



PRIMARY IMMUNODEFICIENCIES

TREATMENTS FOR PRIMARY IMMUNODEFICIENCIES: A GUIDE FOR PATIENTS AND THEIR FAMILIES



WHAT ARE PRIMARY IMMUNODEFICIENCIES?

This booklet explains what primary immunodeficiencies (PIDs) are and how they are treated.

PIDs are a large group of different disorders caused when some components of the immune system (mainly cells and proteins) do not work properly. It is estimated that around 1 in 2000 people are diagnosed with a PID, but some PIDs are much rarer than others. Some are relatively mild, while others are severe. They are usually identified during childhood, but they can also be diagnosed in adults. The treatment for PIDs depends on which part of the immune system is affected.

PIDs are caused by hereditary or genetic defects of the immune system. PIDs are not related to AIDS ('acquired immunodeficiency syndrome'), which is caused by a viral infection (HIV). PIDs are not contagious — it is not possible to 'catch' a PID or to spread it to other people. However, children can inherit PIDs from their parents. People with PIDs may wish to seek advice on the genetics of their condition if they wish to have children.

PIDs are divided into eight groups: predominantly antibody deficiencies; combined T- and B cell deficiencies; other well-defined syndromes; diseases of immune regulation; congenital defects of phagocyte number or function, or both; defects of innate immunity; auto-inflammatory diseases; and complement deficiencies.

- B lymphocytes ('B cells') produce immunoglobulins, also called antibodies. Immunoglobulins are proteins that are able to neutralise invading micro-organisms and help phagocytes to recognise, ingest and kill them.
- T lymphocytes ('T cells') attack invading micro-organisms that are inside host cells, such as viruses. T cells also produce cytokines, which help to recruit and organise other immune cells.
- Phagocytes swallow (or 'ingest') and kill invading micro-organisms.
- Complement are proteins that kill micro-organisms and help other cells in the immune system.

The immune system normally helps the body fight off infections by germs (or 'micro-organisms') such as bacteria, viruses, fungi and protozoa. As their immune systems do not work properly, people with PIDs are more prone than other people to infections. These infections may be more common than is usual, they may be particularly severe or difficult to clear, or they may be caused by unusual micro-organisms. They may occur whatever the season, even in summer.

Treatments for PIDs can:

- Reduce the number and severity of infections.
- Treat other symptoms.
- Help many children and adults with PIDs to enjoy as normal a life as possible.

People with PIDs are normally treated by doctors who specialise in diseases of the immune system. How a patient is treated depends on which PID they have, and on many other factors. The rest of this booklet explains the main treatments involved.

IMMUNOGLOBULIN REPLACEMENT THERAPY

Immunoglobulins are proteins that recognise micro-organisms and help the immune cells to neutralise them. Most PIDs cause the body to produce too few immunoglobulins, or none at all. Immunoglobulin replacement is the most important treatment for these PIDs, as it helps to protect against a range of infections and to reduce autoimmune symptoms. Immunoglobulin is used to treat various PIDs, including common variable immunodeficiency, X-linked agammaglobulinaemia, X-linked hyper-immunoglobulin (HIGM) syndrome, Wiskott-Aldrich syndrome and severe combined immunodeficiency (SCID). Treatment must be given regularly, as it only gives temporary protection, and is usually life-long.

Immunoglobulin is given as an infusion (or 'drip'). The infusion can be given by two different routes. Both routes are effective, and each has advantages and disadvantages.

Intravenous (IV) infusion: this is where immunoglobulin is given straight into the bloodstream through a vein. Each infusion takes 2–4 hours. The main advantages of IV infusion are that it allows high immunoglobulin doses to be given where necessary, and treatment only needs to be given every 3 or 4 weeks. However, a disadvantage is that IV infusions usually need to be given in a hospital or clinic by a doctor or nurse, or at home by a nurse or trained relative. Also, some patients may feel unwell during or after IV infusions (see below).

The dose of immunoglobulin is adjusted to make sure there is the right amount of immunoglobulin in the blood and that infections are controlled. As the various brands of immunoglobulin differ slightly and may be tolerated differently by different individuals, patients and parents should remember which brand they are using so that they can ensure they receive the correct product.

Subcutaneous (SC) infusion: this is where immunoglobulin is given under the skin of the leg, belly or arm using a needle and a portable infusion pump (or 'syringe driver') or 'push' technique. SC infusions only take 1–2 hours but are usually given one or more times a week. SC infusions are useful when there are problems in giving IV infusions. Also, SC infusions can often be given at home by patients themselves, or by parents and carers. However, this is not suitable for everyone. Patients and carers who 'self-treat' at home must be willing and able to keep to the dosing schedule and they are asked to keep a treatment diary. This is only possible after training is provided, or by trained staff.

WHAT ARE THE POSSIBLE SIDE EFFECTS?

Most patients do not experience serious side effects from immunoglobulins. Some patients experience symptoms such as headache, dizziness, fever, chills, nausea, vomiting or pain in the muscles or the back. More severe side effects such as 'aseptic' meningitis, a loss of red blood cells ('haemolytic' anaemia), thromboembolic events (blood clots, e.g. in the heart, brain or lungs) and serious allergic reactions are extremely rare. These side effects are less common with SC immunoglobulin than with IV immunoglobulin. SC infusion sometimes causes swelling and pain at the injection site.

Although immunoglobulin replacement protects against many common and serious infections, it does not prevent all infections. Patients treated with immunoglobulin still need to take precautions against infections, such as good hygiene or in some cases antibiotic treatment. Patients or parents should contact the doctor whenever an infection is suspected. The doctor or nurse can advise on which infections to watch out for.

Immunoglobulin therapies are made from human plasma donated by healthy donors. Immunoglobulin therapies have an excellent safety record. While all biological products carry a very small risk of infection by viruses, with immunoglobulin this risk is minimised by the careful selection of plasma donors, the testing of donations and by the manufacturing process itself.

Immunoglobulin is available in most countries (see www.ipopi.org), but often only from centres that have a specialist in treating PIDs. The way immunoglobulin therapy is paid for (or 'reimbursed') by the healthcare system varies between different countries and healthcare insurance plans. Patients and carers will need to check their local situation and healthcare plan and take advice from their doctor. Patients can also contact their national patient organisation (via www.ipopi.org) for further information.



STEM CELL (OR BONE MARROW) TRANSPLANTATION

Stem cells are immature cells that can divide and mature into many different types of immune cells. Stem cell transplantation is a specialised treatment in which stem cells taken from the bone marrow or cord blood of a healthy donor are given to some patients with certain PIDs when the immune cells are missing or not working properly.

Possible risks of transplantation are that the patient's immune system may attack the donated cells, or the donated cells may attack the patient's body. In order to avoid this, the ideal stem cell donor is a brother or sister of the patient who has cells that match those of the patient. However, sometimes the donor may also be a relative who is not matched with the patient, or a non-relative who is matched to the patient. Some patients need to be given chemotherapy to prepare their immune systems for stem cell transplantation.

Stem cell therapy is provided only by bone marrow transplantation units and its availability varies around the world. Patients and carers will need to check their local situation and healthcare plan, and with their doctor.

Stem cell transplantation can be very effective, but is only used to treat certain types of severe PID, such as SCID, HIGM syndrome, chronic granulomatous disease (CGD), Wiskott-Aldrich syndrome and Duncan's syndrome.

ANTIBIOTICS AND OTHER TREATMENTS

People with PIDs often require antibiotics to treat, and sometimes to prevent, infections. Antibiotics work against infections caused by bacteria. Other medicines may also be needed to fight infections caused by fungi (such as thrush) or viruses (such as chickenpox).

These medicines can usually be taken by mouth, but in some situations they must be given by injection or infusion. Patients with PIDs often need to take these medicines for long periods of time. As with all prescribed medicines, it is important to follow the instructions given by the doctor, nurse or pharmacist.

Other treatments that may be given include:

Granulocyte-colony stimulating factor (G-CSF): G-CSF is sometimes used to boost the production of immune system cells called 'granulocytes' in patients with certain PIDs, e.g. CGD and HIGM. G-CSF is given by SC injection.

Gamma interferon: Gamma interferon is a protein that helps immune system cells to kill invading micro-organisms. Patients with certain PIDs (particularly CGD) may be given gamma interferon to help protect against infections. Gamma interferon is given as a SC injection.

PEG adenosine deaminase (ADA): Patients with ADA-deficiency SCID, a form of severe combined immunodeficiency, lack an enzyme (a type of protein) called ADA. These patients may be given replacement therapy with PEG-ADA via an injection into the muscle.

Gene therapy: This involves correcting the faulty gene in the patient's stem cells. Currently, it has only been used to treat certain severe PIDs for which the faulty gene has been identified, e.g. SCID and CGD. This therapy is still being tested and is not routinely available.

Physiotherapy: People with PIDs sometimes receive physiotherapy to help their breathing, especially if the lungs have been damaged by chest infections.

Treatment for 'autoimmune' symptoms: PIDs can also cause the immune system to attack the body itself — this is called 'auto-immunity'. This can cause pain and swelling in the joints, known as 'arthritis'. It can also cause skin rashes, a loss of red blood cells (anaemia) or platelet cells involved in blood clotting, inflammation of blood vessels, diarrhoea and kidney disease. Patients with some PIDs are also more likely to have allergies and asthma.

Autoimmune problems (such as arthritis) are treated using various medicines that help to stop the immune cells attacking the body. Steroids (or 'corticosteroids') are used most commonly for this. As these medicines suppress the immune system they can increase the risk of infections. These medicines should be used under the guidance of a doctor who specialises in treating people with PIDs. It is important to follow the instructions given with these and any other prescribed medicines.

Complementary medicine: Complementary (or 'alternative') medicines cannot replace the treatment given by the hospital or clinic. Patients or parents should speak with their healthcare team before taking any complementary medicines.

HEALTHCARE TEAM

Patients with PIDs are usually treated at immunology centres or clinics. Regular visits to the centre are usually required, depending on the specific PID and the treatment given. As well as the specialist doctor, several other staff members help care for people with PIDs. These include specialist nurses, physiotherapists, nutritionists or dieticians, and pharmacists.

The immunology centre will normally keep the general practitioner (family doctor) up to date about a patient's treatment. Patients or parents should make sure that other healthcare staff know about the condition — this includes surgeons, dentists, nurses and local pharmacists.

FURTHER INFORMATION AND SUPPORT

This booklet has been produced by the International Patient Organisation for Primary Immunodeficiencies (IPOPI). A companion booklet titled '*Primary immunodeficiencies. Stay healthy! A guide for patients and their families*' is also available. For further information, and details of PID patient organisations in 61 countries worldwide, please visit www.ipopi.org.

Provided by



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.

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

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