Inheritest® CARRIER SCREEN

Alpha-thalassemia

What is alpha-thalassemia?

Alpha-thalassemia is an inherited disorder with variable severity. Individuals with alpha-thalassemia have a deficiency in the production of hemoglobin, which carries oxygen in the blood. Signs and symptoms of alpha-thalassemia are due to a reduction in the amount of hemoglobin that reaches the body's tissues. There are two clinically significant forms of alpha thalassemia: HbH disease and Hb Bart hydrops fetalis syndrome.[1]

What are the symptoms of alpha-thalassemia and what treatment is available?

Signs and symptoms of the more severe Hb Bart hydrops fetalis syndrome appear before birth and may include:[1]

- Hydrops fetalis (abnormal fluid accumulation in the body before birth)
- Severe anemia
- Enlarged liver and spleen (hepatosplenomegaly)
- Heart problems
- Abnormalities of the urinary system or genitalia

Signs and symptoms of the less severe HbH disease usually appear in early childhood and may include:[1]

- Mild to moderate anemia with associated weakness and fatigue
- Enlarged liver and spleen (hepatosplenomegaly)
- Jaundice
- Bone changes

In utero stem cell transplantation or fetal blood transfusions may be available for affected fetuses.[3] Without treatment, most babies with Hb Bart hydrops fetalis syndrome are stillborn or die soon after birth. Mothers of babies affected with Hb Bart hydrops fetalis syndrome may experience serious pregnancy complications, including preeclampsia, premature delivery, or abnormal bleeding.[1,3] Individuals with HbH disease have a shortened lifespan.[1,2] Treatment is supportive and may include red blood cell transfusions.[3]

Alpha-thalassemia is included in newborn screening programs in all states in the United States.[4]

How is alpha-thalassemia inherited?

Alpha-thalassemia is caused by mutations, usually deletions, in the alpha-globin gene cluster.[1] Inheritance is usually autosomal recessive.[3] Each person has two HBA genes, *HBA1* and *HBA2*. Each gene has two copies, one inherited from each parent for each gene (αα/αα). An individual who inherits a mutation in one alpha-globin gene is a silent carrier of alpha-thalassemia (-α/αα) and is not expected to have related health problems. An individual who inherits mutations in two alpha-globin genes is a carrier of alpha-thalassemia and is considered to have alpha-thalassemia trait. Individuals with alpha-thalassemia trait may have symptoms of mild anemia. If both mutations are on the same chromosome ("in cis"), the individual has alpha-o-thalassemia trait (--/αα). If the mutations are on different chromosomes ("in trans"), the individual has alpha-+-thalassemia trait (-α/-α). Individuals with HbH disease have mutations in three alpha-globin genes (--/-α) and individuals with Hb Bart syndrome have mutations in all four genes (--/--).[1,2,]

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Risks for alpha-thalassemia carriers to have an affected child in each pregnancy are shown in the table below.[3] Based on the relevant risk, it is important that the reproductive partner of a carrier be offered testing.

Carrier status of partner	Carrier status of partner	Risk for a child affected with HbH disease (--/-α)	Risk for a child affected with Hb Bart syndrome (--/--)
alpha-0-thalassemia trait (--/αα)	alpha-+-thalassemia trait (-α/-α)	50%	No risk
alpha-0-thalassemia trait (--/αα)	alpha-0-thalassemia trait (--/αα)	No risk	25%
alpha-0-thalassemia trait (--/αα)	silent carrier (-α/αα)	25%	No risk
alpha-+-thalassemia trait (-α/-α)	alpha-+-thalassemia trait (-α/-α)	No risk	No risk
alpha-+-thalassemia trait (-α/-α)	silent carrier (-α/αα)	No risk	No risk
silent carrier (-α/αα)	silent carrier (-α/αα)	No risk	No risk

Who is at risk for alpha-thalassemia?

Alpha-thalassemia can occur in individuals of all races and ethnicities. It is most common in individuals who are of African, Mediterranean, South-East Asian, Indian, and Middle Eastern ancestry. HbH disease and Hb Bart hydrops fetalis syndrome are estimated to be present in at least 1 in 1,000,000 individuals in the Northern Europe and North American general populations. In Southeast Asia, the estimated incidence of Hb Bart hydrops fetalis syndrome is 1 in 200-2,000 births.[1,5]

Having a relative who is a carrier or is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a healthcare provider or a genetics professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

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

Cooley's Anemia Foundation: http://www.thalassemia.org/

Gene Reviews: https://www.ncbi.nlm.nih.gov/books/NBK1435/

References

1. Genetics Home Reference. Alpha thalassemia. Available at https://ghr.nlm.nih.gov/condition/alpha-thalassemia#. Accessed May 30, 2018.
2. Piel,FB, Weatherall DJ. The Alpha-Thalassemias. *N Engl J Med.* 2014; 371: 1908-1916.
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4. National Newborn Screening Status Report. November 2, 2014. Available at: http://genes-r-us.uthscsa.edu/ sites/genes-r-us/files/nbsdisorders.pdf . Accessed May 4, 2018.
5. National Organization for Rare Disorders. Alpha-thalassemia. Available at https://rarediseases.org/rare-diseases/alpha-thalassemia/. Accessed May 30, 2018.