What is haemophilia A?

Haemophilia is an inherited, **serious bleeding disorder** where a person's **blood does not clot properly**, leading to uncontrolled bleeding, which can occur spontaneously or after minor trauma.

It can **significantly reduce the quality of life** of people affected, as well as their family, friends and caregivers.[1]

Haemophilia A is the most common form – affecting

900,000

people worldwide[2,3]

What happens in the blood of a person with haemophilia A?

In a healthy person, proteins called **clotting factors** work together to form a blood clot and help stop bleeding.

People with haemophilia A either **lack or do not have enough** of a clotting factor called **factor VIII**, which leads to their blood not being able to clot properly.

Mild

~48% of those with haemophilia A[4]

Occurs when someone has between **5-40%** of the normal amount of **clotting factor**.[5]

Usually becomes apparent after a **wound or medical procedure**.[6]

Women may also have **problems controlling bleeding** associated with **menstruation or childbirth**.[6]

Moderate

~14% of those with haemophilia A[4]

Symptoms are **similar to mild haemophilia A**, but can also cause:[7]

Occurs when someone has between **1-5%** of the normal amount of **clotting factor**.[5]

Bruising

Bleeding into muscles and joints, which if not treated can lead to long-term pain, swelling and stiffness

Severe

~30% of those with haemophilia A[4]

Occurs when someone has less than **1%** of the normal amount of **clotting factor**.[5]

Potentially **life-threatening and joint bleeding** is more frequent and severe.[7]

People with **severe haemophilia A also experience spontaneous bleeding**.[7]

However, the severity of haemophilia A is not always reflective of bleeding behaviour. While the treatment and management of severe haemophilia A are well-established, there is less information available on the burden of moderate and mild haemophilia A.[8]

The goal for management of haemophilia A should be to eliminate all preventable bleeds regardless of disease severity.

There are many types of haemophilia treatment:

Prophylaxis

Prophylaxis is a preventative, regular treatment involving either factor VIII replacement therapies or non-factor therapies, with the goal to **prevent bleeds** and allow people with haemophilia to **lead active lives and achieve quality of life** comparable to non-haemophilic individuals.[1] It is the **standard of care** for people with severe haemophilia A and some people with moderate haemophilia.[2]

Prophylaxis treatment can be administered intravenously or subcutaneously.[2] Treatment with non-factor therapies can be administered at home **as infrequently as once every two or four weeks**. This makes it easier for people with haemophilia to stick to their treatment, and to live relatively normal lives.[2]

Episodic factor VIII replacement

Episodic factor VIII replacement therapy can be **taken on-demand** (as needed, to treat bleeds) when prophylaxis is not feasible.

It needs to be administered intravenously[2] by the patient or a caregiver.

Finding a vein for medicine infusion during intravenous administration can be difficult for some, especially children.[9]

Treating inhibitors: ITI and bypassing agents

Around one in four...

25-30%

people with severe haemophilia A

and one in 20...

5-10%

people with mild to moderate haemophilia A

... develop inhibitors to factor VIII replacement therapies, respectively.[10]

Inhibitors are antibodies that attack and destroy the replaced factor VIII, because it is recognised as 'foreign'.[11]
As a serious complication of treatment,[12] **many people with haemophilia A live in fear of developing inhibitors.**

People with haemophilia A with inhibitors can be **treated with non-factor therapy prophylaxis.**[2] When non-factor therapy prophylaxis is not available, or for breakthrough bleeds (bleeds which occur during prophylaxis), **treatment infusions of factor VIII replacement** may be needed, as well as a trial of **'immune tolerance induction' (ITI)**, where the patient is given very high doses of factor VIII over a long period of time.[2]

ITI can take many years, is very costly and is ineffective in

~30%

of people.[13,14]

'Bypassing agents' are another treatment option for people with inhibitors, often used after ITI fails. However, these are short-acting, need to be taken often, and give variable bleeding control.[15]

References

1. Flood E, et al. Illustrating the impact of mild/moderate and severe haemophilia on health-related quality of life: hypothesised conceptual models. European Journal of Haematology 2014; 93: Suppl. 75, 9–16.
2. Srivastava, A, Santagostino, E, Dougall, A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020; 26 (Suppl 6): 1-158.
3. Iorio A et al. Establishing the Prevalence and Prevalence at Birth of Hemophilia in Males. Ann Intern Med 2019 Oct 15;171(8):540-546.
4. World Federation of Hemophilia. Report on the annual global survey 2020. [Internet; cited 2022 February].Available from: http://www1.wfh.org/publications/files/pdf-2245.pdf
5. White GC, et al. Definitions in hemophilia. Recommendation of the scientific subcommittee on factor VIII and factor IX of the scientific and standardization committee of the International Society on Thrombosis and Haemostasis. Thromb Haemost. 2001 Mar;85(3):560.
6. Haemophilia Foundation Australia. Living with mild haemophilia. [Internet; cited 2022 February].Available from: https://www.haemophilia.org.au/HFA/media/Documents/Haemophilia/Mild%20haemophilia/Understanding-mild-haemophilia.pdf
7. NHS. Symptoms of haemophilia [Internet; cited 2022 February]. Available from: https://www.nhs.uk/conditions/haemophilia/symptoms/
8. Walsh C et al. Identified unmet needs and proposed solutions in mild-to-moderate haemophilia. A summary of opinions from a roundtable of haemophilia experts. Haemophilia. 2021 February 01; 27(1):125-32.
9. Ljung R. The risk associated with indwelling catheters in children with haemophilia. British Journal of Haematology 2007; 138: 580–586.
10. Gomez K, et al. Key issues in inhibitor management in patients with haemophilia. Blood Transfus. 2014; 12: s319–s329.
11. Wheatall SF, et al. Distinct characteristics of antibody responses against factor VIII in healthy individuals and in different cohorts of hemophilia A patients. Blood 2013; 121: 1039–48.
12. Astermark J. Overview of Inhibitors. Semin Hematol 2006; 43 (suppl 4):S3-S7.
13. Rocino A, et al. Immune tolerance induction in patients with haemophilia a and inhibitors: effectiveness and cost analysis in an European Cohort (The ITER Study). Haemophilia 2015; 10.
14. Marcucci ME, et al. US immune tolerance induction in haemophilia. Clinical Investigation. 2015; 5(3), 331–335.
15. Berntorp, E. Differential response to bypassing agents complicates treatment in patients with haemophilia and inhibitors. Haemophilia. 2009; 15: 3-10.

M-XI-00004042