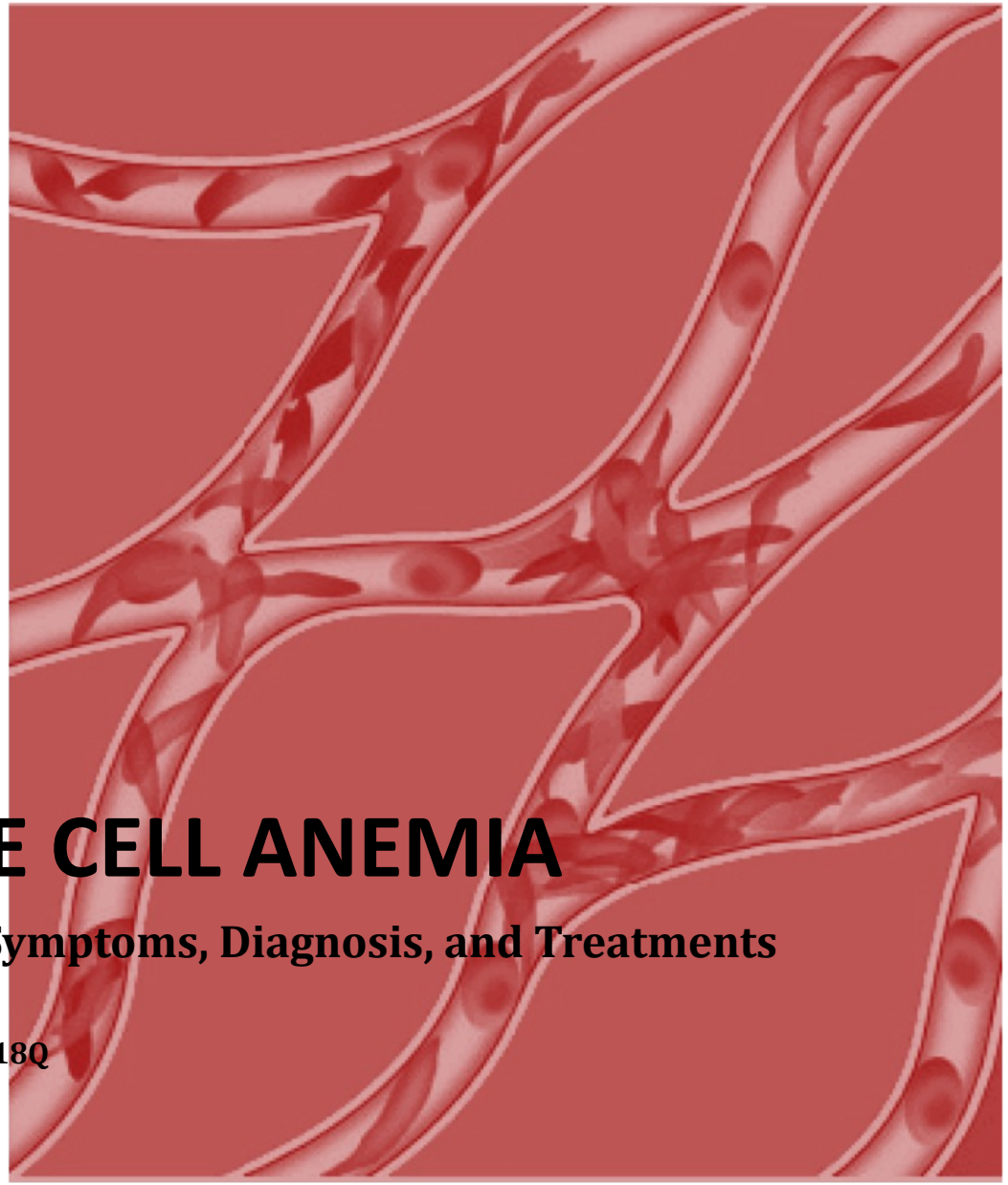


SICKLE CELL ANEMIA

Genetics, Symptoms, Diagnosis, and Treatments

Iris Jovel

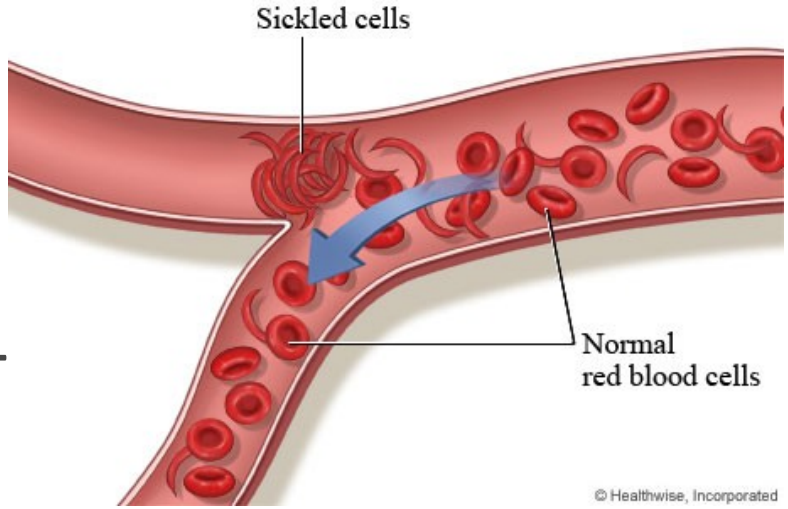
Biochemistry 118Q

THE DISEASE: SICKLE CELL ANEMIA (SCA)

- Most common inherited blood disease in U.S.
- Readily seen in areas with high malaria incidence.
- Autosomal recessive disease. Due to mutation in *hemoglobin beta gene* (*HBB*) gene.
- *HBB* produces Hb protein which carries oxygen in RBCs
- Result: RBCs with abnormal, brittle, sickle shape

IMPLICATIONS OF SICKLE CELL ANEMIA

- Misshapen and rigid RBC fail to pass through blood vessels and capillaries like elastic normal RBC. They become trapped and cause blockage.

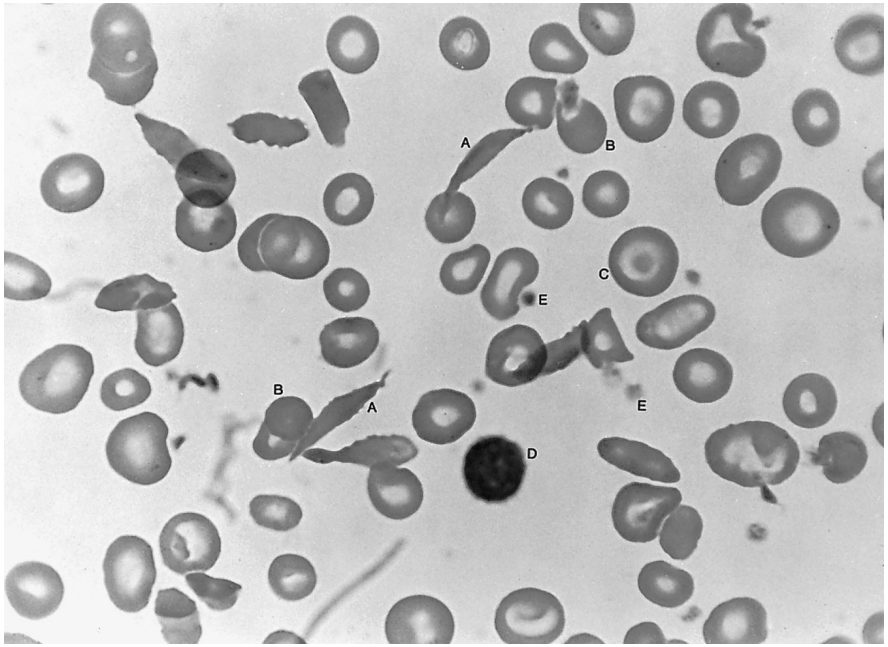


SYMPTOMS AND COMPLICAT

- Anemia
- Vaso-occlusion (pain and damage to organs)
- Dactylitis
- Acute Chest Syndrome (ACS)
- Splenic sequestration (enlargement)
- High risk of infection
- Hemolysis (pulmonary hypertension, jaundice, leg ulcers, aplastic crisis)

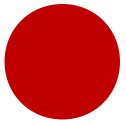
CLASSICAL DIAGNOSIS

- Demonstrating the presence of significant quantities of Hb S by:
  - High Performance Liquid Chromatography (HPLC)
  - Isoelectric Focusing (IEF)
  - Cellulose acetate electrophoresis
  - Blood Smear
  - Hb S Solubility Test

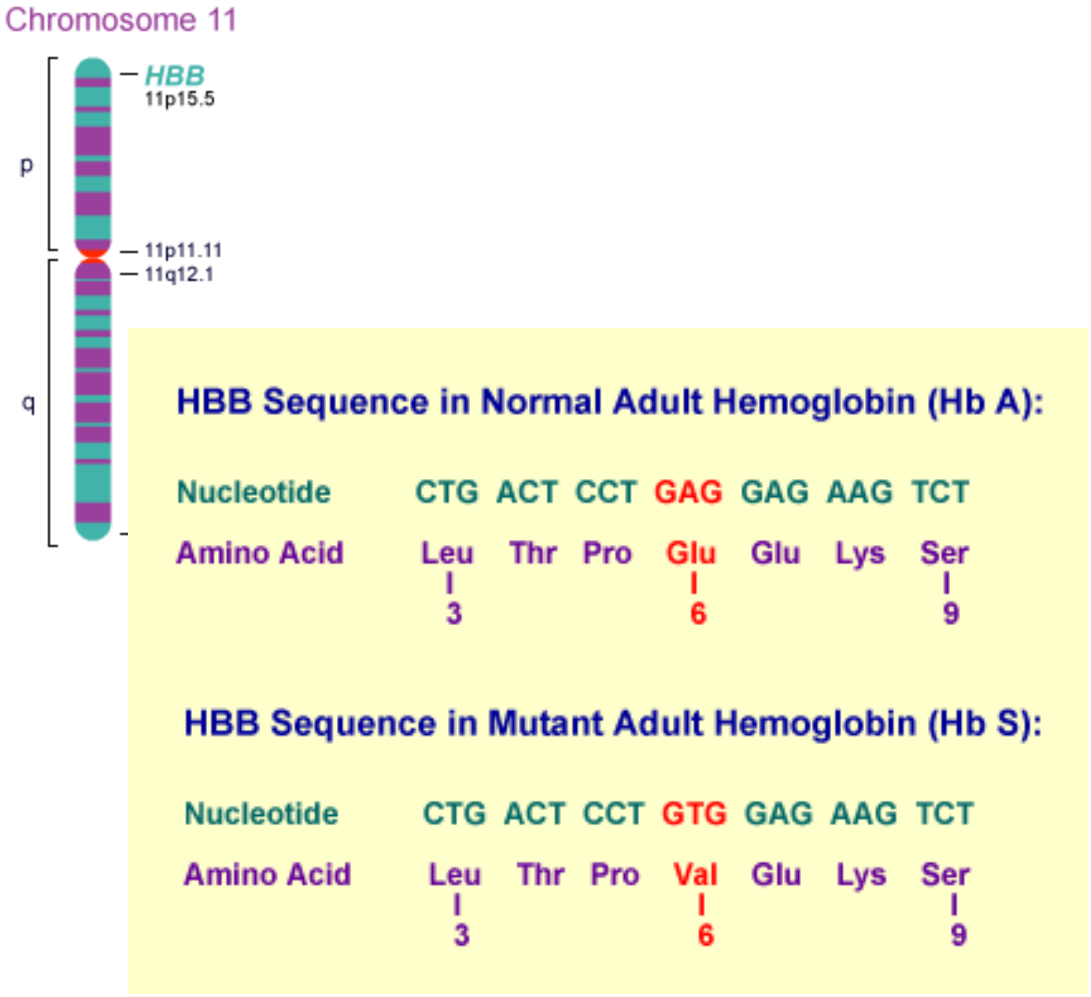


CLASSICAL TREATMENTS

- Management:
  - Education about how to deal with the complications that occur
  - A combination of fluids, painkillers, antibiotics and transfusions
  - Surveillance
  - Splenectomy

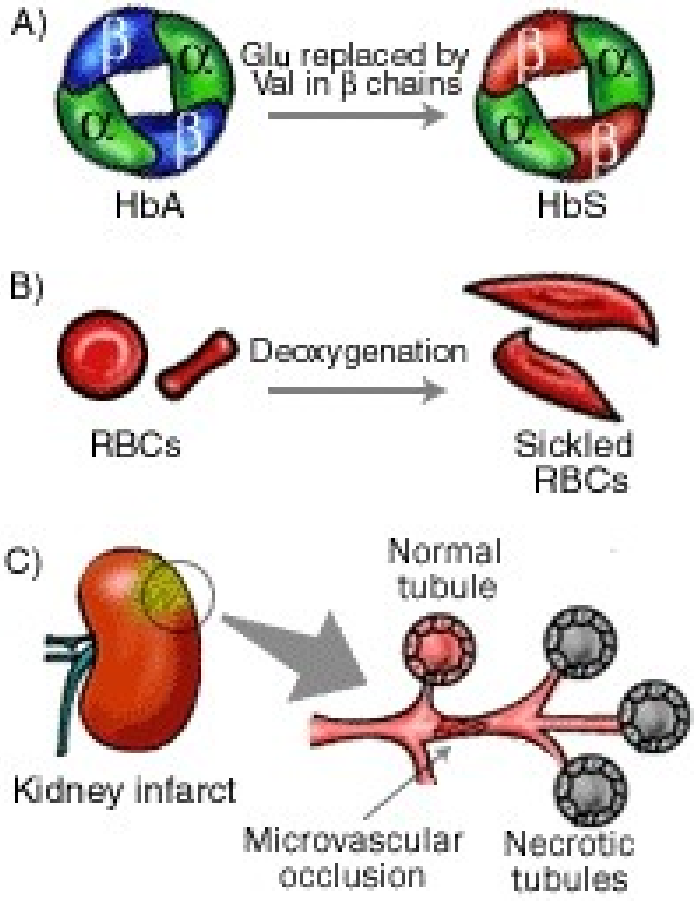


SCA ON A MOLECULAR LEVEL



- A single-nucleotide polymorphism (SNP), A to T, of the β-globin gene on chromosome 11p15.
- 60-70% of SCA is a result of genotype **Hb SS**
- Other SCD come from Hb S coinherited with an abnormal β-globin variant
- Heterozygotes (carriers): **Hb AS**

SCA ON A MOLECULAR LEVEL

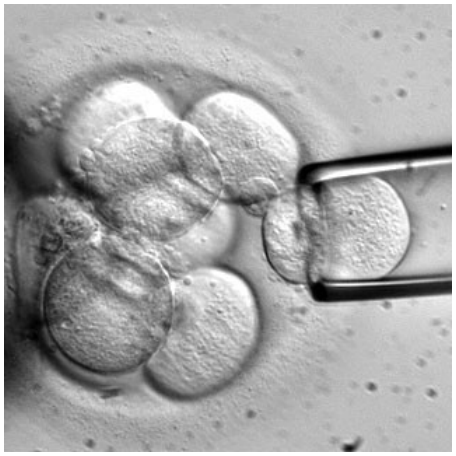


A) Hemoglobin is made up of 4 chains: 2 α and 2 β. In SCA, a point mutation causes the amino acid glutamic acid (Glu) to be replaced by valine (Val) in the β chains of HbA, resulting in the abnormal HbS. **B)** Under certain conditions, such as low oxygen levels, RBCs with HbS distort into sickled shapes.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

NEW FORMS OF DIAGNOSIS AND THERAPY

- *DNA analysis*
- *Targeted mutation analysis*
- *Sequence analysis*
- *Newborn Screening in Neonates*

- *Gene Therapy:*
  - *replacing Hb S with normal allele*
  - *Using induced pluripotent stem cells*
- *Stem cell transplantation (from donors)*
  - Hydroxyurea



REFERENCES

- http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part
- http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gnd&part=
- http://en.wikipedia.org/wiki/Sickle_cell_anemia#Aplastic_crisis
- for images: http://www.google.com/images?hl=en&source=imghp&biw=127 =