Alpha thalassemia is a genetic disorder called a hemoglobinopathy, or an inherited type of anemia. People who have alpha thalassemia make red blood cells that are not able to carry oxygen as well throughout the body, which can lead to anemia. This chronic anemia can include pale skin, fatigue, and weakness. In more severe cases, people with alpha thalassemia can also develop jaundice (yellowing of the eyes and skin), heart defects, and an enlarged liver and spleen (called hepatosplenomegaly).

Alpha thalassemia is more common in people of African, Southeast Asian, Chinese, Middle Eastern, and Mediterranean ancestries.

Causes

We have over 20,000 different genes in the body. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *HBA1* and *HBA2* genes make a protein called alpha-globin. Two of the alpha-globin proteins combine with two other proteins called beta-globins (which are made by the *HBB* gene) to make a normal red blood cell.

Most people have four copies of the genes that make the alpha-globin protein: two copies of the *HBA1* gene (one from each parent), and two copies of the *HBA2* gene (one from each parent). Having all four copies of these genes is symbolized by writing αα/αα. Whether or not someone has alpha thalassemia depends on how many working copies of the alpha-globin gene they have (if someone has a missing or nonworking alpha-globin gene, it is most frequently caused by a deletion):

- Silent alpha thalassemia carrier (also referred to as -α/αα): When there is one missing alpha-globin gene. Silent alpha thalassemia carriers do not usually have signs or symptoms of alpha thalassemia because their three working alpha-globin genes are enough to make up for the one that is missing.
- Alpha thalassemia carrier, or alpha thalassemia trait (also referred to as –/αα or -α/-α): When there are two missing alpha-globin genes. The two missing genes can be on the same chromosome (called the cis position, or –/αα) or there can be one missing gene on each chromosome (called the trans position, or -α/-α). Whether someone is more likely to be a cis or trans carrier for alpha thalassemia can depend on their ethnic background. Some people who have alpha thalassemia trait may have red blood cells that are smaller than normal (microcytosis). Most people who are carriers for alpha thalassemia have no symptoms, but some may experience anemia.
- Alpha thalassemia, or hemoglobin H disease (also referred to as –/-α): When there are three missing alpha-globin genes. This form of alpha thalassemia is extremely variable

and can range from mild to moderate anemia. Some individuals with hemoglobin H disease will have no symptoms, while others may experience yellowing of the eyes and skin (jaundice), bone changes (overgrowth of the upper jaw and a prominent forehead), developmental delays, and gallstones, in addition to other health concerns.
- Alpha thalassemia major, or hemoglobin Bart disease (also referred to as –/–): When all four alpha-globin genes are missing. This is the most severe form of alpha thalassemia, and is characterized by excess fluid build up in the body before birth (hydrops fetalis). Unfortunately, most babies with hemoglobin Bart disease are stillborn or die shortly after birth. Alpha thalassemia major can also include severe anemia, an enlarged liver and spleen (hepatosplenomegaly), and defects of the heart, urinary system, and genitalia.

Alpha thalassemia is inherited in a complex autosomal recessive inheritance pattern, and potential outcomes depend on the parent's specific test results (how many copies of the alpha globin gene do the parents have on each of their chromosomes).

Prenatal testing and/or pre-implantation genetic testing options are available for couples who are identified to be at an increased chance to have a baby with alpha thalassemia.

How common alpha thalassemia is depends on the part of the world someone's family is from. People whose families are from Northern Europe and North America have about a 1 in 1,000,000 chance to have alpha thalassemia. Approximately 4-20 out of every 1000 people whose families are from the Middle East, Southeast Asia, and certain Mediterranean countries have hemoglobin H disease. Exact numbers for how common alpha thalassemia is may not be completely accurate, as many people can have mild or no symptoms and may not even know that they have it.

Medical Management for Alpha Thalassemia

Medical management for alpha thalassemia depends on the severity of symptoms that the person is experiencing. Because people who are silent carriers or those who have alpha thalassemia trait most frequently do not have any health symptoms related to this, no treatment is necessary.

Treatment for hemoglobin H disease may include taking folic acid supplements, blood transfusions (as needed), removal of iron (called iron chelation therapy) due to iron overload, and surgical removal of the spleen (splenectomy). Rarely, a bone marrow transplant (also called a stem cell transplant) may aid in the survival of a child with hemoglobin Bart syndrome. Bone marrow transplants carry many risks, so they are

generally only considered in the most severe cases of alpha thalassemia.

Click here to learn more about scheduling a genetic counseling appointment for pregnancy-related questions.

Click here to learn more about scheduling a genetic counseling appointment for infertility or preconception questions.

Click here to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

ADDITIONAL RESOURCES:

Thalassemia Patients and Friends

Newborn Screening for Hemoglobinopathies

Cooley's Anemia Foundation

Thalassemia International Federation

Thalassemia Support Foundation