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What is Sickle Cell disease?

Sickle cell disease is a group of inherited blood diseases characterized by anemia, pain crises, susceptibility to infection, and organ damage. Sickle cell disease involves defects in 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 are due to the production of abnormally-formed beta-globin chains that results in the formation of structurally abnormal hemoglobin. Under conditions of low oxygen in the body, the abnormal hemoglobin causes the red blood cells to form a sickle shape. Sickled red blood cells break down prematurely, leading to anemia. They also stick together and block blood vessels, causing pain and resulting in inadequate blood supply to the area that can lead to organ damage.[1]

What are the symptoms of Sickle Cell disease and what treatment is available?

Individuals with sickle cell disease usually become symptomatic in infancy or childhood. In addition to anemia, symptoms may include[2]:

- Painful swelling of the hands and feet
- Jaundice (yellowing of the skin)
- Recurrent infections
- Splenic sequestration (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 the lungs causing shortness of breath, chest pain, and rapid heart rate)
- Stroke
- Acute chest syndrome (severe, sudden respiratory condition)

Treatment for sickle cell disease includes hydration and pain management for pain crises, antibiotics, and medications to reduce episodes of blood vessel blockage. Blood transfusions and removal of the spleen may be indicated.[2] Treatment may extend life expectancy for individuals with sickle cell disease into the sixth decade.[3] Stem cell transplantation is an alternative treatment that can be curative; however, it is not without risk.[2]

Sickle cell disease is included in all newborn screening panels in the United States.[4]

How is sickle cell disease inherited?

Sickle cell disease belongs to a group of diseases called beta hemoglobinopathies, which are caused by mutations in the beta-globin (*HBB*) gene.[2] Although there are more than 700 described mutations of the *HBB* gene[5] and a wide range of resultant diseases, sickle cell disease occurs when there is at least one copy of a specific mutation of the *HBB* gene commonly called hemoglobin S (Hb S).[2]

Sickle cell disease is inherited as an autosomal recessive disease. An individual who inherits one copy of the hemoglobin S mutation is a “carrier” and is not typically expected to have related health problems. Individuals who are carriers of the sickle cell disease mutation may also be described as having sickle cell trait. Individuals who inherit two copies of hemoglobin S are affected with sickle cell anemia. Individuals who inherit one copy of hemoglobin S and one copy of a different recessive *HBB* mutation are affected with other forms of sickle cell disease.[2]

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In addition to sickle cell disease, mutations in the *HBB* gene are associated with other types of beta hemoglobinopathies, including beta thalassemia. Beta hemoglobinopathies exhibit significant variability in severity and age at onset, which is related to the specific combination of *HBB* mutations and the presence of any mutations in other globin genes.[2]

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. Carrier detection is best evaluated by combining DNA testing, clinical information, as well as a complete blood count and hemoglobin electrophoresis to assess hemoglobin abnormalities, for the most accurate interpretation.[6]

Who is at risk for sickle cell disease?
Annually there are about 275,000 pregnancies affected with sickle cell disease worldwide.[7] Sickle cell disease can occur in individuals of all races and ethnicities, but is more common in some populations including African, Asian Indian, Hispanic, Mediterranean, and Middle Eastern.[1]

If there is no family history, the risk for an individual of being a carrier depends on an individual's ethnic background.

Estimated Carrier Rate in Select Ethnic Groups* [8]	
African American	1 in 14
Hispanic	1 in 183
Middle Eastern	1 in 360
Native American	1 in 176

- Based on California mandatory and universal carrier screening

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 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?

- 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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