



Genetic Fact Sheets for Parents

Other Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – [http:// www.newbornscreening.info](http://www.newbornscreening.info)

Disorder name: Severe Combined Immunodeficiency
Acronym: SCID

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This fact sheet has general information about Severe Combined Immunodeficiency (SCID). Every child is different and some of this information may not apply to your child specifically. Certain treatments may be recommended for some children but not others. If you have specific questions about SCID and available treatments, you should contact your doctor.

What is SCID?

Severe Combined Immunodeficiency (SCID) is the name for a group of inherited disorders that cause babies to be born without a working immune system. These disorders are also called primary immune deficiency disorders (PID). Newborns with SCID may seem healthy at first because their mother's immune system protects them from infections for the first few weeks of life. However, without necessary treatment, common infections and certain types of vaccines can be life threatening to these infants.

The immune system functions with the help of lymphocytes. Lymphocytes are a type of white blood cells made by the bone marrow.

There are two types of lymphocytes: T cells and B cells.

People with SCID have:

- a severe defect in their T cells, and
- B cells that do not work well.

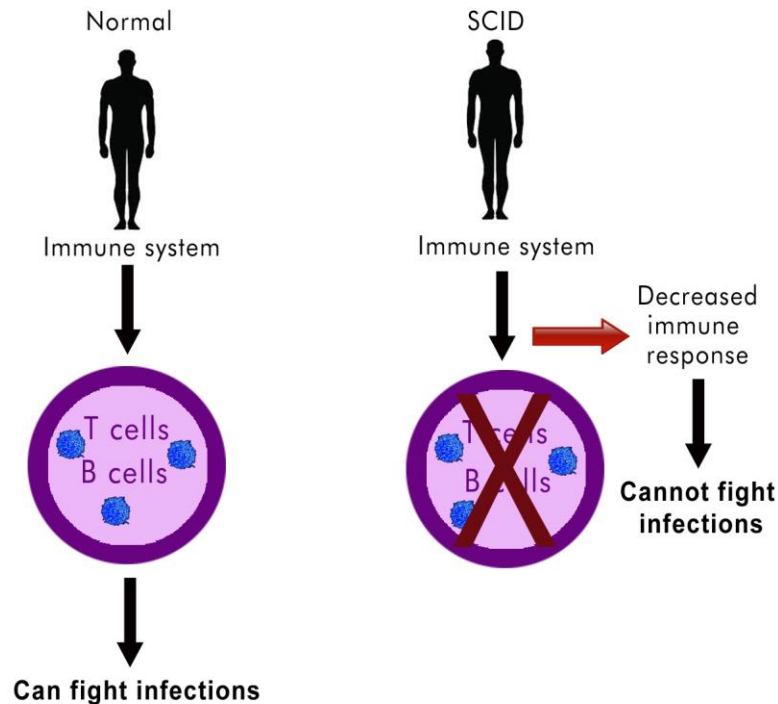
People with SCID are not able to fight off common infections. They also cannot make antibodies to protect themselves.

What causes SCID?

Genes tell the body how to function. People with SCID can have a change in one or more genes that cause SCID. Over 20 different genes are known to cause SCID. Variants, or changes to the DNA code in these genes cause the body to have little or no T cells and B cells. This means that the body is not able to defend itself and make the antibodies that are needed to fight infections. This causes common infections, like a cold or flu, to make the child very sick or may even lead to death.

T cells and B cells are normally made by the body. We cannot get them by eating. SCID is not contagious. You cannot get SCID from living with, touching, or spending time with someone who has SCID.

SEVERE COMBINED IMMUNODEFICIENCY (SCID)



What are the symptoms of SCID?

Symptoms of SCID are usually seen in the first year of life. They can be severe and lead to death. It is important to remember that each child with SCID is different and may experience symptoms differently. Symptoms of SCID may include:

- Failure to thrive (not gaining weight, or not growing at a healthy rate)
- Serious and/or life-threatening infections that happen more than once, are not easily treated, and do not get better with medicine. These infections can include:
 - Meningitis (brain infection)
 - Pneumonia (lung infection)
 - Sepsis (blood infection)
- Opportunistic infections (infections that do not cause disease in healthy people). These can include:
 - Pneumocystis pneumonia (a specific type of pneumonia)
 - Fungal infections
 - Viral infections
- Other infections that may happen more frequently include:
 - Otitis media (ear infection)
 - Sinusitis (sinus infection)

- Skin rashes/infections
- Yeast infections in the mouth or diaper area
- Diarrhea
- Liver infections

SCID does **not** affect a person's intelligence or their ability to learn. Once they get treatment, people with SCID can go to regular school and should be able to reach the same level of education as people without SCID.

An early diagnosis of SCID can lead to early treatment. This can improve the chances for a child to have a good outcome. If it is not treated, SCID will lead to death in infancy or early childhood.

What are the treatments for SCID?

For infants with SCID, the main focus is to prevent infections and treat any active infections.

For prevention, antibiotics and immune globulin may be used. Immune globulin (also called immunoglobulin or gammaglobulin) gives the body antibodies that would normally be made by the B cells. These antibodies help fight infections.

Infants with SCID should also avoid certain types of vaccines called live vaccines. Live vaccines (such as chickenpox, measles, rotavirus, oral polio and BCG and others) contain viruses and bacteria that are weakened and don't harm children with a healthy immune system. In patients with SCID however, these viruses and bacteria may cause severe, life-threatening infections.

Infants with SCID should avoid things that might expose them to CMV (cytomegalovirus). CMV is a common virus that most people have contracted and carry in their bodies. CMV usually does not cause serious symptoms in healthy infants. However, infants with SCID can get sick from CMV. Some sources of CMV include non-irradiated blood products and possibly breast-milk.

For active infections, aggressive antibiotic, antifungal, and antiviral medicines may be used.

Medicines and immune globulin are only short term treatment options. They can only keep patients with SCID healthy temporarily.

Patients with SCID need more permanent treatments. Treatment options are different depending on which type of SCID your infant has and other factors. Permanent treatment options include:

1. **Hematopoietic stem cell transplant (HCT) (also known as a bone marrow transplant):**

In most cases of SCID, children will need a bone marrow transplant (BMT). This is the only treatment that gives children a working immune system that is able to prevent and fight infections.

2. **Enzyme replacement therapy (ERT):**

Some cases of SCID are caused by a shortage of an enzyme called adenosine deaminase (ADA). ADA is found throughout the body but is most active in lymphocytes. A shortage of this enzyme leads to low numbers of T cells and B cells. Enzyme replacement therapy (ERT) with pegademase bovine (PEG-ADA) allows lymphocytes to recover. It may be a long-term treatment option for some children. It is not considered a cure, however, and HCT may still be needed.

3. **Gene therapy:**

Gene therapy can be used to treat SCID. Some clinical trials have shown positive outcomes for children, but this form of therapy is still being studied as there are some risks. Gene therapy is still an experimental treatment. Gene therapy is only available as part of a research study and is not FDA-approved yet. Currently, the only way to receive treatment with gene therapy is to participate in a clinical trial. People with SCID must meet strict eligibility criteria and be informed about the potential risks and benefits of being part of a clinical trial. Your medical team can talk to you more about gene therapy.

What happens when SCID is treated?

Infants with SCID are at risk for fatal infections the moment they are born. So, early diagnosis and treatment are very important. For example, infants with SCID who are treated with BMT before 3.5 months old have a 95% chance of long-term survival and of living a healthy life. BMT treatment after 3.5 months old leads to a 60-70% chance of long-term survival.

With early detection and treatment, patients with SCID are more likely to live healthy lives.

How is SCID inherited?

SCID is inherited in different ways depending on which gene is causing SCID in your family. The most common way SCID is inherited is called X-linked recessive. SCID can also be inherited in an autosomal recessive manner.

In some families, SCID is not inherited. This means that the baby is the first in the family to have SCID.

X-Linked Recessive

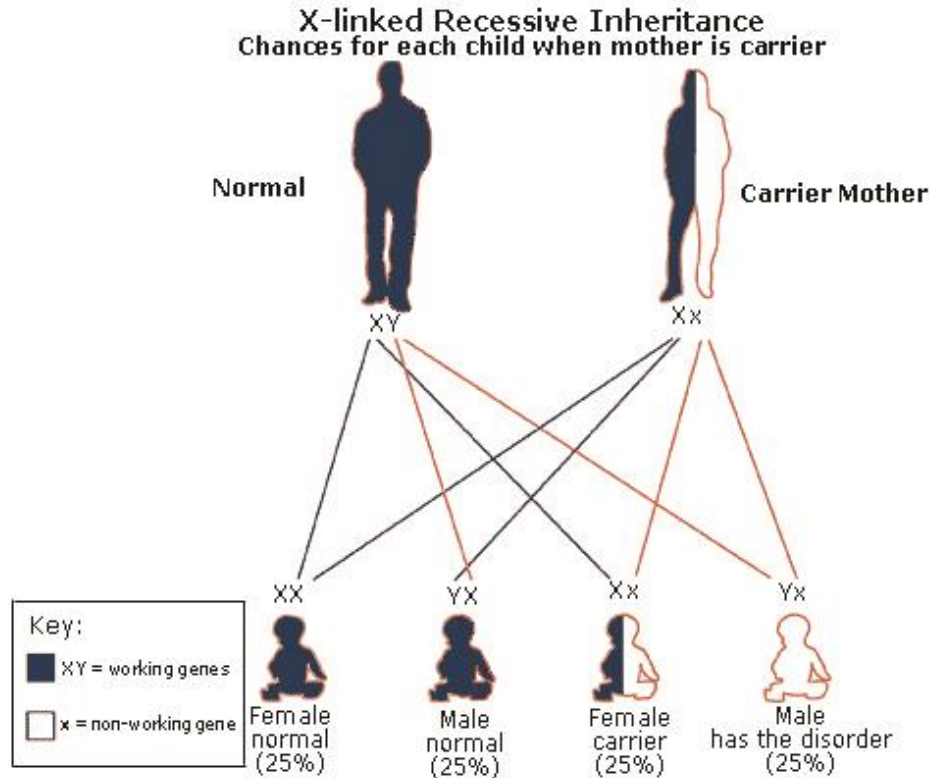
The most common type of SCID is inherited in an X-linked recessive manner. In this type of inheritance, the gene is located on the X chromosome, one of the sex chromosomes. The gene that causes X-linked SCID is called IL2RG. Genes usually come in pairs, with each parent giving one copy to their child. The sex chromosomes, however, are different.

A male inherits one X chromosome from his mother, and one Y chromosome from his father. A female inherits two X chromosomes, one from each parent. When a female has a non-working copy of the gene on one of her X chromosomes, she will not have SCID. This is because she has a second, working copy of the gene on her other X chromosome.

A male with a non-working IL2RG gene for SCID on his X chromosome will have SCID. This is because he does not have a second X chromosome with a working IL2RG gene. Because they only have one copy of the IL2RG gene, it is more common for males to have X-linked recessive SCID than females.

If a mother has one non-working IL2RG gene, she is called a carrier. For carriers, there is a 50% chance that each male pregnancy will have SCID. For carriers, there is a 50% chance that each female pregnancy will be a carrier, like her mother.

A father passes his Y chromosome to his sons and his X chromosome to his daughters. Therefore, if a father has SCID, none of his sons will have SCID and all of his daughters will be carriers.



Autosomal Recessive

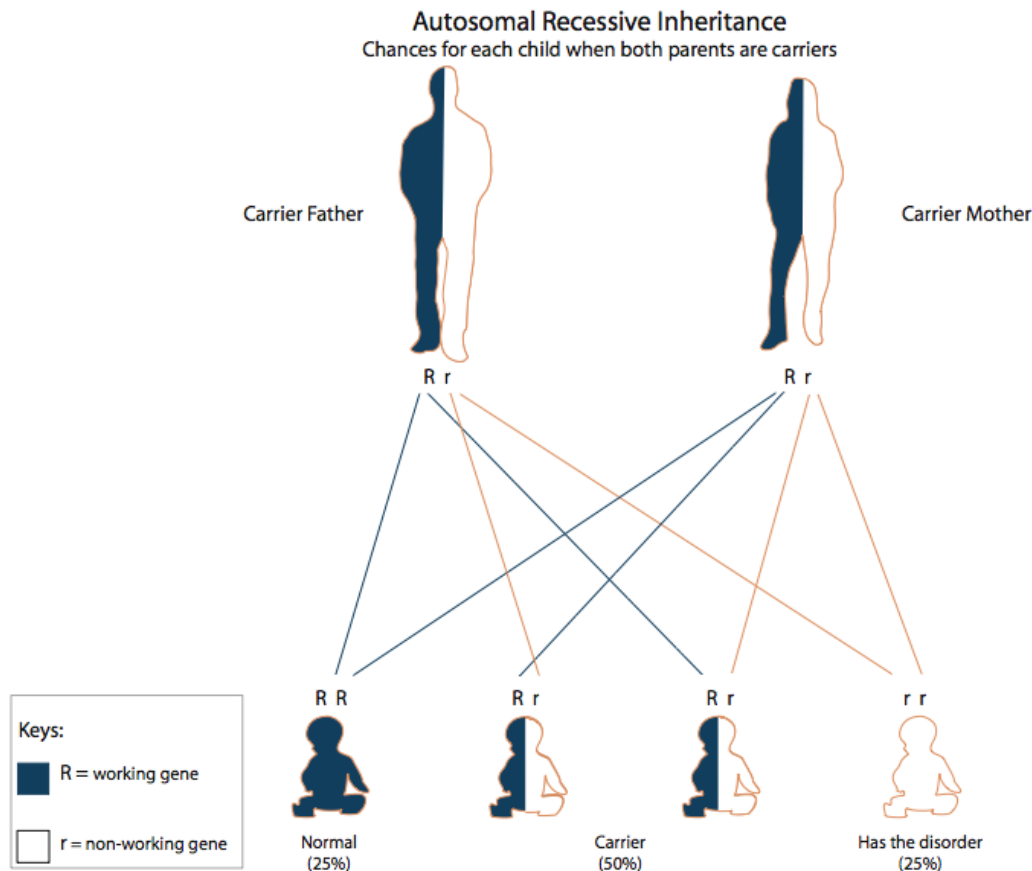
Some types of SCID are inherited in an autosomal recessive manner. There are many different genes that cause autosomal recessive SCID. This type of inheritance affects both boys and girls equally.

In autosomal recessive genetic conditions, we think about the genes other than those inherited on the sex chromosomes. These are the same in both boys and girls. Everyone has pairs of these genes, one from mom and one from dad.

Many genes help make our immune system work the way it should. In children with autosomal recessive SCID, a pair of genes does not work correctly. These children inherit one copy of the non-working gene from each parent.

Parents of children with autosomal recessive SCID are rarely affected, themselves. Instead, each parent has one non-working gene for SCID. They are called carriers. Carriers do not have SCID because their other copy of the gene works correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have SCID. There is a 50% chance for the child to be a carrier, just like the parents. There is a 25% chance for the child to have two working genes.



Genetic counseling is available to families who have children with SCID. Genetic counselors can answer questions about how SCID is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for SCID is available. Over 20 different genes can cause SCID. Genetic testing, also called DNA testing, looks for changes called variants in the genes that cause SCID. DNA testing is typically done on a blood sample.

Even if the genetic cause of SCID in your baby is unknown, he or she can still get therapy for SCID. This information can also be helpful in carrier or prenatal testing, discussed below.

What other testing is available?

Newborn Screening

Newborn screening for SCID is done in all states in the United States. A blood spot from a needle prick on a baby's heel is used to screen for many different conditions. Newborn screening for SCID is done by looking for T cell receptor excision circles (or TRECs for short). TRECs are found in every healthy newborn's blood. They are present when T cells are being produced. Since babies with SCID have few to no T cells, they also have few to no TRECs in their blood.

If a baby has a positive result on the initial SCID newborn screen, it does not mean that he or she has SCID. Low levels of TRECs in the blood can also be caused by prematurity, other less severe immune disorders, or other syndromes. It is also possible for a baby to have a positive screening result, but have a normal immune system. A positive newborn screening result means that further testing must be done to confirm or rule out SCID.

When a parent or both parents are known to be carriers of SCID, newborn screening results are not enough to rule out SCID in a newborn baby. In this case, diagnostic testing should be done, as well as newborn screening.

Confirmatory testing

Two types of testing are used to confirm SCID. These tests are called a complete blood count (CBC) and flow cytometry. These need a blood sample to measure the amount of lymphocytes in an infant's blood. DNA testing may also be done.

Infants who are confirmed to have SCID will then be referred to a pediatric immunologist or infectious disease specialist. The specialist will make recommendations for further treatment and management.

Can you test for SCID during a future pregnancy?

Prenatal genetic testing for SCID is only available if a genetic cause has already been identified in the family. If a genetic cause has been identified, DNA from the fetus can be removed and tested. The sample for this testing is obtained by either CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have SCID. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have SCID or be carriers?

Having SCID

If they are healthy and developing normally, older brothers and sisters of a baby with SCID are unlikely to have SCID. In some cases, siblings should also be evaluated for SCID. Talk to your doctor or genetic counselor if you have questions about your other children.

SCID carrier

Brothers and sisters who do not have SCID still have a chance of being carriers, like their parent(s). Each healthy brother and sister have a chance of being a carrier for SCID. Except in special cases, carrier testing should only be done in people over 18 years of age.

It is important for other family members to be told that they could be carriers. There is a chance they are also at risk to have children with SCID.

How many people have SCID?

The true incidence of SCID is unknown. It is estimated that about 1 in every 58,000 live births in the United States is a baby with SCID.

Does SCID happen more often in a certain ethnic group?

It seems that one of the autosomal recessive forms of SCID happens slightly more often in people of Native American ethnicity. In general, SCID can affect people of all ethnic backgrounds.

Does SCID go by any other names?

SCID is also sometimes called:

- Severe combined immune deficiency
- Severe mixed immunodeficiency syndrome
- Primary immune deficiency

Where can I find more information?

Immune Deficiency Foundation

<http://primaryimmune.org/>

The Jeffrey Modell Foundation

<http://www.info4pi.org/>

National Human Genome Research Institute

<http://www.genome.gov/13014325>

National Marrow Donor Program

http://marrow.org/Patient/Disease_and_Treatment/About_Your_Disease/Immune_System/Severe_Combined_Immunodeficiency.aspx

American Academy of Allergy, Asthma and Immunology

<https://www.aaaai.org/Conditions-Treatments/Primary-Immunodeficiency-Disease/severe-combined-immunodeficiency>

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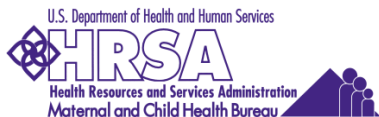
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Severe Combined Immunodeficiency

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