

Understanding your results

Alpha-thalassemia

WHAT IS ALPHA-THALASSEMIA?

Alpha-thalassemia is an inherited blood disorder that causes anemia and prevents your body from getting enough oxygen.

WHAT CAUSES ALPHA-THALASSEMIA?

Alpha-thalassemia is caused by changes to two genes: *HBA1* and *HBA2*. These genes tell the body to make alpha-globin, a critical protein found in hemoglobin. Hemoglobin is the part of a red blood cell responsible for transporting oxygen around the body. If the body does not produce enough alpha-globin, red blood cells do not form properly and cannot carry enough oxygen.

Typically, each person has two copies of the gene *HBA1* and two copies of the gene *HBA2*, for a total of four alpha-globin genes, written: $\alpha\alpha/\alpha\alpha$. When these genes are damaged or missing, the body cannot make enough alpha-globin, which may lead to a spectrum of alpha-thalassemia symptoms.



WHAT ARE THE SYMPTOMS OF ALPHA-THALASSEMIA?

Alpha-thalassemia symptoms vary in type and severity. While it is possible for affected individuals to be symptom-free, many experience anemia symptoms that include pale skin, shortness of breath, poor growth, low energy, frequent infections, and even blood clots. Severe cases of anemia may require regular blood transfusions. Alpha-thalassemia may also be life-threatening during pregnancy or early infancy.

If you have alpha-thalassemia, it's important to speak with your healthcare provider to understand your risks and next steps.

HOW IS ALPHA-THALASSEMIA INHERITED?

Alpha-thalassemia is an autosomal recessive condition, meaning that a couple is at risk of having a child with alpha-thalassemia only if both reproductive parents carry damaged or missing copies of *HBA1* or *HBA2*.

WHAT IS ALPHA-THALASSEMIA TRAIT?

Alpha-thalassemia trait is not a disease. People who have trait usually do not experience any symptoms. Parents may be “trait carriers” meaning they could pass the trait along to their children if their partner is also a carrier (or has alpha-thalassemia). In this case, their children may be at risk of developing an alpha-thalassemia disease.

WHAT DOES THIS MEAN FOR ME?

There are several arrangements of genes that determine whether someone will be unaffected, a carrier, or develop an alpha-thalassemia disease.

Normal, non-carrier ($\alpha\alpha/\alpha\alpha$):



- **Non-working genes:** none
- **Working genes:** four; normal alpha-globin levels
- **Symptoms:** individuals who inherit a complete set of functioning genes do not develop alpha-thalassemia
- **Reproductive impact:** these individuals are not carriers, and so are not at risk of having a child with alpha-thalassemia

Silent carrier ($\alpha\alpha/\alpha-$):



- **Non-working genes:** one
- **Working genes:** three; enough alpha-globin
- **Symptoms:** none

Trait carrier, also called alpha-thalassemia minor ($\alpha\alpha/--$ or $\alpha-/α-$):

- **Non-working genes:** two
- **Working genes:** two; reduced alpha-globin
- **Symptoms:** usually no symptoms, but mild anemia is possible
- **Arrangement:**



Trait carrier (CIS)

- alpha-thalassemia cis ($\alpha\alpha/--$): non-working genes are on the same chromosome



Trait carrier (TRANS)

- alpha-thalassemia trans ($\alpha-/α-$): non-working genes are on different chromosomes

Hemoglobin H disease ($\alpha/--$):

- **Non-working genes:** three
- **Working genes:** one; very little alpha-globin
- **Symptoms:**



- can range from mild to severe anemia
- manageable with proper treatment and routine visits to hematologist
- severe cases may require regular blood transfusions or even a blood marrow transplant

Hemoglobin Bart disease ($--/--$):



- **Non-working genes:** four
- **Working genes:** none; no alpha-globin
- **Symptoms:** these individuals are severely affected and usually die in utero or shortly after birth

WHAT HAPPENS IF I AM A CARRIER?

Being a carrier of alpha-thalassemia typically does not affect your health, but it is important to determine whether you are a silent carrier or have the alpha-thalassemia trait (as described above). Each arrangement of genes poses different reproductive risks and should be discussed in detail with your healthcare provider or genetic counselor.

If you are a carrier, it is also important to have your reproductive partner tested to see if he/she is also a carrier.

WHAT HAPPENS IF MY PARTNER IS NOT A CARRIER?

If your reproductive partner had a negative alpha-thalassemia carrier screen, it is unlikely that you will have a child with alpha-thalassemia. However, no test can thoroughly detect all carriers, so there is a small chance (called residual risk) of your partner being a carrier even after a negative test.

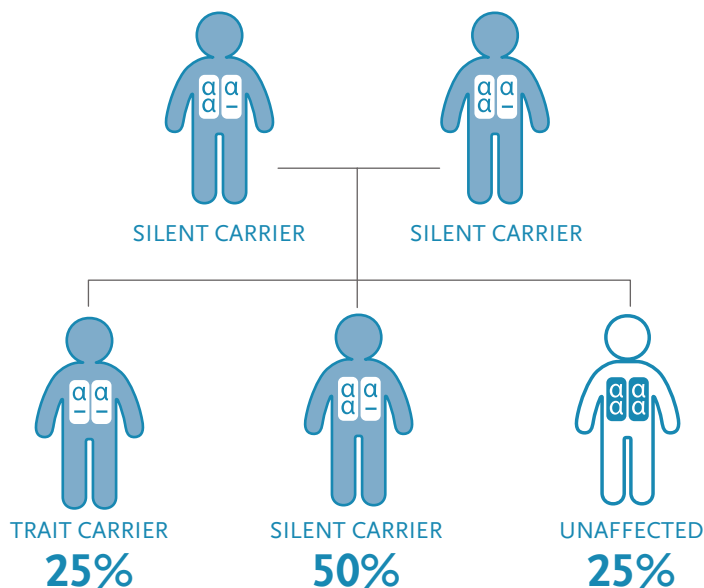
Please speak with your healthcare provider or genetic counselor to understand your options if you are concerned about residual risk.

WHAT DOES THIS MEAN FOR MY CHILD(REN)?

Inheritance of alpha-thalassemia is complicated, and there are different reproductive risks depending on the arrangement of affected genes.

My partner and I are both silent carriers. What is our risk of passing down an affected gene?

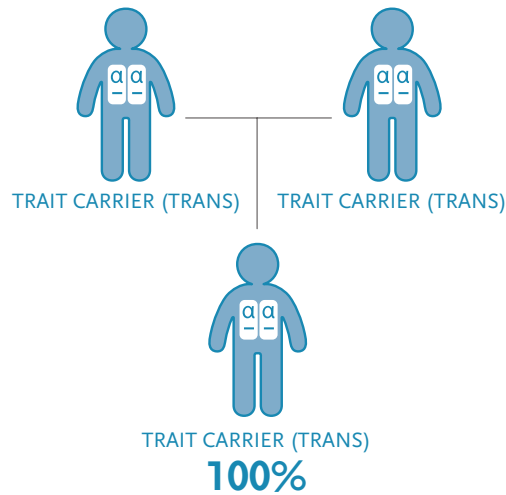
You are not at risk of having a child with a severe alpha-thalassemia disease; however, there is a 25% chance of having a child who is a trait carrier, a 50% chance of having a child who is a silent carrier, and a 25% chance of having a child who is unaffected.



My partner and I are both trait carriers. What is our risk of passing down an affected gene?

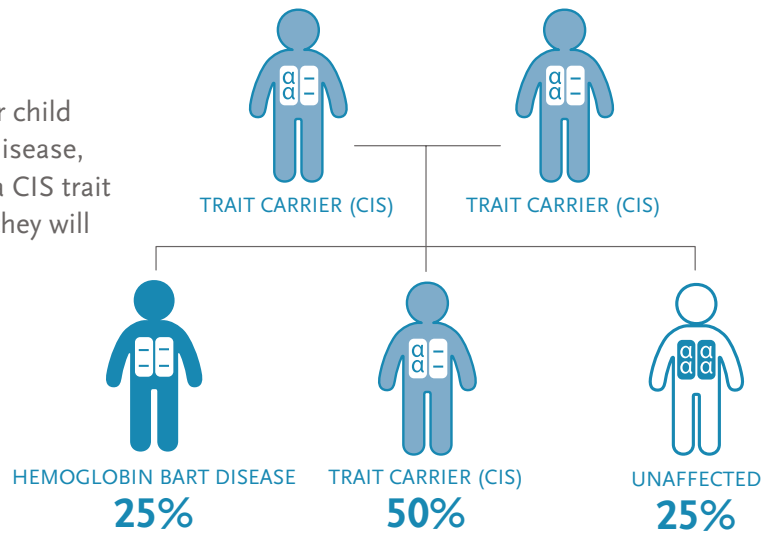
Two trait carriers: both trans

Your child will also be a trans trait carrier.



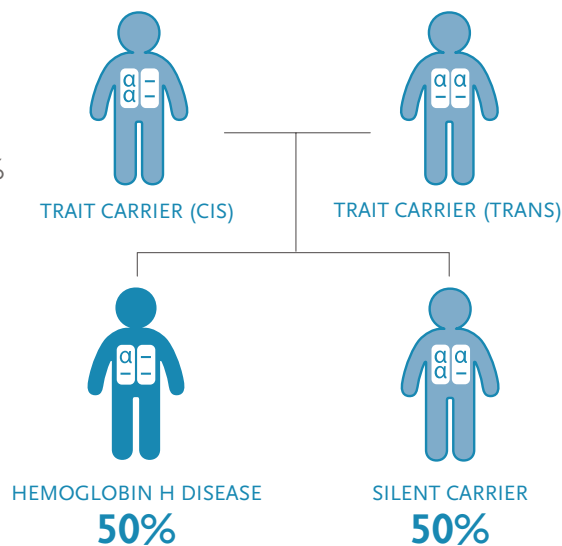
Two trait carriers: both CIS

There is a 25% chance that your child will develop Hemoglobin Bart disease, a 50% chance that they will be a CIS trait carrier, and a 25% chance that they will be unaffected.



Two trait carriers: one CIS, one trans

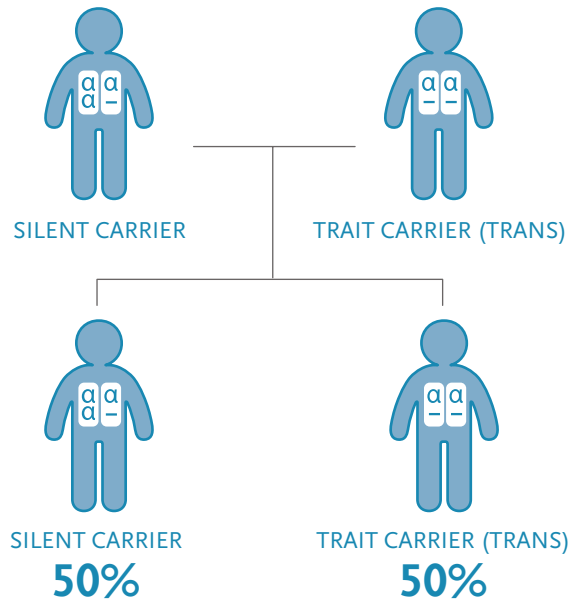
There is a 50% chance that your child will develop Hemoglobin H disease and a 50% chance that they will be a silent carrier.



My partner and I are one silent carrier and one trait carrier. What is our risk of passing down an affected gene?

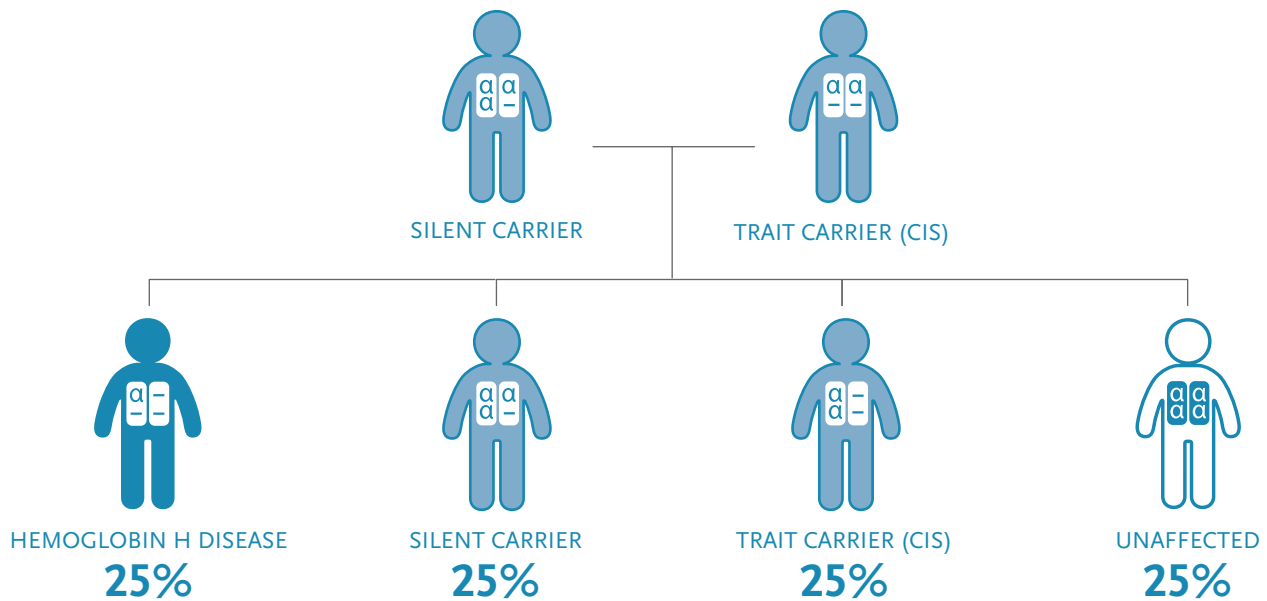
One silent, one trans trait carrier

There is a 50% chance that your child will be a silent carrier and a 50% chance that they will be a trans trait carrier.



One silent, one cis trait carrier

There is a 25% chance that your child will develop Hemoglobin H disease, a 25% chance that they will be a silent carrier, a 25% chance that they will be a cis trait carrier, and a 25% chance of being unaffected.



DO I NEED TO INFORM MY FAMILY MEMBERS IF I AM AN ALPHA-THALASSEMIA CARRIER?

Sharing your test results is a personal choice. Most people who choose to share their test results do so to get support and to help family members assess their own risk. Alpha-thalassemia is an inherited disease so it's possible that your family members may also be carriers who could benefit from testing.

Inheritance of alpha-thalassemia is complicated. If you or your partner are carriers of alpha-thalassemia, speak with your healthcare provider or genetic counselor to understand your reproductive risks and next steps.

WHERE CAN I GET MORE INFORMATION ABOUT ALPHA-THALASSEMIA?

Cooley's Anemia Foundation: www.thalassemia.org

National Heart Lung and Blood Institute: www.nhlbi.nih.gov/health/health-topics/topics/thalassemia

Genetics Home Reference: www.ghr.nlm.nih.gov/condition/alpha-thalassemia