

THE QUEEN'S HEMOPHILIA

Don Steinert MA, RRT, MT



Hemophilia A has been called the "royal hemophilia" because of its prevalence in the royal families of Europe. England's Queen Victoria did not have hemophilia, although she carried the defective gene that causes hemophilia "A" on one of her X chromosomes. The problem arose when she passed the defective gene to two of her daughters-Alice, who transmitted the gene to the imperial families of Russia and Germany, and Beatrice, who passed the gene to the royal family of Spain-and to her son Prince Leopold, who died at age 31 from hemorrhages after a fall. Several of the queen's grandsons and great-grandsons died early in life because of excess bleeding or hemorrhages after surgery or accidents. The Jewish Talmud, which dates to about 400 B.C., decreed that boys whose older brother or male cousins had died from excessive bleeding after circumcision were exempt from this procedure.

Hemophilia A and hemophilia B both result from defects in blood coagulation-the cascade of reactions that causes blood to clot at the site of a wound. A series of proteins were identified that were involved in this cascade. The proteins were numbered in the order they were found; unfortunately, they did not react in the same order! As a result we now have a known reaction process that occurs "somewhat out of order"! A series of twelve primary proteins are found in the blood in an inactive state. When a break in the blood vessel occurs, factor twelve (contact factor) is activated. Activated factor twelve activates factor eleven, which can in turn activate factor nine and so forth down the cascade sequence. The actual order of protein activation is factor twelve, then factor eleven, factor nine, factor eight, factor ten, factor five, factor two and finally factor one. Did you noticed the sequence is out of order? You also probably noticed the total factors did not add up to twelve! This is because some minerals such as calcium and magnesium are necessary as well as factor seven which enters from a different

pathway which will not be discussed in this article.

The interesting thing about this cascade is that all the factors must be present and activated in the prescribed order for a blood clot to form. In the case of hemophilia A, factor eight is missing. This means that the blood clotting process starts just fine and cascades from factor twelve, to eleven, to nine, and then stops because factor eight is missing. The ultimate formation of thrombin (factor two) and fibrinogen (factor one) never takes place, and the patient bleeds. The same process is true of hemophilia B patients who are missing factor nine. The cascade stops at one point sooner than hemophilia A patients.

There are two major types of hemophilia. About 80 percent of patients are type A and 20 percent are type B hemophilia. Both types of hemophilia are caused by defective genes on the X chromosome, the human chromosome that is present in two copies in females and one copy in males. Most hemophiliacs are males because they only need one copy of the defective gene to have the disease. Hemophilia is much less common in females because they need two copies of the defective gene, one on each X chromosome, to have the disorder.

The red blood cells of hemophilia patients are often sickle in shape and cannot carry enough hemoglobin and therefore oxygen. These cells, because of their shape, get stuck in the microcirculation and cause pain for the patient.

The importance of this disease to respiratory therapists is to remember that these patients present with low hemoglobin and hematocrit as well as decrease red blood cell count, and increased activated partial thromboplastin time. The prothrombin time is not affected because it measures the "extrinsic pathway" that I did not talk about. Factors eight and nine, the hemophilia A and B factors, are in the longer pathway (intrinsic pathway) already covered. Respiratory Therapists generally see these patients for the first time in the emergency room when the disease is in active "crisis". The treatment is to administer oxygen and "Factor VIII concentrate" to the patient with hemophilia A, and oxygen and "Factor IX concentrate" to the patient with hemophilia B.

These patients spend a significant portion of their lives in and out of hospitals. Unfortunately, this disease still shortens life span and patients often die at an early age.

There are signs of hope however. With the age of genetic engineering came positive changes. The genes that encode factor VIII and factor IX have both been isolated, and each gene introduced into mammalian cells growing in culture. By this procedure, cell culture lines have been produced that synthesize large quantities of either factor VIII or factor IX. The clotting factors are now purified from these cells and used to prepare concentrates for use in transfusions. As a result, both clotting factors are available in abundant supply for treating these patients. The hope for the future is that techniques for gene replacement will be developed and will essentially cure this disease!

Don Steinert is an Associate Professor in the Department of Nursing and a faculty member in the Respiratory Therapy Program at the University of the District of Columbia.

This button might do more for the Respiratory profession than anything else!



2" metal

\$2.50

Outfit your entire staff with these friendly, professional and memorable (to patients and their families) buttons. Order directly from FOCUS by calling 800-661-5690 *(minimum order 5 buttons)