

# CYSTIC FIBROSIS ADULT CARE... 2012 and Beyond

By Daniel T. Layish, MD



Cystic fibrosis (CF) is the most common fatal genetic disorder in Caucasians. It is inherited in an autosomal recessive pattern. The gene responsible for CF was discovered in 1989. Under normal circumstances, this gene codes for a chloride ion channel. In people with cystic fibrosis this protein malfunctions, or is absent. This leads to an inability to secrete water which then causes dry airway secretions and thick mucus that is difficult to expectorate. This predisposes to recurrent lung infections and bronchiectasis.

Respiratory failure causes 94 percent of all deaths from CF.

In 1970, the median predicted survival for people with cystic fibrosis was only 16 years. It is now 39 years. For people with CF born in the 1990s, the median survival is predicted to be over 40 years. At this time, there are approximately 30,000 people in the United States with cystic fibrosis, almost half are adults. This dramatic improvement in survival in CF is felt to be related to a variety of improvements in treatment (to be detailed below).

Typically, cystic fibrosis is diagnosed early in life. It is estimated that approximately 4% of patients with CF are diagnosed in adulthood. Typically, patients who are diagnosed as adults have milder lung disease and are less likely to have exocrine pancreatic insufficiency. Recently, in the state of Florida newborn screening for cystic fibrosis was instituted. This should certainly dramatically decrease the number of patients who are diagnosed as adults.

The Cystic Fibrosis Foundation recommends that people with CF receive their care in an accredited center. The Adult Cystic Fibrosis Center at the Central Florida Pulmonary Group has been accredited since 1999. It is a multidisciplinary program including pulmonologists, nurses, respiratory therapists, a dietician, and a social worker. This center is one of a minority of Adult Cystic Fibrosis Centers that are run by a private practice. Dr. Daniel Layish and Dr. Francisco Calimano are co-directors of the program, and provide care to approximately one hundred adults with CF. The program is accredited jointly with the Pediatric Cystic Fibrosis Center at Nemours, which is run by Dr. David Geller.

Patients with CF have a very complicated treatment regimen with need for airway clearance, bronchodilators, inhaled antibiotics, and aggressive nutritional support on a daily basis for maintenance. They also have periodic exacerbations which often require hospitalization for intravenous antibiotics

and more aggressive pulmonary care. *Pseudomonas aeruginosa* is the most common pathogen found in adults with cystic fibrosis. However, atypical *Mycobacterial* infections, Methicillin sensitive (and Methicillin resistant) *Staph aureus*, as well as *Aspergillus* can also be seen as well as other organisms. Many patients with cystic fibrosis require maintenance therapy with inhaled antipseudomonal antibiotics. Although azithromycin does not have direct anti-pseudomonal antibiotic efficacy, it has anti-inflammatory properties which make it an important adjunct for many CF patients in whom it is taken three times/week as part of maintenance therapy. Recombinant human DNase has become an important cornerstone in the management of CF airway clearance by decreasing sputum viscosity (by catalyzing extra cellular DNA into smaller fragments).

Cystic Fibrosis is truly a multisystem illness. Approximately 85% of patients with cystic fibrosis have exocrine pancreatic insufficiency and require enzyme supplementations with every meal and snack. Most patients with cystic fibrosis are below their ideal body weight and some adults will require gastrostomy tube placement. Fat soluble vitamin deficiency is common. Cystic fibrosis related diabetes will affect approximately 15% of all patients with cystic fibrosis who are age 35 and above. Cystic fibrosis related diabetes is felt to be related to fibrosis and destruction of the pancreas and is more common in people who have had exocrine pancreatic insufficiency. CF related diabetes has been shown to have components of insulin resistance as well as insulin deficiency. It is a unique form of diabetes, distinct from either Type I or Type II. Many patients with cystic fibrosis have chronic sinusitis and

## The acute airway exacerbation



will require sinus surgery. Osteopenia and osteoporosis are also quite prevalent in patients with cystic fibrosis due to both decreased levels of osteoblasts and increased levels of osteoclasts, as well as vitamin D deficiency.

More and more people with cystic fibrosis are themselves becoming parents. While men with cystic fibrosis are almost always infertile, new techniques may allow some men with cystic fibrosis to become biological fathers. Such techniques include microsurgical epididymal aspiration of spermatozoa with intracytoplasmic sperm injection into the oocyte. Women with cystic fibrosis who are pregnant require careful coordination of care with a high risk obstetrician. In 2000, there were 97 live births to women with CF.

Because of the time required to comply with the complex maintenance treatment regimen for patients with CF (and the increased care needs during exacerbations) it can be difficult for people with CF to maintain a steady income. This can compound the financial burden to patients with cystic fibrosis who require expensive medications. Therefore, the adult CF care center needs to be skilled at assisting patients with career planning, financial resources and disability options.

Lung transplantation has become an option for people with end-stage lung disease due to CF. In general, it is recommended to refer a patient with cystic fibrosis to a transplant center when their FEV1 gets to be below 30% of predicted. Patients with CF require bilateral lung transplant. The median survival 5 years after a lung transplant (for any cause of end stage lung disease) is about 60 percent. If anything, patients with CF tend to do better after lung transplant than those with COPD, pulmonary fibrosis, etc.

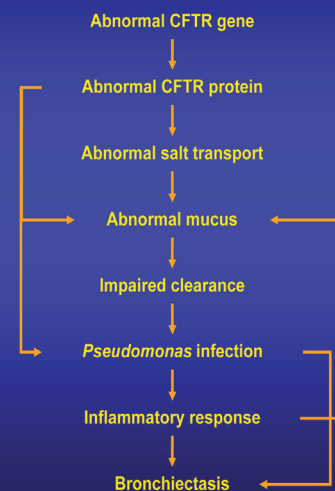
A recent exciting development in the treatment of CF involves an oral medication called Ivacaftor. The results of a randomized study on Ivacaftor were published in the *New England Journal of Medicine* in November 2011 by Dr. Bonnie Ramsey et al. The patients who received Ivacaftor were 55% less likely to have a pulmonary exacerbation than those receiving placebo, their FEV1 went up by 10.6 percent, and they gained 2.7 kg (on average). Lung function improved after 2 weeks on the medication and the results were sustained through 48 weeks. No significant adverse effects occurred with Ivacaftor. This medication may be the first in a new era in the treatment of CF with treatments chosen on the basis of genotype. Ivacaftor is a potentiator of the Cystic Fibrosis Transmembrane Regulator and the patients who received this Medication had a drop in their sweat chloride levels. Thus, Ivacaftor would be the first therapy to impact the core defect of cystic fibrosis. Currently, this medication is only known to be helpful in the approximately 4% of people with CF who carry the G551D mutation. Studies in CF patients with other genotypes are ongoing. It is hoped that this medication will be approved by the FDA later this year.

While the improved life expectancy in CF over the past twenty years has been dramatic, much work remains to be done. Research cannot stop when the average life expectancy remains only 39 years. Hopefully, we will see the day soon when CF will stand for "Cure Found."

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## Pathogenesis of Lung Disease in CF



Collins FS. *Science*. 1992.