Gastrointestinal, Pancreatic, and Hepatobiliary Manifestations of Cystic Fibrosis

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KEYWORDS

- CF and GI manifestations • CF pancreas • CFLD (CF liver disease)
- PERT (pancreatic enzyme replacement therapy)

KEY POINTS

- Gastrointestinal (GI) and hepatic manifestations of cystic fibrosis (CF) deserve special attention, as essentially all patients with CF will experience at least one such complaint during their lifetime.
- GI, pancreatic, and hepatic manifestations of CF are known to have significant effects on growth and nutrition, pulmonary function, and patient-perceived wellness.
- Defects in the CF transmembrane receptor protein affect fluid viscosity, flow, and pH, resulting in the clinical GI, pancreatic, and hepatobiliary manifestations of CF.
- Recognizing and managing GI manifestations is part of a comprehensive, multisystem approach to care.
- Clinicians should be aware of conditions in which diagnostic tests need to be interpreted differently in patients with CF than in the general population.

Pulmonary disease is the primary cause of morbidity and mortality in people with cystic fibrosis (CF), but significant involvement within gastrointestinal (GI), pancreatic, and hepatobiliary systems occurs as well.[1] GI, pancreatic, and hepatic manifestations of CF deserve special attention, as essentially all patients with CF will experience at least 1 such complaint during their lifetime. Additionally, many GI, pancreatic, and hepatic manifestations of CF are known to have significant effects on disease outcomes, including but not limited to (1) growth and nutrition, (2) pulmonary function, and (3) patient-perceived wellness.[1,2]

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The CF transmembrane regulator protein (CFTR) is expressed on the apical epithelium of the intestines and pancreatic and biliary duct systems where it regulates chloride and bicarbonate secretion.[3] Homozygosity of the mutant CFTR gene results in viscous and acidic secretions secondary to deficient surface fluid and bicarbonate efflux. This leads to partial or complete obstruction in the various hollow epithelial-lined structures of the GI tract and is responsible for most GI, pancreatic, and hepatobiliary manifestations of CF.[1,4] The associated increase in local and systemic inflammation is also detrimental to nutrition and growth (**Fig. 1**).

PANCREAS

Severe CFTR mutations (class I–III) are associated with dramatically decreased pancreatic ductal flow and absent digestive enzymes (pancreatic insufficiency [PI]), whereas milder mutations (class IV and V) tend to be associated with decreased flow but to an extent that allows digestive enzymes to flow into the duodenum (pancreatic sufficiency [PS]).[5] The bicarbonate milieu created by pancreatic fluid is essential to neutralize gastric acid so as to optimize the function of pancreatic enzymes, promote micelle formation, and dissolve the enteric coating on exogenous pancreatic enzyme replacement therapy (PERT).[6] The result of alterations in fluid volume, viscosity, and flow is that proenzymes get trapped within the pancreatic ducts, leading to early activation of pancreatic enzymes that inflame and damage the pancreas. Damage begins in utero as early as 17 weeks gestation.[6] Destruction of the pancreas leads to PI in most patients.

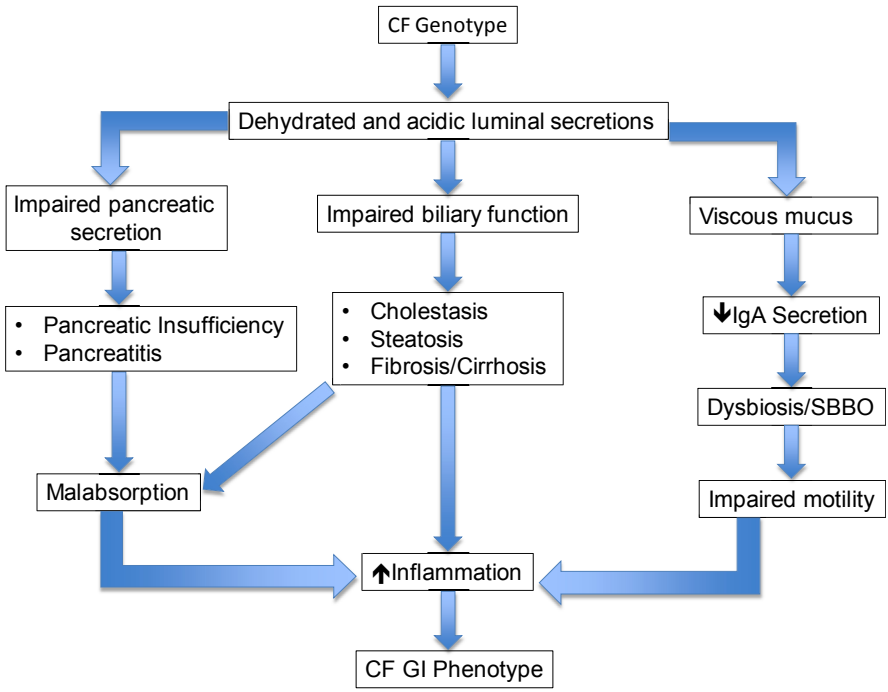

Fig. 1. Diagram illustrating common pancreatic, hepatobiliary, and gastrointestinal manifestations of CF that result in a common end pathway of increased systemic inflammation and CF phenotype.