Sickle Cell Disease

What is Sickle Cell Disease (SCD)?

SCD is a common inherited blood condition that affects the shape of a red blood cell. Red blood cells are normally round or donut-shaped. In people with SCD, the shape of the red blood cell is altered to a sickle or crescent shape. These sickled cells break down faster than normal red blood cells causing low iron (anemia). Additionally, the sickled cells can become stuck in the small blood vessels in the body which causes pain and damages the organs.

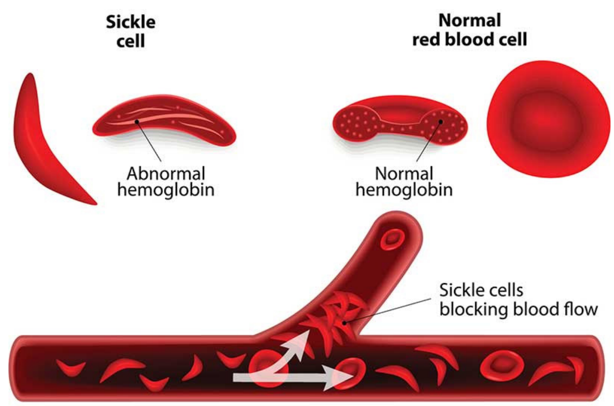


image source: https://wagmc.org/research-2/sickle-cell-disease/

We cannot predict how severe SCD will be or which symptoms a person will have. The symptoms of SCD start in infancy or childhood and may include:

- Recurrent severe pain episodes
- Anemia
- Swelling of hands and/or feet
- Enlarged and/or dysfunctional spleen
- Recurrent infections
- Pulmonary hypertension (high blood pressure in the arteries to the lungs) and other lung diseases
- Strokes, blood clots and other vascular problems
- Kidney diseases
- Gallstones
- Eye diseases
- Heart diseases (heart failure, enlarged heart)
- Delayed growth and puberty
- Increased risk for mental health problems

Anyone can be diagnosed with SCD. It is more common in people of African, Middle Eastern, Mediterranean, Indian Subcontinent, Caribbean, Central and South American ancestry.

What Causes Sickle Cell Disease and How is Sickle Cell Disease Inherited?

A red blood cell is made up of several parts. One of these parts is hemoglobin (Hb). Hemoglobin is made from 2 alpha proteins, 2 beta proteins, iron and oxygen. Hemoglobin takes oxygen to all parts of our body.

The beta globin proteins are made by the beta globin genes. Everyone has 2 copies of the beta globin gene (one copy they inherit from each parent). Sometimes changes occur in these genes that cause these genes to stop working properly. These changes are called disease-causing variants (or mutations). SCD is caused by a variant, called Hemoglobin S (Hb S), in the beta globin gene.

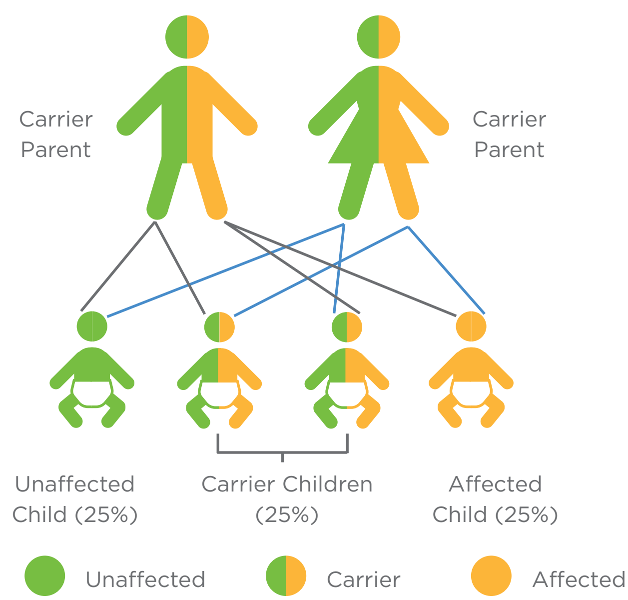
SCD is passed down through a family in an autosomal recessive manner. Autosomal means that both males and females have the beta globin gene. Recessive means a person must inherit 2 copies of the Hb S variant to develop SCD.

People who have one copy of Hb S and one normal working copy of the beta globin gene are called carriers of SCD or have sickle cell trait. Carriers of SCD generally do not have any symptoms of SCD. However, there may be exceptions to this under certain conditions, such as low oxygen environments (ex. high altitude).

When both partners are carriers of one Hb S variant, every pregnancy:

- has a 1 in 4 (25%) chance of inheriting two Hb S variants. The child would have SCD.
- has a 1 in 2 (50%) chance of inheriting one normal working copy of the beta globin gene and one copy of the Hb S variant. The child would have sickle cell trait (like their parents).
- has a 1 in 4 (25%) chance of inheriting two normal working copies of the beta globin gene. The child would not have SCD nor be a carrier of SCD.

Autosomal Recessive Inheritance Pattern



When only one parent is a carrier of SCD, every pregnancy has a 1 in 2 (50%) chance of being a carrier of SCD and a 1 in 2 (50%) chance of having 2 normal working copies of their beta globin gene. They will not have SCD and not be a carrier of SCD.

Sickle Cell Disease and Other Inherited Blood Disorders

Some people are carriers of different blood conditions, such as alpha thalassemia or beta thalassemia. These are common recessive conditions caused by inherited variants in either the alpha globin or beta globin genes. In order to be at risk of having a child with a significant blood disorder, both parents must be carriers of disease-causing variants in the same gene.

I am Considering a Pregnancy, What Now?

Testing options are available for couples who are at risk of having a child with SCD. These tests are optional and should be discussed in more detail with your doctor or genetic counsellor before becoming pregnant or during early pregnancy.

- Before pregnancy – It is possible to test embryos conceived through in vitro fertilization for SCD. This is called PGT-M and is done by fertility clinics. Following testing, couples can transfer embryos not expected to have the condition.
- During pregnancy – SCD can be diagnosed during a pregnancy by:
    - Chorionic villus sampling (CVS) - performed around 11-14 weeks of pregnancy
    - Amniocentesis which is performed after 16 weeks of pregnancy.

  Both procedures have benefits and risks.
- After delivery – A baby can also be tested for SCD after birth.
- Newborn screening – In Ontario, babies are screened for SCD on the heel prick test done shortly after birth. If testing is positive, further blood testing is done on the baby to confirm whether or not the baby has SCD.

Risks to Family Members

Parents, siblings, children of a person who is a carrier of SCD have a 1 in 2 (50%) chance of being a carrier of SCD. We suggest that family members speak to their doctor about testing options.

For more information about this condition, please speak to your doctor or a genetic counsellor.

References:

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