

An estimated 70,000 Americans have **sickle cell anemia disease**. Acute sickle cell pain has been described as more severe than postoperative pain and as intense as cancer pain. Treatment of sickle cell pain. *Pharmacotherapy* 2002; April pp 484-491

### **What is sickle cell anemia disease?**

Sickle cell anemia is an **inherited** disease that affects the red blood cells. The disease was first noted in the USA in the November 1910 issue of *Archives of Internal Medicine*. Dr. James B. Herrick, a Chicago cardiologist described in his article "Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia."

Sickle cell anemia is thought to have evolved as a defense against malaria. Persons with sickle cell anemia or who are carriers of sickle cell disease do not get malaria as frequently as others. Sickle cell disease is most prevalent in areas where there is a high incidence of malaria such as Africa, India, The West Indies, and The Mediterranean (insert Reisberg images).

### **How sickle cells are different:**

Normal red blood cells are disc shaped and concave; they are produced at the rate of nearly 2 ½ million per second and live approximately 120 days. Red blood cells carry oxygen throughout the body and to vital organs by means of blood vessels, veins, arteries and capillaries.

Red blood cells contain hemoglobin, which contains iron. Oxygen is attached to iron that is in the hemoglobin. When sickle cells lose oxygen (deoxygenated) they bend and change form. These cells become long, pointed and crescent shaped like a sickle which is a tool used to cut down tall grasses or weeds.

### **A sickling episode and crisis explained:**

A sickling episode begins when oxygen levels in the body drop due to over exertion, smoking, stress, temperature extremes hot (fever) or cold (hypothermia), or dehydration.

Blood vessel walls narrow (constrict). Hemoglobin S cells, which do not contain oxygen (deoxygenated) become rod like or sickle shaped. (insert image) A glue-like blood vessel wall protein called thrombospondin helps the sickle shaped cells to clump together. These distorted cell clusters cannot get through the constricted blood vessels. (insert image) This log jam of misshapen cells stabbing into the vessel walls, causes a great deal of pain.

Pain from a crisis is most commonly felt the chest, abdomen, lower back, thighs, hips, and knees. Pain can also occur in the bones and is usually symmetric (same place both sides). Pain often begins at night (all pain or just bone pain?) Episodes of pain can be for hours or days even weeks, and usually follow a pattern. Most patients are pain free between episodes but some patients will experience fatigue and symptoms such as numbness or tingling and *scleral icterus*, which is a yellowing (jaundice) in the white portion of the eye.

Some normal red blood cells do get through the narrow blood vessels, but not enough to deliver the amount of oxygen needed by organs in the body. The brain, heart, lungs, liver, pancreas, kidney, and endocrine system all need oxygen to work properly. Without adequate amounts of oxygen the brain cannot send clear messages to the body systems, so muscles get weak, the heart cannot pump, the lungs cannot expand and contract, the kidneys and liver cannot clear the body of poisons or metabolize nutrients, the sex organs won't work properly, and the pancreas cannot manage insulin. The entire body system begins to break down. Pain, organ failure and disease are the consequences.

The blood pH also can contribute to a crisis. The human body functions best with a blood pH at 7.4. If the pH drops below 6.8 or rises above 7.8, death may occur. A person has an alkaline pH at levels higher than 7.4. This condition is called alkalosis or alkalemia. A person has an acidic pH at levels lower than 7.4; this condition is called acidosis or acidemia. An acidic pH can initiate a sickling episode and lead to a crisis.

### **What causes changes in pH:**

Many things can contribute to changes in body or blood pH. What we eat and drink can have considerable influence on these changes. Inadequate fluids, too many sugary foods or soft drinks, too many foods and beverages high in caffeine, not enough fruits and vegetables in the diet, stress, certain medications, tobacco or marijuana smoking and alcohol consumption are among the culprits that will can changes in pH. Disease can also cause acidosis. Damage to the kidney can reduce the ability of the kidneys to excrete acid this leads to acidosis. Other causes include dehydration due to inadequate intake of fluids or diarrhea and vomiting and insulin deficiency due to diabetes or damaged or inflammation of the pancreas (pancreatitis).

Once a sickling episode is triggered, events are set into motion within the sickle cell anemia patient. This cascading chain reaction results in a crisis of extreme pain, sometimes so severe that hospitalization is necessary.

**Who is at risk:**

People whose ancestors come from Africa, Central America (especially Panama), Caribbean nations, India, Mediterranean countries, Near Eastern countries or South America. Most at risk is anyone with a family history of sickle cell disease.

In the USA, an estimated 10 percent of the black population are carriers of sickle cell disease and nearly three percent have sickle-cell disease. According to the US Centers for Disease Control and Prevention, Atlanta 3 of every 1000\* African Americans has sickle cell anemia disease.

**Genes Explained:**

HBB or the hemoglobin beta gene is the gene responsible for sickle cell anemia; HBB is on chromosome 11. When the HBB gene is mutated or flawed it can cause disease.

One HBB gene each is inherited from each parent. If a person inherits two variant (mutated or flawed) copies of this gene, they have sickle cell disease. If they inherit only one variant copy of the gene, they are carriers of the disease. They have the sickle cell trait, but not the disease.

Two carriers can pass one variant copy each to their baby who will then develop the disease. For this reason, sickle cell anemia is one of the diseases most states in the USA screen for at birth. Currently 41 states screen all newborns for sickle cell disease and 11 screen infants of parents who are at high risk for the disease.

The common variants of sickle cell disease are homozygous sickle cell disease (hemoglobin SS disease), compound heterozygous sickle hemoglobin C disease (hemoglobin SC disease) and the sickle  $\beta$ -thalassemias or Hemoglobin Barts - which indicates an alpha thalassemia trait

**Detection:**

Besides DNA analysis, the tests that are used by physicians to detect sickle cell disease include:

Sickledex Hgb S which is one type of blood test that can detect sickle shaped cells. This test initially screens for sickle cell disease. If some cells are present, the doctor will perform hemoglobin electrophoresis to confirm the disease.

Hemoglobin electrophoresis identifies abnormal forms of hemoglobin. Each form of hemoglobin is electrically charged and when removed from red blood cells these cells are placed on a special paper and put into an electromagnetic field. Different forms of hemoglobin migrate at different rates and to special bands on the paper. The bands correspond with cell types. The quantity of cell type on a certain band helps the physician know the severity of the disease. Sickle cell disease and trait, Hemoglobin C or H disease, and thalassemia major or minor can be detected using electrophoresis.

Persons with SS have the most serious form of the disease; these patients will have more severe symptoms and are likely to have a shorter lifespan. Persons with Barts or one sickle variant and one thalassemia variant which is a compound heterozygote, may have serious health consequences similar to the patient homozygous for SS. Those who have Hemoglobin C disease usually only experience a mild form of the disease, as does the patient with sickle cell trait.

**Symptoms, findings and complications** People with sickle cell anemia may have one or several of the following:

- low red cell counts
- nausea or possible vomiting
- weakness
- fatigue
- jaundice
- shortness of breath
- chest pain
- stomach pain
- short torso with long arms, legs, fingers & toes
- bone pain and damage to the bones (which bones: long?)
- enlarged spleen
- priapism (constant erection)

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| <ul style="list-style-type: none"><li>• frequent infections</li><li>• blood in the urine</li><li>• fever</li><li>• strokes</li><li>• leg ulcers</li><li>• eye damage</li><li>• yellow eyes or jaundice</li><li>• early gallstones</li><li>• lung blockage</li><li>• kidney damage and loss of body water into urine</li><li>• blood blockage in the spleen or liver</li><li>• delayed growth</li></ul> |
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Management of sickle cell anemia can be somewhat different for adults, adolescents, teens and children. All sickle cell patients should be under the care of a medical team that understands the disease. Spouse, parents, teachers, caregivers and friends of sicklers should read as much as they can about the disease so that they understand signs that a sickle cell patient is in need of medical attention and know what to do in these times.

**Signs that a sickler is in need of prompt medical attention:**

- Fever
- Chest pain
- Shortness of Breath
- Increasing tiredness
- Abdominal swelling
- Unusual headache
- Any sudden weakness or loss of feeling
- Pain that will not go away with home treatment
- Priapism (erection that will not go away, very painful)
- Sudden vision change

Some small children may not be able to tell a caregiver that they need medical attention. The Oucher scale developed by Mary J. Denyes, PhD, RN and Antonia M. Villarruel, and inspired by Judith E. Beyer, PhD, RN, was designed to help young children communicate the degree of pain being experienced. An example of the scale can be found at <http://www.bestbets.org/cgi-bin/bets.pl?record=00045>

**Sickle cell patient regardless of age:**

- Avoid temperature extremes too hot or too cold because this can be stressful and trigger a sickling episode.
- Get plenty of fluids (1 liter per day minimum) because: fluids help blood flow and keep you from being dehydrated
- Eat a balanced diet with lots of fruits and fresh vegetables because these foods are rich in nutrients that improve hemoglobin levels and the absorption of iron from the diet and most fresh fruits are very high water content
- Take supplements: because some nutrients are difficult to get from the diet and people with SCA need daily supplementation of some nutrients and therapeutic doses of others such as B-complex, folic acid, zinc, and selenium. Always check with your physician about the proper dose for any supplements because doses will be different for age, gender, weight, height and overall health.
- Get adequate rest because being too tired can trigger an episode
- Exercise in moderation but do not over exert yourself because this could trigger an episode
- Stay away from stressful situations or over excitement, which can trigger an episode
- Vital to preventing a painful crisis: keep your vascular system open.
- Don't smoke tobacco or marijuana or be exposed to second-hand smoke of either of these products because use or exposure causes constriction of blood vessels (arteries and capillaries)
- Don't drink alcohol because it robs your body of vitamin B, dehydrates and can cause liver damage. Some over-the-counter products contain significant levels of alcohol, such as cough syrups. Check with your doctor about how to take these products
- Avoid caffeine because caffeine is a diuretic or a substance that makes you lose body fluids; if you lose fluids you become dehydrated. For every cup of caffeine containing beverage (coffee tea cola) you will need to drink two cups of water or eat two servings of fruit to replace lost fluids.

**Exercise for people with sickle cell anemia:**

**Some patients with sickle cell anemia can do mild to moderate exercise without triggering an episode of sickling.**

**Not recommended:**

High-impact sports such as running, jogging, gymnastics or tennis can result in bleeding in the joints. Contact sports such as football, soccer, hockey, basketball are also not recommended. Other strenuous sports such as wrestling, boxing, softball, some forms of dancing, rowing, hiking, rappelling, skating, skateboarding, weight lifting, or judo should be discussed with your physician, as participation in these activities must be evaluated individually.

**Recommended** exercises, depending on the condition of the bones such as the ankles, knees and hips:

Swimming, walking, some forms of dancing, golf, gardening, some resistance exercise such as low settings on the Total Gym EFI Medical systems

What the physician may prescribe:

- Painkillers (over-the-counter or prescribed) as needed
- Prophylactic penicillin until age six to prevent serious infection such as pneumonia or
- Medication such as hydroxyurea, sometimes in combination with EPO (erythropoietin)
- **Nitric Oxide** which can help chest pain
- PCV (pneumococcal conjugate vaccine)
- Blood transfusions
- Iron chelation therapy

**In some cases:**

- Blood exchanges
- Bone marrow transplantation
- Stem cell transplantation
- On the horizon: gene therapy

**Blood transfusions, iron overload and iron chelation therapy:**

People who have repeated blood transfusions will eventually develop transfusional iron overload and they will need iron chelation therapy to remove excess iron. Each blood transfusion contains about 250 milligrams of iron. Iron cannot be excreted by the body and over time the excesses build up in vital organs such as the anterior pituitary, heart, liver and joints. Damage to these organs caused by the excess iron can result in organ failure. It is important to remove the excess iron before damage can occur. Tissue iron levels are measured in serum ferritin, serum iron and TIBC (total iron-binding capacity) These results help the physician to monitor iron build up and to address the excess iron as soon as possible. Usually physicians will allow serum ferritin (which is one measure of tissue iron) to reach 2,000ng/mL before beginning chelation therapy.

Chelation therapy is the removal of iron pharmacologically with an iron-chelating agent such as Desferal. Desferal is not absorbed in the intestinal tract, therefore, this drug must be administered intravenously using a portable battery-operated infusion pump. Generally, the pump is worn at night, where slow infusion of the iron chelating agent is administered over a period of about eight hours, for a duration of four to six nightly infusions per week. Patients might be given an additional two grams of Desferal intravenously for each unit of blood transfused. Desferal is injected separately from blood transfusions.

**Blood exchanges**

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- Bone marrow transplantation
- Stem cell transplantation
- On the horizon: gene therapy