Primary Immunodeficiencies (PIDs)

Primary immunodeficiencies (PIDs) are a group of more than 400 potentially serious disorders, that can lead to frequent or severe infections, swellings and autoimmune problems. PID symptoms often appear in childhood, but some can first occur in adults.

PIDs can be caused by defects in the genes that control the immune system, and may be inherited. PIDs are different to AIDS (acquired immunodeficiency syndrome), that is due to human immunodeficiency virus (HIV).

What are PIDs?

PIDs occur when the immune system does not work normally. The most important function of the body's immune system is to defend against infections and other invaders (such as cancer cells), whilst protecting the body's own cells. Everyone gets infections, however infections in people with PIDs can be:

- Unusually persistent, recurrent or resistant to treatment.
- Due to unusual germs (bacteria, viruses, fungi and parasites).
- Unexpectedly severe.

Some PIDs may increase the chance of autoimmunity or cancer. Autoimmunity occurs when the body doesn't recognise its own cells and attacks them.

Warning signs of PIDs

Early diagnosis of PIDs is important, since delayed treatment can result in complications, that may be life threatening. If someone has two or more of the following signs, they should discuss the possibility of having a PID with their doctor.

CHILDREN	ADULTS
Four or more ear infections within one year	Two or more ear infections within one year
Two or more serious sinus infections within one year	Two or more sinus infections in one year in the absence of allergies
Two or more pneumonias within one year	One pneumonia per year for more than one year
Recurrent, deep skin or organ abscesses	Recurrent, deep skin or organ abscesses
Two or more deep seated infections such as sepsis, meningitis or cellulitis	Infection with normally harmless tuberculosis-like bacteria
Persistent thrush in the mouth, skin or elsewhere after age one	Persistent thrush or fungal infection on skin or elsewhere
Two or more months on antibiotics with little effect	Repeat viral infections (colds, herpes, warts, condyloma)
Need for intravenous antibiotics to clear infections	Need for intravenous antibiotics to clear infections
Failure to gain weight, grow normally, or chronic diarrhoea	Chronic diarrhoea with weight loss
Family history of PID	Family history of PID

This table is adapted from the 10 warning signs developed by the Jeffrey Modell Foundation www.info4pi.org

Types of PIDs

PIDs can be categorised into the following five main groups, according to what part of the immune system is affected.

ANTIBODY DEFICIENCIES

Antibodies, also known as immunoglobulins, are proteins made by specialised white blood cells, called B cells (B lymphocytes). Antibodies recognise germs so they can be removed by the rest of the immune system.

Common variable immunodeficiency (CVID) is the most common form of antibody deficiency and usually presents with recurrent chest and sinus infections. Symptoms can start at any age, although most cases are diagnosed in adults.

X-linked agammaglobulinaemia is an antibody deficiency that is usually diagnosed in male infants. Common symptoms include frequent pus producing infections of the ears, lungs, sinuses and bones, chronic diarrhoea and poor growth.

COMBINED IMMUNODEFICIENCIES

T cells (T lymphocytes) are specialised white blood cells that are essential for the functioning of the immune system. T cells recognise the body's own cells, identify germs and invaders, including cancer, and coordinate the rest of the immune system. They help B cells make good antibodies.

For this reason, most people with T cell problems have combined immunodeficiencies, because both B and T cell functions are affected.

Severe combined immunodeficiency (SCID) is the most serious of these disorders. SCID is usually diagnosed within the first year of life and requires a haematopoietic stem cell (HSCT) transplant to survive.

PHAGOCYTIC CELL DEFICIENCIES

Phagocytes are white blood cells (neutrophils and macrophages), that eat and kill antibody coated foreign invaders. Severe infections can occur if phagocytes are unable to kill germs or move to the site of an infection.

Chronic granulomatous disease (CGD) is the most serious form of phagocytic cell deficiency. In CGD neutrophils can't capture and kill germs. People with CGD have frequent and severe infections of the skin, lungs and bones. They can also develop chronic inflammation, including inflammatory bowel disease (IBD).

IMMUNE DYSREGULATION

Immune dysregulation includes a broad group of disorders that occur when the body's immune system is not being controlled normally, and may react against its own cells. People with immune dysregulation can have fever, damage to organs or blood cells, and increased risk of infection.

Examples of immune dysregulation include immunodysregulation polyendocrinopathy enteropathy x-linked syndrome (IPEX), APECED, autoimmune lymphoproliferative syndrome (ALPS) and autoinflammatory disorders.

COMPLEMENT DEFICIENCIES

The complement system has an important role in the control of inflammation, killing of germs and clearance of damaged cells. Some complement deficiencies can increase the risk of autoimmune disease, whilst others result in severe infections such as meningitis or septicaemia.

Hereditary angioedema (HAE) is a different sort of a complement disorder, that is due to C1 esterase inhibitor deficiency. In people with HAE, the small blood vessels leak fluid into the tissues, causing non-itchy swellings known as angioedema. People with HAE can have unpredictable and sometimes severe swellings (HAE attacks) throughout life, that may be life threatening.

Treatment options

Research and advances in therapies have resulted in improved health and a longer life for people with PIDs.

ANTIBIOTICS

Infections should be treated early, and antibiotics are often required. Some people may be prescribed long term antibiotics (prophylaxis) to reduce infections. Medications against fungi, viruses and parasites may be needed to treat some conditions.

IMMUNOGLOBULIN REPLACEMENT THERAPY (IRT)

Immunoglobulin replacement therapy (IRT) is one of the most effective and commonly used treatments for some PIDs. IRT can be given using intravenous immunoglobulin (IVIG), that is injected into the vein, or given at home using subcutaneous immunoglobulin (SCIG), that is injected under the skin.

These products are derived from blood (plasma), are in limited supply, and access is restricted. Doctors must follow specific guidelines to ensure that the product goes to people most in need.

IMMUNOMODULATION

There is an increasing number of medications used to increase or decrease immune function. Medications may include corticosteroids, biologics such as monoclonal antibodies, and other immunosuppressive drugs.

HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT)

For some people with PIDs, a haematopoietic stem cell transplant (HSCT) may be recommended, due to the severe nature of their condition. These cells are obtained from donated bone marrow or blood. HSCT usually cures the underlying PID, but has risks, and must be performed in specialist centres.

HEREDITARY ANGIOEDEMA (HAE) TREATMENTS

There are two main treatments for severe, acute HAE attacks:

- Purified C1 esterase inhibitor for intravenous use in hospitals or at home.
- Icatibant for emergency treatment, which can be self-administered at home.

Tranexamic acid, danazol or C1 esterase inhibitor are sometimes given regularly to prevent attacks (as prophylaxis) to people with frequent HAE attacks.

Patient support organisations

The following organisations provide support for people with PIDs and their families:

- AusPIPS www.auspips.org.au
- Immune Deficiencies Foundation of Australia (IDFA) www.idfa.org.au
- Immune Deficiencies Foundation of New Zealand (IDFNZ) www.idfnz.org.nz
- HAE Australasia www.haeaustralasia.org.au

For more information go to www.allergy.org.au

To donate to immunology research go to www.allergyimmunology.org.au