Genetic Counseling + Your Family

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NEHA
NEW ENGLAND HEMOPHILIA ASSOCIATION

Genetic Counseling and Your Family

A guide for adults with a suspected bleeding disorder or parents/ caregivers of children with a suspected bleeding disorder

What is a genetic counselor? How can they help me?

A genetic counselor is a healthcare provider specifically trained to discuss genetic conditions and how we may diagnose them. While a genetic counselor is not a doctor, they do work with doctors that specialize in genetics, called geneticists. A genetic counselor can help you reach an answer about if a bleeding disorder is present, and if so, which one. A genetic counselor can provide you with information on who else in the family may be affected as well as your chance for having a child with a bleeding disorder.

Why might I go to see a genetic counselor?

There are many reasons you might go to see a genetic counselor, including:

- Concern about a bleeding disorder
- More bleeding or bruising than is typical when injured
- Frequent nose bleeds
- A really heavy menstrual period
- A bleeding disorder diagnosed by a coagulation factor test that you are looking to find a genetic explanation for
- A family history of a bleeding disorder
- If you are pregnant or plan to become pregnant and want more information on how a bleeding disorder can impact your family
- If you have previously been seen by a genetic counselor/had genetic testing for a bleeding disorder, but no longer have access to the results
- If you have previously been seen by a genetic counselor to discuss a bleeding disorder, and been found to have a VUS (see “What kinds of results might you receive from a genetic test?” section) and would like an update

What can I expect at a genetic counseling visit? What will we discuss?

A genetic counseling visit will be mostly discussion-based. The genetic counselor may ask you some questions about you or your child’s past health and/or some questions about your family history. Please be prepared with any information (the name of a diagnosis, knowledge that someone bleeds more than expected, genetic testing results if available) you have about bleeding disorder diagnoses of other family members. It is okay if this information is incomplete. After that, some visits will include consultation with a geneticist, which might include a physical examination. Then, the genetic counselor will provide some education on bleeding disorders, what testing options are available, and if there is a potential for other family members to be affected by the same condition.

How are bleeding disorders inherited?

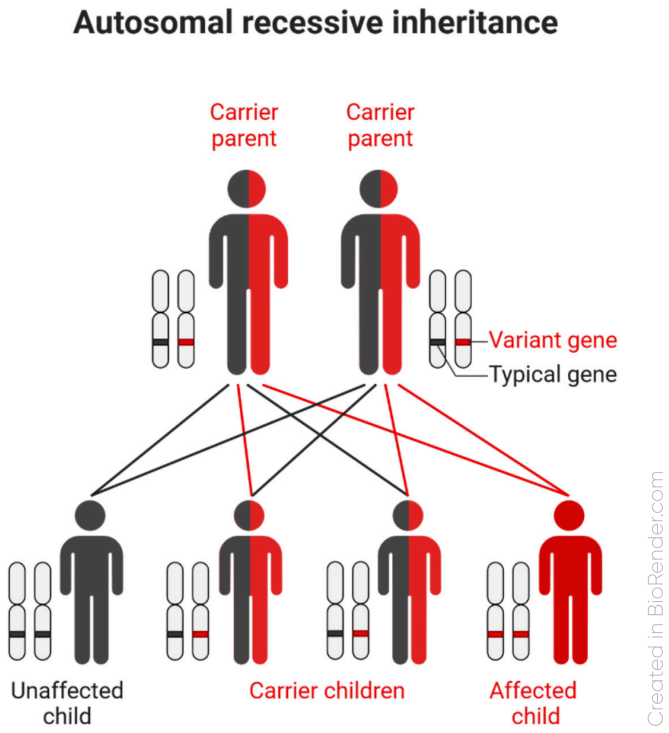
Bleeding disorders have two main inheritance patterns: X-linked and autosomal recessive. Less commonly, bleeding disorders can also have an autosomal dominant inheritance pattern.

All living creatures contain a genetic code, called DNA, that tells their body how to operate and function. Within the DNA, there are chunks of instructions called genes. DNA is compiled into larger, organized units called chromosomes. Humans have 23 pairs of chromosomes, 22 of which are referred to as autosomes and which are the same in everybody, regardless of sex. The last pair is referred to as the sex chromosomes. The sex chromosomes are typically XX or XY, with each letter representing one chromosome in the pair.

A note on language: For this resource, "people with XX chromosomes" will be used to describe individuals that are assigned female at birth (AFAB); this generally includes cisgender women and girls, transgender men, and some non-binary individuals. "People with XY chromosomes" will be used to describe individuals that are assigned male at birth (AMAB); this generally includes cisgender men and boys, transgender women, and some non-binary individuals. Sex is a lot more complicated than just our X and Y chromosomes, with many other factors influencing sex. In this case, when discussing hemophilia, the presence of XX or XY chromosomes is relevant to how these conditions are inherited.

Sometimes, there are differences in the spelling of our genes, which causes our body to not carry out the proper function specified by the gene. This change is called a variant (or previously, a mutation).

Autosomal recessive inheritance means that an individual must inherit two variants, one from each parent, for the condition to show and affect the individual.



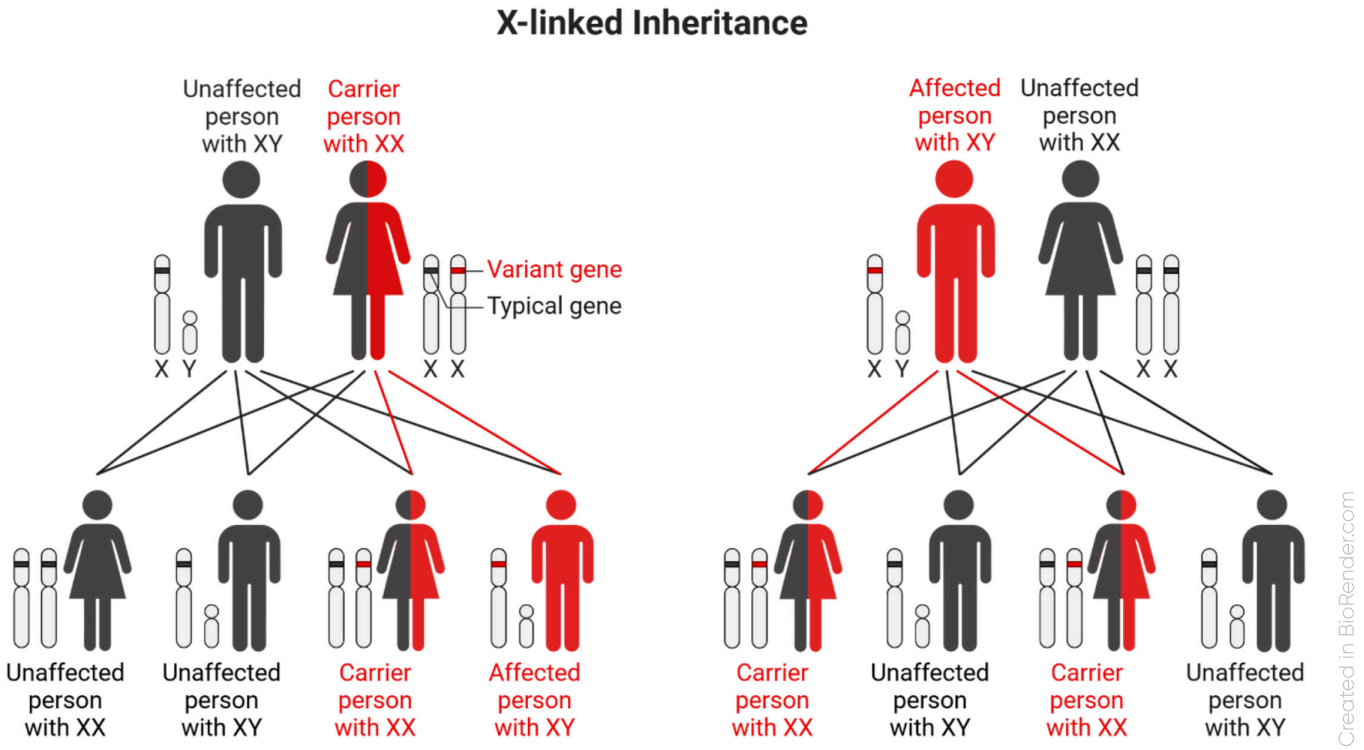
If someone has one variant, they will likely have no or few signs of the condition. These individuals are called carriers. These conditions can appear with little or no family history because carriers are not easily identified. Conditions in this category impact all individuals, regardless of sex. Conditions within this category include some forms of von Willebrand Disease and all of the rare factor deficiencies (1, 2, 5, 7, 10, 11, 12, and 13).

Here is a summary of how autosomal recessive conditions are passed from parents to children:

- If both parents are carriers (shown in the autosomal recessive inheritance figure):
  - 25% or 1 in 4 chance the child will be unaffected
  - 50% or 1 in 2 chance the child will be a carrier
  - 25% or 1 in 4 chance the child will be affected
- If one parent is a carrier and the other is unaffected:
  - 50% or 1 in 2 chance the child will be unaffected
  - 50% or 1 in 2 chance the child will be a carrier
- If one parent is affected and one parent is not affected:
  - All of the children (100%) will be carriers
- If one parent is affected and one is a carrier:
  - 50% or 1 in 2 chance the child will be a carrier
  - 50% or 1 in 2 chance the child will be affected

These percentages remain the same for each pregnancy a couple has, even if they have had children previously; a child being affected or unaffected doesn't have any impact on future pregnancies.

X-linked inheritance involves a gene that is located on the X chromosome. People with XX chromosomes have two copies of the gene while people with XY chromosomes have only one copy of the gene as there is not another copy on the Y chromosome.



People with XX chromosomes with one variant may have no signs of a condition or may have several signs of a condition; this can be variable. Conditions in this category impact people with XY chromosomes more severely. Conditions within this category include hemophilia A and B.

Here is a summary of how X-linked conditions are passed from parents to children:

- If a person with XY chromosomes is unaffected and a person with XX chromosomes is a carrier (shown in the X-linked inheritance figure on the left):
  - 25% or 1 in 4 chance of having an unaffected child with XX chromosomes
  - 25% or 1 in 4 chance of having an unaffected child with XY chromosomes
  - 25% or 1 in 4 chance of having a carrier child with XX chromosomes
  - 25% or 1 in 4 chance of having an affected child with XY chromosomes
- If a person with XY chromosomes is affected and a person with XX chromosomes is unaffected (shown in the X-linked inheritance figure on the right):
  - All of the children with XX chromosomes will be carriers
  - All of the children with XY chromosomes will be unaffected

These percentages remain the same for each pregnancy a couple has, even if they have had children previously; a child being affected or unaffected doesn't have any impact on future pregnancies.

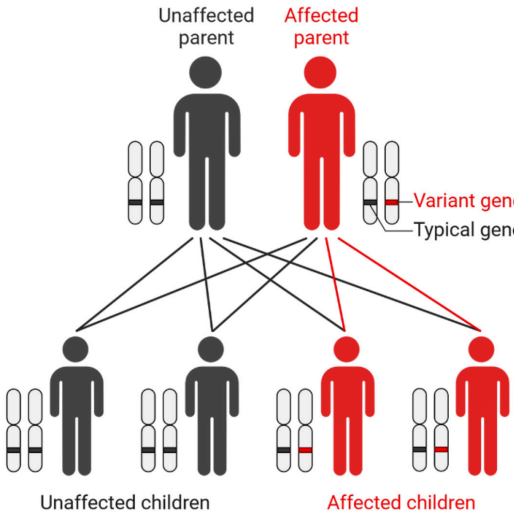
Autosomal dominant inheritance can also be seen with some forms of von Willebrand Disease. In this case, if an individual has a variant, they will be affected. This variant can be passed down from a parent or can be a new variant found in the individual.

What are the testing options?

Bleeding disorders can be diagnosed through coagulation factor tests or genetic tests.

A blood draw is necessary to complete a coagulation factor test. A coagulation factor test will look at the amount of various clotting factors in the blood. If there is a clotting factor whose activity is reduced, a bleeding disorder can be diagnosed. The severity of the condition can be determined based on how reduced the factor activity is.

Autosomal dominant inheritance



Hemophilia Factor Activity

Classification	Clotting Factor activity predicts severity		
	Severe hemophilia	Moderate hemophilia	Mild hemophilia
Hemophilia A	< 1% factor 8	1-5% factor 8	6-40% factor 8
Hemophilia B	< 1% factor 9	1-5% factor 9	6-40% factor 9

**Coagulation factor test is not a reliable test for detecting carriers with XX chromosomes.*

Von Willebrand Factor (VWF) activity in Von Willebrand Disease (VWD)

Type	Features & Factor Function	Inheritance
VWD Type 1	Mildest and most common form of VWD. VWF 20-50% of normal; may also have low factor 8.	Autosomal dominant
VWD Type 2	Multiple subtypes: 2A, 2B, 2M, 2N VWF does not work right (present in the correct quantity, but there is a problem with the factor itself such that it does not work right).	Autosomal dominant or autosomal recessive
VWD Type 2	Most severe form, occurs in less than 5% of cases. No VWF and low factor 8.	Autosomal recessive

A genetic test will look for variants in genes to determine the exact cause of an individual's condition. A genetic test can provide more specific information than a coagulation factor test about the inheritance pattern of a condition and what to expect in the future based on others who have the same variant, though a coagulation factor test will likely provide more specific information on how severely impacted the individual is and may be a better indicator for what to expect as every individual is different. Genetic testing can be done either by blood draw, or in some cases, a cheek swab of the inside of the mouth. The genetic counselor will indicate which of these methods is most appropriate, or in some cases, may let you choose.

What kinds of results might you receive from a genetic test?

Genetic tests have three different types of results.

1. **Positive/Abnormal** - this means that the genetic test found a variant in a gene that is known to cause a bleeding disorder. This result provides an explanation for your/your child's bleeding disorder. Based on these results, the genetic counselor might recommend testing for others within the family. The genetic counselor can provide a note explaining the results which can be given to other family members to help facilitate the testing process.
2. **Negative/normal** - this means that the genetic test did not identify any variants in the genes that were being tested. Genetic testing can only identify variants in the specific genes that are tested, so it is possible that the genetic counselor may discuss further testing options with you, which may include testing a larger number of genes or exome sequencing, in which all of the 20,000 genes in the body are tested. Exome sequencing is a complex test, and details should be discussed with your genetic counselor.
3. **Variant of Uncertain Significance (VUS)** - this means that the genetic test found a variant, but at this time, the scientific community does not have enough information to say whether the variant found is an explanation for you/your child's bleeding disorder. Most of the time (~90%), these spelling changes are found to be harmless. Though it is possible (the other ~10%) that this variant is the cause for the bleeding disorder. It is important to note that VUS's are not considered medically actionable, meaning that you should not make decisions about your/your child's medical care based on this result. Usually with VUS's, genetic counselors do not recommend further testing for the individual or for the family. The genetic counselor will recommend following up every few years to see if there are any updates to the VUS's status that would change this result to a positive or a negative. If there is a change, you will be issued a new report.

How can I get connected with a genetic counselor?

You can talk to your PCP or your child's pediatrician to get a referral. You can also look for genetic counselors in your area using this resource from the National Society of Genetic Counseling: https://findageneticcounselor.nsgc.org.

Genetic Counseling and Kids!

A guide for kids who might have a bleeding disorder

What's going on? Why are you here?

You are here because someone is worried that you might have a bleeding disorder. They may have noticed that when you get hurt, you bleed more than others. You are at this visit so we can try to get some answers about why you bleed more than others.

What is a genetic counselor? How can they help me?

A genetic counselor is someone who is trained to discuss genetic conditions and how we may find them. While a genetic counselor is not a doctor, they do work with doctors. A genetic counselor can find out why you are bleeding more than others. You can ask the genetic counselor any questions that you have.

What will happen during this visit?

This visit will mostly be talking. The genetic counselor may ask you some questions about what you have noticed when you get hurt. They may also ask you some other questions about your health and your body.

This visit might include a physical exam from a doctor. If you are not comfortable with this, please tell the genetic counselor, the doctor, or a trusted adult.

To get an answer about why you bleed more, you may need to have your blood drawn. The doctors will use this blood to find out if there is something missing from your blood that makes it so it does not clot as easily. The doctors may also use this blood to read your genetic code, or DNA, and look for anything out of the ordinary that may explain why you bleed more.

Instead of a blood draw, it is possible that the doctor might want a cheek swab. For this, the doctor will take a cotton swab (like a Q-tip) and rub it against your cheek inside your mouth for 30 seconds on each side.

Genetic Counseling and Kids!

A guide for siblings of an individual who might have a bleeding disorder

What's going on? Why are you here?

You are here because someone is worried that your sibling (brother or sister) might have a bleeding disorder. Someone may have noticed that when your sibling gets hurt, they bleed more than others. This visit is happening so we can try to get some answers about why they bleed more than others.

What can I do?

For now, sit tight! Feel free to play the games or color in the attached booklet. If you have any questions you would like to ask, write them down in the attached notebook. It can be difficult for your family to answer any questions that you have while they are trying to learn what is going on!

It is possible that you may be asked to complete a blood draw or a cheek swab (Q-tip rubbed against the inside of your cheeks) with your sibling or at a later time so that we can better understand why your sibling bleeds more than others. As a family member, it is possible that your genetic code can help us find answers.