# *Sickle Cell Disease*

***1.0 Contact Hour***

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# Sickle Cell Disease

By Joe Knight, PA-C

**Objectives:**

1. Identify the ethnic groups that are most prone to be genetically susceptible to sickle cell disease.
2. List some of the medical consequences of hemolysis.
3. Explain the mechanism-of-action of a sequestration crisis.
4. Explain one of the first physical signs a patient may experience if afflicted with sickle cell disease.
5. Explain the most common cause of death in patients with sickle cell disease.

**Introduction**

Sickle Cell Disease (SCD) is humanity's most common inherited blood disorder, with mortality highest during the first five years of life. Approximately 80,000 Americans, mostly of African or Mediterranean descent, have this affliction. Approximately 1 in 12 African Americans and 1 in 100 Hispanic Americans carry the trait for SCD.[1] Though they may not have the disease, if two parents with the trait have a child, this significantly increases the child's chances of having SCD.

The first case of SCD in the United States was identified in 1910 at the University of Chicago. Medical students were studying blood and were required to sketch what they saw as they put their own blood under the microscope. While most students had drawn round blood cells, one student had abnormal cells that looked like a hooked tool

("sickle") used to cut wheat. The student was from the West Indies, and had recurrent bouts of jaundice and abdominal pain.

SCD occurs in individuals or their descendents from geographic areas where malaria is common; therefore, SCD is common in Africans, Middle Easterners and Southern Europeans. Evidently, the change in the molecule protects against severe infection caused by malaria. Some researchers suspect that when a red blood cell (RBC) is infected with the malaria organism, the cell will sickle and be destroyed by the body's defense mechanism. Over thousands of years, this system probably became incorporated into the genetic structure of those people living in malaria-prone areas, perhaps to provide protection against malaria.

SCD is a chronic condition associated with symptoms due to vascular occlusion and hemolytic anemia. Hemolysis can cause jaundice, anemia, gallstones, pulmonary symptoms and delayed growth.[2]

**Pathophysiology of SCD**

The primary function of hemoglobin is to carry oxygen molecules from the lungs to the rest of the body. In SCD, the molecular structure of the hemoglobin in the RBC is defective, which causes the cell to assume a sickle shape that can't easily pass through small blood vessels and capillaries. While a normal round red blood cell with a normal hemoglobin component can squeeze through capillaries without difficulty, sickled cells become stuck, creating clumps that block blood cells from carrying oxygen to the tissues

in other parts of the body. This logjam of cells and the ensuing oxygen deprivation can cause severe pain, known as a sickle cell crisis. A sickle cell crisis can be triggered by infection, trauma, stress, sudden temperature change or sudden altitude change. Another problem with SCD is the longevity of the red blood cells. While a normal red blood cell lives about 120 days, a sickled cell lives only about 10-15 days. Because sickled red blood cells are too fragile to withstand the mechanical trauma of circulation, the cells break down. This releases the hemoglobin into the bloodstream, causing the yellowish cast (jaundice) to the skin and eyes. The released hemoglobin can also pass through the kidneys and cause dark urine.

**Signs and symptoms**

Patients with SCD usually have symptoms within the first year of life; these symptoms can range from mild to severe. One of the first symptoms is called Hand-Foot syndrome. Swelling of the hands and feet associated with a fever develops as the sickled cells begin to plug the distal capillaries and block the return flow of blood.[1] Vascular occlusion, also known as a sequestration crisis, occurs when blood enters the spleen and the sickled cells either clump together or stick to the endothelium of the blood vessels.[2] So many cells become blocked that eventually only plasma exits the spleen. Some episodes are so severe that if the person is cut, his or her blood resembles pink water instead of the normal dark red of blood. In situations like this, a blood transfusion may be the only thing that can save the person's life. Some hematologists recommend removal of the spleen after one life-threatening episode, while others may allow two or three sequestration episodes to occur before recommending removal of the spleen.

Most children with SCD do not experience a sequestration episode; however, the spleen may slowly die because of multiple blockages of the tiny blood vessels over a long period of time. One of the functions of the spleen is to form antibodies to help prevent infection from occurring; therefore, the affected person may be more susceptible to infection. Other organs can also be affected by SCD, including the kidneys, the brain and lung. Older patients may develop skin ulcers on the lower legs and ankles due to blockage of the capillaries. These problems may take years to decades to develop.

The risk of stroke is a major concern in patients with SCD. Neurological complications may include cerebral infarcts or intracranial hemorrhage, with cerebral infarcts occurring most commonly in children between the ages of two and five.[3] Seventeen percent of children with SCD who do not have neurological symptoms have changes that can be detected using magnetic resonance imaging (MRI);[4] these changes may be associated with learning and behavioral difficulties and may be indicative of an increased risk of more severe brain ischemia in the future. Called silent cerebral infarcts, or SCIs, these lesions can also lead to lower IQ scores and other neurocognitive defects.[5] These infarcts occur due to endothelial changes that lead to a narrowing of the vasculature.[2] Seizures are another concern in children with SCD; seizures are ten times more common in children with SCD compared with the general population.[6]

The sickled cells may also block the flow to the blood vessels that supply the lungs, resulting in an entity called acute lung syndrome. In adult males, the same mechanism may cause priapism, a prolonged, painful erection not due to sexual excitement.[1]

Persistent priapism can damage the vasculature of the penis, and the only treatment is surgical decompression.

## Treatment

Infection is linked to many complications associated with SCD. Despite preventive measures such as prophylactic penicillin and the pneumococcal vaccine, sepsis remains a major concern for patients with SCD and is a common cause of death.[7] Prophylactic penicillin administered daily to children has been shown to reduce the cases of *Streptococcus* pneumonia sepsis by 80%; most children are able to stop the penicillin at aged five.[8] Patients with SCD should also receive annual influenza vaccination.[4] Febrile SCD patients are an emergency situation – the patient should have blood cultures drawn immediately and started on intravenous antibiotics. Chest radiographs and blood counts should also be considered.[2]

Hydroxyurea, an anti-tumor drug, appears to stimulate the production of fetal hemoglobin, a type of hemoglobin found only in neonates. This type of hemoglobin appears to prevent the sickling of cells;[1] however, several problems exist with the use of hydroxyurea for the treatment of SCD. Hydroxyurea is potentially mutagenic and carcinogenic.[9] Cancer and leukemia have been reported in hydroxyurea-treated sickle cell disease patients, but whether the incidence is higher than in the general population is not known.[10]

The only true "cure" for SCD is bone marrow transplantation; however, only about 18% of children with SCD have a healthy, matched donor.[1] Bone marrow/stem cell transplants are used only in cases of severe sickle cell disease for children who have minimal organ damage from the disease.

## On the horizon

Research into the treatment of SCD continues. Sadelain has found promising results using stem cells for the treatment of SCD and other blood disorders.[11] Nelson, et al., have found a higher rate of vitamin B6 excretion in children with SCD. They suspect that vitamin B6 may prevent sickling of cells, and perhaps this information may be useful in developing a treatment for the disease.[12]

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