



## Care of the Adult Patient With Cystic Fibrosis

Barbara S. Aronson  
Melissa Marquis

*Recently published consensus statements and conference proceedings from the Cystic Fibrosis Foundation provide new direction with regard to the etiology, diagnosis, and treatment of the adult patient with cystic fibrosis (CF). Survival has improved through early diagnosis and improved treatment, and aggressive management of complications. The current state of knowledge, the most recent evidence-based treatment options, and essentials of nursing care for the adult patient with CF are outlined.*

**Barbara S. Aronson, PhD(c), APRN, CS,** is an Assistant Professor, Southern Connecticut State University, New Haven, CT.

**Melissa Marquis, RN,** is a Staff Nurse, Cystic Fibrosis Inpatient Coordinator, Hartford Hospital, Hartford, CT.

Cystic fibrosis (CF) is an inherited, autosomal-recessive disease that disrupts ion transport in epithelial-lined organs. The CF gene was first discovered in 1989 and mapped to a single locus on the long arm of chromosome seven. The protein product of the CF gene has been identified as the cystic fibrosis transmembrane conductance regulator (CFTR). CFTR is involved in the transport of chloride and sodium ions across the membranes of cells in the epithelial lining of the ducts of exocrine glands (sweat glands, pancreas, liver, and reproductive systems). When the CFTR malfunctions in the patient with CF, the membrane is unable to transport electrolytes normally, leading to impaired water secretion, salty sweat, and abnormally thick exocrine secretions (Orenstein, Rosenstein, & Stern, 2000). More than 1,000 mutations have been identified on the CFTR gene, creating the innumerable variations in the clinical progression seen in this disease. Probably the most common mutation cited in research is  $\Delta$ F508, which accounts for 66% of the CF mutated alleles worldwide (Yankaskas & Knowles, 1999). This classic CF clinical phenotype

is associated with severe pancreatic insufficiency, obstructive azoospermia, and a variety of pulmonary manifestations (Davis, Drumm, & Konstan, 1996).

Once considered to be only a disease of childhood, CF is now also a disease of adults. Before 1950, the gastrointestinal, nutritional, and pulmonary complications of CF resulted in a median survival of 1 year or less (Yankaskas & Knowles, 1999). Due to a number of basic scientific discoveries and improvements in clinical care, the median survival of CF patients in 1999 rose to 29.1 years (Cystic Fibrosis Foundation Patient Registry, 1999). Adults over 18 years of age now account for more than 37% of patients with CF, and survival past the age of 76 years has been documented (Yankaskas, 2001). CF is one of the most common genetic diseases in Caucasians, with an incidence ranging from 1 in 1,900 to 1 in 3,700 in the United States (Hamosh et al., 1998; Welsh, Ramsey, Accurso, & Cutting, 2001). CF is less frequently found in Hispanic, Asian, and African-American populations (Gibson, Burns, & Ramsey, 2003).

CF is a multi-system genetic disease with a highly variable presentation and course that require comprehensive, multidisciplinary care. Some individuals with CF

**Table 1.**  
**Phenotypic Features Consistent with a Diagnosis of CF**

<p>Chronic sinopulmonary disease characterized by:</p> <ul style="list-style-type: none"> <li>• Persistent colonization/infection with typical CF pathogens (<i>S. aureus</i>, nontypeable <i>H. influenzae</i>, mucoid and nonmucoid <i>P. aeruginosa</i> and <i>B. cepacia</i>)</li> <li>• Chronic cough and sputum production</li> <li>• Persistent chest radiograph abnormalities (bronchiectasis, atelectasis, infiltrates, hyperinflation)</li> <li>• Airway obstruction manifested by wheezing and air trapping</li> <li>• Nasal polyps; X-ray or CT abnormalities of the paranasal sinuses</li> <li>• Digital clubbing</li> </ul> <p>Gastrointestinal and nutritional abnormalities</p> <ul style="list-style-type: none"> <li>• Intestinal: meconium ileus, distal intestinal obstruction syndrome, rectal prolapse</li> <li>• Pancreatic: pancreatic insufficiency, recurrent pancreatitis</li> <li>• Hepatic: chronic hepatic disease including focal biliary cirrhosis or multilobular cirrhosis</li> <li>• Nutritional: failure to thrive, hypoproteinemia and edema, fat-soluble vitamin deficiency</li> </ul> <p>Salt loss syndromes: acute salt depletion, chronic metabolic alkalosis</p> <p>Male urogenital abnormalities resulting in obstructive azoospermia</p>
--

Adapted from Rosenstein & Cutting (1998).

have severe pulmonary and/or gastrointestinal disease, while others have relatively mild disease that presents during adulthood. Outcomes range from early death as a result of pulmonary complications to mild atypical disease diagnosed in the 2nd and 3rd decades of life (National Institutes of Health [NIH], 1997).

### Diagnosing Cystic Fibrosis

In the United States, the majority (71%) of patients with CF are diagnosed by 1 year of age; however, in 8% of the patients, the diagnosis is not made until 10 years of age (Rosenstein & Cutting, 1998). CF now is being diagnosed more frequently in adolescence and adulthood. The older patient tends to have fewer complications, live longer, and have fewer hospitalizations than the individual who was diagnosed as a child (Wideman, Millner, Sexauer, & Fiel, 2000). Confirming a diagnosis early in the course of

the disease avoids unnecessary diagnostic procedures, provides an opportunity for genetic testing and counseling, and ensures access to specialized medical services (Rosenstein & Cutting, 1998).

The diagnosis of CF is suspected in a patient who has typical clinical features of the disease, including chronic sinopulmonary manifestations and exocrine pancreatic insufficiency (see Table 1). Most postpubertal males with CF also have *obstructive azoospermia*, which is sterility due to a blockage or incomplete formation of the vas deferens. The diagnosis of CF typically is confirmed by an elevated sweat chloride concentration (>60 mmol/L) on two separate occasions. In cases where sweat chloride tests are borderline or normal, or in the asymptomatic patient who is at increased risk (for example, an individual with an affected sibling or half-sibling), the diagnosis can be made by identification of CF mutations in each

CFTR gene or the *in vivo* demonstration of abnormal ion transport across nasal epithelium (Rosenstein & Cutting, 1998). In this highly specialized diagnostic test, subcutaneous skin bridges are placed in exact locations within the nasal mucosa, enabling electrical activity to be measured with a high impedance voltmeter. Laboratories performing this test must ensure that equipment is rigorously validated and the protocol for measurement is standardized so the results are reproducible across facilities (Orenstein et al., 2000).

The only acceptable procedure for sweat testing is the quantitative pilocarpine iontophoresis sweat test (Rosenstein & Cutting, 1998). In this test, sweat production is increased by the use of a small electric current carrying the drug pilocarpine. The sweat is collected and analyzed to determine sodium and chloride content; higher concentrations (>60 mmol/L) are consistent with a CF diagnosis. The patient should be told that electrodes are placed on the forearm, thigh, and the back to induce sweat production. Although the procedure does not cause pain, a tingling sensation may be experienced under the electrodes (Daniels, 2003).

Nasal and respiratory epithelia regulate the composition of fluids that surround the respiratory tract by the transport of sodium and chloride ions. The active transport of these ions generates a transepithelial electrical potential difference (PD) which can be measured. The person with CF has a characteristic pattern of abnormal ion transport in the epithelia that may be used to diagnose the disease with relative certainty. As with sweat testing, a raised PD must be duplicated on more than one occasion to confirm the diagnosis (Rosenstein & Cutting, 1998).

Two known CF mutations must be identified in the CFTR gene for the diagnosis of CF to be



confirmed by mutation analysis. The presence of mutations known to cause CF in each CFTR gene makes the diagnosis certain; due to the large number of CF alleles, however, an inability to detect mutations does not mean that the patient does not have the disease. Mutation analysis may also provide genetic information for the patient and family interested in making decisions about future pregnancies (Rosenstein & Cutting, 1998).

### Genetic Considerations

In an autosomal genetic disorder, the gene associated with the disease is not sex linked; both males and females can have the disorder. In a recessive genetic disorder, the normal gene is dominant and the defective gene is recessive, which means that a heterozygous person (with both a defective gene and a normal gene) will not have the disorder but can be a carrier and pass it to his/her children. A homozygous person (with two defective genes passed from the parents) will have the disorder. If both parents are carriers, the risk of having a child with CF is 1 in 4 (25%), regardless of what the outcome of other pregnancies has been (Orenstein, 1997).

According to the NIH Consensus Conference Statement (1997), genetic testing should be offered to adults with a positive family history of CF and to partners of people with CF planning a pregnancy or seeking prenatal testing. The statement does not currently recommend CF genetic testing for the general population or universal screening of newborn infants, although this may become the practice of the future. Genetic counseling services and educational programs should help medical personnel and the public prevent discrimination and stigmatization against patients with CF and their offspring.

### Pulmonary Characteristics of CF

Pulmonary disease is the cause of death in more than 95% of patients with CF (Yankaskas, 2001). Impaired airway mucus clearance is the primary cause of the chronic respiratory inflammation and infection seen in these patients. Once an infection is established, it is rarely eradicated; antimicrobial therapy is used to decrease bacterial load, bacterial virulence, and airway inflammation. Airway wall thickening, persistent neutrophilic infiltration, and plugging of the small and large airways with mucus, inflammatory cells, and bacteria lead to dilatation of the airways and enlarged bronchial arteries (Yankaskas & Knowles, 1999). Symptoms of lung disease progress slowly but tend to worsen during exacerbations of airway infection and inflammation. Pulmonary function, particularly forced expiratory volume (FEV<sub>1</sub>), or the volume of air that can be exhaled in 1 second, deteriorates as lung function declines; exercise tolerance decreases, and exacerbations occur with more frequency. Other late complications include pneumothorax and varying degrees of hemoptysis (Yankaskas, 2001).

### Pulmonary Treatment

The treatment of respiratory infection should be based on the identification and susceptibility patterns of all significant lower respiratory tract pathogens. Because sequential cultures often isolate different bacteria, respiratory cultures should be obtained quarterly and during each exacerbation in patients with CF (Yankaskas, 2001). Sputum cultures should be marked as coming from a patient with CF and transported to the lab within 3 hours. If the patient is unable to produce sputum, oropharyngeal swabs or a bronchoalveolar lavage may be

used to obtain a specimen (CF Foundation, 1994).

The most commonly isolated organisms in patients with CF are *Staphylococcus aureus* and *Haemophilus influenzae*. With advancing age, the mucoid variant of *Pseudomonas aeruginosa* is often dominant (Saiman & Siegel, 2003). *Pseudomonas aeruginosa* may be present in several different colonies in the sputum with different antibiotic sensitivity patterns. Other gram-negative rods that may be found in sputum of CF patients include *Burkholderia cepacia*, *Alcaligenes xylosoxidans*, *Stenotrophomonas maltophilia*, and methicillin-resistant *Staphylococcus aureus* (MRSA) (Beringer & Appleman, 2000).

Patients with cystic fibrosis are treated with antibiotics during an acute pulmonary exacerbation and often with chronic suppressive therapy during remissions. Cystic fibrosis alters the pharmacokinetics of many antibiotics, and patients often require higher doses of *B*-lactams, aminoglycosides, and sulfa drugs (Yankaskas, 2001). Oral drugs are commonly used for suppressive therapy; however, the emergence of bacterial resistance requires parenteral administration during respiratory exacerbations (see Table 2). Two antibiotics with different mechanisms of action that have efficacy against CF pathogens are used to reduce the risk of inducing resistance. Synergy testing offers a way to test the efficacy of combination antibiotics in patients who have multi-resistant organisms in their sputum (Yankaskas, Marshall, Sufian, Simon, & Rodman, 1999). Two-drug antibiotic synergy testing of multiple-resistant isolates may be obtained through a few reference laboratories in the United States.

A clinical response is often not seen for 4 to 7 days after antibiotics are started, and treatment is often needed for 10 to 14 days or

**Table 2.**  
**Typical Parenteral Antibiotic for Respiratory Exacerbations**

Bacteria in Sputum	Drug	Dose (mg)	Dose Interval/Hours	Guidelines for Administration/Toxicity
<i>S. aureus</i> and <i>H. influenzae</i>	Methicillin and Tobramycin (Nebcin®)	200	6	Dilute to < 20 mg/ml for infusion
		10 mg/kg/day	8 or 12	Titrate to peak serum 10-12 mEq/ml Potential for ototoxicity/nephrotoxicity
<i>S. aureus</i>	Cefazolin (Ancef®)	1,000	12	
<i>S. aureus</i> (MRSA)	Vancomycin (Vancocin®)	1,000	12	Infuse over 90 minutes to minimize "red-man" reaction Potential for nephrotoxicity/ototoxicity
<i>S. aureus</i> and <i>P. aeruginosa</i>	Tobramycin (Nebcin®) and Ceftazidime (Fortaz®) or Ticarcillin-clavulanate (Timentin®) or Imipenem-cislatatin (Primaxin®) or Peperacillin (Zosyn®) or Aztreonam (Azactam®)	10 mg/kg/day	8 or 12	Once daily dosing may increase toxicity
		2,000	8	Infuse over 5 minutes
		3,000	6	Platelet dysfunction possible
		500-1,000	6	Doses > 4 gm cause nausea/vomiting
		4,000	6	
2,000	8	Major indication in penicillin allergy		
<i>P. aeruginosa</i>	Tobramycin and <i>B</i> -lactam (above) or Ciprofloxacin (Cipro®)	As above	As above	As above
		As above	As above	As above
		400	12	Interferes with theophylline metabolism
<i>B. cepacia</i>	TMP/SMX (Septra®) and Chloramphenicol (Chloromycetin®)	5 mg/kg (TMP)	6	Potential for nephrotoxicity/hepatotoxicity
		15 mg/kg	6	Neutropenia, photosensitivity Monitor serum levels, can cause leukopenia

Adapted from Yankaskas (2001).

longer (CF Foundation, 1994). Although oral drugs are sometimes used for suppressive therapy, the emergence of bacterial resistance requires parenteral administration during respiratory exacerbations. Multiple routes may be used at the same time to enhance antimicrobial eradication. For example, tobramycin (Tobi®) may be given by inhalation to achieve the desired concentration in large airways and intravenously to reach peripheral air-

ways that are blocked by secretions (Yankaskas, 2001). Aerosol administration of antibiotics is frequently used in CF because drugs can be directly delivered to the site of infection, enabling smaller doses to be given and thus reducing systemic toxicity (Yankaskas, 2001). Serum peak and trough levels are monitored carefully in patients with CF to ensure optimum serum concentrations of aminoglycosides and to help prevent toxicities.

Airway clearance is an essen-

tial component of treatment for all patients with CF. Airway secretions obstruct airflow and impair gas exchange, and contain a number of mediators that contribute to the inflammatory process. Chest percussion with postural drainage, percussion/vibration techniques, breathing exercises, and directed cough techniques have been the mainstay of treatments for decades (Yankaskas & Knowles, 1999). As adjuncts to standard therapies, the following

are also used: the flutter valve, autogenic drainage (AD), forced expiration technique positive expiratory pressure mask (PEP), and high-frequency chest compression (vest) (see Table 3). These therapies are used most commonly in combination, depending on individual patient benefit and preference. The newer techniques do not require the assistance of another person, a distinct advantage for adult patients who wish to live alone or remain independent.

### Other Therapies

Bronchodilators, especially beta-adrenergic agonists and anticholinergics, are used to treat airway hyperactivity and to reverse bronchospasm. Aerosolized solutions such as normal saline, hypertonic saline (3%-12%), or oral mucolytic agents may be used to add liquid to the airways and hydrate secretions. DNA is present in large concentrations in the sputum of patients with CF due to persistent neutrophil influx into the airways as a component of the chronic inflammatory response. Recombinant human Dnase (rhDNase/Pulmozyme®) reduces viscosity of secretions and enhances airway clearance by lysing the extracellular DNA. Although this drug is usually most effective when administered once daily, some patients may require less or more frequent dosing (Orenstein et al., 2000). Hoarseness, voice alterations, and pharyngitis are the major adverse events reported with Dnase; however, these effects are usually self-limiting and do not generally require cessation of the drug (Yankaskas et al., 1999). Other aerosolized therapies are aimed at correcting the fluid and electrolyte imbalance on the mucosal surface of the airway.

The anti-inflammatory drug ibuprofen (Motrin®) can reduce

**Table 3.**  
**Newer Airway Clearance Techniques**

Positive expiratory pressure (PEP)	Series of breaths through a fixed orifice to provide backpressures which help maintain open airways and promote collateral ventilation; this exercise is commonly followed by huffing and coughing.
Active cycle of breathing techniques (ACTB)	Uses low and high-volume huffs interspersed with breathing control. May be done in postural drainage positions.
Autogenic drainage (AD)	Method of controlled breathing in which volume is varied to mobilize secretions from all generations of airways. May also be done passively by varying manually applied extrathoracic pressure.
Oscillating PEP	PEP pressures oscillate at high frequency to promote vibration of airway walls, which loosens secretions; examples include flutter valve, acapella valve.
High frequency chest compression (HFCC)	Applied by a vest through which oscillating airflow creates vibration of the chest wall at varying frequencies and intensities; for example, Therivest®.
Intrapulmonary percussive ventilator (IPV)	Creates crusts of airflow via a mouthpiece at high frequencies to provide a percussive effect within the airways.

Adapted from Lapin & Lapin (2003).

the rate of deterioration in CF respiratory disease in younger patients with mild disease (Yankaskas, 2001). Routine use of corticosteroids in the CF population is not recommended because of unacceptable long-term and short-term side effects; however, they are often used in late-stage disease or during severe respiratory exacerbations to reduce inflammatory airway edema (Yankaskas et al., 1999). Chronic use of alternate-day systemic steroids appears to slow the decline in lung function over time but causes significant toxicity, especially growth retardation, hyperglycemia, and cataract formation (Gibson et al., 2003). Inhaled steroids have the potential to reduce inflammation with-

out significant systemic adverse effects and are widely used in CF, although their efficacy has not been substantiated. CF patients with bronchial hyperresponsiveness may obtain some benefit from inhaled steroids (Gibson et al., 2003).

### Infection Control

In 1999, a multidisciplinary committee with expertise in CF reviewed the relevant literature and developed evidence-based infection control recommendations for patients with CF (Saiman & Siegel, 2003). These guidelines incorporated previously published Healthcare Infection Control Practices Advisory Committee/Centers for Disease Control guide-

lines for preventing health care-associated infections and include recommendations developed by the committee that are specific to patients with CF. They are summarized below.

Standard precautions must be applied to all patients. In addition, transmission-based precautions (contact, droplet, or airborne) must be applied to all patients with documented or suspected infection with highly transmissible or epidemiologically infectious bacteria (for example, *B. cepacia* complex, multidrug-resistant *P. aeruginosa*, MRSA, or *Mycobacterium tuberculosis*). Bacterial pathogens in CF are spread by direct contact, indirect contact, or droplet infection, and health care workers should assume that all patients with CF could have transmissible pathogens in their respiratory secretions (Saiman & Seigel, 2003).

When hands are visibly dirty or soiled with blood, body fluids, or respiratory secretions, they should be washed with an antimicrobial soap and water. Alcohol-based antiseptic hand rubs are now recommended when hands are not visibly soiled with blood or body fluids (Saiman & Seigel, 2003). Hand hygiene should be performed after removing gloves, and before and after contact with any patient (CF or non-CF). Health care workers should wear gloves when caring for patients who require contact precautions and when handling respiratory secretions or objects contaminated with respiratory secretions. Gowns should be worn when caring for patients who require contact precautions or when soiling with respiratory secretions is anticipated (for example, during chest physiotherapy or suctioning). Mask and eye protection or a face shield should be worn when splashes or sprays of secretions, body fluids, blood, or excretions are anticipated. All patients with CF who are

infected or colonized with *B. cepacia* complex, MRSA, or vancomycin-resistant enterococcus (VRE) should be placed in private rooms that do not share common facilities (such as bathroom or shower). Other patients with CF may share rooms with patients without CF who are at low risk for infection (Saiman & Siegel, 2003).

Sources of transmission that have been implicated in hospital outbreaks of CF-related pathogens include contaminated respiratory therapy equipment, multi-dose vials, home nebulizers, and tap water (Saiman, 2001). General guidelines to prevent transmission of these organisms include placing the patient with CF in a private room, rinsing respiratory therapy equipment in sterile water after disinfecting, assuring that all respiratory therapy occurs inside a patient's room, asking the patient to bring personal airway clearance devices from home, and using single-dose vials for aerosol medications.

Families, visitors, and patients should be taught to wash their hands correctly before leaving the patient's room. The patient should contain respiratory secretions in a tissue when coughing to prevent possible contamination of exposed surfaces. The patient with CF needs to know the possible risks of close contact with other CF patients in nonhospitalized settings. Behaviors that increase risk include physical intimacy, assisting with another CF patient's respiratory treatment, sharing personal items, being in a hot tub or whirlpool together, and sharing poorly ventilated areas (for example, bus or airplane). The patient with CF should also be warned to avoid areas where building construction or renovation is occurring due to high *aspergillus* exposure (Saiman, 2001).

### Cystic Fibrosis-Related Diabetes

A frequent complication of CF is glucose intolerance and cystic fibrosis-related diabetes (CFRD), which occurs in approximately 20% to 30% of patients over the age of 20. CFRD is rarely found in children, but occurs more frequently with advancing age (Rodman, 2001). The diagnosis of CFRD is associated with worse pulmonary disease, earlier death, and poorer nutritional status (CF Foundation, 1999a). CFRD shares some characteristics of both Type 1 and Type 2 diabetes, but it has recently been recognized as a separate disease because of features that are unique to the CF population. Although the primary cause of CFRD is insulin deficiency, glucose metabolism is also impaired (Rodman, 2001).

Four different glucose tolerance categories are currently recognized in CF (see Table 4) (CF Foundation, 1999a). In CFRD with hyperglycemia, both the fasting glucose and the postprandial blood sugar are high. CFRD with hyperglycemia is treated aggressively with insulin and nutritional therapy, although the principles of treatment differ from those of either Type 1 or Type 2 diabetes (Yankaskas et al., 1999). In CFRD without hyperglycemia, only the postprandial blood sugar is elevated; this form of diabetes is considered a mild disease and generally not treated unless symptoms are present. The patient with CFRD without hyperglycemia should be told insulin is needed during periods of illness or treatment with corticosteroids, and in the future if fasting hyperglycemia develops (Hardin, Brunzell, Schissel, Schindler, & Moran, 1999).

Cystic fibrosis-related diabetes has an insidious onset and a characteristic pattern of intermittent hyperglycemia between periods of normoglycemia. Although

