

Sickle Cell Disease Learning Points

1. Occurs in 1 in 500 African Americans.
2. The gene is also prevalent in Africans, Arabs, Egyptians, Turks, Greeks, Italians, Iranians, and Asiatic Indians.
3. Newborn screen reveals
 - a. Hgb FS (no A) if homozygous SS disease.
 - b. Hgb FSC (no A) if S-C disease
 - c. Hgb FSA if Sickle β^+ -Thal (double heterozygote)
 - d. Hgb FS (no A) If Sickle β^0 -Thal
4. Once a newborn baby is suspected of having Sickle Cell Disease, he or she is referred to a center for quantitative confirmatory hemoglobin electrophoresis and counseling.
5. For severity of disease: $SS \geq \text{Sickle } \beta^0\text{-Thal} > \text{Sickle } \beta^+\text{-Thal} \geq SC$
6. Typical laboratory values for an SS patient:
 - a. Hgb 7.5 (range 5.5 - 9.5)
 - b. Hct 22 (17 - 29)
 - c. Retic 12% (5 - 25%)
 - d. WBC 12,000 (10,000 - 20,000)
7. Emergencies in Sickle cell patients:
 - a. Vaso-occlusive crisis: localized ischemia/infarction. About a third of the patients have 4-5 episodes a year necessitating 2-3 admissions, lasting typically 5 - 7 days. Treated with **hydration** (one and a half x maintenance IV plus PO). Note: All SS patients are hyposthenuric, i.e. they cannot concentrate their urine secondary to intra-renal medullary sickling so they are high-risk of dehydration. A dilute urine (low specific gravity) does not mean a sickle cell patient is well hydrated!! Treated with **medication** - i.e. narcotics. If old enough use a PCA pump. The right way to start a PCA pump is to IV bolus narcotic until comfortable and then start your basal rate and PCA boluses. Titrate to relief. As a rule sickle cell patients are highly reliable in assessing their own narcotic needs. Treated with **oxygenation** only if patients are hypoxic - do not use O₂ for uncomplicated pain crisis in that this can precipitate an aplastic crisis. Caution: VOC can present similar to other particularly surgical problems such as an acute abdomen, osteomyelitis, septic joint, biliary obstruction, etc. For patients with more than three episodes of severe pain a year, hydroxyurea was shown to decrease the number of crises by half, reduce hospitalization, and decrease the amount of blood transfused and incidence of acute chest syndrome.
 - b. Aplastic crisis (transient cessation of erythropoiesis): like all patients with a chronic hemolytic anemia who have high reticulocytes count any

marrow suppression can lead to symptomatic anemia. Between 70 and 100 percent of episodes are due to infection by human parvovirus B19. Reticulocytopenia begins about 5 days post-exposure and continues for 7 to 10 days. Check CBC and reticulocytes in family members and contacts with Sickle Cell Disease. Check reticulocyte counts often in patients with fever/infection. Treated with simple pRBC transfusions. Infection confers life-long immunity. No cases of recurrent parvovirus B19 infection have been reported in children with sickle Cell Disease. Because infection during the mid-trimester of pregnancy may result in hydrops fetalis and stillbirth, isolation precaution for pregnant staff is necessary.

- c. Infection: 80% of patients younger than 3 years of age, who die, die of *Streptococcus Pneumoniae* sepsis. A landmark randomized, placebo-controlled study of Sickle Cell patients 4 months old and younger (done about 20 years ago) demonstrated that administration of penicillin twice a day prevented 80% of the life-threatening infectious episodes. The current practice is therefore to give prophylactic penicillin until 5 years of age. In addition these patients are getting pneumovax (PPV23) at two years of age and repeated at 5 and 10 years of age. When available prevnar (PPV7) should be given at 2, 4, 6 and 12 months of age. Yearly influenza vaccination is also recommended in all Sickle Cell patients to prevent severe morbidity.
- d. Acute Chest Syndrome: Incidence 21 events/100 patient-years. Mortality 4-9%. Most common complication of surgery and anesthesia.

Definition:

- a. New pulmonary infiltrate on chest x-ray
- b. Fever
- c. Respiratory signs and symptoms (tachypnea, wheezing or cough).

Risk factors: Winter, high sickle hemoglobin and WBC, aseptic necrosis or fracture, cigarette smoke, prior history of ACS.

Causes: Bone marrow embolism, fat embolism, infection (*Chlamydia*, *Mycoplasma*, RSV, *Staphylococcus aureus* and *Streptococcus pneumoniae*).

Treatment:

- a. Supplemental Oxygen
- b. Transfusions (in an emergency, also exchange transfusion to decrease the % S Hgb to < 30%).
- c. Antibiotics (cephalosporin and macrolide)
- d. Incentive spirometry
- e. Bronchodilators (even if there is no wheezing)
- f. Limited hydration (no more than 1.5 times maintenance)

- g. After recovery: Follow PFT, consider hydroxyurea, and in recurrent ACS consider bone marrow transplantation.
- h. Be careful to avoid over-sedation with narcotics.
- e. CNS changes: Another true medical emergency requiring emergent exchange transfusion. Sickle patients are at risk for stroke so any neurologic change should prompt rapid therapy (exchange transfusion) and neuro-imaging studies. Approximately 50% of children with sickle cell disease and a first stroke who do not receive chronic transfusions will develop another stroke within 3 years. Giving blood transfusion on a regular basis (so called, hyper-transfusion regimen) will reduce the incidence of a recurrent stroke to only 10%. Current national recommendations are that transfusion should be continued for at least 5 years.
- f. Splenic sequestration (sudden pooling of a large amount of blood into the spleen leading to acute splenomegaly, profound anemia and hypotension): typically occurs in patients < 3 years old, (but can occur at any age in patients with Hb S-C disease or sickle beta-thalassemia) can present with signs and symptoms of severe hypovolemic shock. Hgb values can be as low as 1-2 gm/dl. Requires emergent transfusion therapy with whole blood or pRBCs and FFP. The goal of transfusion is to prevent shock, not to restore hemoglobin to normal or to the steady state. After transfusion the spleen shrinks and hemoglobin increases more than predicted due to release of trapped RBC from the spleen.
- g. Priapism: Painful erection from intra-penile sickling. The incidence is about 35%. Mean age of onset 15 years. There are no controlled studies which determine the effectiveness of treatment in arresting acute problems and in preventing subsequent sexual dysfunction. Treat with pain meds, hydration, and transfusion. Consider exchange transfusion if not better within 24 hours and surgical therapy if exchange fails. Priapism tends to recur. About 21% of patients with a history of priapism will develop erectile dysfunction.

8. Transfusion.

- a. Alloimmunization: Up to 36% of patients with sickle cell disease will develop either immediate or (more often) delayed transfusion reactions. These may be related to racial and ethnic differences of minor blood group antigen profile. It may also be related to transfused leukocytes and recipient immunogenetics. To address this problem all newly diagnosed patients with Sickle Cell Disease will have a complete red blood cell phenotype. (Preferably before they have been transfused). The transfused

blood should be leukocyte filtered and matched for blood groups C, c, Kell (K), and Kidd (JkA, JkB).

- b. Iron overload. Chronic transfusion can lead to iron overload and hemosiderosis, especially of the heart and liver. Chelation with Desferal is usually started after a cumulative 120ml per kg of transfused blood and a serum ferritin level of 2000 - 2500 mg/ml. Since ferritin is an acute phase reactant and may not be a true reflection of iron stores, the national recommendation is now to perform a liver biopsy for quantitative iron content. Chelation is begun when iron content in the liver is 7 mg/g dry weight or more. Desferal is given at home by pump subcutaneously over 8-12 hours, 5 days a week. For patients who are non-compliant, Desferal can be given in the hospital as a continuous infusion over 48 hours.

Bibliography for sickle Cell Disease

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