IPOPI
INTERNATIONAL
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FOR PRIMARY IMMUNODEFICIENCIES

PRIMARY **IMMUNODEFICIENCIES**

CVID MANAGEMENT

KEY ABBREVIATIONS

CVID	Common Variable Immune Deficiency
CT	Computerised tomography
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IPOPI	International Patient Organisation for Primary Immunodeficiencies
IVIG	Intravenous immunoglobulin
SCIG	Subcutaneus immunoglobulin
PID	Primary immunodeficiency

Common Variable Immune Deficiency (1st edition).

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INTRODUCTION

This booklet explains what Common Variable Immune Deficiency (CVID) is, how it is diagnosed and how it is treated.

Primary immunodeficiencies (PIDs) are rare diseases that occur when components of the immune system are either not present or are not functioning normally. The immune system protects the body from infections. When the immune system is reduced or absent, PIDs leave people vulnerable to infections.

CVID is a PID which affects how the body makes the antibodies that are essential to help fight bacterial, parasitic, viral and fungal infections. Although the effects of CVID vary, most patients have recurrent infections, and some have enlarged lymph nodes and autoimmune disorders. Patients may also have disease-related complications which affect their organs including their lungs, heart, bowel, spleen and liver. For this reason, early diagnosis is important to reduce long-term organ damage.

The following sections explain what CVID is, how it is diagnosed, the symptoms and long-term effects of the condition and how CVID is treated.

WHAT IS CVID?

CVID is usually diagnosed in adults and is the most common PID (as CVID represents approximately 20% of all PIDs). However, diagnosis in children and teenagers can also occur. In most cases, the causes are unknown although a monogenic defect (a single defective gene) has been found in 25% of CVID patients cohorts.

People with CVID are not able to make the full spectrum of antibodies that would usually protect them from bacterial, parasitic, fungal and/or viral infections.

Antibodies are specialised proteins called immunoglobulins. There are three major types of immunoglobulins: immunoglobulin G (IgG), immunoglobulin A (IgA) and immunoglobulin M (IgM). People with CVID have low levels of at least two of these major types of immunoglobulins.

HOW IS CVID DIAGNOSED?

CVID MANIFESTS ITSELF IN MANY DIFFERENT WAYS

Common symptoms of CVID include severe, persistent, unusual and recurrent infections. These may affect the upper respiratory airway (ear, nose and throat) or the lower respiratory airways (bronchi or lungs) but can also affect organs such as the stomach, liver, spleen, kidneys and intestines as well as the skin.

People with CVID may also have enlarged lymph nodes in the neck, chest or abdomen and an enlarged spleen. Other symptoms that may point to CVID include bleeding or bruising, severe anaemia, mouth ulcers that become infected, eye infections and autoimmune diseases.

DIAGNOSTIC CRITERIA

To diagnose CVID, other possible causes of failure to produce antibodies have to be excluded. Blood tests are needed to determine the levels of immunoglobulins in the blood. These tests might also include looking for the immunoglobulins produced against previous vaccinations or known infections. If these are absent, then the person might be immunised again and, after at least 3 or 4 weeks, have their blood rechecked to see if the appropriate amount of antibodies has been produced.

Other tests might include computerised tomography (CT) of the chest if the person has had repeated chest infections, or ultrasound scans of organs such as the spleen.

GENES ASSOCIATED WITH CVID

In recent years, genetic testing has allowed the genes associated with many PIDs to be identified. Although some genes responsible for CVID have been identified in some patients, CVID is thought to be a polygenic disorder (i.e. it is associated with the effects of multiple genes in combination with lifestyle and environmental factors).

Genes that seem to be important in CVID include changes in the *PIK3CD, PIK3R1, NFkB1, NFkB2, ICOS, CD19, CD20* and *CD81* genes. Changes in other genes, including *TAC1, BAFF* receptor and *MSH5* may also be involved.

OTHER CONDITIONS ASSOCIATED WITH CVID

People with CVID may have a range of associated health issues affecting multiple different organs and systems including:

- The lungs. Pneumonia is common in people with CVID and can lead to chronic lung damage, such as bronchiectasis, that may have developed before the CVID was diagnosed.
- Intestinal tract. Symptoms may be abdominal pain, nausea, diarrhea and vomiting, which may be due to infections caused by micro-organisms such as *Salmonella*, or *Campylobacter*, Giardia, etc, or to inflammatory bowel disease. Some patients might experience a liver disease called nodular regenerative hyperplasia.These problems can lead to weight loss.
- Autoimmune disease. People with CVID may produce a specific type of antibody that attacks their own antibodies. These are called autoantibodies. One of the most frequent autoimmune manifestations is anaemia because of auto-antibodies targeting red blood cells.
- Arthritis and painful joints may develop although it is not usually caused by infections within the joints.

Some people may also have a history of lymphoproliferative disorders, malignancy and sarcoid-like granulomas.

WHAT TREATMENT IS SUGGESTED FOR CVID?

IMMUNOGLOBULIN REPLACEMENT THERAPY FOR CVID

People with CVID are not able to fight off bacterial, parasitic, viral or fungal infections as effectively as those with a fully functioning immune system. People with CVID have low levels of IgA, IgG, and/or IgM and immunoglobulin replacement therapy is the optimum treatment for these conditions. Immunoglobulins are purified from the plasma of healthy donors and given to the person with CVID. They may be given by an intravenous (IVIG) or subcutaneous (SCIG) infusion.

The aim of immunoglobulin therapy is to prevent infections and protect the person from the possible chronic effects which can result in damage to their organs, especially their lungs, by bacterial, parasitic, viral and fungal infections. For this reason, people with CVID will usually need lifelong immunoglobulin therapy and it is important to keep to the regimen as prescribed to make sure they are fully protected.

The immunoglobulin dose is determined by how well the therapy protects the person against Infection.
This is done by monitoring the rate and severity of infections and by ensuring that the immunoglobulin trough levels remain within the normal range.
Trough levels are the plasma levels of IgG right before infusions and are normally recorded twice a year in the case of intravenous infusions and at any time in patient on subcutaneos infusions.
The starting dose is determined by the persons' body weight. By increasing the dose of immunoglobulin it might be possible to prevent most of the bacterial infections, but not all (especially the ones affecting the ear, nose, and throat areas as well as the conjunctiva).

ANTIBIOTIC PROPHYLAXIS FOR CVID

Antibiotics are important to help treat acute infections in people with CVID. Some people who experience chronic sinusitis or chronic lung disease may need long-term (prophylactic) antibiotic treatment. These may be broad spectrum antibiotics if the bacteria is unknown or a more specific antibiotic if the bacteria has been identified.

VACCINATIONS FOR CVID

Vaccination is not routinely used for the treatment of CVID but is rather used for its diagnosis as one of the main diagnostic criteria is a poor response to vaccines. However, some people may benefit from active vaccination in addition to immunoglobulin therapy. Some people may also benefit from annual influenza vaccination along with their close family members but this should always be on the advice of an immunologist.
Live vaccines should only be used upon careful immunological evaluation by the immunologist in charge of the PID patient

ADVANCES IN THE TREATMENT OF CVID

Ongoing research has greatly improved our understanding of the pathological processes that result in CVID and this knowledge is opening up new ways to treat the condition. A promising avenue of research is to target signalling pathways inside cells that are not working correctly. A number of signalling pathways seem to be overactive in CVID and new targeted treatments that inhibit the activity of these pathways are being tested.

LIVING WITH CVID

Once a diagnosis has been made and immunoglobulin therapy started, most people can live a relatively normal life. Regular monitoring will be needed for any conditions that were present at the time of diagnosis and to look out for the emergence of any autoimmunity or other potential complications.

FURTHER INFORMATION AND SUPPORT

This booklet has been produced by the International Patient Organisation for Primary Immunodeficiencies (IPOPI). Other booklets are available in this series. For further information and details of PID national patient organisations active worldwide, please visit **www.ipopi.org**.

Provided by

IMMUNO DEFICIENCY UK

Supporting families affected by primary and secondary immunodeficiency

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.

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www.immunodeficiencyuk.org
hello@immunodeficiencyuk.org
0800 987 8986