Understanding haemophilia

CHAPTER 2

KEY POINTS

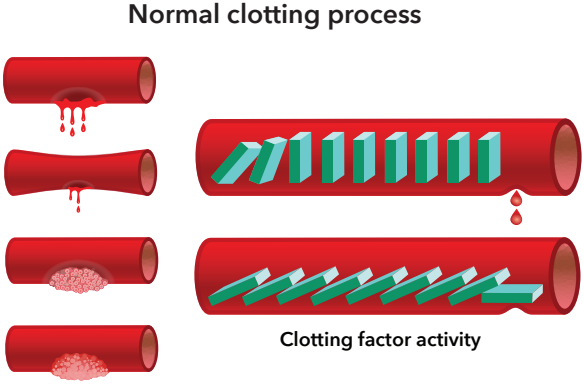
- Haemophilia is an inherited condition caused by a gene alteration.
- There are two types of haemophilia – A and B.
- Haemophilia can be mild, moderate or severe.
- Haemophilia is most commonly diagnosed in boys.
- If you are considering having more children, there is support available to help with your decision.

Haemophilia is an inherited bleeding disorder where blood doesn't clot properly. It is caused when blood does not produce enough of one of the essential clotting ingredients.

These 'ingredients' are clotting factors – proteins in the blood that control bleeding. The missing ingredient that causes haemophilia is usually either factor VIII (8) or IX (9). Roman numerals are used when referring to clotting factors.

Blood clotting and bleeding

Understanding how bleeding starts and stops



Source: Hemophilia in Pictures. © WFH 2005. http://www1.wfh.org/publications/files/pdf-1311.pdf

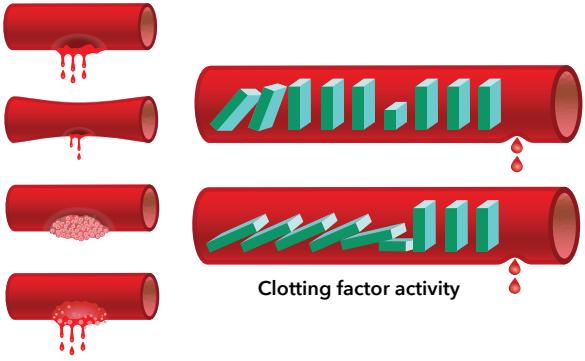
Bleeding starts when a **capillary** (small blood vessel) is injured and blood leaks out.

When this happens, the capillary tightens up to slow the bleeding and blood cells called **platelets** make a plug to patch the hole.

For people without haemophilia, the many **clotting factors** in **plasma** (part of the blood) knit together to make a clot over the plug. This makes the plug stronger and stops the bleeding.

Clotting factor VIII and factor IX are essential to making the blood clot.

Clotting in haemophilia



Source: Hemophilia in Pictures. © WFH 2005. http://www1.wfh.org/publications/files/pdf-1311.pdf

For people with haemophilia, one clotting factor is missing, or the level of that factor is low.

This makes it difficult for the blood clot to form and stay formed, so bleeding continues for a longer period of time. Bleeding does not happen any faster than for someone without haemophilia.

People with haemophilia may experience 'rebleeding' at the site of an injury after the initial bleeding has stopped. This is typical of the bleeding associated with haemophilia.

One aspect of haemophilia treatment involves injecting the missing factor so blood can clot normally. This is called 'factor replacement therapy'.

A person with haemophilia does not bleed any faster than a person without haemophilia, but the bleeding continues for longer if it is not treated.

There is a myth that people with haemophilia bleed to death from a cut. This is NOT true.

Internal bleeding (often referred to as a 'bleed') is the biggest problem for people with haemophilia. Prompt treatment will, however, reduce most problems associated with bleeding.

see Chapter 3 for more information on bleeds and Chapter 4 for more information on treatment.

Types of haemophilia

There are two types of haemophilia, however both have the same symptoms.

- **Haemophilia A** (also called classical haemophilia) is the most common form and is caused by low levels of clotting factor VIII (8).
- **Haemophilia B** (sometimes called Christmas disease) is caused by low levels of clotting factor IX (9).

Haemophilia A is five times more common than haemophilia B.

Severity of haemophilia

Your child may have mild, moderate or severe haemophilia. The severity of haemophilia depends on the amount of clotting factor in their blood.

PARENT TIP

By understanding the severity of your child's haemophilia and their pattern of bleeding over time, you will know what is likely to cause bleeds, how they will affect your child and how best to help them.

The physical effects that your child may experience will depend on whether they have mild, moderate or severe haemophilia. Effects vary from child to child and can even vary between siblings with haemophilia of the same severity. With regular treatment, bleeding episodes can be kept to a minimum.

The 'Severity of haemophilia' table provides a guide to the symptoms of mild, moderate and severe haemophilia.

Severity of haemophilia

The normal level of factor VIII or IX in a person's blood is between 50% and 150%

Severity and factor level	What to expect
Mild haemophilia 5% – 40% of normal clotting factor level	• Usually only bleeding problems following a bad injury, having teeth taken out, surgery or medical procedures that pierce the skin. • Might never have a bleeding problem requiring medical attention. • Might not be diagnosed until later in life if not playing contact sports and have not had any injuries or operations. • Females might have bleeding problems with periods (menstruation) or childbirth.
Moderate haemophilia 1% – 5% of normal clotting factor level	• Might have bleeding problems with minor injuries, such as sporting injuries. • Likely to have bleeding problems after having teeth taken out, surgery, medical procedures and/or a bad injury. • Occasionally have a bleeding episode for no obvious reason ('spontaneous bleeds').
Severe haemophilia Less than 1% of normal clotting factor level	• Often have bleeds into joints, muscles and soft tissues. • Can have bleeding episodes for no obvious reason ('spontaneous bleeds') as well as after surgery, dental work or injuries including minor bumps and knocks.

Please note: this table is a guide only.

Can factor levels change over time?

If a child is born with severe haemophilia, they are likely to have severe haemophilia over their lifetime. The factor levels of people with mild haemophilia can fluctuate over time because their factor levels can be affected by things such as stress, infection or surgery, but generally their levels will remain in the range for mild haemophilia (5-40% of normal clotting factor level).

All babies are born with low levels of some factors, e.g. factor II (2), VII (7), IX (9) and X (10) that gradually increase over the first 6 months of life. If your child has been tested at birth and shows lower levels of factor IX than normal, their factor levels will be retested at 6 to 12 months of age for a more accurate result.

In most cases, families with a history of haemophilia tend to have similar clotting factor levels among the males in their family.

However, the factor levels in females who carry the gene are unpredictable and can vary between female family members. A family with a history of severe haemophilia among the males may have one daughter with mild haemophilia and another daughter who carries the gene but has no bleeding symptoms.

Other bleeding disorders

Haemophilia is just one type of inherited bleeding disorder. There are a number of other inherited bleeding disorders including Von Willebrand disease, rare clotting factor deficiencies and inherited platelet disorders.

Von Willebrand disease (VWD)

Von Willebrand disease (VWD) is the most common inherited bleeding disorder worldwide. Bleeding in people with VWD usually involves the mucous membranes, the delicate tissues that line body passages such as the nose, mouth, uterus, vagina, stomach and intestines. Many people with VWD have bleeding symptoms that are mild, such as bruising easily, nosebleeds, heavy periods, or prolonged bleeding after surgery. However, some have moderate or severe VWD. The symptoms of severe VWD are similar to severe haemophilia, with bleeding into the muscles and joints. With all forms of VWD and levels of severity there can be bleeding problems.

Rare clotting factor deficiencies and platelet disorders

There are other bleeding disorders caused when the body does not produce enough of a specific certain clotting factor, or when the factor does not work properly. These disorders are known as rare clotting factor deficiencies and are very uncommon.

Rare clotting factor deficiencies include factor I (1), II (2), V (5), VII (7), X (10), XI (11), or XIII (13) deficiencies and combined factor V (5) and factor VIII (8) deficiency.

In platelet function disorders, the platelet plug does not form properly, leading to a tendency to bleed for longer than normal or bruise easily. Since platelets have many roles in blood clotting, platelet function disorders can range from mild to severe. Examples of inherited platelet function disorders include Glanzmann thrombasthenia and Bernard-Soulier syndrome.

Parents who have children with these types of bleeding disorders may have similar experiences to parents of children with haemophilia.

For more information about VWD and other rare clotting factor deficiencies and platelet disorders, contact Haemophilia Foundation Australia or visit www.haemophilia.org.au

Understanding how children inherit haemophilia

Haemophilia is an inherited condition and occurs in families. It is caused by a mutation (change or alteration) in the factor VIII or IX gene.

How did my child get haemophilia?

Every person has millions of cells that make up their body. At the centre of each cell are 46 chromosomes arranged in pairs. The chromosomes contain the person's genetic information or 'genes', which determine the person's individual characteristics, such as the colour of their hair or their eyes.

Everyone has the genes responsible for making factor VIII and factor IX. These factors are necessary for blood to clot.

Haemophilia is caused by a mutation (change or alteration) in the factor VIII or IX gene. This altered factor VIII or IX gene affects the way that that the factor VIII or IX is made so that it might be missing or not enough is made for blood to clot properly. It is often called the 'haemophilia gene'.

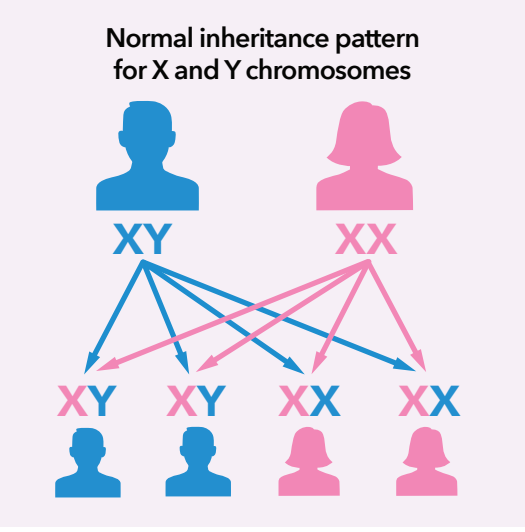
Gene mutation is a normal part of nature. There are many gene alterations that lead to haemophilia, though families inherit the same gene alteration. The specific type of gene alteration also affects the symptoms that people with haemophilia experience.

In families with a history of haemophilia, the gene alteration occurred at some point in previous generations. It is then passed on from parent to child through the generations. Examining the family tree may help to identify where this change occurred.

What if there is no obvious family history of haemophilia?

Around one third of children born with haemophilia do not have an obvious family history of the disorder.

In these cases, the gene alteration may have occurred in a recent generation during reproduction. It may be appearing for the first time in this family in the child or in the child's mother – or sometimes the child's grandmother. The altered gene may have been passed down the current generations from mother to child, without anyone realising until the child was diagnosed with haemophilia.



Haemophilia and the X chromosome

Everyone has a pair of 'sex' chromosomes that determine their sex. Each parent contributes one of these chromosomes to their children.

Females always have two X chromosomes (XX pair): one X chromosome is inherited from each parent. Males have one X chromosome, which they inherit from their mother, and one Y chromosome, which they inherit from their father (XY pair).

For every child any couple has, there are four possible combinations of chromosomes. These are shown in the 'Normal inheritance pattern' diagram.

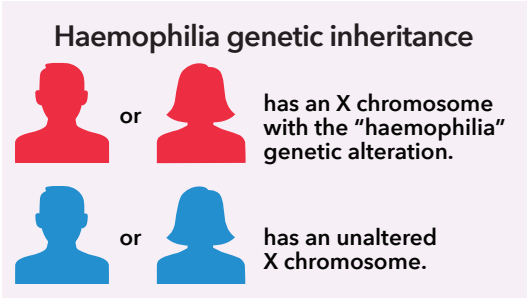
The genes for making factor VIII or IX are located on the X chromosome. An X chromosome with the altered gene causing haemophilia can be passed from parent to child.

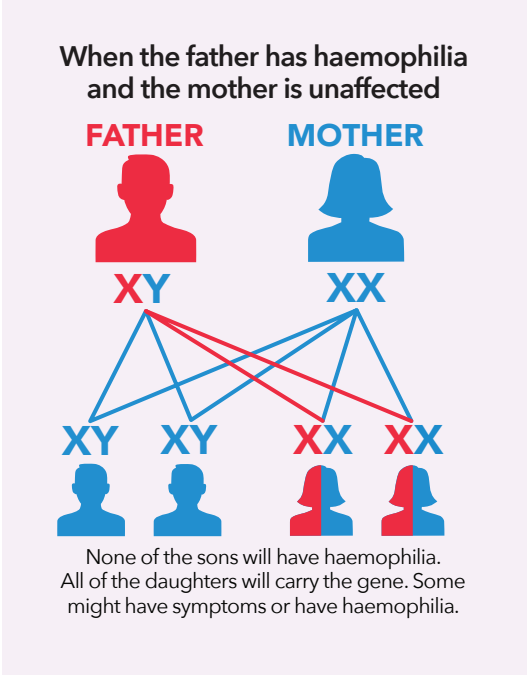
Father with haemophilia

A male with haemophilia carries the altered gene on their X chromosome.

As fathers only pass on the Y chromosome to their sons, none of the sons of a man with haemophilia will inherit the condition.

However, fathers pass on the X chromosome to their daughters. If their father has haemophilia, all of his daughters will inherit the altered gene from him and will carry the gene causing haemophilia. When putting together a family history of haemophilia, daughters whose father has haemophilia are described as 'obligate carriers' as they will always inherit the gene from their father.

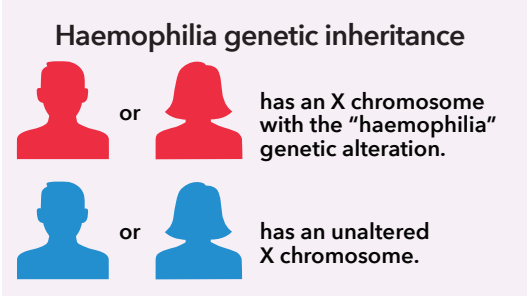


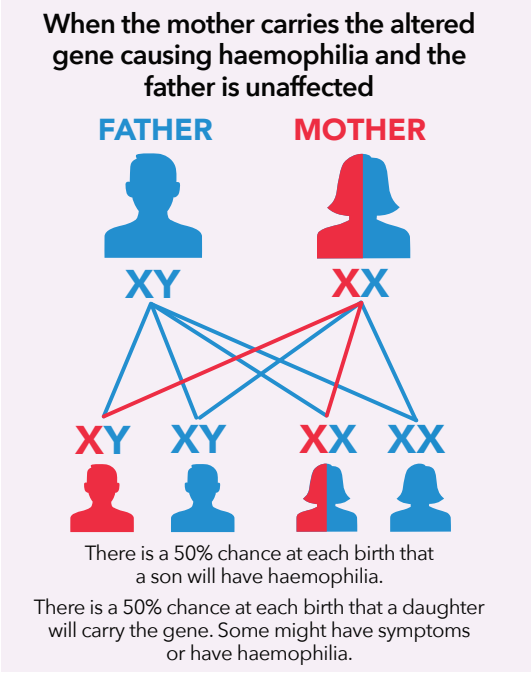


Mother who carries the gene

Mothers pass on one of their X chromosomes to their children.

If the gene alteration responsible for haemophilia is located on one of the mother's X chromosomes, there is a 50 per cent chance at each birth that any of her children will inherit this gene alteration.





If her sons inherit the gene alteration they will have haemophilia.

If her daughters inherit the gene alteration they will carry the gene. Some girls will have normal factor levels and will not have bleeding symptoms. Other girls will have low factor levels and will have haemophilia.

Will my child's children have haemophilia too?

Once haemophilia appears in a family, the altered gene is passed from parents to children through the generations following the inheritance pattern explained in the 'Haemophilia Genetic Inheritance' diagrams.

Sometimes it can seem like haemophilia has skipped a generation. If sons in one generation have not inherited haemophilia, but some or all of the daughters carry the gene, and some of their children have haemophilia, it may seem that haemophilia has skipped a generation.

Haemophilia in girls

While most people diagnosed with haemophilia are male, some females do have haemophilia or bleeding symptoms. Most females with haemophilia have mild haemophilia, but a small number have moderate or severe haemophilia. There are also some females who have factor levels at the lower range of normal but who nevertheless experience abnormal bleeding.

Most females who have one haemophilia X chromosome and carry the gene do not have haemophilia. This is because they have a second X chromosome to generate enough clotting factor in their blood. Some females do, however, have bleeding symptoms from haemophilia, such as heavy periods, easy bruising, poor healing, prolonged bleeding after childbirth and bleeding following surgery, medical or dental procedures or trauma.

In rare cases, they may have moderate or severe haemophilia and also have bleeding into their joints and muscles.

It is recommended that all girls and women in a family with haemophilia visit the Haemophilia Treatment Centre (HTC) at least once to have their factor levels tested and discuss their individual issues. If they have low levels and there is a risk of bleeding, a treatment plan will be needed. This is particularly important to do before a young girl starts menstruating or before surgery or dental work. If you or your daughters are not already patients with the HTC, speak to your family doctor so that they can arrange a referral to a haematologist at the HTC.

Why do bleeding symptoms occur in females?

Bleeding symptoms from haemophilia usually occur in females because of a process called 'lyonization'. In each cell in a female's body, one of her two X chromosomes is turned off or inactivated. Which X chromosomes in a female's body will be turned off appears to be random, but once they are turned off, the X chromosomes will not be turned on again in her lifetime.

If the X chromosome with the altered gene is turned off, that particular cell will produce clotting factor VIII or IX. If the X chromosome with the unaltered gene is turned off, that cell will express the altered gene and follow its genetic instructions: it will not produce clotting factor or the clotting factor it makes will not work properly. A female with low clotting factor levels has had more of her unaltered X chromosomes turned off, which is why she may experience bleeding symptoms. This also explains why a female may have different bleeding symptoms to the males in her family with haemophilia.

You can ask your haematologist at your HTC if your daughter's factor levels needs to be tested.

Genetic testing

A normal factor VIII or factor IX level test will not tell you whether your daughter carries the altered gene causing haemophilia. Some girls and women may have normal factor levels, but still carry the gene.

Talk to your HTC about genetic testing for your daughter. There are a few issues to consider and many people find that these tests give them a lot to think about. Your HTC can help with information and advice about genetic testing and can provide a referral to a genetic counsellor, if needed.

For more information on haemophilia in females, visit www.haemophilia.org.au

Deciding whether to having more children

Choosing to have more children is a very personal decision that involves consideration of:

- you and your partner's personal feelings and beliefs
- your family's lifestyle
- how you deal with haemophilia
- your religion
- family pressures
- how many children you already have
- your chance of having another child with haemophilia
- other family members' experiences with haemophilia.

You don't have to make this decision alone. There is support available to you, including your HTC and genetic counsellors.

See the 'Who can I talk to' section in this chapter for information on the support available to you.

If I have another child, will they have haemophilia?

Whether other children will have haemophilia depends on when the genetic alteration was introduced into your family.

If this is the first time haemophilia has appeared in your family, you may want to have a test to determine where the genetic mutation occurred. Tests usually involve testing other members of your family.

Where there has been a genetic alteration (spontaneous mutation) in your child alone, then your other children may not be affected.

If you have a son with haemophilia: If haemophilia has appeared in the mother's extended family before your son's diagnosis, the mother will carry the gene. If there is no family history of haemophilia there is still a chance the mother may carry the gene and further tests are needed to determine this. If the mother carries the gene, there is a 50 per cent chance with each pregnancy that other children that you have will inherit the gene.

If you have a daughter with haemophilia, it will depend on whether she inherited it from her mother or her father. If your daughter inherited the gene from her mother, there is a 50 per cent chance at each future birth that another son would have haemophilia or another daughter would carry the gene. If your daughter inherited haemophilia from her father, men with haemophilia pass the gene on to all their daughters but not to their sons. Therefore all your other daughters would carry the gene but none of your sons would have haemophilia. If you have another daughter who carries the gene she may or may not have bleeding symptoms and have haemophilia.

The 'Haemophilia Genetic Inheritance' diagrams in this chapter will help you understand your chance of having another child with haemophilia.

Options to consider

There are many different options for couples wanting to have more children. To help sort through the options, you might discuss some of the following questions with your partner:

- How would you feel about having another child with haemophilia?
- How would you feel about not having any more children?
- Would you consider adoption or foster care?
- Would you consider having an antenatal test at 12 weeks to determine whether your child has haemophilia?
- Would you consider termination of pregnancy if the foetus is male or the testing shows they are affected by haemophilia?
- How would you feel about using in-vitro fertilization (IVF) and pre-implantation testing to ensure that the eggs implanted do not contain the haemophilia gene?

Some options may not seem right to you for personal, moral or religious reasons. Some options may not be available in your area.

The choices you make might be different depending on your experience of having children with haemophilia or haemophilia in your family.

Who can I talk to?

While the decision ultimately must be yours and your partner's, there are people you can talk to who can provide you with information and help put things in perspective, including:

PARENT TIP

It is important that the decision you reach is yours and is right for you and your family.

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Haemophilia Treatment Centre (HTC)
Your HTC team is always happy to talk with you. They can explain the options available to you and put you in touch with a range of services, from testing to family planning and genetic counselling.

- ***Genetic counsellor***

  A genetic counsellor can work with you and provide information about the various options for having more children. They can also help with finding out about carrier status.

  Genetic counsellors talk through the options available, provide information on the various options, listen to what your feelings and beliefs are and act as a 'sounding board' while you make your decision.

- ***Haemophilia Foundations***

  Haemophilia Foundations understand the deeply personal nature of this decision. Your local Foundation can provide support but it will not try to make your decision for you. Your local Foundation can also put you in touch with a range of people who can assist with your decision making.

- ***Friends and family***

  Trusted friends and family can offer you guidance and support.

- ***Other families***

  Talking with other families who have faced this question, and finding out how they made their decision may help you. While the decision they made may not be right for you, understanding their opinions can provide you with clarity.

Your HTC can advise you and put you in touch with counselling services. Your local Haemophilia Foundation can help you talk with other families.

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Important note

This resource was developed by Haemophilia Foundation Australia for education and information purposes only and does not replace advice from a treating health professional. Always see your health care provider for assessment and advice about your individual health before taking action or relying on published information.