Cystic fibrosis (CF) is an inherited genetic condition that mainly affects the lungs. However, people with CF can also have issues that affect their digestive system, reproductive system, and other organs in the body. Mucus glands typically produces mucus to cover and protect many different organs, including the lungs. The mucus glands in people who have CF are not able to properly regulate themselves. The mucus glands in people with cystic fibrosis produce more mucus than they should, and it is abnormally thick and sticky. This thick and sticky mucus leads to breathing problems and bacterial infections in the lungs, which can lead to permanent lung damage. Because the digestive system also requires mucus, some individuals with CF will also have thick and sticky mucus that will buildup in the pancreas, causing digestive problems such as diarrhea, malnutrition, poor growth, and weight loss. Because mucus also helps the pancreas to function properly, some individuals may even develop diabetes because of poor insulin production (insulin is made in the pancreas). Most individuals who have CF are found through routine newborn screening.

There are forms of CF (called non-classic) that are not associated with the potentially severe health concerns that people with classical CF have. In men, mucus lines their vas deferens, which are the tubes that carry sperm from the testicles out of the body. Some men with non-classic CF can have a condition called congenital absence of the vas deferens (CBAVD), which is when the vas deferens are blocked by mucus and do not develop properly. Men with CBAVD are infertile without undergoing fertility treatments, but they often will not develop the lung or gastrointestinal symptoms that people with classic CF have.

Causes

We have over 20,000 different genes in the body. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *CFTR* gene makes a protein called the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The CFTR protein works as a channel to move substances called chloride ions in and out of our cells. Moving these chloride ions in and out of our cells is what helps to control the amount of water that is in our tissues. This balance is important for our body to make normal, thin mucus. The CFTR protein also works to move substances called sodium ions in and out of cells, which helps some organs in our body (like the lungs and pancreas) to function how they should.

If someone has a harmful change (called a pathogenic variant) in **both** of their *CFTR* genes (the one they got from their mom **and** the one they got from their dad), then their body is not going to make enough of the CFTR protein. If the body does not have enough CFTR protein, then the cells are not able to move chloride and sodium ions in and out of the cells like they should. This is what leads to the symptoms we associate with CF.

CF is inherited in an autosomal recessive pattern. This means an individual who has CF has inherited two non-working copies of the *CFTR* gene; the one they inherited from their mom is not working **and** the one they inherited from their dad is not working. In the case of autosomal recessive conditions, if you inherit one working *CFTR* gene from a parent and one non-working CFTR gene from a parent, you are called a 'carrier' for CF. Carriers do not have CF, and typically do not have signs or features of CF.

How common CF is depends on someone's ethnic background. It is estimated that CF affects approximately 1 in 2500 to 1 in 3500 newborns that are white, 1 in 17,000 newborns that are black, and 1 in 31,000 newborns that are of Asian descent.

Genetic Testing for CF

Genetic testing for pathogenic variants in the *CFTR* is currently available, but there are a couple different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- Full gene sequencing and rearrangement analysis: Comprehensive testing to search for all currently detectable pathogenic variants in the gene

Diagnosing CF

Many infants with cystic fibrosis will be found through routine newborn screening. Further testing to confirm if a baby has CF can be done either through genetic testing, or sweat testing. The sweat test involves using a small amount of electrical stimulation (not painful but may cause some tingling) to get the body to produce sweat. That sweat is gathered on a paper and sent to the lab, where they measure the amount of a substance called chloride that is in the sweat. If there are larger amounts of chloride in the sweat than expected, that can lead to a diagnosis of CF.

Medical Management for CF

Management of CF is a lifelong process that includes taking steps to prevent lung problems and improve weight gain. The majority of individuals with CF will require medications that will make their mucus thinner and easier to cough up, other medications to open the airway to make breathing easier, and antibiotics for frequent lung infections. In addition, some individuals affected will need Airway Clearance Therapies (ACT), which help them clear sticky, thick mucus through coughing. Those individuals with digestive system problems may require pancreatic enzymes to help digest food properly. Individuals with malnutrition

may also need a high-calorie diet and vitamin supplements for healthy growth and development. With advances in treatment and appropriate management, individuals with classic cystic fibrosis typically live into their late thirties, or longer. Individuals with CBAVD may conceive children through assisted reproductive technologies.

Click here to learn more about scheduling a genetic counseling appointment for pregnancy-related questions.

Click here to learn more about scheduling a genetic counseling appointment for infertility or preconception questions.

Click here to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

Additional Resources:

Cystic Fibrosis Foundation

GeneReviews

Genetics Home Reference

Newborn Screening and CF