Quest Diagnostics®

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Cystic Fibrosis

Cystic fibrosis (CF) is one of the most common genetic diseases. It is caused by mutations in the cystic fibrosis transmembrane conductance regulator *(CFTR)* gene. It's a chronic, progressive condition.

CF and ethnicity

People of any race or ethnicity can inherit CF. But it's most common in Caucasians and Ashkenazi Jewish people. This is because the mutation carrier rate is higher in these people.

Race/Ethnicity	Mutation Carrier Rate[1]	Birth Prevalence[2]
Ashkenazi Jewish	1 in 24	1 in 2,270
Non-Hispanic Caucasian	1 in 25	1 in 2,500
Hispanic	1 in 58	1 in 13,500
African American	1 in 61	1 in 15,100
Asian	1 in 94	1 in 35,100[a]

[a] 95% confidence interval is 13,700 to 128,000.

Pathogenesis

The CFTR protein is a chloride channel. It regulates (or channels) the flow of chloride ions and water into and out of cells. Mutations in the CFTR gene result in a defective chloride channel. As a result, various tissues don't get enough water. This causes mucus in the lining of the tissues to be unusually thick and sticky. This mucus clogs airways and ducts and causes the characteristic symptoms of CF.

Symptoms of CF

Symptoms all stem from lack of proper chloride and water balance and thick, sticky mucus.

- High salt content in the sweat
- Persistent coughing, wheezing, shortness of breath, and frequent lung infections caused by mucus in the lungs; subsequent permanent lung damage is the most common cause of death from CF[1]
- Inadequate weight gain and poor growth due to malnutrition; blocked ducts in the pancreas prevent enzymes from digesting food, leading to the malnutrition
- Meconium ileus resulting from blocked intestines
- Male infertility resulting from blocked vas deferens
- Liver disease resulting from blocked liver ducts

The genetics of CF

CF is an autosomal recessive disease. "Autosomal" means that the gene is not located on a sex chromosome. "Recessive" means that 2 mutated genes must be inherited, one from each parent, for a child to get the disease. If both parents are carriers, but not affected, each of their children has a:

- 25% chance of getting a mutated gene from both parents. In this case they have CF.
- 25% chance of getting a normal gene from both parents. In this case they do not have CF and can't pass a CF mutation to their children.
- 50% chance of getting a normal gene from one parent and a mutated gene from the other. In this case they don't have CF but can pass the CF mutation to their children.

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Not all people with CF have the same symptoms. The severity of symptoms can vary too. Symptoms can start in infancy or may not appear until years later. The symptoms each person has depend in part on which mutations they have.

Screening and diagnosis of CF

Women should be offered carrier screening before becoming pregnant. This genetic blood test helps them understand their risk for having a child with CF. If it reveals that a woman is a CF mutation carrier, her partner can then be screened. If both are carriers, they have several options. For example, they could have in vitro fertilization followed by genetic testing of the embryo. Or they could have fetal diagnosis done once they get pregnant. Women who were not screened before getting pregnant can be screened early in pregnancy. This is not optimal, since fetal diagnosis is the only option when both parents are carriers.

CF screening is a standard part of newborn screening in the United States. The immunoreactive trypsinogen (IRT) test is used for this purpose. It measures the amount of trypsinogen in blood. A positive IRT test result must be confirmed. This is because conditions other than CF can also cause the pancreas to release trypsinogen.

A genetic test or a sweat test can be used to confirm a positive IRT. The sweat test is also commonly used to diagnose CF in people who show symptoms later in life. It measures the amount of sodium chloride (salt) in the sweat. A positive result can be confirmed by a second sweat test or by genetic testing.

How the laboratory can help

Quest Diagnostics offers tests for carrier screening and diagnosis of CF. Two screens are offered. Both include the 23 mutations recommended by the American College of Medical Genetics and Genomics (ACMG) and the American Congress of Obstetricians and Gynecologists (ACOG). One screen includes a total of 32 mutations. The other, the CFvantage® Cystic Fibrosis Expanded Screen, includes 155+ mutations; it can detect more cases of CF than can the 32-mutation panel. Both are appropriate for use in all ethnicities.

Race/Ethnicity	Detection Rate for CFvantage Test, %[a]	Detection Rate for 23-Mutation Panel, %[1]
Ashkenazi Jewish	95	94
Non-Hispanic Caucasian	90	88
Hispanic	88	72
African American	78	64
Asian	53	49

[a] Based on a subset of 78 mutations detectable by the panel, including the 23 ACMG/ACOG-recommended mutations.[1,5-12]

Surviving with CF

Survival has increased dramatically in the last 60 years[3]:

- In the 1950s, most people with CF didn't live to go to the first grade.
- In 1985, the median survival was about 25 years.
- In 2007, the predicted survival was 37.4 years.

Thanks to research and earlier diagnosis and treatment, survival continues to increase.

Quick facts about CF in the United States

- More than 10 million people are CF carriers.[3]
- About 30,000 people have CF.[3]
- Nearly half the people with CF are age 18 or older.[4]
- About 1 in 3,700 people are born with CF.[3]
- About 1,000 new cases are diagnosed each year.[3]
- More than 75% of people with CF are diagnosed by age 2.[3]

References

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Several tests are offered for diagnosing CF in people with symptoms. When the familial mutation is unknown, doctors can start with 1 of the 2 screening panels. Detection of 2 mutations in a screening panel confirms a diagnosis of CF. Detection of 0 or 1 mutation can be followed up with a sequencing test that can detect more mutations. Doctors can choose between a test that sequences the entire gene and tests that sequence only part of the gene (eg, 1 or 2 exons). The latter are best when the familial mutation is known and is not part of the screening panel. That's because they cost less than the full gene sequencing test. Doctors can also choose a test that can detect deletions and duplications. These CF-related changes are less common and are not detected in the sequencing tests.

Quest also offers genetic testing for diagnosing CF in a fetus. It can be done using a specimen from amniocentesis or chorionic villus sampling. It should only be ordered when both parents have a known CF mutation. A maternal blood sample must also be available to rule out contamination from maternal cells.

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