



Carrier Screening in the Ashkenazi Jewish Population

*Helping you make
an informed decision*



What is carrier screening?

Inherited, or genetic, disorders are passed from parents to their children. This often occurs even when neither parent has the disease. For a child to inherit 1 of these disorders, both parents must have at least 1 altered gene that causes the disorder; that is, both parents must be carriers of an altered gene.

Carrier screening tells you what your chance, or risk, is for carrying an altered gene that causes 1 of these disorders. Carrier screening can also tell you what your chance is of having a child with the disorder. Carrier screening cannot, however, tell you if your child *will* have the disorder. Additional testing is needed for that. This brochure will help you understand exactly what information can be obtained from carrier screening and how the information can help with family planning.

Why is there carrier screening just for Ashkenazi Jewish people?

Ashkenazi Jewish people are those whose ancestors originated from Eastern Europe. There are a number of serious disorders that occur more often in these people than in the general population. Since the frequency of these serious disorders is higher in Ashkenazi Jews, it makes sense to screen Ashkenazi Jewish people but not people from other ethnic groups that have a lower frequency.

Which disorders are included in Ashkenazi Jewish carrier screening?

Eight disorders can be included in Ashkenazi Jewish carrier screening: Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Niemann-Pick disease, and Tay-Sachs disease. Depending on your personal and family history, 1 or maybe all of these disorders will be included in your screening. Some information about each disorder is listed in Table 1.

Table 1. Disorders Commonly Inherited by Ashkenazi Jews

BLOOM SYNDROME	
Disease Frequency*	1 in 40,000
Carrier Risk†	1 in 100
Symptoms	Increased risk for infection and cancer, increased sensitivity to sunlight, blotches on face (light or reddish), reduced fertility (women), infertility (men), maximum height less than 5 ft.
Life Expectancy (years)	13-30
CANAVAN DISEASE	
Disease Frequency*	1 in 6,400
Carrier Risk†	1 in 40
Symptoms	Enzyme deficiency leading to degeneration of brain, generalized weakness, mental retardation, seizures, feeding difficulties, blindness
Life Expectancy (years)	<20
CYSTIC FIBROSIS	
Disease Frequency*	1 in 2,500
Carrier Risk†	1 in 25
Symptoms	Mucus build-up in lungs leads to breathing difficulties and many lung infections; poor digestion of food; reduced fertility (women), infertility (men)
Life Expectancy (years)	30
FAMILIAL DYSAUTONOMIA	
Disease Frequency*	1 in 3,600
Carrier Risk†	1 in 30
Symptoms	Nervous system disorder leading to poor regulation of body temperature and blood pressure, poor recognition of heat and pain, poor swallowing reflex leading to vomiting and malnutrition, and lack of tears leading to eye irritation and injury
Life Expectancy (years)	<30
FANCONI ANEMIA GROUP C	
Disease Frequency*	1 in 32,000
Carrier Risk†	1 in 89
Symptoms	Decrease in red blood cells (anemia), white blood cells (neutropenia), and platelets; deformities of the arm, leg, kidney, or heart; short stature; frequent bleeding and bruising; increased risk of cancer
Life Expectancy (years)	Young adulthood
GAUCHER DISEASE, TYPE 1	
Disease Frequency*	1 in 1,000
Carrier Risk†	1 in 13
Symptoms	Enzyme deficiency leading to accumulation of a fatty substance in the liver, spleen, and bone marrow; bone and joint pain; bone fracture (crack, break, splinter); anemia; easy bruising and bleeding
Life Expectancy (years)	6-80‡
NIEMANN-PICK DISEASE (TYPE A)	
Disease Frequency*	1 in 40,000
Carrier Risk†	1 in 90
Symptoms	Enzyme deficiency leading to accumulation of fat in liver, spleen, brain and lymph nodes; poor growth; enlarged liver and spleen; many infections; loss of brain function
Life Expectancy (years)	2-3
(TYPE B)	
Disease Frequency*	Less than 1 in 40,000
Carrier Risk†	Less than 1 in 90
Symptoms	Enzyme deficiency leading to accumulation of fat in liver, spleen, brain and lymph nodes; poor growth; enlarged spleen and liver; lung infections; very low levels of HDL (good) cholesterol leading to heart disease
Life Expectancy (years)	40-50
TAY-SACHS DISEASE	
Disease Frequency*	1 in 3,600
Carrier Risk†	1 in 30
Symptoms	Severe mental retardation, loss of coordination and movement of arms or legs, seizures, blindness, deafness
Life Expectancy (years)	3-5

* How often the disease occurs in the Ashkenazi Jewish population.

† Risk of an Ashkenazi Jew without a personal or family history of the disorder.

‡ Depends on severity of symptoms and treatment received.

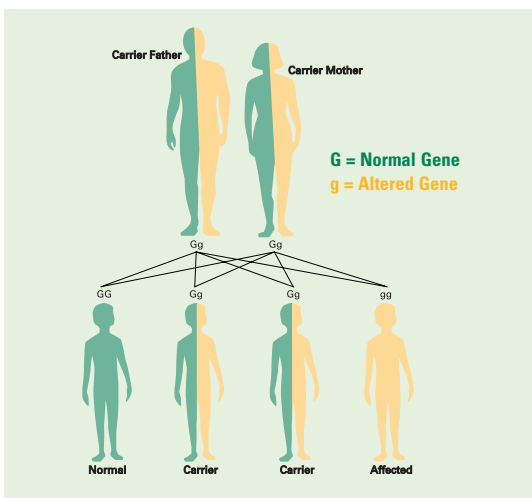
What is a genetic disease carrier?

For each inherited characteristic, we receive 1 gene from our mother and 1 from our father. People who receive 1 altered gene and 1 normal gene for a particular disorder are called carriers because they “carry” an altered gene, yet do not have the disorder. These carriers have a 50% chance of passing the altered gene on to each of their children. However, in order for a child to inherit the disorder, he or she must receive an altered gene for that disorder from *both* parents. A child cannot inherit the disorder when only 1 parent is a carrier.

How is the altered gene inherited when both parents are carriers?

In the figure below, both the mother and the father are carriers, so each carries 1 altered gene (g) and 1 normal gene (G). Each of their children has:

- A 25%, or 1 in 4, chance of inheriting 2 altered genes and having the disorder.
- A 25%, or 1 in 4, chance of inheriting 2 normal genes. This child would not have the disorder and would not be a carrier.
- A 50%, or 2 in 4, chance of inheriting 1 altered gene. This child would not have the disorder but would be a carrier, just like the parents.



Who should have Ashkenazi Jewish carrier screening?

This is a decision that you and your partner must make. Generally, carrier screening is offered to couples of any ethnic group when 1 partner is a known carrier or actually has 1 of the genetic disorders described earlier. It is also offered to individuals of any ethnic group who have a family history of 1 of these disorders, such as those who already have a child with a disorder or those who have a close relative with a disorder. In these situations, carrier screening is usually performed only for that particular disorder, rather than for all of the disorders.



Carrier screening is also offered to Ashkenazi Jews who don't have a personal or family history of any of these disorders but wish to know their chances of having a child with 1 of these disorders. In this situation, carrier screening may be performed for all 8 disorders.

Carrier screening for a single disorder may be offered to a non-Ashkenazi Jewish person who is the reproductive partner of a carrier-positive Ashkenazi Jewish person. Non-Jewish partners are sometimes tested because these disorders occur in other ethnic groups too, although less often.

You may wish to consider *your* risk of being a carrier. Table 1 lists the carrier risk for Ashkenazi Jewish people who do not have a personal or family history of the disorder. If someone in your family has 1 of these disorders, your risk of being a carrier of an altered gene for that disorder is as high as 2 in 3.

If you have 1 of these disorders, your risk of being a carrier is 1 in 1 or 100% because you have to have 2 altered genes to have the disorder.

Remember that carrier screening provides information about your child's chances of inheriting 1 of these disorders but cannot tell you if you will, or will not, pass on a disorder to your child.

How is Ashkenazi Jewish carrier screening done?

Some disorders can be caused by more than 1 alteration or "mutation" in the gene. For example, more than 1,000 mutations have been discovered in the cystic fibrosis gene. The screening tests, however, detect only the more common mutations. Table 2 lists the number of mutations that are detected by the screening tests performed at Quest Diagnostics Incorporated. Using these tests, more than 95 out of 100 mutations can be found, as shown in Table 2.

Table 2. Percentage of Gene Mutations Found by the Screening Test

DISEASE	NUMBER OF MUTATIONS DETECTED	PERCENTAGE (%) OF MUTATIONS FOUND*
Bloom syndrome	1	97
Canavan disease	4	99
Cystic fibrosis	25	97
Familial dysautonomia	1	>98
Fanconi anemia group C	1	99
Gaucher disease	4	96
Niemann-Pick disease	4	>95
Tay-Sachs disease	3	up to 98

* Applies only to those of full Ashkenazi Jewish heritage.

Ashkenazi Jewish carrier screening is performed on a small sample of your blood. During the test, the laboratory will find out if you carry 1 of the more common mutations. Your doctor will provide the lab with information about any personal or family history of the disorders to help with interpretation of the results. Your blood can be screened for the presence of altered genes for 1 or all of the disorders, depending on what you and your partner decide.



What does a negative screen mean?

Your “pretest” risk of being a carrier is shown in Table 1, assuming that you are of full Ashkenazi Jewish heritage and that you have no personal or family history for the disorder. Ashkenazi Jewish carrier screening provides additional information that modifies that pretest risk. A negative screen means that the lab didn’t find any mutations related to the disorder(s). Your “posttest” risk of being a carrier is therefore lower than your pretest risk. You’re also less likely to have a child with the disorder. Since the screening test detects only the most common mutations in the genes, a negative screen doesn’t guarantee that you’re not a carrier.

What does a positive screen mean?

A positive screen means that the lab found a mutation in 1 of your 2 genes and that you're a carrier. There is a 50% chance that you'll pass this altered gene on to your child. Even if you do pass the altered gene on to your child, it doesn't necessarily mean that your child will have a disorder. Your child's chances of having a disorder also depend on whether or not your partner is a carrier for that particular disorder or has the disorder.

If your partner has a negative carrier screen, your chance of having a child with a disorder is less than if your partner's screen were positive; however, there is a 50%, or 1 in 2, chance that your child will be a carrier for that disorder. The only way you and your partner could have a child with the disorder is if your partner has a rare mutation in 1 of his or her genes that was not detected in the screen. The chance of this happening depends on your partner's race and family history. Your doctor or a genetic counselor can give you more specific information.

If your partner is also a carrier, then your child has a 25%, or 1 in 4, chance of inheriting the disorder. There is a 50%, or 1 in 2, chance that your child will not have the disorder but will be a carrier. Finally, there is a 25%, or 1 in 4, chance that your child will not even be a carrier.

If your partner has the disorder and you are a carrier, then there is a 50%, or 1 in 2, chance that your child will have the disorder. There is also a 50% chance that your child will be a carrier and not have the disorder.

A positive screen also means that other members of your family are at higher risk of being a carrier.

Remember that the risk described above will be the same for *each* child you and your partner conceive (that is, for each pregnancy). Also remember that Ashkenazi Jewish carrier screening can only tell you the risk of your child having the disorder; it cannot tell you if any of your children will actually have the disorder.

What family planning options are available?

If your carrier screen is negative and if you do not have any close relatives with 1 of the disorders, you can plan your family knowing that it's very unlikely for you to have a child with the disorder(s) screened for. This is true even if your partner is a carrier, because 2 altered genes are necessary to have a child with 1 of these disorders. Remember, however, that there is no guarantee your child won't have 1 of these disorders.

If you and your partner are both carriers for the same disorder, you may want to learn what it's like to live with and take care of a person with that disorder. You may also want to know about medical procedures that tell whether an unborn

child has inherited the disorder. For example, in chorionic villus sampling (CVS), a tissue sample is obtained from the placenta between the 10th and 12th weeks of pregnancy. This



sample is then analyzed for the mutations that were found in the parents' genes. In another procedure called amniocentesis, a sample of amniotic fluid, the fluid that surrounds and protects your baby, is collected between the 14th and 18th weeks of pregnancy. This fluid contains cells that have washed off your baby's skin. These cells are tested for the parents' altered genes. You may also want to learn about other methods of getting pregnant, such as using an egg or sperm from a donor who is not likely to be a carrier of the disorder. Finally, you may wish to explore the option of adoption. Your doctor or genetic counselor can help you learn more about these options and their associated risks and benefits. The information will help you make the best decisions for you and your family.

In summary...

Ashkenazi Jewish carrier screening

- determines your risk of carrying an altered gene that can cause 1 of these disorders,
- determines your risk of passing that gene on to your child, and
- determines your child's risk of having a disorder if both you and your partner are screened.

A negative screen means that

- none of the common gene mutations were found in your blood sample,
- you're much less likely to pass an altered gene on to your child, and
- you're much less likely to have a child with a disorder.

Remember, a negative screen doesn't guarantee that you're not a carrier and that you can't pass on an altered gene to your child.

A positive screen means that

- you are a carrier,
- you might pass the altered gene on to your child, and
- your child might have a disorder if your partner also carries an altered gene for the same disorder.

Ashkenazi Jewish carrier screening cannot tell you for sure if you will, or will not, have a child with 1 of these disorders. Carrier screening will, however, give you important information that will help you make the best possible decisions for you and your family.



For more information, visit these Web sites:

- **Canavan Foundation**
<http://www.canavanfoundation.org/index.php>
- **Cystic Fibrosis Foundation**
<http://www.cff.org/index.cfm>
- **Fanconi Anemia Research Fund, Inc.**
<http://www.fanconi.org>
- **Genetic Disease Foundation**
<http://www.geneticdisease.org/index.html>
- **Familial Dysautonomia Foundation**
<http://www.familialdysautonomia.org>
- **National Gaucher Foundation**
<http://www.gaucherdisease.org>
- **National Niemann-Pick Disease Foundation, Inc.**
<http://www.nnpdf.org>
- **National Tay-Sachs and Allied Diseases Association, Inc.**
<http://www.ntsad.org/index.htm>

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