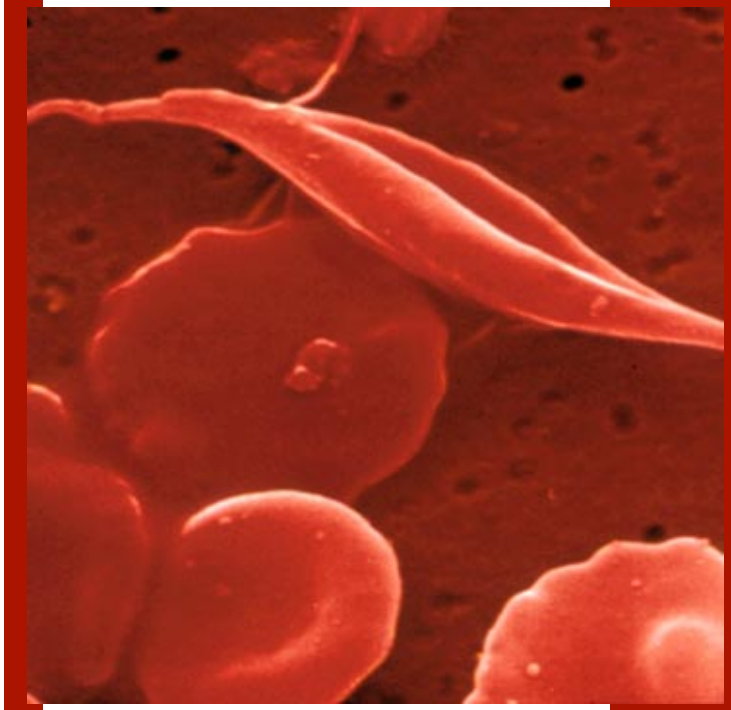

Sickle Cell Anemia

Diagnosis, Treatment, & Genetics

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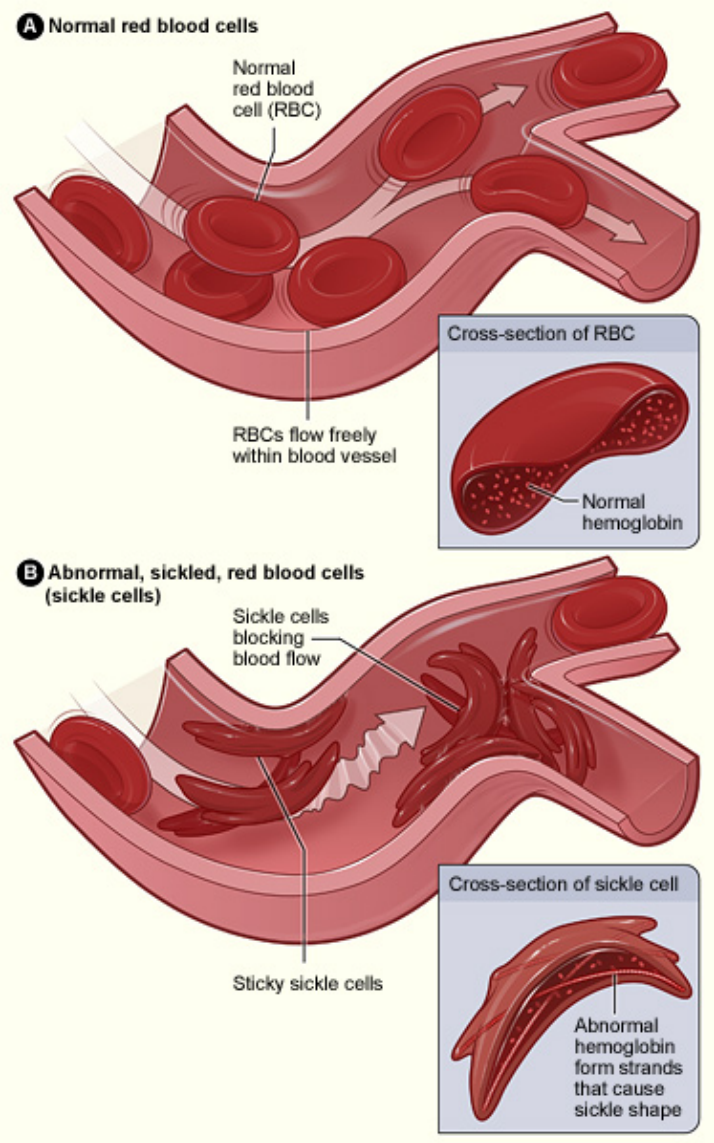
Sickle Cell Anemia

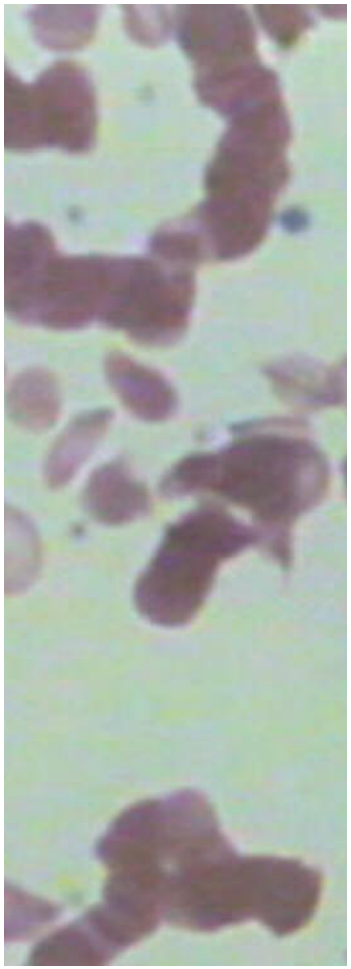
- SCA is the most common inherited blood disorder.
- Red Blood Cells assume an abnormal, rigid, sickle shape.
- SCA is an autosomal recessive disease; two abnormal genes are required for the mutation to be fully expressed.
- Higher concentration of carriers in regions where malaria is or was common. Heterozygous carriers are somewhat protected from malaria.

Symptoms

- Anemia
- Vaso-occlusion
- Dactylitis
- Acute Chest Syndrome
- Jaundice
- Immuno-compromised
- Vision problems
- Enlarged spleen
- Hemolysis



Classical Diagnostic Methods



- Hematologic Testing

  1. High Performance Liquid Chromatography – demonstrates significant quantities of Hb S.

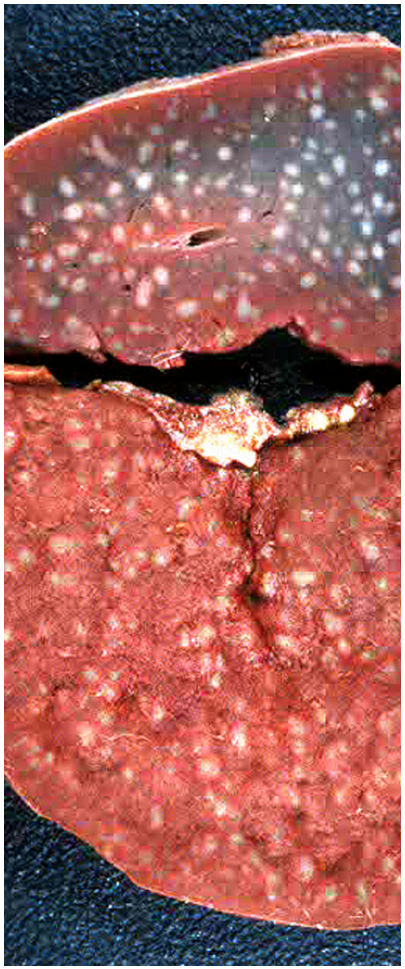
  2. Blood Smear- search for sickled cells or fragments of RBC's.

  3. HB S Solubility Test - utilizes the relative insolubility of deoxygenated Hb S in solutions of high molarity. Bad diagnostic tool for Sickle Cell Disease (differentiating between different types).

  4. Cellulose Acetate and Citrate Agar Electrophoresis- hemoglobin will migrate in specific patterns.

Sickle Cell Anemia is only one type of Sickle Cell Disease, and it is characterized by hemoglobin S replacing both beta-globin subunits in hemoglobin. Many classical methods search for this protein variation.

Classic Treatment



- Lifelong comprehensive care is required.
- Combination of fluids, painkillers (especially during painful vaso-occlusive crisis), and antibiotics [cyanate, analgesics, opioid administration, folic acid, penicillin].
- Blood transfusions in the case of an acute chest crisis.
- Treatment aimed at avoiding crises and relieving symptoms.
- Bone Marrow Transplants- potential cure for people with severe SCA or children.
- Surgeries- correct vision problems or to remove spleen.

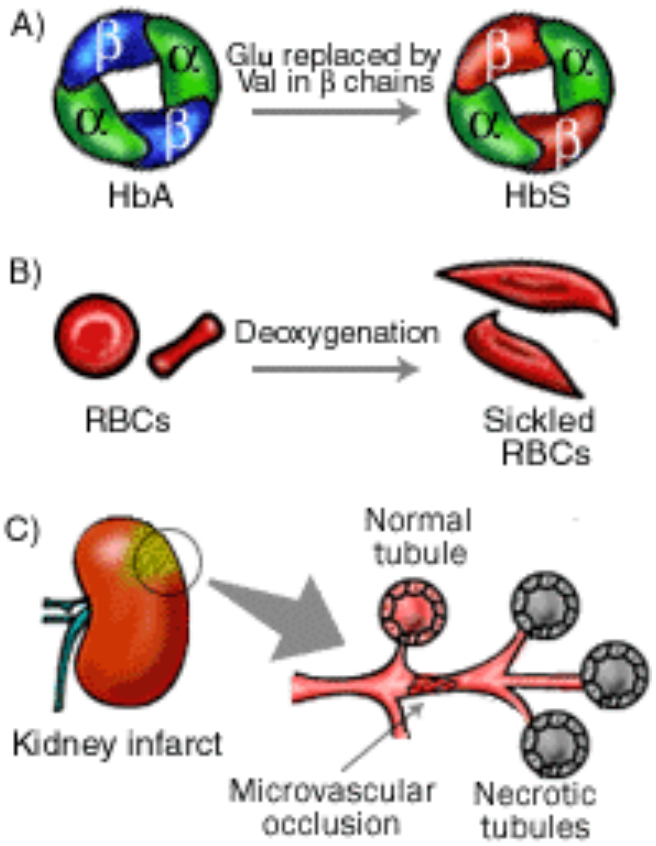
Novel Diagnostics & Therapies

- SCA is a disease caused by a single point mutation in the HBB gene (11p15.5). Hemoglobin normally consists of a chain of four subunits – two alpha-globin and two beta-globin. This SNP is simply a replacement of one Adenine with a Thymine in the HBB gene. which thus in turn causes one glutamic acid to be replaced by valine in the amino acid chain. This mutation causes the abnormal production of beta-globin, called HbS. Other mutations can also cause various abnormal structures, such as HbC.

- Knowledge of gene mutation and its variation allows for better genetic testing.
- Isoelectric focusing, especially for newborns.
- DNA testing for gene.
- Targeted mutation analysis and sequence analysis (latter often primary test to detect mutations associated with β -thalassemia hemoglobin variants).

Novel Diagnostics & Therapies

- Fetal hemoglobin
- Hydroxyurea- stimulates production of fetal hemoglobin. Effective in preventing painful crises (prevents sickling).
- Knowledge of gene mutation variations also helps with stem cell transplantations for those with severe disease.
- Experimental treatments are under way for gene therapy.
- Insert normal gene into bone marrow.
- Turn off gene for abnormal hemoglobin and turn on gene for fetal hemoglobin.
- There has been success in expressing normal human beta-globin in a mouse model via retroviral vectors.
- Gene therapy using induced pleuripotent stem cell lines.
- Many trials currently recruiting.



A) Hemoglobin is made up of 4 chains: 2 α and 2 β. In SCA, a point mutation causes the amino acid glutamic acid (Glu) to be replaced by valine (Val) in the β chains of HbA, resulting in the abnormal HbS. **B)** Under certain conditions, such as low oxygen levels, RBCs with HbS distort into sickled shapes. **C)** These sickled cells can block small vessels producing microvascular occlusions which may cause necrosis (death) of the tissue.

Resources

http://www.ncbi.nlm.nih.gov/books/bv.fcgi?highlight=sickle%20cell%20anemia&rid=gnd.section.98

http://en.wikipedia.org/wiki/Sickle-cell_disease

http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=sickle

http://ghr.nlm.nih.gov/condition=sicklecelldisease#treatment

http://www.mayoclinic.com/health/sickle-cell-anemia/DS00324/DSECTION=treatments%2Dand%2Ddrugs

http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene&cmd=Retrieve&dopt=Graphics&itool=books&referralid=gnd.section.98&list_uids=3043