Inherited Immune System Disorders
Severe Combined Immunodeficiency (SCID)

Inherited immune system disorders are diseases in which part of the body's immune system is missing or does not work. People with an immune system disorder are less able to fight infections. While these disorders are rare, there are about 100 different types, which range from mild to severe. About 50,000 people in the United States have some type of inherited immune system disorder.

Inherited immune system disorders are also called primary immune deficiency disorders. They are called “primary” because they begin in a gene that affects the immune system. Genes carry an inherited code of instructions that tells the body how to make every cell and substance in the body. (Secondary immune deficiencies are caused by something outside the body, such as a virus or chemotherapy.)

Immune system disorders and transplant

People with severe inherited immune system disorders are at high risk for life-threatening infections. For some severe disorders, the only known cure is a bone marrow or cord blood transplant (also called a BMT).

Severe Combined Immunodeficiency (SCID) and Transplant

Severe combined immunodeficiency (SCID) is the name for a group of inherited immune system disorders. SCID disorders are the most severe of the inherited immune system disorders. Babies are born with these disorders, which can become life-threatening within the first year of life. SCID is rare. About 1 in 500,000 babies are born with SCID.

Causes of SCID

Inherited immune disorders are also called primary immune deficiency disorders. They are caused by a mutation (mistake) in a gene that affects the immune system. Genes carry an inherited code of instructions that tells the body how to make every cell and substance in the body.

Some types of SCID are caused by a gene mutation on the X chromosome, which comes from the mother. Disorders inherited on the X chromosome appear only in males. A female with the mutated gene will not have the disease but will be a carrier. This means she may pass the mutated gene on to her children.

Other types of SCID appear when a gene mutation is inherited from both parents (the child has two copies of the same gene mutation). These disorders appear in both males and females. In most cases, no one knows what causes the mutation to appear the first time. Once a mutation appears, it can be passed from parent to child through many generations.
SCID and the Immune System
The immune system is made up of organs and cells that work together to protect the body from infection and disease. The immune system uses white blood cells to fight infections. The white blood cells mark and attack cells that they do not recognize as belonging in the body.

There are several types of white blood cells, each with its own role. In children with SCID, the immune system does not work well because of problems with certain types of white blood cells known as lymphocytes. There are three types of lymphocytes:

- B cells make antibodies. Antibodies attach to foreign cells and mark them to be attacked.
- T cells direct B cells to make antibodies against foreign cells. T cells also direct the rest of the immune system when to attack or stop attacking foreign cells. They also help in the attack.
- Natural killer cells (NK cells) destroy infected cells and cancer cells.

The three types of lymphocytes work together, and all three types are needed for the immune system to function normally. In children with SCID, the T cells and, in some cases, also the B cells do not work well or do not develop. Sometimes, the natural killer (NK) cells are affected as well.

Symptoms and Diagnosis of SCID
Children with SCID are at risk for life-threatening infections. From their first months of life, they have infections that may be frequent, severe, long-lasting or hard to treat. Infections may occur in the lungs (pneumonia), around the brain and spinal cord (meningitis) or in the blood stream. Many babies also get diarrhea that does not go away. Babies with SCID do not gain weight or grow at a healthy rate (failure to thrive). A baby diagnosed with SCID needs immediate treatment. Without effective treatment, most children with SCID die of infection with failure to thrive within the first year of life.

Diagnosis
If a baby shows signs of a possible immune disorder, a doctor can do a blood test to count the number of lymphocytes (the white blood cells affected in SCID) and test their function. Babies with SCID will have very low numbers.

Families affected by SCID may want to talk with a genetic counselor about family planning and the chances of having children with the disorder. Early diagnosis can enable early treatment and improve a child’s chances of a good outcome.

Types of SCID
There are several types of SCID. Two of the more common are:

- Classical X-linked SCID – Almost half of patients with SCID have classical X-linked SCID (sometimes called “boy in the bubble” disease). It is inherited on the X chromosome and appears only in boys.
- ADA deficiency SCID – About 15% of patients with SCID have adenosine deaminase (ADA) deficiency. These patients have low levels of the enzyme ADA. Lack of ADA leads to low numbers of T cells and B cells. This type of SCID can appear in either girls or boys.
Treatment for SCID

Preventing Infections
For children with SCID, the first concern is to prevent infections. Children with SCID need to be protected from germs. This includes keeping them away from crowds and sick people. They are often treated with antibiotics to prevent infection.

They will also be given intravenous immune globulin (IVIG). Immune globulin is also called immunoglobulin or gammaglobulin. It contains antibodies that would normally be made by healthy B cells to help the body fight infection. Immune globulin is usually infused into a vein. Patients with SCID will probably get one IVIG infusion a month. Each infusion may take from one to five hours. Treatments may be given in a doctor’s office, hospital outpatient unit or at home. Many people have no side effects from IVIG infusion, but some people may have side effects such as chills, headaches, fever, nausea and chest tightness. These can usually be controlled with medicine or adjustments to the rate of infusion.

Enzyme Therapy for ADA Deficiency SCID
The standard treatment for ADA deficiency SCID is treatment with a form of the ADA enzyme called PEG-ADA. Treatment with PEG-ADA is effective in about 90% of children. However, some also still need IVIG treatments.

Gene Therapy
A treatment option being studied in clinical trials is gene therapy. Gene therapy has been a successful treatment for some patients with ADA deficiency SCID. At first, gene therapy also appeared to be a promising treatment for X-linked SCID, but some children treated with gene therapy developed leukemia. New trials of gene therapy are in progress.

Transplant and SCID
The only known cure for SCID is a bone marrow or cord blood transplant (also called a BMT).

A bone marrow or cord blood transplant replaces the child’s abnormal blood-forming cells with healthy blood-forming cells from a family member or unrelated donor or cord blood unit.

The donor must closely match the patient’s tissue type. The best donor is usually a matched sibling. Each sibling has a 25% chance of being a suitable match, but since SCID is inherited, many children with SCID do not have a healthy matched sibling. Doctors may also use one of the child’s parents or another partly matched family member as a donor. Each parent’s tissue type matches half of the child’s tissue type (a haploidentical match). Haploidentical transplants have had disappointing outcomes for many other diseases treated with transplant. However, for SCID, survival rates have been high enough to make them a good option for patients who do not have a matched sibling donor.

For children without a suitable family donor, doctors may search the National Marrow Donor Program (NMDP) Registry for an unrelated adult donor or cord blood unit.

Unlike transplants for most other diseases, a transplant for SCID may not include a preparative regimen of high-dose chemotherapy. The preparative regimen destroys cells in the bone marrow to make room for the donated cells. It also destroys immune cells so they cannot attack the donated cells. Some children with SCID do not need a preparative regimen because they have so few immune cells.
Factors that Affect SCID Transplant Outcomes
Patient, disease and transplant factors can affect a child’s chances of survival and his or her quality of life after transplant. In general, a child has a higher likelihood for a good outcome when:

- A transplant is done early, within the first few months of life, if possible.
- The child has not had severe infections or shown a failure to thrive.
- The child has a type of SCID with normal B cell function.
- The donor is a close match. A matched sibling offers the highest likelihood of success, but a partly matched (haploidentical) family member or an unrelated donor or cord blood unit can also provide a good outcome.

Whether or not a preparative regimen is used can affect some of the risks of a transplant. Without a preparative regimen, a child avoids risks of serious side effects from the high-dose chemotherapy. However, other risks are increased. The risk that the transplant will not engraft (make new blood cells for the body) is slightly higher. The risk that the child will not develop the B cell function needed for a normal immune system may also be higher. A child who does not develop normal B cell function will need ongoing treatment with IVIG to help his or her immune system fight infection.

Whether or not the donor’s cells are filtered to remove T cells (T-cell depleted) can also affect the outcome. T cells play an important role in the immune system, but they are also involved in a transplant complication called graft-versus-host disease (GVHD). GVHD can range from mild to life-threatening. Whether or not the transplant is T-cell depleted depends on the donor used and the transplant center.

Making Treatment Decisions
If your child has SCID, it is important to see a doctor who is an expert in these disorders. If your doctor has not treated other patients with SCID, ask him or her to refer you to an expert for consultation.

A doctor who is an expert in SCID can talk with you about the best treatment for your child and explain the possible risks and benefits. For children with ADA deficiency, enzyme therapy is the first option. For other types of SCID, the first choice may be a transplant. A transplant has serious risks and is not an option for all children, but it can offer some children with SCID the chance for a cure of their disease.

Transplant Timing and Limitations
In general, it is best to have a transplant as soon as possible. Children with SCID are at risk for dying of infection before they can receive a transplant. Children who have had severe infections or show failure to thrive may be too weak to tolerate a transplant.

The NMDP’s Office of Patient Advocacy (OPA) continually develops resources and materials to help patients, family members and doctors with questions about marrow or cord blood transplantation. In addition to print, audio and visual materials, OPA has bilingual (Spanish/English) case managers and LanguageLine interpreter services available for callers. All OPA materials and services are free and confidential. Call the OPA toll-free at 1 (888) 999-6743. Outside the United States call (612) 627-8140, or visit marrow.org/patient