Cystic Fibrosis

Description/Etiology
Cystic fibrosis (CF) is a fatal, autosomal recessive, multisystem disorder that is characterized by exocrine gland dysfunction. CF results from a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which is located on chromosome 7 and regulates the flow of chloride ions across the membranes of cells that produce mucus, sweat, saliva, tears, and digestive enzymes. The mutation results in abnormal secretions and thick mucus that obstruct glands and ducts, which damages tissues and severely impairs the pulmonary, gastrointestinal, endocrine/metabolic, and reproductive systems.

Diagnosis of CF requires a positive quantitative pilocarpine iontophoresis (commonly called a sweat chloride test) or positive genetic testing, along with one of the following: typical chronic obstructive pulmonary disease, documented exocrine pancreatic insufficiency, and documented CF in a sibling or first cousin. CF should be differentiated from asthma, pneumonia, celiac disease, immunodeficiency states, and bronchiectasis.

Although the onset, pattern of signs and symptoms, and progression of CF vary, respiratory failure is the cause of death in 90% of patients. Adolescents with CF are typically thinner and shorter than others in their age group. The thick mucus produced in the lungs of patients with CF inhibits clearance of bacteria and results in recurrent, persistent lung infections with pathogens such as Pseudomonas aeruginosa and Staphylococcus aureus.

Treatment is primarily supportive, including pharmacotherapy, physical therapy, respiratory therapy, and education about the importance of exercise and good nutrition. Liver, pancreas, or lung transplantation can be attempted in some cases of severe CF. CFTR modulators are a newer group of medications that can improve lung function in patients with certain CF-causing mutations. Patients with CF caused by any of nine specific mutations in the CFTR gene (i.e., G551D, G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D) can be treated with the CFTR potentiator ivacaftor (Kalydeco); the drug is approved for use in patients ≥ 2 years of age to decrease the frequency of pulmonary exacerbations and improve lung function. Orkambi, which combines ivacaftor with the CFTR corrector lumacaftor can be used to treat patients with CF who are ≥ 12 years of age and are homozygous for the F508del mutation. Symdeko combines ivacaftor with the CFTR corrector tezacaftor and is approved for use in patients ≥ 12 years of age who are homozygous for the F508del mutation or who have at least one CFTR mutation shown to be responsive to the drug combination. Current mutation classifications from the Clinical and Functional Translation of CFTR Project can be found at https://cftr2.org/.

Facts and Figures
CF is the most common lethal genetic disease in Whites in the United States, affecting 1 in 3,200–3,500 Whites of Northern European origin, 1 in 15,000–17,000 Blacks, 1 in 9,200–9,500 Hispanics, and 1 in 31,000 Asian Americans. About 5% of Whites are carriers of a mutated CFTR gene. More than 1,800 CF-causing mutations of the CFTR gene have been identified.

The Cystic Fibrosis Foundation Patient Registry 2017 Annual Data Report includes the following information regarding CF in the U.S. in 2017:
29,887 persons in the U.S. were living with CF; 880 were newly diagnosed, with 58% of these cases detected by newborn screening. The mean age at diagnosis was 3 years. The median age of all persons with CF was 19.3 years. 12% of children and 35% of adults with CF had CF-related diabetes (CFRD). 53% of eligible patients were receiving CFTR modulators. 46% and 26% of patients tested positive for *P. aeruginosa* and methicillin-resistant *S. aureus* (MRSA) lung infections, respectively. 43% of adults and 24% of children received IV antibiotics for treatment of pulmonary exacerbations. The predicted median survival among patients with CF born during the period 2013–2017 is 44 years. 269 patients received organ transplants, including 250 lung, 11 liver, and eight kidney transplants.

**Risk Factors**
The primary risk factor for development of CF is family history. A child born to parents who are both carriers has a 25% chance of developing CF and a 50% chance of becoming a carrier.

**Signs and Symptoms/Clinical Presentation**
Signs and symptoms of CF include meconium ileus in newborns; increased anterior/posterior chest diameter; digital clubbing; dry or productive cough; wheezing; constipation; abdominal distention; foul-smelling, fatty stools; decreased weight gain and growth; recurrent pneumonia and bronchitis; and bloody sputum.

**Assessment**

**Patient History**
• Ask about patient and family medical history, including family incidence of CF

**Physical Findings**
• Respiratory: thick secretions, dyspnea, tachypnea, nasal polyps, signs of respiratory failure, pneumothorax, cyanosis, bronchiectasis, emphysema
• Gastrointestinal: pancreatitis, ulcers, gastroesophageal reflux, bowel obstruction, rectal prolapse, gallstones, enlarged liver and spleen, malabsorption, biliary cirrhosis
• Reproductive: infertility, undescended testicles or hydrocele in males, amenorrhea in females
• Endocrine/metabolic: ↑ salty sweat; electrolyte imbalance; ↓ levels of vitamins A, D, E, and K; metabolic alkalosis

**Laboratory Tests**
• Sweat test showing ↑ Na and ↑ Cl > 60 mmol/L in children and > 80 mmol/L in adults confirms the CF diagnosis
• Sputum culture and Gram stain can detect bacteria responsible for recurrent infection
• Liver function tests might show ↑ alanine transaminase (ALT) and ↑ aspartate transaminase (AST), indicating liver dysfunction
• Stool 72-hour fecal fat test might identify ↑ fat and ↓ albumin levels
• ABGs might show ↓ PaCO₂
• Genetic screening/DNA testing confirms the diagnosis and identifies carriers of CF
• Newborns with suspected CF are tested by immunoreactive trypsinogen assay (IRT)

**Other Diagnostic Tests/Studies**
• Pulmonary function tests can show abnormalities in lungs, forced vital capacity (FVC), and pulmonary diffusing capacities; pulmonary function tests are routinely performed with an exercise challenge test 2–3 times/year in patients with CF
• Chest X-ray and CT scan can show hyperinflation, unexpanded lungs, hyperaeration, bronchiectasis, bronchial wall thickening, and cystic lesions

**Treatment Goals**

**Promote Optimal Respiratory Status and Reduce Risk of Related Complications**
• Assist with resuscitation for patients who are in respiratory failure and assess patient status, including taking vital signs, evaluating all physiologic systems (especially pulmonary, gastrointestinal, and endocrine/metabolic), and reviewing laboratory/other diagnostic results
• Administer prescribed bronchodilator (e.g., inhaled beta2-agonistsalbuterol and ipratropium) to decrease airflow obstruction; provide supplemental oxygen if < 90%
• Administer nebulized hypertonic saline or recombinant human deoxyribonuclease (DNase [Dornase alpha]), as ordered, to thin airway mucus
• Administer prescribed oral corticosteroids and NSAIDs to improve pulmonary function. When given to children, corticosteroids are given on alternating days to reduce risk for impaired growth
• Administer a CFTR modulator, if prescribed
• Monitor for signs and symptoms of respiratory infection and note characteristics of sputum; administer antibiotics to treat respiratory tract infection that are prescribed in increased doses and for longer periods of time compared with those ordered for persons without CF
  – Oral antibiotics include ciprofloxacin, cephalexin, and tetracycline
  – Aerosolized antibiotics include intermittent use of tobramycin
  – IV antibiotics include oxacillin, ticarcillin, and clavulanic acid
• Request referral to physical therapy as appropriate and to respiratory therapy for patient evaluation and treatment with chest physiotherapy to loosen secretions and sputum using standard percussion and postural drainage techniques and teaching “huffing” (i.e., forced expiration)

Promote Optimal Gastrointestinal and Metabolic Status and Reduce Risk of Complications
• Monitor appetite, food intake, and growth; request referral to a registered dietitian for patient evaluation and patient/family education about nutrition. Provide pancreatic enzyme supplements with meals/snacks (for more information, see Evidence-Based Care Sheet: Cystic Fibrosis: Nutritional Management)
• Monitor for dehydration and increased water intake; administer prescribed salt supplements
• Administer prescribed insulin for patients who have CFRD
• Administer prescribed enema (e.g., barium enemas for meconium ileus in newborns, diatrizoate sodium or GoLYTELY/NG for adults), as appropriate
• Monitor for abdominal pain and constipation and monitor color, frequency, and consistency of stools
• Follow facility pre- and postsurgical protocols if patient becomes a candidate for surgery (e.g., for resolution of meconium ileus in newborns: for liver, pancreas, or lung transplantation); reinforce pre- and postsurgical education and verify completion of facility informed consent documents

Promote Emotional Well-Being and Educate
• Assess patient (as age-appropriate)/parent anxiety level and coping ability; provide emotional support and educate about CF pathophysiology, potential complications, treatment risks and benefits, and individualized prognosis; request referral to a mental health clinician for counseling and a social worker for identification of support groups and other CF services, as appropriate
• For pediatric patients, follow facility protocols regarding parental involvement in patient care and rooming-in
• Educate about the importance of regular exercise (e.g., jogging, swimming) and good nutrition to improve breathing and maintain ideal weight

Food for Thought
• Regular exercise reduces the rate of lung decline and improves QOL in patients with CF
• Although infertility is common in both men and women with CF, advances in the management of CF have led to a significant increase in lifespan such that an increasing number of patients with CF are likely to consider parenthood. Successful pregnancies in women with CF require special attention to managing nutrition, airway clearance, and treatment of respiratory infections
• CFRD is a complex disorder that is distinct from diabetes mellitus, type 1 (DM1) and diabetes mellitus, type 2 (DM2). Its onset is insidious and not associated with an autoimmune process; it is characterized by severe, but not complete, insulin deficiency and somewhat decreased insulin sensitivity. Although it is associated with microvascular complications, it is not associated with macrovascular complications. Insulin is the treatment of choice; oral medications are not effective

Red Flags
• Risk of developing colorectal cancer (CRC) is increased 5–10-fold in adults with CF and 25–30-fold in adults with CF who have received an organ transplant
  • CRC screening via colonoscopy with CF-specific bowel preparation should begin at 40 years in adults with CF.
    Patients older than 30 years of age who receive a solid organ transplant should begin CRC screening within 2 years of transplantation (Hadjiliadis et al., 2018)
• In patients with CF, respiratory viruses, including those that cause influenza, can result in lung function decline and even risk of death
What Do I Need to Tell the Patient/Patient’s Family?

› Educate about the prescribed treatment regimen (e.g., chest physiotherapy, breathing treatments, and proper use of medication), strategies for preventing infection (including routine vaccinations [e.g., seasonal influenza]), and dietary and exercise requirements

› Promote a regular schedule of meal and snack times, particularly for children

› Emphasize the value of independence for older children and adolescents with CF and educate that participation in school and exercise activities is important. Educate to avoid smoking, use of recreational drugs, and alcohol

› Encourage women with CF who are planning to conceive to receive genetic counseling and testing. Educate that all fifty states now require CF screening for newborns

› Educate that more information can be obtained through the Cystic Fibrosis Foundation at https://www.cff.org/

References


