

Thalassemia

Thalassemia is a general name for a group of inherited blood diseases. They involve abnormalities in hemoglobin, the oxygen-carrying part of the red blood cells. There are two main kinds of protein, called alpha and beta globin, in each molecule of hemoglobin. Individuals with thalassemia do not produce enough of one (or occasionally both) of these proteins. As a result, their red blood cells may be abnormal and unable to carry enough oxygen throughout the body.

The two main types of thalassemia are called alpha and beta thalassemia. Individuals with alpha thalassemia do not produce enough alpha globin, and those with beta thalassemia lack sufficient beta globin. There are a number of different forms of both alpha and beta thalassemias, with symptoms ranging from mild to severe.

Thalassemia is among the most common inherited disorders caused by a single abnormal gene. According to the World Health Organization, more than 350,000 babies worldwide are born each year with severe forms of thalassemia and other related disorders affecting hemoglobin. Thalassemia occurs most frequently in people of Italian, Greek, Middle Eastern, Southern Asian and African ancestry.

What is alpha thalassemia?

There are at least four main types of alpha thalassemia. These mainly affect people of Southeast Asian, Chinese and Filipino ancestry. There are four genes that control the production of alpha globin. The severity of the condition is determined by how many of these genes are missing or abnormal.

- **Silent carrier**, the mildest form, in which one alpha globin gene is missing or abnormal. These individuals generally have no symptoms, but can pass on the genetic abnormality to their children.
- **Alpha thalassemia minor**, in which two alpha globin genes are missing or abnormal, usually does not cause major health problems. However, affected individuals may have significant anemia, and can pass the condition on to their children.

- **Hemoglobin H disease**, in which individuals have only one normal alpha globin gene. The condition results in abnormalities in the red blood cells and rapid destruction of these cells. The result is mild to moderate or even severe anemia. While most individuals with hemoglobin H disease live fairly normal lives, they eventually may develop complications such as an enlarged spleen, frequent infections, and gallstones. They should receive regular medical care to detect and treat these complications.
- **Alpha thalassemia major**, the most severe form, results from having no genes for the production of alpha globin. Affected fetuses suffer from severe anemia, heart failure and fluid buildup. They usually are stillborn, but some die in the first hours after birth. In rare cases, babies diagnosed and treated before birth have survived.

What is beta thalassemia?

There are three main forms of beta thalassemia, which range from very severe to having no effect on health.

- **Thalassemia major**, the most severe form, also is called Cooley's anemia, named after the doctor who first described it in 1925.
- **Thalassemia intermedia** is a mild Cooley's anemia.
- **Thalassemia minor** (also called thalassemia trait) may cause no symptoms, but mild anemia and other changes in the blood do occur.

What are the symptoms of beta thalassemia?

Most children with thalassemia major appear healthy at birth but, during the first year or two of life, they become pale, listless and fussy, and have a poor appetite. They grow slowly and often develop jaundice (yellowing of the eyes and skin). The condition is diagnosed with blood tests.

Without treatment, the spleen, liver and heart soon become greatly enlarged. Bones become thin and brittle; facial bones become distorted, and children with thalassemia often look alike. Heart failure and infection are the leading causes of death among children with untreated thalassemia major.

Children with thalassemia intermedia may develop some of the same complications, although, in most cases, the course of the disease is mild for the first two decades of life.

What is the treatment for beta thalassemia?

The use of regular blood transfusions and antibiotics has improved the outlook for children with thalassemia major. Children with thalassemia intermedia usually do not require transfusions, although these may be recommended if complications start to develop.

Children with thalassemia major are treated with regular transfusions (generally, every 2 to 3 weeks) aimed at keeping their hemoglobin level near normal. This prevents many of the complications of thalassemia. This treatment enhances the child's growth and well-being, and usually prevents heart failure and bone deformities.

Unfortunately, repeated blood transfusions lead to a buildup of iron in the body, which can damage the heart, liver, pancreas and other organs. There is a drug (deferoxamine), called an iron chelator, which binds to iron and helps the body rid itself of the excess. The drug usually is administered nightly via a mechanical pump that infuses the drug slowly underneath the skin while the child is sleeping.

Individuals with beta thalassemia major who are treated with regular blood transfusions and iron chelation live 30 to 40 years or longer. Because intensive chelation treatment was introduced only in the 1960s, continuing studies may show that treated individuals are living even longer.

Beta thalassemia has been cured in more than 1,000 patients worldwide using bone marrow transplants. However, this form of treatment is possible only for a small minority of patients who have a suitable bone marrow donor, and the transplant procedure is still risky and can result in death. Scientists are evaluating whether a transplant using umbilical cord blood (which, like bone marrow, contains unspecialized cells called stem cells that produce all other blood cells) from a newborn sibling may be as effective as a bone marrow transplant, while posing fewer risks.

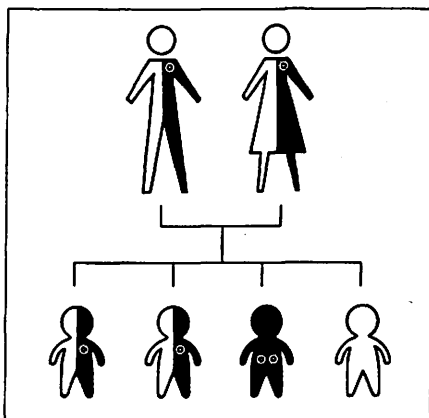
How is the disease transmitted?

All forms of thalassemia are inherited. The disease cannot be caught from another person who has it. Thalassemia is passed on through parents who carry the thalassemia genes in their cells.

When both parents carry alpha thalassemia genes, any child that they have is at risk for inheriting a more severe form of this condition. Individuals who know they have one of these disorders, those with family histories of these disorders, and those from countries where they are common should consider consulting a genetic counselor to find out whether their children could be at risk. (Doctors can provide referrals to genetic counselors, or individuals can find them by contacting a major medical center.)

When two individuals with beta thalassemia trait become parents, there is a 25 percent chance (one in four) that any child they have will inherit a thalassemia gene from each parent and have a severe form of the disease. There is a 50 percent (two in four) chance that the child will inherit one of each kind of gene and have the trait like its parents; and a 25 percent (one in four) chance that the child will inherit two normal genes and be completely free of the disease. The odds are the same for each pregnancy when both parents have the beta thalassemia trait.

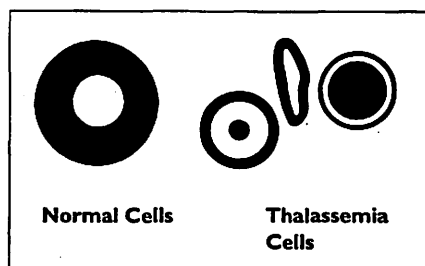
Until recently, pregnancy was rare in women with thalassemia major. A 1999 study suggested that pregnancy appears safe for a woman with well-treated thalassemia who does not have heart problems. As long as her partner does not carry a gene for thalassemia, her children will not be at risk of thalassemia — although all will be carriers.



Chances with each pregnancy that baby may have beta thalassemia or beta thalassemia trait (see text).

Is there a test for thalassemia?

Yes. Blood tests and family genetic studies can show whether an individual has any form of thalassemia or thalassemia trait. In addition, prenatal testing using chorionic villus sampling (CVS) or amniocentesis can detect or rule out thalassemia in the fetus. Early diagnosis is important so that treatment can prevent as many complications as possible.



What research on thalassemia is taking place?

Scientists are working on better ways to remove excess iron from the body in order to prevent or delay iron overload. They are developing and testing the safety and effectiveness of oral iron-chelating drugs, which could greatly simplify treatment of this disease.

Researchers also are testing a drug that could be injected (with a brief shot) two or three times a week. March of Dimes grantees are among the many scientists seeking to develop an effective form of gene therapy that may, someday, offer a cure for thalassemia. Gene therapy may involve inserting a normal alpha or beta globin gene into the patient's stem cells, possibly allowing these immature blood cells to produce normal red blood cells.

Another form of gene therapy may involve using drugs or other methods to reactivate the patient's genes for fetal hemoglobin. All humans produce a fetal form of hemoglobin before birth; after birth, natural genetic switches "turn off" production of fetal hemoglobin and "turn on" production of adult hemoglobin. Scientists are seeking ways to activate these genetic switches so that they can make the blood cells of patients with thalassemia produce more fetal hemoglobin to compensate for their deficiency of adult hemoglobin. Initial studies of rare individuals with genetic traits that allow them to produce only fetal hemoglobin show that they generally are healthy, demonstrating that fetal hemoglobin can be a fine substitute for adult hemoglobin.

In addition, improved bone marrow transplantation methods may lead to wider use of the technique as a treatment for thalassemia.

For further information about thalassemia, contact:

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