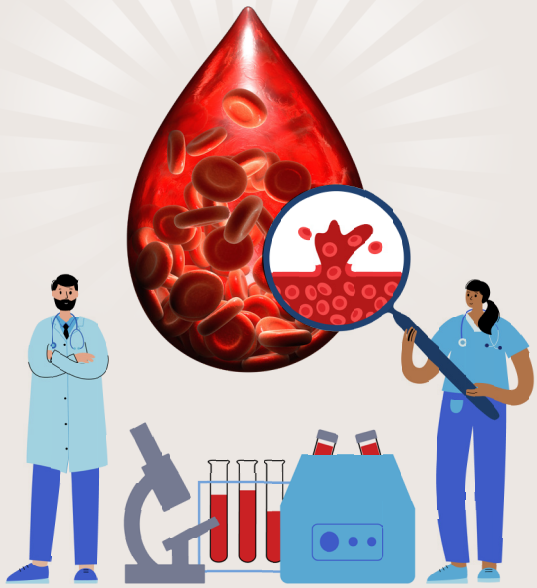


The Journey of Haemophilia

World Haemophilia Day:
A Day to Celebrate Progress

Xiaofu (1973–1996) was born in Hong Kong with severe haemophilia, a condition that prevented his blood from clotting properly. This makes even the smallest injury a life-threatening event for him. Yet, he longed to run, jump and play like other children. And he ran and played, chasing after a childhood he was never meant to have; only to find himself back in the hospital again and again. Through it all, his mother stood by him; helping with his injections of clotting factors and fighting alongside him.

As Xiaofu grew, so did his dreams. He managed to get into university and became a gifted writer. He chased after a future that finally seemed within reach. But fate dealt a cruel blow. The very treatment that had kept him alive was tainted. Xiaofu had unknowingly received contaminated blood products and was now infected with HIV. In an era when a HIV diagnosis was literally a death sentence, his life became a countdown.

But Xiaofu did not surrender. With time running out, he turned his pain and suffering into poetry and stories. His final masterpiece, *Boundless Sky,* became his defiance against fate - a voice that would live on beyond himself. The book told the life stories of Xiaofu and a group of fellow haemophilia patients, showcasing their struggles and perseverance, while revealing their genuine bonds of love and friendship. And when Xiaofu was gone, his mother wrote a book about her son's battle with HIV. In 2001, this was adapted into the film *Forever and Ever.*

WHAT IS HAEMOPHILIA?

Haemophilia, a rare and complex genetic disorder, has long been a daunting challenge for patients, their families and the medical community. The annual observance of World Haemophilia Day on 17 April every year serves as a poignant reminder of the remarkable strides made in understanding and managing this condition.

When you get a cut or injury, your body has a system in place to stop the bleeding and heal the wound. Three main things work together to form a blood clot:

- **Blood Vessels:** When you get injured, the blood vessels around the wound tighten to slow down the bleeding. They also expose special parts inside the blood vessels that help with clotting.

- **Platelets:** These are tiny cells in your blood that act like little "plugs." When you get hurt, platelets stick to the injury site and form a temporary plug to stop the bleeding.

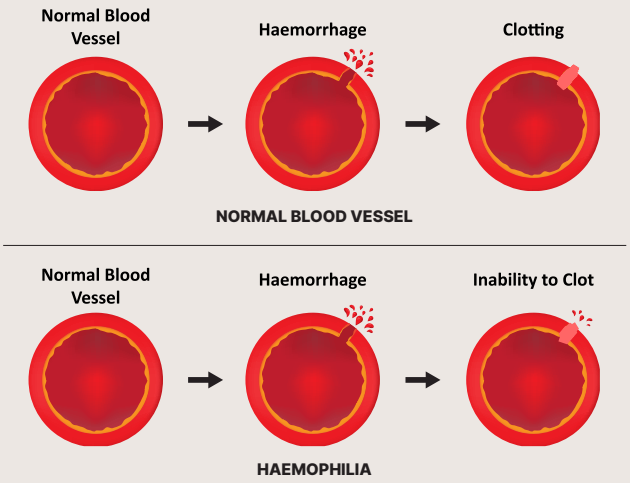
- **Coagulation factors:** These are special proteins in your blood that work like a chain reaction. They are always ready to go, but only become active when you get hurt. These proteins work together to turn another protein (fibrinogen) into a sticky substance called fibrin. Fibrin forms a mesh over the platelets, creating a strong and stable blood clot that fully stops the bleeding. These protein factors are differentiated using Roman numerals.

TYPES OF HAEMOPHILIA

Haemophilia A results from a factor VIII deficiency, while haemophilia B is caused by a factor IX deficiency. Both are inherited bleeding disorders. Haemophilia is linked to the X chromosome. Since men have only one X chromosome, they are more likely to be affected. Women have two X chromosomes, so they need both X chromosomes to carry the mutated gene to have haemophilia.

If a woman has only one mutated X chromosome, she is considered a carrier. Female carriers of haemophilia have one normal gene and one mutated gene, typically resulting in about 50% of normal clotting factor levels, which is usually enough to prevent excessive bleeding. However, some carriers experience symptoms similar to males with mild haemophilia. In such cases, their treatment is similar to that of males with mild haemophilia.

Haemophilia A (1 in 5,000 live male births) is more prevalent than haemophilia B (1 in 30,000 live male births). According to the World Federation of Haemophilia (WFH) report in 2023, the number of people in Singapore living with haemophilia was estimated to be 592, but only 280 were reported.



SYMPTOMS AND LONG-TERM PROBLEMS

Most babies with severe haemophilia will show first signs of bleeding in the first 18 months of life. These can include easy bruising, bleeding into joints (haemarthrosis), bleeding after injury to the mouth, or bleeding after medical procedures. In newborns, bleeding commonly occurs in the central nervous system, head (cephalohaematoma), and at sites of medical interventions like circumcision, heel sticks or intravenous cannula insertions. As children begin to crawl, bruising and bleeding into joints and muscles become more frequent. In older children and adults, bleeding typically affects the joints, muscles, central nervous system, the mouth, urinary tract and gastrointestinal tract.

Serious long-term problems can include brain damage after bleeding in the brain, and joint damage from repeated bleeding into joints. This joint damage can lead to joint destruction, weakened muscles, chronic pain, stiff joints and ultimately, disability. Nerve damage can also occur due to pressure buildup in the muscles (compartment syndrome) during bleeding episodes. Finally, bone weakening and a higher risk of fractures can also happen.

MANAGEMENT

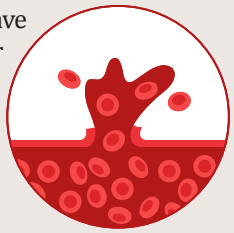
Managing haemophilia effectively is a complex undertaking which requires a multidisciplinary approach. Integrated care should be instituted as soon as the diagnosis of haemophilia is made. Counselling and guidance on psychosocial challenges and genetic inheritance should also be instituted. It is crucial for families and caregivers, especially those with newborns recently diagnosed with haemophilia, to receive proper education about the condition.

It is essential to focus on clinical management of acute bleeding episodes (on demand treatment), and prevention of complications from these bleeding episodes. Preventive (prophylactic) therapy, which involves administering clotting factors even without active bleeding, is highly effective in reducing both bleeding episodes and long-term complications like chronic joint damage. It also lowers the risk of bleeding in the brain. Preventing bleeds (prophylaxis) with clotting factor replacement in haemophilia comes with considerable costs and difficulties. These include the frequent need for intravenous access, potentially requiring a central venous catheter which carries risks of infection and blood clots. Regular intravenous infusions are necessary, impacting daily routines and family life.

The overall cost of this treatment is another major factor as clotting factors are expensive. Many individuals who could benefit from prophylaxis may not have access to factor infusions due to the high costs and/or limited resources. With the increased use of factor replacement, life expectancy for people with haemophilia has improved over time. In resource rich areas, their life expectancy now closely matches that of the general population.

Clotting factors can come from either donated blood products or be produced through recombinant (genetically engineered) technology. A significant number of people with haemophilia contracted HIV and hepatitis C through factor infusions before donated blood was routinely screened for these viruses and before plasma-derived factor products underwent pathogen inactivation. Serologic testing for HIV in blood products was not introduced until the mid-1980s, and the first recombinant products were not introduced until the 1990s. HIV infection was first reported in a person with haemophilia in 1982. Haemophiliacs born in the 1970s to early 1990s were estimated to be the most affected by HIV and AIDS as depicted in the story of Xiaofu.

In recent years, gene and cell therapy have made headlines as promising treatments for haemophilia. These cutting-edge approaches aim to correct the underlying genetic defects that cause haemophilia, potentially offering a cure or long-term disease management.



CONCLUSION

This year, the global bleeding disorders community unites once again to celebrate World Haemophilia Day, expanding the recognition of medical milestones beyond haemophilia to include all bleeding disorders. The theme for this year, "Access for All: Women and Girls Bleed Too," highlights an urgent and often overlooked issue.

Despite advancements in care, women and girls with bleeding disorders (WGBDs) remain underdiagnosed and underserved. It is time for change. As a global community, we have the power and the responsibility to ensure they receive the recognition, diagnosis, treatment, and care they deserve. By doing so, we not only transform lives, but also strengthen the entire bleeding disorders community - creating a future where access to care is truly for all. PRIME

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