CYSTIC FIBROSIS: A GENETIC DISEASE WITH A HIGH UNMET MEDICAL NEED

Cystic fibrosis is a life-limiting genetic disorder that reduces the flow of salt and water across cell membranes leading to the buildup of abnormally thick, sticky mucus that clogs the lungs and the pancreas. CF also affects other organs in the body including the liver, intestines, sinuses, and reproductive system.[1,2]

CF is caused by a defect in the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The CFTR protein controls the flow of salt and water into and out of the body's cells. Mutations in the *CFTR* gene can make a CFTR protein that doesn't work correctly.[5] While more than 2,000 mutations in the *CFTR* gene have been identified, most are rare. To date, only about 100 of these mutations have been confirmed to cause CF. It takes two CF-causing mutations to have CF.[3, 6] CF affects approximately 30,000 in the United States with an average incidence of only about 1,000 new cases annually.[3,4]

The median predicted age of survival for a person with CF born today is approximately 41 years, but today's median age of death remains in the late twenties.[3,4] Nationwide screening of newborns for CF has been in place since 2010. 72% of patients are diagnosed before the age of two and 97% have been tested for their genetic mutations. The *F508del* mutation is most prevalent, occurring in almost 87% of US patients with CF. Forty-seven percent of these patients have two copies of the mutation. Other mutations each have a prevalence of less than 5% (see Figure 1).[3]

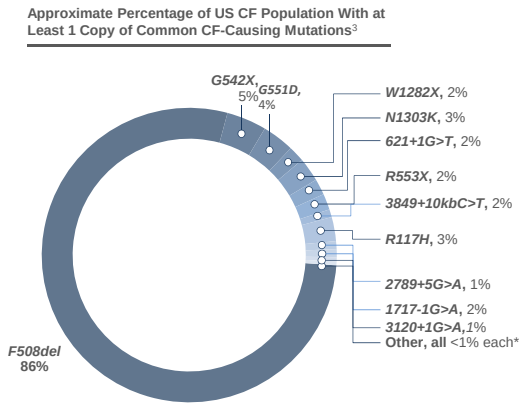

Figure 1

*Note: Due to heterozygosity, percentages are not intended to sum to 100%. Common mutations occurring in ≤1% of the CF population include *3120+1G->A, I507del, D1152H, R1162X, 3659delC, 1898+1G->A, G85E, R560T, R347P, 2184insA,R334W, A455E, Q493X, 2184delA*

CF is a progressive, life-limiting condition that can significantly impact a patient's quality of life.

The buildup of thick, sticky mucus in the lungs of a person with CF can lead to serious lung infections. This mucus also obstructs the pancreas and prevents the body's enzymes from breaking down food and aiding the absorption of vital nutrients.[1]

Acute pulmonary exacerbations are a common consequence of CF and often require hospitalizations and/or treatment with intravenous antibiotics.[7] The number of exacerbations a person with CF experiences per year increases with age. In 2013, almost 50 percent of people with CF were 18 years of age and older and in that year, adults aged 18-30 were the most likely to have at least 1 pulmonary exacerbation.[3] In 2007, approximately 30% of pediatric and 48% of adult patients experienced 1 or more exacerbations requiring hospitalization and in 2013, 35% of persons with CF required IV antibiotics to treat an exacerbation.[3,4,7]

CF patients typically visit a CF center every quarter to be followed by a team of providers that may include pulmonologists, dieticians, social workers, and respiratory/physical therapists.[3] The level of care required involves an intricate regimen of multiple medications and therapies that can take hours each day to prepare and administer.[2]

While there is no "typical" day for a patient with CF, daily treatment often includes:[8]

- Airway clearance by chest physiotherapy or chest wall oscillation for 20-30 minutes, up to 3 times a day, to help loosen and get rid of the thick mucus in the lungs
- Consumption of oral pancreatic enzymes at every meal and at snack times to help in the absorption of vital nutrients
- Use of inhaled medications that may contain antibiotics for lung health and infection control or other inhaled therapies to keep airways clear

References:

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[4] Cystic Fibrosis Foundation. CFF 2013 Annual Data Report to the Center Directors. Bethesda, MD:CFF;2014.

[5] Ratjen F, Tullis E. Chapter 46 – Cystic Fibrosis. *Clinical Respiratory Medicine (Third Edition)*. Philadelphia: Mosby: 2008:593-604.

[6] Sosnay PR, Siklosi KR, Van Goor F, et al. Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. *Nat Genet.* 2013;45(10):1160-1167.

[7]Newton TJ. Respiratory care of the hospitalized patient with cystic fibrosis. *Respir Care*, 2009:54(6):769-775.

[8]Cystic Fibrosis Foundation. Frequently asked questions. http://www.cff.org/AboutCF/Faqs/. Accessed on January 24, 2015.