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Key Inforbits

- What is Sickle Cell Disease?
- Signs and Symptom
- Risk Factors for Developing Sickle Cell
- Diagnosis
- Treatment
- Prevention of Complications in Sickle Cell Disease

World Sickle Cell Day, June 19

What is Sickle Cell?[1,2]

Roughly 70,000 to 100,000 Americans have sickle cell disease. Sickle cell disease or SCD is the most common of all genetic blood disorders and is a major health problem in today's society. SCD is a genetically inherited red blood cell disorder that affects the hemoglobin which is the protein that helps carry oxygen throughout the body. People who are born with this disease typically do not start showing signs or symptoms until around five to six months of age. A normal red blood cell is shaped like a disc, very flexible, and can move through the blood vessels with ease. With SCD, the red blood cells are shaped like a crescent-or "sickle"-shaped. When the red blood cells are shaped this way, they are not as flexible and will inhibit blood flow which causes blockages within the blood vessels. When these sickled red blood cells become congested, blood flow to the organs is reduced. This puts the patient at a higher risk for other health problems. Unfortunately, sickle cell disease is a lifelong illness and without treatment can lead to other serious health problems such as stroke and organ damage.

Normal red blood cell Sickled red blood cell

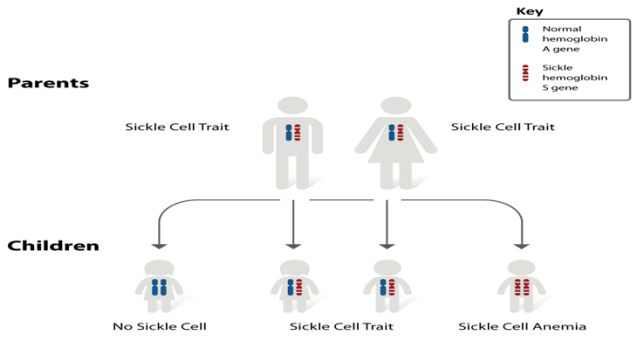
https://kidshealth.org/en/teens/sickle-cell-anemia.html

Signs and Symptoms[1,2]

Each person handles their sickle cell differently. The most common problems with SCD are the "pain crisis" and anemia. These painful episodes often begin in childhood and commonly occur as dactylitis, a condition that affects the small bones of the hands and feet. The "pain crisis" is caused by the crescent shaped blood cell causing the blood cells to clump together and block the blood vessels, preventing oxygen from flowing to the organs. This results in organ failure. The anemia is caused by the sickle-shaped cells breaking down faster than normal red blood cells. Normal red blood cells have a life span ranging from 90 to 120 days before new ones are made. Since sickled red blood cells can burst abruptly and only last 10 to 20 days. The most common signs of anemia include extreme tiredness and irritability. Dark urine, jaundice, and stunted growth are other common symptoms that are typically seen in patients that have SCD.

Risk Factors for Developing Sickle Cell[2-4]

Since SCD is an inherited disorder, people who have SCD inherited two faulty hemoglobin genes known as hemoglobin S. To have "normal" genes, a person must have two hemoglobin A genes. A person can have the hemoglobin A gene and a hemoglobin S gene and still be healthy. A carrier of the sickle cell trait (hemoglobin S gene) can pass it onto their children. To have two faulty hemoglobin S genes, both parents must be carriers. If both parents are carriers, there is a 25% chance that their child will have sickle cell disease. There is a 50% chance that the child will inherit one of the hemoglobin S genes and one regular gene-meaning that the child is now a carrier. There is also a 25% chance that they will have a child with only hemoglobin A genes-meaning the child is not a carrier nor do they have sickle cell. SCD is more common among particular ethnic groups. African-Americans, Hispanic-Americans, and people of Middle Eastern, Asian, Indian, and Mediterranean descent are more predisposed to this condition. These ethnicities are more at risk of being affected by SCD due to evolving traits that developed to help protect against malaria. Roughly, 1 in 13 African-American babies are born with the sickle cell trait. Roughly, 1 in every 365 African- American babies are born with sickle cell disease. This disease also affects roughly 1 in every 16,000 Hispanic-Americans. Tiki Barber, a former National Football League player for the New York Giants, has SCD and helped launch the "Be Sickle Smart" campaign to help raise awareness for the disease.



https://www.nhlbi.nih.gov/sites/default/files/inline-images/scd_inheritance_0_0.jpg

Diagnosis of Sickle Cell Disease[1,4,5]

In the United States, sickle cell disease is a mandatory part of the fetal routine work up that happens after birth. Unborn babies can be diagnosed before birth by gathering a sample of amniotic fluid or a sample from the placenta, if both of the parents are sickle cell disease carriers. This can be performed as early as 8 to 10 weeks in pregnant women. For after birth, a blood test is performed to check for the hemoglobin S gene. Anyone showing signs or symptoms of sickle cell can have the blood test performed with a doctor's recommendation. Even though these tests are available. they can not predict the severity of the disease. Early detection of SCD can help improve survival and with the right treatment, can help reduce disease related complications.

Treatment of Sickle Cell Disease[1,6,7,8]

For some patients, a cure for sickle cell disease is possible. A blood and bone marrow transfusion can be performed to possibly cure a patient's sickle cell. This transfusion is a tricky process because a "perfect" bone marrow donor must be found. The blood and bone marrow transfusion currently has 84% chance of event free survival. Unfortunately, it also has a 5% chance of death due to the procedure and 10% of patients will have a relapse of their SCD including signs and symptoms. Clinical trials are currently underway for a new therapy called LentiGlobin. This is a gene-based therapy where physicians would use the patient's own stem cells and add them to a corrected gene (hemoglobin A). This treatment would help the body create normal red blood cells. Blood transfusions are also used for management of symptoms. These transfusions are used to help reduce the amount of sickle hemoglobin levels in the patient's body and reduce the risk of stroke. No oral treatment has been found for SCD remission. However, there are treatment options to manage symptoms.

Table 1: Drug Treatment Options for Sickle Cell Disease

Drug ***Brand/Generic*** **Manufacturer**	**Class**	**Dose/ Dosage form**	**How it Works for Patients**
Hydroxyurea *Hydrea* *Droxia* Manufactured by: E.R. Squibb and Sons	AntiMetabolite	Oral Capsule: 200 mg, 300vmg, 400vmg, 500vmg Oral Tablet: 100vmg, 1000vmg	Drug of choice. Reduces "pain crisis" by increasing RBCs to flow through the vessels.

L-Glutamine *Endari* Manufactured by: AIE Pharmaceuticals	Amino acid	Only the Endari oral powder is available for sickle cell disease. Oral Powder: 5 g	Reduces the frequency of "pain crisis". *Can be used in combination with Hydroxyurea
Crizanlizumab *Adakveo* Manufactured by: Novartis Pharma AG	IgG2 kappa monoclonal antibody	Monthly Intravenous Transfusion: 100 mg/10ml Only approved for patients over the age of 16.	Reduces "pain crisis" by preventing the sickled cells from clotting. *Can be used in combination with Hydroxyurea
Voxelotor *Oxbryta* Manufactured by: Global Blood Therapeutics	HbS polymerization inhibitor	Oral Tablet: 300 mg and 500mg Oral Soluble Tablet: 300 mg Only approved for patients over 4.	Reduces risk of anemia by improving blood flow through the body *Can be used in combination with Hydroxyurea
Ferriprox *Deferiprone* Manufactured by: Chesi Global Rare Diseases	Iron-chelating agent	Oral Solution: 100 mg/mL Oral tablet: 500 mg and 1000 mg	Reduces the risk of anemia *Can be used in combination with Hydroxyurea

Unfortunately, all of the drugs used to help manage SCD have a variety of side effects including neutropenia, arthralgia, increased ALT and AST, vomiting, oropharyngeal pain, and pyrexia.

Prevention of Complications in Sickle Cell Disease[1,9,10]

Sickle cell disease comes with a wide range of complications. Even though a cure for SCD is rare, there are many ways to manage the complications of the disease.

- The transcranial doppler (TCD) ultrasound screening is used to help identify children, aged 2 to 9 years who are at an increased risk of stroke due to SCD.
- Patients with SCD are at a higher risk of infection and it is recommended that children take daily penicillin orally twice a day to reduce the risk of bloodstream infection. This therapy starts as early as 2 months and continues until the patient is at least 5 years of age.
- These patients should also maintain adequate hydration to also help them prevent the pain crisis. Dehydration causes the sickle red blood cells to have a higher risk of clumping together.
- Since the SCD patient population is considered high-risk, these patients should be up to date on their vaccines including COVID-19, annual influenza vaccine, and the pneumococcal polysaccharide vaccine.
- Decongestants may cause blood vessel constriction and should be avoided in this patient population.
- SCD patients need to limit alcohol consumption. Excessive amounts of alcohol causes dehydration within the body. This puts the patients at an increased risk of blood clotting.

- Patients should be screened annually to avoid retinopathy. SCD causes blockages within the vessels that deliver oxygen to the eyes. When this blood is blocked, it can result in vision loss.
- Patients should drink plenty of fluids during long flights of over 4 hours.
- SCD patients should avoid smoking. Smoking is linked to acute chest syndrome in this patient population.

Summary

The most prevalent hereditary blood disorder, known as SCD, is a significant public health issue today affecting 70,000 to 100,000 Americans. Hemoglobin, the protein that aids in carrying oxygen throughout the body, is impacted by SCD, a genetically transmitted red blood cell condition. Unfortunately, sickle cell disease is a lifelong condition that, if left untreated, can result in major health issues like organ damage and stroke. The "pain crisis" and anemia are the two most typical SCD issues. The most typical symptoms of anemia are excessive fatigue and irritability. Two defective hemoglobin genes, or hemoglobin S, are inherited by people with SCD. Due to developing features that emerged to help defend against malaria, certain ethnic groups with SCD have a higher incidence of being affected. There may be a cure for SCD in some patients involving a blood and bone marrow transfusion. To manage symptoms and complications, there are various therapy choices; however, currently no oral medication is efficacious for SCD remission. Everyone has a role in preventing and becoming aware of the prevention of sickle cell disease.

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The Last "dose" ...

"Although the world is full of suffering, it is also full of the overcoming of it."

– Helen Keller (1880-1968)

American Author, disability rights advocate, political activist and lecturer

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