CFTR Gene and Cystic Fibrosis

Description

Cystic fibrosis (CF) is an inherited disease characterized by the buildup of thick, sticky mucus that can damage many of the organs in the body. In people with cystic fibrosis, the body produces mucus that is abnormally thick and sticky. This abnormal mucus can clog the airways, leading to severe problems with breathing and bacterial infections in the lungs. These infections cause chronic coughing, wheezing, and inflammation. **The disorder's most common signs and symptoms include progressive damage to the respiratory system and chronic digestive system problems.** Symptoms and severity vary depending on the pathogenic variants present in a person. Over time, mucus buildup and infections result in permanent lung damage, including the formation of scar tissue (fibrosis) and cysts in the lungs. Death due to complications of CF can vary from childhood well into adulthood. Cystic fibrosis used to be considered a fatal disease of childhood. With improved treatments and better ways to manage the disease, many people with cystic fibrosis now live well into adulthood. The most common cause of CF is pathogenic change(s) in the CFTR gene.

Hereditary Pancreatitis

Most people with cystic fibrosis also have digestive problems. Some affected babies have meconium ileus, a blockage of the intestine that occurs shortly after birth. **Other digestive problems result from a buildup of thick, sticky mucus in the pancreas. In people with cystic fibrosis, mucus blocks the ducts of the pancreas, reducing the production of insulin and preventing digestive enzymes from reaching the intestines to aid digestion.** Problems with digestion can lead to diarrhea, malnutrition, poor growth, and weight loss. In adolescence or adulthood, a shortage of insulin can cause a form of diabetes known as cystic fibrosis-related diabetes mellitus (CFRDM).

Congenital Bilateral Absence Of The Vas Deferens

Adults with cystic fibrosis caused by CFTR gene mutations experience health problems affecting the respiratory, digestive, and reproductive systems. **Most men with cystic fibrosis have congenital bilateral absence of the vas deferens (CBAVD),** a condition in which the tubes that carry sperm (the vas deferens) are blocked by mucus and do not develop properly. Although the testes usually develop and function normally, sperm cannot be transported through the vas deferens to become part of semen. As a result, men with this condition are unable to father children (infertile) unless they use assisted reproductive technologies.

This condition can occur alone or as a sign of cystic fibrosis. Many men with CBAVD do not have the other characteristic features of cystic fibrosis; however, some men with this condition may experience mild respiratory or digestive problems. Women with cystic fibrosis may experience complications in pregnancy.

Frequency - How Often Does Cystic Fibrosis Occur?

Cystic fibrosis is more common in the Caucasian (white) and Ashkenazi Jewish populations and less common in other ethnic groups. CF occurs in about 1 in 2,500 Caucasian newborns and 1 in 2,300 newborns of Ashkenazi Jewish descent. Cystic fibrosis is less common in other ethnic groups, with 1 in 17,000 African Americans and 1 in 31,000 Asian Americans newborns born with CF.

Normal Function of the CFTR Gene And Genetic Changes

Mutations in the CFTR gene cause cystic fibrosis. The CFTR gene provides instructions for making a protein called the cystic fibrosis transmembrane conductance regulator. This protein functions as a channel across the membrane of cells that produce mucus, sweat, saliva, tears, and digestive enzymes. The channel transports negatively charged particles called

chloride ions into and out of cells. The transport of chloride ions helps control the movement of water in tissues, which is necessary for the production of thin, freely flowing mucus. Mucus is a slippery substance that lubricates and protects the lining of the airways, digestive system, reproductive system, and other organs and tissues. The CFTR protein also regulates the function of other channels, such as those that transport positively charged particles called sodium ions across cell membranes. These channels are necessary for the normal function of organs such as the lungs and pancreas. Mutations in the CFTR gene disrupt the function of the chloride channels, preventing them from regulating the flow of chloride ions and water across cell membranes. As a result, cells that line the passageways of the lungs, pancreas, and other organs produce mucus that is unusually thick and sticky. This mucus clogs the airways and various ducts, causing the characteristic signs and symptoms of cystic fibrosis.

Other genetic and environmental factors likely influence the severity of the condition. For example, mutations in genes other than CFTR might help explain why some people with cystic fibrosis are more severely affected than others. However, most of these genetic changes have not been identified.

Pattern of Inheritance - How Is Cystic Fibrosis Inherited?

This condition is inherited in an autosomal recessive pattern. This type of inheritance requires the presence of two copies of a pathogenic variant in the gene for a person to have the genetic disease. Both parents must be carriers of a pathogenic variant in the gene in order to be at risk to have an affected child. **The child must inherit a pathogenic variant from each carrier parent in order to be affected.** If both parents are carriers, there is a 1 in 4 chance that a baby will inherit two mutated copies of the gene and be affected. The parents of an individual with an autosomal recessive condition are carriers, each carry one copy of the mutated gene, but they typically do not show symptoms of the condition.

What Does It Mean To Be A Carrier?

There are generally no signs or symptoms associated with being a carrier for CF. However, the risk to have a child affected with CF is increased, especially for certain ethnicities. Testing of reproductive partners is recommended for carriers of CF.

Carrier Rates

Ethnicity	Detection Rate	Carrier Frequency
African/African American	>99%	1 in 65
Ashkenazi Jewish	>99%	1 in 25
East Asian/South Asian/Southeast Asian	>99%	1 in 90
General Population	>99%	1 in 25
Hispanic American	>99%	1 in 46
Northern European Caucasian	>99%	1 in 25

Clinician References

OMIM [Cystic fibrosis: 219700] (http://www.ncbi.nlm.nih.gov/omim)

Gene Reviews: CFTR-related disorders (http://www.ncbi.nlm.nih.gov/books/NBK1116/)

Patient and Family Resources

Genetics Home Reference: Cystic fibrosis (http://ghr.nlm.nih.gov/)

Genetic Alliance: Cystic fibrosis (http://www.diseaseinfosearch.org/)