SICKLE CELL ANEMIA

Genetics, Symptoms, Diagnosis, and Treatments

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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 COMPLICATIONS

- 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.
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

- for images:
  http://www.google.com/images?hl=en&source=imghp&biw=127