CVIDs

# Common variable immune deficiency disorders (CVIDs)

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IMMUNO DEFICIENCY UK

Supporting families affected by primary and secondary immunodeficiency

# About this booklet

This booklet provides information on common variable immune deficiency disorders (CVIDs). It has been produced by the Immunodeficiency UK Medical Advisory Panel and Patient Representative Panel to help answer the questions patients and their families may have about these conditions but should not replace advice from a clinical immunologist.

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Second edition October 2018



Published by Immunodeficiency UK (www.immunodeficiencyuk.org)




# Summary


Common variable immune deficiency disorders (CVIDs) is the name for a group of conditions that affect how the body's immune system makes antibodies and fights bacterial infections.

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

Antibodies belong to a particular type of protein called immunoglobulin, which is 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 and saliva. IgA 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 of antibody are made against the germs that an individual has met during the course of his or her life.

People with a CVID have either low levels of immunoglobulins in their blood or none at all; all are unable to make functionally efficient antibodies of the IgG or IgA types, though some patients do make IgM antibodies. This means that those affected can't fight infection 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 are usually bacterial, but may also be viruses, parasites and fungi. The infections particularly affect the ears, sinuses, chest, lungs and gut – places that come into daily contact with infectious agents.

CVIDs are a range of different immune deficiencies, and the diagnosis is often used inappropriately to cover more severe 'combined immunodeficiencies' in which antibodies and immune T-cells do not work. The disorder is called 'variable' because of the extent and type of immune deficiencies. Furthermore, the clinical course varies from patient to patient. In some patients, there is a decrease in both IgG and IgA in the blood; in other patients, levels of all three major immunoglobulin types (IgG, IgA and IgM) may be decreased.

Since CVID patients are susceptible to bacterial infections owing to missing antibodies, the aim of treatment is to replace those antibodies with immunoglobulins purified from the blood of healthy donors. Immunoglobulin therapy, combined with antibiotics for breakthrough infections, means that people with a CVID can live relatively normal lives with no restrictions on the type of jobs they can do. For example, some patients with a CVID work in sectors that carry a higher risk of infection, such as the healthcare sector and farming industry.

Immunoglobulin therapy aims to prevent both infections and the development of chronic lung disease that results from pneumonia, known as bronchiectasis. The outlook for patients with a CVID depends partly 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 immunoglobulin therapy.

## How did I get a CVID?

In most cases of CVID, the causes are unknown. A CVID usually occurs in people with no apparent history of the disorder in their family. About 90% of CVID patients are diagnosed in adulthood. Only 5% have a close relative who is also affected, and these relatives may have a different type of antibody failure with an identifiable genetic susceptibility.

The few people (< 10%) with antibody failure presenting in childhood are called 'CVID' but may have a more severe primary immune deficiency (PID). Most people do not develop symptoms until they are very much older, with age at diagnosis ranging from 16 to 80 years of age. The search for the causes of antibody failure is ongoing, though common viruses have largely been excluded.

## What are the symptoms of CVIDs?

Here are some common features that you may recognise and which, if repeated, persistent or severe, 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, e.g. chronic giardiasis (a parasitic infection) resulting in persistent diarrhoea or weight loss
- Enlarged spleen (found only on examination by a doctor)



- Bleeding or bruising, owing to low platelet numbers in the blood
- Severe anaemia, owing to destruction of the red blood cells (haemolysis)
- Skin infections, such as abscesses or boils
- Oral ulcers in association with repeated infections
- Eye infections, such as conjunctivitis
- Autoimmune diseases, joint and bowel problems.

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

The diagnosis of a CVID is challenging because a doctor needs to exclude other reasons for the failure of antibody production. A hallmark of a CVID is recurring 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 the investigative process.

Diagnosis is confirmed by blood tests that check 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 known infections. If antibodies are not present in the blood, then the patient will have to be immunised again and blood taken 3–4 weeks later for retesting, to ensure that the previous negative test result was significant.

Lots of different genes may be altered in CVID, and sometimes genetic testing reveals that patients with more severe or unusual forms of a CVID have another related PID, often a combined immunodeficiency. Some centres offer genetic testing to families of affected children as part of clinical trials or studies.

**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 a 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 a CVID is replacing the missing antibodies using immunoglobulin 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 thigh). It is usually needed every day or week for subcutaneous therapy or every 2–4 weeks for intravenous therapy, depending on the individual. Patients can usually be taught to do the treatment for themselves at home. The dose is monitored by looking at how well the treatment protects the patient against infections, since adequate therapy reduces the rate and severity of bacterial infections and may prevent them entirely. A 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 immunoglobulin therapy, and levels of IgG.

Additional treatments may be needed for people affected by chronic sinusitis or chronic lung disease. Such treatments include 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 and/or related immune suppressant medicines.

As much more is being learned about the disease processes in CVIDs, finding better targeted treatments is an active research area for many immunology centres.



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

Some people with a 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 of a CVID, 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 and improve your lung health.

### Autoimmunity in CVID

People with a CVID may produce damaging antibodies that attack their own tissues (autoantibodies). These autoantibodies can attack and destroy blood cells (e.g. red blood 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 a CVID may develop painful inflammation of one or more joints, known as arthritis. 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 a CVID can often have gut problems, such as abdominal pain, bloating, nausea, vomiting and diarrhoea. Involvement of the gut – or as doctors refer to it, the gastrointestinal tract – may in some instances interfere with normal growth in children or lead to weight loss in adults, owing 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.

## Immunisations

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

## More questions about CVIDs?

Then type 'FAQs on CVIDs' into the 'I'm looking for...' section of the home page of our website, at **www.immunodeficiencyuk.org**.

Other useful booklets available from Immunodeficiency UK include:

- Immunoglobulin therapy
- Antibiotics in PID
- Looking after your lungs.

'My CVID diagnosis was a major turning point for me. I was daunted to begin with but, after doing a bit of research and hearing about other patients' experiences, everything suddenly made sense and I finally knew what I was dealing with. I've been managing my own immunoglobulin replacement therapy ever since and although I need antibiotics to deal with some infections, I generally feel well and in complete control of my health.

'I'm approaching my 600th subcut anniversary (having never missed one). I work full time and have travelled extensively, so I'm very positive about having CVID and leading a full and normal life!'

Lorna Byrne (diagnosed in 2005)



## Glossary of terms

**abscess** a collection of pus that has built up within a tissue of the body.

**anaemia** a condition resulting from having fewer red blood cells than normal or where each red blood cell has less haemoglobin in it than normal. It results in tiredness.

**antibody** a type of protein (immunoglobulin) that is produced by certain types of white blood cells (plasma cells – a type of B-cell). The role of antibodies is to fight bacteria, viruses, toxins and other substances foreign to the body.

**arthritis** a condition that causes pain and inflammation in a joint.

**autoantibodies** antibodies that attack the body's own tissues.

**autoimmunity/autoimmune** when an individual's immune system attacks the body's own tissues or vessels.

**biopsy** a procedure to remove a piece of tissue or a sample of cells from your body so that it can be studied in a laboratory.

**bronchiectasis** a widening of the tubes (bronchi) that lead to the air sacs of the lung; this can happen because of repeated bouts of infections.

**chronic** a chronic condition is a health condition or disease that is persistent or otherwise long-lasting in its effects, or a disease that comes with time.

**coeliac disease** a disease that is caused by the immune system reacting adversely to gluten, a product found in wheat, barley and rye. It causes inflammation of the bowel and leads to diarrhoea and/or malabsorption. The condition is reversible by avoiding gluten.

**conjunctivitis** inflammation of the eye.

**corticosteroids** also known as steroids. These are medicines used to reduce inflammation and that affect the way the immune system works.

**CT scan** also known as a CAT scan. A specialised X-ray test that gives pictures of the inside of the body.

**deficiency** a lack or shortage.

**depigmentation** lightening of the skin.

**gastrointestinal tract** this is the lining of body parts that run from the mouth to the bottom. It can also be referred to as the gut.

**giardiasis** an infection of the digestive system caused by tiny parasites called Giardia intestinalis (also known as Giardia lamblia or Giardia duodenalis).

**immune deficiency** when the immune system's ability to fight infectious disease is compromised or entirely absent.

**immunoglobulin replacement therapy** a plasma-based treatment. The immunoglobulin contains antibodies that help fight infection. This treatment can be given through a vein or through the skin.

**immunoglobulins** proteins (globulins) in the body that act as antibodies. They work to fight off infections. They are produced by specialist white blood cells (plasma cells/B-cells) and are present in blood serum and other body fluids. There are several different types (IgA, IgE, IgG and IgM), and these have different functions.

**intravenous** inside or into a vein; e.g. an immunoglobulin infusion is given directly into a vein.

**lymph nodes** small bean-sized organs of the immune system that are distributed widely throughout the body. They are the home for the many types of cells that are important in fighting infections.

**malabsorption** a failure to fully absorb the nutrients from food in the gut.

**otitis media** inflammation or infection of the ear.

**platelets** blood cells that work to prevent bleeding in the body by producing blood clots.

**pleurisy** inflammation of the lining of the lungs.

**respiratory tract** the airway passage involved in breathing that leads from the mouth/nose to the lungs.

**sinuses** air-filled spaces within the bones of the face and around the nose. Infection of the sinuses is called sinusitis.

**subcutaneously** injected under the skin in the lower stomach or thigh. This is used as a way of giving immunoglobulin.

**vitiligo** a disease that causes the loss of skin colour in patches.



## Notes

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# About Immunodeficiency UK

**Immunodeficiency UK is a national organisation supporting individuals and families affected by primary and secondary immunodeficiency.**

We are the UK national member of IPOPI, an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website has useful information on a range of conditions and topics, and explains the work we do to ensure the voice of patients with primary and secondary immunodeficiency is heard. If we can be of any help, please email us or call on the number above, where you can leave a message.

Support us by becoming a member of Immunodeficiency UK. It's free and easy to do via our website. Members get monthly bulletins.

Immunodeficiency UK is reliant on voluntary donations. To make a donation, please go to **www.immunodeficiencyuk.org/donate**

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Supporting families affected by primary and secondary immunodeficiency

Supported by an educational grant from Biotest

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