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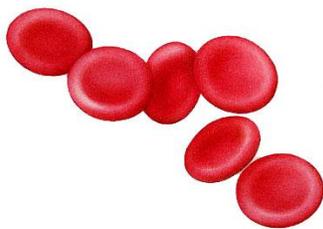
Guest editors: Azita Fathi, Pharm.D. and Jason Thomas, Pharm.D., PGY1 Pharmacy Practice Residents



Key Inforbits

- Sickle cell disease pathology
- Risk factors for complicated disease
- Screening and diagnosis
- Treatment
- Prevention of complications
- Did you know?

June 19 is World Sickle Cell Disease Day



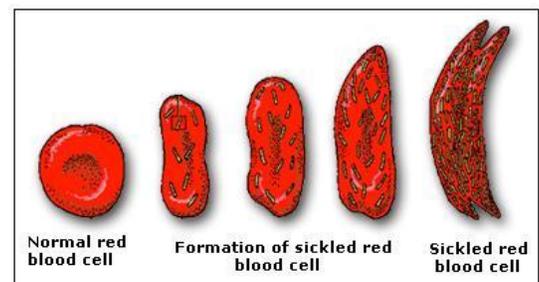
http://explow.com/red_blood_cell

Sickle Cell Disease: Pathology

Sickle cell disease (SCD) represents the most common of all genetically acquired diseases and is a sizeable health problem, both in terms of patients affected and disease-induced sequelae. Due to the changing demographics of SCD, the disease is now being increasingly seen in Western regions of the world, though at one time it was thought to reside predominantly in sub-Saharan Africa, the Middle East, and parts of India. Nonetheless, these latter regions still possess a higher incidence of reported SCD of 1 child per 500 children, whereas the observed United States rate currently stands at 1 child in 5000 children.

SCD is a genetically inherited disorder and is brought about by a point mutation in a specific gene, or segment of DNA designed to encode protein production. Because of this aberration of the β -globin gene, irregular hemoglobin molecules result which cannot bind oxygen molecules as effectively as native hemoglobin. Over time, the physical and oxidative stresses brought on by this change have significant implications at the cellular level, and one of these is the crystallization of affected hemoglobin molecules. Once this occurs, the red blood cell to which hemoglobin is bound begins to physically elongate, morphologically transforming into the characteristic “sickled” erythrocyte. These sickled cells are not only more prone to lysing but also are responsible for a variety of adverse ramifications.

The aggregation of sickled red blood cells causes adverse complications throughout the body that are most typically observed as vaso-occlusive crises. Once inside smaller capillaries and venules, because of their irregular shape, these affected red cells can inhibit blood flow to key organ systems. Consequentially, a multitude of untoward effects can ensue, including tissue ischemia, necrosis, and ultimately target organ damage. Another result of these vaso-occlusive events is a greatly increased perception of pain secondary to tissue ischemia and necrosis. These first painful episodes often occur in childhood and are manifested as dactylitis, a condition affecting the small bones of the hands and feet.



[http://demos.biamedia.com/ompdemos/www.itriagehealth.com/disease/anemia-\(low-red-blood-cell-count\).html](http://demos.biamedia.com/ompdemos/www.itriagehealth.com/disease/anemia-(low-red-blood-cell-count).html)

Approximately 50-60% of all emergency room visits by pediatric patients with SCD are due to such pain crises. Over time, a myriad of complications can occur as a result of SCD, several of which are listed below:

Table 1. Pathologic features of sickle cell disease.

Cardiac	Pulmonary	Hepatobiliary	Renal	Musculoskeletal
✓ Cardiomegaly	✓ Edema	✓ Hepatomegaly	✓ Acute renal failure	✓ Degenerative changes
✓ Infarction	✓ Emboli	✓ Intrahepatic cholelithiasis	✓ Pyelonephritis	✓ Septic arthritis
✓ Arrhythmias	✓ Pulmonary hypertension	✓ Viral hepatitis	✓ Medullary carcinoma	✓ Osteonecrosis
✓ Heart failure				✓ Osteomyelitis

Adapted from, Malowany JI, Butany J. Pathology of sickle cell disease. Semin Diagn Pathol. 2012;29:49-55.

1. Malowany JI, Butany J. Pathology of sickle cell disease. Semin Diagn Pathol. 2012;29:49-55.
2. Meier ER, Miller JL. Sickle cell disease in children. Drugs. 2012;72:895-906.

Risk factors for complicated SCD



Though all cases of SCD are inherited genetically through the point genomic mutation, they are highly variant in their presentations, with some patients experiencing frequent crises and others being affected minimally in comparison by the disease. The following are suggested to be indicative of SCD associated with target organ complications:

<http://www.wepsicklecell.org/what/>

Table 2. Predictors and Outcomes of SCD Complications

Predictors	Outcomes
Hemoglobin concentration < 8.1 g/dL	Death, stroke, leg ulcers
Hemoglobin concentration > 8.9 g/dL	Pain, ACS, AVN
Fetal hemoglobin concentration < 8.1 mg/dL	Death, ACS, pain, leg ulcers
Steady-state WBC < 11.8 x 10 ⁹ / L	Death, ACS
α-thalassemia present	AVN
α-thalassemia absent	Stroke
↑ pain rate	Adult death, AVN
Acute anemia	Death, stroke

Abbreviations: ACS = acute chest syndrome
AVN = avascular necrosis
WBC = white blood cell count

Adapted from, Buchanan GR, DeBaun MR, Quinn CT, et al. Sickle cell disease. Hematology Am Soc Hematol Educ Program. 2004;1:35-47.

1. Kinney TR, Sleeper LA, Wang WC, et al. Silent cerebral infarcts in sickle cell anemia. Pediatrics. 1999;103:640-645.
2. Miller ST, Sleeper LA, Pegelow CH, et al. Prediction of adverse outcomes in children with sickle cell disease. N Engl J Med. 2000;342:83-89.

Screening and Diagnosis

- Early detection can help improve survival and prevent or reduce the number of disease related complications.
- Testing to detect the presence of hemoglobin S in newborns is mandatory in the United States. All positive tests are confirmed through a second blood test.
- Prenatal screening through DNA analysis of chorionic villus or amniotic fluid is available for those individuals with a globin gene mutation and may be performed as early as 10 weeks into the pregnancy.
- Sickle solubility tests are nonspecific and should not be used to make a diagnosis



<http://www.sicklecelldisease.org/index.cfm?page=research-screening-overview>

1. Sickle cell anemia [Internet]. Bethesda: National Heart, Lung, and Blood Institute; 2011 Feb 1 [cited 2012 May 19]. Available from: <http://www.nhlbi.nih.gov/health/health-topics/topics/sca/>
2. Steinberg MH. In the clinic: sickle cell disease. *Ann Intern Med.* 2011; 155(5): ITC3 1-15.
3. Sickle cell tests [Internet]. American Association for Clinical Chemistry; 2012 May 18 [cited 2012 May 19]. Available from: <http://labtestsonline.org/understanding/analytes/sickle/tab/test>
4. SCDAA research and screening [Internet]. Baltimore: Sickle Cell Disease Association of America. <http://www.sicklecelldisease.org/index.cfm?page=research-screening-overview>. Assessed May 19, 2012.

Treatment

- Hydroxyurea is the only drug FDA approved for the treatment for sickle cell disease. It is a cytotoxic drug used to increase fetal hemoglobin (HbF) levels. HbF levels >20% are associated with fewer vaso-occlusive crises. Bone marrow studies should be obtained at baseline and periodically throughout the course of therapy.
- Transfusions, simple or exchange, are another method often used to reduce sickle hemoglobin levels and prevent stroke. Simple transfusions only require peripheral venous access and are less likely to lead to alloimmunization. Exchange transfusions, on the other hand, reduce sickle hemoglobin levels more rapidly and have less potential of causing hyperviscosity.
- The only cure for sickle cell disease is a successful stem cell transplant which has been reported to provide event free survival in 84 % of patients; however, transplantation is not always successful. Five percent of patients will experience death as a result of the procedure and another 10% of patients will experience disease recurrence. .

1. Steinberg MH. In the clinic: sickle cell disease. *Ann Intern Med.* 2011; 155(5): ITC3 1-15.
2. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. *Lancet.* 2010; 376: 2018-31.
3. Sickle cell anemia [Internet]. Bethesda: National Heart, Lung, and Blood Institute; 2011 Feb 1 [cited 2012 May 19]. Available from: <http://www.nhlbi.nih.gov/health/health-topics/topics/sca/>

Prevention of Complications

- Individuals with sickle cell disease are at higher risk of infection because of altered splenic function. As such, it is recommended that children with sickle cell disease receive the following:
 - Annual influenza vaccinations starting at 6 months of age.
 - Pneumococcal polysaccharide vaccine (PPSV) starting at 2 years of age.
 - Daily penicillin prophylaxis starting as early as 2 months of age and continuing until at least 5 years of age.

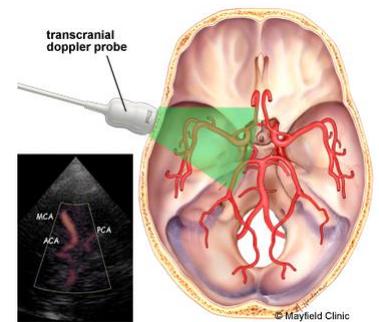


- Severe pain is usually indicative of a “sickle cell crisis” and most often due to vascular occlusion. The pain can last anywhere from 2-10 days. At home, nonopioid analgesic therapy or oral opioid therapy combined with increased fluid intake, rest, warm baths and heating pads may suffice for some. Others may require hospital admission for administration of parenteral opioids and IV fluids.
- Acute chest syndrome is a serious, potentially deadly complication of sickle cell disease. Signs and symptoms include fever, chest pain, cough, and chest infiltrates. Patients with acute chest syndrome require prompt treatment and hospitalization.
- Other complications of sickle cell disease include renal failure, leg ulcers, retinopathy, biliary tract and liver disease, neurocognitive dysfunction and priapism. Patients should be counseled regarding the seriousness of sickle cell disease and the importance of monitoring for complications.

1. O’Bryant CI, Utz KJ. Anemias. In: Koda-Kimble MA, Young LY, Alldredge BK, Corelli RL, Guglielmo BJ, Kradjan WA, Williams BR, eds. Applied therapeutics: the clinical use of drugs. 9th ed. Philadelphia: LWW; c2009. Chapter 86, Pg 12-14
2. Steinberg MH. In the clinic: sickle cell disease. Ann Intern Med. 2011; 155(5): ITC3 1-15.
3. Sickle cell anemia [Internet]. Bethesda: National Heart, Lung, and Blood Institute; 2011 Feb 1 [cited 2012 May 19]. Available from: <http://www.nhlbi.nih.gov/health/health-topics/topics/sca/>

Did you know?

- “In studies in which MRI is used, up to 20% of children with sickle-cell disease have silent brain infarcts” and the risk of a recurrent stroke is greater than 60%.
- **PREVENTION IS KEY**
 - Transcranial Doppler blood flow tests can help identify those at risk of stroke
 - Screening should start at age 2
 - Those found to be at risk for stroke should be considered for long term blood transfusions. Such transfusions have been reported to help reduce the risk by 90%.



<http://www.mayfieldclinic.com/PE-sah.HTM>

1. Steinberg MH. In the clinic: sickle cell disease. Ann Intern Med. 2011; 155(5): ITC3 1-15



The last “dose” ...

We make a living by what we get, we make a life by what we give.
 Sir Winston Churchill [British politician (1874 - 1965)]

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