THALASSEMA

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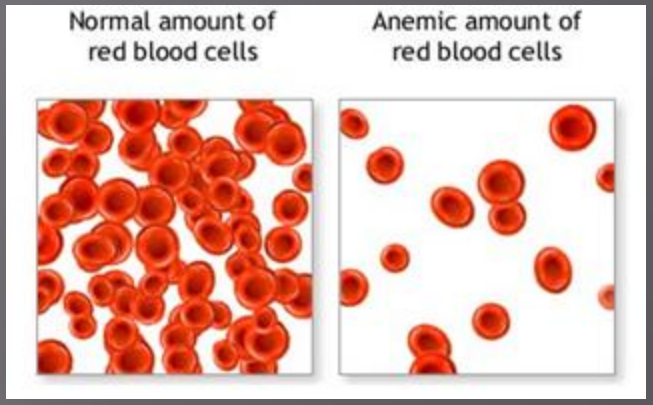
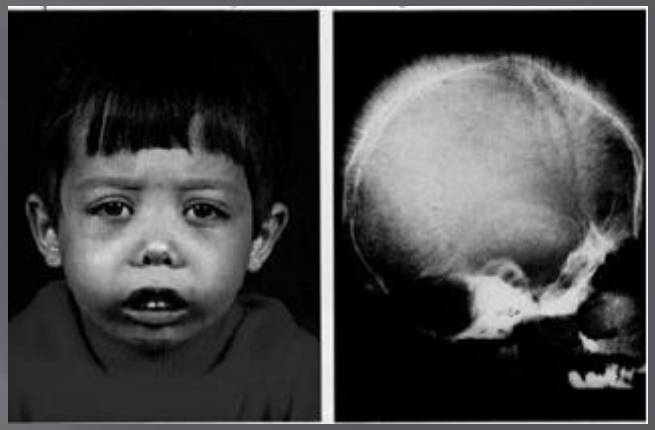
SB11QHG-1 (Period 3)

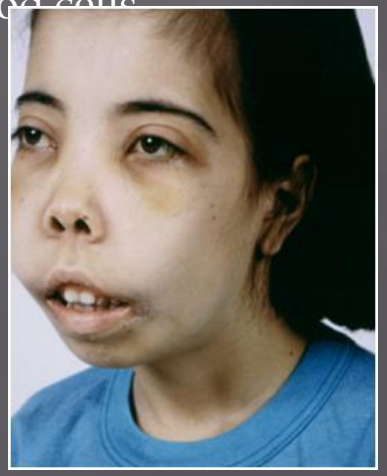
Dr. Nedwidek Human Genetics

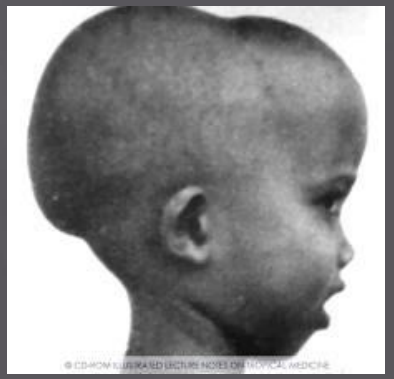
Physiology

- Early childhood onset
- Two types of thalassemia:
  - Alpha thalassemia and Beta-thalassemia
  - Alpha thalassemia is caused by a deletion
  - Beta-thalassemia is caused by a mutation
- Caused by over 200 different mutations
- Patients with thalassemia are immune to malaria
- Geographic Bias:
  - Most common in the Mediterranean or south Asia
- Thalassemia affects hemoglobin in red blood cells
  - Hemoglobin binds to oxygen and transports it to cells around the body
- Main symptom is anemia: deformed red blood cells
- Other symptoms include
  - Jaundice
  - Facial Bone Deformities
  - Hepatosplenmegaly
    - Large spleen
  - Constant fatigue



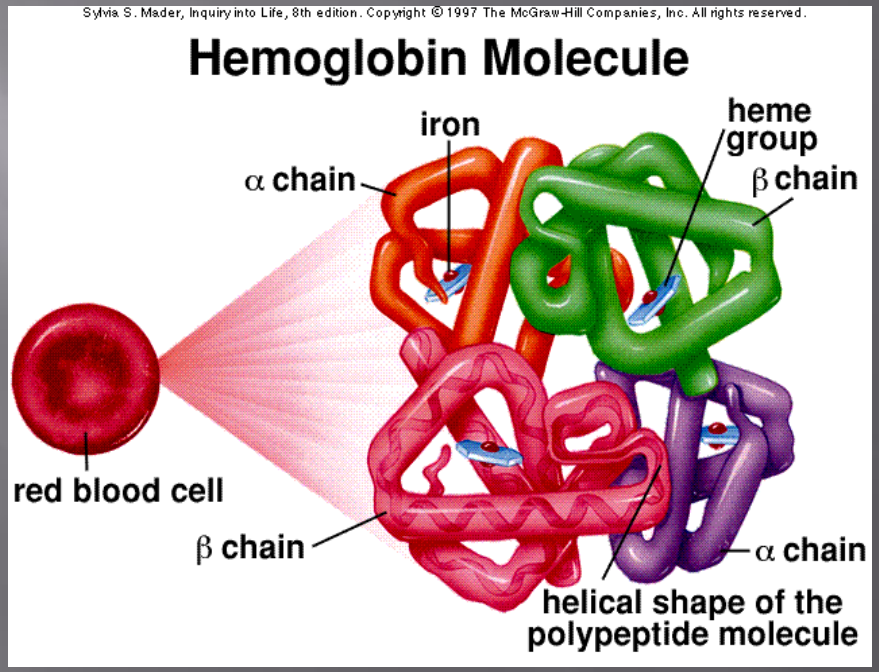


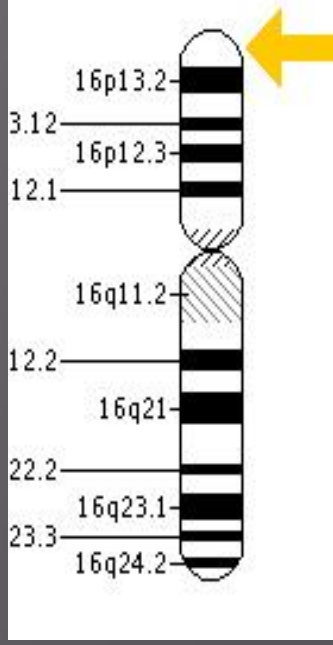


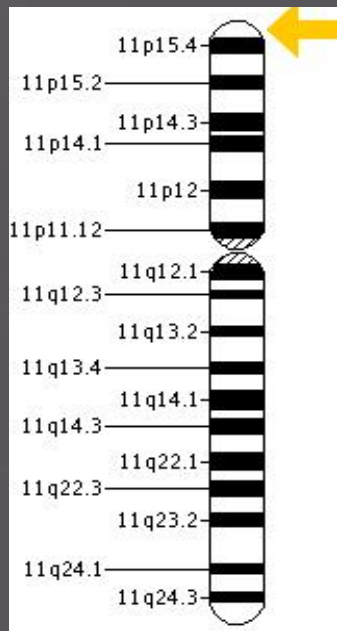


Molecular Cause

- Autosomal Recessive, though it sometimes can be autosomal dominant
- Alpha-thalassemia is caused by deletions on chromosome 16
  - Leads to deletion of HBA1 gene or HBA2 gene in alpha globin
  - Genotypes:
    - Silent Carrier
      - (-a/aa) or (-/aaa)
    - Alpha-thalassemia trait
    - Alpha thalassemia minor
      - (-a/-a) or (--/aa)
    - Hb H disease
      - (--/-a)
    - Hydrops Fetalis
      - (--/--)







- Beta-thalassemia is caused by deletions on chromosome 11
  - Leads to deletion of HBB gene in beta globin
    - Beta-thalassemia Minor
    - Beta-thalassemia Intermedia
    - Beta –thalassemia Major
- Both alpha and beta globin are in the hemoglobin in red blood cells

Current Treatments

- Currently the most effective diagnosis is a physical exam (for phenotypes) and a CBC (complete blood count) with a blood test.
- Prenatal Detection is also available.
- No major treatment needed for patients with beta-thalassemia minor, alpha thalassemia minor, or silent carrier. They do need frequent blood tests to make sure their condition does not get worse.
- More severe patients require regular blood transfusions
  - This has several limitations
    - Blood transfusions causes iron buildup
    - After 100 blood transfusions, they will develop is hemosiderosis
    - Iron cleating therapy must be paired with blood transfusions
      - Deferoxamine (under the skin) = Pump
      - Deferasirox (oral) = Pill
- For patients with even more severe symptoms, a bone marrow transplant can be given. Though this is a cure, it is not ideal, and not recommended for most patients.
  - Patients are given high doses of radiation and drugs that destroy all defective bone marrow
  - Compatible donors are usually hard to find
- Treatment of individual symptoms is sometimes recommended

Proposal

- Bone marrow produces about 95% of the body's blood cells
- Stem cell treatment seems to be a good cure
  - Injection of hematopoietic stem cells; cells that mature into healthy RBCs
  - Injected into the body by IV (intravenous therapy)
- Three types of Stem Cell Transplant
  - Autologous Stem Cell Transplant
    - Patient (as an adult) is his own donor
  - Allogeneic Stem Cell Transplant
    - Stem cells are taken from a donor and cultivated
  - Umbilical Cord Stem Cell Transplant
    - Stem Cells are taken immediately after a baby is born from the umbilical cord
- Umbilical Cord Stem Cell Transplant is the best therapy
  - Before patients reach childhood, their hemoglobin is normal
  - This transplant is done early on since there is only a limited number of cells in the umbilical cord cells and must be used as early as possible
- Limitations:
  - New and very limited information about this process
  - Many diseases that can occur from this therapy

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