

Common Variable Immune Deficiency

Subjects: [Genetics & Heredity](#)

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Common variable immune deficiency (CVID) is a disorder that impairs the immune system.

genetic conditions

1. Introduction

People with CVID are highly susceptible to infection from foreign invaders such as bacteria, or more rarely, viruses and often develop recurrent infections, particularly in the lungs, sinuses, and ears. Pneumonia is common in people with CVID. Over time, recurrent infections can lead to chronic lung disease. Affected individuals may also experience infection or inflammation of the gastrointestinal tract, which can cause diarrhea and weight loss. Abnormal accumulation of immune cells causes enlarged lymph nodes (lymphadenopathy) or an enlarged spleen (splenomegaly) in some people with CVID. Immune cells can accumulate in other organs, forming small lumps called granulomas.

Approximately 25 percent of people with CVID have an autoimmune disorder, which occurs when the immune system malfunctions and attacks the body's tissues and organs. The blood cells are most frequently affected by autoimmune attacks in CVID; the most commonly occurring autoimmune disorders are immune thrombocytopenia, which is an abnormal bleeding disorder caused by a decrease in cells involved in blood clotting called platelets, and autoimmune hemolytic anemia, which results in premature destruction of red blood cells. Other autoimmune disorders such as rheumatoid arthritis can occur. Individuals with CVID also have a greater than normal risk of developing certain types of cancer, including a cancer of immune system cells called non-Hodgkin lymphoma and less frequently, stomach (gastric) cancer.

People with CVID may start experiencing signs and symptoms of the disorder anytime between childhood and adulthood; most people with CVID are diagnosed in their twenties or thirties. The life expectancy of individuals with CVID varies depending on the severity and frequency of illnesses they experience. Most people with CVID live into adulthood.

There are many different types of CVID that are distinguished by genetic cause. People with the same type of CVID may have varying signs and symptoms.

2. Frequency

CVID is estimated to affect 1 in 25,000 to 1 in 50,000 people worldwide, although the prevalence can vary across different populations.

3. Causes

The cause in CVID is unknown in approximately 90 percent of cases. It is likely that this condition is caused by both environmental and genetic factors. While the specific environmental factors are unclear, the genetic influences in CVID are believed to be mutations in genes that are involved in the development and function of immune system cells called B cells. B cells are specialized white blood cells that help protect the body against infection. When B cells mature, they produce special proteins called antibodies (also known as immunoglobulins). These proteins attach to foreign particles, marking them for destruction. Mutations in the genes associated with CVID result in dysfunctional B cells that cannot make sufficient amounts of antibodies.

In about 10 percent of cases, a genetic cause for CVID is known. Mutations in at least 13 genes have been associated with CVID. The most frequent mutations occur in the *TNFRSF13B* gene. The protein produced from this gene plays a role in the survival and maturation of B cells and in the production of antibodies. *TNFRSF13B* gene mutations disrupt B cell function and antibody production, leading to immune dysfunction. Other genes associated with CVID are also involved in the function and maturation of immune system cells, particularly of B cells; mutations in these genes account for only a small percentage of cases.

All individuals with CVID have a shortage (deficiency) of two or three specific antibodies. Some have a deficiency of the antibodies called immunoglobulin G (IgG) and immunoglobulin A (IgA), while others, in addition to lacking IgG and IgA, are also deficient in immunoglobulin M (IgM). A shortage of these antibodies makes it difficult for people with this disorder to fight off infections. Abnormal and deficient immune responses over time likely contribute to the increased cancer risk. In addition, vaccines for diseases such as measles and influenza do not provide protection for people with CVID because they cannot produce an antibody response.

3.1. The Gene Associated with Common Variable Immune Deficiency

- *TNFRSF13B*

4. Inheritance

Most cases of CVID are sporadic and occur in people with no apparent history of the disorder in their family. These cases probably result from a complex interaction of environmental and genetic factors.

In rare cases, CVID is inherited in an autosomal recessive pattern, which means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

In a few cases, this condition is inherited in an autosomal dominant pattern, which means one copy of an altered gene in each cell is sufficient to cause the disorder.

When CVID is caused by mutations in the *TNFRSF13B* gene, it is often sporadic and the result of a new mutation in the gene that occurs during the formation of reproductive cells (eggs or sperm) or in early embryonic development. When *TNFRSF13B* gene mutations are inherited, they can cause either autosomal dominant CVID or autosomal recessive CVID.

Not all individuals who inherit a gene mutation associated with CVID will develop the disease. In many cases, affected children have an unaffected parent who has the same mutation. Additional genetic or environmental factors are likely needed for the disorder to occur.

5. Other Names for This Condition

- common variable hypogammaglobulinemia
- common variable immunodeficiency
- CVID
- immunodeficiency, common variable

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