

What is Thalassemia Trait ?



Introduction

Being tested
for the
thalassemia trait
is easy

This book contains basic information about the thalassemia trait.

Whether you have been diagnosed with the thalassemia trait or are simply interested in finding out more about it, we encourage you to consult your physician or a hematologist. If you carry the thalassemia trait and are considering having children, we also suggest that you seek the advice of a genetic counselor.

The Cooley's Anemia Foundation's message concerning the thalassemia trait is simple:

Being tested for the thalassemia trait is easy. And it is in everyone's best interest, working in partnership with the health care professional of their choice, to be informed and take responsibility for their own health care.

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Because it is a genetic trait and not a health condition, except for extremely rare cases, the thalassemia trait has no symptoms and requires no treatment

What is the thalassemia trait?

If you have been diagnosed with the thalassemia trait, this is simply another way of saying that you carry the genetic trait for thalassemia.

A genetic trait is a kind of message or code contained in your body. You may pass this code on to your children, and they may pass it on to their children.

You may, for instance, carry the genetic trait for blue eyes, even if you yourself have brown eyes.

Thalassemia trait is not a disease or condition but a kind of genetic possibility that you pass on to your descendants.

The thalassemia trait is not a disease.

Medical personnel often tell people who carry the thalassemia trait that they "have thalassemia" which can lead trait carriers to believe that they have some kind of health-threatening medical condition. This is not true.

Medical terminology refers to the thalassemia trait as "thalassemia minor." So while it may be technically correct to say that trait carriers "have thalassemia" (or, more properly, "thalassemia minor"), trait carriers should be aware that carrying the genetic trait for thalassemia is not the same thing as having a disease.

The thalassemia trait requires no medical treatment.

Physicians sometimes mistakenly prescribe iron supplements for thalassemia trait carriers, usually because they mistake the small size of the trait carrier's red blood cells with iron-deficiency anemia.

The only way to properly determine the need for iron supplements is to have a physician test iron levels in the patient's blood. Without a test of blood iron levels, iron supplements should not be prescribed for thalassemia trait carriers.

The thalassemia trait cannot become worse or turn into a serious disease.

Because the thalassemia trait is a genetic trait and not a health condition, it cannot "become worse" or change into one of the more serious forms of thalassemia that may require medical treatment.

Similarly, except for extremely rare cases, the thalassemia trait has no symptoms and requires no treatment.

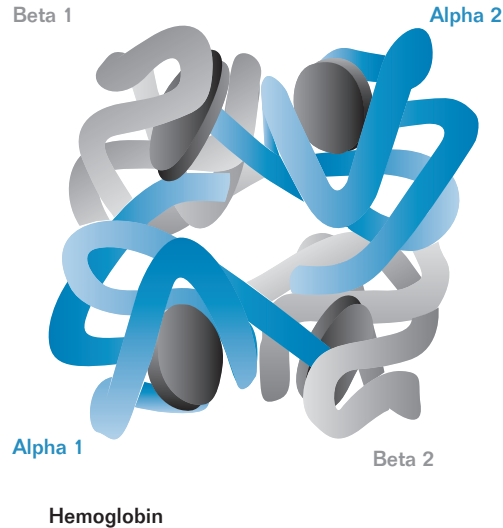
Why should I be concerned about the thalassemia trait?

Even though the thalassemia trait has no symptoms and cannot directly affect your health, it can indirectly affect your health and directly affect the health of your children. Doctors may mistake your thalassemia trait for a different condition and prescribe unnecessary and potentially harmful tests or treatments.

Also, when two thalassemia trait carriers have a child, there is a one-in-four chance with each pregnancy that the child will be born with a serious blood disorder.

What is Thalassemia?

To understand how thalassemia affects the human body, you must first understand a little about how blood is made



Thalassemia is the name of a group of genetic blood disorders.

To understand how thalassemia affects the human body, you must first understand a little about how blood is made.

Blood carries oxygen from your lungs to other parts of your body. Oxygen is carried inside the red blood cells by a substance called hemoglobin.

Hemoglobin is made of two different kinds of proteins, called alpha and beta globins. These globin proteins are made by genes located on pairs of chromosomes. If one or more of these globin-producing genes is abnormal or missing, there is a drop in globin production.



When only one beta globin gene or one or two alpha globin genes are missing (as is the case with trait carriers), the drop in globin production is so small it rarely affects the person's health.

But when two beta globin genes or three alpha globin genes are missing (as is the case with the more serious thalassemia disorders), the drop in globin production is so great that the red blood cells do not form properly and the blood cannot carry enough oxygen.

The result is anemia that begins in early childhood and lasts throughout life. When all four alpha genes are missing, the result is usually death in the womb.

Since thalassemia is not a single disorder but a group of related disorders that affect the human body in similar ways, it is important to understand the differences between the various types of thalassemia.

Alpha Thalassemia

Physicians often mistake alpha thalassemia minor for iron deficiency anemia and prescribe iron supplements that have no effect on the anemia.



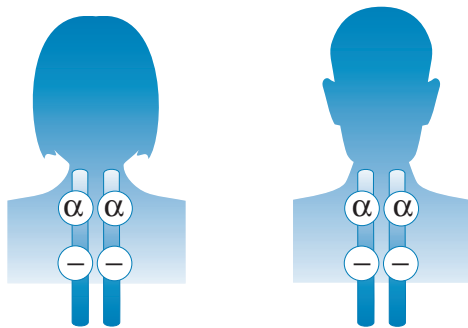
Normal alpha globin genes chromosomes 16

People who do not produce enough alpha globin protein have alpha thalassemia. It is commonly found in Africa, the Middle East, India, Southeast Asia, southern China, and occasionally the Mediterranean region.

Alpha globin is made by four genes, two on each strand of the chromosome 16. Individuals who have one or two abnormal alpha globin genes have alpha thalassemia trait.

An individual with alpha thalassemia trait defined by the presence of one abnormal alpha globin gene is said to have the **silent carrier state**. This condition, in which one of the four alpha globin genes is missing or defective, generally causes no health problems because the lack of alpha globin protein is so small that there is no anemia.

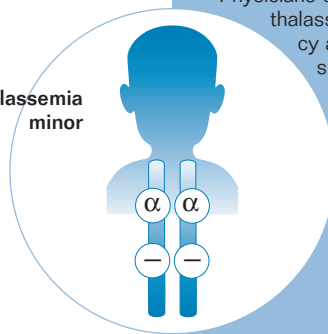
It is called "silent carrier" because of how difficult it is to detect. Silent carrier state is "diagnosed" by deduction when an apparently normal individual has a child with hemoglobin H disease or alpha thalassemia minor. It can also be diagnosed by special DNA testing.



If **both parents** carry **alpha thalassemia minor** in which the two abnormal genes of each parent are on opposite chromosomes, their children will inherit **alpha thalassemia minor**.



alpha thalassemia minor



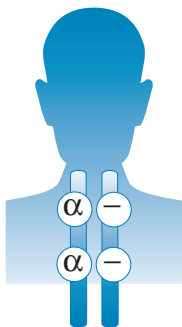
An individual with alpha thalassemia trait defined by the presence of two abnormal alpha globin genes is said to have **alpha thalassemia minor**.

Alpha Thalassemia Minor.

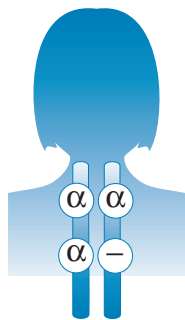
In this condition, in which two of the four alpha globin genes are missing or defective, the lack of alpha globin protein is somewhat greater. Patients with this condition have smaller red blood cells and a mild anemia, although they do not experience symptoms.

Physicians often mistake alpha thalassemia minor for iron deficiency anemia and prescribe iron supplements that have no effect on the anemia. Both abnormal alpha globin genes may be on the same chromosome (cis position) or one may be on each chromosome in the pair (trans position).

if...



one parent has **alpha thalassemia minor** with two abnormal alpha globin genes on the same chromosome



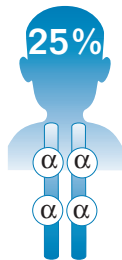
and the other parent has the **silent carrier state** with a single abnormal alpha globin gene on one chromosome

The alpha thalassemia traits combine in different ways to produce blood disorders that range from mild to severe in their effect on the human body.

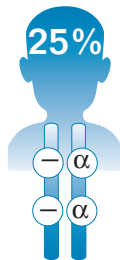
..then

there is a 25% chance with each pregnancy that their child will be born with **hemoglobin H disease** in which three of the four alpha globin genes are abnormal.

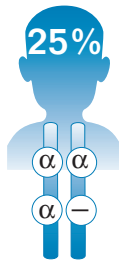
In this condition, the lack of alpha protein is great enough to cause moderate to severe anemia and may cause serious health problems such as an enlarged spleen, bone deformities and fatigue.



normal hemoglobin

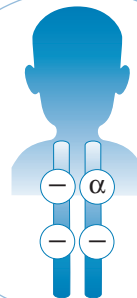


alpha thal trait

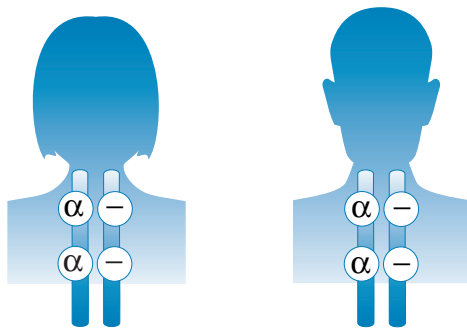


alpha thal silent carrier

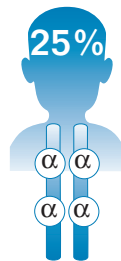
25%
hemoglobin H
disease



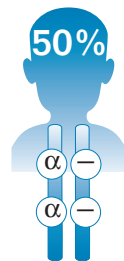
if...



both parents carry alpha thalassemia minor with two abnormal alpha globin genes on the same chromosome

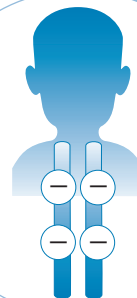


normal
hemoglobin



alpha thal
trait (cis Type)

25%
hydrops fetalis
(alpha thal major)



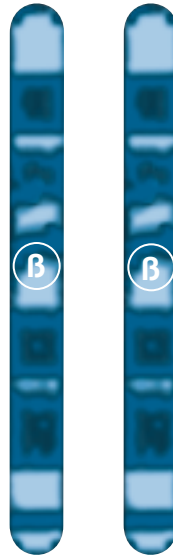
..then

there is a 25% chance with each pregnancy that their child will inherit **hydrops fetalis** or **alpha thalassemia major**, in which all four alpha globin genes are abnormal.

Most individuals with this condition die before or shortly after birth. In some extremely rare cases, in utero blood transfusions have allowed the birth of children with hydrops fetalis who then require life-long blood transfusions and medical care.

Beta Thalassemia

In beta thalassemia trait, one of the two genes is abnormal but the lack of beta protein is not great enough to cause problems in the normal functioning of the hemoglobin



Normal beta globin genes
chromosomes 11

People who do not produce enough beta protein have beta thalassemia. It is found in people of Mediterranean descent such as Italians and Greeks, and is also found in the Arabian Peninsula, Iran, Africa, Southeast Asia, and southern China.

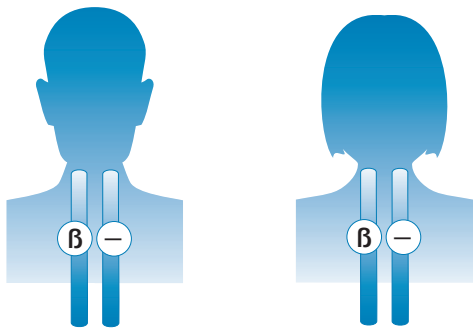
Beta globin is made by two genes, one on each chromosome 11. Individuals who have one abnormal beta globin gene have beta thalassemia trait.

BETA THALASSEMIA MINOR or BETA THALASSEMIA TRAIT.

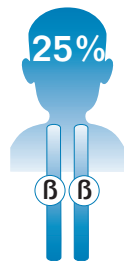
In beta thalassemia trait, one of the two genes is abnormal but the lack of beta protein is not great enough to cause problems in the normal functioning of the hemoglobin. A person with this condition simply carries the genetic trait for beta thalassemia and will usually experience no health problems other than a mild anemia.

As in alpha thalassemia minor, physicians often mistake the small red blood cells of the person with beta thalassemia minor as a sign of iron-deficiency anemia and incorrectly prescribe iron supplements.

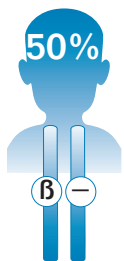
if...



both parents carry the **beta thalassemia trait**,



normal
hemoglobin



beta thal
trait

25%
Cooley's anemia



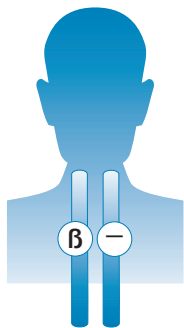
..then

there is a 25% chance with each pregnancy that their child will inherit two abnormal beta globin genes. In its most severe form, this may cause **beta thalassemia major** or **Cooley's anemia**, a blood disorder in which the lack of beta protein causes a life-threatening anemia that requires regular blood transfusions and extensive ongoing medical care. Lifelong transfusions lead to iron overload which must be treated with chelation therapy to prevent early death from organ failure.

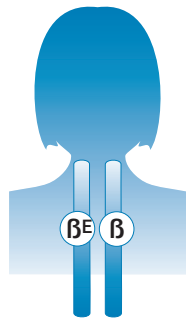
In a somewhat milder form, the inheritance of two abnormal beta globin genes may cause **beta thalassemia intermedia**, in which the lack of beta protein in the hemoglobin causes a moderately severe anemia and significant health problems including bone deformities and enlargement of the spleen.

Due to the wide range in severity of this condition, the borderline between thalassemia intermedia and thalassemia major can be confusing. When a patient is more dependent on blood transfusions he is likely to be classified as thalassemia major.

if...



one parent carries the **beta thalassemia trait**



and the other parent carries the **hemoglobin E trait**

The beta thalassemia trait can also combine with "variant" hemoglobins to produce other related blood disorders.

..then

there is a 25% chance with each pregnancy that their child will be born with **E beta thalassemia**, a moderately severe anemia that has similar symptoms to beta thalassemia intermedia but on occasion may be as severe as thalassemia major.

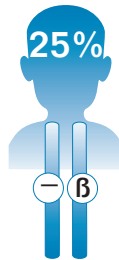
Hemoglobin E is one of the most common abnormal hemoglobins. It is usually found in people of Southeast Asian ancestry, such as Cambodians, Vietnamese and Thai.



normal hemoglobin



hemoglobin E trait

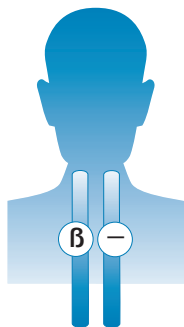


beta thalassemia trait

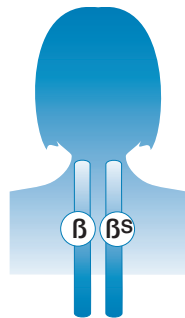
25%
E beta thalassemia



if...



one parent carries the **beta thalassemia trait**



and the **other parent** carries the **hemoglobin S trait** (the abnormal hemoglobin found in people with sickle cell disease)



..then

there is a 25% chance with each pregnancy that their child will be born with **sickle beta thalassemia**. Hemoglobin S is commonly found in people of African or Mediterranean ancestry, such as Africans, Italians, Greeks, Turks, and in people from the Caribbean.

The severity of the condition varies according to the amount of normal beta globin produced by the beta gene. When no beta globin is produced by the beta gene, the condition is almost identical to sickle cell disease. When some beta globin is produced by the beta gene, the condition is less severe.



normal hemoglobin



sickle cell trait



beta thal trait

25%
sickle-beta
thalassemia



Who Carries the Thalassemia Trait?

Thalassemia was originally believed to be common only to people of the Mediterranean region, such as Italians, Greeks and Turks. (An early name for thalassemia major or Cooley's anemia was Mediterranean anemia.)

It is estimated that over 2 million people in the United States carry the genetic trait for thalassemia



Since then, scientists have discovered that the thalassemia trait is found in people of many other regions, including the Arabian Peninsula, Africa, the Indian subcontinent, China, Southeast Asia, and the Caribbean.

Today, due to the migration and intermarriage of different ethnic populations, the trait for thalassemia is found in people with no obvious ethnic connection to the disorder. For this reason, the New York State Department of Health provides couples seeking a marriage license with information about thalassemia.



Thalassemia Trait Testing

Finding out if you
have the genetic
trait for thalassemia
begins by
determining the size
of your red blood
cells

Finding out if you have the genetic trait for thalassemia begins by determining the size of your red blood cells.

If you have a routine blood test known as a Complete Blood Count, or CBC, already on file at your doctor's office, ask your doctor to look at the Mean Corpuscular Volume, or MCV. The MCV reading determines the size of your red blood cells. For adults, if the MCV reading is less than 75 and you are not iron deficient, you may be a trait carrier. For children, the MCV reading may be lower and varies according to their age.

If your MCV reading indicates that you may have the thalassemia trait, your doctor should then perform additional tests to confirm that you have the thalassemia trait and to determine what kind.

Although the MCV reading is a good indicator of whether a person may have either the alpha or the beta thalassemia trait, finding out for certain if you have either trait involves additional tests.



Special tests called hemoglobin electrophoresis and quantitation of hemoglobin A2 and hemoglobin F are a reliable way of determining whether or not a person has the trait for beta thalassemia (beta thalassemia minor). These tests are available at most large hospitals and clinics.

Testing for alpha thalassemia trait (alpha thalassemia minor) is usually done by a process of exclusion; people who have low MCV (not due to iron deficiency), a normal hemoglobin electrophoresis, quantitative hemoglobin A2 and quantitative hemoglobin F, and are of the appropriate ethnic origin are presumed to have alpha thalassemia minor.

In some circumstances, more definitive "molecular" testing is performed to determine the presence or absence of thalassemia trait. As these genetic tests are developed further, they will be used more widely to test for thalassemia trait.

Remember that the first step to finding out if you have the thalassemia trait is easy. Just call your doctor and ask him or her to check your MCV reading. Testing for thalassemia can be done at most hospitals. When you go in for your test bring this book with you to share with your doctor.

Prenatal Testing for Thalassemia

Inform your obstetrician about your thalassemia trait. Discuss what it might mean for your unborn child



If you have alpha or beta thalassemia trait and are considering having a child or are already pregnant, your partner should be tested to see if he or she has the thalassemia trait. If you both have thalassemia trait, there are several things you can do.

Inform your obstetrician about your thalassemia trait. Discuss what it might mean for your unborn child. If necessary, share this book with your doctor.

If you want to determine whether your unborn child has any form of thalassemia, there are two kinds of tests you can request.



AMNIOCENTESIS

Amniocentesis is performed in the second trimester of pregnancy, after about 15 weeks of gestation. Using ultrasound as a guide, the doctor withdraws 2-3 tablespoons of amniotic fluid from the mother's womb through a very thin needle inserted in the mother's abdomen. Fetal cells that are floating free in the amniotic fluid are then analyzed for the thalassemia mutations.

CHORIONIC VILLUS SAMPLING (CVS)

CVS can be performed somewhat earlier than amniocentesis, at about 10-11 weeks of pregnancy. In this test, the doctor removes a small sample of the chorionic villi, or the cells that will form the placenta. The cells are removed either with a thin needle inserted in the mother's abdomen or with a thin catheter inserted in the vagina. These cells, which contain the same genetic information as the fetus, are analyzed for the thalassemia mutations.

If you are interested in either of these tests, ask your obstetrician to refer you to a prenatal testing center.

About the Cooley's Anemia Foundation

The Cooley's Anemia Foundation is the only national non-profit health organization dedicated to serving patients afflicted with various forms of thalassemia, most notably the major form of this genetic blood disease, Cooley's Anemia

The Foundation's mission is:

- Advancing the treatment and cure for this genetic blood disease.
- Enhancing the quality of life of patients.
- Educating the medical profession, thalassemia trait carriers and the public about thalassemia.

For more information about thalassemia and what the Cooley's Anemia Foundation is doing to fight it, call 800-522-7222 or visit our website (www.cooleysanemia.org)

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