

Hemophilia

Hemophilia is the earliest known hereditary bleeding disorder. When injured, hemophiliacs tend to have a slow clotting (coagulation) process because of the lack of necessary blood factors (proteins). Consequently, those patients have prolonged bleeding after injury or surgery.

Hemophilia is clinically classified into two types: hemophilia A (classic hemophilia) associated with the deficiency of clotting factor VIII, and hemophilia B (also known as Christmas Disease) in which factor IX is affected. It is estimated that 1 in 5,000 to 10,000 males are born with hemophilia A worldwide accounting for 85% of global hemophilia cases. The remaining cases (15%) exhibit type B hemophilia at the rate of 1 in 20,000 to 34,500 males worldwide.

The amount of the clotting factor in the blood identifies the severity of both types of hemophilia. Patients with less than 1% level of the normal clotting factor have severe hemophilia. Unfortunately, most hemophiliacs (70%) have this severe form with serious complication of spontaneous bleeding into joints and muscles. In contrast, moderate hemophilia with rare bleeding events will result when the corresponding clotting factor is about 5% of the normal level.

Risk Factors

Mutations in the genes encoding for blood clotting factors VIII and IX result in hemophilia A and B, respectively. Both genes are located on the X chromosome which presents as two copies in females (XX) but one copy only in males (XY). Therefore, if a female has a mutation in one copy, she usually does not develop the disease, but becomes a silent carrier of the trait since the other copy of the gene compensates with a normal product. Having two defective copies of a gene is the only cause of hemophilia in females,

though it occurs rarely. On the other hand, males are more affected than females because they have only one copy of the X chromosome. Male patients do not transmit the disease to their sons because they are not responsible for transmitting the X chromosome, but rather the Y chromosome (responsible for male characteristics), but all their daughters will be carriers.

Diagnosis and Management

Patients with severe hemophilia are usually diagnosed after few months of birth due to serious bleeding problems. On the other hand, patients with the milder form of the disease may be diagnosed only when they accidentally have a severe injury.

Tests are widely available for hemophilia. Since both hemophilia types (A and B) cause the same complications but are treated differently, distinguishing the type of hemophilia via special blood test is extremely important in deciding a proper treatment regimen. This is because hemophilia A patients are treated with a supply of factor VIII, whereas type B hemophiliacs necessitate factor IX compensation.

Previously, treatment modalities in hemophilia involved pooling of plasma products from a very large number of donors, thus carrying the potential risk of transmitting infectious diseases, such as hepatitis and AIDS, through blood transfusion. Factors deficient in hemophilia A and B are now synthesized using new biotechnology methods which resulted in removing these risks of infection. Difficulties sometimes arise in some patients when the transfused clotting factor is recognized as a foreign substance and the immune system will try to fight it. Furthermore, managing irreversible joint damage and life-threatening hemorrhage may present a serious challenge for both healthcare providers and the patients.

It is recommended that people affected with hemophilia do specially monitored exercises on a daily basis to strengthen their muscles and joints, particularly the elbows, knees, and ankles, to prevent bleeding problems. Many recommended exercises include standard sports warm-up and training exercises such as stretching of the calves, ankle circles, elbow flexions, and quadriceps sets.

Hemophilia in Arab Populations

Although hemophilia is not as prevalent as other genetic blood disorders (G6PD deficiency, thalassemias, sickle cell disease) in most all Arab countries, it is the most prevalent form of inherited bleeding syndromes (IBS) in the region. In agreement with world data, hemophilia A accounts for the majority of Arab patients with IBS (Saudi Arabia 72%, Egypt 60%, Iraq 53%, Jordan 26%), whereas hemophilia B occurs less frequently (Egypt 20%, Iraq 8%, Jordan 7%, Saudi Arabia 4%).

A Disease that Shaped History

Although effective treatment has only become available in recent decades, hemophilia was recognized, though not named, in ancient times. The earliest written references to what appears to be hemophilia are encountered in the Babylonian Talmud of the second century CE. Rabbinical rulings exempted male boys from circumcision if two previous brothers had died of bleeding after the procedure. The Jewish physician Moses Maimonides (1135-1204) applied this ruling to the sons of a woman who had married twice, thus, apparently appreciating the maternal inheritance of the condition. However, the first medical professional to describe a disease was the Arabic physician Albucasis (1013-1106) who described families whose males died of bleeding after only minor injuries.

While many other such descriptive and practical references to the disease appear throughout historical writings, modern scientific analysis does not begin until 1803 when Dr. John Conrad Otto, a physician in Philadelphia, clearly appreciated the three cardinal features of hemophilia: an inherited tendency of males

to bleed. Yet, the first use of the word “hemophilia” appears in a description of the condition written in 1828 by Hopff, while he was a student at the University of Zurich. Hemophilia B was only distinguished from the more common type in 1952, and is often referred to as “Christmas disease” after the surname of the first child reported with this condition.

Hemophilia has often been called *The Royal Disease* because several members of noble families in Europe were affected by it. Queen Victoria (1819-1901), Queen of England from 1837 to 1901, was a carrier. Victoria bore nine children. The third, Alice (1843-1878), and the ninth, Beatrice (1857-1944), were carriers of the hemophilia gene. The eighth, Leopold (1853-1884), was a hemophiliac.

The condition transmitted through Alice and Beatrice to several royal families in Europe, including Spain, Germany, and Russia. Victoria's youngest daughter, Beatrice, passed the hemophilia gene on to her granddaughter, Victoria-Eugenie (1887-1969), who married King Alfonso XIII of Spain (1886-1941). Of the four sons she bore him, two had hemophilia and both died from minor car accidents.

Most fatefully, Victoria's second daughter, Alice, passed the gene on to two of her daughters, one of whom, Alexandra (1864-1918), married Czar Nicholas of Russia in 1894. Alexandra bore the Emperor four daughters before finally giving birth to a son and heir, Alexei, in 1904. The parents were ecstatic, but a short time later, they were devastated to learn that the boy was hemophiliac. Many times Alexei suffered extreme pain from internal bleeding that he would pass out, and several times he almost died.

The Empress was driven nearly insane trying to protect her son, and turned to the monk Grigori Rasputin (1869-1916) for comfort. It was claimed that Rasputin was successful at treating the Tsarevich's hemophilia. He used hypnosis to relieve Alexei's pain. The use of hypnosis not only relieved pain, but may have also helped slow or stop the boy's hemorrhages. Soon Rasputin was giving Alexandra advice not only on her son, but on the way the country should be run. The illness of the heir to the Tsar's throne and the strain it placed on the Royal family combined with Alexandra's German blood and the power wielded by the monk Rasputin were all factors leading to the Russian Bolshevik Revolution of 1917 changing the course of history.