Severe combined immunodeficiency (SCID)

Severe combined immunodeficiency (SCID) is the most serious form of primary immunodeficiency and is usually diagnosed in early infancy. It is a rare disorder, thought to affect less than ten Australian children born each year.

SCID is a primary immunodeficiency disease

Primary immune deficiencies, such as SCID, are caused by defects in cells of the immune system and are usually inherited. This contrasts with secondary immunodeficiency diseases such as acquired immunodeficiency syndrome (AIDS), which is caused by infection with human immunodeficiency virus (HIV).

SCID is usually an inherited disorder

Children usually inherit SCID from their parents, by either of the following ways:

- X-linked - this means that it only affects boys but is transmitted by their mothers, who are called 'carriers'. A daughter of a carrier mother has a 50% chance of being a carrier herself. Each son of a carrier mother has a 50% chance of being affected by the disorder.
- Autosomal recessive disorders - in this situation both parents are carriers and each child, whether a girl or a boy, has a 25% chance of being affected. Sometimes the autosomal recessive form of the disease is caused by a deficiency of an enzyme called adenosine deaminase, which is found by means of a special blood test.

What is SCID?

The main role of the immune system is to fight foreign invaders such as bacteria, moulds and viruses. About half the white blood cells in healthy people are T cells (T lymphocytes), which are the most important cells in the immune system. One of the roles of T cells is to help another type of white blood cell (B cells) to produce antibodies. In SCID neither the T cells nor the B cells work properly. In fact, blood from SCID babies usually doesn't even have any T cells. So, even if the blood of SCID babies contains B cells, the B cells cannot make antibodies without T cells.

Babies are usually born protected against sicknesses like tetanus, diphtheria, chickenpox, polio and most types of meningitis. After birth the antibodies start to gradually disappear from the baby's blood and by age 6 months they are practically gone. The amount of antibody in the blood is shown by the Immunoglobulin G (IgG) level.

Babies with SCID can't produce IgG so once the IgG from the mother has gone, they easily get the types of infections that antibodies are good at preventing.

How is SCID diagnosed?

The diagnosis of SCID in babies is based on a number of findings, including:

- very low numbers of T cells (T lymphocytes) in the blood
- the T cells that do exist do not work properly
- an inability to make antibodies
- very low levels of gammaglobulin or immunoglobulins in the blood once the antibodies of the mother have disappeared (around a few months of age)

Children with SCID are prone to infections

Babies with SCID are susceptible to severe infections of the lungs, especially by Pneumocystis carinii or by cytomegalovirus (CMV). Symptoms include poor growth rate and chronic diarrhoea. It is extremely important for survival beyond the age of two years that infections are properly treated and the condition is corrected at an early age. Exact diagnosis of the cause or causes of infections is vital, as this allows the correct antibiotics to be chosen. Sometimes this means doing a lung biopsy to take a sample of infected lung tissue to test for viruses and other microbes.

Treatment options depend on the cause of SCID

Depending on the cause of SCID, there are three main treatment options, in addition to specific treatment of infections with appropriate antibiotics:

1. Deficiency of adenosine deaminase

Deficiency of the enzyme Adenosine Deaminase can sometimes be treated by replacing the missing enzyme with injections of purified enzyme, which has been specially treated. This special treatment makes the enzyme last long enough in the blood for it to work.

2. Missing antibodies or immunoglobulins

These can be replaced by immunoglobulin replacement therapy.

3. T cell disorders

These can only be corrected by bone marrow transplantation. Bone marrow transplantation provides a new source of T cells. The purpose of bone marrow transplantation is to give the child with SCID a new source of bone marrow stem cells. Stem cells are so named because of their ability to develop into all types of blood cells including T cells and B cells which produce antibodies. The success of bone marrow transplantation varies according to the:

- severity of SCID
- number of infections, especially around the time of the transplant
- type of treatment the bone marrow has to receive to reduce the risk of rejection, such as removal of the T cells (or 'T cell depletion') - bone marrow contains T cells which can recognise that tissues of the patient are foreign to the donor's tissues
- need for conditioning, whereby the bone marrow of the patient with SCID is suppressed prior to transplantation, to improve the ability of the new marrow to grow properly (or 'take')
- source of the bone marrow - transplantation of bone marrow cells from a family member with identical 'tissue typing' of human leukocyte antigens (HLA) greatly decreases the risk of rejection and of graft-versus-host disease (see below). For cases where an HLA identical sibling is not available it has been

found that most children with SCID can receive bone marrow from either parent, although T cell depletion and conditioning may be required.

Cord blood transplants may be an alternative to bone marrow transplants

It has recently been found that blood taken from the umbilical cord and afterbirth contains high numbers of stem cells. Cord blood harvested from the afterbirth may therefore be an alternative to bone marrow for transplantation.

Graft versus host disease

The bone marrow or cord blood stem cells need to come from a healthy donor with normal immune function. The transplant cells are inevitably contaminated with T cells from the donor. These T cells can recognise the foreignness of the patient's tissues and start to attack them (as would happen if the T cells were still in the donor and were called upon to reject an invader like a tumour, skin graft or infection). This attack causes a condition called graft versus host disease (GVHD). A patient with GVHD might develop fever, measles like rash or diarrhoea and it can be very serious. Strategies to reduce the risk of GVHD include:

(i) selection of a donor with matching tissues (HLA matching)
(ii) T cell depletion of the donor marrow
(iii) preventative drug treatment after the transplant (such as cyclosporine or methotrexate).

Immune function gradually restores after transplantation

After a successful bone marrow transplant immune function is gradually restored, taking about a year to be fully developed. Even though a 'take' of the bone marrow can usually be diagnosed within a month of the transplant, it is generally much longer before the child can be considered to be cured of the SCID condition and no longer in danger of serious infections. During that time children are usually kept isolated, especially from other children. They receive immunoglobulin replacement therapy and antibiotics to prevent some of the most common serious infections that can affect children with this condition. After a year they can start to have childhood immunisations.

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

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

- Immune Deficiencies Foundation of Australia (IDFA) www.idfa.org.au
- Immune Deficiencies Foundation of New Zealand (IDFNZ) www.idfnz.org.nz

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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