Primary Immunodeficiencies (PID)

Primary immunodeficiency (PID) diseases are a group of potentially serious disorders in which inherited defects in the immune system lead to increased infections. There are currently more than 150 primary immunodeficiency diseases, with new disorders being described regularly.

What are primary immunodeficiency diseases?

One of the most important functions of the body's normal immune system is to protect against infection. Although everyone experiences infections of one form or another, some people have infections that seem to fall beyond the scope of normal immune defence.

Such cases may be explained by inherited defects of the immune system, known as primary immunodeficiency diseases. Many of these rare diseases appear in childhood, but some emerge for the first time in adulthood.

Examples of infections in people with primary immunodeficiency diseases include:

- Infections that are unusually persistent, recurrent or resistant to treatment
- Infections involving unexpected spread or unusual organisms
- Infections that are unexpectedly severe

Primary immunodeficiency diseases are inherited

Primary immunodeficiency diseases are caused by defects in the genes that control the immune system, and are therefore inherited.

Primary immunodeficiency diseases are not related to AIDS (acquired immunodeficiency syndrome) which is due to infection with human immunodeficiency virus (HIV).

What are the warning signs of primary immunodeficiency diseases?

Many people with primary immunodeficiency diseases have experienced similar patterns of symptoms. These can be called warning signs and symptoms:

1. Eight or more ear infections within one year
2. Two or more serious sinus infections within one year
3. Two or more months on antibiotics with little effect
4. Two or more pneumonias within one year
5. Failure of an infant to gain weight or grow normally
6. Recurrent deep skin or organ abscesses
7. Persistent thrush in mouth or elsewhere on skin after age one
8. Need for intravenous antibiotics to clear infections
9. Two or more deep seated infections such as sepsis, meningitis or cellulitis
10. Family history of primary immune deficiency.

What types of primary immunodeficiency diseases exist?

Primary immunodeficiency diseases cause increased susceptibility to infections as well as other problems. For simplicity, these diseases can be categorised into four groups according to what part of the immune system is affected:

1. ANTIBODY DEFICIENCIES

Antibodies are proteins made by specialised white blood cells: B cells (B lymphocytes) and plasma cells. The function of antibodies is to recognise infectious agents so that they can be blocked. Two examples of antibody deficiencies are:

- **Common Variable Immunodeficiency (CVID)** is the most common form of antibody deficiency, usually presenting with recurrent chest and sinus infections in childhood or early adulthood, although most cases are diagnosed in adults. Early recognition can prevent permanent damage to the lungs called bronchiectasis.
- **X-linked Agammaglobulinaemia** can present in infancy, later childhood or adulthood. Infants with this deficiency develop recurrent pus producing infections of the ears, lungs, sinuses and bones and can get infections in the bloodstream and internal organs. They are also susceptible to certain viruses such as hepatitis and polio.

2. COMBINED IMMUNE DEFICIENCIES

T cells (T lymphocytes) are specialised white blood cells that are critical to a healthy immune system. People who lack T cells also tend to have weak antibody defences, and this is called combined immunodeficiency. These disorders are very rare and hereditary. The most common is **X-linked Severe Combined Immunodeficiency (SCID)** which is due to a defective gene for T cell growth. Patients are usually diagnosed within the first year of life and require gene therapy or bone marrow transplantation to survive.

3. COMPLEMENT DEFICIENCIES

The complement system consists of a group of proteins that attach to antibody coated foreign invaders like bacteria and viruses. People with complement deficiencies lack may develop antibodies that react against the body's own cells and tissues. The most common of these deficiencies is **C2 Deficiency**. This defect can cause an autoimmune disease such as Systemic Lupus Erythematosus (SLE) or can result in severe infections such as meningitis. The illnesses usually appear in childhood or in early adulthood. **Hereditary angioedema (HAE)** is another example of a complement disorder, due to C1 inhibitor deficiency,

4. PHAGOCYTIC CELL DEFICIENCIES

Phagocytes include white blood cells (neutrophils and macrophages) that engulf and kill antibody coated foreign invaders. Phagocytes can be defective either in their ability to kill pathogens or in their ability to move to the site of an infection. In either case, the defect results in increased infections. The most severe form of phagocytic cell deficiency is **Chronic Granulomatous Disease** which is an inherited deficiency of molecules needed by neutrophils to kill certain infectious organisms. People with chronic granulomatous disease develop frequent and severe infections of the skin, lungs and bones and develop localised, swollen collections of inflamed tissue called granulomas.

Improved therapy can lead to a better and longer life

Research has led to improved therapy for people with primary immunodeficiency diseases.

Treatment options include:

I. ANTIBIOTICS

The use of antibiotics to treat and prevent infections and an action plan for early management of infections are key elements in the treatment of primary immunodeficiency diseases.

II. IMMUNOMODULATION

Immune system molecules, such as interferon gamma, can be used to improve immune function and reduce infection in primary immunodeficiency diseases.

III. IMMUNOGLOBULIN REPLACEMENT THERAPY

One of the most effective and most commonly used treatments for primary immunodeficiency diseases is immunoglobulin replacement therapy, to replace antibody levels. This can be injected into the vein (intravenous immunoglobulin or IVIG) about once a month, or administered at home in certain cases using injections under the skin (subcutaneous immunoglobulin or SCIG). These products must be restricted because of limited supply and doctors need to follow specific guidelines to ensure that the product goes to those most in need.

To ensure future supplies of immunoglobulin replacement therapy people can assist by regularly donating plasma to the Australian Red Cross Blood Service. To find out how, where and when you can donate plasma, phone the Australian Red Cross Blood Service on 13 14 95.

IV. BONE MARROW TRANSPLANTATION

For patients with combined immunodeficiency diseases, transplantation of bone marrow cells from a family member with identical human leukocyte antigens (HLA) can result in normal immune function. Tissue typing of human leukocyte antigens (HLA) greatly decreases the risk of rejection and of graft versus host disease (GVHD).

V. OTHER TREATMENTS

There are several other treatments available for disorders associated with primary immunodeficiency diseases.

Is there any support for people in Australia and New Zealand with primary immunodeficiencies?

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

- 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/

Glossary of terms

Antibodies
Blood proteins which kill germs

B cell (B lymphocyte)
Type of lymphocyte (specialised white blood cell) which develops into a cell that produces antibodies

Conditioning
Use of drugs, anti-lymphocyte serum or radiotherapy to suppress immune function to allow bone marrow to engraft. **Antilymphocyte serum** is **s**erum raised in horses which contains antibodies that destroy the white blood cells which could cause graft rejection

Gammaglobulin
Part of the blood which contains antibodies

Immunodeficiency (also referred to as immune deficiency)
Lack of the ability to develop immunity following immunisation or infection

Immunoglobulin
Blood proteins which have the function of antibodies. **IgG (immunoglobulin G)** is the main type of immunoglobulin.

IVIG or SCIG
Immunoglobulin replacement therapy methods, used to enhance immune defence by replacing missing antibodies, using antibodies derived from the blood donor pool

Stem cell
Type of cell present in bone marrow which has the ability to grow and to form red and white blood cells and platelets

T cell (T lymphocyte)
Type of lymphocyte (specialised white blood cell) necessary for immunity to viruses, moulds, protozoa (single celled organisms like giardia, malaria, toxoplasmosis). Although antibodies are made by B cells, they require the help of T cells to do so effectively. **T cell depletion** is a process to physically remove T cells which purifies and enriches the stem cells in bone marrow and lessens the chance that the transplant will attack the body of the patient who receives it.

ASCIA is the peak professional body of clinical immunology/allergy specialists in Australia and New Zealand
Website: www.allergy.org.au
Email: info@allergy.org.au
Postal address: PO Box 450 Balgowlah NSW 2093 Australia

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