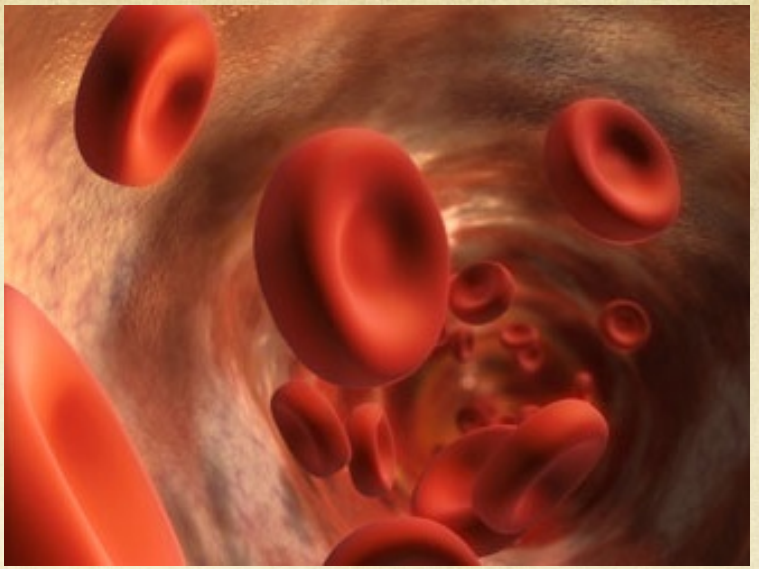


Hemophilia A (F8)

"Classic Hemophilia"

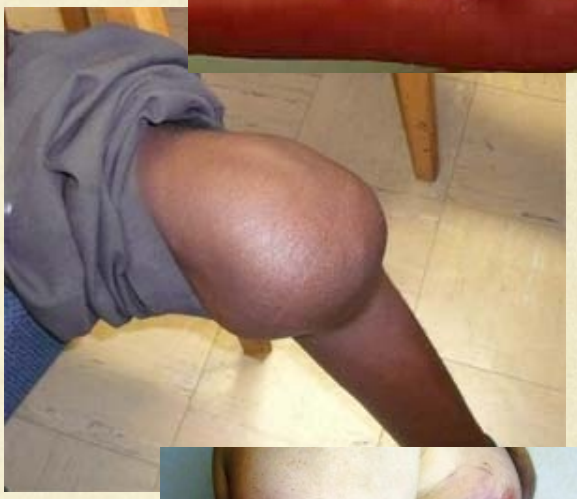
Hoa Mai

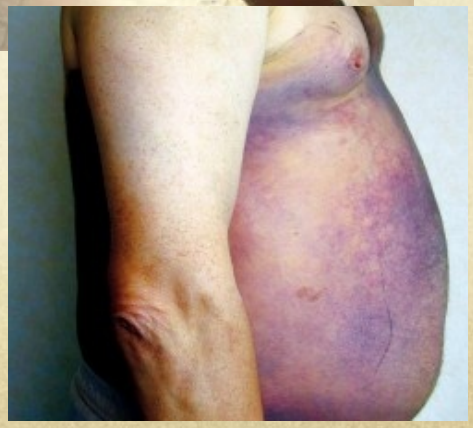
BIOC 118Q: "Genomics & Medicine"

Winter 2011

Hemophilia A

- Symptoms:
  - Slow blood clotting process
  - Prolonged, excessive bleeding after injury, surgery, or tooth extraction
  - Easy bruising
  - Spontaneous heavy bleeding
  - Hematuria
  - internal bleeding in joints and muscles
    - Swelling, pain, and decreased function in joints
    - hemorrhage in joints → necrosis, contractures, and neuropathy

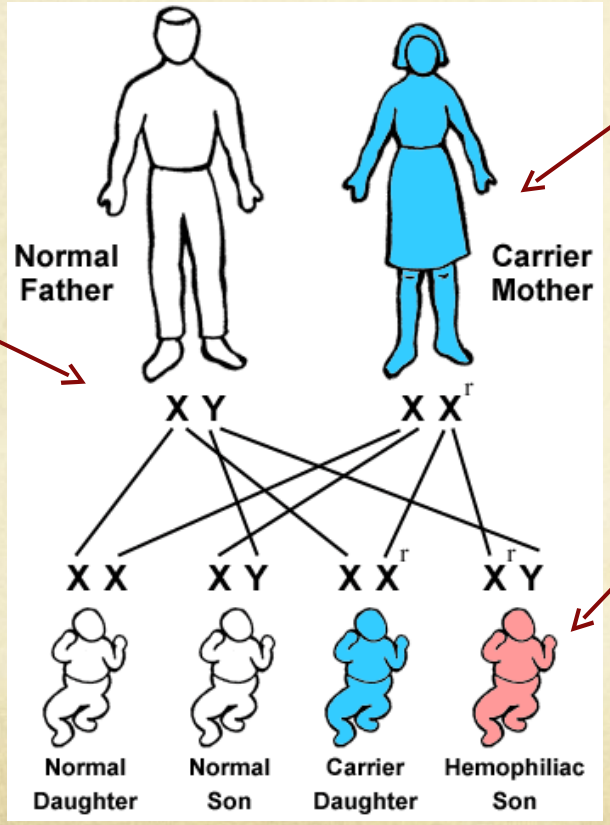




Mendelian Sex-Linked Trait

- HEMA F8 gene
- Altered protein coagulation factor VIII
- X-linked, recessive trait

Cannot be passed from father to son.



Heterozygous females: 1 normal allele can offset effects by altered allele.

Gene inherited from a carrier mother.

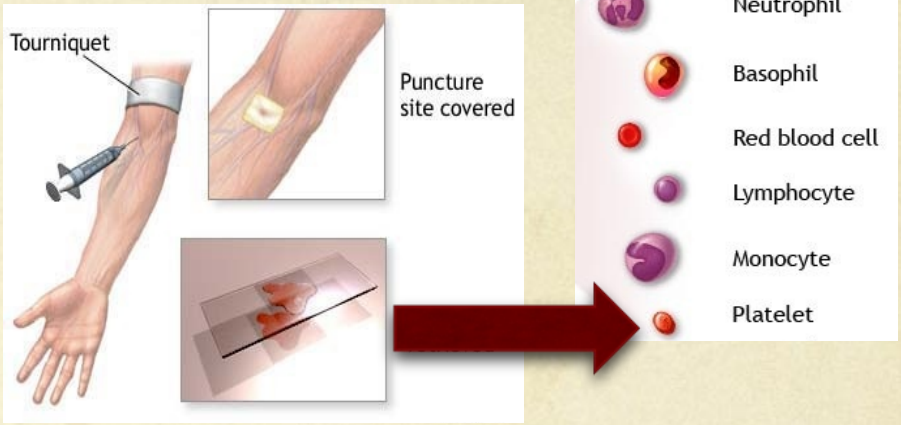
Males: 1 altered allele is enough to cause the disease

Primarily affects males → 1/1,500 male newborns

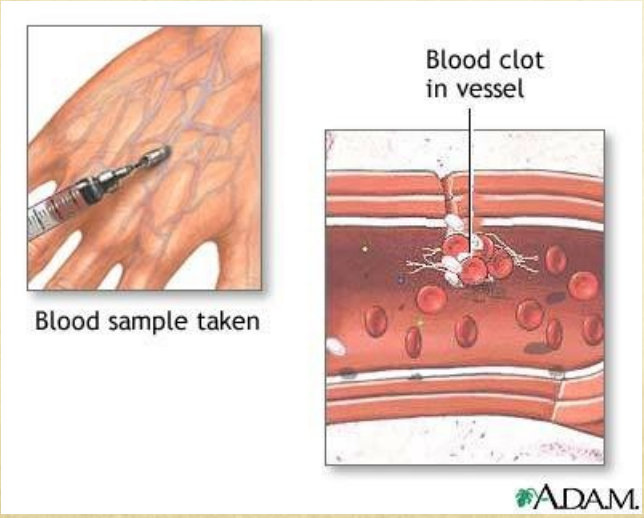
Traditional Diagnostic Methods

- Diagnosed when symptoms appeared

  (1st episode of unusual bleeding)
- Blood tests used to detect:
  - platelet count and function analysis
  - Bleeding time tests
  - Factor VIII assays
- Time of diagnosis depends on severity
  - Severe → first 2 years of life
  - Moderate → 5-6 years
  - Mild → later in life



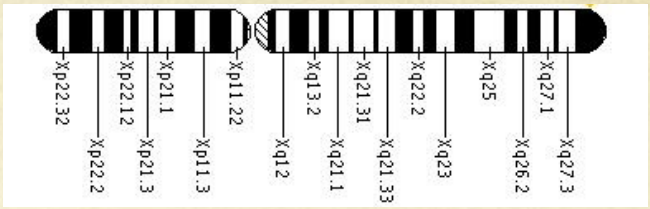
Traditional Treatment



- mid-1960s: infusion of factor VIII concentrations from donor plasma
- Complications:
  - 1979 to 1985: many individuals contracted HIV and hepatitis C
  - 30% develop alloimmune inhibitors for factor VIII
  - infusion of processed plasma with recombinant Factor VIII concentrate
  - Desmopressin (dDAVP): synthetic analog

Novel Diagnostics

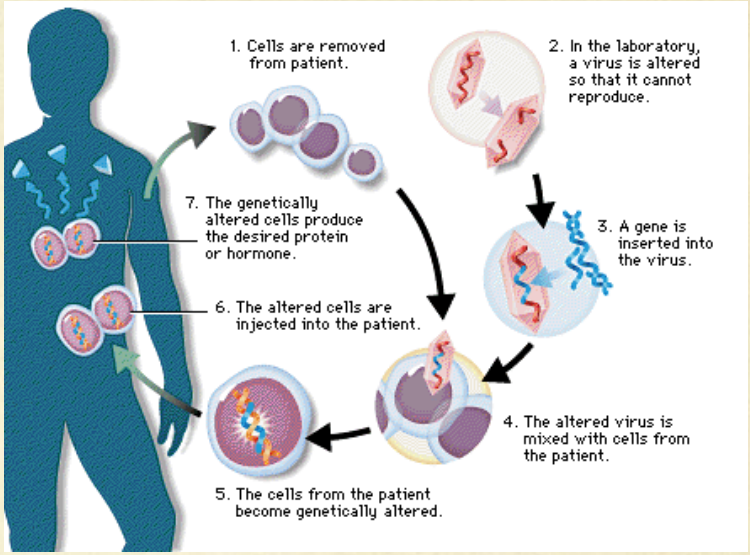
F8 gene



- PCR or Southern blotting → an F8 intron 22-A or intro 1 in 50% of severe cases
- Others: large deletions, insertions, frameshift, nonsense and missense mutation
- Identification of the specific F8 mutation can determine severity and the likelihood of inhibitor development
- Genetic counseling

Novel Treatments

- 140 federally funded hemophilia treatment centers (HTCs)
- Prophylactic treatment
- Longer-acting factor VII concentrates still under clinical trials
- More research on immune tolerance therapy to avoid alloimmune inhibitors
- Use retroviral vector systems to insert Factor VIII gene into DNA of cells
- Clinical trials for gene replacement therapy has been discontinued



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