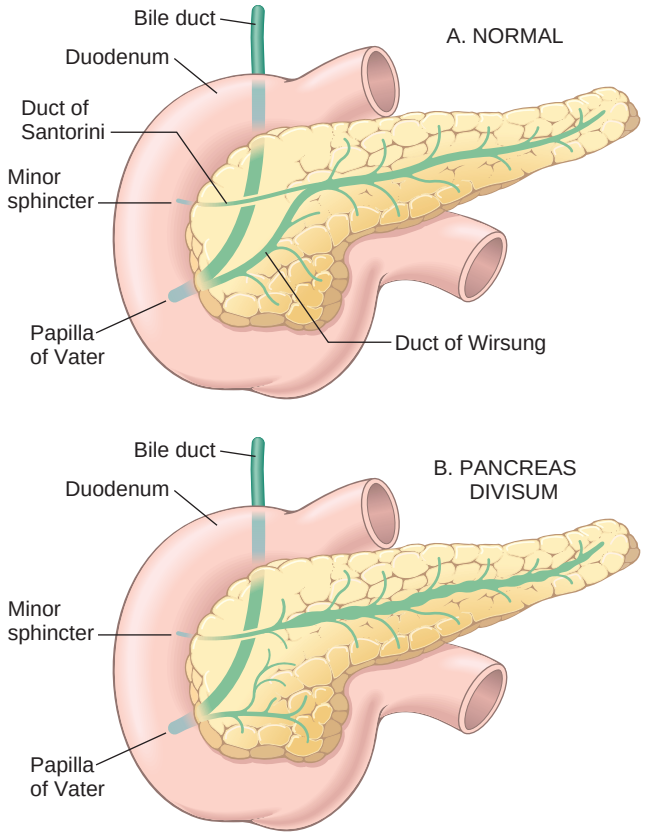

Figure 19-1 Pancreatic ductal anatomy. **A,** The normal ductal anatomy. **B,** The ductal anatomy in pancreatic divisum. (Adapted from Gregg JA, et al: Pancreas divisum: results of surgical intervention. Am J Surg 1983; 145:488-492.)

Meckel diverticula, and ileum. Although usually incidental findings, these embryologic rests, composed of normal-appearing pancreatic acini, glands, and sometimes islets of Langerhans, may cause pain from localized inflammation, or, rarely, may incite mucosal bleeding.

Agenesis. Very rarely the pancreas fails to develop (agenesis). Some cases of agenesis are caused by homozygous germline mutations involving *PDX1*, a gene encoding a homeobox transcription factor that is critical for pancreatic development.

Pancreatitis

Pancreatitis is divided into two forms, acute and chronic, each with its own characteristic pathologic and clinical features. As we will discuss, both are initiated by injuries that lead to autodigestion of the pancreas by its own enzymes. Under normal circumstances, the following mechanisms protect the pancreas from self-digestion by its secreted enzymes:

- Most digestive enzymes are synthesized as inactive proenzymes (zymogens), which are packaged within secretory granules.
- Most proenzymes are activated by trypsin, which itself is activated by duodenal enteropeptidase (enterokinase) in the small bowel; thus, intrapancreatic activation of proenzymes is normally minimal.
- Acinar and ductal cells secrete trypsin inhibitors, including serine protease inhibitor Kazal type 1 (SPINK1), which further limit intrapancreatic trypsin activity.

Pancreatitis occurs when these protective mechanisms are deranged or overwhelmed. As discussed later, the clinical manifestations of pancreatitis vary widely. Acute attacks may be mild and self-limited or present as a life-threatening acute inflammatory process; with recurrent or persistent pancreatitis, there may be permanent loss of pancreatic function.

Table 19-1 Etiologic Factors in Acute Pancreatitis

Metabolic
Alcoholism
Hyperlipoproteinemia
Hypercalcemia
Drugs (e.g., azathioprine)
Genetic
Mutations in genes encoding trypsin, trypsin regulators, or proteins that regulate calcium metabolism
Mechanical
Gallstones
Trauma
Iatrogenic injury
Operative injury
Endoscopic procedures with dye injection
Vascular
Shock
Atheroembolism
Vasculitis
Infectious
Mumps

Acute Pancreatitis

Acute pancreatitis is characterized by *reversible* pancreatic parenchymal injury associated with inflammation and has diverse etiologies, including toxic exposures (e.g., alcohol), pancreatic duct obstruction (e.g., biliary calculi), inherited genetic defects, vascular injury, and infections. Acute pancreatitis is relatively common; the annual incidence in Western countries is 10 to 20 cases per 100,000 people. Biliary tract disease and alcoholism account for approximately 80% of cases of acute pancreatitis in Western countries (Table 19-1). Gallstones are present in 35% to 60% of cases, and pancreatitis develops in about 5% of patients with gallstones. The proportion of cases of acute pancreatitis caused by excessive alcohol intake varies from 65% in the United States to 20% in Sweden to 5% or less in southern France and the United Kingdom. The male-to-female ratio is 1:3 in the group with biliary tract disease and 6:1 in those with alcoholism.

Pathogenesis. **Acute pancreatitis results from inappropriate release and activation of pancreatic enzymes, which destroy pancreatic tissue and elicit an acute**