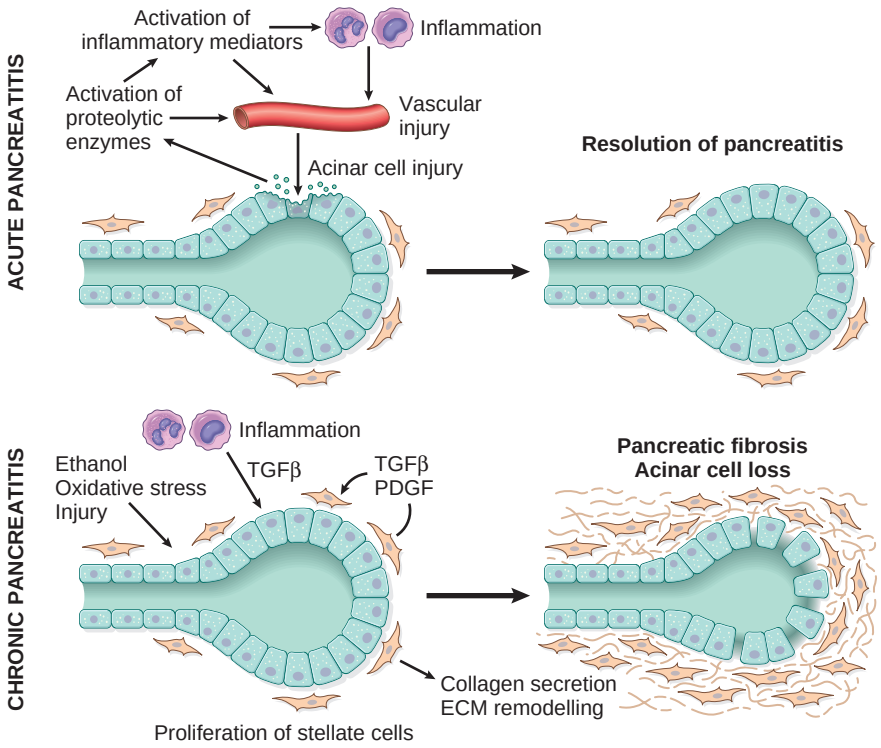

Figure 19-5 Comparison of the mediators in acute and chronic pancreatitis. In acute pancreatitis acinar injury results in release of proteolytic enzymes, leading to a cascade of events including activation of the clotting cascade, acute and chronic inflammation, vascular injury, and edema. In most patients, complete resolution of the acute injury occurs with restoration of acinar cell mass. In chronic pancreatitis, repeated episodes of acinar cell injury lead to the production of profibrogenic cytokines such as transforming growth factor β (TGF-β) and platelet-derived growth factor (PDGF), resulting in the proliferation of myofibroblasts, the secretion of collagen, and remodeling of the extracellular matrix (ECM). Repeated injury produces irreversible loss of acinar cell mass, fibrosis, and pancreatic insufficiency.

- The key feature of all of these causes is that they promote the inappropriate activation of digestive enzymes within the substance of the pancreas
- Clinical features include acute abdominal pain, systemic inflammatory response syndrome, and elevated serum lipase and amylase levels

Chronic Pancreatitis

Chronic pancreatitis is defined as prolonged inflammation of the pancreas associated with *irreversible* destruction of exocrine parenchyma, fibrosis, and, in the late stages, the destruction of endocrine parenchyma. The prevalence of chronic pancreatitis ranges between 0.04% and 5%; most affected patients are middle-aged males. **The most common cause of chronic pancreatitis by far is long-term alcohol abuse.** In addition to alcohol, chronic pancreatitis has been associated with the following conditions:

- Long-standing *obstruction* of the pancreatic duct by calculi or neoplasms
- *Autoimmune injury* to the gland
- *Hereditary pancreatitis,* as discussed under acute pancreatitis; up to 25% of chronic pancreatitis has a genetic basis

Pathogenesis. Chronic pancreatitis most often follows repeated episodes of acute pancreatitis. It has been proposed that acute pancreatitis initiates a sequence of perilobular fibrosis, duct distortion, and altered pancreatic secretions. Over time and with multiple episodes, this can lead to loss of pancreatic parenchyma and fibrosis.

Chronic pancreatic injury, whatever its cause, leads to local production of inflammatory mediators that promote fibrosis and acinar cell loss. While the cytokines produced during chronic and acute pancreatitis are similar, fibrogenic factors tend to predominate in chronic pancreatitis. These fibrogenic cytokines include transforming growth factor β (TGF-β) and platelet-derived growth factor, which induce the activation and proliferation of periacinar myofibroblasts (pancreatic stellate cells), resulting in the deposition of collagen and fibrosis (Fig. 19-5).

Autoimmune pancreatitis is a pathogenically distinct form of chronic pancreatitis that is associated with the presence of IgG4-secreting plasma cells in the pancreas. Autoimmune pancreatitis is one manifestation of IgG-related disease (Chapter 6), which may involve multiple tissues. Autoimmune pancreatitis may mimic the signs and symptoms of pancreatic carcinoma. It is important to recognize because it responds to steroid therapy.

MORPHOLOGY

Chronic pancreatitis is characterized by fibrosis, atrophy and dropout of acini, and variable dilation of pancreatic ducts (Fig. 19-6*A*). Grossly, the gland is hard, sometimes with visibly dilated ducts containing calcified concretions. These changes are typically accompanied by a chronic inflammatory infiltrate around lobules and ducts. The ductal epithelium may be atrophied or hyperplastic or may show squamous metaplasia. Acinar loss is a constant feature. There is usually relative sparing of the islets of Langerhans, which become embedded in the sclerotic tissue and may fuse and appear enlarged, but in advanced disease the islets also are lost. Chronic pancreatitis caused by alcohol abuse is characterized by ductal dilatation and intraluminal protein plugs and calcifications (Fig. 19-6*B*). **Autoimmune pancreatitis** is characterized by a duct-centric mixed inflammatory cell infiltrate, venulitis, and increased numbers of IgG4-secreting plasma cells.