

Answers to Commonly Asked Questions About Common Variable Immunodeficiency (CVID)

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Why Is CVID Referred to as “Common Variable” When It Is Not Common?

The prevalence of CVID is about one in 25,000 people, which makes CVID a rare medical condition. However, when looking at the genetic causes of primary immunodeficiency diseases (PIs), CVID is one of the most prevalent. Therefore, in the realm of PIs, CVID is quite common. CVID is referred to as variable because of the symptoms associated with it — infections, gastrointestinal (GI) issues, lymphoma, etc. — that vary from person to person. As such, there are many different symptoms and different clinical courses in people who have the same disorder.

Why Does CVID Take So Long to Diagnose?

Historically, it has been a challenge to get the proper testing for diagnosing CVID because it is a rare condition. According to the most recent studies, diagnoses are being made earlier, but we have a long way to go to get CVID diagnosed quickly after the onset of symptoms in most patients. Older studies showed it took a decade or more to diagnose CVID. Today, on average, it takes about five to seven years to diagnose CVID; however, some patients still aren't diagnosed for 10 to 20 years or more.

There has been a lot of effort to raise awareness about PIs over the years. And, while awareness has improved, CVID is still very rare. So, one reason it takes so long to diagnose is because most physicians and healthcare practitioners are either not familiar with the disease, or they may have heard about it in their training, but have forgotten about it. Therefore, CVID is not something they're thinking about or testing for.

Another reason CVID can take so long to diagnose is that there is a perception that PIs are a pediatric problem — something that is diagnosed at birth or early in life. So, many adults have to battle the myth that it doesn't happen to adults or that they would have already been diagnosed.

In addition, finding the right doctor to diagnose CVID can be a challenge. The symptoms of CVID can be similar to other common conditions: sinus infections, bronchiectasis, bowel issues, etc. These are conditions that a lot of physicians see as run-of-the-mill; but they're not, if they keep recurring. It takes a certain healthcare practitioner to know that recurring infection is not normal. And, while infection is the hallmark of CVID, there are also many other symptoms and complications. For instance, if the primary symptom is GI problems

or granulomatous disease, physicians don't equate that to an immune deficiency, and CVID gets overlooked.

Finally, today, doctors specialize in certain areas of medicine, and through no fault of their own, they often don't look at the big picture. As such, individuals have to run into the right specialist or seek out the physician who will look at the big picture of various symptoms and conduct the appropriate testing.

Yet, even when physicians think of CVID as a possible diagnosis, they often don't know what tests to conduct or how to interpret those tests. This is a particular challenge, so physicians who are not familiar with CVID are being encouraged to refer patients to a practitioner who is familiar with the disease. Unfortunately, there is a relative shortage of specialists who have a strong interest in this kind of immunology.

How Is the Time of CVID Diagnosis Calculated?

Studies that look at the time to diagnose CVID base it on the date from when a patient first started to record recurrent infections or presenting symptoms to when they were tested and diagnosed. This is an inexact science, however, because it relies on backward tracking and recollection.

Does CVID Run in Families, and Is There Genetic Testing for It?

Even though it is believed CVID is caused by genetic mutations, only about 10 percent of diagnoses are clearly familial. Ninety percent are sporadic, which means the disease shows up in only one person in the family. Therefore, only a small minority of patients have inherited CVID. The problem with such testing, though, is that a genetic mutation can be identified in only about 15 percent of all CVID cases. In the other 85 percent, the genetic mutation is unknown. Genetic testing is relatively expensive, so without a high rate of success, it is often not clinically useful outside of the research setting. Much more research needs to be conducted to understand the genetics related to CVID.

What Is the Difference between Hypogammaglobulinemia and CVID?

Hypogammaglobulinemia is a nonspecific diagnosis. Basically, it describes a laboratory value that shows antibody levels are low, but gives no other information on the condition. CVID, on the other hand, has specific criteria: low IgG plus low IgA and/or IgM levels. Therefore, hypogammaglobulinemia is a general diagnosis, whereas CVID is a more specific diagnosis.

It's possible for children to have transient hypogammaglobulinemia, which means their IgG levels are low, but they become normal as they age. This sometimes occurs in children under 5 years old because the development of the immune system is delayed. Therefore, because it could be transient, physicians generally

don't like to diagnose children with CVID until they're older than 5 years. In most patients, CVID is diagnosed after puberty.

What Is the Risk of Serious Disease with CVID, and What Can Be Done to Prevent It?

Historically, the major risk of CVID is overwhelming infection (bacteria in the bloodstream, meningitis, etc.). The good news is that infections have dramatically been reduced in patients who are diagnosed and properly treated with immune globulin (IG). And, these days, serious complications such as chronic lung disease (which occurs in 25 percent to 30 percent of patients) resulting from bronchiectasis may be prevented or slowed with IG therapy.

But, there are other conditions, like granulomas and lymphoma, that aren't likely related to infection and cannot be prevented with IG treatment. There are also autoimmune diseases (ADs) associated with CVID, ranging from low blood cell counts and arthritis to lupus. Additionally, 20 percent of CVID patients also have serious GI problems, ranging from irritable bowel disease, Crohn's disease, ulcerative colitis, malabsorption, giardia, etc. A final serious complication occurs with the spleen and lymph nodes. A third of CVID patients will develop problems with the spleen and lymph nodes, but these problems are largely benign. Approximately 8 percent of the time, these problems can result in lymphoma. Unfortunately, we don't have any way to prevent any of these conditions; we can only recognize them early and treat the symptoms as they arise.

In short, infectious problems can be treated with IG; other conditions can't. Therefore, it's important for CVID patients to have regular follow-up with their physician to identify any other conditions that may arise and treat them early.

Can CVID Patients Have an Autoimmune Disease but Test Negative for It?

One of the challenges in dealing with CVID and its associated complications is that patients don't make antibodies well. This includes autoantibodies, and because ADs are typically diagnosed based on autoantibody assays, CVID patients may have all the signs and symptoms of an AD, but their autoantibody lab tests may be normal. In addition, IG therapy may interfere with the lab tests that look for autoimmunity, which can make them unreliable for CVID patients. Therefore, these patients need to find a rheumatologist who will conduct a comprehensive physical examination for an AD and recognize that the lab tests won't necessarily test positive for it.

Are CVID Patients Treated with Medications Other Than Immune Globulin?

IG is the primary treatment for CVID. It is the only proven treatment for preventing infectious complications. However, there are a lot of other medications that might be used to treat complications of CVID. These include antibiotics (although chronic prophylactic antibiotics are not commonly prescribed), immunosuppressant drugs to treat ADs, GI problems or lung problems, and chemotherapy to treat lymphoma, which rarely occurs. ■