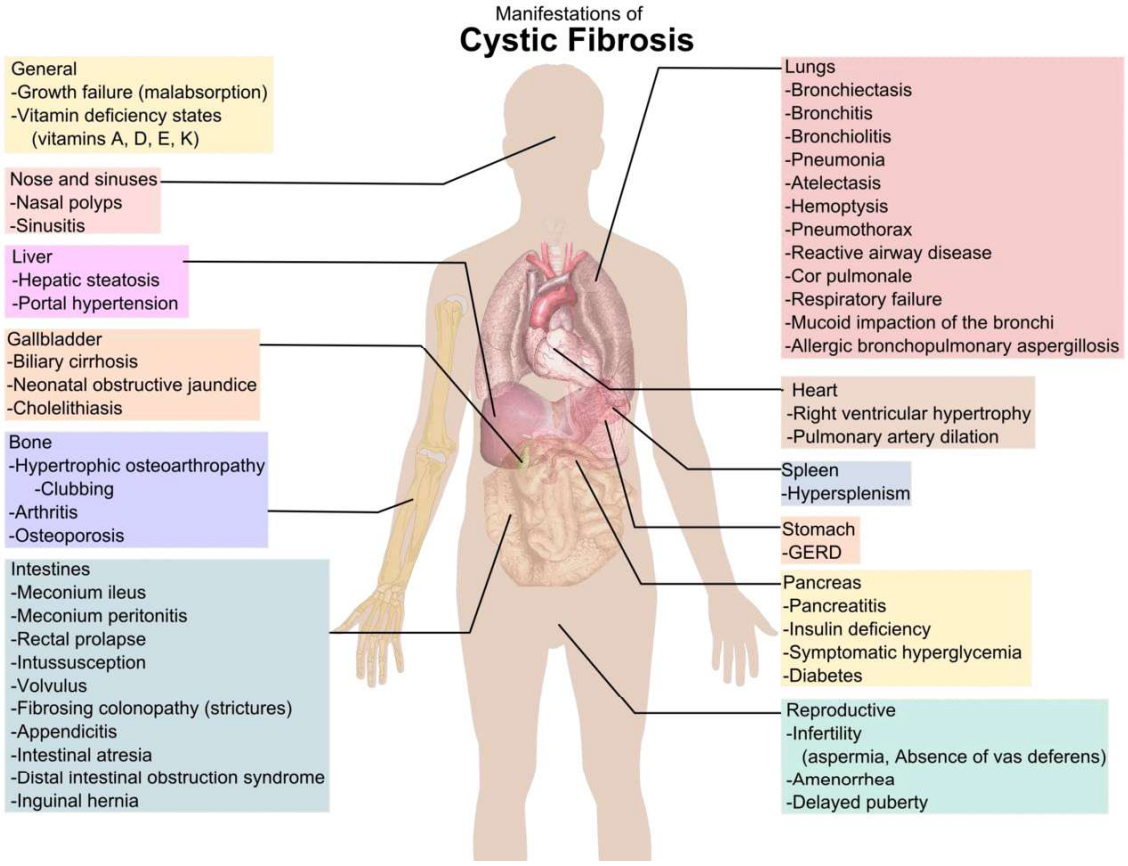
Cystic Fibrosis information sheet

Cystic fibrosis is a recessive multi-system genetic disease characterized by abnormal transport of chloride and sodium across epithelium, leading to thick, viscous secretions in the lungs, pancreas, liver, and intestine.

CF is caused by a mutation in the gene for the protein cystic fibrosis transmembrane conductance regulator (CFTR). This gene is required to regulate the components of sweat, digestive juices, and mucus. Although most people without CF have two working copies of the CFTR gene, only one is needed to prevent cystic fibrosis. CF develops when neither gene works normally and therefore has autosomal recessive inheritance.

Individuals with cystic fibrosis can be diagnosed before birth by genetic testing, or by a sweat test in early childhood. Ultimately, lung transplantation is often necessary as CF worsens.

Symptoms



Diagnosis

Cystic fibrosis may be diagnosed by many different methods including newborn screening, sweat testing, and genetic testing. As of 2016 in the United States, 62 percent of cases are diagnosed shortly after birth as part of newborn screening programs. The newborn screen initially measures for raised blood concentration of immunoreactive trypsinogen. Some states conduct a DNA test

simultaneously with the trypsinogen test. Infants with an abnormal newborn screen need a sweat test in order to confirm the CF diagnosis.

Cystic fibrosis is the most common life-limiting autosomal recessive disease among people of European heritage. In the United States, close to 40,000 individuals have CF. The median age at diagnosis for all people with CF is 4 months. Approximately 1 in 25 people of European descent and one in 30 of Caucasian Americans is a carrier of a cystic fibrosis mutation. Although technically a rare disease, cystic fibrosis is ranked as one of the most widespread life-shortening genetic diseases. It is most common among nations in the Western world. In the United States, 1 in 4000 children are born with CF. Cystic fibrosis is diagnosed in males and females equally.

Management

While there are no cures for cystic fibrosis there are several treatment methods. The management of cystic fibrosis has improved significantly over the past 70 years. While infants born with cystic fibrosis 70 years ago would have been unlikely to live beyond their first year, infants today are likely to live well into adulthood. Recent advances in the treatment of cystic fibrosis have meant that an individual with cystic fibrosis can live a fuller life less encumbered by their condition. The cornerstones of management are treatment with CFTR modulators, if eligible, proactive treatment of airway infection, and encouragement of good nutrition and an active lifestyle. Management of cystic fibrosis continues throughout a patient's life, and is aimed at maximizing organ function, and therefore quality of life. At best, current treatments delay the decline in organ function. Because of the wide variation in disease symptoms treatment typically occurs at specialist multidisciplinary centers, and is tailored to the individual. Targets for therapy are the lungs, gastrointestinal tract (including pancreatic enzyme supplements), the reproductive organs (including assisted reproductive technology (ART)) and psychological support.

The most consistent aspect of therapy in cystic fibrosis is limiting and treating the lung damage caused by thick mucus and infection, with the goal of maintaining quality of life. Intravenous, inhaled, and oral antibiotics are used to treat chronic and acute infections. Mechanical devices and inhalation medications are used to alter and clear the thickened mucus. These therapies, while effective, can be extremely time-consuming for the patient. One of the most important battles that CF patients face is finding the time to comply with prescribed treatments while balancing a normal life.

Prognosis

The improved prognosis of cystic fibrosis, combined with earlier diagnosis through screening, has already started to result in a change in attitude. Many factors will influence the prognosis of a person with cystic fibrosis. These factors include treatment compliance, efficacy of treatment, and access to health care. Life expectancy for people with CF depends largely upon access to health care. In 1959, the median age of survival of children with cystic fibrosis was six months. In the United States, the predicted median survival age for infants born in 2019 with CF is 48.4 years, based upon data compiled by the Cystic Fibrosis Foundation.

The U.S. Cystic Fibrosis Foundation compiles lifestyle information about American adults with CF. In 2020, the foundation reported that 93% had graduated from high school and 68% had at least some college education. Employment data revealed 16% of adults were disabled and 8% were

unemployed. Marital information showed that 50% of adults were single and 45% were married or living with a partner. In 2020, 619 American women with CF were pregnant.

Research and Therapies

In 2012, the U.S. Food and Drug Administration approved ivacaftor (Kalydeco) for individuals with at least one G551D mutation ages 6 and older. Today, it is approved in the U.S. to treat people with CF ages 2 and older who have one of 38 ivacaftor-responsive mutations in the CFTR gene. Ivacaftor is designed to act upon a non-functional but properly localized CFTR protein to help to open the chloride channel in CF cells. There were no safety issues in the trials and the treatment groups met the primary endpoint for improved lung function and secondary endpoints of reduced pulmonary exacerbations, increase in weight, and increase in quality-of-life measures.

In 2015, ivacaftor in combination with lumacaftor (Orkambi) was approved for individuals age 12 and older who are homozygous for the F508del mutation; in 2016, the age limit was reduced to age 6. Lumacaftor is designed to move defective CFTR protein to the proper place in the airway cell membrane and improve its function as a chloride channel.

In 2020, a combination drug with ivacaftor, tezacaftor, and elexacaftor (Trikafta) was approved for individuals age 12 and older who have at least one copy of the F508del mutation; in 2021 the approval was expanded to include children aged 6 and up. Tezacaftor and elexacaftor are both designed to correct the folding of CFTR protein.

Almost 90% of CF patients are eligible for either Kalydeco, Orkambi, or Trikafta based on their CF mutations. An unmet medical need continues to exist for the remaining 10% of the global CF population of approximately 105,000 individuals. Companies are now working towards developing novel combination therapies to address the unmet medical need in about 10% of CF patients who do not carry at least one F508del mutation, which is the most common CF-causing variant observed globally, as well as gene therapies that could address all mutations.

A comprehensive and interactive summary of all drugs either approved or in development for CF can be accessed on the CF Foundation's website at https://www.cff.org/trials/pipeline