Sickle cell disease is a genetic disorder called a hemoglobinopathy, or an inherited type of anemia. Most people's red blood cells are a round shape, like a doughnut, and they deliver oxygen throughout our bodies to keep everything working correctly. People who have sickle cell anemia have red blood cells that are shaped like a sickle, or a banana. Red blood cells that are this shape can not carry as much oxygen around the body as normal red blood cells. Red blood cells that have the sickle shape break down and die more quickly than they should, which results in anemia. Anemia can cause shortness of breath, fatigue, pale complexion, and delayed growth and development in children.

Individuals with sickle cell anemia generally show some symptoms early in childhood, although the severity can vary greatly between people. Some other common health issues people with sickle cell are anemia (low number of red blood cells), swelling of the hands and feet, high blood pressure, heart failure, organ damage, and infections.

Because of their shape, there is also a chance that these sickled blood cells can get stuck in veins or arteries and lead to a blockage. This blockage prevents blood from flowing to part of the body and can cause a sickle cell pain crisis, which is when there is severe pain because a part of the body is not getting the necessary blood flow. This pain can be throbbing, sharp, dull, or stabbing, and can last anywhere from several hours to several days. This lack of oxygen can also cause organ damage, stroke, cognitive delays, blindness, ulcers, and gallstones.

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 *HBB* gene makes a protein called beta-globin. Two of the beta-globin proteins combine with two proteins called alpha-globins (which are made by the *HBA1* and *HBA2* genes) to make a normal red blood cell.

People who have sickle cell anemia have a specific change (called a pathogenic variant) in both of their *HBB* genes that changes the beta-globin protein. That altered protein is what gives the red blood cell it's sickle shape (called hemoglobin S).

In more rare instances, someone can inherit the specific variant in their *HBB* gene for sickle cell from one parent, and then can inherit a different pathogenic variant in the *HBB* gene they get from their other parent. It is also possible for someone to inherit the sickle cell *HBB* gene variant from one parent, and then inherit a pathogenic variant in the genes that make the alpha-globin proteins (*HBA1* and *HBA2)*. These different combinations are overall

thought to be rare.

Sickle cell anemia is inherited in an autosomal recessive pattern. This means an individual who has the sickle cell anemia has inherited two copies of the *HBB* gene (one from each parent) that **both** have the sickle cell variant. If someone has one normally functioning *HBB* gene, and one *HBB* gene that has the sickle cell variant in it, they are called a 'carrier' for sickle cell anemia (also called sickle cell trait).

It is estimated that approximately 8%-10% of African Americans are carriers for sickle cell anemia. Some research has shown that as many as 1 in 2 to 1 in 3 individuals from parts of sub-Saharan Africa have sickle cell trait. It is also thought to be more common in people with Hispanic, South Asian, Southern European, and Middle Eastern populations.

People with sickle cell trait do not have sickle cell anemia, and most do not have any direct health consequences because of it. However, in rare extreme conditions, people with sickle cell trait can develop some of the symptoms of sickle cell anemia. These situations include an increase in atmospheric pressure (can happen with activities such as scuba diving), low oxygen levels (can happen during strenuous physical activity), high altitudes, and dehydration.

Medical Management for Sickle Cell Anemia

Much of the treatment for sickle cell anemia surrounds avoiding circumstances that increase the chance for complications and having a plan to manage complications as they arise. It is recommended for people with sickle cell anemia to avoid dehydration, extreme temperature or physical exertion/exhaustion, high altitudes, and recreational drugs that may affect the heart. If someone is having a pain crisis, hydration and medications can be used to help manage the pain and risk for related complications.

There are also some screening tests that are recommended for people with sickle cell anemia that can include blood work and imaging such as Doppler ultrasound, chest x-ray, ECG, and abdominal ultrasound. Women who have sickle cell anemia that are pregnant can have an increased risk for preterm labor, blood clots, and infections, so it is important that they work closely with their medical team to make sure they taking all the necessary precautions.

A research study that was done in 1994 estimated that the average person with sickle cell anemia lives to be in their 40s. However, some more recent studies have shown that as our understanding and treatment of sickle cell anemia improves, there has been shift toward a

longer lifespan and fewer childhood deaths. There are also more treatments that are being developed that will likely further increase the life expectancy of people who have sickle cell anemia.

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

American Sickle Cell Anemia Association

Sickle Cell Adult Provider Network

Sickle Cell Disease Association of America

Sickle Cell Information Center