

Severe Combined Immunodeficiency

Introduction

This booklet is intended for families who have a baby diagnosed with Severe Combined Immunodeficiency (SCID). We hope that it will help you to understand something about this disorder, and help you to manage the first few weeks and months after the diagnosis has been made.

What is SCID?

'SCID' is the name given to a group of rare inherited disorders which cause severe abnormalities of the immune system. This happens when white blood cells, responsible for fighting infection, are missing or working poorly. Their absence or poor function results in serious and often life threatening infections. Three types of white blood cell can be affected: T and B lymphocytes and natural killer (NK) cells ([see diagram below](#)). Not all cases of SCID are identical but all children with SCID have poorly working immune systems and will need protection from infection.

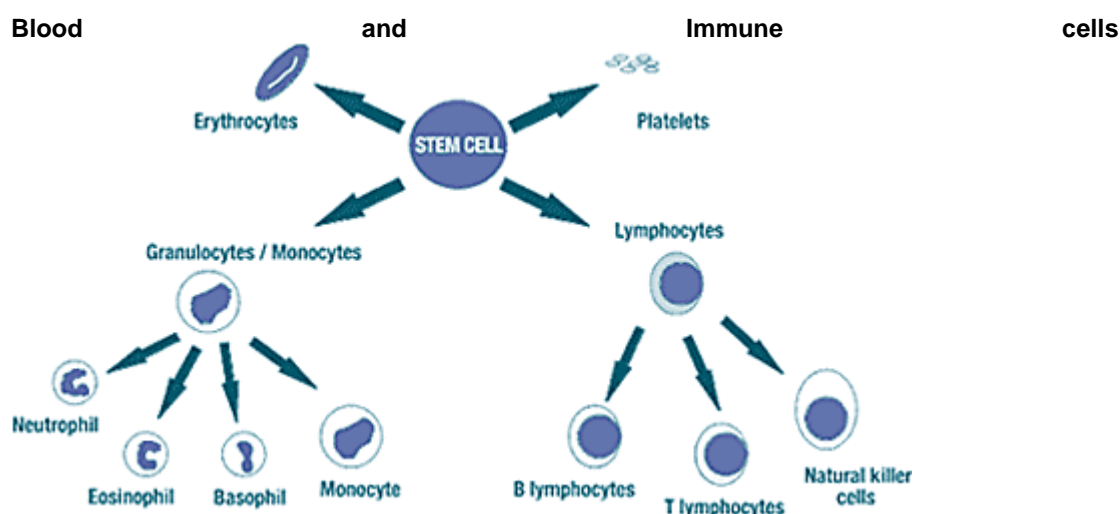
The first case of SCID was reported in 1950 and, following a number of isolated reports of affected children, the term SCID was introduced to describe the syndrome. Before the advent of modern medication and treatment, most affected babies did not survive beyond their first year. Today we understand much more about SCID. Treatment is now available that can reduce the risk of serious infection, and in many cases, cure the disorder.

About blood cells and immunity...

Just under half of the volume of blood consists of blood cells which are tiny and can only be seen if you look down a microscope. The rest of the blood volume is plasma, a watery liquid which contains dissolved proteins, sugars, fats, salts and minerals.

There are three main types of cells in the blood which you may have heard of: red blood cells, white blood cells and platelets. It is the white blood cells that play an important role in defending the body against infection. All blood cells are derived from immature cells known as a stem cells, sometimes referred to as "mother cells". Some stem cells can be found in the blood, but the richest supply is found in the bone marrow.

The following diagram will help you to understand which blood cells are affected in SCID and will be useful to refer to during discussions about the condition.



Stem cells are cells that are capable of giving rise to all blood cells.

Red blood cells are also known as erythrocytes or red blood corpuscles. They contain haemoglobin which transports oxygen to all parts of the body.

Platelets or thrombocytes play a vital role in blood clotting or coagulation. Low levels of platelets may cause bleeding that is difficult to control.

White blood cells or leukocytes protect the body against infection and fight it when it occurs. There are three main types of white blood cell: granulocytes, monocytes and lymphocytes.

Granulocytes: The most common granulocytes are called neutrophils. They are responsible for isolating and destroying invading bacteria, literally 'swallowing' bacteria. For this reason they are known as phagocytes. Other granulocytes are eosinophils and basophils and play a part in allergic reactions.

Monocytes: These play a role in protecting against certain infections such as fungal infection and tuberculosis (TB) and in cleaning up debris from sites of infection or injury. They can leave the blood stream and are then referred to as tissue macrophages.

Lymphocytes: These play a central role in the immune system. There are several different types of lymphocytes and these are the blood cells specifically affected in SCID:

B Cells sometimes referred to as B lymphocytes, recognise and attack germs or foreign attackers. They produce specific antibodies that fight a specific invader. These antibodies are sometimes referred to as gammaglobulins or... **Immunoglobulins** These work by recognising and binding to infecting organisms, 'marking' them for destruction by other cells in the immune system. There are five main types of antibodies: IgA, IgD, IgE, IgG and IgM, of which IgA, IgG and IgM are the most common.

T Cells also known as T lymphocytes, also recognise and attack specific germs or foreign attackers. They play an important role in co-ordinating the immune defences and kill organisms by secreting toxic chemicals called lymphokines. T cells are especially important for killing viruses.

NK Cells or Natural Killer cells are able to kill cells directly. They kill a variety of target cells (eg. tumour cells, virus infected cells, transplanted cells).

What causes SCID?

SCID is caused by a defect or mutation in a child's genetic make-up. It is an inherited condition - passed on in families in the same way as physical characteristics are passed from parent to child.

It may be helpful to explain the background. In the centre of every cell in our bodies there are 46 string like structures known as chromosomes. The chromosomes are arranged into 23 matching pairs. For ease of identification the chromosome pairs are numbered according to size from one to 23. The last pair - number 23 - are the sex chromosomes which determine whether a child is male or female. Think of each pair of chromosomes as a double string of thousands of beads. Each bead is a gene. Each gene is responsible for a certain characteristic (hair colour for instance).

Scientists know that each gene is responsible for producing a particular protein many of which are necessary for the development of a normal immune system. A defect in one of these genes results in absence of the protein that is necessary for a functioning immune system. There are a number of different genes that can be affected, each causing a different type of SCID.

These important findings now enable doctors to make a much more specific diagnosis. The names given to the different types of SCID are based on the particular protein or gene that is deficient - for example you may hear the terms gamma chain deficiency, JAK 3 kinase deficiency, purine nucleoside phosphorylase (PNP) deficiency, adenosine deaminase (ADA) deficiency, MHC class II deficiency or recombinaise activating gene (RAG) deficiency.

How is SCID inherited?

There are two main ways in which SCID can be inherited. These are autosomal recessive type inheritance and X-Linked inheritance.

Autosomal Recessive Type Inheritance: We are all carriers of around three to five different genetic disorders. Most often we never know about them because the fault lies in one gene of one chromosome and the other healthy half of the pair switches on to compensate for the faulty one. A problem only arises if your partner carries the same faulty gene as you, and your child inherits both faulty chromosomes (see diagram on page 6). If coincidentally both parents carry the same faulty gene, there is a 25% chance of the child inheriting the two affected copies (and therefore developing SCID), a 25% chance of inheriting the two unaffected copies (in which case there are no problems) and a 50% chance of inheriting one faulty gene from either one of the parents, thus making the child a carrier. Because undetected gene mistakes may be found in several family members, autosomal recessive inheritance is most common in children whose parents are related to each other. Approximately 60% of all cases of SCID are inherited in this way.

X-Linked Inheritance: In X-Linked SCID (otherwise known as gamma chain deficiency) the faulty gene is carried on the X chromosome (one of the sex chromosomes). Females have two X chromosomes, men have one X and one Y. A mother will pass on one of her X chromosomes to her baby while a father will pass on either an X or Y chromosome thus determining the sex of the child. If the mother has an affected gene on one of her X chromosomes there is a 50% chance that her child will inherit the affected one, and a 50% chance of inheriting the unaffected one.

If the affected gene is inherited and the child is a girl, the father's healthy X chromosome will compensate for the affected one passed on by her mother and the girl will be a carrier. If the child is a boy, the father will have passed on his Y chromosome which is not able to compensate for the affected X chromosome and the child will have SCID. Hence only boys will inherit X-Linked SCID, girls can only be carriers.

If a mother carries the affected gene for X-Linked SCID, there is a 25% chance of having either: an unaffected boy; an affected boy; an unaffected girl or a carrier girl (see diagram below). Approximately 40% of all cases of SCID are thought to be caused in this way.

Figure 1: Autosomal Recessive Inheritance

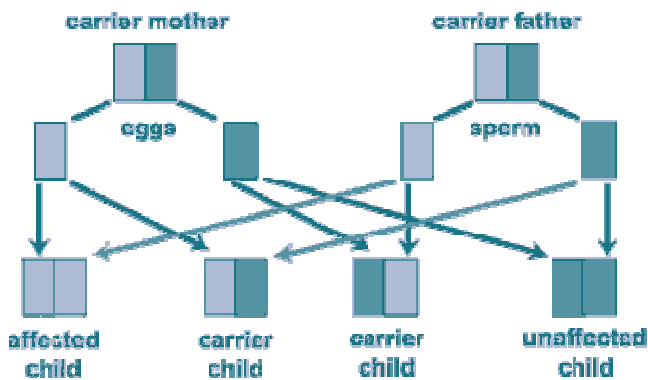
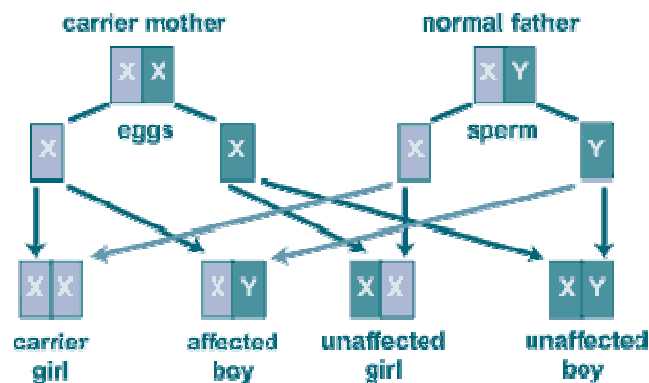


Figure 2: X-Linked Inheritance



What does SCID mean for my baby?

Sometimes, babies seem well at birth and for the following weeks. This is probably because they are partly protected by antibodies passed from mother to baby across the placenta during the last few months of pregnancy.

However the first signs of problems generally occur within the first three to six months. As your baby's immune system is not working properly, he or she will become highly susceptible to infection. You are likely to find that your baby suffers infections more frequently than other children - run of the mill problems such as coughs and colds will seem more severe and last longer than would usually be expected, requiring repeated and prolonged courses of treatment. The more common childhood infections such as thrush (candida), chicken pox (varicella), measles virus (rubella) and cold sore virus (herpes simplex) can also be dangerous for a baby with SCID and may even be life threatening.

Germs in the environment which children are often exposed to, but do not cause disease if the immune system is healthy, can be devastating for a child with SCID. In particular pneumocystis carinii (PCP), aspergillus, cytomegalovirus and cryptosporidium are examples of infections that can cause severe pneumonia, liver disease and severe diarrhoea in children with SCID.

As a result of repeated infections, your baby may not feed well and may not gain weight as fast as you would expect. Many infants with SCID suffer from chronic diarrhoea even when an infection cannot be identified, and this also contributes to poor weight gain. Skin rashes are common, and may be caused by candida infection (thrush), or sometimes by a reaction in the skin caused by maternal blood cells which have crossed the placenta at birth.

How is a diagnosis made?

Before parents know their baby has SCID many seek help from their GP because of repeated infections, poor weight gain or feeding problems. If you or your GP are worried about a possible problem, your GP usually makes a referral to a local paediatrician. Sometimes the first indication that something is wrong can be a serious life threatening infection which causes a rapid deterioration in the baby's condition. It may be necessary for the baby to be admitted to an intensive care unit for emergency treatment. During the course of routine investigations, SCID may be suspected.

Depending on the type of SCID, it may be possible to diagnose or at least suspect the disorder by performing a simple blood test known as a full blood count. However, it will be necessary to perform more specialised immune blood tests to confirm this.

Once SCID is suspected, your child will be referred to a specialist centre.

What will happen to my child?

There are two specialist centres in the country that care for and treat children with SCID - here at Great Ormond Street Hospital for Children and at Newcastle General Hospital.

Your child will be referred to one of these centres, and will usually in the first instance need to be admitted. The immediate priorities will be to provide a environment which protects from infection, the appropriate tests and assessments made and initial treatment given. You and your family will also need time to learn about SCID and will need time to ask questions and discuss all aspects of care with the team members.

Preventing infection is the most important aspect in the management of SCID. Your child will normally be admitted to a room or an area with 'filtered air' (to remove germs). Your child will usually be restricted to this room and will not be able to mix with other children or go to the playroom. This can be one of the most difficult aspects of SCID. No baby likes to be separated from those closest to them. You will be able to stay with your baby and will be encouraged to continue to feed, care for and play with him or her as much as you want. While the doctors, nurses and play specialists you meet will be very closely involved, they can never be a substitute for you. Your baby will need you and close members of the family for as much time as you can possibly give. You will be told about the ways that you can avoid passing on infection, such as washing your hands thoroughly. If you have a lot of family and friends it will be necessary to keep visitors to a minimum too.

Tests and assessment

Soon after admission it will be necessary to perform further blood tests to confirm the diagnosis of SCID. It is possible to examine all the different blood cells and determine which cells are missing or working poorly. More specialised tests will be carried out to determine the precise genetic abnormality. A range of investigations will be necessary to see if your baby has any undetected infection and will include chest X rays and scans and samples of blood, urine, faeces, and mucus from the throat.

What treatment will my child need initially?

Most children with SCID will have similar symptoms and will receive the same treatments whatever the type of SCID.

If your child is having many blood tests and needs a number of intravenous medications, or intravenous nutrition, it is usual to put in a central line (sometimes called a central venous catheter catheter). This is a latex tube which is put into a large vein and fixed to the skin surface usually on the chest, under general anaesthetic. It requires a small operation to put it in, but it allows blood to be taken and medicine to be given without the need for any needles.

Medication: Your child will need antibiotics, anti-viral and (in some cases) anti-fungal medicines to protect against serious infection. Most medicines can be given in the form of syrups. If your baby has an infection it may be necessary to give the medicines into a vein, through a drip.

Immunoglobulin (antibody) therapy: Your child will not be able to produce enough natural antibody to fight infection. It is possible to replace some of the missing antibody by giving treatment with immunoglobulin. Immunoglobulin is a solution of purified human antibodies which have been removed from normal blood donations. It provides temporary protection against infection and it is given either intravenously (into a vein) or subcutaneously (injection into the skin). Your child will receive regular immunoglobulin therapy from the time of diagnosis up until approximately six months after a bone marrow transplant. Because it is derived from donor blood, giving immunoglobulin carries a small risk of transmitting viruses. You will have the chance to discuss immunoglobulin therapy in more detail and the method by which it will be given with the immunologist or nurse specialist caring for your child before treatment starts.

Blood Transfusions: Your child may need blood, platelet or plasma transfusions. It is important that these treatments are given, but precautions need to be taken first. If your child needs a transfusion, he or she will receive specially prepared 'irradiated' blood. Irradiating donor blood preserves the red blood cells and platelets but removes any immune cells which may cause a bad reaction. The donor blood will also be screened to ensure it does not contain a virus called cytomegalovirus (CMV) - which could cause problems for a child with SCID. Your child's blood, platelet or plasma transfusion will be labelled "CMV negative" and "irradiated".

Further support your child may need

Feeding: If you are breast-feeding we will do our best to encourage and support you to continue. Facilities are available for you to express and store your breast milk when necessary. Whatever your chosen method of feeding, it is possible that despite all efforts to maintain sufficient feeding, your baby may need some extra calories, vitamins and minerals. These can be given in special drinks or medicines. If your baby has difficulty taking enough feed he or she may need to be given extra feeds through a naso-gastric tube (a tube inserted into the stomach through the nose). If your baby is still not tolerating feeds it may be necessary to give feeding called TPN (total parenteral nutrition), in which all the nutrients and calories are given intravenously, directly through a drip into a vein.

What does SCID mean for the family?

Your baby will need all the love and attention you can possibly give, and parents need to call upon all their inner strength to share their love and support amongst the family. It is to be expected that repeated hospitalisation, separation from extended family, blood tests and uncomfortable procedures will contribute to a great deal of stress and anxiety and even guilt. While all health care professionals work as a team to help you through, it is vital that parents identify ways to help them cope with the overwhelming and unexpected demands this will put upon them.

In addition to supporting your sick child you may have other children who will feel left out. Recruit as much help as possible from family and friends to enable you to spend some "special" time with your other children.

You will need to spend time and energy in maintaining relationships with your partner too. During difficult times some parents can feel very close and united, sharing decisions and helping each other cope with the overwhelming problems they face. However most couples at some time or other will find it very difficult to cope with the immense demands put upon them while at the same time maintaining their closeness and unity. With so many other things to think about it is easy to forget to make time to talk to your partner. Ask about support groups and counselling services. Having a sick child tests even the strongest relationship so don't be afraid to ask for help early.

As part of our regular care for you and your child we have a team psychologist and team social worker who may be able to help you with the particular problems you are facing. They are available to discuss your worries and help you to identify sources of help should you wish to.

Can I care for my baby with SCID at home?

Once your baby is established on all necessary treatment and is gaining weight, it may be possible to go home for a period of time before bone marrow transplant. The ward staff will contact your local doctors and community nurses beforehand to make arrangements if any particular treatments need to be given whilst you are at home. You will always be able to ring the hospital and speak to an immunologist or a nurse if you are worried at any time.

Whilst most parents are delighted to get home, it can be a worrying time. Anxiety about catching or passing on an infection can make life very stressful and you may worry that you might forget to do something or unwittingly pass on infection. Remember that your home is probably as safe, if not safer, than hospital as long as you take a few sensible precautions. The following information is intended as a practical guide to help you at home. If you have specific questions not covered here please always ask for advice from your doctor or specialist nurse.

Keeping your child safe at home

Infection is probably the greatest specific risk for a child with SCID whether at home or in hospital. Your home should be kept as clean as possible without going to extremes. You do not need to use elaborate isolation procedures, shampoo carpets or wash the walls. You simply cannot remove every germ from your home and so common sense precautions need to be taken without going over the top.

General household cleaning: The most useful thing is to dust and vacuum around once a week and give hard floors a wash with a mild detergent. In the kitchen, dishcloths and tea towels which harbour infection should be washed regularly. Paper towel is preferable for drying hands and soaking up spills. Kitchen surfaces should be cleaned with a mild detergent or disinfectant. Bathroom floors and equipment such as sinks, baths, bidets, showers and loos should be washed with a mild disinfectant around once a week. Children's toys which may have got dirty with sticky hands or saliva should be rinsed with warm soapy water. Bed linen should be laundered around once a week. You do not need to wash your child's clothes separately or with any special soap powders.

Feeding and food hygiene: The hospital dietician will advise and help you regarding feeding your child at home. Tap or bottled water may very rarely contain germs harmful to children with incomplete immunity. All drinking water, whatever the age of your child, should be boiled and cooled before drinking. If you are bottle feeding, continue to sterilise all bottles and teats. As for all small babies, scrupulous hand-washing with a mild soap before making feeds and careful preparation and storage of milk are vital in order to prevent food poisoning infections. Check that your fridge works properly and if you are cooking all your own baby food, be extra careful to cook foods thoroughly and use only the freshest ingredients. In order to reduce the risk of food poisoning, certain foods with a high bacteria content should be avoided such as unpasteurised milk and cheese, all soft cheeses, raw eggs, paté, honey, raw shellfish and supermarket pre-packed pre-washed foods. Higher risk foods such as take-away foods and pre-prepared meals should also be avoided as much as possible. Eating utensils can be washed along with the household washing up or in the dishwasher. Dry utensils well before storing them.

Personal hygiene: Caring for your child's skin is vital so examine your baby in all the cracks and crevices for sore areas or spots and rashes. The use of barrier creams and regular nappy changes are important to prevent sore areas developing. If your child has any teeth, make sure you brush them twice a day, and watch out for oral thrush (white spots in the mouth). If you notice any possible signs of infection let your doctor know as soon as possible. As well as normal baby care, ensure that face cloths or sponges are washed regularly and that the changing mat and equipment are kept clean. Keep loo seats down to deter exploring hands.

Contact with others: As far as is practical keep visitors to your home, especially young children, to a minimum. However, brothers and sisters should be allowed to mix and play with your child with SCID unless they have cold sores, coughs or colds. People who have already had chicken pox are unlikely to pass on the disease to your baby. If anyone, including family members, comes in close contact with chicken pox before having had the disease themselves it is wise to keep them away. If you have older children at school who have not had chicken pox, ask the school to let you know if chicken pox is going round. If so you should telephone your immunology centre for advice. If a family member unexpectedly develops chicken pox at home you need to try to limit their contact with your baby and notify your immunologist as soon as possible who will tell you if any further treatment is necessary.

Going out: There is no need to remain inside your home feeling isolated. Fresh air and exercise are of great benefit. Enjoy walks in the park and in open spaces with a friend but avoid crowded or confined areas such as shopping centres, public transport, funfairs and cinemas. In the garden or park, it is best to put your child on a towel or rug - garden soil can be a source of serious infection especially if there is dog or cat litter around.

Smoking: Smoky environments are harmful for all babies and can make them prone to chest infections. If you or any family members do smoke and cannot give up, try to only smoke outside or keep well away from your child and his or her bedroom.

House renovations: Dust from building work, especially in old buildings, may contain a fungus called *Aspergillus* which can cause serious infection. Put off any major redecoration work you had planned on your home and avoid old buildings or building sites where major building work is being carried out.

Pets: Pets are important family members but they carry infectious organisms in their saliva and other secretions. If it is difficult to keep your child away from your pet, it may be appropriate to ask a friend to look after your pet for a few months. If not, try to restrict contact between your child and pet, keep your pet clean and healthy and always remind family members to thoroughly wash hands after handling or feeding them.

Vaccinations: For a baby with SCID, some vaccinations may be dangerous and others are ineffective and unnecessary. You should not let your child have live vaccines such as polio vaccination, measles mumps and rubella (MMR) or BCG. In addition, the polio virus can be excreted by people who have recently been immunised, so anyone in close contact with your child requiring polio immunisation should have the alternative 'killed polio' vaccine, which is available from your doctor. Your child will be receiving regular immunoglobulin treatment and this will provide protection against a number of germs including diphtheria, pertussis and tetanus (DPT). The normal triple vaccination programme is therefore unnecessary whilst the child receives regular immunoglobulin therapy.

Bone Marrow Transplant

Bone Marrow Transplant (BMT) offers the only long-term "cure" for SCID at present. The aim is to replace the faulty immune system with an immune system from a healthy donor. Healthy bone marrow is rich in stem cells, from which all the cells of the immune system develop, and it is possible to take bone marrow from a healthy individual and give it by transfusion into the child with SCID. A BMT is not an operation like a heart or kidney transplant. Stem cells contained in the donor bone marrow are able to find their way from the bloodstream to the child's bone marrow where they start to produce healthy blood cells. A BMT does involve a number of risks, and complications can arise - some of which are temporary, others of which can be life-threatening.

You will have the opportunity to discuss this in detail with your immunologist and BMT consultant on a number of occasions. Early during your stay in hospital, blood will be collected from your family to determine the tissue type of each of the immediate family members. If a family member is found to have an identical, tissue type to the affected baby, he or she will be selected to be the bone marrow donor. If there is no suitable family donor an unrelated donor will be sought from the world-wide donor panels. Donating bone marrow involves having a general anaesthetic but it is a relatively minor procedure, involving minimal risk to the donor. Before the BMT can be arranged you will meet members of the transplant team who will ensure that you have ample opportunity to see the BMT unit, discuss your worries and to ask questions. The BMT will usually be carried out in your own room on the BMT unit and you will be admitted a few days before the chemotherapy drugs are given.

It is usually necessary to have chemotherapy drugs to prepare the body to receive a new immune system. Chemotherapy is given to reduce the chance of rejection of the new bone marrow by the child's own immune cells. If a perfectly matched bone marrow donor has been found within the immediate family then chemotherapy is not always necessary. However, in all other circumstances chemotherapy is required. Not all children will receive exactly the same drug combinations. There are a number of side effects related to chemotherapy which you should know about. This and other information is covered in detail in the Primary Immunodeficiency Association booklet "Bone marrow transplantation for Primary Immunodeficiencies".

In the future...

Now, more than ever, developments and improvements are being made that are transforming life for children with SCID. Better diagnostic techniques and genetic technology, better treatments and better medications enable children with SCID to proceed through bone marrow transplant safely. The future too holds some exciting developments.

Gene therapy is currently undergoing clinical trials in selected patients and has been successful in correcting or 'curing' a small number of children affected by X-linked SCID. Gene therapy aims to correct the underlying genetic abnormality causing SCID. For the child, gene therapy is a relatively straightforward procedure and if successful would offer a cure. The process being tested involves taking stem cells from an affected child's blood or bone marrow and then, under laboratory conditions, manipulating and correcting these cells using complex gene technology. Once corrected the cells are returned a few days later by transfusion into the child. As in a bone marrow transplant, these new stem cells find their way to the bone marrow where they start to produce healthy immune cells. This is known as somatic gene therapy - altered genetic material is only present in the child's own immune cells and cannot be passed on to offspring. People worry about the idea of gene therapy because of the possibilities of eugenics (generating an improved population through selection of its best characteristics for breeding). Manipulating genes that can be passed on to offspring is known as germ line gene therapy and is not permitted by law.

Pre-natal diagnosis and screening

If you have a family history of SCID and you or close members of your family are planning future pregnancies, it may be possible to offer you genetic counselling and pre-natal diagnosis. You should let your doctor know if you are planning a baby or as soon as you find out you are pregnant.