Cystic Fibrosis Carrier Screening:

Helping you make an informed decision

Quest Diagnostics®

What is cystic fibrosis carrier screening?

Inherited, or genetic, diseases like cystic fibrosis (CF) are passed from parents to their children. This occurs even when neither parent has the disease. For a child to inherit CF, both parents must have an altered gene that causes CF; that is, both parents must be carriers of an altered CF gene.

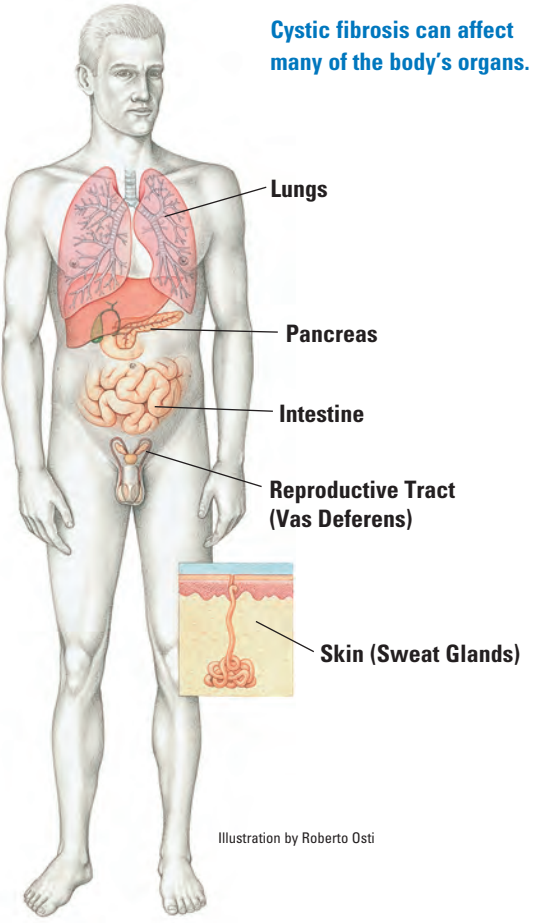
CF carrier screening tells you what your chance, or risk, is for carrying an altered CF gene. Carrier screening can also tell you what your chance is of having a child with CF. Carrier screening cannot, however, tell you if your child *will* have CF. Additional testing is needed for that. This brochure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

What is cystic fibrosis?

CF is an inherited disease that occurs most often in people whose ancestors come from Northern and Western Europe. In Northern European Caucasians and people of Ashkenazi Jewish descent, approximately 1 infant out of every 3,000 live births will be born with CF. People of other ethnic groups also have CF, but not as frequently. For example 1 in 8,500 Hispanic Americans, 1 in 15,000 African Americans, and only 1 in 35,000 Asian Americans will be born with CF.

People who have CF have high levels of sodium and chloride (salt) in their sweat. More importantly,

a thick, sticky mucous in the lungs causes persistent coughing and wheezing as well as frequent lung infections including pneumonia. Some affected children have difficulty gaining weight even though they eat normally. These children have very low amounts of pancreatic enzymes and cannot break down food normally to extract the nutrients needed for growth. All these symptoms can be either mild or severe.



Infertility (not being able to have children) is also common in people with CF, especially in men. Although men with CF produce sperm, they are almost always born without the vas deferens, the tube that carries sperm from the testes. This condition is called congenital bilateral absence of the vas deferens (CBAVD). Since sperm cannot be carried from the testes, these men don't release sperm during sex and, consequently, are infertile. CBAVD may occur in men who don't have other CF symptoms as well as in those who do. Many women with CF, on the other hand, are able to have children even though some have reduced fertility.

Although CF is not curable, there are some treatments that greatly increase the life span for patients with CF. For example, digestive problems are often treated with special high-protein, high-calorie diets and vitamins. In addition, capsules are taken at each meal to replace the missing pancreatic enzymes. Lung symptoms are treated with physical therapy that can sometimes clear the mucus from the lungs. Antibiotics and other medications are also used. Despite treatment, half of the people born with CF die by the age of 37 years, primarily from lung disease.

What is a cystic fibrosis carrier?

For most inherited characteristics, we receive 1 gene from our mother and 1 from our father. People who receive 1 altered CF gene and 1 normal gene are called CF carriers because they "carry" an altered CF gene, yet do not have CF. These carriers have a 50% chance of passing the altered CF gene on to each of their children. However, in order for a child to inherit CF, he or she must receive an altered CF gene from

both parents. A child cannot inherit CF when only 1 parent is a carrier. People with CF are also carriers, since they "carry" 2 altered CF genes. They will pass on an altered CF gene to each of their children.

Who should have cystic fibrosis carrier screening?

This is a decision that you, your partner, and your doctor must make. Carrier screening is offered to:

- all couples who are currently pregnant
- those who are planning a pregnancy
- couples in which 1 partner has CF
- individuals who have a family history of CF, such as those who already have a child with CF or those who have a close relative with CF

Men with CBAVD (see previous section: "What is cystic fibrosis?") often are carriers for, or have, CF. Since these men can still father children by having a special medical procedure in which sperm are removed directly from their testes, they and their partners may also want to be screened.

You may wish to consider *your* risk of being a carrier. This is based on your personal and family history of CF and the frequency of CF in your ethnic group. Table 1 lists the risk of being a carrier for various groups. You may also want to consider the ability of the test to find the altered CF genes that occur in your ethnic group as shown in Table 2 and described in the next section ("How is cystic fibrosis carrier screening done?"). Remember that carrier screening provides information about your child's chances of inheriting CF, but cannot tell you if you will, or will not, pass on CF to your child.

Table 1. Risk of Being a CF Carrier[1]

Risk Factor	Risk
	HIGH RISK
Personal or family history	
Individuals with CF	1 in 1
Individuals with a family history of CF	As high as 2 in 3
Ethnicity*	
Ashkenazi Jewish people	1 in 24
Non-Hispanic Caucasian	1 in 25
Hispanic American	1 in 46
African American	1 in 65
Asian American	1 in 94
	LOW RISK

*This risk is based on ethnicity alone; it does not include risk from personal or family history.

How is cystic fibrosis carrier screening done?

More than 1,700 changes have been discovered in the CF gene. The screening test, however, identifies only the more common changes. Thus, the test is better at finding CF carriers in some ethnic groups than in others. For example, the test can detect 88% of the changes found in the Non-Hispanic Caucasian group, but only 72% of the changes found in the Hispanic American group. Table 2 shows how well the Quest Diagnostics test can find altered CF genes in each ethnic group.

Table 2. Percentage of CF Gene Changes Found by the Screening Test[3]

Ethnic Group	Percentage of CF Gene Changes Found
Ashkenazi Jewish people	94%
Non-Hispanic Caucasian	88%
African American	65%
Hispanic American	72%
Asian American	49%

CF 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 changes to the CF gene. Your doctor should provide the lab with information about your race, ethnicity, and any personal or family history of CF to help with interpretation of the results.

What does a negative screen mean?

As shown in Table 1, your risk of being a CF carrier is based on your ethnic group and your personal or family history. CF carrier screening provides additional information that modifies your "pre-test" risk. A negative screen means that the lab didn't find any changes in your CF genes, so your actual risk of being a CF carrier is lower than your pre-test risk. You're also less likely to have a child with CF. Since the screening test detects only the most common changes in the CF gene, 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 change in 1 of your 2 CF 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 CF. Your child's chances of having CF also depend on whether or not your partner is a CF carrier or has CF.

If your partner has a negative CF carrier screen, your chance of having a child with CF 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 CF carrier. The only way you and your partner could have a child with CF is if your partner has a rare change in 1 of his or her CF 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 there is a 25%, or 1 in 4, chance that your child will have CF. There is a 50%, or 1 in 2, chance that your child will not have CF, 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 CF, then there is a 50%, or 1 in 2, chance that your child will have CF. There is also a 50% chance that your child will be a carrier and not have CF.

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 CF carrier screening can only tell you the risk of your child having CF; it cannot tell you if any of your children will actually have CF.

What family planning options are available?

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

If you and your partner are both CF carriers, you may want to learn what it's like to live with and take care of a person with CF. You may also want to know about medical procedures that tell whether an unborn child has inherited CF. For example, in chorionic villus sampling, a tissue sample is obtained from the placenta between the 10th and 12th week of pregnancy. This sample is then analyzed for the changes that were found in the parents' CF 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 week of pregnancy. This fluid contains cells that have washed off your baby's skin. These cells are tested for the parents' altered CF 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 CF carrier or using preimplantation genetic diagnosis in conjunction with in vitro fertilization. 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…

Cystic fibrosis carrier screening

- determines your risk for carrying an altered gene that can cause CF
- determines your risk for passing that gene on to your child
- determines your child's risk of having CF if both you and your partner are screened

A negative screen means that

- none of the common CF gene changes were found in your blood sample
- you're much less likely to pass an altered CF gene on to your child
- you're much less likely to have a child with CF

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

A positive screen means that

- you are a CF carrier
- you might pass the altered CF gene on to your child
- your child might have CF if your partner is also a carrier

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

Reference:

1. Richards CS, Bradley LA, Amos J, et al. Standards and guidelines for CFTR mutation testing. *Genet Med.* 2002:4:379-391.

2. American College of Medical Genetics. Technical standards and guidelines for CFTR mutation testing. 2006 ed. http://www.acmg.net/Pages/ACMG_Activities/stds-2002/cf.htm#Table1. Accessed May 10, 2010.

3. Committee on Genetics, American College of Obstetrics and Gynecology. ACOG Committee Opinion. Number 325, December 2005. Update on carrier screening for cystic fibrosis. *Obstet Gynecol.* 2005;106:1465-1468.

This brochure is for informational purposes only and is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by your doctor. Always talk with your doctor about the meaning of your test results and before you stop, start, or change any medication or treatment.

PP0490 08/2010

Quest Diagnostics®