

Cystic Fibrosis

Cystic fibrosis (CF) is a fatal, inherited disease found in humans and characterized by buildup of thick, sticky mucus, particularly in the respiratory and digestive tracts. The abnormally thick mucus prevents the pancreas from functioning normally; it often leads to digestive problems and chronic lung infections. Cystic fibrosis is most prevalent in Caucasian individuals, and approximately 1 in every 29 individuals in the US is a carrier for the mutated CF gene. There are an estimated 30,000 reported cystic fibrosis cases in the US, and 70,000 reported cases worldwide, although the international number is undoubtedly low due to underreporting or early deaths.

Unlike disorders such as Down Syndrome and Fetal Alcohol Syndrome, CF does not cause characteristic visible abnormalities. However, infants born with CF typically have a low birth weight, are sick, and may be diagnosed with failure to thrive. Abnormally thick and sticky mucus buildup, particularly in the respiratory tract, causes chronic lung infections that can lead to life-threatening illness. The buildup of mucus in the lungs often causes persistent coughing, wheezing, and shortness of breath. The mucus may also obstruct the pancreas, hindering the body's ability to break down food and absorb nutrients. When the pancreatic ducts are blocked, the individual may grow abnormally slowly and fail to gain weight, despite having a good appetite. Males with CF are usually sterile. While there is no cure for the disease, scientific research has made it possible to detect the disease in the early stages of development when treatments can alleviate certain symptoms.

Cystic fibrosis is an autosomal recessive disorder, meaning that it is not inherited solely from the mother or father as in sex-linked disorders. Rather, cystic fibrosis is inherited when an individual receives a mutated copy of the gene associated with cystic fibrosis from both parents. When an individual has only one copy of the mutated gene, the functional gene is able to compensate for the defect and the individual is healthy. Two parents who are carriers for the mutated gene have a twenty-five percent chance of passing the disease on to their child, a fifty percent chance that their child will be a carrier for the gene, and a twenty-five percent chance that their child with neither have CF nor carry a CF gene. The mutated gene may remain undetected in many individuals simply because they never have children with another CF carrier, and if they never have any offspring with CF, they will likely never know themselves to be carriers.

Mutations to the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene causes approximately seventy percent of cystic fibrosis cases, although its frequency varies in different ethnicities. Geneticist Lap-Chee Tsui discovered the CFTR gene in 1989 along with his team of researchers at The Hospital for Sick Children in Toronto, Canada. Tsui's interest in genetic diseases, and CF in particular, led him to seek out the underlying genetic cause for CF while analyzing the genes on human chromosome 7. Tsui and his team discovered that the gene that contains the instructions for production of the CFTR protein, when mutated, was responsible for the majority of cystic fibrosis cases.

Although the CFTR protein contains 1,480 amino acids, the most common mutation to the CFTR gene causes the deletion of a single amino acid in the CFTR protein. Certain specialized epithelial cells that generate mucus in the stomach lining, nasal cavity, and lungs have the CFTR protein in their cell membranes. The CFTR protein regulates the passage of chloride ions through a channel in the membrane that adjusts the percentage of water that these cells secrete. The deletion of the amino acid mentioned above renders these specialized skin cells unable to regulate their chloride channels properly, making the mucus they produce thick and sticky.

People with CF produce sweat with a very high salt content. Salty sweat results from the faulty CFTR protein's inability to regulate the amount of sodium ions, chloride ions, and water that leave the cell.

While most cases of cystic fibrosis result from the single amino acid deletion, well over a thousand additional mutations of the CFTR gene have been found that account for a small percentage of cystic fibrosis cases.

Adults and children can be tested to see if they carry the mutated CF gene. Genetic carrier testing analyzes a sample of the DNA from each parent via a mouth swab or blood sample that is examined for any mutations in the CF gene. Carrier testing is highly accurate, but some mutations are undetectable. Therefore, a person who tests negative for a cystic fibrosis mutation may be a carrier.

For parents that are known carriers for the disease, doctors can conduct prenatal screening such as chorionic villus sampling (CVS) or amniocentesis to determine if the fetus has the genetic disorder. Doctors perform CVS after nine weeks of pregnancy; in CVS, a tiny piece of the placenta is taken and tested for the presence of the CFTR gene, among other cystic fibrosis mutations. A doctor performs amniocentesis at approximately fifteen to twenty weeks of pregnancy. In amniocentesis, the doctor takes a small sample of the amniotic fluid surrounding the fetus. The cells there are then cultured in a lab and examined for cystic fibrosis mutations.

Cystic fibrosis has traditionally been tested in children with a sweat test, which involves sampling the sweat of an individual who might have CF in order to determine if the salt content is higher than normal. However, with the advent of genetic testing, use of the sweat test has diminished. Health professionals conduct newborn screening for CF by taking a blood sample at birth, and sometimes taking a second blood sample several weeks later. All US states test newborns for CF. Prenatal screening may also be performed as a precautionary measure when there is a known family history of the disease. Early screening allows people to live longer and improves their quality of life because it allows for earlier awareness and medical intervention.

Prior to the 1950s, individuals with CF rarely lived to attend elementary school. New advances in medicine now allow longer and higher quality lives for those with the disease and many with cystic fibrosis are currently living into their 30s and 40s. Lap-Chee Tsui's research has led to advances in cystic fibrosis science and medicine that have exposed the developmental cause of this disorder.

Sources

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