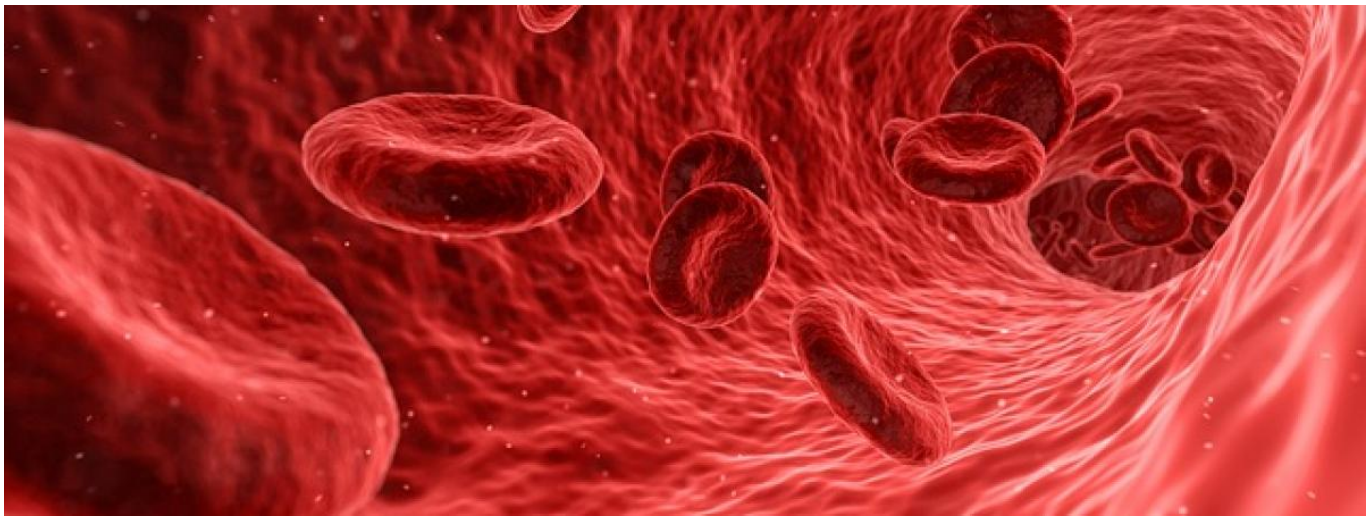
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In haemophilia, the blood doesn't clot properly. Blood transfusions can help but one Oxford scientist, Professor George Brownlee, discovered a much safer treatment - a drug so important that it is listed on the World Health Organization List of Essential Medicines. In an exclusive interview, Professor Brownlee reveals how he came up with the pioneering treatment.

Professor Brownlee gained his PhD in Natural Sciences from Cambridge in 1967. His supervisor had been Dr Frederick Sanger [7], the biochemist who won the Nobel Prize twice.

Inspired by his hard working, supportive mentor, Professor Brownlee became interested in genetics, studying the structure of the influenza virus. His work on haemophilia B began when he was appointed Chair of the Sir William Dunn School of Pathology [8] in 1980 (the place where penicillin was developed). Professor Brownlee explained that he chose to focus on haemophilia B because he was keen to discover the genetic basis of this disease, knowing that to do so could revolutionise its treatment.

I asked him a few questions.

What is haemophilia B?

"Haemophilia B is a rare inherited bleeding disorder. For blood to clot [9], bodily injury activates a number of different proteins (called clotting factors) that kick-start a chain reaction in the blood, culminating in the formation of a clot.

In haemophilia B, there's inadequate production of a clotting factor called Factor IX (9). The disease occurs in about 1 in 30,000 males in the United Kingdom. Females are not affected. Before modern treatment haemophilia was life-threatening. Patients were often wheelchair bound from a young age because of bleeding into joints causing mobility problems."

Before modern treatment haemophilia was life-threatening.

What is the difference between haemophilia A & B?

“Both are blood clotting disorders and both are inherited. Different clotting factors are deficient in haemophilia A and B. In haemophilia A [10], there is a shortage of Factor VIII (8); it’s about 5 times more common than haemophilia B.”

Why is haemophilia B called the Christmas disease and the Royal disease?

“Stephen Christmas was the first patient in whom haemophilia B was recognized, in 1952. This defined two forms of haemophilia - now called haemophilia A and B.

It has been called the Royal disease because it occurred in the English Royal family. Queen Victoria was a carrier of haemophilia, although she did not know it until she had an affected son Leopold. She passed on the disease through her daughters, Beatrice and Alice, to the Spanish and Russian Royal families.

The defect was finally discovered in 2009 by genetic studies of DNA of Victoria’s granddaughter, Tsarina Alexandra, and her affected son Alexis and youngest daughter Anastasia (killed by the Bolsheviks in the Russian revolution of 1918). DNA testing of their exhumed bones showed that a single genetic defect in the Factor IX gene caused the disease.”

What did you and your team discover?

“My Oxford team managed to clone the Factor IX gene in 1981-2. We then introduced cloned Factor IX DNA into rat cells, causing them to produce human Factor IX, which, to our delight, was biologically active (and so would work to help clotting when given to humans).

We also carried out research on why a small number of haemophilia B patients amazingly recovered from the disease at puberty (the so called ‘Leyden patients’). To my knowledge, this is the only example of a genetic disease which can show spontaneous recovery (other examples of genetic diseases include cystic fibrosis and Huntington’s disease).”

A life-saving treatment

A large-scale method for manufacturing Factor IX was established in the US and became available just before the millennium. It is now the medicine of choice [11] to treat most haemophilia B patients. It carries no risk of contamination by viruses such as HIV [12] or hepatitis viruses. This had formerly been a serious problem as pooled blood from blood donors had been the only treatment.

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Professor Brownlee returned to his earlier interest in influenza, working with Professor Ervin Fodor resulting, among other discoveries, in improved vaccines for children. He wrote a book [13] on the life of Frederick Sanger, and he is currently sorting through his laboratory notes and papers to donate to the Bodleian Library in Oxford.

Oh, and he’s also writing a book on rare snowdrops. Intricate beauty seems to be a recurring theme in his career, whether it’s in DNA, protein structure or indeed in tiny flowers.

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