BORN IN THE BLOOD

People with the inherited bleeding disorder haemophilia lack factors that cause the blood to clot. The disease affects thousands of people around the world and has even played a part in historic events. By Neil Savage.

COAGULATION CASCADE

When damage occurs to blood vessels, exposure of the blood to collagen in the cell walls and material released by the cells triggers the activation of clotting factors. One factor activates the next factor in a series of events (some not depicted here) that eventually produces fibrin. Fibrin forms a mesh to hold together a plug of platelets to form a clot (platelets are a type of cell that circulates in the blood to help coagulation)¹.

MISSING FACTOR IX = HAEMOPHILIA B

About 20% of cases².

**AT LEAST 172,000
PEOPLE WORLDWIDE
HAVE HAEMOPHILIA**

MISSING FACTOR VIII = HAEMOPHILIA A

About 80% of cases².

OF ALL THE PEOPLE WITH HAEMOPHILIA...

60%

Have severe haemophilia (clotting factor in the blood is less than 1% of the level in normal, healthy people)³. Bleeding after injury, spontaneous bleeding, risk of joint damage. Median age at diagnosis is one month.

25%

Have mild haemophilia (clotting factor levels of 6–30%)³. Bleeding only after serious injury, accidents or surgery. Heavy menstrual bleeding in women. Median age at diagnosis is 36 months, though it is often not diagnosed until after a serious injury.

15%

Have moderate haemophilia (clotting factor levels of 1–5%)³. Bleeding after injury, some spontaneous bleeding, risk of joint damage. Median age at diagnosis is eight months.

TREATMENT TIMELINE

About two-thirds of the world's population lacks access to prophylaxis with clotting factors because the cost of treatment is too high.

1840

1840s

First blood transfusions for bleeding episodes.

THE ROYAL DISEASE

Queen Victoria became a carrier of haemophilia through what is believed to have been a spontaneous genetic mutation⁴.

Queen Victoria
1819–1901

Prince Albert
1819–1861

Victoria passed it on to one son, who died of bleeding, and two daughters.

Haemophilia spread throughout European royalty, including Victoria's great-grandson, Alexei Romanov, son of the last Russian tsar, Nicholas II.

The 'mad monk' Rasputin claimed to be able to treat Alexei's haemophilia, and his influence with the tsar's family is credited with contributing to the Russian revolution.

In 2009, DNA tests on Alexei's remains showed that Victoria carried haemophilia B.

Alexandra
1872–1918

Alexei
1904–1918

Nicholas II
of Russia

INHERITANCE PATTERN

The mutations causing haemophilia are carried on the X chromosome. Women are usually carriers, with a 50% chance of having sons with haemophilia or daughters who are carriers. Men with haemophilia will have no sons who are haemophiliacs, but all their daughters will carry the gene. In rare cases, female carriers or girls with both X chromosomes affected will have haemophilia; fewer than 10% of cases occur in females. Approximately one-third of cases arise from spontaneous mutation⁵.

An estimated 40,000 haemophiliacs worldwide were infected with HIV, including 70–90% of those with severe haemophilia⁶.

40,000

The cost of prophylaxis treatment could reach \$300,000 per child per year⁷.

\$300,000

1900

1923

First use of plasma replacement therapy

1950s–1960
Fresh frozen plasma requires large volume transfusions

Mid-1960s
Cryoprecipitate (a concentrate of blood components made from frozen plasma) allows smaller transfusions

1970
Freeze-dried clotting factors allow home-based prophylaxis

1970s–early 1980s
Haemophiliacs contract hepatitis and HIV from blood products

1989
Genetically engineered factor VIII, no risk of HIV or hepatitis

1987
Heat-treated factor VIII reduces risk of blood-borne pathogens

2000

1997
Genetically engineered factor IX

Future
Gene therapy

2014
First extended-life clotting factors approved

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