

Hemoglobinopathies in Pregnancy

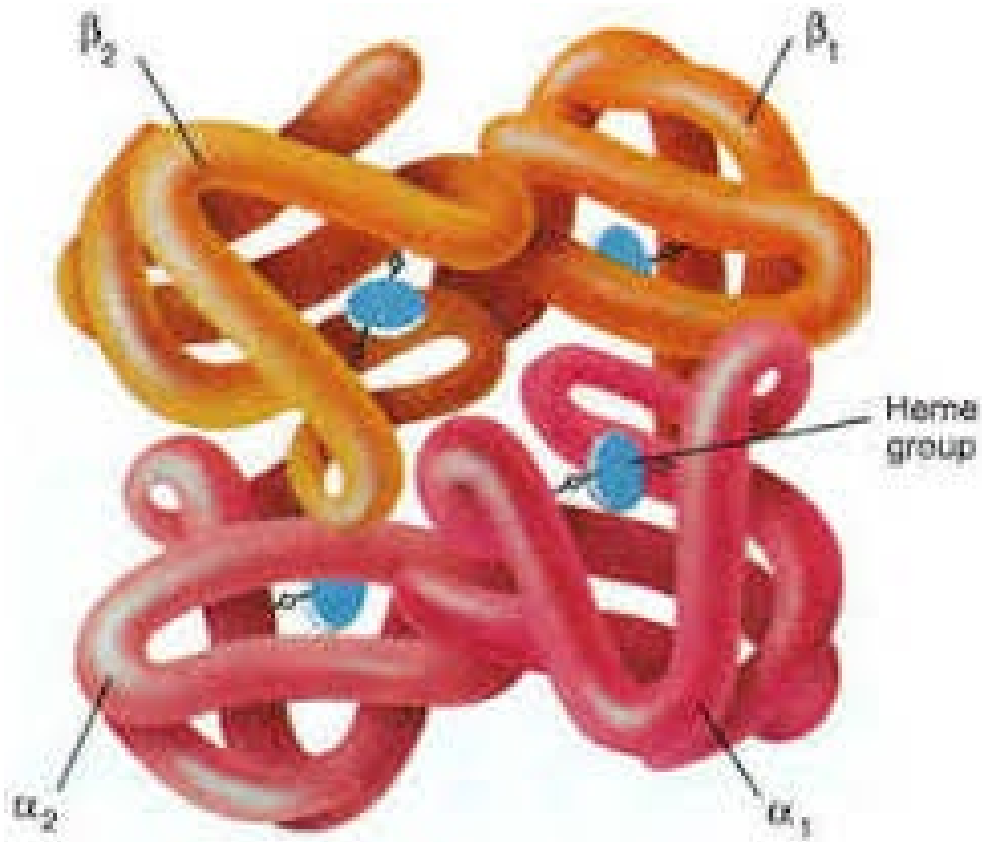
Pregnancy ECHO

Lauren Theilen, MD

May 4th, 2018



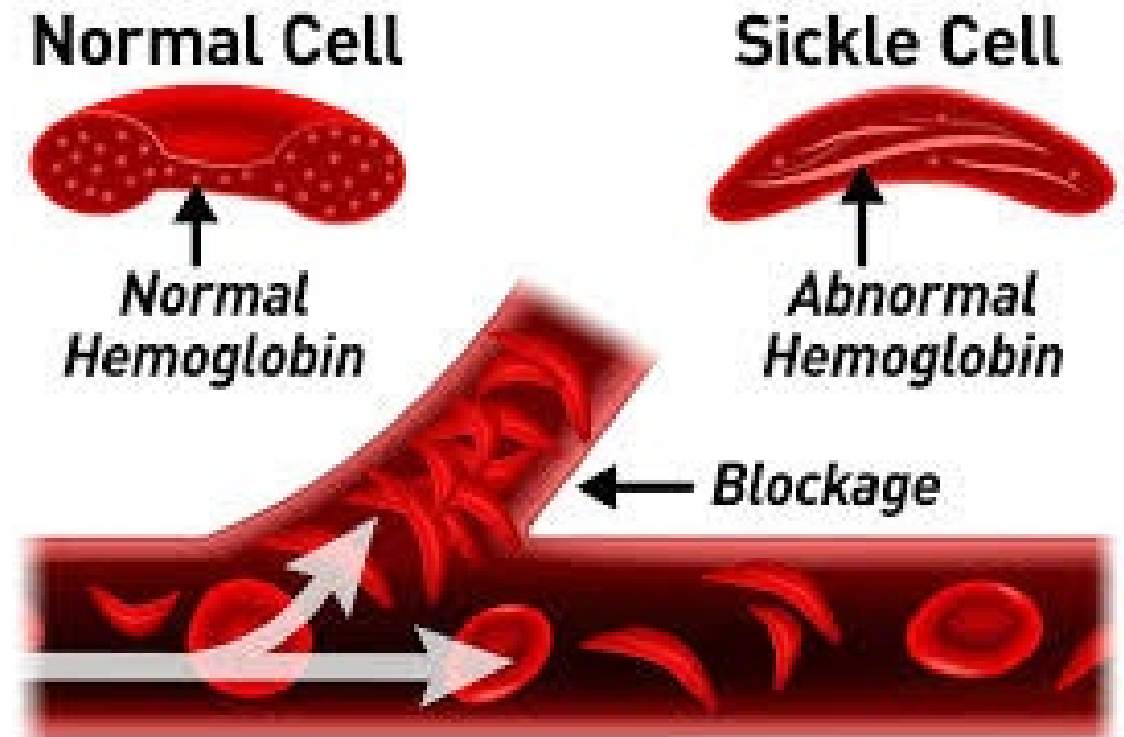
Hemoglobin structure



- 4 interlocking polypeptide chains with attached heme molecules
 - Hemoglobin A = 2 alpha + 2 beta
 - Hemoglobin F = 2 alpha + 2 gamma
 - Hemoglobin A₂ = 2 alpha + 2 delta
- Hemoglobinopathies = single-gene disorders
 - Structural hemoglobin variants
 - Thalassemias

Sickle cell disease – pathophysiology

- A group of autosomal recessive disorders of beta globin structure
 - Hb S
 - Hb C
- Under conditions of decreased oxygen tension, red blood cells become distorted
 - Vaso-occlusion
 - Hemolysis



Sickle cell disease – complications

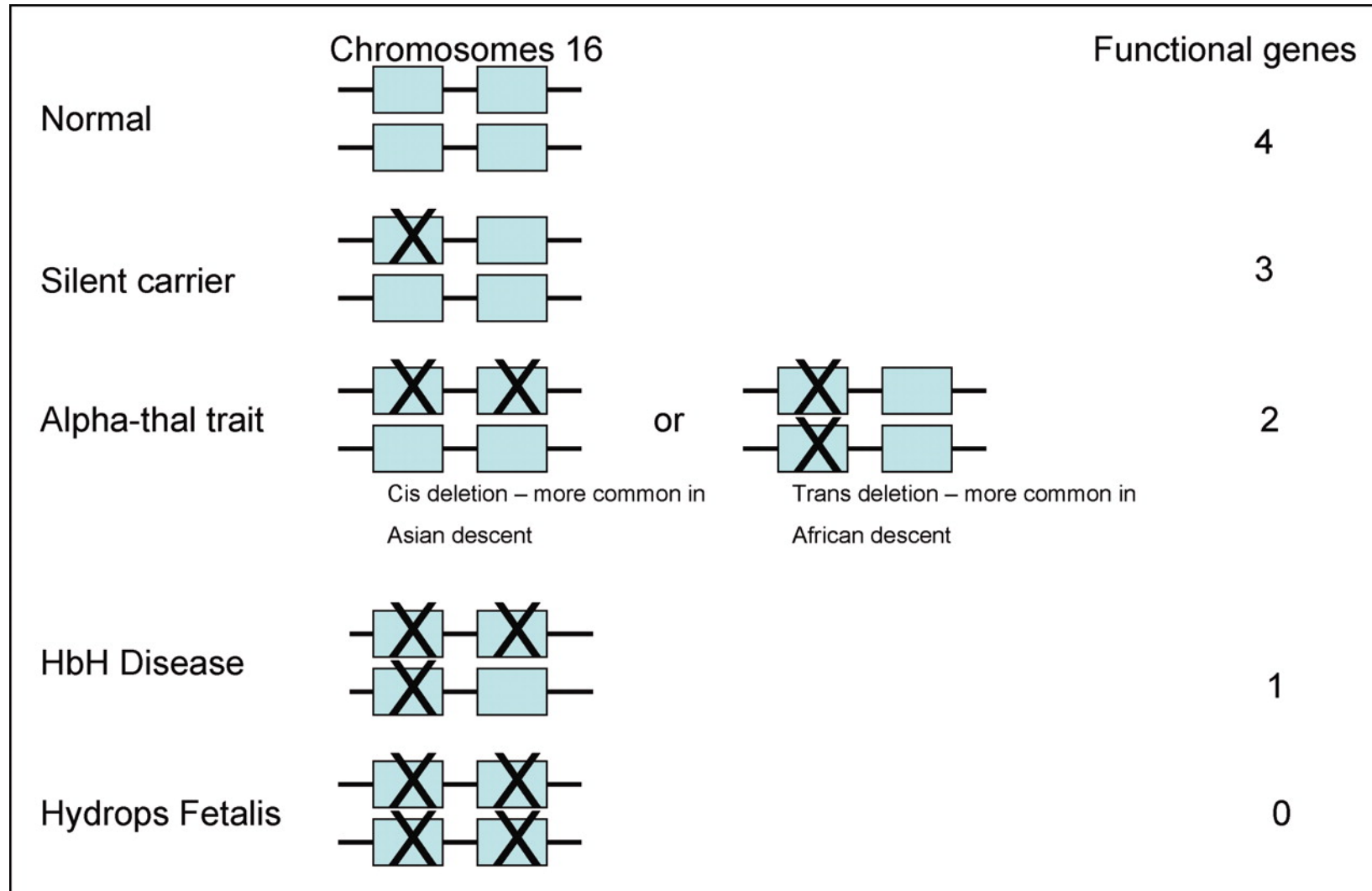
- **Pain:** distinguish acute painful episode from life-threatening crisis
- **Infection:** bacteremia, meningitis, pneumonia
- **Multiorgan failure:** requires prompt exchange transfusion
- **Anemia:** chronic compensated hemolysis, crises
- **Neurologic:** stroke, TIA, epilepsy, PRES
- **Pulmonary:** acute chest syndrome, pulmonary hypertension
- **Renal:** chronic kidney disease, hypertension, renal infarct
- **Skeletal:** dactylitis, osteoporosis, osteomyelitis, avascular necrosis
- **Cardiac:** cardiomyopathy, myocardial infarction, dysrhythmia
- **Hepatobiliary:** acute ischemia, transfusional iron overload
- **Pregnancy:** IUGR, IUFD, preeclampsia

Thalassemias

- Reduced synthesis of globin chains* leading to microcytic anemia
- Classified according to globin chain affected
 - Alpha
 - Beta
- Different molecular mechanisms arose in different parts of the world

*Can also have structural changes in alpha globin chains (Hb Constant Spring, Hb Qong Sze), but these are much less common.

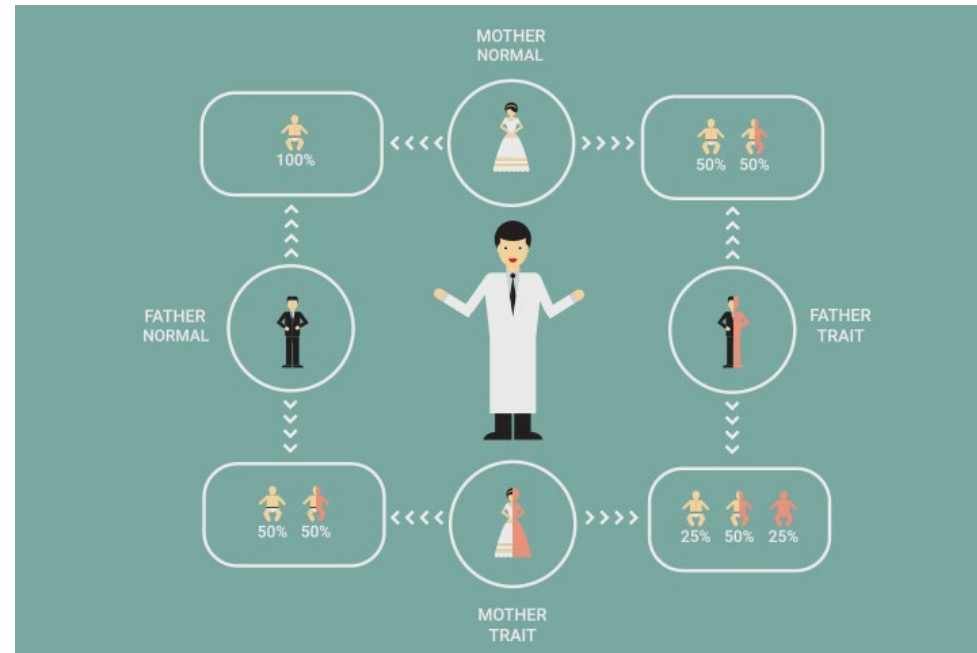
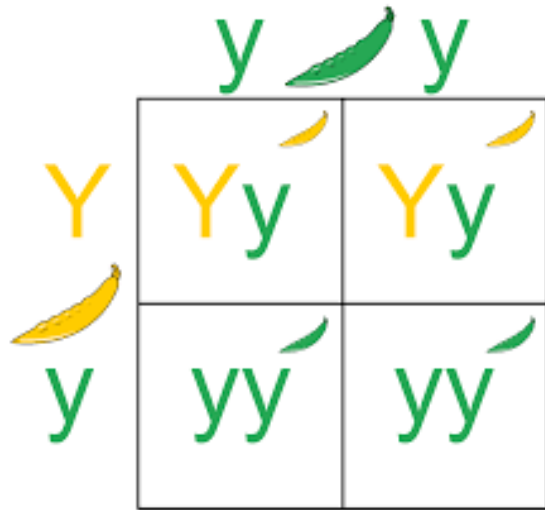
Alpha thalassemia



Beta thalassemia

- Mutation in beta globin gene causing either absent or deficient beta chain production
- Heterozygotes have beta-thalassemia minor
 - Often seen in association with Hb S
 - If no normal beta chain production, results in clinically severe sickle cell-beta thalassemia with no production of Hb A
- Homozygotes have either beta-thalassemia major or beta-thalassemia intermedia
 - Depends on the degree of beta chain production associated with the specific mutation

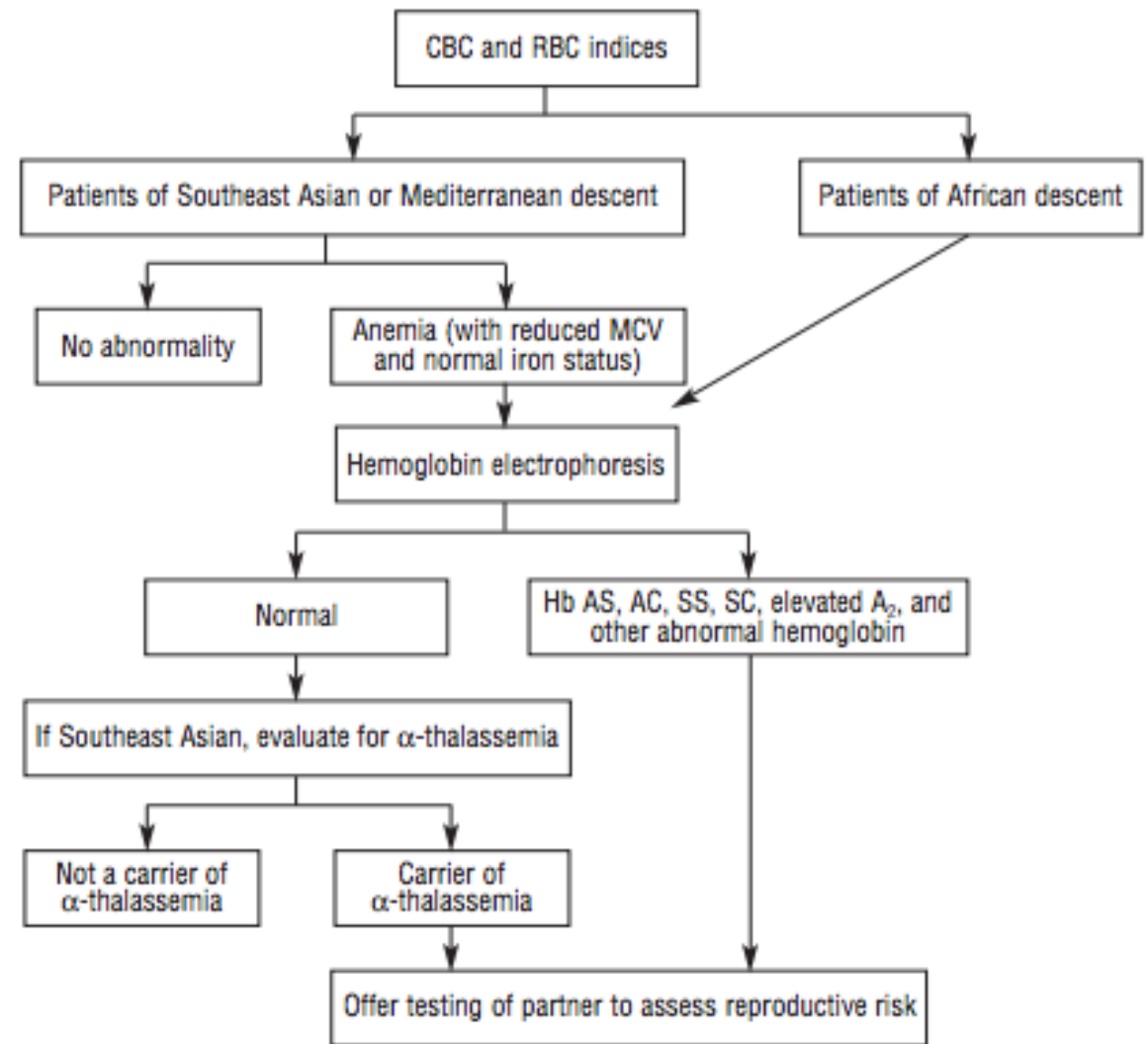
Genetic counseling



- Hemoglobinopathies are heritable conditions
 - Autosomal recessive, with some caveats
- Ethnicity not always a good predictor of risk

Screening

- Start with CBC/MCV
 - Part of routine prenatal labs
- Hemoglobin electrophoresis
 - African descent
 - Microcytic anemia with normal ferritin
 - Solubility testing inadequate
- DNA-based testing for alpha globin gene deletions
 - Microcytic anemia with normal ferritin AND normal hemoglobin electrophoresis



Summary of clinical pearls

- Offer carrier screening to individuals at increased risk for being hemoglobinopathy carriers
- CBC and hemoglobin electrophoresis are appropriate initial lab tests for hemoglobinopathy screening
 - NOT solubility testing
- Offer genetic counseling to couples at risk for having a child with sickle cell disease or thalassemia
- Pregnant women with sickle cell disease or thalassemia should be co-managed with hematology and MFM

A microscopic view of numerous red blood cells, which are biconcave discs, floating in a fluid medium. The cells are rendered in shades of red and pink, with some showing a distinct central pallor. The background is a soft, out-of-focus pinkish-red.

Questions?