

Radiographic evidence of sinusitis occurs in most patients with CF and is associated with organisms similar to those recovered from lower airways, suggesting the sinus may serve as a reservoir for bacterial seeding.

■ PATHOGENESIS

Cystic Fibrosis Transmembrane Conductance Regulator CFTR is an integral membrane protein that functions as an epithelial anion channel. The ~1480-amino-acid molecule encodes a passive conduit for chloride and bicarbonate transport across plasma membranes of epithelial tissues, with direction of ion flow dependent on the electrochemical driving force. Gating of CFTR involves conformational cycling between an open and closed configuration and is augmented by hydrolysis of adenosine triphosphate (ATP). Anion flux mediated by CFTR does not involve active transport against a concentration gradient but utilizes the energy provided from ATP hydrolysis as a central feature of ion channel mechanochemistry and gating.

CFTR is situated in the apical plasma membranes of acinar and other epithelial cells where it regulates the amount and composition of secretion by exocrine glands. In numerous epithelia, chloride and bicarbonate release via CFTR is followed passively by flow of water through other pathways, aiding mobilization and clearance of exocrine products. Along respiratory mucosa, CFTR is necessary to provide sufficient depth of the periciliary fluid layer (PCL), allowing normal ciliary extension and mucociliary transport. CFTR-deficient airway cells exhibit depleted PCL, causing ciliary collapse and failure to clear overlying mucus ([Video 291-1](#)). In airway submucosal glands, CFTR is expressed in acini and may participate both in the formation of mucus and extrusion of glandular secretion onto the airway surface ([Fig. 291-1](#)). In other exocrine glands characterized by abrogated mucus transport (e.g., pancreatic acini and ducts, as well as bile canaliculi, and intestinal secretions), similar pathogenic mechanisms have been implicated. In these tissues, a driving force for apical chloride and/or bicarbonate secretion is believed to promote CFTR-mediated fluid and electrolyte release into the lumen, which confers proper rheology of mucins and other exocrine