ROBERSON MUSEUM AND SCIENCE CENTER

Post-Visit Anastasia: Hemophilia "The Royal Disease"

Grade Level: 6th through Adult
NY State Standards: M S & T 2, 4, 5, and 7
Pennsylvania State Standards: S & T and 3.1, 3.2, 3.3. and 3.7

Objective: After participating in the "Anastasia/DNA Extraction" program at Roberson Museum and Science Center, students will further explore the royal descendants of Queen Victoria as they married into the various royal houses of Europe. Students will explore the family trees that resulted from these marriages and trace the presence of the disease, known as the "Royal Disease" within these family trees. Students will learn more about the science behind this disease and make predictions as they become familiar with the concepts presented in this activity.

Materials:

- Pencil
- Copies of Family Trees (1/Student) or Projected on an Elmo

Procedure:

1. Part I: Historical Background

a) Hemophilia has played an important role in Europe's history. Hemophilia became a popular phenomenon when it suddenly cropped up in the children of Great Britain's Queen Victoria (b: 1819 - d: 1901). It became known as the "Royal Disease" because it spread to the royal families of Europe through Victoria's descendants.

b) Victoria had always been worried about the "quality" of the blood of the British royal family. She felt it needed to be revitalized, this can be seen through a letter to her daughter Victoria where she writes, "I do wish one could find some more black eyed Princes and Princesses for our children! I can't help thinking what Dear Papa said… that it was in fact when there was some little imperfection in the pure Royal descent that some fresh blood was infused…. For that constant fair hair and blue eyes makes the blood so 'lymphatic'….it is not as trivial as you may think, for Darling Papa…often with vehemence said: 'We must have some strong blood!'"

c) It is doubtful at the time of the writing of this letter that Queen Victoria knew exactly what was wrong with her family's blood. Hemophilia first appeared in Victoria's family in her eighth child, Prince Leopold, Duke of Albany. Leopold had suffered hemorrhages and was always described as being very "delicate." He died at the age of 31 after a minor fall.

d) Her son's hemophilia upset and confused the Queen. She protested that it did not originate on her side of the family. There were some who whispered about a curse. The traditional view is that there was a mutation in either the Queen or in her father, Edward Duke of Kent. From there it spread to Victoria and the Royal Houses of Europe as Monarchs arranged marriages to consolidate political alliances.

e) The students will trace the history of hemophilia as it popped up in Spain, Russia, and Prussia by looking at their family trees. But before we do this let us understand a little more about the disease itself and how it is passed down from generation to generation.

2. Part II: What is Hemophilia?

a) Hemophilia is an X-linked recessive disorder characterized by the inability to clot blood properly. X-linkage describes the fact that the gene for hemophilia is carried on the X-Chromosome. A recessive gene is defined as one that will be expressed in the absence of a dominant gene.

b) In order for blood to clot, numerous biological processes must occur. One of these processes is called "Factor 8." The hemophiliacs that we are discussing today, those with the "Royal Disease," and indeed most hemophiliacs, lack "Factor 8."

c) Why do they lack Factor 8? Because of a mutation in their DNA that has caused them to have a faulty gene, they cannot produce Factor 8.

d) At the time of Queen Victoria hemophilia was untreatable and very few hemophiliacs survived to reproduce due to small cuts or internal hemorrhaging even after a minor bruise.

e) Today hemophiliacs are treated with blood transfusions and infusions of a blood derived substance known as anti-hemophilic factor to help blood clot.

f) Hemophilia affects males (1/10,000) much more than females (1/100,000,000). This occurs because the gene for Factor 8 is carried on the X-chromosome.

g) Since males only have one X-chromosome, if the chromosome is defective, hemophilia will immediately show up. Females on the other hand have two X-chromosomes. If one is defective, the other is normal and will compensate. So the female will be a carrier with normal blood clotting ability. For a female to be a hemophiliac, she must have two abnormal X-chromosomes. This is quite rare.

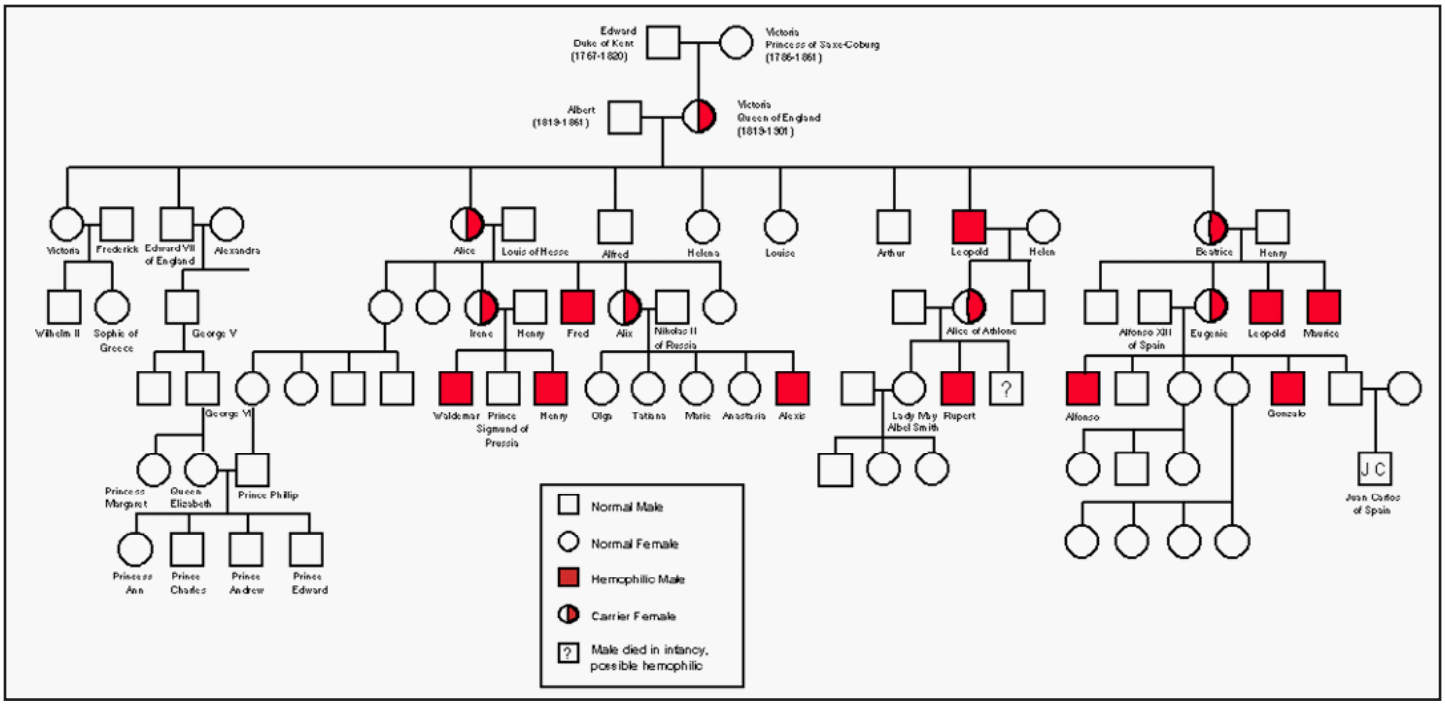
3. Part III: Analysis of Royal Family Trees

a) #1 Queen Victoria's Family Tree

First let's look at Queen Victoria's son **Leopold's** Family (see Queen Victoria's Family Pedigree). His daughter **Alice of Althlone** had one hemophiliac son Rupert and two other children, a boy and a girl, whose status is unknown. a) **What is the probability that her son was hemophiliac?** Answer: 50% because Alice can give her sons either a normal or an abnormal X (Alice has two X-chromosomes. One is normal and one carries the gene for hemophilia. Therefore, since each child will get one of his or her X-chromosomes form each parent, Alice will give either a normal or an abnormal X-chromosome to her children (remember boys inherit a Y instead of an X chromosome). Thus, once again the answer is 50%). b) **What is the probability that her daughter is a carrier?** Answer: 50% same reasoning as above. c) **What is the probability that her daughter is a hemophiliac?** Answer: 0% her father would have had to be a hemophiliac and her mother would also have had to give her the abnormal X. However, we know that Alice's husband was normal. (To better explain this we know that to be a female hemophiliac you would have to have two abnormal X-chromosomes. Since females have two XX chromosomes and males have and XY chromosome combination, Alice would have to give her abnormal X to this "hemophiliac" daughter and Alice would have had to have had a hemophiliac for a husband who could have also passed on a bad X in order to produce a daughter with two bad X's that would be a hemophiliac. We know that Alice's husband was normal. So, this was not possible).

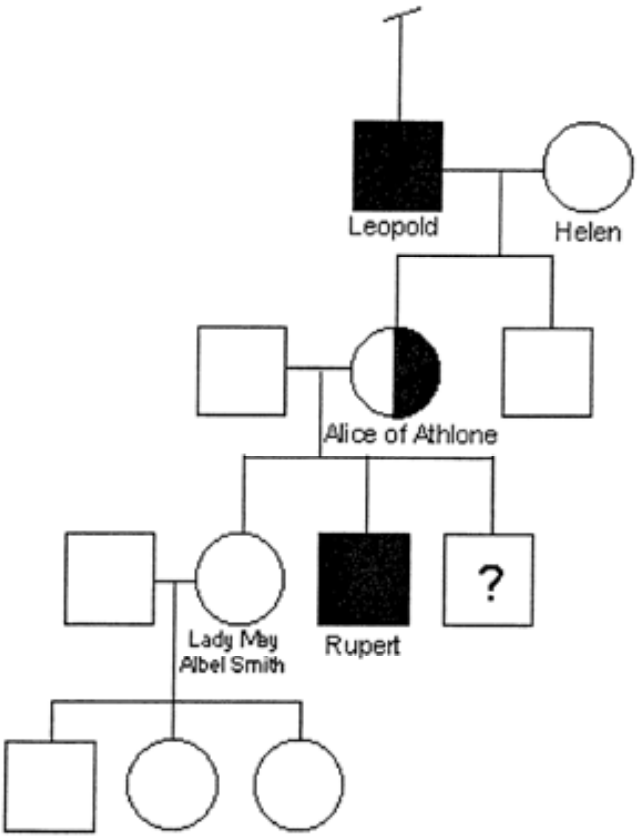
b) Fortunately, Leopold was the only one of Victoria's sons who suffered from hemophilia. Her other sons, Edward, Alfred, and Arthur were unaffected. Since the present royal family of England descended from Edward VII (b: 1841 – d: 1910), the first son, the lineage is now free from hemophilia.

Queen Victoria's Family Pedigree



This pedigree continues on the next page.

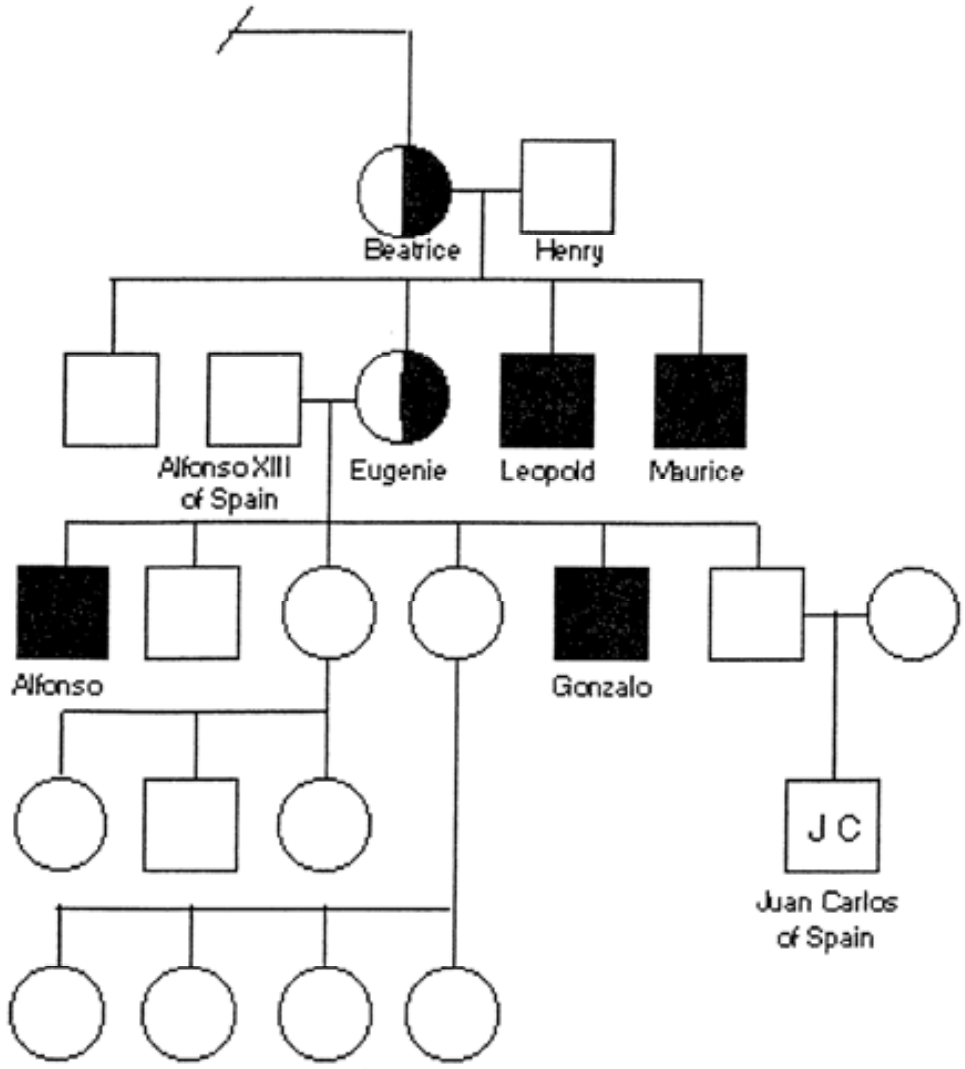
Queen Victoria's Family Pedigree continued with son Leopold's descendants



c) #2 The Spanish Connection
Victoria's youngest child, **Beatrice**, gave birth to one daughter, one normal son, and two hemophiliac sons.
a) **Look at the family tree titled "Princess Beatrice's Family Pedigree" and identify which of Beatrice's children received the hemophilia gene; why can you make this conclusion?** Answer: Eugenia is the normal daughter although she is a carrier. Leopold and Maurice are both hemophiliacs because their squares are colored in.

Notice that Beatrice's daughter Eugenie married King Alfonso XIII of Spain and had six children, one of whom was the father of Juan Carlos, the current King of Spain. **Would you predict that Juan Carlos was normal, a carrier, or a hemophiliac?** Answer: Juan Carlos would be normal because Eugenia's son was his father and he was normal and his mother was also normal.

Princess Beatrice's Family Pedigree

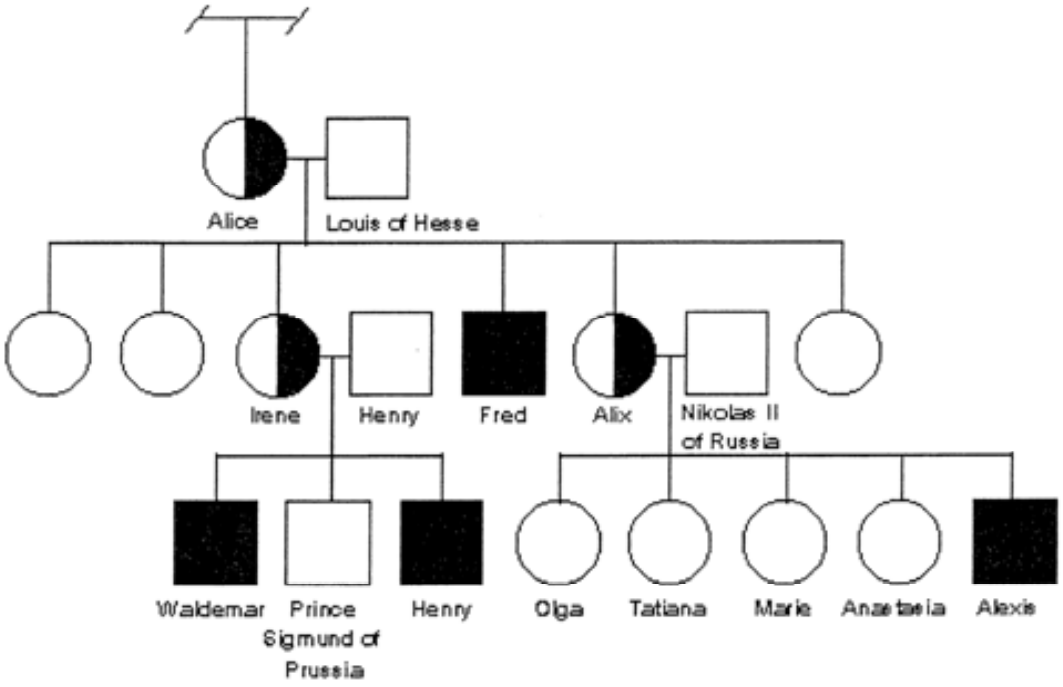


d) #3 The German and Russian Families

Queen Victoria's third child Alice passed hemophilia to the German and Russian imperial families. Of Alice's six children, three were afflicted with hemophilia. Her son **Frederick** died at a young age. Alice's daughter **Irene**, a carrier married her first cousin Prince Henry of Prussia, and gave birth to two hemophiliac sons. Alice's other daughter, **Alix**, was also a carrier. **Alix (Alexandra Feodorovna)** (b: 1872 – d: 1918) married Tsar Nikolas II (b: 1868 – d: 1918), and carried the disease into the Russian imperial family. (Alix was offered to marry Prince Albert Victor Duke of Clarence and Avondale (b: 1864 – d: 1892), brother of George V (b: 1865 – d: 1936). If she had done so this would have reintroduced hemophilia back into the British Royal Family!) Alexandra and Tsar Nikolas had four daughters, Olga, Tatiana, Marie, and Anastasia and one son the young Alexis, heir to the Russian Throne. Within a few months of his birth it was apparent that Alexis had hemophilia. Alexis' parents were so distressed about his condition that they turned to a spiritualist monk, Rasputin, who claimed he could help Alexis. Alexandra gave an unlimited amount of trust to Rasputin because she claimed he was the only one who could calm him and relieve his sufferings. All of these children, along with their parents, were eventually murdered during the Russian Revolution.

In 1995, a 63 year old man named **Eugene Romanov**, a resident of the former Soviet Union, turned up. He shared both the disease and the last name of the royal family of Czarist Russia. He proclaimed to be the grandson of Nikolas II's youngest daughter, Anastasia, whose body had never been recovered. Eugene Romanov claimed that Anastasia was raised by a farmer, and later she married a nephew of her adopted parents and had a daughter, Eugene's mother. a) **According to Eugene's argument, and the Romanov Pedigree, what was the likely hemophilic status of Eugene's mother and grandmother?** Answer: Eugene's grandmother, Anastasia, must have been a carrier who passed the afflicted X-chromosome on to Eugene's mother. Both were carriers. b) **What about his father and grandfather?** Answer: We can assume they were normal but we don't really know. They only pass a Y chromosome on to Eugene. c) **Is his argument plausible?** Answer: It could be.

The Romanov Pedigree



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