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.”
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 overwhelms 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
Listen, PI.
I’ll tell you who’s in charge.

Treat PI on your own terms with CUVITRU

For people living with primary immunodeficiency (PI) 2 years of age or older

CUVITRU™ [Immune Globulin Subcutaneous (Human)] 20% solution gives you and your doctor control over your treatment—from the number of infusion sites to how much, how fast, and how often you infuse.¹

Number of infusion sites
Infuse using 1 to 4 sites simultaneously

Infusion volume
Infuse up to 60 mL per site, as tolerated

Infusion rate
Infuse at rates up to 60 mL per hour per site, as tolerated *

Infusion frequency
Infuse daily up to once every 2 weeks, at regular intervals

Weekly infusions typically were completed in under an hour * using 1 or 2 sites.¹

You and your doctor will determine if CUVITRU is right for you and if so, what regimen is best.

*Recommended to infuse first 2 infusions at 10-20 mL per hour per site.
¹Median: 0.95 hours; range: 0.2-6.4 hours.
We’ve got patients with PI covered

Eligible patients with PI can save up to $5,000† on their out-of-pocket deductible/co-payment/co-insurance costs within a 12-month period for all Shire Ig products, including CUVITRU [Immune Globulin Subcutaneous (Human)] 20% solution.

For more information on MyIgCoPayCard and other support programs, visit MyIgSource.com or call 855-250-5111

†Not valid for prescriptions reimbursed, in whole or in part, by Medicaid, Medicare, Medigap, VA, DoD, TRICARE or any other federal or state healthcare programs, including state pharmaceutical assistance programs, and where prohibited by the health insurance provider or by law. Commercial insurance must cover medication costs for prescribed Shire Immune Globulin (Ig) treatment for primary immunodeficiency (PI) and allow for copay or co-insurance assistance. Shire reserves the right to change or discontinue this program at any time without notice. Please see full treatment-specific Terms and Conditions on product web sites for additional program restrictions and eligibility requirements or call MyIgSource for more information (855-250-5111).

Please see the Indication and Important Safety Information on the adjacent page, and the Brief Summary of the FDA-approved patient labeling on the back page of this ad.
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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S17659 02/17
Low rate of infusion site reactions even when infused at higher volumes and rates per site\textsuperscript{1,2}

- **2 out of every 3 people** who received CUVITRU had **no infusion site reactions**
- The most common infusion site reactions are 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

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.

**Please see the Indication and additional Important Safety Information on the inside of this fold out page, and the Brief Summary of the FDA-approved patient labeling on the back page of this ad.**
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 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.

These are not all of the possible side effects with CUVITRU. 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 information provided here is not comprehensive. To learn more, talk about CUVITRU with your healthcare provider or pharmacist. The FDA-approved patient labeling can be found at www.CUVITRU.com or by calling 1-800-423-2090.

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U.S. License No. 2020

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 food. 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