endocrine insufficiency in the absence of pain. Other patients are asymptomatic and are found to have chronic pancreatitis incidentally on imaging.

The pain of chronic pancreatitis is typically epigastric, often radiates to the back, is occasionally associated with nausea and vomiting, and may be partially relieved by sitting upright or leaning forward. The pain is often worse 15 to 30 minutes after eating. Early in the course of chronic pancreatitis, the pain may occur in discrete attacks; as the condition progresses, the pain tends to become continuous.

The pain of chronic pancreatitis is poorly understood. Possible causes include inflammation of the pancreas, increased intrapancreatic pressure, neural inflammation, and extrapancreatic causes, such as stenosis of the common bile duct and duodenum.

Glucose intolerance occurs with some frequency in chronic pancreatitis, but overt diabetes mellitus usually manifests late in the course of disease. Diabetes in patients with chronic pancreatitis is different from typical type 1 diabetes in that the pancreatic alpha cells, which produce glucagon, are also affected, increasing the risk of hypoglycemia.

Clinically significant endocrine or exocrine insufficiency (i.e., protein and fat deficiencies) does not occur until more than 90% of pancreatic function is lost. Steatorrhea usually occurs before protein deficiencies because lipolytic activity decreases faster than proteolysis. Malabsorption of fat-soluble vitamins (A, D, E, K) and vitamin B_{12} may also occur, although clinically symptomatic vitamin deficiency is uncommon. Because reduced vitamin D absorption can result in osteoporosis, osteopenia, and fractures, periodic assessment of vitamin D levels and bone densitometry are recommended.

Diagnosis and Differential Diagnosis

Because direct biopsy of the pancreas has considerable risk, the diagnosis of chronic pancreatitis is typically based on indirect tests of pancreatic structure and function. Marked structural changes usually correlate with severe functional impairment. In early chronic pancreatitis, however, mild abnormalities of pancreatic function can precede the morphologic changes seen on imaging. Studies of pancreatic structure may remain normal even with advanced deterioration of pancreatic function.

Laboratory evaluations of serum pancreatic enzymes, such as amylase and lipase, are frequently normal in the setting of well-established chronic pancreatitis, even during painful exacerbations. Serum pancreatic enzymes neither confirm nor exclude the diagnosis.

Tests of Function

Function tests assess pancreatic secretory reserve of ductal function capacity for secretion of bicarbonate ions (HCO_3^-) in fluid or acinar function for secretion of digestive enzymes. Direct tests involve stimulation of the pancreas through the administration of hormonal secretagogues. Indirect tests measure the consequences of pancreatic insufficiency, and although more widely available, the results usually are not abnormal until enzyme output has declined by more than 90%. They are insensitive to early pancreatic insufficiency. Clinicians have preferentially relied on noninvasive methods to circumvent the challenges associated with direct pancreatic function tests. Clinically available indirect tests of pancreatic function include analyses of fecal fat, fecal elastase, and serum trypsin.

The secretin stimulation test takes advantage of the normal response of pancreatic ductular cells to secrete HCO_3^- in response to physiologic and exogenously administered secretin. The observation that HCO_3^- production is impaired early in the course of chronic pancreatitis led to the use of this test to diagnose early-stage disease (sensitivity of 95%). The test involves oral placement of a double-lumen gastroduodenal catheter for aspiration and quantitative measurement of pancreatic enzyme and HCO_3^- production before and after stimulation with intravenous secretin. This quantitative measure of pancreatic secretion and enzyme activity is primarily performed for patients with suspected chronic pancreatitis who have chronic abdominal pain but negative or equivocal results of imaging studies. Peak pancreatic fluid HCO_3^- concentrations of less than 80 mEq/L represent pancreatic insufficiency.

The secretin stimulation test has been infrequently used in clinical practice because the study is labor intensive and is associated with discomfort. Endoscopic collection methods have simplified pancreatic fluid collection and made the test more suitable for clinical use.

The 72-hour fecal fat determination is sometimes used for detection of steatorrhea (fecal fat >7 g/24 hours), but the test is not specific for pancreatic exocrine insufficiency. The test also lacks sensitivity because steatorrhea occurs only in advanced chronic pancreatitis. Because the quantitative fecal fat test is inconvenient, unpleasant for patients, and prone to laboratory error, a qualitative assay is used preferentially in clinical practice to assess for malabsorption.

Determination of fecal elastase is the most commonly used noninvasive test for the diagnosis of pancreatic exocrine insufficiency. Elastase, a protease synthesized by pancreatic acinar cells, is useful for evaluating insufficiency because it is stable in stool, unaffected by pancreatic enzyme replacement, and correlates well with stimulated pancreatic function test results. Mild or severe exocrine insufficiency is based on fecal elastase values of less than 200 or 100 µg/g of stool, respectively.

Low concentrations of serum trypsin are relatively specific for advanced chronic pancreatitis. However, they are not sensitive enough to be helpful for most patients with mild to moderate pancreatic disease.

Tests of Structure

Findings that suggest chronic pancreatitis include ductal abnormalities (e.g., dilation, stones, duct irregularity), parenchymal abnormalities (e.g., calcification, inhomogeneity, atrophy), gland contour changes, and pseudocysts. Imaging studies may be normal or inconclusive in the early stages of disease.

Plain film radiography of the abdomen can detect pancreatic calcifications in approximately 20% of individuals with alcohol-induced chronic pancreatitis. The study should be the first diagnostic test performed when pancreatitis is suspected because it is simple and inexpensive. Calcifications not detected on plain films are more readily apparent by CT (E-Fig. 38-4). CT scans may show supportive findings of pancreatic ductal dilatation, atrophy of the pancreas, and fluid collections (e.g., pseudocysts). Sensitivity and specificity