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.
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.

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