Cystic fibrosis

Health & Medicine, Disease

Cystic fibrosis (CF) also known as mucoviscidosis is an inherited disease that causes the body to produce mucus that's extremely thick and sticky. The mucus in people with CF is thicker than normal because CF affects cells in the epithelium, the layer of cells that lines the passages in the body's organs. In a person who does not have CF, the epithelial cells produce a thin, watery mucus that acts like a lubricant and helps protect the body's tissues. In a person with CF, however, the thicker mucus doesn't move as easily.

This thick, sticky mucus clogs passages in many of the body's organs and infection sets in. The two organs that are most affected are the lungs and pancreas, where the thick mucus causes breathing and digestive problems (Warrell, 2003). The thicker mucus has trouble moving out of the lungs, so bacteria can remain and cause infections. The thick mucus can also be found in the pancreas — an organ that produces proteins called enzymes that flow into the intestine to support the body's digestion process.

Because the mucus can block the path between the pancreas and the intestines, people with CF have trouble digesting food and getting the vitamins and nutrients they need from it (Warrell, 2003). CF can also affect the liver, the sweat glands, and the reproductive organs (McPherson & Pincus, 2006). Cystic fibrosis is caused by mutations (changes) in a gene on chromosome 7, one of the 23 pairs of chromosomes that children inherit from their parents. Cystic fibrosis occurs because of mutations in the gene that makes a protein called CFTR (cystic fibrosis transmembrane regulator) (Warrell, 2003).

A person with CF produces abnormal CFTR protein — or no CFTR protein at all, which causes the body to make thick, sticky mucus instead of the thin, watery kind. People who are born with CF have two copies of the CF gene. In almost all people born with CF, one gene is received from each parent. This means that the parents of kids with CF are usually both CF carriers — that is, they have one normal and one defective gene — but the parents may not have CF themselves because their normal gene is able to " take over" and make the necessary CFTR protein(McPherson & Pincus, 2006).

Each child born to parents who are both CF carriers has a 1 in 4 chance of having the disease. Cystic fibrosis occurs most frequently in Caucasians of northern European descent, in whom the CF gene is most common — although people of other heritages can get the disease, too (McPherson & Pincus, 2006). People who have a close relative with CF are also more likely to carry the CF gene — approximately 12 million Americans, or 1 in every 20 people living in this country, is a CF carrier and most of them don't know it (www. cff. org).

Parents can be tested to see if they carry the CF gene, but because there are hundreds of specific CF gene mutations (not all of which are known), genetic testing for CF won't detect everyone who is carrying a CF gene. Doctors can also perform tests during pregnancy so prospective parents can find out more about the chances that their child will have CF. However, these tests also won't always detect a CF gene. Based on statistics, there is 1 in every 1600 Caucasian births and 1 in 17 000 African American births has a CF

incidence(McPherson & Pincus, 2006). Approximately 1 in every 20 Caucasians is a carrier.

Cystic Fibrosis is the #1 genetic killer of children and young adults in the United States. Also, 1 in 20 Americans - more than 12 million - is an unknowing, symptomless carrier of the disease. Whether male or female everyone is equally likely to inherit CF. Worldwide, about 70, 000 people have cystic fibrosis. Ninety percent are diagnosed before the age of 17(www. cff. org). A documented history of CF can be traced in the 1930s. Prior to that, most cases of CF were misdiagnosed as hard coughs, pneumonia or chronic bronchitis. However, people in the 18th century were already aware of what CF is.

There was a popular German saying that states, “ A child whose forehead tastes like salt when kissed will soon die. ” In 1936, A Swiss pediatrician Dr. Guido Fanconi published a paper about the disease. He called the illness “ celiac syndrome” which he noted as changes in the pancreas as observed in children. (1938) Dr. Dorothy Hansine Andersen of the Babies Hospital in New York named the disease as “ Cystic Fibrosis”. She was the first doctor to give the disease its earliest best description which she also theorized that the condition is caused by Vitamin A deficiency. During the 1940s, Drs.

Sidney Farber and Harry Shwachman changed the theories on the nature of CF. They connected the abnormal secretion of thick mucus to the disease. The idea that Vit. A deficiency is the cause was confronted by some researchers including the person who proposed the idea, Dr. Anderson. Antibiotics, particularly penicillin became part of the treatment for this

condition. In the 1950s, Dr. Paul di Sant' Agnese developed the sweat test (the standard test now used for diagnosing CF) as a result of the abnormalities in sweat electrolytes that he discovered during the heat wave in New York in during that time.

Dr. Schwachman laid the foundation for the modern way of treating CF. the treatment included proper nutrition. On the same year, Dr. Archie Norman began studies on high fat diets in treating the disease in London. In the 1960s, organizations specializing CF research were formed in this decade. These organizations were initiated by parents of children afflicted with the disease, as well as the rare patients who lived to see adulthood. (1962) the CF predicted median survival age is 10 years.

On the same year, a total of 30 Cystic Fibrosis Foundation-accredited care centers are now in operation. In 1970s, the feature for this decade was the groundwork on proper neonatal screenings. The Cystic Fibrosis Foundation in the United States also pioneered the use of the patient registry during this decade and the number of the foundation’s accredited care centers totals more than 100 in the year 1978. In the 1980s, the Cystic Fibrosis Foundation creates the Research Development Program, a network of research centers at leading universities and medical schools nationwide (USA).

In 1988, the foundation launched the Cystic Fibrosis Services Pharmacy and in the following year a team of CF foundation supportees scientists discovered the defective CF gene and its protein product (CFTR) thus opening the door to understanding the disease at its most basic level. In 1990s, CF researchers achieve “ proof of concept” that gene therapy (in the

lab dish) is possible. (1994) the Food and Drug Administration (FDA) approves Pulmozyme, which is proven to thin the tenacious, sticky mucus in the lungs - and is the first drug developed specifically for CF.

The time taken to develop Pulmozyme is less than half of the industry average. (1997) the CF Foundation establishes the Therapeutics Development Program. On the same year, the FDA approves TOBI, the first aerosolized antibiotic designed for CF, which is proven to reduce hospital stays and improve lung function. In the 21st Century, scientists supported by the Cystic Fibrosis Foundation map the entire genetic structure of the most common cause of CF lung infections-thePseudomonas aeruginosa bacterium. Researchers can identify the function of specific genes and find ways (drugs) to turn off the bad ones.

In 2002, a CF study shows azithromycin improves CF lung health. (2003) the foundation supported scientists at Structural GenomiX, Inc. determine the 3-dimensional structure of a portion of the CFTR protein, opening the door to more drug discovery opportunities. In 2004, Cystic Fibrosis Foundation Therapeutics-supported studies in Australia and at the University of North Carolina show that hypertonic saline helps clear CF mucus. It is proven to improve lung function and reduce hospital stays, and becomes a therapeutic option. (2006) the predicted median age of survival for those with CF increases from 10 to 37 years.

On the same year, VX-770, a drug in development by Vertex Pharmaceuticals with support from the CF Foundation, enters clinical trials. The drug is one of the first compounds to attack the root cause of CF, and

works at the cellular level to open chloride channels that do not function correctly in people with the disease. (2007) Vertex Pharmaceuticals selects a second potential drug known as VX-809 for development. Like VX-770, VX-809 addresses the root cause of CF, but it works by helping the defective CF protein move to its proper place in the cell.

Gilead Sciences, Inc. applies for FDA approval for its inhaled antibiotic therapy, aztreonam lysine, which has been shown to improve respiratory symptoms in CF patients. In 2008, the Foundation and Vertex Pharmaceuticals achieve a “ proof of concept,” showing that it is possible to treat the root cause of CF. During Phase 2 studies of VX-770, trial participants, all of whom carry the G551D mutation of CF, show unprecedented improvements in key signs of the disease. (2009) All 50 states and the District of Columbia now require newborns to be screened for CF.

Finally, last year 2010, VX-809, a second Vertex drug aimed at treating the basic CF defect, shows encouraging results in a Phase 2a clinical trial. More than 30 potential therapies are in the Foundation’s drug discovery and development pipeline. The more drugs in the pipeline, the greater the odds of producing successful therapies and a cure for CF. The FDA approves Cayston® (aztreonam for inhalation solution), the first inhaled antibiotic for the treatment of CF approved in more than a decade. Cayston treats Pseudomonas aeruginosa and was made possible by significant support from the Cystic Fibrosis Foundation.