



Understanding and Treating Common Variable Immunodeficiency

By Ronale Tucker Rhodes, MS

While CVID is a “common” immune deficiency disease, as its name implies, it is far from a common disease. And in the majority of cases, it is diagnosed after years of illness.

It could be said that Jenny Gardner is the face of common variable immune deficiency (CVID). Not because she is alone in suffering from the disease. Hardly. It’s because she has become one of the many strong vocal advocates for patients with CVID and other immune deficiency diseases. Jenny’s story is a glaring example of what many individuals endure in their lifelong struggle with this disease. It is a story of suffering through years of illness before finally being diagnosed, fighting a losing battle with insurance companies to be reimbursed for the expensive treatment, and continuing to battle the effects of the illness despite treatment.

What Is CVID?

People with CVID have deficient numbers of serum immunoglobulins (IGs), which are antibodies that fight off infection. Why people develop CVID is unknown, but the disease is the most common of the immune deficiency diseases, hence the name “common,” and the degree and type of IG deficiency varies, hence the name “variable.” Some patients treated with immune globulin (IG) have a deficiency in both IgG and IgA antibodies, while others may be deficient in all three types of antibodies: IgG, IgA and IgM.¹

CVID affects approximately one person in 50,000 worldwide and occurs in males and females equally and in all races. It can occur in infants, young children, adolescents or even those ages 20 years to 40 years and older. And, while peaks of onset occur in children ages 1 to 5 years and in young adults ages 16 to 20 years, more than two-thirds of patients are 21 years or older when diagnosed,² and in the majority of patients, diagnosis is not made until the third or fourth decade of life.¹

That is the case with Jenny, who was sick all of her life but who wasn’t diagnosed until age 45. This was after being told many times that her illness was psychological and that she was a hypochondriac. “I was so frustrated,” explains Jenny. “I told one doctor that he needed to get more creative, as I’d been told that before. But something was wrong with me, and I wanted answers.”

Symptoms of CVID

Symptoms of CVID can occur in the first few years of life, as with Jenny, or they may not develop until the second or third decade, or even later.¹

Symptoms include recurring infections of the respiratory tract, such as sinus infections, otitis, bronchitis and pneumonia, which is caused by bacteria, including streptococ-

cus pneumonia, hemophilus or moraxella.³ If severe lung infections repeatedly occur, it's possible that permanent damage to the bronchial tree may result and a chronic condition of the bronchi can develop, causing widening and scarring of the breathing tubes (known as bronchiectasis).¹

Patients also frequently experience diarrhea and chronic lambliaiasis (an intestinal infection). Occasionally, infections of the skin, urinary tract and herpes zoster (shingles) may occur. And, rarely, patients will experience cytomegaly virus infection, viral meningitis and tuberculosis. Approximately 20 percent of patients also develop autoimmune complications, such as rheumatoid arthritis (in the knees, ankles, elbows and wrists), vitiligo (a skin condition), hemolytic anemia, thrombocytopenia and neutropenia.³ And, CVID patients have an increased risk of cancer, especially cancer of the lymphoid system, skin and gastrointestinal tract.¹

Fortunately, unless complications have developed, CVID patients do not experience physical abnormalities. However, some patients may have an enlarged spleen and lymph

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nodes. And, if chronic lung disease has developed, patients may not be able to exercise due to decreased lung capacity. In some cases, gastrointestinal disorders may cause decreased growth in children or weight loss in adults.¹

Jenny's symptoms ran the gamut. "If any bug was going around, I got it and was sick the longest. Strep throat was a constant problem," says Jenny. When she was 8, she had rheumatic fever, which kept her out of school for three months, and she was sick so much throughout junior high and high school that the school district sent someone to her home to investigate her parents. "I might have been the first home-school patient," says Jenny. As an adult, in addition to repeatedly becoming ill, including a bout with German measles, she went through three sinus surgeries.

Causes of CVID

Despite 40 years of research, what actually causes CVID is unknown. It's possible that genetic factors may be involved. For instance, in approximately 20 percent of CVID patients, a first-degree family member has a selective IgA deficiency. When more than one family member is affected with CVID, approximately 5 percent of patients have a concurrent IgA deficiency. However, no clear pattern of inheritance has been observed.⁴

Jenny has no family members who also have been diagnosed with CVID. However, she has tried to make a genetic connection, since her physician told her it is not uncommon for this disease to skip a generation or two, and it's possible that someone in her family may have had the disease but not known it. Her brother "seems to get everything that comes around," says Jenny, but he is able to fight off the infections with the help of antibiotics.

Research also has shown the involvement of a small group of genes in some patients. Patients with CVID appear to have normal numbers of B lymphocytes, but those fail to mature into plasma cells capable of making the different types of Igs. Other CVID patients lack T lymphocyte function, which is necessary for a normal antibody response. And, yet other CVID patients have excessive numbers of cytotoxic T lymphocytes, whose role in the disease is unclear.¹

Diagnosing CVID

To diagnose CVID, the patient's history is examined to look for types of infections and their severity and frequency, and the family history is explored to determine whether there have been relatives diagnosed with primary immunodeficiency or those who have an unusual susceptibility to infections. This is followed by a physical exam to rule out other possible reasons for a high rate of infections, which could include the suppression of normal immune responses due to malnutrition, injuries such as burns, drugs such as corticosteroids, diseases such as leukemia and infections such as mononucleosis, measles, chicken pox and AIDS. In children, the physical examination should show whether the child is growing well and is well-nourished. A severely immunodeficient child is likely to look sickly and pale.

If an infection is present, samples of mucus, sputum and stool will be cultured to determine the type of germs involved. Common bacteria typically elicit antibodies. Therefore, sinus and respiratory infections, which often are due to bacteria, suggest an antibody deficiency. On the other hand, viruses and fungi stimulate T cells. Therefore,

infections caused by viruses and fungi point to a T cell defect. Recurrent infections involving the skin or soft tissues often can be traced to problems with phagocytes, and blood-borne infections caused by encapsulated bacteria, including meningitis, may be linked to complement deficiencies.

If CVID is suspected, lab tests are necessary. These include a complete blood count to measure the levels of red and white blood cells, as well as platelets; a quantitative immunoglobulin test that measures IgG, IgM and IgA antibody levels in the blood; a blood test to show if the blood contains antibodies to the usual childhood immunizations (i.e., tetanus, measles, pertussis and diphtheria); a complement test using a sample of the blood to indicate how effectively the complement system is working; and skin tests that are similar to tuberculosis tests to show how well T cells are functioning.⁵

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Jenny suffered from infections and illness for years before she finally got lucky and was diagnosed. This happened when she was required to change insurance carriers and was able to pick from a new list of doctors. “I called a friend who is a nurse, and I asked her to tell me who was the best at allergy and immunology,” says Jenny. Her friend referred her to a doctor who, after unsuccessfully treating her for allergies, tested her IG numbers and diagnosed her with CVID.

Treatment for CVID

While there are a number of treatment options for CVID, the most common is IG therapy to provide the patient with protective antibodies. IG almost always brings improvement of symptoms. Generally, intravenous IG (IVIg) is dosed at 400 mg/kg every three to four weeks. Subcutaneous administration of immunoglobulin (SCIG) also can now be performed with a variety of dosing schedules to suit the preference of the patient, with the overall goal of administering a total of 400 mg/kg every three to four weeks.

Prophylactic antibiotics may help patients with chronic sinusitis or chronic lung disease. Antibiotics also may help control small bowel bacterial overgrowth. For those with

bronchiectasis, physical therapy and postural drainage will remove the secretions from the lungs and bronchi.^{1,5}

Jenny was started with gamma globulin injections, and when that didn’t work, she was treated with IVIG. She was first administered 5 grams, and that was increased to 10, and then 15, 20, 30 and 40. However, she continued to get sick, although not quite as often, and she suffered from terrible IVIG side effects, including migraines and nausea, and she would often need to recuperate in bed for two or three days afterward. Because of the side effects, Jenny was sent to another doctor for a second opinion: He ran extensive tests and told her that her dosage was too low. After being prescribed 50 grams, her insurance carrier cut it back to 40 and she again was frequently ill. Jenny is also frequently treated with antibiotics.

While many people never have a problem with reimbursement for their IG treatments, unfortunately many others do. Jenny just happens to be one of those. In addition to not getting the number of grams of IG she needed, Jenny also began experiencing another problem. Her insurance carrier was forcing her doctor to buy the least expensive IG brand, so every month, Jenny was infused with a different IG product. Then, in 2006, her insurance company canceled her policy, and after her COBRA plan expired, she was unable to convert that plan into a private individual plan. And, while she qualified for disability in the state of Florida, where she resides, she is ineligible for a Medigap/supplemental insurance plan until age 66, leaving her responsible for paying for 20 percent of the cost of her IVIG treatments. She appealed, but she was told that “it was cheaper to let me die than to treat me,” says Jenny. “That really got to me.” Age 66 is still five years away for Jenny, and she still has no insurance. Today, she relies on both clinical trials and patient assistant programs to receive her IVIG. “Every day, I am fearful that I will not have either of these available to me, and it really worries me,” explains Jenny.

Managing Day to Day

Even with treatment, CVID patients may still experience infections and their consequences. For Jenny, who was a vice president of a national bank in Florida, chronic illness caused her to leave that job and work as an administrator at her church, where her pastor insisted that her illness and doctor appointments would not be a problem. However, that pastor moved on to another church and his replacement was not so sympathetic. Jenny quit that job as well, and since January 2000, she has been on disability.

While patients can’t prevent infections from occurring,

there are some things they can do to help to manage their disease. For instance, they should eat a normal, balanced diet with sufficient vitamins and fiber. Those with chronic gastritis or diarrhea should make sure to peel fruit, wash salads well and cook vegetables, and they should keep away from raw eggs, mussels and whipped ice cream. While immune stimulants have not been proved in any clinical trials to help, they do in some cases. However, patients should take caution if immunosuppressive substances have been prescribed. Light fitness training is recommended, but high-performance sports training is not advised.

Patients should be sure to get annual checkups and regular blood checks. Should patients be exposed to someone who is ill, they should keep their distance as best as possible. If patients become ill, they should be examined by a physician to determine the causal bacteria type and to be prescribed the appropriate antibiotics. It should be noted that blood screening tests for bacterial antibodies in CVID patients usually result in false negative readings. A serious infection may be present with or without a fever.

Another precaution: Live virus vaccines such as polio, measles and yellow fever should not be administered to CVID patients.

Last, women with CVID who are pregnant may require an increase in the frequency of IgG infusions. And, for the safety of the child, the choice of antibiotics may be an issue. These patients also should discuss the risk of inheritance with their doctor.³

Future Outlook

Fortunately, IG therapy combined with antibiotic therapy has greatly improved the outlook of CVID patients, helping them to decrease the number of infections and, in many cases, prevent the development of chronic lung disease. However, the future for patients depends on how much damage occurred prior to diagnosis and treatment, as well as their ability to get treatment. This is why advocacy efforts to spread the awareness of CVID and its symptoms for more timely diagnoses for patients, as well as to enact legislation that will provide adequate reimbursement for the expensive IG therapy, is crucial.

Jenny, who advocates at both the local and national level, advises that others who advocate for patients need to make sure that work is done at home before going to the national level. Her first advocacy trip was to her state Capitol in Tallahassee, Fla. She was then asked by the Immune Deficiency Foundation to accompany the organization on a lobbying trip to Washington, D.C. Since then,

Jenny has been on numerous local and national lobbying trips. "If anyone had told me 10 years ago that I would be doing this and that I would actually find it very fulfilling, I would have said 'no way,'" exclaims Jenny. "It can be very daunting, especially in the beginning. When I first went to Washington, it was all about me. But it only took one day

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to talk to other patients and hear their stories to realize that I needed to do this for the patients. I am especially concerned for the children with this disease. It's not about me anymore; it's about the entire patient community. Sometimes, I think we are just spinning our wheels, and then I look back and see what has been accomplished, and I realize that baby steps turn into victories." ■

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References

1. Immune Deficiency Foundation. *Patient & Family Handbook for Primary Immunodeficiencies*, 4th ed. Chapter 2: Common Variable Immune Deficiency (CVID). Accessed at www.immunedisease.com/about-pi/types-of-pi/common-variable-immunodeficiency-cvid.html.
2. Schwartz, RA. Common Variable Immunodeficiency Epidemiology. Medscape Reference. Accessed at emedicine.medscape.com/article/1051103-overview#a0199.
3. Schwartz, RA. Common Variable Immunodeficiency Causes. Medscape Reference. Accessed at emedicine.medscape.com/article/1051103-clinical#a0217.
4. Schwartz, RA. Common Variable Immunodeficiency History. Medscape Reference. Accessed at emedicine.medscape.com/article/1051103-clinical#a0218.
5. National Institutes of Health. When the Body's Defenses Are Missing: Primary Immunodeficiency. Accessed at www.nichd.nih.gov/publications/pubs/primary_immuno.cfm.