CYSTIC FIBROSIS

GENETIC TESTING

LabCorp
Laboratory Corporation of America

What is cystic fibrosis?

Cystic fibrosis (CF) is an inherited disease that in its classic form is characterized by progressive lung damage, chronic digestive problems, decreased pancreatic function, and male infertility. It involves abnormalities in a protein, cystic fibrosis transmembrane conductance regulator (CFTR), which controls the movement of chloride (salt) and water across cell membranes, resulting in excess salt in the sweat glands and the production of abnormally thick mucus. The symptoms of cystic fibrosis are due to the thickened mucus that clogs the airways and various glands in the body.[1]

What are the symptoms of cystic fibrosis and what treatment is available?

Cystic fibrosis is a disease that varies in severity and age at presentation, even within families. Signs of CF may be visible on prenatal ultrasound but typically occur in infancy or childhood. Classic CF is characterized by lung, pancreatic, and gastrointestinal symptoms, as well as infertility and a reduced life expectancy. Some individuals may experience fewer or milder symptoms, which can include isolated male infertility.[2] Some individuals may reach adulthood and not be aware that they have the disease.[3]

Symptoms of CF may include[1,2,4]:

- Meconium ileus (intestinal blockage due to abnormallythick fetal stool) may be visible on prenatal ultrasound or detected at birth
- Salty tasting skin
- Chronic sinus and lung disease (coughing, wheezing, sinusitis, and frequent infections)
- Poor growth and weight gain
- Pancreatic insufficiency (causing diarrhea and a reduced ability to digest and absorb nutrients from food)
- Pancreatitis (inflammation of the pancreas)
- Diabetes
- Infertility in males due to congenital absence of the vas deferens (CAVD)
- Distal intestinal obstruction syndrome (intestinal blockage due to undigested material)
- Liver disease

There is no cure for cystic fibrosis. Treatment may include respiratory therapy, antibiotics, and nutritional and pancreatic enzyme supplementation. New medications are becoming available that treat the underlying protein defect. In severely affected individuals, lung transplantation may be considered.[2] The average life expectancy for individuals with classic CF is 38 years.[5]

Cystic fibrosis is included on all newborn screening panels in the United States.[6]

How is cystic fibrosis inherited?

Cystic fibrosis is an autosomal recessive disease caused by mutations in the *CFTR* gene.[1] An individual who inherits one copy of a *CFTR* gene mutation is a "carrier" and does not usually have related health problems. An individual who inherits two mutations in the *CFTR* gene, one from each parent, is expected to be affected.

If both members of a couple are carriers, the risk for having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for cystic fibrosis?

Cystic fibrosis can occur in individuals of all races and ethnicities, but it is most common in individuals of Ashkenazi (Eastern European) Jewish and Caucasian ancestry.[3] In the United States, the incidence is approximately 1 in 3500.[5]

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

How is cystic fibrosis diagnosed?

- Cystic fibrosis is included on all newborn screening panels in the United States.[6]
- Positive screening results are typically confirmed with diagnostic testing, such as a sweat chloride test.

Genetic tests for *CFTR* mutations are available and may be used to confirm a diagnosis of cystic fibrosis, identify

Estimated Carrier Frequency for Select Ethnic Groups[3]

Population	Carrier Frequency
Ashkenazi Jewish	1 in 24
Caucasian	1 in 25
Hispanic	1 in 58
African American	1 in 61
Asian American	1 in 94

carriers of *CFTR* mutations, or determine whether a developing baby (fetus) is affected.

- *CFTR* full gene sequencing is a procedure that reads the instructions (DNA) that make up the *CFTR* gene. This is a way to identify the presence of an altered *CFTR* gene in a person's cells, which may help a doctor confirm the diagnosis of cystic fibrosis.
- Duplication/deletion testing is a way to find out whether the *CFTR* gene contains mutations resulting from the presence of extra (duplicated) or missing (deleted) parts of DNA code.

Genetic tests for CF can be performed on:

- A sample of blood.
- Cells obtained by swabbing the inside of the mouth (buccal swab).
- Prenatal samples of amniotic fluid (the watery substance that surrounds a fetus) or chorionic villi (a small piece of tissue taken from the placenta).

What possible genetic test results can be reported and what do they mean?

- **Negative:** After scanning the *CFTR* gene, no detectable mutations were found. This test does not detect all possible mutations in the gene. For this reason, a negative result cannot completely rule out the presence of a gene mutation that is causing a person's symptoms.
- **Positive – Abnormal:** After scanning the *CFTR* gene, 2 mutations were found. Along with a person's signs and symptoms, a positive genetic test may confirm a diagnosis of cystic fibrosis.
- **Positive – Carrier:** After scanning the *CFTR* gene, 1 mutation was found. It is likely that this person is a carrier of cystic fibrosis. A CF carrier may benefit from genetic counseling to discuss how his/her carrier status may affect family planning and to find out whether other members of his/her family are at risk and should consider having a CF screening test.
- **Variant of unknown significance:** After scanning the *CFTR* gene, a mutation was found that has not been reported before. It is unclear if the mutation is the cause of a person's signs and symptoms. Genetic testing of family members may provide more information. If all affected family members have the same mutation, then it is likely to be linked to the inherited disorder. If some affected family members do not have the mutation, it is less likely to be linked to the disorder.

Gene sequencing test results should be combined with clinical findings and reviewed by a heath professional who specializes in medical genetics.

Where can I get more information?

If you have questions or want more information about genetic testing for cystic fibrosis, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at **www.nsgc.org**.

Other information resources include:

- Cystic fibrosis.com: **www.cysticfibrosis.com**
- Cystic Fibrosis Foundation: **www.cff.org**
- Cystic Fibrosis Research Inc.: **http://www.cfri.org/home.shtml**

Note: This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

References

1. Cystic Fibrosis Genetics Home Reference Available at: http://ghr.nlm.nih.gov/condition/cystic-fibrosis Accessed on: March 14, 2012
2. Moskowitz SM et al. Cystic fibrosis. Gene Reviews. Available at http://www.ncbi.nlm.nih.gov/books/NBK1250/. Accessed: Mar 10, 2012.
3. Update on carrier screening for cystic fibrosis. ACOG Committee Opinion Number 486. American College of Obstetrics and Gynecologists. *Obstet Gynecol.* 2011; 117: 1028-1031.
4. Zielenski J. Genotype and phenotype in cystic fibrosis. *Respiration.* 2000; 67:117-133.
5. Cystic Fibrosis Patient Registry 2010 Annual Data Report. Cystic Fibrosis Foundation.
6. National newborn screening status report: Updated 2/15/12. Available at http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf Accessed Mar 12, 2012.

LabCorp
Laboratory Corporation of America

www.LabCorp.com

Contact Us

For more information about LabCorp, the testing services we provide, and where to find a specimen collection lab near you, visit **www.labcorp.com.**