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CARRIER SCREEN

Beta hemoglobinopathies

What are beta hemoglobinopathies?

Beta hemoglobinopathies are a group of inherited disorders of red blood cells characterized by mild to severe anemia. Individuals with beta hemoglobinopathies have defects in one of the beta-globin chains of hemoglobin,[1-4] the oxygen-carrying molecule in the blood. Symptoms of beta-hemoglobinopathies are due to structurally abnormal hemoglobins, or to reduced or absent production of hemoglobins.[1,2]

What are the symptoms of beta hemoglobinopathies and what treatment is available?

Beta hemoglobinopathies due to structural changes in hemoglobin include sickle cell disease. Individuals with sickle cell disease usually become symptomatic in infancy or childhood and symptoms may include:[1,4]

- Hemolytic anemia
- Jaundice (yellowing of the skin)
- Susceptibility to recurrent infections
- Acute splenic sequestration crisis (blockage of blood vessels in the spleen causing enlargement and restriction of blood flow from the spleen)
- Recurrent pain crises (severe pain in the extremities, head, chest, abdomen, or back)
- Pulmonary hypertension (high blood pressure in blood vessels supplying the lungs)
- Stroke
- Acute thoracic syndrome (severe, sudden respiratory condition)

Beta hemoglobinopathies due to decreased production of hemoglobin are also known as thalassemias. The severe form of beta thalassemia is known as thalassemia major and the less severe form as thalassemia intermedia. Individuals with thalassemia major typically become symptomatic before age two and symptoms may include:[2,4]

- Severe anemia
- Jaundice (yellowing of the skin)
- Failure to thrive (poor weight gain and growth)
- Hepatosplenomegaly (enlarged liver and spleen)
- Skeletal deformities that result from expansion of the bone marrow
- Delayed puberty
- Secondary complications that can include cardiomyopathy and liver disease

Individuals with thalassemia intermedia usually become symptomatic later in life, with milder symptoms such as moderate anemia, slow growth, and skeletal abnormalities.[2]

Treatment for sickle cell disease may include hydration, pain management, antibiotics, and medication to reduce episodes of blood vessel blockage, blood transfusions, and splenectomy.[4] Treatment may extend life expectancy for individuals with sickle cell disease into the sixth decade.[4]

Sickle cell disease is included in all newborn screening panels in the United States.[5]

Treatment for thalassemia major may include blood transfusions, chelation therapy to reduce the build-up of iron, and bone marrow or cord blood transplantation.[4] With treatment, the life expectancy of individuals with beta thalassemia major is 50 to 60 years.[4]

How are beta hemoglobinopathies inherited?

Beta hemoglobinopathies are autosomal recessive diseases caused by mutations in the beta-globin (*HBB*) gene.[1,2] An individual who inherits one copy of an *HBB* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two mutations in the *HBB* gene, one from each parent, is expected to be affected with a beta hemoglobinopathy.

If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child 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 of carrier status, carrier detection is best evaluated by combining information from clinical assessment, complete blood count, hemoglobin electrophoresis, and DNA testing.[6]

Who is at risk for beta hemoglobinopathy?

Each year, throughout the world, there are approximately 42,000 pregnancies affected with beta thalassemia and approximately 275,000 pregnancies affected with sickle cell disease.[7] Beta hemoglobinopathies can occur in individuals of all races and ethnicities. Selected carrier frequencies for populations in which beta hemoglobinopathies are more common are provided below.

Beta thalassemias[8,9]

Population	Carrier frequency
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

Sickle cell disease[10]

Population	Carrier frequency*
African American	1 in 14
Hispanic	1 in 183
Middle Eastern	1 in 360
Native American	1 in 176

*Based on California mandatory carrier screening

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

Center for Disease Control and Prevention: http://www.cdc.gov/ncbddd/thalassemia/index.html

Thalassemia International Foundation: http://www.thalassaemia.org.cy

Sickle Cell Disease Association of America: http://www.sicklecelldisease.org

Center for Disease Control and Prevention: http://www.cdc.gov/ncbddd/sicklecell/index.html

March of Dimes: http://www.marchofdimes.com/baby/birthdefects_sicklecell.html

American Sickle Cell Anemia Association: http://www.ascaa.org/index.php

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