

What is Beta Thalassemia?

Beta thalassemia is an inherited disease characterized by mild to severe anemia, poor growth, enlargement of the spleen, and skeletal changes. It involves a deficiency of one of the components of hemoglobin, the oxygen-carrying molecule in the blood. Soon after birth, the majority of hemoglobin is comprised of iron and four globin chains, two alpha-globin and two beta-globin chains. Symptoms of beta thalassemia are due to reduced production of the beta-globin chains (β^+) or no production of beta-globin chains (β^0). This, in turn, results in decreased hemoglobin levels which causes anemia and other associated health problems. Beta thalassemia is also known as Cooley's anemia and Mediterranean anemia.^{1,2}

What are the symptoms of Beta Thalassemia and what treatment is available?

Beta thalassemia is classified into two types, thalassemia major, the severe form, and thalassemia intermedia, a less severe form.²

Individuals with thalassemia major typically present before two years of age with severe anemia, which can become life-threatening if not treated. The symptoms may also include:¹

- Jaundice (yellowing of the skin)
- Failure to thrive (poor weight gain and growth)
- Feeding problems
- Irritability
- Recurrent fevers
- Hepatosplenomegaly (enlarged spleen)
- Skeletal changes that result from expansion of the bone marrow
- Increased risk for abnormal blood clots
- Secondary complications that can include cardiomyopathy and liver disease

Treatment for thalassemia major is life-long and involves regular blood transfusions to correct the anemia, and chelation therapy to reduce the build-up of iron in the body. Bone marrow and cord blood transplantation are alternative treatments that can be curative; however, they are not without risk.¹ With treatment, the life expectancy of individuals with beta thalassemia major now extends beyond age 40.³

Individuals with thalassemia intermedia usually present with these symptoms later in life than individuals with thalassemia major. Disease severity can range from a severe form treated with blood transfusions to a form characterized by mild anemia in otherwise asymptomatic adults.³

How is Beta Thalassemia inherited?

Beta thalassemia belongs to a group of diseases called beta hemoglobinopathies, which are caused by mutations in the beta-globin (*HBB*) gene¹. Beta thalassemia is, in most cases, an autosomal recessive disease. An individual who inherits one copy of a recessive beta thalassemia mutation is a "carrier" and is not expected to have related health problems. On routine blood work, many carriers are found to have small red blood cells, which alone can be misinterpreted as iron-deficiency anemia.⁴ A carrier may also be described as having beta thalassemia minor.¹

Depending on the specific mutations present, an individual who inherits two mutations in the *HBB* gene, one from each parent, is expected to be affected with beta thalassemia or another form of beta hemoglobinopathy,



including sickle cell disease. Beta hemoglobinopathies exhibit significant variability in severity and age of onset, which is often related to the specific combination of *HBB* mutation(s) and the presence of any mutations in other globin genes¹. To date, more than 700 *HBB* mutations have been described⁵.

If both members of a couple are carriers of a recessive *HBB* gene mutation, the risk of having a child who inherits two *HBB* mutations is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing. For the most accurate interpretation, carrier detection may be best evaluated by combining DNA testing, clinical information, as well as a complete blood count and hemoglobin electrophoresis.⁶

Who is at risk for beta thalassemia?

Annually, there are about 42,000 pregnancies affected with beta thalassemia worldwide⁷. Beta thalassemia can occur in individuals of all races and ethnicities, but it is more common in some populations, including individuals of African, Chinese, Mediterranean, Middle Eastern, South Asian, and Southeast Asian ancestry.¹

African American	1 in 75
East Asian	1 in 50
Mediterranean	1 in 20
Middle Eastern	1 in 30
South Asian	1 in 20
Southeast Asian	1 in 30

Having a relative who is a carrier or who 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 physician or genetics health 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?

- Cooley's Anemia Foundation: <http://www.thalassemia.org>
- March of Dimes: http://www.marchofdimes.com/baby/birthdefects_sicklecell.html
- Center for Disease Control and Prevention: <http://www.cdc.gov/ncbddd/thalassemia/index.html>
- Thalassemia International Foundation: <http://www.thalassaemia.org.cy>



References

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