Haemoglobinopathies: Sickle cell anaemia

Hemoglobinopathies?

- What are they?
  - Disorders where the production of normal adult hemoglobin in partly or completely suppressed or replaced by a variant hemoglobin.

Hemoglobinopathies

- Catagories
  - Inherited abnormality of the structure of one of more of the globin chains
  - Inherited abnormality related to the rate of synthesis of one or more of the globin chains
  - Failure of the normal switch from fetal hgb (HbF) to adult hgb (HbA)

Broad Classification System for Hemoglobin Disorders

- **Qualitative**:
  - Hemoglobins differ in sequence of amino acids composing globin chain
  - Disorders called hemoglobinopathies
- **Quantitative**:
  - Characterized by decreased production of hemoglobin resulting from decreased synthesis of one particular globin chain
  - Called thalassemia

Qualitative Disorders

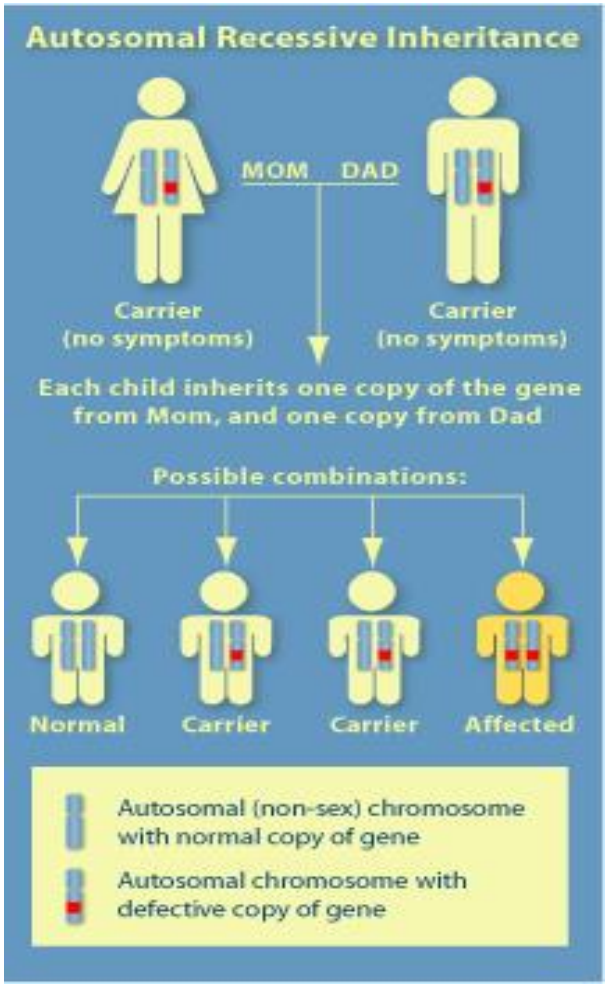
- **Qualitative** abnormalities in globin structure, usually involving beta-chain.
- Heme portion is normal
- Arise from single amino acid substitution or deletion
  - Rarely see multiple substitutions.

- May or may not cause abnormal laboratory test results.

Sickle Cell Anemia and Sickle Cell Trait

Introduction to Sickle Cell Anemia

- Most common hemoglobinopathy
- Autosomal co-dominant
- Hemoglobin A and Hemoglobin S produced.
  - AS is sickle cell trait.
  - SS is sickle cell disease. Patient is homozygous for HbS (SS). Results in very severe anemia.



Frequency

- African Americans
  - Sickle cell disease occurs in 0.3-1.35%
  - Sickle cell trait occurs in 8-10%
- Is worldwide disorder

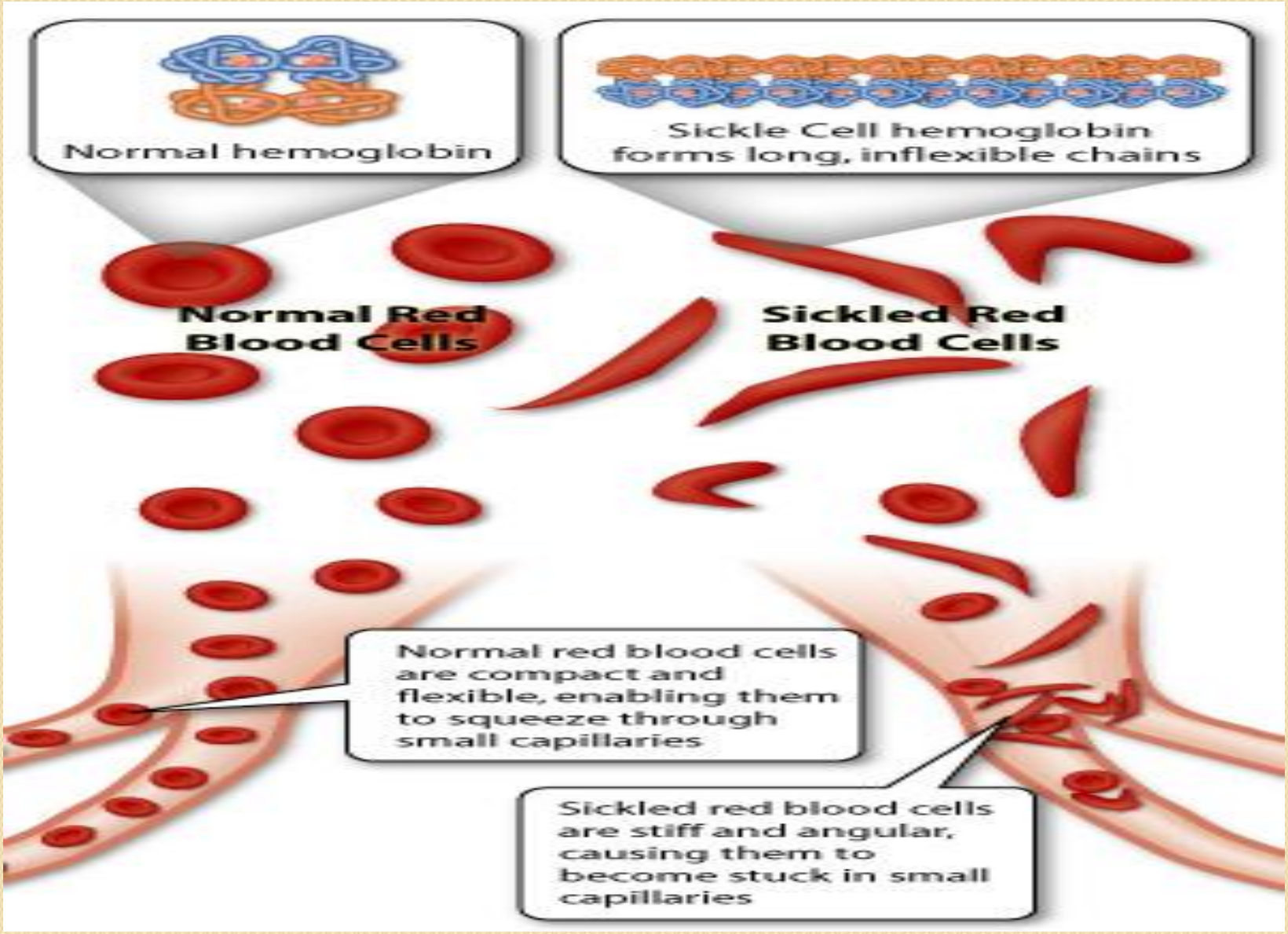
How and Why Cells Sickle

- Hb S forms from a point mutation for the sixth amino acid in the Beta chain.
- Valine substituted for glutamic acid.

- One benefit for AS persons is increased resistance to malaria

Pathophysiology of Sickle Cell Anemia

- SS cells may look normal when fully oxygenated; Sickling occurs when O_2 decreased.
- Other causes of sickling include decrease in pH and dehydration of patient.
- Cells become rigid, impeding blood flow to tissues. Tissue death, organ infarction, and pain result.
- Sickling is reversible up to a point.
- Have both extravascular hemolysis and intravascular hemolysis.


Normal hemoglobin
Sickle Cell hemoglobin forms long, inflexible chains
Normal Red Blood Cells
Sickled Red Blood Cells
Normal red blood cells are compact and flexible, enabling them to squeeze through small capillaries
Sickled red blood cells are stiff and angular, causing them to become stuck in small capillaries

Clinical Findings of Sickle Cell Anemia

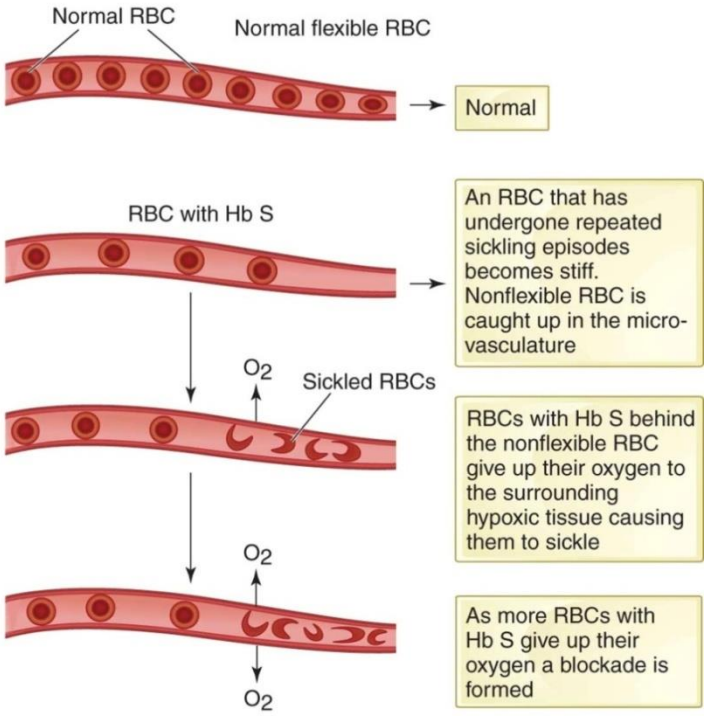
- Clinical signs appear at 6 months of age
- Have all physical symptoms of anemia
- Growth and sexual maturation slower
- Crisis – very painful. Anything that deoxygenates blood acts as trigger (exercise, illness and airplane flights). Sickle cells get stuck in capillaries.
- Strokes

Sickle Cell Anemia: Clinical features

- Organs Affected:
  - Liver: Enlarges, malfunctions, jaundice, hyperbilirubinemia
  - Heart: Cardiomegaly, iron deposits
  - Spleen: Enlarges leading to infarction and fibrosis Eventually shrivels and becomes nonfunctional
  - Skin: Develop ulcers, jaundice
  - Kidney: Hematuria and eventual failure
  - Lungs: Infarction
  - Brain: Strokes
  - Blood: Hemolytic anemia

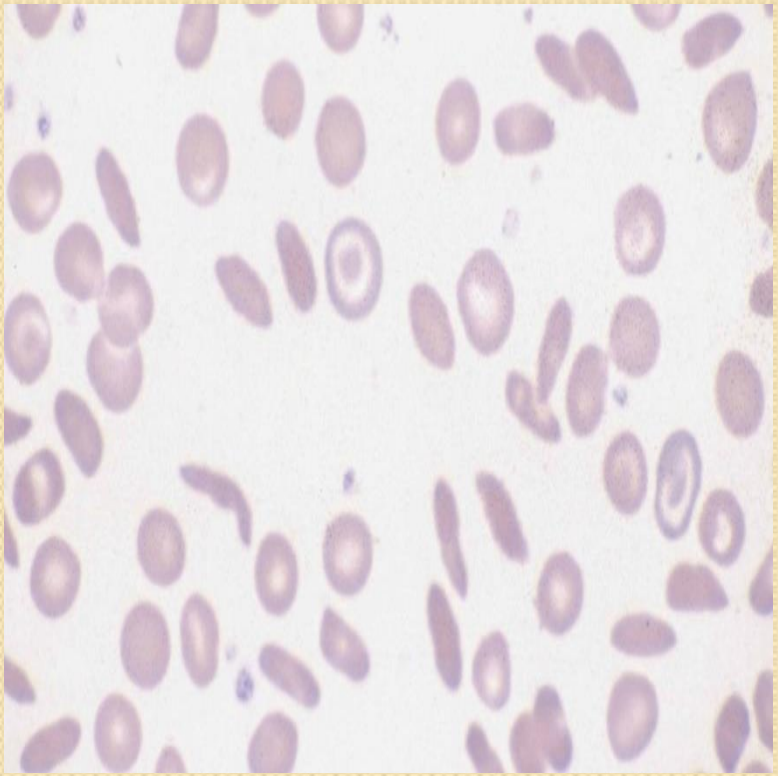
Pathophysiology of Sickle Cell Anemia

- Have three types of crises:
  - **Aplastic crisis**: associated with infections which causes temporary suppression of erythropoiesis.
  - **Hemolytic crisis**: Results in exaggerated anemia.
  - **Vaso-occlusive crisis**: Associated with severe pain. Hallmark symptom of sickle cell anemia.



Peripheral Blood Findings in Sickle Cell Anemia

- Hb 6-10 g/dL
- Marked aniso and poik
- Sickle cells and Target cells
- Ovalocytes and Schistocytes
- NRBCs with Polychromasia
- Increased Retics
- Basophilic Stippling
- Howell Jolly Bodies and Pappenheimer Bodies
- Leukocytosis with left shift
- Thrombocytosis



Special Hematology Tests in Sickle Cell Anemia

- Electrophoresis on cellulose acetate
  - Hb S present @ 85-100%
- Sickling Test – Positive
- Osmotic Fragility – Decreased
- Sed Rate – Decreased

Chemistry Tests in Sickle Cell Anemia

- LDH increased
- Bilirubin – increased
- Haptoglobin decreased

Sickle Cell Anemia: Treatment

- Prevention of infection
- Reduce organ damage
  - Hydroxyurea (it is believed to induce production of Hgb F). Using chemotherapeutic agents
  - Avoidance of situations that could cause a crisis
- Minimize pain
- Blood transfusion
- Median age at death
  - Male: 42
  - Female: 48

Sickle Cell Trait

- Heterozygous AS with more HbA than HbS, so condition is compensated for
- Patient often has normal life span
- Usually asymptomatic with occasional episodes of hematuria
  - Sickling can occur with drastic reduction of oxygen tension such as severe respiratory infection, air travel in unpressurized aircraft, anesthesia or congestive heart failure
  - Exercise that causes a buildup of lactic acid can cause sickling due to lowered pH

Laboratory Features: Sickle Cell Trait

- Normal CBC – Few target cells or sickle cells may be present.
- Sickle solubility test – positive.
- Electrophoresis – Both A and S present.

Referenes

- McKenzie, S. B. (2010). *Clinical Laboratory Hematology* (2nd ed.). Upper Saddle River, NJ: Pearson Education, Inc.
- http://learn.genetics.utah.edu/content/disorders/whataregd/sicklecell/