

# Hemophilia A Inheritance

By Heather Bauman

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Try the Interactive Inheritance Tool. Visit [PersonalizeHemA.ca](https://PersonalizeHemA.ca).



## Hemophilia A is a result of insufficient levels of factor VIII

Hemophilia is a bleeding disorder where blood does not clot properly. Hemophilia A, also known as classical hemophilia, is a genetic bleeding disorder caused by insufficient levels of a blood protein called factor VIII, a clotting factor. Clotting factors are proteins essential for proper blood clotting to stop bleeding.



## The role of the X chromosome in producing factor VIII

A person's genes provide the instructions on how to make proteins, such as factor VIII. In people with hemophilia A, there is a mutation (difference from normal) in the gene for factor VIII protein which causes the body to produce too little factor VIII.

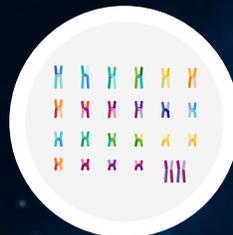
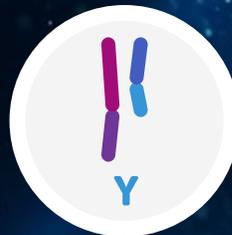
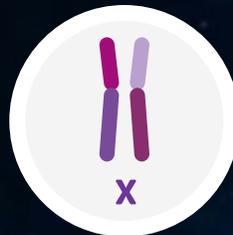
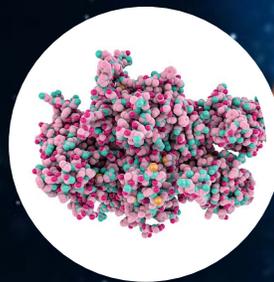
The genes responsible for producing factor VIII are situated on the X chromosome. This makes hemophilia a sex-linked or X-linked genetic disorder.

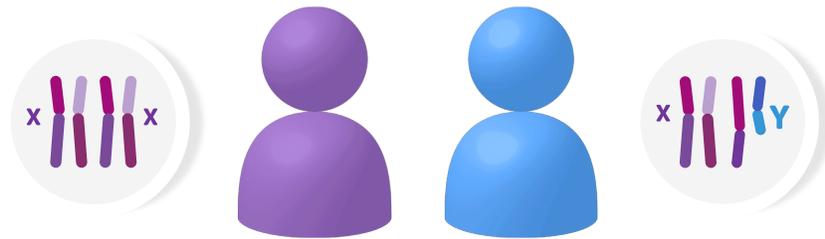
The X chromosome is one of the two sex chromosomes in humans (the other is the Y chromosome).

The sex chromosomes form one of the 23 pairs of human chromosomes in each cell.

The X and Y chromosomes determine whether a person's sex is male or female.

Approximately 70% of hemophilia A cases are inherited in an X-linked pattern. In the remaining 30%, cases occur spontaneously without a previous family history of the disorder.





## X chromosome gene mutation

Females inherit an X chromosome from each parent (XX), whereas males always inherit their X chromosome from their mother and their Y chromosome from their father (XY).

Females who have a mutated gene present on only one of their X chromosomes are called heterozygous or a carrier for the disorder.

- They usually do not display symptoms of the disorder because they have another normal/healthy copy of the gene to compensate for the copy with the disease-causing mutation.
- Some females do have bleeding symptoms, but they are usually milder than those of males with hemophilia.
- In rare cases, a female who is heterozygous can have bleeding symptoms that are just as serious as those of a male with hemophilia.

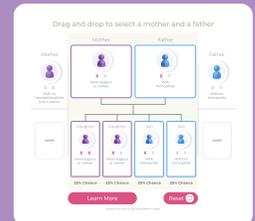
There are no genes for clotting factors on the Y chromosome. Since males have only one X chromosome, if they inherit an X chromosome that contains a mutated gene, they will develop the disease.

## Hemophilia A inheritance patterns

Inheritance patterns are used to describe how genetic variations are distributed through families. Looking at these patterns helps to predict disease risk in family members.

Use our hemophilia inheritance pattern tool to understand what might happen based on the genetics of a mother and father.

- Select from possible hemophilia traits in a mother and father to see what the chances are of the children inheriting the mutated gene that affects the creation of factor VIII.
- Try different combinations to see the different possibilities.

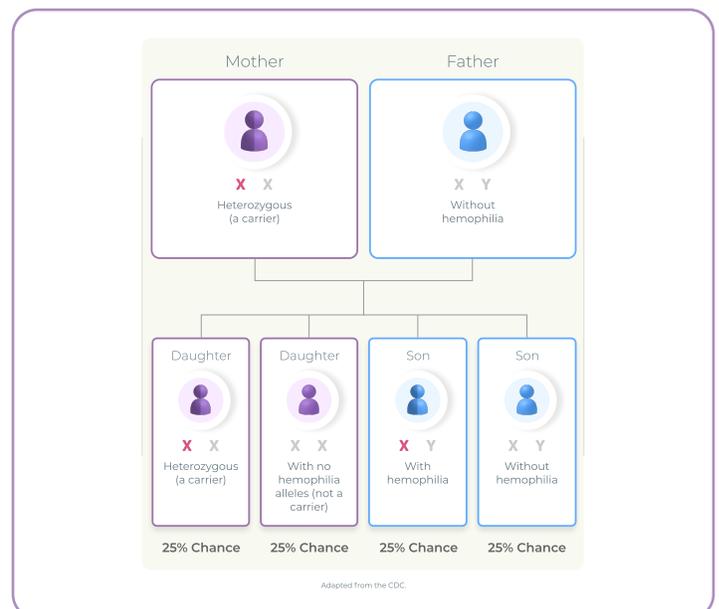


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## If a mother is heterozygous for hemophilia and the father does not have hemophilia:

- Each son has a 1 in 2 (50%) chance of getting his mother's mutated gene.
- Each daughter has a 1 in 2 (50%) chance of getting her mother's mutated gene and being heterozygous.

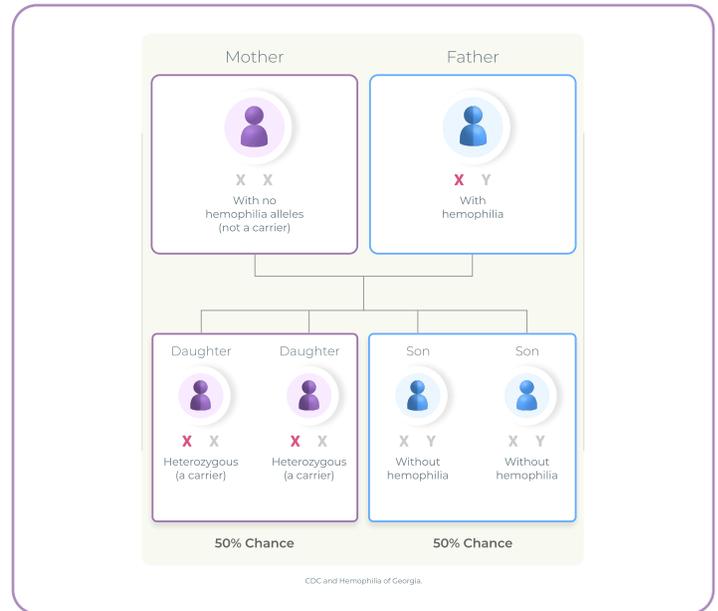
Overall, there is a 1 in 4 (25%) chance for each pregnancy that the baby will be a son with hemophilia and a 1 in 4 (25%) chance that the baby will be a heterozygous daughter. There is a 1 in 2 (50%) chance that the baby (either a son or a daughter) will not get the disease-causing gene at all and, therefore, can't pass it down to their children.



## If the father has hemophilia and the mother does not have a gene for hemophilia:

- A father who has hemophilia passes his only X chromosome down to all his daughters.
  - Daughters will always be heterozygous.
- A father passes down his Y chromosome to his sons; therefore, he cannot pass down a mutated gene to them.
  - Sons will not have hemophilia.

Overall, there is a 1 in 2 (50%) chance that the baby will be a son who does not have hemophilia and a 1 in 2 (50%) chance that the baby will be a daughter who is heterozygous (a carrier).



## If the father has hemophilia and the mother is heterozygous:

In the rare circumstance that the father has hemophilia, and the mother is a carrier, there is a chance that a daughter is homozygous (or doubly heterozygous) meaning there are two mutated genes.

- Each son has a 1 in 2 (50%) chance of getting his mother's mutated gene.
- There is a 1 in 2 (50%) chance of a daughter being heterozygous – getting the mutated gene from the father and the non-mutated gene from the mother.
- There is a 1 in 2 (50%) chance of a daughter being homozygous – getting the mutated gene from the father and the mutated gene from the mother.

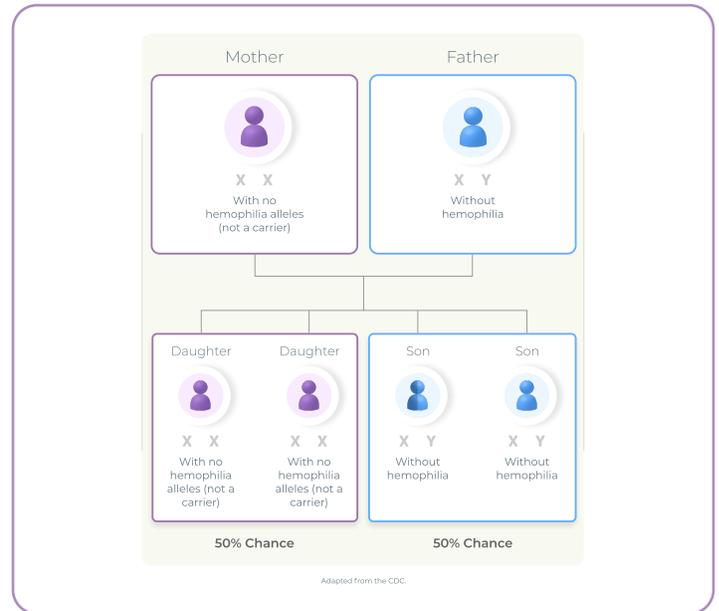
Overall, there is a 1 in 4 (25%) chance for each pregnancy that the baby will be a son with hemophilia and a 1 in 4 (25%) chance that the baby will be a heterozygous daughter. There is a 1 in 4 (25%) chance that the baby will be a homozygous daughter and a 1 in 4 (25%) chance a son will not get the disease-causing gene at all and, therefore, can't pass it down to their children.



## Can hemophilia occur if the father does not have hemophilia and the mother does not have a gene for hemophilia?

Although rare, it is possible for a child to have a spontaneous mutation on their X chromosome in the gene for factor VIII protein.

Of all hemophilia A cases, 30% occur without a previous family history of the disorder. In Canada, that is fewer than 1 in 33,000 people.



Talk to your healthcare team if you are interested in genetic testing for Hemophilia A.

## About the Author



**Heather Bauman** graduated from the University of Alberta with a Bachelor of Science in Nursing in 2005. She has been working in the bleeding disorder clinic for over 4 years.

Prior to this role, Heather worked in pediatric oncology and taught clinical courses for the Faculty of Nursing (University of Alberta) for 9 years. She serves on the Stollery Oncology/Hematology Quality Council and is a Western Nursing Representative for the Canadian Association of Nurses in Hemophilia Care (CANHC). For the past 3 years (pre-Covid), she has attended Camp Kindie (summer camp) with bleeding disorder patients. Her interests include tennis, snowboarding, and traveling.