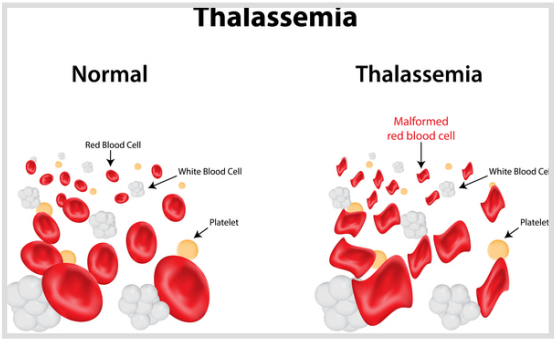
Alpha-Thalassemia

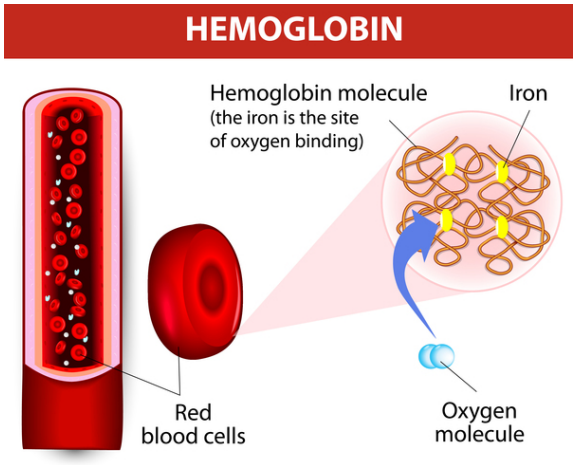
Overview

What is alpha-thalassemia?

Alpha-thalassemia is an inherited blood disorder. Inherited means alpha-thalassemia is passed down from parents to children through genes in the same way traits for hair or eye color are passed down. A child or adult with this condition may experience mild to severe anemia.



There are 4 subtypes of alpha-thalassemia: alpha-thalassemia silent carrier, alpha-thalassemia carrier, hemoglobin H disease (HbH disease), and alpha-thalassemia major. Alpha-thalassemia major is also known as hemoglobin barts syndrome (Hb barts syndrome). Screening measures are available to identify individuals at risk for alpha-thalassemia.



What causes alpha-thalassemia?

Hemoglobin is an iron-rich protein found in red blood cells. It is the protein in red blood cells responsible for carrying oxygen throughout the body.

Hemoglobin is made up of smaller proteins known as alpha and beta. In alpha-thalassemia, there is not enough alpha protein (known as alpha-globin) produced. As a result, there are fewer healthy red blood cells carrying oxygen throughout the body. This leads to varying degrees of anemia.

What are the genes involved in alpha-thalassemia?

There are 2 copies each of the *HBA1* and *HBA2* gene for a total of 4 alpha-globin genes. Alpha-globin genes instruct the body to make the alpha-globin part of the hemoglobin protein. The number of alpha-globin genes damaged or missing determines the subtype of alpha-thalassemia.

Symptoms

Individuals that are silent carriers of alpha-thalassemia typically exhibit no symptoms and are not expected to need medical treatment. This is also true for individuals that are carriers for alpha-thalassemia.

1) HbH disease: Individuals with this subtype show a broad range of symptoms. The onset of HbH disease is usually in early childhood. However, some affected individuals may not present at all or not present until adulthood.

(a) Presenting symptoms

- Lack of energy (fatigue)
- Slow growth and development (failure to thrive)
- Yellow skin and eyes (jaundice)
- Increased spleen and liver size (hepatosplenomegaly)
- Possible bone changes

(b) Possible later onset symptoms

- Gallstones
- Episodes that involve the destruction of red blood cells (hemolysis) in response to infections or exposure to certain medications

2) Alpha thalassemia major: If this subtype is identified before birth, treatments may be initiated but successful outcomes are rare. Without treatment, there is a high risk of infant death. All symptoms listed below onset before birth (prenatally).

(a) Prenatal symptoms

- Fluid buildup in baby's heart and lungs (pleural and pericardial effusions)
- Fluid buildup under baby's body tissues (generalized edema)
- Increased spleen and liver size (hepatosplenomegaly)
- Larger than normal placenta

Treatment and Management

The treatment options differ between individuals affected by HbH disease and alpha-thalassemia major.

1) HbH disease

(a) Blood transfusions: Affected individuals receive donated blood through a tube placed in the vein of the arm. This procedure is known as a blood transfusion and restores the number of red blood cells in the body. While some individuals with HbH disease require frequent blood transfusions, others may only require occasional blood transfusions in the event of illness or before undergoing surgery.

(b) Iron chelation therapy (medication): Iron overload may occur in individuals with HbH disease undergoing blood transfusions. Iron buildup is toxic to the body and the body is unable to naturally rid itself of iron. Medications called iron chelators bind to iron in order to prevent damage to healthy body tissues.

(c) Management: This includes regular blood tests and physicals, avoidance of iron-containing therapies to prevent iron overload risk, avoidance of certain medications, and psychosocial support.

2) Alpha thalassemia major

(a) Intrauterine blood transfusions: If alpha thalassemia major is identified before birth, blood transfusions may be performed in some medical centers.

(b) Investigational therapies: Investigational therapies refer to therapies that are currently under study. If interested in learning more, please visit https://www.clinicaltrials.gov.

Diagnosis

Your doctor or genetic counselor is able to discuss the screening measures listed below with you.

1) Parental screening measures: Testing is available prior to or during a pregnancy to determine a person's chance to pass on alpha-thalassemia to their offspring. Complete blood count (CBC) and hemoglobin electrophoresis are blood tests that examine properties of the hemoglobin protein. Additional tests are used to distinguish alpha-thalassemia from iron-deficiency anemia.

2) Prenatal screening measures: If both parents are identified as carriers, further tests may be performed in the baby.

(a) Chorionic villus sampling (CVS): A small tissue sample from the placenta is tested around the 11th week of the pregnancy.

(b) Amniocentesis: Fluid surrounding the baby called amniotic fluid is taken out for testing between the 15th to 20th weeks of pregnancy.

Common Populations

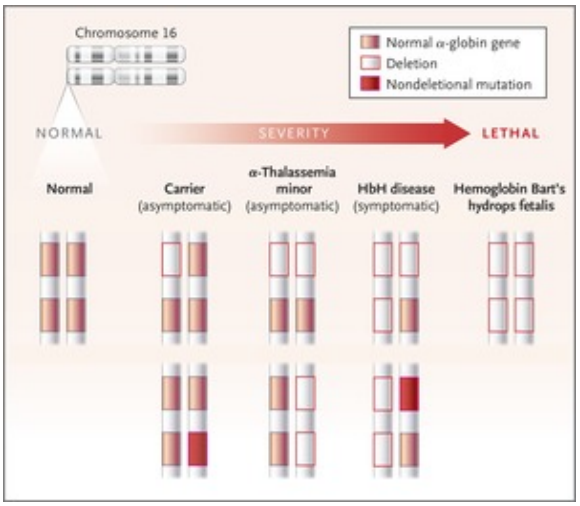
Alpha-thalassemia is prevalent in regions such as the Mediterranean, Africa, the Middle East, and Central and South Asia. Individuals with these ancestral backgrounds are at increased risk to be carriers of alpha-thalassemia.

Carriers from South Asia are at greater risk to have a child with alpha-thalassemia major. Carriers from other regions are typically not at risk to have a child with alpha-thalassemia major. However, these populations still have a chance to have a child with HbH disease (see Inheritance section below).

Inheritance

Individuals with alpha-thalassemia have either 1, 2, 3 or 4 missing or damaged alpha-globin genes. A higher number of missing or damaged alpha-globin genes corresponds with less alpha-globin produced. There is no alpha-globin production in individuals with alpha-thalassemia major.

1) Alpha-thalassemia silent carrier: Individuals have 3 working genes, and 1 non-working gene.



2) Alpha-thalassemia carrier: Individuals have 2 working genes, and 2 non-working genes. Genes are contained within structures in the body called chromosomes. Carriers differ based on whether the missing or damaged genes are on the same chromosome (cis) or on different chromosomes (trans). Cis carriers are at risk to have children with either HbH disease or alpha-thalassemia major, depending on their partner's carrier status. Trans carriers are not at risk for having children with alpha-thalassemia major, since they will always pass down their 1 working gene. Although, there is still a risk for their children to develop HbH disease.

3) HbH disease: Individuals have 1 working gene, and 3 non-working genes.

4) Alpha-thalassemia major: Individuals have 4 non-working genes.

Additional Information and Resources

Government resources

Center for Disease Control and Prevention (CDC): https://www.cdc.gov/ncbddd/thalassemia/facts.html
National Institute of Health (NIH): https://www.clinicaltrials.gov/
National Center for Biotechnology Information (NIH resource): https://www.ncbi.nlm.nih.gov/books/NBK1435/
Medline Plus (NIH resource): https://medlineplus.gov/genetics/condition/alpha-thalassemia/

Other resources

Johns Hopkins Medicine: https://www.hopkinsmedicine.org/health/conditions-and-diseases/alpha-thalassemia
My46 Trait Profile: https://www.my46.org/trait-document?trait=Alpha-thalassemia&type=profile
National Organization for Rare Diseases: https://rarediseases.org/rare-diseases/alpha-thalassemia/
Kids Health: https://kidshealth.org/en/parents/thalassemias.html
Cooley's Anemia Foundation: https://www.thalassemia.org
Nature: https://www.nature.com/articles/gim9201117

Images

Hemoglobin/cell images: https://medlineplus.gov/genetics/condition/alpha-thalassemia/
Family image: https://www.cdc.gov/ncbddd/thalassemia/facts.html
Chromosome image: https://www.nejm.org/doi/10.1056/NEJMra1404415

Written by: Shivani Bhatt