

Common Variable Immune Deficiency

Summary

Common Variable Immune Deficiency (CVID) is the name for a group of conditions that affect how the body's immune system makes antibodies and fights infections.

If you have CVID you are unable to make protective antibodies and therefore become susceptible to infections. Both males and females can be affected by CVID. The clinical features of CVID can vary from mild in those who suffer from infections only to severe in those with disease-related complications.

Antibodies belong to a particular type of protein, called immunoglobulin, normally found in blood and body fluids. There are three major types of immunoglobulin, known as:

- Immunoglobulin G [IgG] - the most abundant and common immunoglobulin, found in blood and tissue fluids. IgG functions mainly against bacteria and some viruses.
- Immunoglobulin A [IgA] - found in blood, tears, saliva, and protects the tissues of the respiratory, reproductive, urinary and digestive systems.
- Immunoglobulin M [IgM] - found in the blood, IgM functions in much the same way as IgG but is formed earlier in the immune response.

All types are made up of antibodies against the germs that an individual has met during the course of their life.

People with CVID have either low levels of immunoglobulin in their blood or none at all; they are unable to make functional antibodies of the IgG or IgA types though some patients do make IgM antibodies. This means those affected can't fight infection against mainly bacteria, but also viruses, parasites and fungi, as well as people with a fully working immune system can. Patients may have severe, persistent or repeated infections, often from the same germ. These infections often particularly affect the ears, sinuses, chest, lungs or gut, places that come into daily contact with infectious agents.

CVID covers a range of different deficiencies. The disorder is called 'variable' because of the extent and type of immune deficiencies; in addition to this the clinical course varies from patient to patient. In some patients, there is a decrease in both IgG and IgA in the blood; in others, all three major immunoglobulin types, IgG, IgA and IgM, may be decreased.

Since CVID patients are susceptible to bacterial infections due to missing antibodies, the aim of treatment is to replace those antibodies with purified immunoglobulins from the blood of healthy donors. Replacement immunoglobulin (Ig) therapy combined with antibiotics for breakthrough infections, means that people with CVID can live relatively normal lives with no restrictions on employment; many patients with CVID work in healthcare or on farms.

The Ig therapy aims to prevent both infections and the development of chronic lung disease. The outlook for patients with CVID depends on how much damage has occurred to their lungs or other organs before diagnosis and how successfully infections can be prevented in the future by Ig therapy.

How did I get CVID?

In most cases of CVID, the causes are unknown, CVID can occur in people with no apparent history of the disorder in their family. About 90% of CVID patients are diagnosed in adulthood but only 5% have a close relative who is affected.

A few people (<10%) with CVID may have symptoms in childhood, but most people do not develop symptoms until they are very much older, with ages at diagnosis ranging from 16 to 80 years of age.

What are the symptoms of CVID?

Here are some common features that you may recognise and that may have led your clinician to a diagnosis of CVID:

- Sinusitis – inflammation of the air-filled spaces (paranasal sinuses) that surround the nose
- Ear infections such as otitis media
- Throat infections such as tonsillitis or laryngitis
- Chest infections such as bronchitis, pneumonia or pleurisy
- Enlarged lymph nodes in the neck, chest or abdomen
- Stomach and intestinal infections giardiasis (a parasitic infection) resulting in persistent diarrhoea or weight loss
- Enlarged spleen (only found on examination by a doctor)
- Bleeding or bruising (due to low platelet numbers in the blood)
- Severe anaemia due to destruction of the red cells (haemolysis)
- Skin infection, such as abscesses, boils
- Oral ulcers in association with repeated infections
- Eye infections such as conjunctivitis
- Autoimmune diseases, joint and bowel problems

How is CVID diagnosed and why can diagnosis take a long time?

The diagnosis of CVID is challenging because your doctor needs to exclude other reasons for the failure of antibody production. A hallmark of CVID is reoccurring infections, but infections at any age are common and, even when low immunoglobulins are found, it may take some time for the significance of this to be determined. Sometimes, doctors find it hard to recognise when a person has 'too many' infections and that makes the diagnosis difficult to pin down.

Delay in diagnosis can be serious if infections are severe. In particular pneumonia may cause structural scarring of the lungs (known as bronchiectasis).

Those affected can feel very frustrated and angry when a diagnosis is finally made, especially if they have suffered for a long time without recognition of the cause of their symptoms.

Making the diagnosis

A clinical immunologist usually makes the diagnosis of a CVID. Tests may be intensive at the beginning of this investigative process.

Diagnosis is confirmed by blood tests. These tests check to see if there are low levels of serum IgG and IgA and usually IgM. The doctor will also test for the presence of antibodies to previous immunisations or infections. If antibodies are not present in the blood, then you will have to be immunised again and blood taken 3 to 4 weeks later for retesting, to ensure that the previous negative test was significant.

Other tests may include:

- A Computer Tomography (CT) chest scan. Patients who have had multiple chest infections may have permanent damage to the tubes in the lungs, known as bronchiectasis. This is easily diagnosed on the CT scan. To take a CT scan, the scanner rotates around the patient, building three-dimensional image that helps the doctor to see precise detail.
- Taking samples of any infected body fluids (e.g. pus or diarrhoea) and testing for what germs are present so that the doctor can decide which antibiotics might work best.
- An ultrasound scan of organs involved in the immune system such as the spleen.

Treatment

The main treatment for CVID is replacing the missing antibodies using immunoglobulin (Ig) replacement therapy. This treatment can be given intravenously (dripped into a vein through a needle in the arm or hand) or subcutaneously (injected under the skin in the lower stomach or thighs). This treatment is usually needed every week for subcutaneous therapy or every 2-4 weeks for intravenous therapy, depending on the individual. The dose is monitored by looking at how well the treatment protects you against infections, since adequate therapy reduces the rate and severity of bacterial infections and may prevent them entirely. **Your doctor will also do blood tests periodically (typically every 3-6 months, although this may be more frequent depending on your centre's local policies) to check the safety of the IgG therapy, and your levels of IgG.**

Additional treatments may be needed for people affected by chronic sinusitis or chronic lung disease. This includes long-term treatment with broad-spectrum antibiotics or more specific antibiotics if the bugs causing the infection are known. If lung problems have developed such as bronchiectasis, where the airways of the lungs become abnormally widened leading to a build-up of excess mucus physical therapy such as physiotherapy and specific exercises may be needed to remove the mucus from the lung airways. Rare disease related lung complications may sometimes require treatment with corticosteroids.

Are there any associated health problems with CVID and how will my health be monitored?

Yes some people with CVID, but not all, may have or may develop other health problems. Monitoring is usually by infrequent blood tests and for some people annual scans or tests of breathing function.

Your clinical immunologist will be on the look out for the complications and will work with other clinical specialists to offer you the most appropriate advice and treatments.

Lung problems

If chronic lung disease, such as bronchiectasis, has developed before diagnosis, those affected may have a reduced ability to exercise. Your doctor may refer you for 'lung function tests'. These are tests that measure how well your lungs are working. You may be referred to a physiotherapist and specific exercises may be recommended to remove the mucus from the lung airways to improve your lung health.

Autoimmunity in CVID

People with CVID may produce damaging antibodies that attack their own tissues (autoantibodies). These autoantibodies can attack and destroy blood cells (e.g. red cells, or platelets) resulting in severe anaemia or very low platelet counts. Other autoimmune diseases include thyroid failure, skin changes with areas of depigmentation (vitiligo) or a form of intestinal malabsorption often mistaken

for coeliac disease.

Painful joints and arthritis in CVID

Some people affected by CVID may develop painful inflammation of one or more joints known as polyarthritis. Arthritis associated with CVID can involve large joints such as knees, ankles, elbows and wrists with smaller joints such as finger joints rarely affected. Infection must be excluded; joint fluid may be removed using a fine needle and analysed for the presence of bacteria or Mycoplasma, as this rare pathogen can sometimes be the cause of joint infections leading to pain and destruction of the joint.

In the absence of infection, symptoms of joint inflammation usually disappear with immunoglobulin therapy.

Gut problems in CVID

People affected by CVID can often have gut problems such as abdominal pain, bloating, nausea, vomiting and diarrhoea. Involvement of the gut or as the doctors refer to it, the gastrointestinal tract, may in some instances, interfere with normal growth in children or lead to weight loss in adults, due to malabsorption of nutrients from food. This may be due to infection with a range of common organisms, such as Giardia, salmonella or campylobacter. These infections can be successfully treated.

Sometimes a small sample (biopsy) of bowel tissue is taken for examination to exclude infection and search for a cause. If unexplained inflammation is found, a non-absorbable corticosteroid may be given by your doctor.

Immunisation

Not all vaccines are safe to be administered to patients with CVID and therefore you should discuss any recommended or required vaccinations with your clinical immunology team, before receiving a vaccine.

This patient information was reviewed by the PID UK Medical Advisory Panel and Patient Representative Panel (February 2014; review date February 2015).

About Primary Immunodeficiency UK

Primary Immunodeficiency UK (PID UK) is a national organisation supporting individuals and families affected by primary immunodeficiencies (PIDs). Our website provides useful information on a range of conditions and topics and explains the work we do to ensure the voice of PID patients is heard.

If we can be of any help please contact us at hello@piduk.org or on 0800 987 8986 where you can leave a message. Visit www.piduk.org for further information.

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