Hemophilia A

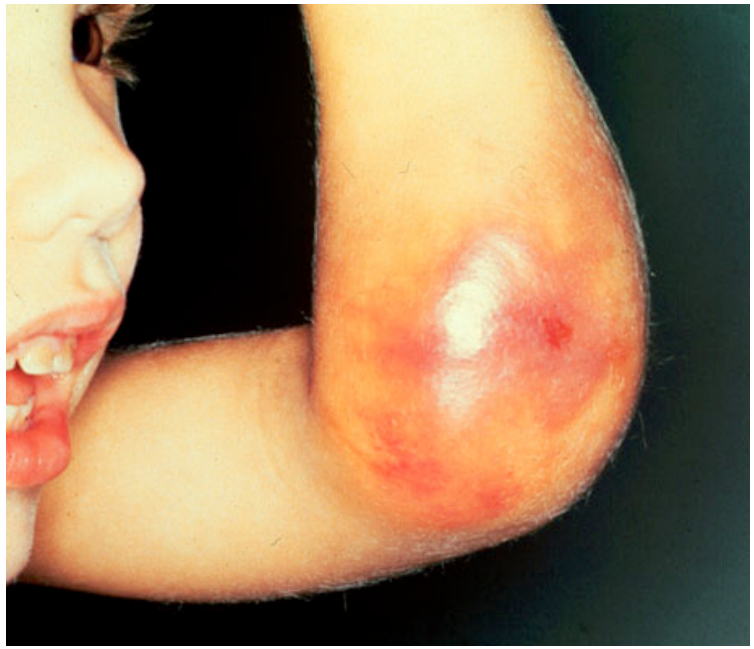
Angela Torney

English royal family--descendants of Queen Victoria

Rasputin & Russian royal family

Classical Diagnosis

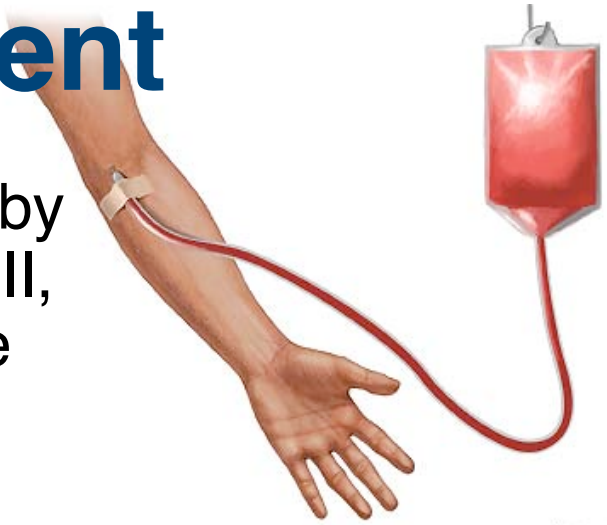
- Symptoms:
  - Excessive bleeding from cuts, surgery, or tooth removal
  - Bleeding into joints and muscles (may cause swelling, pain, necrosis, contractures, neuropathy)
  - Hematuria (presence of blood in urine)
  - Easy bruising
  - Intracranial hemorrhage after mild head trauma



- Blood tests can be used to diagnose hemophilia: platelet count and function analysis, bleeding time tests, and factor VIII assays.

http://www.pathguy.com/lectures/hemophilia.jpg

Classical Treatment



- Because hemophilia is caused by a deficiency of clotting factor VIII, therapies involve increasing the level of factor VIII.
- **Treatments:**
  - **Mild hemophilia (6-35% of normal factor VIII levels):** Take dDAVP, a synthetic analog of the hormone that stimulates release of stored factor VIII in the lining of blood vessels.
  - **Moderate hemophilia (1-5%):** Need replacement therapy (blood transfusions) only when bleeding occurs. Before doing an activity with a high risk of bleeding, dDAVP should also be taken as a precaution.
  - **Severe hemophilia (<1%):** Need consistent replacement therapy. Prevents bleeding that could cause permanent damage to joints, muscles, or other parts of the body. Therapy may be given at home two or three times a week.

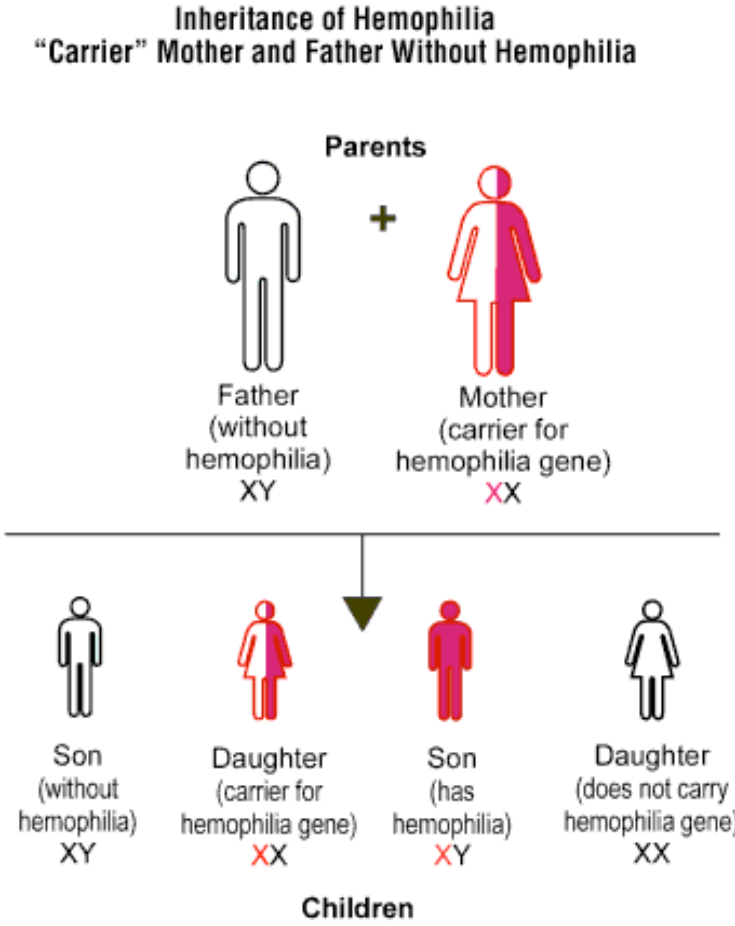
http://www.dhmc.org/shared/adam/graphics/images/en/19449.jpg

Classical Treatment *(cont'd)*

- **Complications?**
  - While replacement therapy is effective in most cases, 10-15% of treated individuals will develop neutralizing antibodies that impede treatment.
  - Immunizations may be necessary because of increased risk of exposure to Hepatitis B and HIV during transfusions.

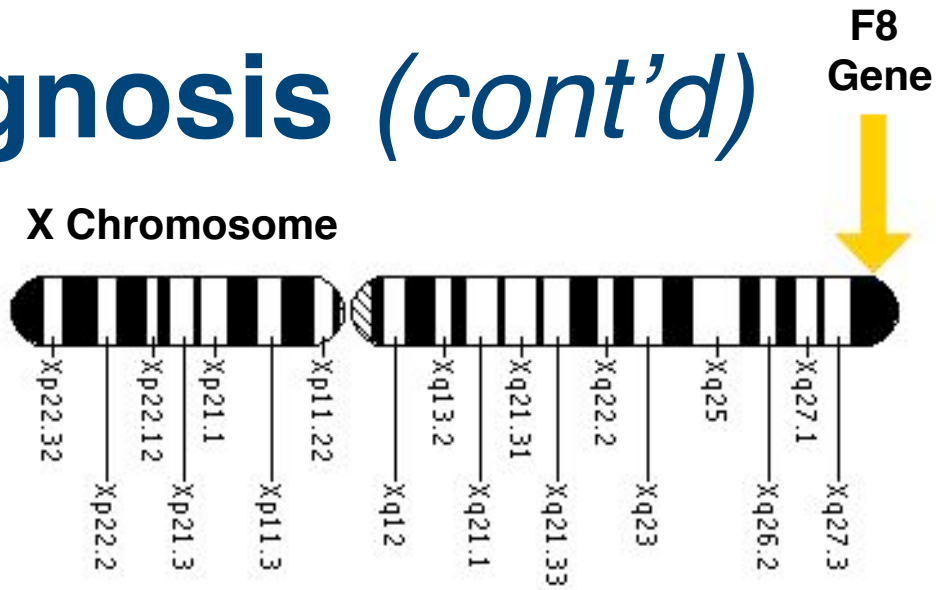
Genetic Diagnosis

- Inheritance:
  - Hemophilia is an inherited, X-linked recessive trait.
  - Heterozygous female carriers may exhibit slightly decreased coagulability but no other symptoms.
  - Males will inherit the disease if their mothers are carriers.
- Hemophilia affects 1 in 10000 males and 1 in 100000000 females.



http://www.daviddarling.info/images/hemophilia_inheritance_1.gif

Genetic Diagnosis *(cont'd)*



- Hemophilia is caused by mutations in the gene which provides instructions for making clotting factor VIII, the **F8 gene**.
- Location = **Xq28**, meaning that the F8 gene is located on the long arm (q) of the X chromosome at position 28.
- The most common mutation in people with severe hemophilia is an **inversion of a large segment of the F8 gene**. A large inversion will entirely eliminate the activity of factor VIII.
- Other mutations causing hemophilia **change, delete, or insert base pairs**. These mutations may lead to the production of an abnormal factor VIII, which cannot participate effectively in blood clotting.

http://ghr.nlm.nih.gov/gene=f8

Genetic Treatment

- All clinical trials for gene therapy have been discontinued because of complications and failure to achieve significantly higher factor VIII levels.
- Therefore, the classical treatments of replacement therapy and dDAVP are still in use pending new discoveries.

Sources

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- “F8 Gene.” *Genetics Home Reference.* 28 September 2008. http://ghr.nlm.nih.gov/gene=f8
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