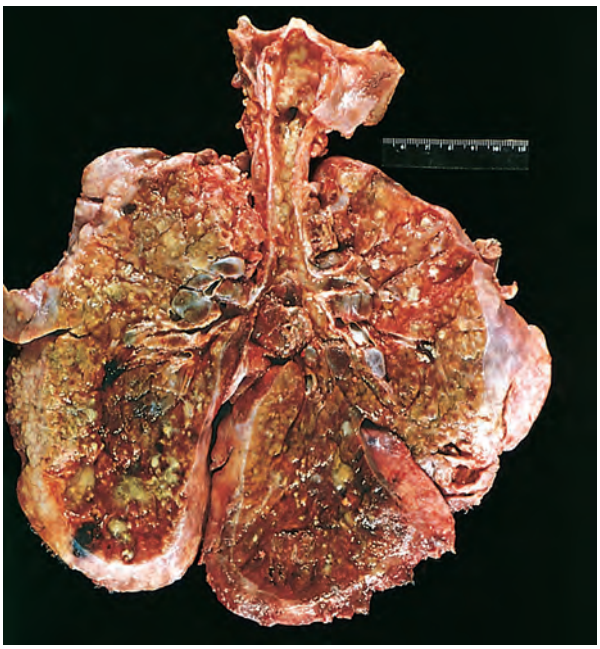

Figure 10-21 Lungs of a patient dying of cystic fibrosis. There is extensive mucus plugging and dilation of the tracheobronchial tree. The pulmonary parenchyma is consolidated by a combination of both secretions and pneumonia—the green color associated with *Pseudomonas* infections. (Courtesy Dr. Eduardo Yunis, Children's Hospital of Pittsburgh, Pittsburgh, Pa.)

the mucus-secreting cells. Superimposed infections give rise to severe chronic bronchitis and bronchiectasis (Chapter 15). In many instances, lung abscesses develop. *Staphylococcus aureus*, *Haemophilus influenzae*, and *Pseudomonas aeruginosa* are the three most common organisms responsible for lung infections. As mentioned earlier, a mucoid form of *P. aeruginosa* (alginate-producing) is particularly frequent and causes chronic inflammation. Even more sinister is the increasing frequency of infection with another group of pseudomonads, the *Burkholderia cepacia* complex, which includes at least nine different species; of these, infections with *B. cenocepacia* are the most common in cystic fibrosis patients. This opportunistic bacterium is particularly hardy, and infection with this organism has been associated with fulminant illness ("cepacia syndrome"), longer hospital stays, and increased mortality. Other opportunistic bacterial pathogens include *Stenotrophomonas maltophilia* and *nontuberculous mycobacteria*; *allergic bronchopulmonary aspergillosis* also occurs with increased frequency in cystic fibrosis.

Azoospermia and infertility are found in 95% of the males who survive to adulthood; **congenital bilateral absence of the vas deferens** is a frequent finding in these patients. In some males, bilateral absence of the vas deferens may be the only feature suggestive of an underlying *CFTR* mutation.

Clinical Features. Few childhood diseases are as protean as cystic fibrosis in clinical manifestations (Table 10-5). The symptoms are extremely varied and may appear at birth to years later, and involve one organ system or many. Approximately 5% to 10% of the cases come to clinical attention at birth or soon after because of *meconium ileus.* Distal intestinal obstruction can also occur in older individuals, manifesting as recurrent episodes of right lower quadrant pain sometimes associated with a palpable mass of meconium, with or without associated intussusception, in the right iliac fossa.

Exocrine pancreatic insufficiency occurs in the majority (85% to 90%) of patients with cystic fibrosis and is associated with "severe" *CFTR* mutations on *both* alleles (e.g., *ΔF508/ΔF508*), whereas 10% to 15% of patients with one "severe" and one "mild" *CFTR* mutation *(ΔF508/R117H)* or two "mild" *CFTR* mutations retain enough pancreatic exocrine function so as not to require enzyme supplementation (*pancreas-sufficient* phenotype). Pancreatic insufficiency is associated with protein and fat malabsorption and increased fecal loss. Manifestations of malabsorption (e.g., large, foul-smelling stools, abdominal distention, and poor weight gain) may appear during the first year of life. The faulty fat absorption may induce deficiency of the fat-soluble vitamins, resulting in manifestations of avitaminosis A, D, or K. Hypoproteinemia may be severe enough to cause generalized edema. Persistent diarrhea may result in rectal prolapse in up to 10% of children with this disease. The *pancreas-sufficient* phenotype is usually not associated with other gastrointestinal complications, and in general, these individuals demonstrate excellent growth and development. A subset of patients with pancreas-sufficient cystic fibrosis have recurrent bouts of pancreatitis associated with acute abdominal pain and

Table 10-5 Clinical Features and Diagnostic Criteria for Cystic Fibrosis

Clinical Features of Cystic Fibrosis
1. *Chronic sinopulmonary disease manifested by*
a. Persistent colonization/infection with typical cystic fibrosis pathogens, including *Staphylococcus aureus*, nontypeable *Haemophilus influenzae*, mucoid and nonmucoid *Pseudomonas aeruginosa, Burkholderia cepacia*
b. Chronic cough and sputum production
c. Persistent chest radiograph abnormalities (e.g., bronchiectasis, atelectasis, infiltrates, hyperinflation)
d. Airway obstruction manifested by wheezing and air trapping
e. Nasal polyps; radiographic or computed tomographic abnormalities of paranasal sinuses
f. Digital clubbing
2. *Gastrointestinal and nutritional abnormalities, including*
a. Intestinal: meconium ileus, distal intestinal obstruction syndrome, rectal prolapse
b. Pancreatic: pancreatic insufficiency, recurrent acute pancreatitis, chronic pancreatitis
c. Hepatic: chronic hepatic disease manifested by clinical or histologic evidence of focal biliary cirrhosis, or multilobular cirrhosis, prolonged neonatal jaundice
d. Nutritional: failure to thrive (protein-calorie malnutrition), hypoproteinemia, edema, complications secondary to fat-soluble vitamin deficiency
3. *Salt-loss syndromes: acute salt depletion, chronic metabolic alkalosis*
4. *Male urogenital abnormalities resulting in obstructive azoospermia (congenital bilateral absence of vas deferens)*
Criteria for Diagnosis of Cystic Fibrosis
One or more characteristic phenotypic features, OR a history of cystic fibrosis in a sibling, OR a positive newborn screening test result
AND
An increased sweat chloride concentration on two or more occasions OR identification of two cystic fibrosis mutations, OR demonstration of abnormal epithelial nasal ion transport

Adapted with permission from Rosenstein BJ, Cutting GR: The diagnosis of cystic fibrosis: a consensus statement. J Pediatr 132:589, 1998.