Primary immunodeficiencies **in adults**

IPOPI
INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES

Introduction

This booklet explains what primary immunodeficiencies (PIDs) are, and how they are managed in adults.

PIDs are a large group of different disorders caused when some components of the immune system (mainly cells and proteins) do not work properly. People with PIDs are more prone than other people to catching infections. PIDs can also cause the immune system to attack the body itself – this is called 'auto-immunity' and it can lead to various symptoms such as pain and swelling in the joints ('arthritis').

PIDs are caused by defects in the genes (the DNA) responsible for the immune system. These defects can be inherited from the parents and they can manifest themselves at any age, although most cases are diagnosed at young adult or late adult ages. Although some PIDs are diagnosed in children, others are more often identified during adulthood. For example, common variable immunodeficiency (CVID), the most common PID diagnosed in later life, occurs in around 1 in 25,000 people and is most often diagnosed in adults. Immunoglobulin A deficiency, immunoglobulin G subclass deficiency and complement deficiencies are other PIDs that are often diagnosed in adolescents or adults. Chronic granulomatous disease (CGD) and X-linked agammaglobulinemia are examples of other PIDs that are usually identified in children, but which are sometimes diagnosed during adulthood.

Adults often suffer from PIDs for many years before the condition is diagnosed. This is an important issue because the sooner the condition is diagnosed, the sooner treatment can be given to reduce the risk of infections and other complications.

PIDs are serious, chronic disorders. However, with modern treatments and some common sense health precautions most people with PIDs can lead long, full and active lives. Adults with PIDs have important roles in making decisions about their own therapy, in adhering to the treatment provided, and in looking after their own health. In order to fulfil these roles, patients should learn as much as possible about PIDs and their management.

This booklet explains how PIDs are diagnosed, the available therapies, and the implications of these conditions for the lives of patients and their families. It is intended to help adults who are newly diagnosed with PIDs and young people with an existing PID who have reached adulthood.

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Diagnosis and treatment of PIDs

Warning signs

Whatever the age of the patient, it is most important that PIDs are diagnosed as early as possible. A PID is usually first suspected because a person suffers infections that are unusually frequent or severe, or they do not respond normally to treatment, or if they are caused by unusual types of bacteria, viruses or fungi. The most common types of infections seen in adults with PIDs are infections of the respiratory tract, which include those of the sinuses, airways (bronchitis) or lungs (pneumonia), and those of the digestive system (causing diarrhoea).

Diagnostic tests

In the diagnosis and treatment of PIDs it is important, wherever possible, to consult a doctor specialising in diseases of the immune system (an immunologist) where one is available, as well as a general practitioner (family doctor) who is in contact with the immunologist.

Doctors use various laboratory tests to investigate the immune system in patients whom they suspect may have a PID. They count the number of immune system cells in the blood (especially cells called T and B cells) and test how well these cells are able to multiply and kill infecting microorganisms. Importantly, they also measure the amount of immunoglobulins in the blood. Immunoglobulins (which are also called 'antibodies') are proteins that recognise infecting micro-organisms and help immune cells to destroy them. Most PIDs (with the exception of hyperimmunoglobulin M and hyperimmunoglobulin E syndromes) cause the body to produce too few immunoglobulins, or none at all. Other tests used include those for levels of 'complement', which are proteins that kill micro-organisms and assist other immune cells.

Patients who have symptoms of PIDs may also be tested for human immunodeficiency virus (HIV) infection. PIDs are genetic conditions and they are completely unrelated to HIV. However, because HIV also causes people to be prone to infections, an HIV test may be done to exclude this. During the diagnosis of PIDs, patients may also be tested for autoimmune diseases and certain cancers that can cause symptoms similar to those of PIDs.

Treatments

Immunoglobulin replacement therapy is the main treatment for most people with PIDs. Immunoglobulin replacement helps to protect against infections and reduces some autoimmune symptoms if these are present. Immunoglobulin replacement is given as an infusion either into a vein (intravenous immunoglobulin, or 'IVIG') or under the skin (subcutaneously, abbreviated to 'SC' or 'subcut'). In some cases, immunoglobulin can be given at home by adult patients themselves, or by their partners or carers. By reducing the need for visits to the hospital or clinic, this can be more convenient and can lessen the intrusion of treatment on patients' personal, family and working lives.

Other specialised treatments for PIDs are sometimes used, depending on the particular PID present. These include:

Granulocyte-colony stimulating factor: used to boost the production of immune cells called granulocytes by the bone marrow when levels of these cells are low, e.g. in patients with severe congenital neutropenia or CD40 ligand deficiency.

Gamma interferon: used to boost the immune system, particular in patients with CGD.

PEG adenosine deaminase: used in patients in whom an absence of this enzyme causes severe combined immunodeficiency (SCID).

Stem cell transplantation: stem cells normally mature into many types of immune cells. Stem cell defects causing some severe PIDs (e.g. SCID) can be corrected by giving the patient stem cells taken from a healthy donor.

Gene therapy: this involves correcting the faulty gene causing some PIDs (e.g. CGD and SCID). This therapy is still being tested and is not yet routinely available.

These treatments are generally expensive and their availability varies in different parts of the world. PID treatments are constantly evolving and patients should try to keep up to date with new developments.

People with PIDs also often require medicines to treat or prevent infections caused by bacteria (antibiotics), fungi (antifungals, for example against thrush) and viruses (antivirals, for example against chickenpox).

People with PIDs should watch out for signs of infection and report any signs to their immunologist or specialist doctor.

IPOPI has produced specific booklets on IPOPI diagnosis and treatments. These can be found at www.ipopi.org.

Long-term effects of PIDs

Modern treatments allow people with PIDs to live longer and healthier lives than ever before. However, these conditions do cause a variety of long-term health problems and patients need to monitor their health and report any changes to their clinic, hospital or physician. This section provides only a broad indication of the health issues people living with a PID may encounter. Each individual patient will be affected by his or her condition differently and so it is important that specific issues are discussed in person with a doctor.

People with PIDs need to monitor their own health carefully and report any problems to their hospital, clinic or family doctor.

Lung disease complications

People with PIDs can suffer chronic (i.e. long-term), recurrent respiratory infections that over time can damage the lungs. Bronchiectasis is a serious condition in which the airways of the lungs (bronchi) are abnormally widened and subject to a build-up of mucus. This causes coughing and breathlessness and renders sufferers even more susceptible to infections. Immunoglobulin replacement therapy and antibiotics are used to help prevent chronic lung disease.

Patients with PIDs can also develop other kinds of chronic, damaging inflammation in various organs of the body, including the lungs, liver and spleen. In particular, patients with CVID sometimes develop nodules (called 'granulomas') in the lungs and other organs. In the lungs this condition can cause breathless and reduce a patient's capacity to exercise.

Autoimmune disease progression

Autoimmune disease can affect various parts of the body, including the:

- Joints, causing pain and inflammation (arthritis).
- Skin, causing rashes and swelling.
- Liver and spleen, causing enlargement of these organs ('hepatomegaly' and 'splenomegaly', respectively).
- Intestines, causing inflammatory bowel disease.
- Blood cells, causing a loss of the red blood cells that normally carry oxygen from the lungs to the tissues (anaemia) or the platelet cells involved in blood clotting.

Immunoglobulin replacement therapy is the main treatment used to control autoimmune disease. Other drugs that suppress the immune system (such as corticosteroids and an antibody therapy called rituximab) are also sometimes used. These 'immunosuppressive' treatments need to be administered carefully by an immunologist.

Neurodegenerative disease progression

Ataxia telangiectasia (AT) is a PID that causes abnormalities in the brain. Patients with AT can have various symptoms, including unsteadiness when standing or walking, and problems with the eyes and with speaking and swallowing. These symptoms can become worse over time. There is some evidence that people with other PIDs can also suffer from a deterioration of the nervous system, although little is known about this.

Cancers

Patients with many PIDs are at an increased risk of certain kinds of cancer. The cancer risk differs between PIDs. For example, patients with CVID are at an increased risk of cancer of the lymph system (lymphoma), stomach, breast, bladder and cervix.

Effects of PID treatments

Immunoglobulin replacement therapy causes few side effects. Some people experience headaches or symptoms of allergy during or soon after the infusions, but in most cases these are short-lived and respond to simple treatments. In rare instances patients can have severe reactions to immunoglobulin replacement and so any new product should be given under the care of a physician. Over time, IV immunoglobulin can damage the veins into which it is infused. Other PID treatments are generally well tolerated and usually do not cause long-term side effects. Taking antibiotics often or for long periods can cause potentially serious diarrhoea. Antibiotics called quinolones can cause joint damage, especially in children and adolescents, when given for long periods to protect against infections (so-called 'prophylaxis').

Disabilities

Some symptoms of PID can interfere with patients' normal activities. For example, arthritis in the knees, ankles and hands, and serious chronic lung disease can be disabling. Patients with disabling symptoms should seek advice on measures to help them overcome these problems, for example by making changes in the home or work environment.

Access to PID treatments

Older people with PIDs may find it increasingly difficult to attend clinic appointments, especially if they have problems with mobility and travelling. Depending on the way healthcare is provided where they live, they may also find it harder to fund PID care in later life. In some countries the hospital or clinic may provide homecare services to help in these situations. National PID patient organisations may be able to provide helpful advice.

Living with a PID

Staying healthy

People with PIDs need to take various simple precautions to help themselves stay healthy. Simple precautions to avoid infections are particularly important. These include:

- Personal hygiene, including washing hands and good dental hygiene.
- Making sure cuts and grazes are properly dressed.
- Not smoking (in order to reduce the risk of infections and lung disease) and avoiding smoky environments where possible.
- Eating a nutritious, balanced diet.
- Getting enough rest and sleep.
- Undertaking suitable types of activities and exercise. While patients with PIDs can enjoy most sports and activities, they should ask their doctor about any necessary precautions.

It is very important that patients with PIDs do not smoke because smoking increases the risk of lung infections and chronic lung disease.

These issues, and others, are also discussed in the IPOPI booklet entitled, ‘Stay healthy! A guide for patients and parents’ (www.ipopi.org).

Emotional impact of PIDs

Newly diagnosed patients with PIDs can experience various negative emotions. They may feel afraid of the condition and its complications, or frustrated and angry that the condition has affected them. Feelings of isolation and self-pity may also occur, as may feelings of guilt from being a burden to other people. It may take some time to come to terms with the diagnosis. Over time, these emotions may cause stress or depression. People with PIDs, and their friends and family members, should watch out for signs of these conditions and seek advice if these occur.

Ideally, patients should take advantage of emotional support from the people around them, for example from family members, friends or professional services. The family doctor, or the team at the PID clinic or hospital, may also be able to help. For example, in some cases they may be able to arrange counselling. It can also help to be in contact with other people with PIDs to share experiences, concerns and emotions, and this can be done via national patient support groups (visit www.ipopi.org).

Relationship aspects

People with PIDs must decide how much they tell people about their condition, and when. They may be afraid that a potential partner might be put off by the condition or worried about demands these conditions can place on both patients and the people around them. In some cases these concerns can result from misunderstandings about PIDs. In particular, patients can reassure their partners that PIDs are completely unrelated to HIV/AIDS and cannot be caught or transmitted. When it comes to sexual relations, people with PIDs should nevertheless ensure that they practise safe sex to avoid infections.

Inheritance of PIDs

Doctors have identified the precise genetic defects causing some PIDs, and the way these can be passed from parents to children. In some cases this is a complicated matter. For example, although CVID is thought to be inherited, no definitive genetic cause has yet been demonstrated. Around 10% of people diagnosed with CVID have relatives with CVID (or another PID).

Ideally, people with a PID who wish to have children should seek genetic counselling so that they are aware of the risks of passing on their PID to their children. Genetic testing to identify the defect present can only be done by specialised laboratories. It is expensive and is not available in all countries. National PID patient organisations can provide further information about availability of genetic testing in specific countries.

Employment issues

Patients with severe PIDs or associated disabilities may find some types of work difficult or impossible. However, in most cases, PIDs need not limit the kinds of work that patients can do. Patients may need to be absent from work at times to attend scheduled clinic appointments or during periods of illness due to infections or other complications. Ideally, patients and employers will work together to find solutions to minimise the disruption to work caused by these episodes. For example, the ability to work from home at times may be helpful where this is possible.

If someone with a PID believes that they are discriminated against by an employer because of their condition, they should find out about the laws relating to discrimination in their country. The national PID patient organisation may be able to provide advice in these matters.

Travel

PIDs need not restrict travel in most cases. However, certain precautions are important, especially when travelling internationally. For example, diarrhoea is common when travelling in some parts of the world (especially in Africa, the Middle and Far East, and South America) and this may be severe and prolonged in patients with PID. The risk of diarrhoea can be reduced by avoiding salads, raw foods, seafood, ice cubes and ice cream, and by drinking only boiled or bottled water. Travellers may also need to take tablets to protect against malaria in certain areas of the world. Patients should ask their doctor for advice on these and other precautions, such as vaccinations, before they travel. For example, vaccination against yellow fever, a serious viral illness, is normally recommended in healthy individuals travelling to some parts of sub-Saharan Africa, South America and parts of the Caribbean, and is required for entry into some countries. However, as the yellow fever vaccine is a ‘live’ vaccine it should not be given to patients with PIDs caused by T cell defects or to members of their household.

Patients must make sure they have all necessary medications available to them during their travels, in case these are not available in the countries visited. An explanatory letter from their immunologist, addressed to border or medical authorities in the countries visited, is often useful and in some cases necessary — especially when patients travel with their medication. A sample letter is available at the IPOPI website (www.ipopi.org), together with other travel precautions. Patients who experience problems while travelling should contact their local national PID patient organisation.

Health insurance

In many countries healthcare is funded via personal health insurance policies. Following a diagnosis of a PID, people who live in such countries will need to check that their policy covers their new needs. Patients or their doctors should check if the diagnosed PID is on the national list of chronic diseases and whether the treatment is on the list of essential medicines. The immunologist or family doctor will normally be able to help in ensuring that the policy is updated and changed, as necessary. Thereafter patients with PIDs should ensure that they do not let their coverage lapse.

Primary immunodeficiencies

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 patient organisations in 43 countries 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.

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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