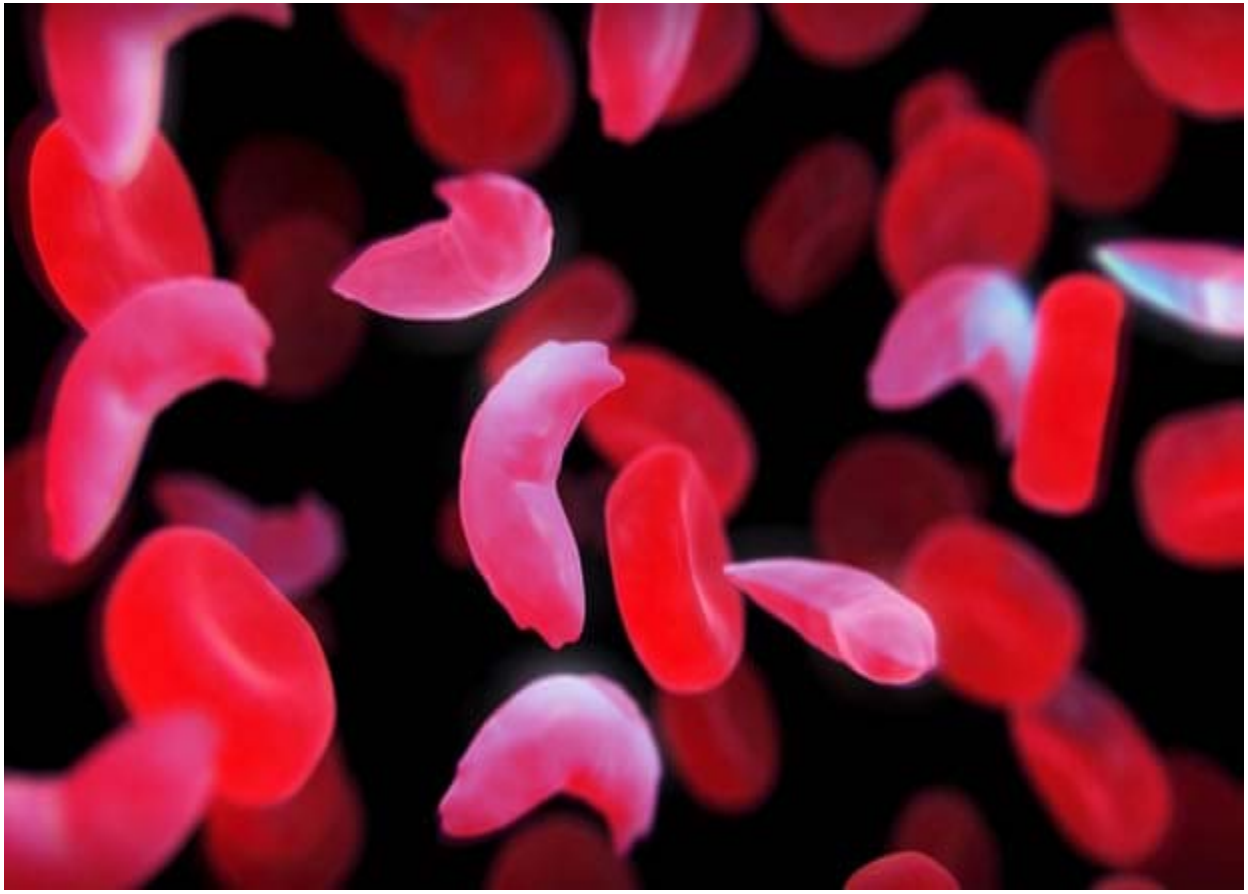
Sickle Cell Anemia



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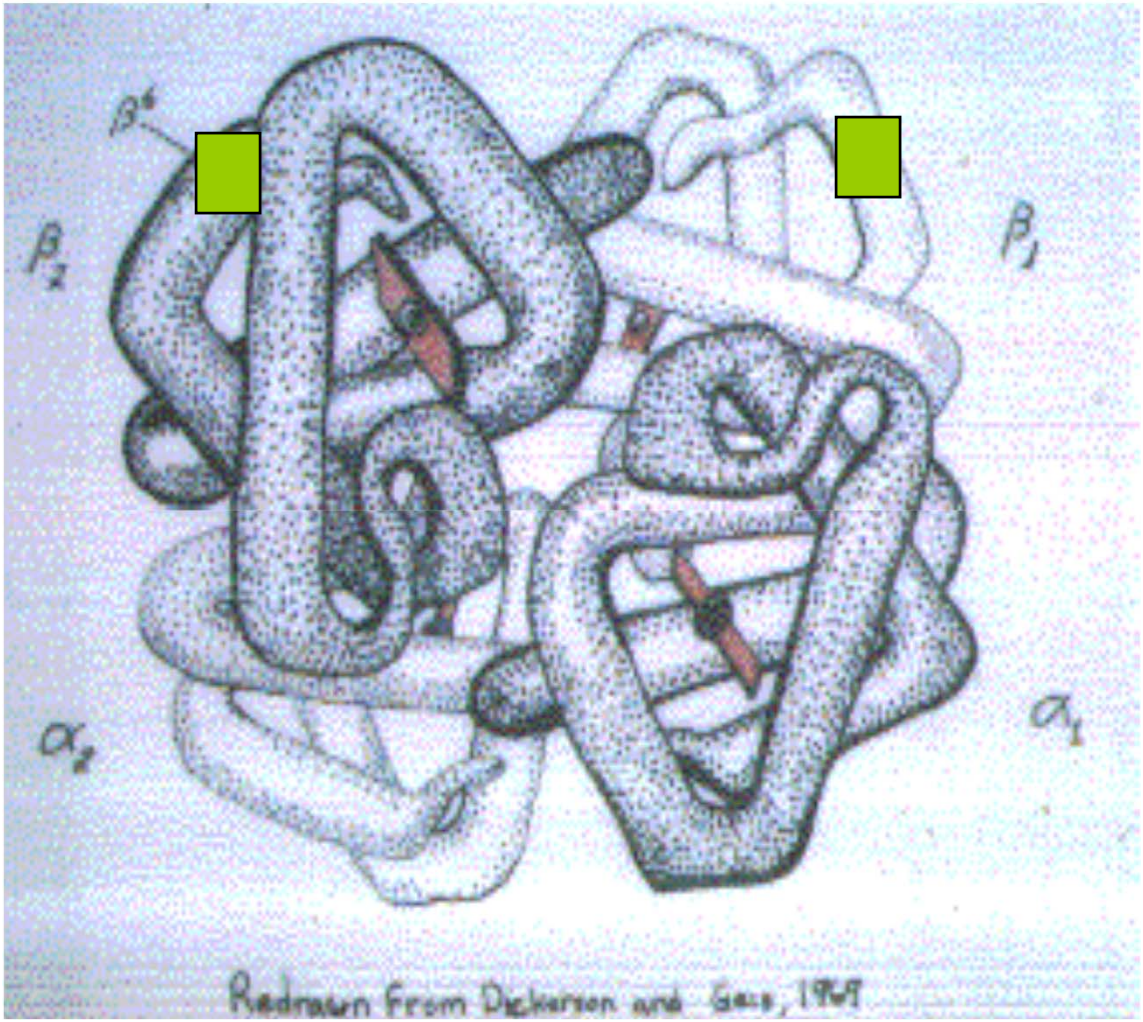
Objectives

- Explain to a patient the cause of sickle cell anemia
- Distinguish between sickle cell trait and sickle cell disease
- Identify the clinical features of Sickle Cell Disease
- Discuss measures to prevent a sickle cell crisis
- Based on a patient case develop a treatment plan for a patient experiencing a sickle cell crisis

What is Sickle Cell Disease?



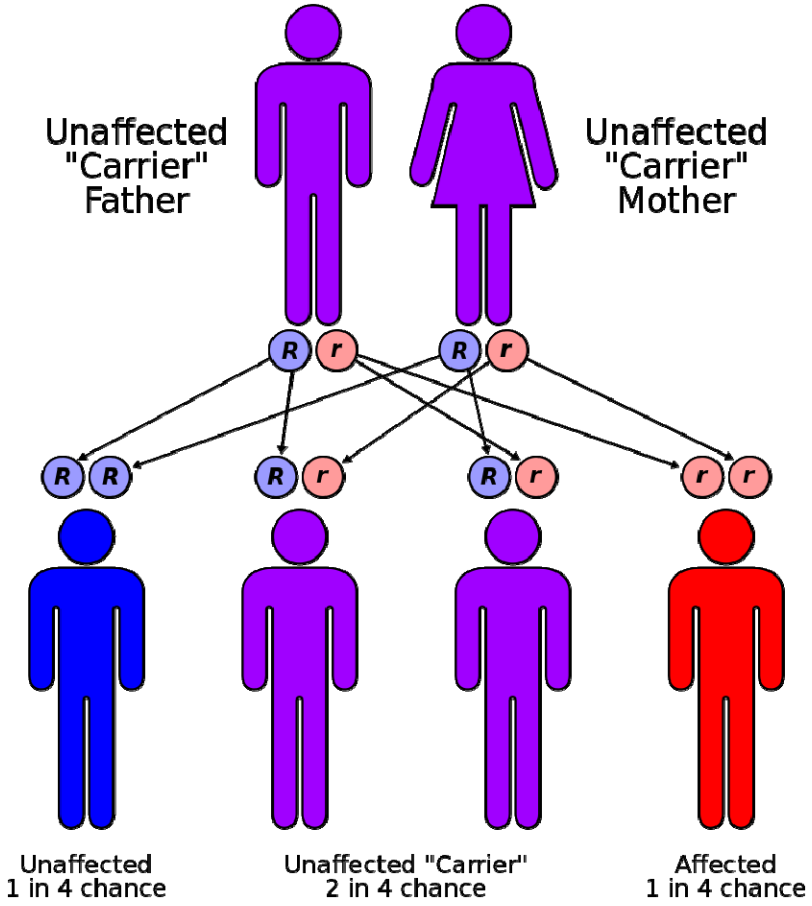
A person with sickle cell disease has one different substance in the way it makes hemoglobin. This substance is the amino acid valine in one spot where there should be glutamic acid.

This one change causes the chemical to form long strings when it lets loose of its' oxygen. This causes the red cell to become deformed into a "sickle" shape.

Frequency

- Hgb SS disease occurs in 0.15% of African American newborns
- 8-10% of African Americans in the U.S. are carriers of Hgb S gene

Carriers


Unaffected
"Carrier"
Father
Unaffected
"Carrier"
Mother
R
r
R
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R
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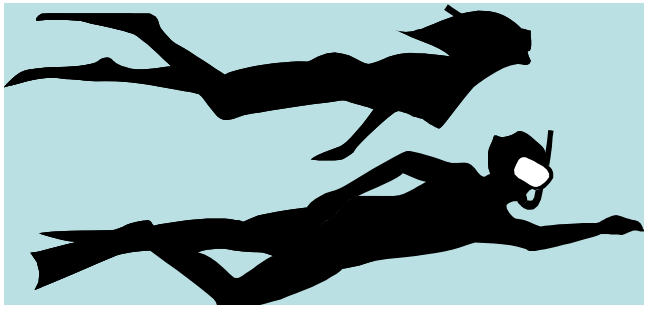
R
r
r
r
Unaffected
1 in 4 chance
Unaffected "Carrier"
2 in 4 chance
Affected
1 in 4 chance

Trait vs.. Disease

Sickle cell trait is present in one out of ten African Americans. About half of the hemoglobin in the red cell is sickle and the cell will exhibit sickling when under severe conditions of low oxygenation. Hematuria or blood in the urine is the most common problem. There are case reports of people with sickle cell trait having more severe sickle related problems when placed under severe conditions such as extreme pressure and low oxygen conditions. Those with trait should be advised of the risks of extreme physical activity, severe pressure changes, deep sea diving, and the possibility of hematuria.



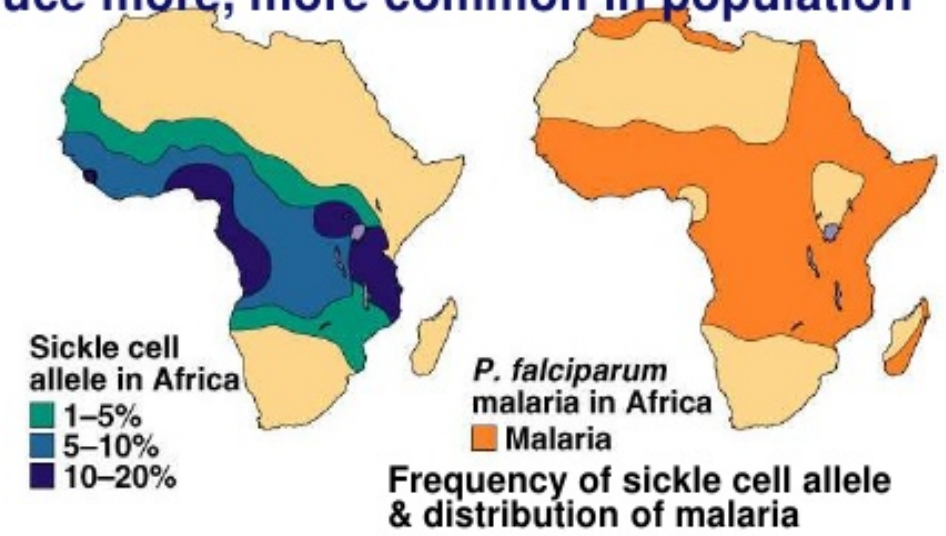
Survival advantage against Plasmodium infection (malaria)

- Heterozygotes for the sickle cell gene are relatively protected against malaria, while patients who are homozygous for the sickle cell gene, suffer from sickle cell disease and are highly prone to the lethal effects of malaria.
  - This is because the malarial parasite cannot undergo multiplication in a sickle-shaped red blood cell for the following reasons:
  - The body sends sickled red blood cells to the spleen for elimination, consequently destroying the parasite.
  - Since the cell membrane of the sickled red blood cell is stretched by its unusual shape, it becomes porous. The sickled cell "leaks" nutrients, like potassium, that the parasite needs to survive, so the parasite dies.

Heterozygote Advantage

- In tropical Africa, where malaria is common:
  - homozygous dominant (normal)
    - die or reduced reproduction from malaria: H^bH^b
  - homozygous recessive
    - die or reduced reproduction from sickle cell anemia: H^sH^s
  - heterozygote carriers are relatively free of both: H^bH^s
    - survive & reproduce more, more common in population

Hypothesis:
In malaria-infected cells, the O_2 level is lowered enough to cause sickling which kills the cell & destroys the parasite.

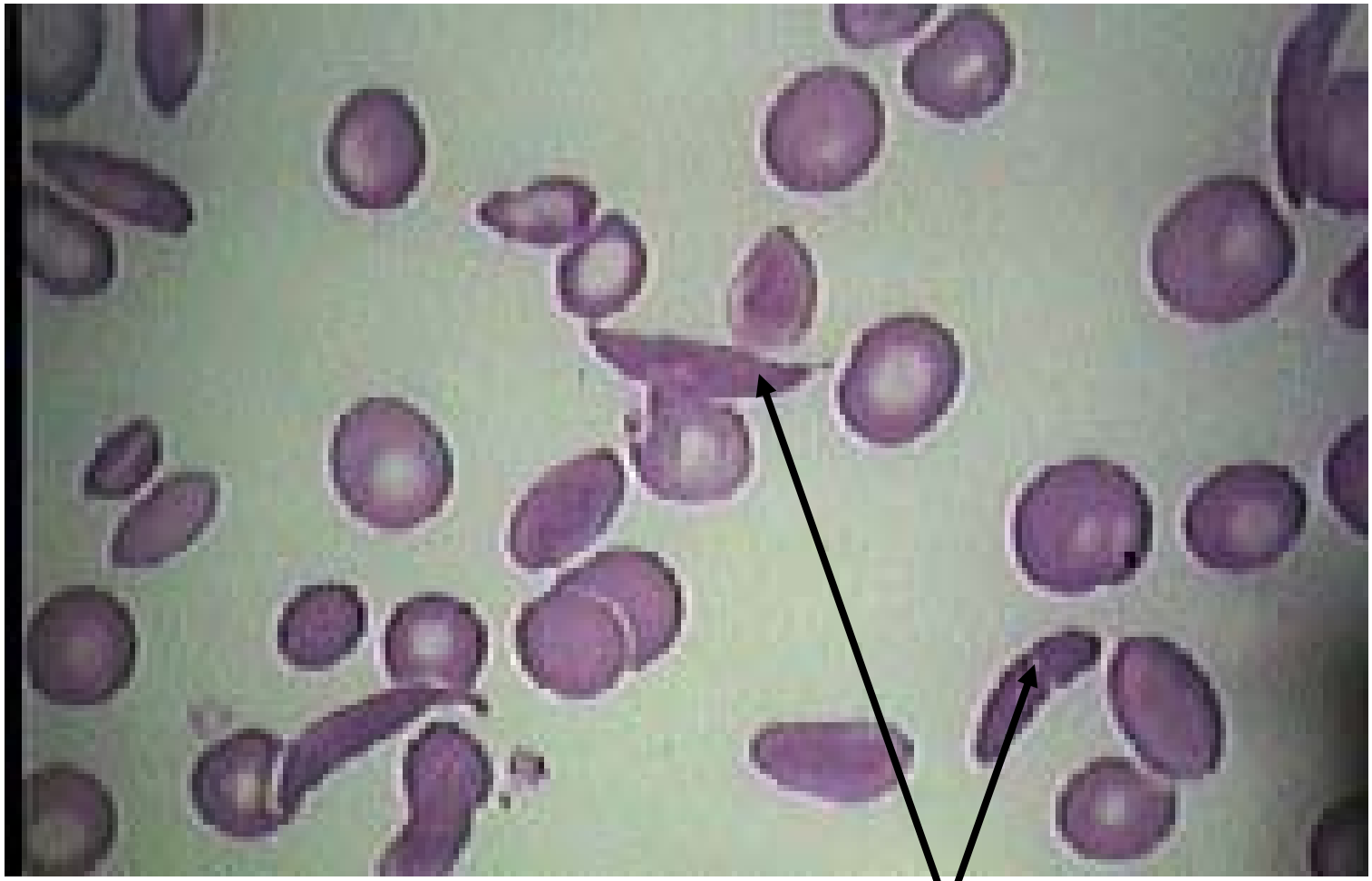


Frequency of sickle cell allele & distribution of malaria

Sickle Cell: Pathophysiology

- Deoxygenation of mutant Hb leads to
  - ↑ K^+ efflux
  - ↑ cell density / dehydration
  - ↑ polymerization
- Sickled cells adhere to endothelial cells
- Endothelial factors ↑ vasoconstriction
- Blood flow ↓ promotes vaso-occlusion
- “Vicious cycle” with decreased blood flow, hypoxemia / acidosis, increased sickling
- Some cells become irreversibly sickled

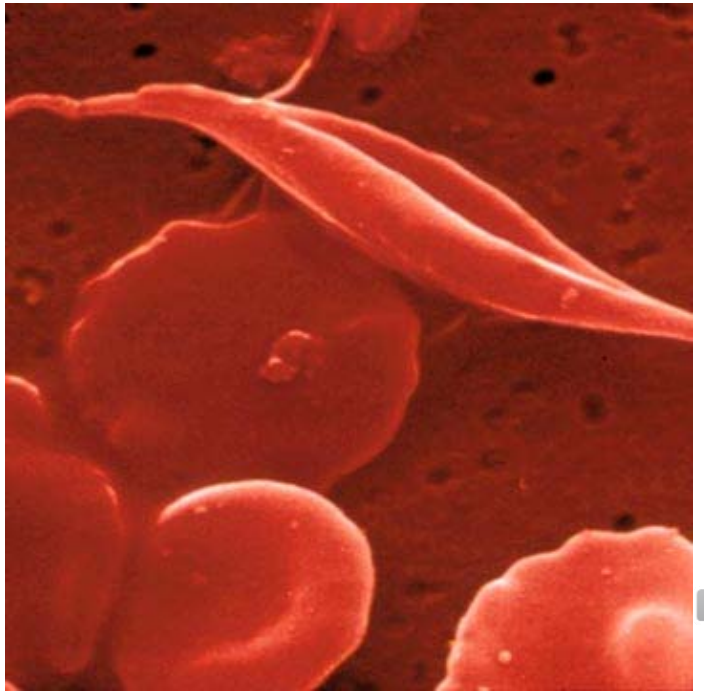
Diagnosis - Blood Smear



Sickle red cells

Clinical Features of Sickle Cell Anemia

- **Painful episodes**
- **Pneumococcal disease**
- **Acute chest syndrome**
- **Splenic infarction**
- **Splenic sequestration**
- **Stroke**
- **Osteonecrosis**
- **Priapism**
- **Retinopathy**
- **Leg ulcers**
- **Gallstones**
- **Renal abnormalities**
- **Osteopenia**
- **Nutritional deficiencies**
- **Placental insufficiency**
- **Pulmonary hypertension**



Clinical Features of Sickle Cell Anemia

Associated with *higher* hemoglobin	Associated with *lower* hemoglobin
Painful episodes	Stroke
Acute chest syndrome	Priapism
Osteonecrosis	Leg Ulcers
Proliferative retinopathy	

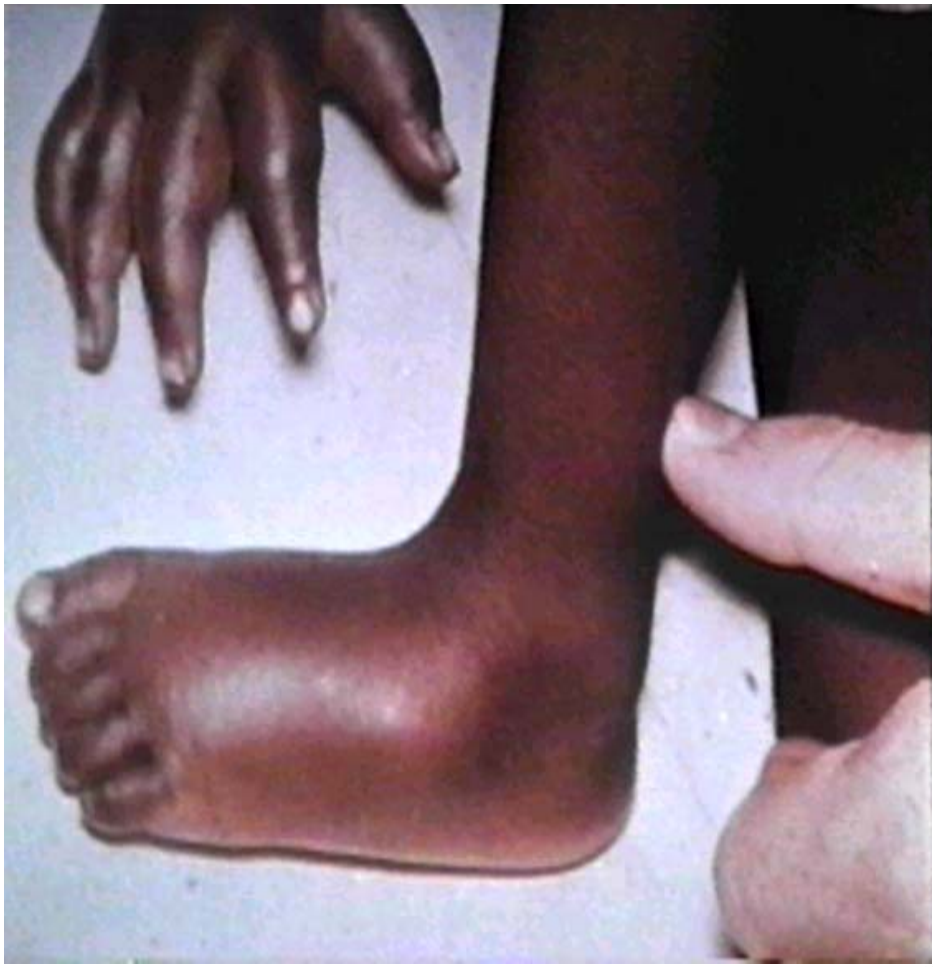
Manifestations

- Generally, no symptoms are seen in the 1st 6 months of life due to circulating fetal hemoglobin
- Dactylitis (aka hand-foot syndrome)
  - Painful, symmetric swelling of hands and feet
  - Due to ischemic necrosis of small bones of hands and feet
  - Due to rapidly expanding bone marrow, choking of blood supply

Hand Foot Syndrome - Dactylitis

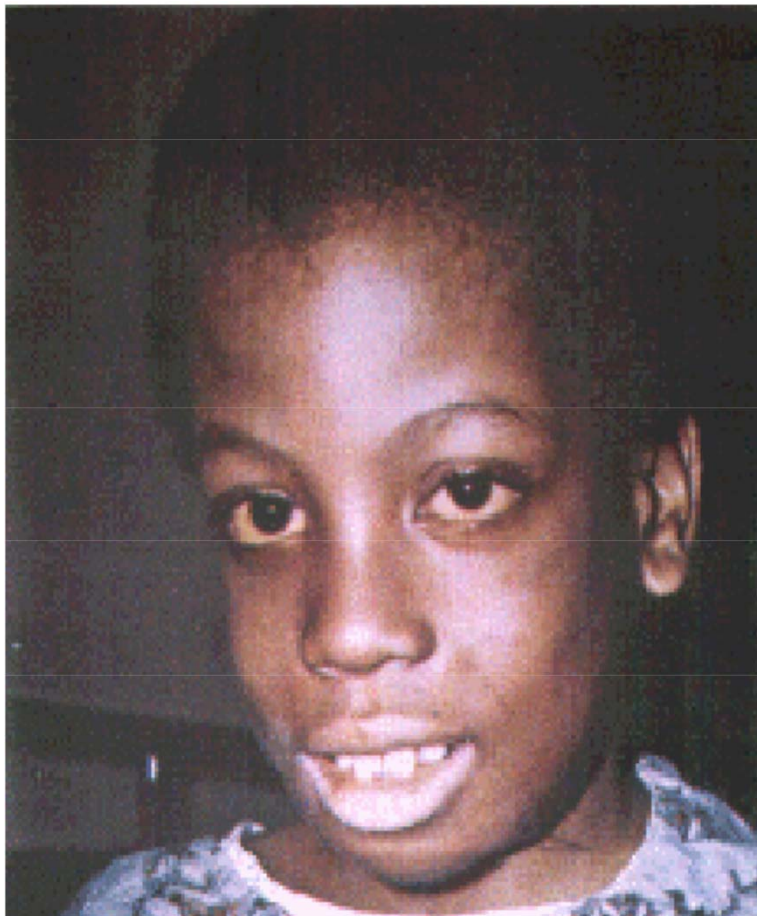
Sickle dactylitis is one of the first complications in sickle cell syndromes with the highest incidence between ages six months and two years.

The sickle red cells cause painful swelling of the hands and feet. This is treated with fluids and pain medication. It usually will go away in a few days without any problems.



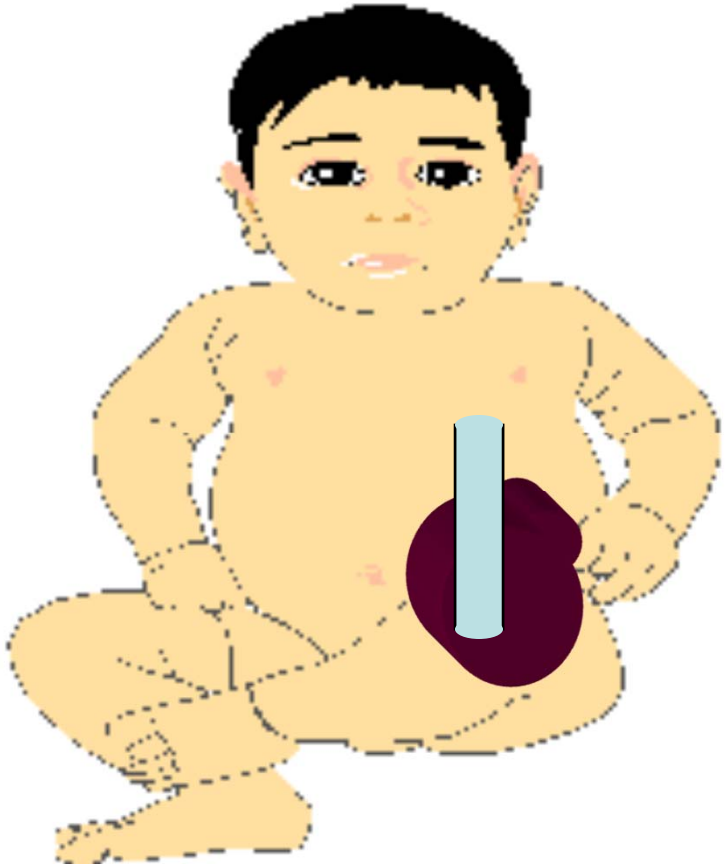
Anemia - Jaundice

Anemia or a low red blood cell count, is lifelong, starting in the first year of life. The average red cell life is reduced from a normal of 120 days down to an average of 10 to 20 days in sickle cell anemia. This produces anemia, a high reticulocyte count, and a bone marrow factory that is producing 3 to 4 times more red cells than normal. Other problems related to the anemia are yellow eyes or jaundice (elevated indirect bilirubin),which later in childhood and early adult life can cause gallstones



What is Splenic Sequestion

- Sudden trapping of blood within the spleen
- Usually occurs in infants under 2 years of age
- May be associated with fever, pain, and respiratory symptoms.
- Circulatory collapse and death can occur in less than thirty minutes.

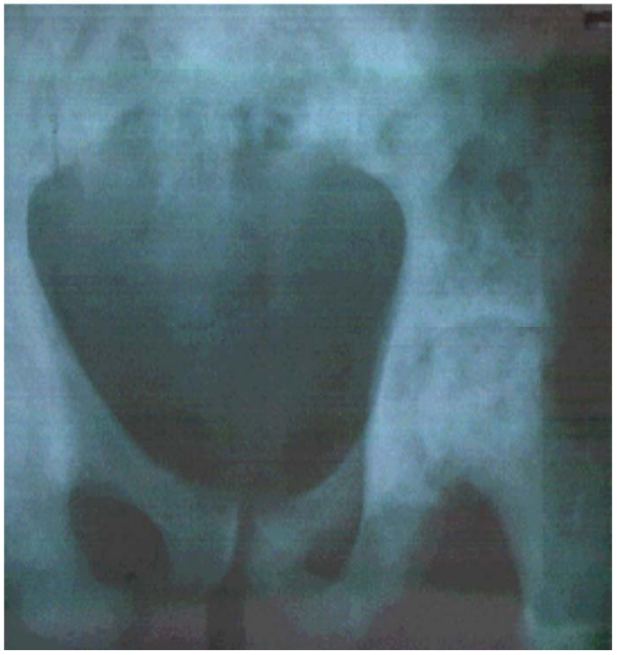


Treatments For Splenic Sequestion

- Intravenous fluids
- Blood transfusion as necessary
- Spleen removal or splenectomy

Bone Pain

More prolonged and constant pain can be seen with bone infarction, sickle arthritis, and aseptic necrosis of the femur or humerus. With chronic pain, non-steroidal anti-inflammatory medications should be used. *TENS units, relaxation techniques, occupational and physical therapy approaches may be useful in reducing pain and maintaining a good lifestyle. *

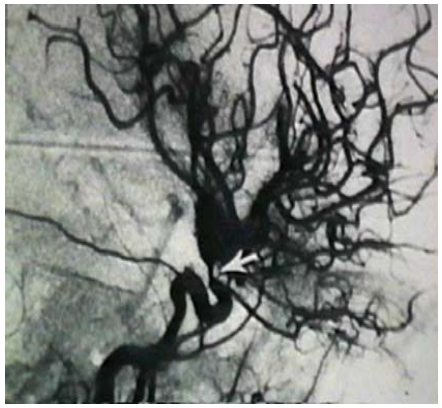


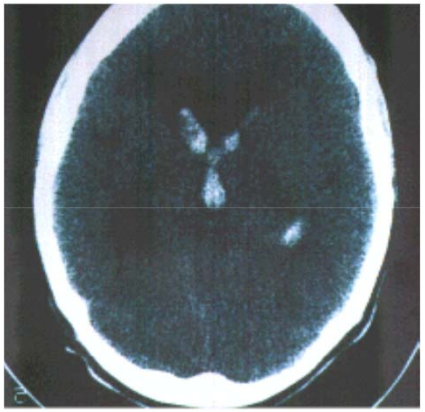
TENS stands for **transcutaneous electrical nerve stimulation**. The output of the **unit** is a stimulating pulse that excites the nerves and blocks pain signals being sent to the brain.

Strokes

Strokes are a blockage of blood flow to a part of the brain caused by the sickle cells. The symptoms include one sided weakness, numb feelings, seizures, slurred speech or facial weakness. Treatment is with chronic transfusion to maintain the Hb S level at less than 30% to prevent recurrences or even prevent the first stroke.

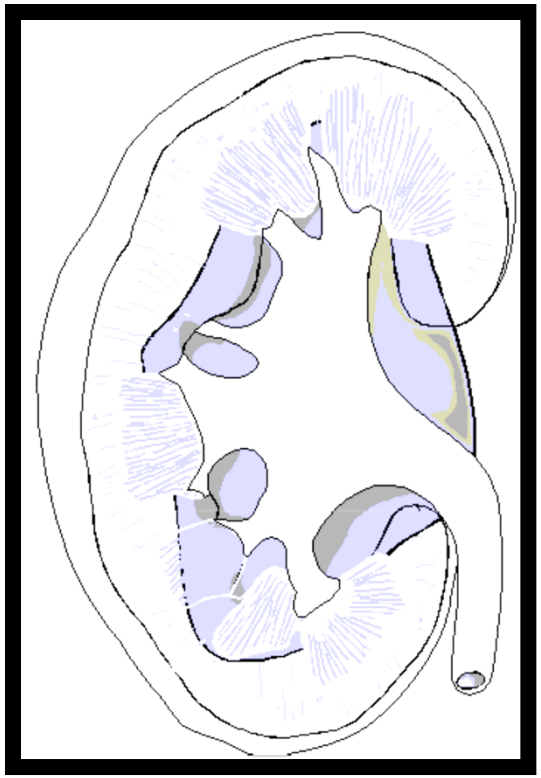
Present evidence suggests that the need for transfusion may be life-long and complications such as alloimmunization, iron overload, and exposure to infectious disease may be common complications. Bone marrow transplantation may, in the future, offer these children the best chances for a more normal life.



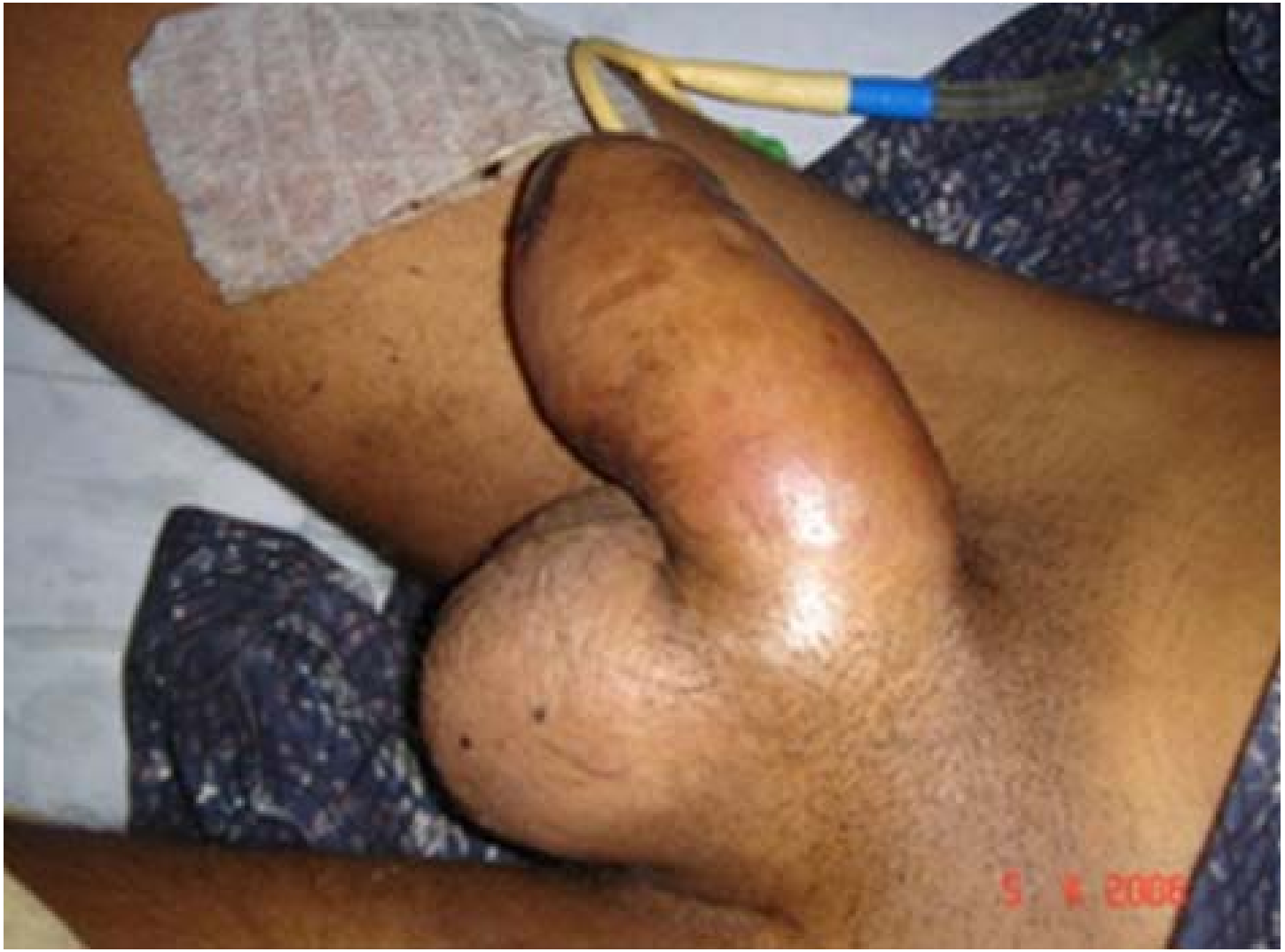


Kidney

Kidney damage starts very early and progresses throughout life causing complications in many individuals with sickle syndromes. The kidneys may not filter normally, passing protein and/or excessive amounts of water.

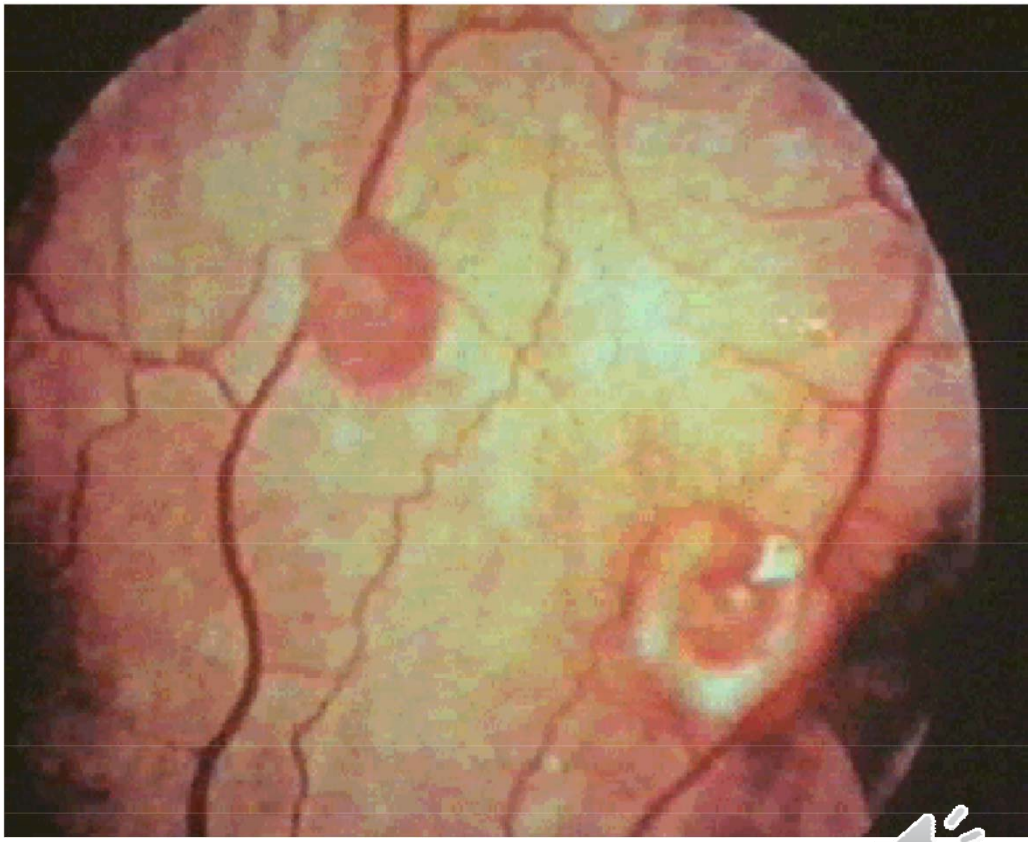


Priapism



Eye Problems

Sickle cells can cause damage to the blood vessels in the eye, especially in SC disease. New weaker blood vessels may form and break open and bleed. Early treatment with laser therapy can prevent such bleeds.



Sickle Cell Crisis

A sickle cell crisis is pain that can begin suddenly and last several hours to several days. It happens when sickled red blood cells block small blood vessels that carry blood to the bones.

The patient might have pain in the back, knees, legs, arms, chest or stomach. The pain can be throbbing, sharp, dull or stabbing. How often and how bad the pain gets varies a lot from person to person and from crisis to crisis.

Preventive Measures
Counseling Pearls for Patient

- Don't drink a lot of alcohol.
- Don't smoke.(If patient smokes, recommend smoking cessation).
- Exercise regularly but not so much that you become really tired. When exercising, drink lots of fluids.
- Drink at least eight 12-ounce glasses of water a day during warm weather.
- Reduce or avoid stress. Talk to your doctor if you're depressed or have problems with your family or job.
- Treat any infection as soon as it occurs. When in doubt, see your doctor.
- Wear warm clothes outside in cold weather and inside in air-conditioned rooms during hot weather. Also, don't swim in cold water.
- Try to be positive about yourself.
- Tell your doctor if you think you might have a sleep problem, such as snoring or if you sometimes stop breathing during sleep.
- If you have another medical condition, like diabetes, get treatment and control the condition.
- If you are pregnant or plan to become pregnant, get early prenatal care.
- Only travel in commercial airplanes. If you have to travel in an unpressurized aircraft, talk to your doctor about extra precautions.

Treatment

- For suspicion of stroke
  - Exchange transfusion
- For priapism
  - Analgesia, hydration
  - Partial exchange transfusion

Treatment

- For respiratory distress
  - Antibiotic coverage
  - Supplemental oxygen
  - Partial exchange transfusion
- For splenic sequestration
  - Repletion of intravascular volume
  - Severe anemia, transfuse

Treatment

- Hydration- 1.5 times maintenance
- Analgesia
  - ibuprofen
  - Acetaminophen +/- codeine
  - Ketorolac
  - Opiates

Treatment

- Outpatient
  - Vaccinations
  - Pneumococcal, meningococcal, influenza vaccines

- Bone marrow transplant (BMT), also called a stem cell transplant, involves replacing bone marrow affected by sickle cell anemia with healthy bone marrow from a donor. The procedure usually uses a matched donor, such as a sibling, who doesn't have sickle cell anemia. For many, donors aren't available. But stem cells from umbilical cord blood might be an option.

L-glutamine oral powder (Endari®)

- Endari (L-glutamine oral powder) reduces oxidant damage to red blood cells by improving the redox potential of nicotinamide adenine dinucleotide (NAD), a coenzyme that has been identified as the primary regulator of oxidation.
- Endari is specifically indicated to reduce the severe complications of sickle cell disease (SCD) in adult and pediatric patients age 5 and older.
- Endari is supplied as a powder for oral administration.

Endari®

Administer Endari orally, twice per day at the dose based on body weight according to Table 1.

Table 1. Recommended Dosing

Weight in kilograms	Weight in pounds	Per dose in grams	Per day in grams	Packets per dose	Packets per day
less than 30	less than 66	5	10	1	2
30 to 65	66 to 143	10	20	2	4
greater than 65	greater than 143	15	30	3	6

Mix Endari immediately before ingestion with 8 oz. (240 mL) of cold or room temperature beverage, such as water, milk or apple juice, or 4 oz. to 6 oz. of food such as applesauce or yogurt. Complete dissolution is not required prior to administration.

Side Effects

- Adverse effects associated with the use of Endari may include, but are not limited to, the following:
- constipation
- nausea
- headache
- abdominal pain
- cough
- pain in extremity
- back pain
- chest pain (non-cardiac)

Hydroxyurea

- Start: 15 mg/kg/day as single dose; monitor patient's blood count every two weeks
- Titrate by 5 mg/kg/day q12wk
- Dose is not increased if blood counts are between acceptable range and toxic
- Not to exceed 35 mg/kg/day
- Discontinue therapy until hematologic recovery if blood counts are considered toxic; may resume treatment after reducing dose by 2.5 mg/kg/day from dose associated with hematological toxicity

Hydroxyurea

- When taken daily, hydroxyurea reduces the frequency of painful crises and might reduce the need for blood transfusions and hospitalizations. Hydroxyurea seems to work by stimulating production of fetal hemoglobin — a type of hemoglobin found in newborns that helps prevent the formation of sickle cells.
- Hydroxyurea increases the risk of infections, and there is some concern that long-term use of this drug might cause problems later in life for people who take it for many years. More study is needed.

Hydroxyurea Side Effects

- Fever, sore throat, cough, congestion, or other signs of infection
- Unusual bruising or bleeding
- Vomit that's bloody or looks like coffee grounds
- Bloody or black, tarry stools