinic holds an event for families who receive care there, but we haven’t been able to attend one. We live on a farm, and the events usually occur during farming/haying season. My goal is to one day go to one of the events!

Trudie: Tell us about the Kelker’s Kids program.

Kelly: Kelker’s Kids is a program through the Billings Clinic Foundation that provides financial assistance to families of children with cancer or other serious blood disorders. It’s staffed by amazing individuals who go out of their way to ensure the comfort and well-being of every child they treat. They treat us like we’re family; we’ve been coming here for six years, and even though we could look for someplace closer, this is the place we want to bring them.

Trudie: Beyond infusions, how has the clinic helped you and your family?

Kelly: I love the clinic and the staff. They have a room with toys and games to keep the kids entertained, and they always give them gifts. We have been going there since the kids were babies. It’s like a second home once a month. They have also helped us with travel and lodging. We feel very fortunate.

Trudie: Tell us about your fundraising efforts for Kelker’s Kids.

Kelly: I really wanted to give something back, so I joined a company that sells books to get the hostess benefits. In less than two weeks, I raised $1,000 from our great little town to purchase Cuddle Bear books by Claire Freedman and Gavin Scott, and the bear plush toys that go with them. I donated these items so that the Kelker’s Kids clinic could give a book and a bear to each child who has to go through the same thing my boys do. An infusion clinic is a scary place for a child, and it’s scary for them to go through this type of medical procedure. This was a small way to help brighten a child’s day.

Trudie: What has living with chronic illness in your family taught you?

Kelly: It’s taught me that life is precious, something I see people take for granted every day. We live to the fullest each day, and we say I love you every day. It definitely has taught us to be strong together as a family.

Trudie: Any advice to other parents dealing with a similar diagnosis?

Kelly: Let your kids live a normal life. As long as they get their regular infusions, they will be just fine. We let our kids run around on the farm and get dirty like normal kids. They go to a public school and have amazing friends. Their childhood years are worth living, so don’t let their disease hold them back from anything. Medicine has improved so much in the last 40 years, and there have been significant advances that allow people with diseases like this to live a much more normal life.

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.
Let’s Not Talk About ‘It’

By Stacy Oliver

WELCOME TO THE back of this magazine. Good for you! You made it this far. You’ve read quite a bit about immune globulin (IG). Whether you are new to IG infusions or IG has been a part of your life for years, there is always something to learn. Each issue that comes out, I am in awe of what I discover in these pages. I’m a big fan of talking about IG and how it can become part of a balanced, fulfilling life.

But, I’m taking a little break in this column. You might be reading this magazine in the doctor’s office. Maybe you grabbed a copy from your doctor’s office and brought it home. Or, you could be thumbing through it while getting your infusion. Any way you look at it, you are surrounded by the topics of your condition and IG. Well, I’m breaking away from everyone else in this issue, and I’m not going to talk about it. In this column, I’m just going to tune out. Because sometimes that’s what we need to do. Sometimes, for a little while, it’s time to talk about everything else. We spend enough time at the doctor, with family, friends and our home nurse, at outpatient treatment, in therapy, etc., talking about what we have and how miraculous IG is. Believe me, I like walking and am thankful every day for IG, but I can get pretty preoccupied with my illnesses to the exclusion of what else is going on around me. There are so many more thoughts that can float through my mind and should.

So, the “floors are wet” sign is going up in this column, and I am walking around the topic of IG for a minute to clear my mind. Here, I’m going on a stroll to take my mind to different places of thought:

Aren’t sloths fascinating creatures? They remind me to slow down mentally and physically. If you see me hanging upside down, just go with it.

I’ve noticed the more I watch my dogs sleep, the more it makes me tired. Why is the sound of a puppy snoring so soothing, and my husband doing it so annoying?

Very dark chocolate (over 72 percent) every day in small amounts really does boost a person’s mood.

I carry a Sudoku book with me wherever I go. If I’m early and have to wait, for any reason, I try to exercise my mind. It’s relaxing and invigorating at the same time.

I like watching older movies and seeing items that I no longer use: rotary phones, phonographs, typewriters. I wonder if really young people, those under 20, know what they are?

Whew, that was a nice stroll around my mind. Now, having rested our minds, we can return to a fresh take on the topic of IG. We could do this daily in the form of meditation or yoga. Or, maybe, it’s just a matter of being present while we are engaged in something, anything, besides our condition and getting our IG. That’s called mindfulness, and there are all sorts of books about it.

So, you’re almost at the finish line and are close to finishing the magazine. Have fun getting to the end. Back to the fascinating world of IG. I do love the word “immunoglobulin.” Too bad I can’t use it in a game of Scrabble as a triple word score! Hey, stop strolling around my mind, you’ll get lost in there.

STACY OLIVER was diagnosed in 2008 with multifocal motor neuropathy (MMN). She is the assistant director of the Center for the Writing Arts at Northwestern University, and she is working on her supersecret identity as Neuropathy Girl, who will one day save the world after her infusion and a nap.
Too Sick to Go Out? Check Out These Apps for Independence

By Ilana Jacqueline

GROWING UP WITH a chronic illness made becoming “independent” a bit of a pipe dream for me. I was 19 and still yelling for my mom in the middle of the night to help get me to the emergency room. How was I going to live on my own when my disease was not only out of control, but getting worse every day? There were days I could barely get out of bed, let alone go grocery shopping, drive my car or run errands. But whether it was with courage or just a huge amount of forced ignorance, I did move out. And, I learned how to cope on the fly.

Turns out we’re living in a fabulous age of technology, and sometimes being independent is as easily found as searching for an app on your smartphone. Here are some apps to help keep your life going, even when your body has given up.

A girl’s gotta eat. And sometimes a girl just can’t get it together to go to the grocery store. So when the shelves are bare and your latest sinus infection has you seeing stars, have somebody else do the driving, walking and standing behind the lady paying in pocket change at checkout. I recently became a big fan of Shipt (www.shipt.com). It’s kind of like Uber for grocery shopping. After signing up for a membership, you can pick your local grocery store, choose your products and then someone will do the shopping for you! You can even request special items, and if the person doing your shopping has questions, he or she can text or call you. Deliveries generally show up within an hour of ordering. If you buy $35 worth of groceries, there’s no shipping fee! If you don’t, the shipping fee is still only $7.

Want the meals already cooked for you? Plenty of apps offer food delivery from restaurants that don’t deliver. Apps like Grubhub (www.grubhub.com), UberEats (www.uber eats.com) and Delivery Dudes (deliverydudes.com) are affordable, convenient and have large networks.

Some days, not only can I not drive, but I can barely get out of bed. This is a problem for my dog who expects to be walked three times a day. There’s a great app called Barkly (barkly.us) that lets you choose from local dog walkers. The website states that customers are matched with local, background-checked and trained dog walkers available to take out a dog in as little as 60 minutes notice. The app delivers premium care through pick-up/drop-off notifications and detailed walk reports, including a GPS map of the route, photos from the visit, instant feed-

back and encrypted cashless transactions.

There’s nothing like getting home from a long hospital stay only to get in your car and realize you have almost no gas. Thankfully, there’s an app called Yoshi (www.startyoshi.com) that has a simple fix. Yoshi is a weekly gas delivery service that comes to you. For a small monthly fee plus the price of gas, they fill up your tank. And, you don’t even have to be there. Just leave your car in a designated area, pop the fuel tank and let them make life just a little easier for you.

Of course, if I’m going anywhere after a long stay in the hospital, it’s usually to get a haircut or replenish my makeup drawer. If I can’t leave the house just yet, I can sign into GlamSquad (www.glam squad.com) whose staff will come to my apartment and do my nails, hair or makeup, without me ever having to step foot in Sephora.

I don’t even have to face another foreign dressing room again if I don’t want to! I’ve discovered a great program for fashion called Stitch Fix (www.stitchfix.com). Fill out a fashion profile and your personal stylist will send you a huge box full of clothes, shoes, bags and jewelry — all your style. Keep what you like, and use their free envelope to send back what you don’t. You can also choose a price range so you only shop for what you can afford.

Sometimes being independent is as easily found as searching for an app on your smartphone.

Turns out there are a lot of ways to be independent these days. With a phone, paid membership and a little texting, I’m practically a normal, healthy person.

ILANA JACQUELINE is a 27-year-old dysautonomia and primary immune deficiency disease patient from South Florida. She’s been writing professionally since 2004 on everything from health and wellness to celebrities and beauty. Her blog www.letsfeelbetter.com is both a personal collection of anecdotes about life with chronic illness, as well as a resource for patients of all ages.
Dealing with Teen Anxiety
By Jessica Leigh Johnson

THE TEEN YEARS are a stage in life marked by great emotional and physical change, increasing responsibility and the need to make major life decisions. So it’s no surprise that most teenagers are familiar with anxiety. It’s a normal part of the adolescent years, as these are some of the most stressful times in life. Playing sports, leading busy social lives and balancing heavy loads of school work, all while preparing for the future, can be overwhelming at times. But add a chronic illness on top of the already heavy burden most teenagers carry, and life can become quite challenging. Living with a chronic illness ranks as one of the leading risk factors for anxiety among teenagers. Other factors that may increase the risk of teen anxiety include being female, experiencing traumatic events during childhood, having a personality that is prone to worrying and using drugs or alcohol.1

Worries About the Future
People of all ages worry about the future from time to time, and during adolescence, when the future is a big unknown, it’s normal to feel anxious or apprehensive. But young people living with chronic illness have many more health-related concerns relating to the future such as: What will happen to my health as I get older? Will my condition get worse over time? Will I eventually become restricted in my activities? Will I be able to support myself or my family? How long will I be able to live independently before becoming dependent upon my family?2

As parents, it’s hard to watch our chronically ill teens deal with such a heavy burden in this already rocky period between childhood and adulthood. Fortunately, there are things parents and their teens can do to help them cope with stress and anxiety, and smooth the transition into adulthood.

Find a Support Network
Young people who are dealing with anxiety related to their chronic illness should reach out to friends and family, even doctors or counselors, about the unique issues they are facing. Having more information about their condition can lessen the fear of the unknown and help reduce levels of anxiety.

Whether it’s online or in a clinical setting, parents and teens are encouraged to find a support group with others in a similar situation. Simply having someone to talk to who understands can be a great stress-reducer, because knowing you’re not alone in your feelings and experiences can temper anxiety. Local support groups for specific conditions, as well as groups for parents, teens and families, can be found by asking the teen’s doctor or other healthcare provider, or by calling the local hospital for a referral.3

Learn How to Relax
It’s commonly known that relaxation reduces stress and anxiety. But many teenagers don’t truly know how to relax. Sitting in front of the TV or playing video games may seem like it’s relaxing to the body, but it isn’t relaxing to the mind, and may actually cause more tension. In the same way, drinking alcohol or smoking may seem to calm the nerves, but the state of relaxation they lead to is only temporary, and when these vices are unavailable, the body can become jittery or go through symptoms
of withdrawal. For true stress reduction, teens should get in the habit of practicing a relaxation technique such as deep breathing, meditation or yoga — all of which have a physical effect on the brain. According to D’Arcy Lyness, PhD, at TeensHealth, “Deep breathing helps to relax a major nerve that runs from the diaphragm to the brain, sending a message to the entire body to let go and loosen up.”

Enjoy the Outdoors and Exercise
Every once in a while, it’s good for teens to remove themselves from the environment causing them the most anxiety, whether that’s school or work, or even home. Getting outside and venturing into more natural surroundings by taking a walk in the park or a hike in the woods can help teens feel more at peace. Low-impact activities such as walking, hiking, trail biking or snowshoeing offer the additional benefit of exercise. According to Harvard University, aerobic exercise also has a positive impact on the head, not just on the heart: “It has a unique capacity to exhilarate and relax, to provide stimulation and calm, to counter depression and dissipate stress” by reducing levels of the body’s stress hormones such as adrenaline and cortisol. “It also stimulates the production of endorphins, the body’s natural painkillers and mood elevators.”

Anxiety vs. a Mental Health Disorder
It’s quite normal for teens to have trouble adjusting to life with a chronic condition. Immediately following diagnosis, feelings such as worry, sadness or fear are to be expected. For most teens, whether they have a chronic illness or not, anxiety is often a harmless phase that only lasts for a while and goes away on its own. For example, levels of stress and worry may be heightened when exam time approaches. However, there are a variety of mental disorders that can affect teens. If the symptoms of anxiety persist, or if they occur more days than not over a six-month period, they may be signs of a more serious, ongoing problem such as an anxiety disorder. If parents notice their teens exhibiting any of the following symptoms or behaviors, they should contact their child’s healthcare provider right away:

• Excessive crying
• Big changes in appetite or weight
• Not sleeping or sleeping too much
• Talking about feeling hopeless or worthless
• Loss of interest in family, friends or activities they once enjoyed
• Increase in reckless or risk-taking behavior
• Increased irritability

Any mental health issue, especially a chronic one, can be debilitating. A teenager’s body can respond to depression or anxiety with physical symptoms such as pain, shortness of breath or nausea in the same way it might respond to a physical illness. To complicate matters, sometimes mental problems such as anxiety can actually be caused by a physical condition. Getting proper care for both physical and mental issues is important, and trying to self-diagnose is not a good idea.

Because it can be difficult to determine the root cause of anxiety, the first step when symptoms develop is to visit the teen’s primary care doctor. The doctor will ask for a list of symptoms, how long they’ve been present and whether they’re constant or come and go. During an examination, the doctor will check for underlying physical problems that could be causing the symptoms, and help determine what type of mental health professional, or what kind of therapy, if any, might be best for the patient.

Managing Anxiety Is Key
Chronic illness places an extra burden on teens during a time when they’ve already got quite a load to bear. Hopefully by practicing relaxation techniques, exercising and finding support in the community, teens with chronic illness can find ways to manage any stress or anxiety they may experience because of their condition.

It’s quite normal for teens to have trouble adjusting to life with a chronic condition.

References
Healthy Hydration to Minimize IVIG Side Effects

By Trudie Mitschang

FOR MANY patients treated with intravenous immune globulin (IVIG), infusion day is wrought with potential pitfalls due to a host of common side effects. While most side effects fall into the mild to moderate category, they can nonetheless be bothersome. Patients report symptoms that include headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea and hypotension. Headaches and migraines tend to be relatively common, both of which can be treated with antihistamines, nonsteroidal anti-inflammatory drugs and steroids, both before and after an infusion.

Apart from medication, healthcare providers agree that it’s a good idea to stay well-hydrated before, during and after infusions, since adequate hydration has been proven to help alleviate many unwanted side effects of IVIG therapy. “We encourage patients to begin hydrating with nonalcoholic/noncaffeinated liquids several days prior to their infusion, during their infusion and a day or two after their infusion,” says Leslie Vaughan, senior vice president of clinical programs at NuFACTOR Specialty Pharmacy. “We encourage them to try to follow the standard eight-by-eight rule: Consume eight 8-ounce glasses of water each day.”

Water Versus Other Beverages

While medical professionals agree that water is the best choice when it comes to hydrating, there are many other options for those who find plain water to be somewhat “boring.” Sports drinks such as Gatorade contain both water and valuable electrolytes like sodium and potassium. The downside of sports drinks is they can contain sweeteners and may not be a healthy choice for some patients, especially those who are diabetic. Still, if there are no contraindications and a sports drink encourages hydration, especially for a child who may not be getting enough fluids, it is still a preferable choice to not hydrating at all. Sports drinks may also be diluted with water to minimize sugar intake. “If someone wants to use a sports/electrolyte drink, I think it would be best to limit it to a small portion of their fluid consumption rather than the majority. Simple water does the trick,” says Vaughan.

Another option for hydration that has fewer calories, less sodium and more potassium than a sports drink is coconut water. This increasingly popular beverage is low in calories, naturally fat- and cholesterol-free and has more potassium than four bananas. Coconut water has a sweet, nutty taste and contains easily digested carbohydrates in the form of sugar and electrolytes. It is a clear liquid that comes from the center of young, green coconuts. On average, unflavored coconut water contains 5.45 calories, 1.3 grams of sugar, 61 mg of potassium and 5.45 mg of sodium per ounce, compared to Gatorade that has 6.25 calories, 1.75 grams of sugar, 3.75 mg of potassium and 13.75 mg of sodium.

Yet another option is fitness water. This cross between plain water and sports drink is popular. Products like Propel water are lightly flavored and infused with added vitamins and minerals. Although often sweetened, fitness waters contain fewer calories and electrolytes than sports drinks, but offer more taste than plain water. Again, if there are no contraindications, this is a good option.

When it comes to keeping young patients hydrated, Pedialyte is a popular choice because it quickly replaces fluid and electrolytes lost in children and infants. Pedialyte meets the requirements of the American Academy of Pediatrics Committee on Nutrition to help prevent dehydration and is lower in sugars than most sports drinks (100 calories per liter compared to approximately 200 calories in Gatorade). It does not contain sucrose, although flavored versions use the synthetic sweeteners sucralose and ascesulfame potassium. While Pedialyte is marketed for children, it has been gaining popularity among adults as well.

In some instances, patients may require hydration during IVIG therapy. According to Vaughan, NuFACTOR typically recommends D5W hypotonic saline solution because it is the only solution compatible with IVIG and can run at the same time via a Y-site. Keep in mind that D5W is not recommended for diabetic patients. “If the doctor requests normal saline, the patient will need to have it before and/or after their IVIG, or it would need to be run through a separate IV line,” says Vaughan.

A Case-by-Case Situation

Whether patients choose to hydrate with plain water, flavored or other hydration beverages, it’s always a good idea to check with the doctor or infusion provider about each individual’s unique situation. For example, sodium is not recommended for patients with congestive heart failure or high blood pressure, while diabetic patients should avoid beverages containing added sugar and sweeteners. “As pharmacists, we always take comorbidities into consideration,” says Vaughan. “For example, we wouldn’t recommend a lot of fluid for someone with concomitant heart failure or renal disease, which is why each case needs to be individually evaluated.”

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.
**Vita Coco 100% Pure Coconut Water**

Vita Coco is pure vitamin and mineral-rich coconut water. It is a good source of potassium, fat and cholesterol-free water, and comes in eco- and socially-responsible Tetra Pak packaging with a resealable cap. Each bottle contains 11.1 ounces. $17.99 (12-pack); Amazon.com

**Pedialyte Oral Electrolyte Maintenance Solution, Unflavored**

Pedialyte is ready to use and requires no mixing or dilution. It contains balanced electrolytes to replace losses and provide maintenance requirements, as well as glucose to promote sodium and water absorption. Each bottle contains 33.8 ounces. $4.99; Target.com

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**SALUS Infusion Water Bottle**

This water bottle contains an infuser in which fruits and flavors such as strawberries, limes, melons, oranges, mint leaves, cinnamon sticks, etc., can be added to water or other beverages. It has a flip top, is U.S. Food and Drug Administration-approved and is made of BPA-free material. The bottle holds 25 ounces of liquid. $10.99; Walmart.com

**Propel Water**

Each of Propel’s nine flavors provides electrolytes while also providing vitamin B and antioxidant vitamins C and E. It contains no fruit juice and is naturally flavored. Each container has 16.9 ounces. $5.38 (12-pack); Walmart.com

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**Gatorade Thirst Quencher Variety Pack**

This variety has six each of fruit punch, lemon-lime and orange flavors. Each 12-ounce, 80-calorie bottle contains electrolytes and sugars for rehydration. $8.68 (18-pack); Walmart.com
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