Managing Disease

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Supporting the Immune System with Probiotics

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- A pregnancy registry is available for Flublok. Contact: Protein Sciences Corporation by calling 1-888-855-7871.

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**Fungal Infections in PIDD Patients**

“Individuals with primary immune deficiencies often require recurrent courses of antibiotics, which can lead to an imbalance in the normal bacteria and fungi (normal flora) that inhabit all of our protective barriers such as the skin, gastrointestinal tract and oral mucosa.”

**MINDY HERMANN, MBA, RDN**  
*Food and Nutrition Writer, and Communications Consultant*

**Probiotics for the Immune System**

“The promises for probiotics are wide-reaching and include benefits for the immune system.”

---

**VALARIE KINNEY**  
*Mother of Three Children with CVID*

**IG Chronicles: “Please Hear Me”**

“Parenting teenagers is hard. Parenting teenagers with chronic illness is even more difficult.”

---

**E. RICHARD STIEHM, MD**  
*Professor of Pediatrics, David Geffen School of Medicine, University of California, Los Angeles*

**Rare Hypogammaglobulinemic Disorders Due to Immunoglobulin Loss**

“A diagnosis of immunoglobulin loss is suspected when the IgG level is disproportionally low, some antibody function is present, and albumin and lymphocyte levels are markedly reduced.”

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Therapies for Immune Deficiencies

Immune deficiencies are rare and complicated diseases. When immune systems go awry, patients often depend on immune globulin (IG) to replace the essential proteins their bodies need to remain infection-free, as well as other medicines to keep them well. Yet, there are also nonmedicinal therapies that can help. That’s the focus of this issue, which looks at the causes of immune deficiencies, the health issues they pose and treatments, both medicinal and nutritional.

There are more than 150 primary immunodeficiency diseases (PIDDs) — all having in common that they are caused by an abnormality in the number and/or function of the body’s immune defenses that leaves patients susceptible to repeated infections. As two specialists at the National Institutes of Health’s National Institute of Allergy and Infectious Diseases describe in our feature “Fungal Infections in PIDD Patients,” there are many types of fungi that can cause problems for the immune deficient. But, it is the type of PIDD that determines susceptibility and how severe infections can be. Fortunately for these patients, there are many antifungal medications, as well as various ways infections can be prevented.

While many PIDDs are caused by defects of immunoglobulin (IgG) production (the proteins that fight infection), some very rare PIDDs are caused by increased loss of IgG through five different body sites, which makes replacement therapy much more difficult. Dr. Stiehm, a pediatric immunologist and author of our article “Rare Hypogammaglobulinemic Disorders Due to Immunoglobulin Loss,” illustrates these cases of IgG loss in insightful vignettes that outline the symptoms, treatments and diagnoses.

Of course, as is true for any disease, medicinal therapies are not a cure-all. Lifestyle also can affect how well patients are able to function daily with these diseases, especially with the often-related conditions that ensue. For example, many immune deficient patients also suffer from gastrointestinal issues, and as nutritionist Mindy Hermann explores in our article “Probiotics for the Immune System,” this nutritional remedy is under extensive study for its benefits to the immune system. Not only can probiotics help balance intestinal microorganisms, they may improve cell-mediated immunity, activate cells that stimulate immune responses and have a positive influence on IgA production.

While probiotics are still unproven health remedies and their claims are not approved by the U.S. Food and Drug Administration, the Agency for Healthcare Research and Quality has determined they have few negative side effects. And, in addition to probiotics, there are other natural health remedies that can stimulate the immune system, including multivitamins, antifungal supplements, teas and more. A sampling of these can be found in our article titled “Natural Therapies for Fungal Infections.”

Of course, all patients should always discuss the use of any type of supplement with their physicians prior to taking them.

I hope you benefit from the information presented and enjoy the many other articles in this edition of IG Living.

Ronale Tucker Rhodes, MS
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1. Marketing Research Bureau data, June 2012
Reader: I have primary immune deficiency disease (PIDD), and I have suffered from severe dry eye for several years. My physician and I have tried several things, and we have discussed the possible use of Restasis (cyclosporine). However, he is concerned that it works as an anti-inflammatory and may have an adverse effect on my immune system. Do you know of anyone suffering from PIDD who has used Restasis, and if so, if there are any benefits or side effects?

Michelle and Leslie: Using Restasis should be fine since it is intended to work locally and is administered directly to the eye with little to no systemic absorption. According to the manufacturer’s website, in clinical studies of Restasis (cyclosporine ophthalmic emulsion), “there was no increase in infection, interaction with other drugs, increase in intraocular pressure or detectable systemic drug absorption in the blood for up to 12 months of treatment.”

Reader: My mother was prescribed Vigam for many years, and she has now been switched to another brand. After her first two infusions, she experienced bad headaches. After her third dose, she had extreme lower-back and upper-thigh pain along with the headache. Both blood and urine tests found nothing. Is this common?

Michelle and Leslie: From a manufacturing standpoint, each brand of immune globulin (IG) is different in terms of contents, including sodium, sugar or no sugar, type, etc. Therefore, people tolerate each brand differently. While headache is a common side effect of IG infusions, pain in the lower back and upper thighs is not, and the manufacturer would want to know about these side effects. It sounds like your mother is not tolerating the alternate brand and should be switched back to Vigam or another product that is available.

Reader: I have myasthenia gravis (MG), and my insurance carrier has denied coverage for Rituxan (rituximab). Is Rituxan covered under any insurance plan?

Leslie: Rituxan currently has U.S. Food and Drug Administration (FDA) approval for the treatment of rheumatoid arthritis, non-Hodgkin’s lymphoma, chronic lymphocytic leukemia and two types of polyangiitis. Most insurance companies develop specific criteria for coverage of expensive therapies such as Rituxan, one of which is an FDA indication. Therefore, part of the challenge you are experiencing relates to the use of Rituxan for an indication that is not yet approved by the FDA.

Since the use of Rituxan for MG is considered off-label, the first attempt to get authorization for Rituxan will almost always receive an automatic denial by an insurance company. The good news is there are quite a few articles that have been published in peer-reviewed journals that give positive evidence for the use of Rituxan in treating MG.

You (and your physician) should be able to appeal the denial from the insurance company. Your appeal letter should provide the information on positive response to therapy from the literature. The letter should also include your current status with the types of symptoms you experience, the treatments you are currently on, any treatments that have been tried and failed, and, if appropriate, a specific reason your physician wants to wean you off of a medication (for example, long-term steroid use can increase the risk of developing diabetes, osteoporosis, etc.).

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

LESLIE J. VAUGHAN, RPh, is senior vice president of clinical services at NuFACTOR Specialty Pharmacy.
Did You Know?

Immunology 101:
Diagnosing an Antibody Deficiency: Case 5, Part 2: Does a Chronic Sinus Infection Always Indicate an Antibody Deficiency Is Present?
By Terry O. Harville, MD, PhD

IN THE LAST issue, we began the discussion of an approximately 7-and-a-half-year-old girl being evaluated for a possible immunodeficiency due to chronic sinusitis that had not improved with antibiotic treatment. She was reported to have initially been a well child but began having problems with recurrent ear infections and bouts of sinusitis around 3 years of age. Additionally, the family history of recurrent problems with sinusitis was suspicious for antibody deficiency.

Her physical examination revealed features that may typically be present in children with allergic disease (Dennie's lines, allergic shiners, nasal crease with allergic salute, etc.). However, her nasal mucosa (tissue inside of the nose) was red. It is typically pale with allergic disease but will be red with sinusitis. There was tenderness over her cheeks (maxillary sinuses), and her upper molars were tender to pressure, which may occur with maxillary sinusitis. Additionally, she had tenderness of the bridge of her nose between her eyes, which is found with ethmoidal sinusitis. The frontal sinuses are not yet developed at her age, and there was no tenderness above the eyes. Examination of her mouth revealed somewhat enlarged tonsils and evidence of post-nasal drip on the back of her throat. Inspection of her ears demonstrated tympanic membranes (ear drums) that had become thickened, possibly scarred, and had lost some of the normal architectural features expected to be found during visual inspection. Her ears had the appearance of having been chronically infected. And, the skin of her upper, posterior arms was rough to the touch (some call this chicken-skin or chicken-flesh appearance). This is known as keratosis pilaris, and it is often found in persons with allergic disease. Therefore, the physical examination revealed a child with allergic features, apparent sinusitis and findings consistent with recurrent ear infections.

Allergy skin testing was performed, and she exhibited large reactions to multiple allergens (grass, weed and tree pollens; mold spores; dust mite dander). Testing of her blood revealed a normal white blood count with a normal lymphocyte count. Her CH50 complement activity test was normal. All of her serum immunoglobulin levels were normal average for age, except for an elevation in the IgE level, as commonly found with allergic disease. A CT scan revealed that all of her sinuses appeared to be extensively affected by infections (pansinusitis), which is consistent with the history and physical examination. Serum for pre-immunization pneumococcal titers was sent, and while waiting the four weeks for the serum for post-immunization titers to be sent, specific therapy was begun.

Her sinusitis was initially treated by IV infusion of ceftriaxone (strong antibiotic) and methylprednisolone (strong anti-inflammatory corticosteroid) in the clinic. When one has significant long-standing sinusitis, oral antibiotics may be woefully insufficient. Further, the swelling caused by the infection can prevent the fluid that has built up in the sinuses from being able to drain. A strong antibiotic may be necessary, and treatment with corticosteroids may be necessary to reduce the inflammation and swelling.

She was further treated with a month-long course of cefprozil (oral antibiotic). Unfortunately, in the current age of trying to reduce the unnecessary usage of antibiotics, physicians may try to treat sinusitis with a five-day course of a long-acting antibiotic (e.g., azithromycin) or with seven, 10 or 14 days of other antibiotics. In general, almost all cases of sinusitis need at least three weeks, and under many circumstances four weeks of oral antibiotics.

Within a few days of the IV medications, she had significant improvement in her symptoms, and the symptoms were fully resolved after the month of oral antibiotics. The allergic disease symptoms were treated with daily dosing of cetirizine and montelukast, and with as-needed additional dosing of hydroxyzine.

We will continue with this case next issue, discussing the pre-/post-immunization titers and the patient's diagnosis.

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

Disclaimer: This case report is intended as an illustration for education purposes only. It does not necessarily represent an individual or precise information from patient files.
Research

Did You Know

A baby born with severe combined immunodeficiency (SCID) has received the world’s first gene therapy cure to “reboot” her body’s defense systems and give her a chance of life outside of a sterilized environment. Nina Warnell was initially placed in isolation, given antibiotics and antiviral drugs to tackle infections, and was placed on the bone marrow transplant list, but no donor could be found. At one point, Nina began to slowly recover and put on weight, and doctors created an artificial immune system for her by prescribing 15 medications per day and immune globulin transfusions every three weeks.

When Nina was 17 months old, doctors at Great Ormond Street Hospital in the United Kingdom suggested the gene therapy cure. Doctors there harvested Nina’s bone marrow and re-engineered it using a new type of “reprogrammed virus” to splice the vital gene she is missing into her DNA profile. The re-engineered bone marrow was re-inserted into her body, and they hope a fully functioning immune system will develop. As part of the treatment, Nina underwent a session of chemotherapy to wipe out her existing bone marrow so that the new one can grow in its place. Doctors estimate a 60 percent to 90 percent chance of success.

Medicines

Baby with SCID Trials
First Gene Therapy Cure

The European Commission has granted Baxter marketing authorization in all European Union (EU) member states for the use of HyQvia as replacement therapy for adults with primary and secondary immunodeficiencies. HyQvia is a combination of human normal immune globulin 10% and recombinant human hyaluronidase, which facilitates the dispersion and absorption of the medicine, and is infused subcutaneously. Baxter will introduce HyQvia in select countries during 2013 and plans to expand the launch to other EU countries in 2014.

The approval was based on results from a Phase III, prospective, open-label, non-controlled multi-center clinical trial that evaluated the safety and efficacy of HyQvia in the prevention of acute serious bacterial infections and the pharmacokinetic parameters compared with immune globulin administered intravenously. During the study, patients were infused a three- or four-week dose of the treatment in a single subcutaneous site. The rate of validated acute serious bacterial infections was 0.025 per patient per year, which is below the required efficacy threshold of 1.0. In the tolerability assessment of HyQvia, the most frequently reported adverse reactions were infusion site reactions (20 percent), headache (3 percent), fatigue (1 percent) and pyrexia (1 percent).
The U.S. Food and Drug Administration has expanded the administration options and approved a new vial size for Hizentra, immune globulin subcutaneous (human), 20% liquid. The new dosing option includes dosing once every two weeks (biweekly) for people diagnosed with primary immunodeficiency disease (PIDD). The approval is based on the principles of pharmacoanalytics and pharmacokinetic modeling.

Hizentra is the first and only 20% subcutaneous immune globulin that is self-administered weekly or biweekly to deliver consistent levels of IgG to help protect those with PIDD against infections. “To provide the best care to PI patients, therapy needs to be individualized to meet particular needs. Fortunately, today we have options on treatment administration, dose and dosing interval,” said Richard L. Wasserman, MD, PhD, clinical professor of pediatrics, University of Texas Southwestern Medical School. “With the approval of biweekly dosing, Hizentra provides PI patients with an additional option to be in greater control of their lives.”

The new 10 g (50 mL) vial size for Hizentra, which became available in October, will reduce the number of vials that patients must use when higher doses are required, thus increasing administration efficiency and reducing complexity of care. “CSL Behring remains dedicated to providing every patient with options that will enhance his or her treatment experience,” said Lynne Powell, senior vice president, North America Commercial Operations at CSL Behring. “The availability of Hizentra in a 10 g vial will reduce vial preparation for infusion, therefore saving time for both patients and their caregivers.” In addition to the new 10 g vial, Hizentra is available in 1 g (5mL), 2 g (10 mL) and 4 g (20 mL) vials.

**Did You Know?**

Immunology is still a very new specialty, and the optimal treatments have not been fully defined for most immune deficiencies. A significant barrier to defining the best treatment for each disorder is the rarity of patients. Any one center may have only a handful of patients and, therefore, the individual physician and nurse never accumulate sufficient patients to compare different treatments. Another barrier is the lack of information about what each patient feels has worked most effectively. One strategy to improve knowledge about treatment and outcomes is to assemble large collections of patients and compare them across different treatments and centers. This is the “big data” approach, and it has been instrumental in refining therapy for conditions like diabetes and cystic fibrosis. The purpose of USIDNET is to assemble and maintain a registry of people with primary immunodeficiency diseases (PIDDs). The project was started in 1992 and now contains information on more than 50 diseases and more than 3,000 patients. For big data to work, more patients are needed. Three thousand sounds like a lot, but USIDNET has been able to analyze only a few of the questions that are so pressing. Future questions to be answered are: Does antibiotic prophylaxis prevent lung disease? Are higher doses of intravenous immune globulin beneficial? What types of autoimmune disease occur, and how are they best treated? How well do patients feel they are doing? To help answer these questions, all patients with a PIDD are asked to register with USIDNET by contacting Tara Caulder, registry manager, at contact@usidnet.org or by calling (866) 939-7568 or (443) 632-2543.
Autoimmune Corner

Research

**IVIG Most Common Retreatment for Refractory Kawasaki Disease**

A recent study shows that a second dose of intravenous immune globulin (IVIG) is the most common treatment for refractory Kawasaki disease (rKD). However, several regional variations exist, possibly due to the influence of regional experts.

KD, also known as mucocutaneous lymph node syndrome, causes inflammation of blood vessels throughout the body, which can lead to coronary aneurysm and heart attack, making KD the most common cause of acquired heart disease in children in developed countries. The current standard of care for KD is a single 2 g/kg dose of IVIG infused over 10 to 12 hours, accompanied by aspirin (80 to 100 mg/kg/day by mouth in four divided doses). Fevers persistent more than 36 hours after initial treatment represent rKD, for which there are no current national guidelines or standards for treatment.

In the study, researchers examined data from the Pediatric Health Information System, a clinical and financial database of care provided at 43 nonprofit, freestanding children’s hospitals in the U.S. Data from 40 of these hospitals were deemed complete enough for analysis and were collected from Jan. 1, 2005, to June 30, 2009. Subjects were included if they received at least one dose of IVIG and had a principal diagnosis of KD. To be considered rKD, the subject must have received additional treatment after the initial diagnosis of rKD.

Researchers found that the most commonly used treatment after initial IVIG treatment was retreatment with IVIG (65 percent), followed by intravenous methylprednisolone (27 percent) and then infliximab (8 percent). Significant regional variation was observed, with hospitals in the Northeast using methylprednisolone most frequently for rKD (55 percent) and hospitals in the West using infliximab (29 percent) compared with other regions.

Research

**Study Indicates Possible Autoimmune Process in ME/CFS**

A recent study shows the first direct association between plasmacytoid dendritic cells (pDCs) and human endogenous retroviral (HERV) proteins in patients with myalgic encephalomylitis (ME), or chronic fatigue syndrome (CFS), which suggests an underlying autoimmune process may be implicated. Researchers, who conducted the study to determine if autoimmunity is a factor in some subgroups of patients with ME/CFS, investigated the guts of individuals with ME/CFS for the presence of HERV proteins. They found that in eight out of 12 individuals with ME, immunoreactivity to HERV proteins was observed in duodenal biopsies. In contrast, no immunoreactivity was detected in any of the eight controls. Immunoreactivity to HERV proteins was uniquely co-localized in cells that are consistent with pDCs. Although the significance of HERV proteins present in the pDCs of individuals with ME has yet to be determined, these data raise the possibility of an involvement of pDCs and HERV proteins in ME pathology.
Three recent studies suggest that a high-salt diet may be behind rising rates of autoimmune diseases such as multiple sclerosis (MS). According to the studies, high-salt diets increased levels of a type of immune cell linked with autoimmune disease, and mice genetically engineered to develop MS got much worse when they ate what amounted to a high-salt Western diet compared with mice who had more moderate salt intake. The results suggest, say researchers, that salt may play a previously unknown role in triggering autoimmune diseases such as MS or type 1 diabetes in individuals who are already genetically predisposed.

In the first study, researchers investigated the link between salt and autoimmunity through studies of the gut microbiome (a census of gut microbes and cell function) in 100 healthy individuals. They noticed that when people in the study visited fast food restaurants more than once a week, there was a marked increase in their levels of destructive inflammatory cells, which the immune system produces to respond to injury or foreign invaders, but which attack healthy tissues in autoimmune diseases.

In another study, researchers were investigating what factors induce the activity of a type of autoimmune cell known as a T helper 17, or a Th17 cell, which can promote inflammation that is important for defending against pathogens, but have been linked to diseases like MS, psoriasis, rheumatoid arthritis and ankylosing spondylitis. They identified a specific gene known as SGK1 that plays an important role in the Th17 cells’ development. The SGK1 gene had not been seen in T cells before, but it has been known to play a role in absorbing salt in the gut and kidneys.

Putting this together with the first study, another set of researchers investigated whether a high-salt diet could induce the destructive immune system response that is the hallmark of autoimmunity. They found that adding salt to the diet of mice induced the production of Th17 cells and that mice genetically engineered to develop a form of MS had a more severe disease than mice fed a normal mouse diet.

“It’s not bad genes. It’s not bad environment. It’s bad interaction between genes and the environment,” said Dr. David Hafler, a professor of immunobiology at Yale University in New Haven, Conn., and senior author of the first study. According to Hafler, the findings now need to be studied in people. He has received permission to test the effects of lowering the salt intake in the diets of individuals with MS to see if their symptoms improve. And, while it’s likely to be years before the link is confirmed, Hafler says that for patients already at risk of autoimmune disease, reducing dietary salt may be a good idea.
Did You Know

Diagnosing Kawasaki Disease

Researchers at the Rady Children’s Hospital in San Diego are testing a new tool to help in the earlier diagnosis of children with KD.

By Ronale Tucker Rhodes, MS

IT IS ESTIMATED that the number of kids who are accurately diagnosed with Kawasaki disease (KD) is just the “tip of the iceberg,” says Adriana Tremoulet, MD, MAS, a pediatric infectious disease specialist at Rady Children’s Hospital in San Diego, Calif. In the U.S., there are approximately 5,000 to 7,000 cases of KD diagnosed annually, but there are many people who present later with conditions that likely are a result of KD being misdiagnosed or undiagnosed. One of the most common conditions is a high risk of heart disease. Specialists like Dr. Tremoulet and her colleagues know that if KD could be diagnosed when symptoms present, the risk of serious outcomes is greatly reduced. And, they may be very close to developing such a diagnostic tool.

What Is KD?

KD, a form of vasculitis, is a rare childhood disease in which the walls of the blood vessels throughout the body become inflamed. In some cases, KD affects the coronary arteries that carry oxygen-rich blood to the heart, which causes some kids with KD to develop serious heart problems.

It’s unknown what causes KD, but it’s believed to be a trigger combined with genetic factors, even though no trigger in kids diagnosed with KD has been found. The disease affects children of all races, ages and genders, although it occurs most often in children of Asian or Pacific Island descent. It is also more likely to affect boys than girls, and most cases occur in children younger than 5 years old.

During the acute phase of KD, one of the main symptoms is a fever that lasts longer than five days, which remains high even after treatment with standard medicines. Also during this phase, a child may be irritable, have a sore throat, joint pain, diarrhea, vomiting and stomach pain. Other classic signs of the disease include swollen lymph nodes in the neck; a rash on the mid-section of the body and in the genital area; red, dry, cracked lips and a red, swollen tongue; red, swollen palms of the hands and the soles of the feet; and redness of the eyes.

Unfortunately, not all kids have classic signs of KD. And, some kids with classic signs may actually have other illnesses that present with similar signs. Therefore, many of these kids go undiagnosed until long-term damage has occurred. This damage, which can present after two to three weeks of the start of symptoms, includes the peeling of fingers and toes, sometimes in large sheets, as well as damage to their coronary arteries.

Rady Children’s Hospital

The Kawasaki Disease Clinic at Rady Children’s Hospital, follows the health status of more than 1,200 children with KD and treats 80 to 90 new patients per year. The clinic is directed by Jane Burns, MD, who was involved with the first intravenous immune globulin (IVIG) study with KD patients (IVIG is a U.S. Food and Drug Administration-approved indication for KD).

The cutting-edge Kawasaki Disease Research Center supports clinical, laboratory and epidemiologic investigation into the etiology, pathophysiology and natural history of the disease. Currently, the center is conducting a number of studies, including the long-term outcome for adults who suffered from KD in childhood, the epidemiology of KD, and genetics and gene expression of KD, among others. But, the newest study launched this year focuses on diagnostics.

A KD Diagnostic Tool in the Works

For approximately five years, researchers at the Kawasaki Disease Research Center have been working to develop the right combination of physical biomarkers and clinical indications to diagnose KD. To do this, they have collected clinical and lab data, as well as blood and urine, from the repository of kids with KD and without, and then combined them to show which combination increases the likelihood that a child has KD. Just last year, they collaborated with researchers at Stanford University and developed an algorithm of that data that appears to be 80 percent accurate in distinguishing between kids with KD and kids with symptoms that are not KD. “Eighty percent is
great, but 100 percent would be better,” says Dr. Tremoulet.

So, using that algorithm, they launched a diagnostic test validation study in September in the Rady Children’s Hospital emergency room. The clinical trial will include a total of 60 kids at the beginning of diagnosis and 60 kids who have a separate illness, and it will last for three to four years (three years of enrollment, and another year of analysis). After conducting the trial locally, it will have to be tested in nonchildren emergency rooms and then move on to a multicenter study conducted nationally. The ultimate goal is to use the algorithm to develop a tool that will diagnose kids with KD early and, hence, reduce the number of children and adults who suffer serious issues that occur as a result of a KD misdiagnosis.

“One of the hard parts about KD is you have to have a very good clinical eye,” explains Dr. Tremoulet. So, we’re testing [the algorithm] with clinicians who are ER physicians who see kids with a whole host of diseases. Ultimately, what we want is a test that is generalizable.”

**A Highly Motivated Team**

The researchers involved in this new study are highly motivated for good reason. “What’s motivated us to do this work is that, on a monthly basis, we see probably three to five children who develop significant peeling of their fingers, which is a sign of missed KD,” says Dr. Tremoulet. “Some of the most difficult cases to hear about are the young adults in their mid-30s who may be suffering a heart attack or die suddenly from having had missed KD as children. We are hoping that our diagnostic test will detect children early and prevent such devastating outcomes.”

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

**Sources**

Fungal Infections in PIDD Patients

PIDD patients are more prone to certain types of infections. Knowing which ones they are most susceptible to and how they are most commonly treated can help to minimize the risk.

By Alexandra F. Freeman, MD, and Anahita Agharahimi, MSN, CRNP
Individuals with primary immune deficiencies (PIDDs) are at greater risk for recurrent infections compared with those with normal immune systems. PIDD patients frequently have a genetic defect that causes an abnormality in the number and/or function of one or more components of the immune system that fights infections. These infections can be predominantly viral, bacterial or fungal, depending on the type of white blood cells affected by the specific immune deficiency. For instance, neutrophil abnormalities lead to recurrent bacterial and mold infections; B lymphocytes typically lead to bacterial infections, more specifically those that antibodies prevent such as Streptococcus pneumoniae (pneumococcus) and Haemophilus influenzae; and T lymphocytes frequently lead to recurrent viral infections and yeast infections such as Candida. Other types of immune system abnormalities lead to other specific recurrent infections.

Individuals with PIDDs often require recurrent courses of antibiotics, which can lead to an imbalance in the normal bacteria and fungi (normal flora) that inhabit all of our protective barriers such as the skin, gastrointestinal tract and oral mucosa. This imbalance, in turn, increases vulnerability to other types of infections such as yeast infections and Clostridium difficile (C. diff) infections.

**What Are Fungi, and What Diseases Do They Cause?**

Fungi are categorized as eukaryotes, organisms whose cells are larger and more complex in their makeup compared with bacteria, which lack nuclei inside the cells, and viruses, which require assistance from host cells (the cells it infects) to replicate. For medical purposes, fungi are divided into three groups: yeasts, molds and those that can exist as both yeasts and molds (dimorphic fungi).

Yeasts commonly include Candida species and Cryptococcus species, with Candida being the more common. Candida are a part of human normal flora and mostly reside in the mouth, gastrointestinal tract and vagina. Problems arise when their numbers multiply in these areas due to the eradication of normal bacteria from antibiotic use, medications like corticosteroids that weaken the immune system, or when the improper function of the immune system allows them to replicate unchecked. Candida can cause infections in the mouth, known as thrush, which appear as white plaques on the inside of the cheeks and tongue. It can also cause vaginal yeast infections and diaper rash in infants and young children. And, it can cause infections on the skin surrounding the fingernails (paronychia) or the fingernails and toenails themselves (onychomycosis). Candida can enter the bloodstream and cause more severe infections when the normal skin barriers are compromised such as with central venous access lines (long-term IV access) that are sometimes needed for various treatments. These invasive infections usually cause fever and more acute illness compared with the more mild infections such as thrush and vaginal yeast infections. Ringworm is also caused by yeasts, including Trichophyton and Microsporum species, that cause rashes on the skin or scalp. Tinea versicolor is caused by the yeast Malassezia furfur and causes a rash usually on the trunk.

 Cryptococcus is a yeast that can be found in the soil, in wild bird droppings and around certain plants. In healthy individuals, it rarely causes problems. However, in immune deficiencies with T lymphocyte abnormalities, it can usually cause lung infections when it is inhaled. The lung infection can look like a mass on chest imaging scans but rarely causes many symptoms. However, Cryptococcus can spread to the brain and cause meningitis. The meningitis symptoms may evolve over weeks to months, which is different from bacterial meningitis, which rapidly causes significant illness. This may present with symptoms such as headaches, personality changes or vision changes.

Molds are fungi that grow as multicellular organisms that usually have branches called hyphae. The most common mold responsible for causing infections is Aspergillus. Aspergillus species grow in almost all oxygen-rich environments. It is rare for people with normal immune systems to have infection from mold, although breathing in high quantities of molds can make asthma and other lung diseases worse. Problems with the neutrophil white blood cells, either due to a PIDD (e.g., chronic granulomatous disease,
or CGD) or to chemotherapy, can cause severe mold infections that require long-term antifungals and possibly surgery to cure. In CGD, pneumonias from molds can cause chest pain, cough and fever and may worsen slowly over weeks compared with bacterial infections that usually cause more symptoms rapidly. Molds can cause less severe, but still problematic, chronic pulmonary infections in individuals with bronchiectasis (irreversible dilation of part[s] of the bronchial tubes) or other structural lung problems. People with asthma or cystic fibrosis can develop an allergy to molds and have allergic sinus or lung disease, known as allergic bronchopulmonary aspergillosis (ABPA) or allergic fungal sinusitis. ABPA normally causes wheezing and productive cough with usually brown-colored mucous plugs. Allergic fungal sinusitis causes thick mucous that often requires sinus surgery to clear. Both ABPA and allergic fungal sinusitis improve typically with steroids such as prednisone.

Dimorphic fungi that are mainly responsible for causing infections include Histoplasmosis, Blastomycosis and Coccidioidomycosis. Histoplasmosis is found in the soil mostly in the Ohio River Valley and lower Mississippi River area and usually causes a self-limited lung infection with a dry cough. Blastomycosis grows in moist or wet environments and vegetation and is found most frequently around the Great Lakes. Coccidioides is found in the soil of primarily the Southwestern United States and causes valley fever, which is a flu-like illness with cough. All three can cause infections in individuals with normal immune systems, but the infections are not usually severe and frequently clear without any medications. Those with PIDDs can develop significant infection affecting the respiratory, neurologic and dermatologic systems from these organisms.

**What PIDDs Lead to Fungal Infections?**

As mentioned earlier, individuals with PIDDs have increased risk for certain fungal infections, and the type of PIDD determines the susceptibility to the infection and the severity of illness.

CGD is caused by a problem in the neutrophil oxidative burst, which is the chemical end product of neutrophil activity that kills certain bacteria and fungi. This abnormal killing ability of neutrophils leads to susceptibility to infections with molds, most commonly with the Aspergillus species. These mold infections are usually of the lung, skin or bone and can cause fever and sometimes localizing symptoms to the site of infection. Diagnosis is best made by taking a biopsy and sending the sample for fungal and bacterial cultures so that specific treatment can be given.

Severe combined immune deficiency (SCID) is caused by severe abnormalities in T lymphocytes along with B and/or NK lymphocytes. Affected individuals present early in life as infants with recurrent, severe bacterial and viral infections, as well as failure to grow normally. Lymphocytes are also important for the control of yeasts, and infants with SCID frequently have yeast infections causing thrush and diaper rash.

Hyper IgE (Job’s) syndrome is caused by mutations in a gene called STAT3, which is needed for T lymphocytes to mature into a special type of T lymphocyte called a Th17
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Please see additional Important Safety Information on next page and brief summary of full prescribing information for Hizentra on adjacent pages.
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Important Safety Information (continued)

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. Your doctor will monitor for potentially serious reactions that have been seen with Ig treatment, including thrombotic events (blood clotting); aseptic meningitis syndrome (brain swelling); osmotic nephropathy (a kidney condition); hemolysis (a blood problem) and transfusion-related acute lung injury.

The most common drug-related adverse reactions in the clinical trial for Hizentra were injection-site reactions (swelling, pain, redness, heat or itching); 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.

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

Please see brief summary of full prescribing information for Hizentra on adjacent pages.

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.

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*Based on an equivalent dose in grams.


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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.

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**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.

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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.

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

**Dosage**
Before switching to Hizentra, obtain the patient's serum IgG trough level to guide subsequent dose adjustments.
Weekly: Start Hizentra 1 week after last IGIV infusion

- Initial weekly dose = Previous IGIV dose (in grams) x 1.53
  No. of weeks between IGIV doses
- Biweekly: Start Hizentra 1 or 2 weeks after the last IGIV infusion or 1 week after the last weekly Hizentra infusion. Administer twice the calculated weekly dose.
- Adjust the dose based on clinical response and serum IgG trough levels (see Dose Adjustment).

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

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**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

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**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 pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
- May carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

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

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

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**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.

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**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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Based on September 2013 version
cell. Th17 cells are involved in the control of yeast on the skin and mucous membranes, and individuals with abnormal Th17 cells can have trouble with Candida in the mouth (thrush), as well as fingernail Candida infections and recurrent vaginal yeast infections. Less frequently, there can be more severe infections from Cryptococcus, Histoplasmosis, and Coccidioides. These can cause gastrointestinal infections and, in the case of Cryptococcus and Coccidioides, can cause meningitis.

**Individuals with PIDDs have increased risk for certain fungal infections, and the type of PIDD determines the susceptibility to the infection and the severity of illness.**

STAT1 immune deficiency is caused by gain of function mutations in a gene called STAT1, which also leads to abnormal Th17 function. Therefore, yeast infections occur affecting the mouth, skin, fingernails and vagina. Severe Coccidioides infections also can occur in patients with gain of function STAT1 mutations.

APECED (autoimmune polyendocrinopathy candidiasis ectodermal dystrophy) is an autoimmune disorder in which autoantibodies (antibodies that the body makes against some of its own proteins) can cause a deficiency in the inflammatory proteins made by Th17 cells leading to mucosal and skin yeast infections.

**What Are Treatments for Fungi?**

Several antifungal medications exist for fungal infections. Following are the most frequently used medications. The use of any of these medications, with their potential side effects and interactions with other medications/herbals, should always be discussed with one’s medical team beforehand.

**Polyene Antifungals:**
- Nystatin is used topically to treat thrush or skin infections with Candida. With thrush, it is usually administered as a swish and spit. Side effects are rare.
- Amphotericin has activity against many fungi and is used frequently for severe infections. Amphotericin use is limited due to its intravenous administration and risk for kidney toxicity.

**Azole Antifungals:**
- Miconazole/clotrimazole are topical medications primarily used for Candida infections.
- Fluconazole is a medication taken by mouth used most frequently to treat Candida infections but can be used for Cryptococcal or Coccidioides infections if mild or after an initial course of amphotericin. Main side effects include abnormal elevations in liver enzymes, which are usually reversible. At high doses, hair may thin.
- Itraconazole has activity against both yeasts and molds. For molds, it is usually used for prophylaxis or treatment of mold infections. It can be used for some infections with Histoplasmosis as well. Similar to fluconazole, it can affect the liver.
- Voriconazole has excellent activity against many yeasts and molds. In addition to liver enzyme abnormalities, it can also increase risk for sun sensitivity and sunburn.
- Posaconazole is very similar to voriconazole in its activity against yeasts and molds. It does not increase risk for sun sensitivity, but is only dispensed in a liquid formulation.

**Echinocandin Antifungals:**
- Caspofungin, micafungin and anidulafungin have excellent activity against yeasts, and are sometimes used for molds, usually along with other antifungals such as voriconazole. Unfortunately, they are only available as intravenous medications at this time.

**Allylamine Antifungal:**
- Terbinafine is used frequently for skin or nail fungal infections either as a pill or in a cream.

**What Are Ways to Prevent Fungal Infections?**

Fungi are found in abundance throughout the environment, and exposure cannot be totally avoided. But, there are ways to avoid high-risk exposures. Molds are common outdoors in shady, damp spots, as well as in areas of decomposing vegetation. Mulch and hay can have increased amounts of mold, and avoiding exposure to it through activities such as gardening and hayrides or barns if one is susceptible to infection is often advised. Buildings with ongoing renovations may often have high amounts
Several antifungal medications exist for fungal infections.

Prophylactic antifungals are used in the setting of certain PIDDs to try to prevent fungal infections. CGD is one example of this, as it is recommended that prophylactic antifungals such as itraconazole be administered daily to prevent mold infections. Fluconazole is used sometimes as prophylaxis for PIDDs characterized by mucocutaneous candidiasis.

Future Directions

There has been an increased amount of research regarding the human normal microbiome (normal flora) in recent years, focusing on areas such as the skin, intestines and vagina, where there are lots of normal bacteria and yeasts. It is hoped that this research will help us understand more about how antibiotics and other treatments disrupt the normal flora and how we can then prevent overgrowth of certain microbes leading to infection. Improving this disruption will hopefully diminish some of the Candida infections.

An increasing number of medications are being evaluated as well to combat fungal infections, especially since molds and yeast can cause very severe infections and death in severely immunocompromised patients such as those undergoing bone marrow transplants. In addition, vaccines are being studied for the prevention of fungal infections.

Selected References


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Probiotics for the Immune System

By Mindy Hermann, MBA, RDN

While probiotics are unproven remedies, they are actively being studied for the benefits they may have on the immune system and for relief from intestinal problems.
The dairy case, particularly the yogurt section, is the epicenter of an exciting and growing area of interest: probiotics. The promises for probiotics are wide-reaching and include benefits for the immune system. But, as with any such trend, it is important to separate the helpful from the hype.

**Probiotics = For Life**

The word *probiotics* means “for life,” a name that refers to the ability of probiotics to boost populations of microorganisms such as bacteria that live in the human body. The official definition of probiotics was developed by the Food and Agriculture Organization of the United Nations in 2001. It states that probiotics are live microorganisms that when administered in adequate amounts confer a health benefit on the host. This definition was carefully crafted, and each part of the definition describes an important feature of probiotics:

- **Probiotics are microorganisms, typically certain types of bacteria but also other forms of microscopic life.** It’s important to note that not all bacteria, or even all bacteria in yogurt and other dairy products, are probiotics. The only bacteria that can be called probiotics are those strains that have a scientifically proven connection to health.
- **Only live organisms can be characterized as probiotics.** Bacteria and other organisms that no longer are alive cannot aid other organisms in the body and, as such, are not probiotics. Foods that contain probiotics may be marked “live and active” on the label, meaning that the bacteria cultures are guaranteed by the manufacturer to be alive.
- **Probiotics must be consumed in adequate amounts.** This ensures that enough of them make it alive through the digestive process (stomach acid and various digestive enzymes destroy bacteria and other microorganisms) and remain alive until they reach the large intestine. This requires starting with a lot of cultures. Yogurt and other fermented foods are rich in microorganisms, including probiotics. One teaspoon of yogurt with live and active cultures has approximately half a billion^1^ bacteria cultures!
- **Not all bacteria improve the health of microorganisms in the body.** The probiotic classification pertains only to those with health benefits that can include positive effects on the immune system.
- **While microorganisms that break down lactose offer a benefit to people who are lactose-intolerant, these microorganisms are not considered probiotics because they act on milk and dairy products rather than directly on the body.

All probiotics have three-part Latin names. The first part is their genus, the second is their species and the third refers to their strain. For example, one three-part Latin name is *Lactobacillus* (genus) *rhamnosus* (species) GG (strain). Different strains have different characteristics, just like the difference between dogs (*Canis lupus familiaris*) and common wolves (*Canis lupus lupus*).

**Probiotics and the Body’s Natural Microorganisms**

The human body is filled with microorganisms, including bacteria, viruses and other microscopic life. Trillions of microorganisms live on the skin, and trillions more live in the digestive tract, which starts at the mouth and ends at the anus. So many microorganisms — approximately 100 trillion^2^ — live in the average intestine that their total weight adds up to about 2.5 pounds. Collectively, the body’s microorganisms are called its microbiota. The specific composition of each person’s microbiota is different and is determined by genetics, exposure to microorganisms in early life, diet, health and medications.

**Only live organisms can be characterized as probiotics.**

A healthy microbiota has numerous important roles in the body. It helps support the development of a strong immune system. It forms a protective layer or barrier in the intestine that blocks pathogens and harmful substances from entering the bloodstream through the intestinal wall. It also helps maintain a balance in the intestine between beneficial and harmful microorganisms. When the microbiota does not function properly, as in certain immune deficiency disorders, pathogenic microorganisms can take hold, causing discomfort and illnesses such as inflammatory bowel disease and Crohn’s disease.^4^

Certain probiotics, namely the types of bifidobacteria and lactobacilli that commonly are added to yogurt and probiotics supplements, work by boosting the overall health of the microbiota and gut barrier. They accomplish this in several ways: boosting mucus production on the surface of the intestine; preventing harmful bacteria from proliferating, sticking to^5^ or traveling through the intestinal wall; and stimulating the production of immunoglobulin A (IgA), the primary antibody associated with mucosal immunity.^6^
The relationship between probiotics and relief from intestinal problems is actively being studied. Some findings show that probiotics help relieve infectious diarrhea, but more research is needed to determine which strains are the most effective. Research results also suggest that probiotics, by restoring a healthy balance of organisms in the microbiota, may help alleviate the symptoms of inflammatory bowel disease, Crohn’s disease, ulcerative colitis and other disorders—some of which are more common in people who are immune-compromised.

**Approximately 70 percent of the body’s immune system is located in the intestinal tract.**

**How Probiotics May Boost the Immune System**

Approximately 70 percent of the body’s immune system is located in the intestinal tract. Known as GALT (gut-associated lymphoid tissue), its primary immune responses in the intestine target dietary proteins that could be potential allergens, as well as pathogenic bacteria, viruses and parasites. An unhealthy or unbalanced microbiota may lead to inadequate immune responses and is thought to contribute to the development of autoimmune diseases, diabetes and other illnesses. Conversely, a healthy balance of microorganisms in the intestine aids the immune system by interacting with intestinal innate and adaptive immune development and functions.

Researchers, encouraged by the tremendous potential and limited downside of probiotics, are actively trying to figure out how they work to enhance the intestinal immune response. Several possible mechanisms have been put forth:

- **Improve communication.** By helping balance intestinal microorganisms, probiotics enhance the ability of the microbiota to communicate, or “cross-talk,” with the immune cells located in the intestinal mucosa. Failures in this communication are thought to contribute to the development of autoimmune and auto-inflammatory diseases.

- **Boost T cells.** Probiotics appear to have a beneficial effect on T cells, lymphocytes (white blood cells) that are involved in cell-mediated immunity. It has been shown that a variety of strains of lactobacillus, a probiotic bacteria, improve the health of T cells and increase the ability of these blood cells to destroy harmful bacteria.

- **Activate cells that stimulate immune responses.** Dendritic cells are cells in the immune system that intercept and deliver antigens to T cells and B cells, where the adaptive immune response takes place. They help regulate both innate and adaptive immunity by producing anti-inflammatory cytokines and chemokines (both are compounds that signal the immune system). Certain probiotic strains help activate dendritic cells while also suppressing the inflammation process caused by pathogens. Probiotics also stimulate immune cells to better tell the difference between harmful and beneficial bacteria.

- **Stimulate IgA production.** The positive influence of probiotics on IgA in the intestinal mucosal lining may improve immune function.

The relationship between probiotics and reduced inflammation has been shown in short-term studies to aid symptoms of irritable bowel syndrome (IBS) and certain types of colitis, which are not immune diseases. But, results of longer-term IBS studies vary. However, to date, probiotics have not definitively been shown to be effective in inflammatory bowel disease, Crohn’s disease or several other conditions. Additionally, despite probiotics’ promising effects on the intestinal immune system, studies have not yet demonstrated that they benefit disorders involving the immune system. Long-term studies on large groups of people are needed to determine whether different combinations of probiotics, given at specific stages in the disease process, might lead to beneficial results. Thus, for now, probiotics are not part of mainstream therapy for inflammatory bowel disease and other immune-related intestinal disorders.

**Adding Probiotics to the Diet**

Although probiotics are considered to be unproven remedies and the U.S. Food and Drug Administration has not approved any health claims for probiotics, many people add them to their diet with the thought that they can’t hurt and possibly can help. The most common products with probiotics are yogurts that contain probiotic cultures in addition to their traditional yogurt cultures, a variety of dairy and non-dairy beverages, and probiotic supplements. When deciding on a probiotic food or supplement, it must continue to be taken on a regular basis in order to get any potential benefit; once stopped, the microbiota is likely to go back to the way it was before beginning probiotics.
Always look for package information on the strains of probiotics that are supplied in the products being considered. Different strains have different potential effects on particular conditions in the body.\textsuperscript{16} research on one strain is not applicable to others, different people do not have the same response to a specific probiotic, and results from animal studies do not necessarily apply to humans.\textsuperscript{2,15}

Furthermore, no strains or combinations of strains have yet been proven to improve immune disorders.

Exact dosages can’t be found on most products, but foods and supplements will list the species and strain. Some will state that the cultures are live and active, and supplements will list the approximate number of cultures.

In 2011, the Agency for Healthcare Research and Quality looked at the safety of probiotics and concluded that they have few negative side effects. However, long-term safety has not yet been studied extensively in healthy populations or in people who have chronic illnesses or immune deficiency diseases and who consistently take daily doses.\textsuperscript{15}

That is why it is important to consult with a doctor or other health professionals before starting a probiotics regimen. Additionally, probiotics should not take the place of scientifically proven medications or treatments.\textsuperscript{16}

Because probiotics are live microorganisms, they need to be handled properly to ensure that they stay alive. A package statement that lists the number of live cultures in a product pertains to the product when it leaves the manufacturing facility. Improper handling during shipping and storage can kill the bacteria, and, unfortunately, there is no way of knowing that a product might have been mishandled. However, if a product package calls for refrigeration and it is being sold from a room-temperature shelf, it shouldn’t be purchased. For freshness, products with the latest expiration date should be chosen, and package instructions for storage at home should be followed.

The field of probiotics is rapidly changing, with new research findings continuing to be published and new products hitting the store shelves. Patients should rely on reputable sources for information on scientifically proven relationships between probiotics and immune system disorders. And, when choosing among brands, reviews from reputable third parties and other users should be taken into account, and a product and dosage schedule that makes the most sense for the patient should be considered.

MINDY HERMANN, MBA, RDN, is a food and nutrition writer and communications consultant in metropolitan New York. She gets her probiotics from yogurt, which she tries to eat daily.

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Most patients with low serum immunoglobulins (IgGs) have defects of immunoglobulin production (e.g., X-linked agammaglobulinemia, common variable immunodeficiency, etc.). These patients respond well to immunoglobulin (IG) replacement therapy since the IG, given either intravenously (IV) or subcutaneously (SC), persists in the circulation for 20 to 25 days. However, there are some patients who have low IgG levels because of increased IgG loss. In these illnesses, the IgG half-life is markedly reduced, often as rapid as two to three days, making replacement therapy a severe challenge. The sites of IgG loss, in order of increasing frequency, are into the skin, lung or thorax, peritoneum, urine and gastrointestinal tract. The following clinical vignettes illustrate these routes of IgG loss.

Case 1: Jimmy, Age 6 Months, IgG Loss Into the Skin

Shortly after birth, Jimmy developed an itchy rash on his cheeks and arms. He was the first child of allergic parents. The pediatrician diagnosed atopic dermatitis (eczema) and prescribed skin lubrication, local steroids and a soy formula. Over the next several months, his skin condition worsened despite multiple creams and baths, higher-potency steroid ointment and two courses of systemic steroids. Jimmy’s constant itching and crying at night prevented him and his parents from getting a good night’s sleep. When he developed purulent areas on the skin and a low-grade fever, he was referred to an allergist/immunologist who noted a weeping infected dermatitis and enlarged lymph nodes.

Skin cultures showed *Staphylococcus aureus*. His white blood count was 14000 cell/μL with 82 percent polymorphonuclear cells. His IgG levels were 52 mg/dL IgG (low), 45 mg/dL IgM (normal), 15 mg/dL IgA (low) and 437 IU/mL IgE (high). Blood chemistries were normal except for an albumin level of 3.2 g/dL. Antibody levels to tetanus and *Hemophilus influenzae* were nonprotective despite immunizations to these pathogens. Alpha-1 antitrypsin

# Rare Hypogammaglobulinemic Disorders Due to Immunoglobulin Loss

Five clinical vignettes illustrate how hypogammaglobulinemia can be caused by increased immunoglobulin loss, rather than decreased immunoglobulin production.

By E. Richard Stiehm, MD
was not present in the stool, excluding protein loss in the gastrointestinal tract.

The infant was hospitalized for intensive skin care, intravenous antibiotics and IVIG therapy, which resulted in marked improvement.

Diagnosis: Exudative atopic dermatitis with hypogammaglobulinemia

Comment: Low IgG levels have been reported in severe atopic dermatitis secondary to loss of IgG and other serum proteins into the skin. This is more common in young infants and often aggravated by transient hypogammaglobulinemia in infancy. Other disorders with protein loss through the skin include severe burns or blistering dermatitis such as Stevens-Johnson syndrome. IG has been used with some success in all of these conditions.

Case 2: John, Age 3, IgG Loss Into the Lung or Thorax

Johnny has never been in good health. He was diagnosed shortly after birth with cyanotic congenital heart disease due to a single ventricle. At age 2, he required a Fontan open-heart surgical operation, which redirects venous blood from the body into the lung via the pulmonary arteries. This lessened the cyanosis for more than a year, but he then developed increasing dyspnea. A chest X-ray showed complete opacification of the right lung.

Laboratory tests revealed an IgG level of 150 mg/dL (low) and an absolute lymphocyte count of 155 cells/μL (very low; normal is greater than 1500 cells/μL). Bronchoscopy revealed an obstruction of the main right main stem bronchi with a gelatinous fibrinoid material infiltrated with mononuclear cells. Multiple bronchial lavages with activated plasminogen led to marked improvement.

Diagnosis: Plastic bronchitis (bronchial casts) with hypogammaglobulinemia and lymphopenia

Comment: The Fontan procedure may result in diminished lymphatic flow from the lungs and/or thoracic duct damage, leading to extravasation of lymphoid fluid and white cells into the bronchi. In severe cases, the entire bronchial tree may be involved resulting in the formation of a cast of the entire bronchi. Additional heart surgery and bronchial lavage are only partially successful.

Other conditions associated with loss of IgG into the thorax include interference with thoracic duct cyst flow by accidental ligation during surgery, deliberate cannulation for immunosuppression or obstruction by enlarged lymph nodes or tumors. Large pleural effusions may also result in hypogammaglobulinemia.

Case 3: Pedro, Age 8, IgG Loss Into the Peritoneum

Pedro has been on triweekly peritoneal dialysis for three years because of IgA nephropathy and renal failure, and he is on the waiting list for kidney transplantation. He suddenly developed abdominal pain, a fever of 102 degrees and diarrhea, and his abdomen was very tender. A diagnosis of peritonitis was made. The indwelling peritoneal catheter was removed, and a culture showed Streptococcus pneumoniae. His serum IgG was 280 mg/dL (low), and IgM and IgA levels were normal. Pneumococcal titers were nonprotective despite a recent Pneumovax vaccine. Intraperitoneal and systemic antibiotics were given, and he made a good recovery.

With increased IgG loss, the IgG half-life is markedly reduced, often as rapid as two to three days, making replacement therapy a severe challenge.

Diagnosis: Peritonitis, peritoneal dialysis and hypogammaglobulinemia

Comment: Infection is a constant risk with peritoneal dialysis and is often aggravated by hypogammaglobulinemia due to loss of IgG in the peritoneal fluid removed during dialysis. There is decreased immune responses to vaccines, particularly pneumococcal vaccines. In addition, chronic renal failure results in decreased cellular immunity, adding to these patients’ propensity to infection.

Loss of IgG into the peritoneal space may also be caused by chylous ascites. The milky lymphatic fluid contains lipids, fat globules, IgG and other serum proteins. It is caused by congenital lymphoid abnormalities, peritoneal lymphadenopathy, infection, cirrhosis or cancer. Hypoalbuminemia is usually present.

Case 4: Aziz, Age 10, IgG Loss Into the Urine

Aziz developed gradual onset of leg swelling and puffiness around the eyes following a short-lived respiratory infection. His parents noted pallor, lessened energy and a persistent cough. His pediatrician’s tests showed mild anemia, a low
Case 5: Marianne, Age 18, IgG Loss Into the Intestines

Marianne had gradual onset of abdominal pain, loose stools and recurrent sinus infections. She sought medical attention when she noted symmetrical swelling of the ankles and a slight weight loss. Laboratory tests showed mild lymphopenia of 1400 cells/µL and a low IgG of 125 mg/dL. Her IgM and IgA levels were normal, but her albumin level of 2.5 g/dL was reduced. Alpha-1 antitrypsin levels in the stool were markedly elevated, indicating loss of protein into the gastrointestinal tract. A small intestinal biopsy showed markedly distended lymphatic channels. A fat-free diet and medium chain triglyceride supplements led to considerable improvement. The hypogammaglobulinemia was treated with weekly SCIG infusions.

Diagnosis: Primary intestinal lymphangiectasia with hypogammaglobulinemia

Comment: The markedly dilated lymphatics present in intestinal lymphangiectasia results in leakage of lymphatic fluid into the intestinal lumen and loss of serum proteins and cells. These and decreased absorption of fat-soluble vitamins lead to abdominal symptoms, undernutrition and peripheral edema. Intestinal lymphangiectasia can be a primary disorder (as in Marianne’s case) or secondary to gastrointestinal inflammatory disorder, chronic infection or lymphatic obstruction following surgery, thoracic duct abnormalities or mesenteric lymphadenopathy.

Discussion

In all of the cases of hypogammaglobulinemic disorders discussed, IgG loss is greater than IgG production, which is normal or increased. Since functional antibody is continually produced, the patients rarely have increased susceptibility to infection unless the hypogammaglobulinemia is profound (IgG is less than 200 mg/dL). Edema lymphopenia and depressed cellular immunity may be present.

Secondary hypogammaglobulinemia due to excessive loss can also result following repeated plasmapheresis, massive blood loss due to trauma or surgery, or multiple blood sampling in tiny premature infants.

A diagnosis of immunoglobulin loss is suspected when the IgG level is disproportionately low, some antibody function is present, and albumin and lymphocyte levels are markedly reduced. A shortened IgG half-life can be documented by giving a large dose of IVIG (i.e., sufficient to elevate the IgG to 1000 mg/dL) followed by serial IgG levels. Sophisticated studies using radiolabeled IgG were done in the past to document rapid IgG turnover, but are rarely done these days.

Treatment of the hypogammaglobulinemia is a challenge since IgG is rapidly lost. If Ig is necessary because of recurrent infection, SCIG should be used at least weekly to maintain a more constant trough level.

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

References

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How Not to Say the Wrong Thing

It works in all kinds of crises — medical, legal, even existential. It’s the “Ring Theory” of kvetching. The first rule is comfort in, dump out.

By Susan Silk and Barry Goldman

When Susan had breast cancer, we heard a lot of lame remarks, but our favorite came from one of Susan’s colleagues. She wanted, she needed, to visit Susan after the surgery, but Susan didn’t feel like having visitors, and she said so. Her colleague’s response? “This isn’t just about you.”

“It’s not?” Susan wondered. “My breast cancer is not about me? It’s about you?”

The same theme came up again when our friend Katie had a brain aneurysm. She was in intensive care for a long time and finally got out and into a step-down unit. She was no longer covered with tubes and lines and monitors, but she was still in rough shape. A friend came and saw her and then stepped into the hall with Katie’s husband, Pat.

“I wasn’t prepared for this,” she told him. “I don’t know if I can handle it.”

This woman loves Katie, and she said what she did because the sight of Katie in this condition moved her so deeply. But it was the wrong thing to say. And it was wrong in the same way Susan’s colleague’s remark was wrong.

The Ring Theory

Susan has since developed a simple technique to help people avoid this mistake. It works for all kinds of crises: medical, legal, financial, romantic, even existential. She calls it the Ring Theory.

Draw a circle. This is the center ring. In it, put the name of the person at the center of the current trauma. For
Katie’s aneurysm, that’s Katie. Now, draw a larger circle around the first one. In that ring, put the name of the person next closest to the trauma. In the case of Katie’s aneurysm, that was Katie’s husband, Pat. Repeat the process as many times as you need to. In each larger ring, put the next closest people. Parents and children before more distant relatives. Intimate friends in smaller rings, less intimate friends in larger ones. When you are done, you have a kvetching order. One of Susan’s patients found it useful to tape it to her refrigerator.

Here are the rules. The person in the center ring can say anything she wants to anyone, anywhere. She can kvetch and complain and whine and moan and curse the heavens and say, “Life is unfair” and “Why me?” That’s the one payoff for being in the center ring.

Everyone else can say those things, too, but only to people in larger rings.

When you are talking to a person in a ring smaller than yours, someone closer to the center of the crisis, the goal is to help. Listening is often more helpful than talking. But if you’re going to open your mouth, ask yourself if what you are about to say is likely to provide comfort and support. If it isn’t, don’t say it. Don’t, for example, give advice. People who are suffering from trauma don’t need advice. They need comfort and support. So say, “I’m sorry” or “This must really be hard for you” or “Can I bring you a pot roast?” Don’t say, “You should hear what happened to me” or “Here’s what I would do if I were you.” And don’t say, “This is really bringing me down.”

If you want to scream or cry or complain, if you want to tell someone how shocked you are or how icky you feel, or whine about how it reminds you of all the terrible things that have happened to you lately, that’s fine. It’s a perfectly normal response. Just do it to someone in a bigger ring.

**Comfort IN, Dump OUT**

There was nothing wrong with Katie’s friend saying she was not prepared for how horrible Katie looked, or even that she didn’t think she could handle it. The mistake was that she said those things to Pat. She dumped IN.

Complaining to someone in a smaller ring than yours doesn’t do either of you any good. On the other hand, being supportive to your principal caregiver may be the best thing you can do for the patient.

Most of us know this. Almost nobody would complain to the patient about how rotten she looks. Almost no one would say that looking at her makes them think of the fragility of life and their own closeness to death. In other words, we know enough not to dump into the center ring. Ring Theory merely expands that intuition and makes it more concrete: Don’t just avoid dumping into the center ring, avoid dumping into any ring smaller than your own.

Remember, you can say whatever you want if you just wait until you’re talking to someone in a larger ring than yours.

And don’t worry. You’ll get your turn in the center ring. You can count on that.

**SUSAN SILK** is a clinical psychologist. **BARRY GOLDMAN** is an arbitrator and mediator and the author of The Science of Settlement: Ideas for Negotiators.
Let’s Talk!
By Trudie Mitschang

Velvet Bolingbroke is a 16-year-old who was diagnosed at the age of 4 with chronic inflammatory demyelinating polyneuropathy (CIDP). CIDP is a very rare condition, especially in children. It damages the myelin sheath (the fatty covering that wraps around and protects nerve fibers) of the peripheral nerves. As a result, messages sent throughout her body don’t always reach their destination, and her muscles start to weaken. Velvet lives with her parents in Ottery, Somerset, United Kingdom.

Trudie: You were diagnosed with CIDP at a young age. What has treatment been like?
Velvet: Initially, I was prescribed high-dose steroids (prednisolone), and over the years, they have been reduced according to how stable my disease is. If I get too weak, the doctors raise the dosage to increase my strength. Unfortunately, over the last couple of years, the steroids haven’t worked, so several other treatments have been tried. These include intravenous immune globulin (twice), plasmapheresis (which I couldn’t finish because the Perm cath being used cracked, so they had to stop the treatment and take the line out), azathioprine and, just recently, a course of cyclophosphamide. Now, I am taking mycophenolate mofetil, but I'm not sure if this treatment will work because it is in the same family as azathioprine, which caused me kidney problems.

Trudie: When did your health start to decline?
Velvet: Since 2011, I have used a wheelchair as I am unable to walk. The right side of my body is extremely weak, especially my right arm. My left side is a lot stronger, and I tend to use it more, which is why I am left-handed. I have trouble swallowing, and since last May, have been fed by a nasogastric tube. I also have scoliosis and respiratory problems, and I use a BIPAP (a portable ventilator) every night.

The worst year I have experienced with my condition was 2012 because I was in hospital for more than 130 days. As a result, I hardly went to school, but I did do my schoolwork at home, and I finally went back to school in January 2013.

Trudie: You’ve been working on a business idea. What are your career goals?
Velvet: I am going to need a job when I leave school, so my dad is helping me to start my own business using a computer to create imaginative photos. It’s a great job because I am quite restricted, but I can still use a computer.

Trudie: You recently underwent physical therapy. Tell us about that.
Velvet: During the first three weeks of my school summer holiday, I did an intense course of rehabilitation. This was given to me because all my muscles and joints are very weak, and my physiotherapists wanted to try to strengthen them to help me stand and walk like I used to. This treatment was given to me in Great Ormond Street Children’s Hospital by two fantastic physiotherapists who worked very hard to help me restore my strength and confidence again.

Trudie: What did your therapy entail?
Velvet: Before my rehab began, my muscles were measured to see how strong or weak they were. Then, the hard work began. My exercises varied every day from dry land physiotherapy to hydrotherapy (in a swimming pool). The exercises were mostly focused on my legs and hips. The dry land physiotherapy mainly consisted of exercises on a gym bed like rolling, knee balancing and lots of tummy muscle work. However, near
the end of the second week of rehab, I did some standing, but I had to wear leg supports so my legs wouldn’t give way. In the water, the exercises were completely different as I had to perform a few lengths of walking, standing and swimming on my front, and much more. Also, in the water, I did a couple of arm exercises to help strengthen them too.

**Trudie:** Did the rehabilitation help?

**Velvet:** When I first started my session of rehabilitation, I was feeling quite nervous. But as the days went on, I gained more and more confidence in myself, and as a result, I became much more successful in doing my exercises. After my three-week session, I felt a little stronger in my legs as I seemed to be doing better transfers from my chair. On my last day, my joints were measured again to see whether there was any improvement, and out of 10 different joints measured, one of them was down a little, one stayed the same and the remaining eight showed an increase between 5 percent and 50 percent. Overall, the physiotherapy benefited me as far as my strength and confidence.

**Trudie:** How do you keep a positive attitude?

**Velvet:** I have had some really tough times, but I still have been able to enjoy my life. I have been to Disneyland Paris twice and a number of great shows in London. But, the happiest part of my life is having my mum and dad always there to support me or to give me a cuddle when I’m upset. I keep positive because I am sure that one day something will come along to help me.

**TRUDIE MITSCHANG** is a staff writer for IG Living magazine.
Life as a 20-Something
10 Rules for Surviving Chronic Illness in Your 20s
By Ilana Jacqueline

THERE ARE TONS of things no one tells you about your 20s. Like the fact that you’ll probably be in credit card debt for the next 10 years. Or, that you’ll be expected to make new friends who are like you when you have almost zero definition of what you are like. Not to mention that you will be able to visually tell if you ate carbs the night before based on the size of your muffin top.

Add to that your basic life-with-chronic-illness woes: how to tell friends about your disease, when to bring up your latest hospitalization on your first date, and how to get out of that party so you can go home and crash — and it’s basically a minefield of situations ranging from incredibly awkward to downright dangerous.

That said, and some 23 years of chronic illness behind me, here are 10 rules to surviving chronic illness in your 20s:

1. Say goodbye to your pediatrician. If those lollipops you’re collecting at the pediatrician’s office are sitting next to your college class schedule, you’ve overstayed your welcome.

2. Don’t be afraid to get a second opinion. Just because you’ve been seeing a doctor for a long time doesn’t mean he’s the best (or only) doctor out there. This is your 20s; nothing wrong with a little experimenting.

3. Insurance is a language; get fluent. If you’re lucky enough to have insurance these days, do yourself a favor and get familiar with your plan. Whether you’re on your parents’ plan (which you can be until age 26!) or you’re getting healthcare through federal programs or your own job, you’ll still want to know ahead of time what’s covered.

4. It’s a small world, until it’s not. In high school, you may not have had the energy, time or luck to get to know other students with chronic illnesses. Now is a good time to put a little effort forth to join or create a local support group, look for local patients online or volunteer in your college’s office of student disabilities.

5. Learn to keep yourself in check. Literally. Make a list if you really have to. Are you sleeping every night? Are your symptoms getting out of control? Are your medications all working like they should? It’s easy to let the management of your disease get lost in the millions of other things in life that you’re responsible for.

6. Drop the drama. I operate under the rarely used 20-something philosophy that my life is plenty exciting. I don’t need to create drama; my colon is probably going to do that for me. So when it comes to fair-weather friends and partners I couldn’t trust with my goldfish, let alone my immune system, I’m just not in that place right now.

7. Budget for emergencies. Maybe your friends have a rainy day fund; in your case, you’d better have the resources to withstand a tsunami. If you’re unable to work from home or the hospital, it’s good to put up to half of your weekly paycheck into savings. If you can’t budget with money, budget with knowledge of available resources for personal funding by researching charitable funds (like the Chronic Disease Fund www.cdfund.org) or government assistance.

8. Suck it up, but don’t be a hero. Having a flare-up on your sister’s wedding day? Time to take a mouthful of Imodium and suck it up. Being pressured to eat four pieces of cake by your obnoxious aunt who keeps pinching your skinny arms? Don’t be a hero; just say “No.” Learn who, where and when it’s worth it to put yourself through a little suffering, but don’t give away your energy to people who don’t deserve it and won’t appreciate it.

9. Don’t take it personally. People don’t always “get” why you have to coordinate parts of your life around your chronic illness. Whether you’re leaving a party early or carrying around half a pharmacy in your purse, seemingly rude comments are generally coming from a place of misunderstanding. Don’t take it personally; take it as an opportunity to educate someone about your disease.

10. It isn’t who you are; it’s just what you have. You’re not just a person who is chronically ill. You are a person, and you happen to also be chronically ill. You are a person, and you are someone who is chronically ill. You are a person, and you happen to also be chronically ill. Don’t let your disease define your personality. You are so much more than an illness, and when you stop thinking of yourself in that box, others will too.

ILANA JACQUELINE is a 23-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.
WHEN I WAS DIAGNOSED with common variable immune deficiency and interstitial lung disease in 2004, I was so relieved. At last, I knew why I had been taking more than 10 antibiotics a year, and why being healthy was always such a struggle. All at once, my endless list of questions had suddenly been answered. Not only was my frustrating search over, but my new journey had begun — even if I didn’t know where I was going. From what the doctors told me, it seemed pretty simple: intravenous immune globulin therapy every month and the labs to go with it, and I should be good as new.

Is it ever really that simple? With one diagnosis came another and another. My relief has become dread. It feels like I can’t catch a break. I’m in my 20s, and I already have a textbook size medical record! Every time I go to the doctor, I fear that something else will be added to my list of diagnoses or prescriptions. I feel trapped. The idea that I have to undergo these treatments “for life” scares me, and now I have been upgraded from once to twice a month. The thought that I have to carry my 5-pound sparkly bag of pills with me everywhere I go is such a burden. And, then, to top it off, experimental treatments and pulmonary rehab have been added to my agenda.

I don’t know if I just need to accept my situation or if I should keep wondering if it will ever change. I want to be better already! I don’t want any more surprises. Between all of the quality control, illness management and organizing my treatment dates and appointments, there’s no time for me. I keep asking myself the age-old chronically ill question: Am I my illness? It sure feels that way.

I feel like I am teetering on the edge of two worlds. I have a strong desire to be well and continue on the path that I have always imagined since I was a little girl, but I have to accept that my path has changed. My life is going to be different now, and not just different for me but for my family. And, it certainly will be a different life from the lives of most people I will meet.

I still have this strong desire to work, go out with my friends and spontaneously take a trip somewhere. But I know the 20-something lifestyle isn’t healthy for me. I find myself asking my friends, “You mean we are going out at 10 p.m.?” when in my head I am thinking I am usually in bed 30 minutes later. What makes things a little more complicated is that it is still hard for many of my friends to understand what I am and have been going through. Besides the fact that I looked a little strange to them because of the prednisone-induced weight gain and moon face, they just always assumed that I had “let myself go.” This frustrates me to my core! But I know I can’t make them understand or teach them to have empathy. I have to learn for myself that I’m a hero and that I’m a survivor and a fighter. What matters most is that I know what I’m going through, and I know how well I can cope.

I have always known, perhaps instinctively, that I would need to find balance. I need to do things that make me feel like I’m leading a “normal” life, while always calibrating it with activities and habits that will keep me healthy.

What I have come to realize is that, with time, what felt so foreign or abnormal and such a burden has become my standard for living. I have adapted and persevered by adopting a new way of thinking. I have simply prioritized differently. It now seems like all I have to do is juggle a full schedule and, OK, carry a bigger purse for my many supplies.

EVER FECSKE MAZZA was diagnosed with CVID and interstitial lung disease in 2004. She is a new mom of a sweet little boy named Boston, and loves every minute of it! She lives in Los Angeles, Calif., with her husband, and when she isn’t changing diapers and playing with her son, she enjoys wedding planning, baking, flower arranging, cooking, shopping and anything that sparkles!
IG Chronicles
“Please Hear Me”

TEENAGERS. Can’t live with ‘em, can’t duct tape them to a tree in the middle of a remote forest — where nobody can hear their pleas for a better phone or a later curfew or another $20 — because, apparently, it’s illegal or something. Whatever.

My 15-year-old daughter has blue hair. Actually, at the moment, it’s bleach blonde with blue streaks. In the past two years, her hair has been dark blue, hot pink, purple and, in the holiday spirit of Christmas, fire engine red. It drives my mother crazy. She can’t understand why I let her do it.

My daughter and I argue. A lot. There are some arguments I absolutely must win — such as whether or not she attends her monthly infusion appointments — and some I feel are just not worth the time and effort to fight about — like the temporary color of her hair.

Parenting teenagers is hard. Parenting teenagers with chronic illness is even more difficult. I worry about all the typical issues most parents do: drugs, alcohol, sex, teen pregnancy. But it’s more than that. When a teenager lives with a chronic illness, each of these worries expands exponentially, because there could always be added ramifications.

I worry that excessive alcohol consumption could wreak havoc on an already weakened immune system. I worry what damage smoking cigarettes or pot would cause to asthmatic lungs already injured by infections. I worry that a split-second decision to have sex, just once, could leave my daughter with an STD that would ravage her body or result in a pregnancy she couldn’t possibly be healthy enough to support.

But, then again...

Then again, I realize that I need to let my kids grow up. I know that when I was a teenager, I did … well … some stupid things. I want to protect my children from every single boogeyman in the world.

I also know I can’t.

When my kids were first diagnosed — really, even before that, when they were sick all the time and we weren’t sure why — I had control. They were young, and I was the boss. If they seemed ill, I cancelled plans and kept them home. I had the power to make them take their meds, or hog-tie them into a car seat for a nebulizer treatment. (Yes, a car seat. My little one was quick to run and hard to catch.)

I have four children. All of them have asthma, and the three youngest live with common variable immunodeficiency (CVID). My girls are 17 and 15, and at 11 and 13, my boys are just at the cusp of teen angst. As they are all growing older, it’s hitting me that my supermom powers are becoming rather impotent. It can be difficult to convince a headstrong, rebellious teenager to take her meds, or hog-tie them into a car seat for a nebulizer treatment. (Yes, a car seat. My little one was quick to run and hard to catch.)

I worry that excessive alcohol consumption could wreak havoc on an already weakened immune system. I worry what damage smoking cigarettes or pot would cause to asthmatic lungs already injured by infections. I worry that a split-second decision to have sex, just once, could leave my daughter with an STD that would ravage her body or result in a pregnancy she couldn’t possibly be healthy enough to support.

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Then again, I realize that I need to let my kids grow up. I know that when I was a teenager, I did … well … some stupid things. I want to protect my children from every single boogeyman in the world.

I also know I can’t.

When my kids were first diagnosed — really, even before that, when they were sick all the time and we weren’t sure why — I had control. They were young, and I was the boss. If they seemed ill, I cancelled plans and kept them home. I had the power to make them take their meds, or hog-tie them into a car seat for a nebulizer treatment. (Yes, a car seat. My little one was quick to run and hard to catch.)

I have four children. All of them have asthma, and the three youngest live with common variable immunodeficiency (CVID). My girls are 17 and 15, and at 11 and 13, my boys are just at the cusp of teen angst. As they are all growing older, it’s hitting me that my supermom powers are becoming rather impotent. It can be difficult to convince a headstrong, rebellious teenager to take her meds, or hog-tie them into a car seat for a nebulizer treatment. (Yes, a car seat. My little one was quick to run and hard to catch.)

I wonder if this imaginary tattoo artist would accept a letter of explanation from our infectious disease guy? The possibility is slightly comforting.

I’ve always tried to be open with my kids by explaining that while their illnesses should never be used as an excuse to limit their futures, they do need to think. Think through decisions that may have a little bit more impact on them because of CVID and asthma and everything else.

Last week, we received a baby shower invitation from a high school classmate of my daughter’s. I blinked a bit. The mother-to-be is a girl who has spent many sleepovers at our home; a girl whose hair I used to braid; a girl who — just a blink of time ago — was a little girl, just like my own.

I felt this warranted another one of those little mother-daughter “talks,” and cleared a space at our old
wooden kitchen table for that purpose. Rather helplessly moving around the clutter that overruns our table (my Susie Homemaker skills are decidedly deficient), I catch her attention.

“Let’s sit down. I want to discuss something with you, Savannah.”

Hands halt, fingers aquiver over her iPod.

“Mom, is this about the baby shower?”

“Kind of … well …,” (The speed of my speech is increasing at a ridiculous rate, and my words begin to tumble over one another.) “I think we should talk about the consequences of teenage pregnancy, and even though we hope everything goes well for your friend and her future is bright and happy … we should talk about … um…”

Eyes roll. The expression on her face clearly implying, “My mom is so lame, it’s going to kill me.”

“Oh. My. God. MOM. Please don’t tell me this is another sex talk. Not again.”

“Well, honey, it’s just that you need to understand the difficulties something like this could cause for you, having the medical issues you have…”

I drift off. I know where I want this conversation to go, I’m just not positive how to get there.

“MOM. We don’t need to talk about this again. I heard you the last time. And the time before that. I hear you, I hear you.”

I hope she does. I hope she does. Please hear me.

VALARIE KINNEY is the mother of four children, three of whom are diagnosed with common variable immunodeficiency. Her blog titled Organizing Chaos and Other Misadventures can be read at organizingchaosandothermisadventures.wordpress.com.

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“WELL, HAVE YOU TRIED steamed broccoli?” the rogue “nice” lady ahead of me in the “15-or-less-items” line at our neighborhood super-duper megastore suggested, watching me place my five items (to her 40) on the checkout belt. The five items I was about to purchase didn’t settle well with her: two bags of sour Gummi Bears, one cinema-sized Whoppers and one bulk half-pound of Jelly Bellys — all “bribe eats” for my PIDD (primary immune deficiency disease) kids’ intravenous immune globulin (IVIG) infusions the following day. I tried to explain to “nice-but-misinformed lady” in the 10 or so minutes we were waiting in the express lane — ample time for her to really study my purchases — that a treat for a kid getting IVs once every four weeks wasn’t such a terrible thing and that our family doesn’t eat Ho Hos for dinner. “Not-so-nice and getting-on-my-last-nerve, extremely judgmental lady” dug in her sensible shoes’ 2-inch heels: “Well, then you more than anybody should be including healthy choices in your kids’ diets!” I looked down at my tattered flip-flops, trying to look ashamed so she’d leave me alone. Finally, “not-nice-at-ALL, terribly misinformed, express lane-abuser, on-my-last-nerve, extremely judgmental, sensible, ugly-shoe lady” and her uber-stuffed shopping cart bid us farewell.

Trying to get our PIDD kids to eat better has been a battle from the get-go. In their teens now, all three know raw carrots are better than candy corn, steamed broccoli is better than brownies, and fish is better than french fries. I live in a household that thinks bacon is the “candy bar of meat” and that cheesecake isn’t really dessert because it has the word cheese in it. And, since everybody knows that cheese is good for you, we should be able to eat as much cheesecake as our little (or big) hearts desire!

I have tried every trick in the book to sneak “good stuff” into my family’s diet, and I’ve failed miserably. I was convinced my kids’ taste buds had been blown to bits by Pop Rocks candy, and that all those sinus infections razed their palates so they wouldn’t be able to tell the difference! Not so. They knew my Saturday morning pancakes had yogurt and whole wheat flour in the batter, they could taste prunes in the brownies, and they knew their favorite lasagna was made with “some sort of vegetable mush that is coating the back of my throat!”

Humiliated I couldn’t get my family to even try hummus, I turned to an acquaintance who sold vitamins and other types of dietary supplements and who hunted me down after learning about our kids’ diagnoses. She showed me a “sample pack” of vitamins and herbal capsules that strangely resembled a dozen eggs.

“Suzie, those pills are huge!” I clamored. “I don’t think a pelican can swallow all those pills, let alone my kids!”

“Well, let’s just start with the Gummi supplements that have a day’s worth of iron, potassium, fiber and….” Suzie rattled off the laundry list of ingredients, but I wasn’t paying much attention; she had me at Gummi vitamins.

That night at the dinner table, I brought out a bear-shaped container stuffed with colorful Gummi vitamins, but I didn’t say a word about what really was in the so-called “candy.”

“If you can take just one little ‘mouse bite’ of broccoli, I’ll give you a
Gummi Bear!” I bribed.

“Right now?” Caleb, one who protests vegetables the loudest, cried.

“Right now,” I countered with a grin.

Very slowly and ever so cautiously, Caleb selected a stem of broccoli. He looked up at me for approval, and I gave him a smile and a wink and hopefully enough encouragement to stick the darned thing in his mouth! His hand shook as the fork and broccoli journeyed dangerously close to his mouth. The dinner table was silent; even Jackson, our faithful black Labrador, stood at attention (read: begging as always). You could cut the tension with a knife and smell the stress coming from the table (or was it the broccoli?). Ever so slowly and meticulously, the forkful of broccoli inched its way forward. Finally, Caleb reluctantly placed the forkful into his mouth first brushing past his lower lip then coming to a stop in the middle of his tongue. Caleb’s teeth closed with his head bowed between his arms that crossed on top of the table. The rest of us peered at him in awe of his feat; I never thought I’d see the day, so I gave him an extra Gummi Bear for his efforts. My PIDD kid finally had something other than meat digesting and blessing his “starving” immune system.

We finally settled down from Caleb’s brilliant performance (I was hoping for an encore), and despite my exhaustion from Battle Broccoli, I made my way upstairs to congratulate Caleb one last time.

As I stepped onto the stair’s landing, I heard a subtle “Mooooom” coming from the kids’ bathroom.

“Mom, is that you?”

“I’m coming!” trying to do my best to figure out to whom the groan belonged.

I opened the door and saw Caleb taking care of business but with a very strange look on his face, a look that oddly reminded me of his broccoli encounter earlier in the evening.

“You OK?” I asked tentatively, as I didn’t think I could prepare myself for what I was about to see.

“Look at what broccoli did to my poop! I’m never, ever, gonna eat that stuff ever again!”

Sure enough, floating in the toilet water was a fluorescent green blob of human waste that belonged to Caleb. I was flabbergasted, overwhelmed and scared all at the same time. Once I got Caleb settled down from his traumatizing toileting and managed to get him back into bed, I saw a very familiar container of Gummi Bears trying their best to be vitamins.

“Um, what are you doing with the Gummi Bears in your room?” I asked. I was so angry with Caleb at this point, I didn’t know whether to deal with his disobedience or his discolored droppings.

“You know how much I love Gummi Bears, and just one after I ate broccoli wasn’t enough for me. I had a weak moment, and, Mom, please don’t be mad at me!” Caleb confessed, crying into his stuffed cocker spaniel.

I motioned to Caleb to hand over the container while my rage slowly melted away. I made sure Caleb was OK, tucked him in for the night and decided the green gobs of poo goo were enough punishment for a day, until I saw how many Gummi Bears had disappeared.

“Caleb, how many bears did you eat?”

“Um. OK, you got me. I ate a bunch of them. I couldn’t help myself! They tasted so good! There is something about them because they don’t taste like normal Gummi Bears!”

“Well, I don’t think it was the broccoli that caused your, uh…”

“Poop to look like little green men?” Caleb saved me from having to describe his excrement.

“I just noticed the ingredient list, and it’s quite colorful — literally!” I said.

I know my rep, Suzie, was quite clear about what vitamins and minerals were in the Gummi Bears; however, she forgot to mention the other ingredients like Lake Blue 5, Red 1, Yellow and Green 6. I kinda determined that was the reason Caleb had an interesting experience in the loo.

After we read over the ingredients, Caleb turned to me and said, “Mom, I just pooped a rainbow.”

Yes, Gummi Bear vitamins are still in our diet, but we now know that one or two is about all our bodies need. We are also having fun seeing if colorful vegetables like eggplant, squash, artichokes and red bell peppers will, “in the end,” tint our intestinal tract.

CHERYL L. HAGGARD is a stay-at-home mom and has three children, two of whom have CVID. She and her husband, Mark, also operate Under the Hood Ministries at www.underthehoodministries.org.
Parenting: PIDD and the Helicopter Parent

It’s difficult not to be overprotective of kids with chronic illness, but as many child health specialists advise, it’s better to let them learn how to handle their own issues and, at some point, to let go of the reins altogether.

WHEN MY PRIMARY immunodeficiency disease (PIDD) kid was in the third grade, he was faced with many issues — both medical and social. My wife and I decided to sit down with the principal of his elementary school to explain his disease and hope to settle some of the social issues that were troubling him. In a condescending tone, she explained the educational principles that guided her school, and then stated we should stop being “helicopter parents.” My response: “If it’s my son you’re talking about, I’m going to be a ‘helicopter parent.’

Helicopter parent is a new term that has entered the lexicon of parenting in the past decade. These are overprotective parents who “hover” over their children, watching their every move and intervening when their children are faced with the slightest provocation. As parents of PIDD kids, the temptation to hover over our children is even greater. We don’t know which bruise or scrape will be the one to land our children in the ER or on long-term antibiotics. But, how much of a service are we doing to our children with continual hovering over every part of their lives?

The Problem with Overprotective Parents

“Being protective is good, but too much of a good thing always turns out to be bad. There are a lot of negative influences and situations that children face today. It’s natural for parents to be concerned about their safety, but sometimes they go overboard and cocoon their children in fear,” states Marila Fernandes, a licensed school psychologist. “[Parents] have to understand that they will not always be there to protect their children, and soon they will be adults who will have to fend for themselves. It’s better if they teach their children how to cope with difficult situations and deal with problems positively rather than shielding them from reality.”

It is a complex task to maintain a balance between being too protective and not affecting children’s independence. And, many child psychologists have opinions about this. According to clinical psychologist Anita Karambalkar, “We need to teach [kids] self-confidence and moral values, and let them live their lives. When parents say yes to everything their children want, when the children face the real world and get their first no, it can shatter the young adult’s confidence.” Dieter Wolke, PhD, of the University of Warwick adds: “I compare it to the parent who does all their child’s homework. You wouldn’t be surprised if the child then couldn’t pass an exam.” Overprotective parents who perform tasks for their children because they hate seeing their children struggle are sending a message to their children that they are not capable of doing an adequate job or that they don’t trust their children to make the right choices.

Why are some parents overprotective? Dr. Robyn Silverman, a child development specialist, considers a number of reasons. In some cases, parents perceive that when they do something for their child, it comes out better. Other parents feel a need for control in a world that is unpredictable and scary. Some parents have a fear of failure and hate to see their children struggle. Some parents fear that their children will succeed and no longer need them as much as they did at one time. Still others feel entitled to check in with their children at any given time. Many are living their lives vicariously through their sons and daughters who are doing things that the parents might not have been able to do when they were younger.

Pediatrician Ramon Resa agrees. He says that when children cannot explore their worlds because their overprotective parents are hovering over them, they become prisoners in their own homes. If their mom or dad is continually right there next to them, children invariably look to their parents to give them answers instead of figuring things out for themselves and learning to handle situations on their own. Also, when parents do too much
protecting in an effort to make their children’s lives stress-free, it often has the opposite effect; instead, many children become depressed and suffer anxiety disorders.

The Problem with Bullies

Several issues ago, my parenting column focused on bullies. Surprise! There are sociopaths on middle school campuses across the United States and the world. These power-seeking agents tend to pick on those who are weaker or have less cachet in the school community. Unfortunately, in many cases, it is our PIDD kids who are on the outside looking in. Our children have had numerous illnesses that cause them to miss school and make it more difficult to socialize. Many become targets of middle school sociopaths. Unfortunately, the children of overprotective helicopter parents are not afforded the tools to handle bullying. A mom or dad might bring it to the attention of a school administrator and walk their kids to class, but there will come a time when an administrator or a parent cannot be there.

In a study on child abuse and neglect (published in the April 2013 issue of Child Abuse & Neglect: The International Journal), researchers investigated the association between parenting behavior and peer victimization between 1970 through 2012. “Overprotection” was categorized as a negative parenting behavior. Conversely, authoritative parenting, parent-child communication, parental involvement, support, supervision, and warmth and affection were classified as positive parenting behaviors. What they found was that the incidences of bullying were 26 percent more common for children of overprotective parents. The authors further noted that victims of bullying are at high risk of developing a host of physical and mental health problems such as anxiety and depression, borderline psychiatric symptoms and increased risk of self-harm, suicidal ideation, and even suicide itself.

Wolke, who was one of the study’s authors, noted that the results “should serve as a reminder that advising parents that being supportive and involved — though not overly involved — lowers the odds their children will be a victim of bullying. Be clear that overprotection increases this risk. Children need support, but parents should not try to buffer their children from all negative experiences.” He added that parents ought to “allow children to have some conflicts with peers to learn how to solve them rather than intervene at the smallest argument.”

When to Stop Hovering

Obviously, we are not going to leave our 5-year-old at the mercy of school sociopaths. My son had surgery in the third grade to remove precancerous lesions from his scalp. Unfortunately, the stitches began coming out before the incision was healed. His pain became the target of jokes by his classmates. When his teacher refused to act, we confronted the teacher and the principal, and eventually pulled him from that school.

However, we should not keep the reins as tight as our children get older. According to Fernandes, it “depends on the age of the child, but if you are in sync with children, you will be surprised by how well they will guide you to help them become confident, achieving adults.” At some point, we must let the reins go altogether.

When parents hover over their children and do everything for them, they are preventing them from maturing. One of the most important jobs we have is to prepare our children to be independent and productive adults. For parents of children with PIDD, that includes preparing them to plan and follow through with their infusions for a time when we are not there. Today, as a high school freshman, my son is free to succeed or fail on his own; I promise to pick him up if the result is bad. As for his infusions, I am making it more and more his responsibility. He will be changing over to subcutaneous infusions soon, and he will be in charge of preparing his injections and placing his own line. I will not always be around for him. The best that I can do is prepare him for a long, healthy and independent life.

MARK T. HAGGARD is a high school teacher and football coach, and has three children, two of whom have CVID. He and his wife, Cheryl, also operate Under the Hood Ministries at www.underthehoodministries.org.
Natural Therapies for Fungal Infections

By Annaben Kazemi

There are many types of fungal infections, all of which can be itchy and annoying. Because fungal infections are “opportunistic,” people with weakened immune systems are particularly prone to their curse, and treatment can become complex and take longer. Often, prescription medications are needed. However, there are over-the-counter precautions that can be taken to prevent reoccurrence and help treat infection.

Reinstate Balance

Fungus enters the body through the airways and digestive system. It is kept in check by healthy bacteria and internal flora. Bacteria also aid the production of vitamin B and lactase. However, it is easy for the system to become unbalanced. Preservatives, additives and the use of antibiotics, oral contraceptives or alcohol can destroy the healthy bacteria in the body and allow fungus to grow unchecked. Dietary changes and antifungal supplements can help restore balance. For instance, adding an acidophilus probiotic supplement can re-establish the body’s healthy bacteria. And, taking a multivitamin supplement can boost the body’s supply of antioxidants and minerals.

Fight Fungus with Food

Fungus needs carbohydrates and sugar to thrive, so people who have a fungal overgrowth tend to crave these kinds of foods. Most nutritionists agree that sugar, yeast, dairy, wheat, caffeine, nicotine and alcohol are the main culprits because they help yeast to grow. Therefore, a diet that is high in protein with few carbohydrates and sugars, as well as avoiding foods that might contain fungi such as corn and peanuts, is recommended. In addition, replacing sugary processed foods in the diet with gluten- and allergen-free food products can help.

Another approach is to eat larger amounts of foods that may suppress the growth of yeast. For example, garlic is believed by some nutritionists to have natural anti-fungal properties and may help to prevent candidiasis. While fresh garlic is considered best, garlic supplements offer the advantage of reduced odors and ease of consumption. Foods also can help individuals infected with oral thrush, which can change how foods taste and are enjoyed and make eating and swallowing difficult. These individuals should avoid acidic, spicy or hot foods because all of these can irritate the insides of the mouth. Instead, soft, cool, bland foods are recommended. And, liquid food supplements can be tried to ease swallowing and to keep or add weight during an oral infection.

Rotate Supplements

There are many natural antifungal supplements that can fight fungus in the body. Caprylic acid, olive leaf extract, apple cider vinegar, undecylenic acid, grapefruit seed extract and neem all contain antifungal properties. There also are supplements that incorporate one or more of these properties. Some nutritionists think it’s best to use a few different antifungal supplements and to rotate them every few weeks to maintain their effectiveness. This is because fungus can learn to adapt to antifungals that are taken every day.

Talk with a Healthcare Professional

The U.S. Food and Drug Administration suggests patients consult with a healthcare professional before using any dietary supplement. These professionals can discuss the safety of a particular product, whether the product is appropriate for patients’ needs, and whether there could be contraindications with other medications.

Annaben Kazemi is the patient advocate for IG Living magazine.

References

Probiotic Pearls

Probiotic Pearls are probiotic supplements that come in a tiny round shape to make them easy to swallow. They are made with True Delivery technology — a triple-layer softgel that protects live probiotics inside from heat, moisture, air and stomach acid so that the live probiotics are released into the intestine where they are needed most. They require no refrigeration. Probiotic Pearls come in five different styles: Acidophilus Pearls that contain active cultures. Pearls YB that are yeast-balancing lactobacillus; Pearls IC, intensive care pearls to provide digestive support; Pearls Elite, high-potency pearls that deliver five billion probiotics and Pearls Immune, the only probiotic supplement with Activ-Ferrin to help strengthen natural defenses.

(800) 783-2286; www.pearlsprobiotics.com

Allergy Research Group

Laktoferrin with Colostrum 90 Vegetarian Caps provides purified lactoferrin in a base of colostrum, and is prepared with lysozyme. Colostrum contains immunoglobulins IgG, IgA and IgM, nucleotides, gamma-interferon, orotic acid, enzymes and vitamins A, E and B12. Other ingredients include hydroxypropyl methylcellulose, microcrystalline cellulose and L-leucine. The nutrients are of the highest purity and do not contain preservatives, diluents or artificial additives. Other available products include Laktoferrin 90 and Laktoferrin 120 Vegetarian Caps.

(800) 545-9960; www.allergyresearchgroup.com/Laktoferrin-with-Colostrum-90-Vegetarian-Caps-p-119.html

Mega Resveratrol

Mega Resveratrol comes in 250 mg and 500 mg vegetarian capsules and powder. Mega Resveratrol’s vegetarian caps contain 99 percent pure resveratrol with no fillers, additives or preservatives. Pure resveratrol refers to a product that contains only trans-resveratrol, the active ingredient and the beneficial substance in resveratrol. Ninety-nine percent resveratrol contains 99 percent of pure trans-resveratrol. The company manufactures the product in small batches so it will always be fresh.

(877) 909-6342; megaresveratrol.net

Barlean’s Organic Oils

Barlean’s offers a line of omega-3 products, including flax oils, flax oil blends, greens, forti-flax, fish oils, omega swirls (omega-3 supplements that have been emulsified) and more. The company’s newest oil is its Wild & Whole Krill Oil. All products are stamped with a six-month freshness date, and each lot of flaxseed used to manufacture the oils is stringently tested and 100 percent guaranteed to be both all-organic and non-genetically modified. The products are packaged in black, opaque drip-free plastic bottles made of high-density polyethylene (HDPE). The capsules used for greens are vegetarian caps made from plant cellulose. And, the gelatin capsules used to encapsulate the oil products are all made at the company’s in-house, state-of-the-art encapsulation facility from bovine-based gelatin, glycerin and water and are caramel coated as a darkening agent to suppress the damaging effect of light on the oils.

www.barleans.com

Enjoy Life Foods

Enjoy Life offers a line of gluten- and allergen-free food products, including crunchy cookies, soft baked cookies, granolas, chewy bars, decadent bars, seed and fruit mixes, chocolate for baking, chocolate bars, plentils, cereals and more. They are made of all-natural ingredients and do not contain hydrogenated oil, white sugar or GMOs. Many items are rich in fiber, protein, omega-3 fatty acids, and vitamins and minerals. The website features recipes, and healthcare professionals can obtain free samples for their patients.

www.enjoylifefoods.com
These organizations provide information about various disease states, which can be found by conducting a search of the disease state name.

- Advocacy for Patients with Chronic Illness: www.advocacyforpatients.org
- The Alliance for Biotherapeutics (fair access to plasma therapies): www.bioalliance.org
- American Autoimmune Related Diseases Association (AARDA): www.aarda.org
- American Chronic Pain Association (ACPA): www.theacpa.org
- Band-Aides and Blackboards: www.lehman.cuny.edu/faculty/jfleitas/bandaides
- eMedicine from WebMD: emedicine.medscape.com
- FamilyDoctor.org: www.familydoctor.org
- Johns Hopkins Medicine: www.hopkinsmedicine.org
- KeepKidsHealthy.com (pediatrician’s guide to children health and safety): www.keepkidshealthy.com
- Mayo Clinic: www.mayoclinic.com
- National Committee for Quality Assurance (detailed report cards on health plans, clinical performance, member satisfaction and access to care): www.ncqa.org
- National Heart, Lung and Blood Institute: www.nhlbi.nih.gov/health/health-topics/by-alpha
- National Institutes of Health: health.nih.gov/see-all-topics.aspx
- National Organization for Rare Disorders (disease-specific support groups and virtual communities for patients and caregivers): www.rarediseases.org
- Office of Rare Diseases Research: rarediseases.info.nih.gov
- Patient Advocate Foundation (patient access to care, maintenance of employment and financial stability): www.patientadvocate.org
- WebMD (medical reference): www.webmd.com

**IG MANUFACTURER WEBSITES**
- Baxter: www.baxter.com
- Bio Products Laboratory: www.gammaplex.com
- CSL Behring: www.csblehring.com
- Grifols: www.grifolsusa.com
- Kedrion: www.kedrionusa.com
- Octapharma: www.octapharma.com

**For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.**

### General Resources

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

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

- **Evans Syndrome**
  - **ONLINE PEER SUPPORT**
  - Evans Syndrome Research and Support Group: www.evanssyndrome.org

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

- **Idiopathic Thrombocytopenic Purpura (ITP)**
  - **WEBSITES**
  - ITP Support Association – UK: www.itsupport.org.uk
  - Platelet Disorder Support Association: www.pdsa.org

- **Kawasaki Disease**
  - **WEBSITES**
  - American Heart Association: www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Kawasaki-Disease_UCM_308777_Article.jsp#.T1T2boePWEO
  - Kawasaki Disease Foundation: www.kdfoundation.org

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

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The nonprofit Patient Services Incorporated, www.patient servicesinc.org, specializes in health insurance premium, pharmacy co-payment and co-payment waiver assistance for people with chronic illnesses. (800) 366-7741

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Sources

For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.
Multifocal Motor Neuropathy (MMN)

WEBSITES
- The Neuropathy Association: www.neuropathy.org

Multiple Sclerosis (MS)

WEBSITES
- All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
- Multiple Sclerosis Association of America: www.msaa.com
- National Multiple Sclerosis Society: www.nationalmssociety.org

ONLINE PEER SUPPORT
- Friends with MS: www.FriendsWithMS.com
- MSWorld’s Chat and Message Board: www.msworld.org

Myasthenia Gravis (MG)

WEBSITES AND CHAT ROOMS
- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org

ONLINE PEER SUPPORT
- Genetic Alliance: www.geneticalliance.org

Myositis

WEBSITES
- International Myositis Assessment and Clinical Studies Group: www.niehs.nih.gov/research/resources/collab/imacs/main.cfm

ONLINE PEER SUPPORT

- Michigan Immunodeficiency Foundation: www.facebook.com/groups/108048062584350
- Myositis Association Community Forum: tmacommunityforum.ning.com
- Myositis Support Group: www.myositissupportgroup.org
- Myositis Support Group – UK: www.myositis.org.uk

Pemphigus and Pemphigoid

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

Peripheral Neuropathy (PN)

WEBSITES
- Neupathy Action Foundation: www.neuropathyaction.org
Sources

Online Peer Support
- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: http://idffriends.org/forum
- IDF Friends: http://idffriends.org
- Jeffrey Modell Foundation Message Board: www.info4pi.org

Education and Disability Resources
- Americans with Disabilities Act of 1990: www.ada.gov Provides protection for people with disabilities from certain types of discrimination, and requires employers to provide some accommodations of the disability.
- Individuals with Disabilities Education Improvement Act of 2004: ideia.ed.gov/explore/home
- National Disability Rights Network: www.ndrn.org This website offers a search tool to find resources in your state to assist with school rights and advocacy.
- Social Security: www.ssa.gov/disability
- U.S. Department of Education Website: www2.ed.gov/parents/landing.html?exp=4 This federal government website offers a parents section titled “My Child’s Special Needs.”
- Michigan Immunodeficiency Foundation: www.facebook.com/groups/108048062584350
- Rhode Island peer group: health.groups.yahoo.com/group/RhodeIslandPIDD

Scleroderma
WEBSITES
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Scleroderma Center: www.hopkinsmedicine.org/rheumatology/clinics/scleroderma_center.html

OTHER RESOURCES

Online Peer Support

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

Other Resources

Medical Research Studies
- ClinicalTrials.com: www.clinicaltrials.com This site has a registration form to request that you be notified about recruitment for future studies.
- ClinicalTrials.gov: www.clinicaltrials.gov A registry of federally and privately supported clinical trials conducted in the United States and around the world.

Food Allergies
- Allergic Disorders: Promoting Best Practice: www.aaaai.org
- American Partnership for Eosinophilic Disorders: www.apfed.org
- Food Allergy and Anaphylaxis Network: www.foodallergy.org
- World Allergy Organization: www.worldallergy.org

Product Information
- Influenza and the influenza vaccine: www.cdc.gov/flu or call (800) CDC-INFO: (800) 232-4636
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Pump and Infusion Sets Websites
- EMED Technologies: www.emedtc.com
- Marcal Medical Inc.: www.marcalmedical.com
- Intra Pump Infusion Systems: www.intrapump.com
- Micrel Medical Devices: www.micrelmed.com
- Norfolk Medical: www.norfolkmedical.com
- RMS Medical Products: www.rmsmedicalproducts.com
- Smith Medical: www.smiths-medical.com/brands/cadd

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.

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