fibrosis carriers and had a 40-fold increased risk of pancreatitis. The presence of an *N34S SPINK1* mutation increased the risk 20-fold. A combination of two *CFTR* mutations and an *N34S SPINK1* mutation increased the risk of pancreatitis 900-fold. Knowledge of the genetic defects and downstream alterations in protein expression has led to the development of novel genetic therapy in cystic fibrosis children that potentiates the CFTR channel resulting in improvement in lung function, quality of life, and weight gain. Table 371-5 lists recognized causes of chronic pancreatitis and pancreatic exocrine insufficiency.

AUTOIMMUNE PANCREATITIS (TABLE 371-6)

Autoimmune pancreatitis (AIP) is an uncommon disorder of presumed autoimmune causation with characteristic laboratory, histologic, and morphologic findings. In type 1 AIP, the pancreas is involved as part of an IgG4 systemic disease (Chap. 391e) and meets HISORt criteria as defined below. The characteristic pancreatic histopathologic findings include lymphoplasmacytic infiltrate, storiform fibrosis, and abundant IgG4 cells. AIP type 2 is histologically confirmed idiopathic duct centric pancreatitis with granulocytic infiltration of the duct wall (termed GEL), but without IgG4 positive cells and systemic involvement. Although AIP was initially described as a primary pancreatic disorder, it is now recognized that it is associated with other disorders of presumed autoimmune etiology, and this has been termed IgG4 systemic disease (Chap. 391e). The clinical features include IgG4-associated cholangitis, rheumatoid arthritis, Sjögren's syndrome, ulcerative colitis, mediastinal fibrosis and adenopathy, autoimmune thyroiditis, tubulointerstitial nephritis, retroperitoneal fibrosis, chronic periaortitis, chronic sclerosing sialadenitis, and Mikulicz's disease. Mild symptoms, usually abdominal pain, and recurrent acute pancreatitis are unusual. Furthermore, AIP is not a common cause of idiopathic recurrent pancreatitis.

Weight loss and new onset of diabetes may also occur. An obstructive pattern on liver tests is common (i.e., disproportionately elevated serum alkaline phosphatase and minimally elevated serum aminotransferases). Elevated serum levels of IgG4 provide a marker for the disease, particularly in Western populations. Serum IgG4 normally accounts for only 5–6% of the total IgG4 in healthy patients but is elevated to values >280 mg/dL in those with AIP. CT scans reveal abnormalities in the majority of patients and include diffuse enlargement, focal enlargement, and a distinct enlargement at the head of the pancreas. ERCP or MRCP reveals strictures in the bile duct in more than one-third of patients with AIP; these may include common bile duct strictures, intrahepatic bile duct strictures, or proximal bile duct strictures, with accompanying narrowing of the pancreatic portion of the bile duct. This has been termed autoimmune IgG4 cholangitis. Characteristic histologic findings include extensive lymphoplasmacytic infiltrates with dense fibrosis around pancreatic ducts, as well as a lymphoplasmacytic infiltration, resulting in an obliterative phlebitis.

The Mayo Clinic HISORt criteria indicate that AIP can be diagnosed by the presence of at least two of the following: (1) *h*istology; (2) *i*maging; (3) *s*erology (elevated serum IgG4 levels); (4) *o*ther organ involvement; and (5) *r*esponse to glucocorticoid *t*herapy, with improvement in pancreatic and extrapancreatic manifestations.

Glucocorticoids have shown efficacy in alleviating symptoms, decreasing the size of the pancreas, and reversing histopathologic features in patients with AIP. Patients may respond dramatically to glucocorticoid therapy within a 2- to 4-week period. Prednisone is usually administered at an initial dose of 40 mg/d for 4 weeks followed by a taper of the daily dosage by 5 mg/wk based on monitoring of clinical parameters. Relief of symptoms, serial changes in abdominal imaging of the pancreas and bile ducts, decreased serum γ-globulin and IgG4 levels, and improvements in liver tests are parameters to follow. A poor response to glucocorticoids over a 2- to 4-week period should raise suspicion of pancreatic cancer or other forms of chronic pancreatitis. A recent multicenter international report reviewed 1064 patients with AIP. Clinical remission was achieved in 99% of type I and 92% of type II AIP patients with steroids. However, disease relapse occurred in 31% of type I and 9% of type II AIP patients. For treatment of disease relapse in type 1 AIP, glucocorticoids were successful in 201 of 295 (68%) patients, and azathioprine was successful in 52 of 58 patients (85%). A small number of patients responded favorably to 6-mercaptapurine, rituximab, cyclosporine, and cyclophosphamide. Types 1 and 2 AIP are highly responsive to initial glucocorticoid treatment. Relapse is common in type 1 patients, especially those with biliary tract strictures. Most relapses occur after glucocorticoids are discontinued. Patients with refractory symptoms and strictures generally require immunomodulator therapy as noted above. Appearance of interval cancers following a diagnosis of AIP is uncommon.

TABLE 371-6 CLINICAL FEATURES OF AUTOIMMUNE PANCREATITIS (AIP)

- Mild symptoms, usually abdominal pain, but without frequent attacks of acute pancreatitis
- Diffuse swelling and enlargement of the pancreas
- Two-thirds of patients present with either obstructive jaundice or a "mass" in the head of the pancreas mimicking carcinoma
- Diffuse irregular narrowing of the pancreatic duct (MRCP or ERCP)
- Increased levels of serum gamma globulins, especially IgG4
- Presence of other autoantibodies (ANA), rheumatoid factor (RF)
- Can occur with other autoimmune diseases: Sjögren's syndrome, primary sclerosing cholangitis, ulcerative colitis, rheumatoid arthritis
- Extrapancreatic bile duct changes such as stricture of the common bile duct and intrahepatic ducts
- Pancreatic calcifications (rare)
- Pancreatic biopsies reveal extensive fibrosis and lymphoplasmacytic infiltration
- Glucocorticoids are effective in alleviating symptoms, decreasing size of the pancreas, and reversing histopathologic changes

Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography.

Clinical Features of Chronic Pancreatitis Patients with chronic pancreatitis seek medical attention predominantly because of two symptoms: abdominal pain or maldigestion and weight loss. The abdominal pain may be quite variable in location, severity, and frequency. The pain can be constant or intermittent with frequent pain-free intervals. Eating may exacerbate the pain, leading to a fear of eating with consequent weight loss. The spectrum of abdominal pain ranges from mild to quite severe, with narcotic dependence as a frequent consequence. Maldigestion is manifested as chronic diarrhea, steatorrhea, weight loss, and fatigue. Patients with chronic abdominal pain may or may not progress to maldigestion, and ~20% of patients will present with symptoms of maldigestion without a history of abdominal pain. Patients with chronic pancreatitis have significant morbidity and mortality and use appreciable amounts of societal resources. Despite steatorrhea, clinically apparent deficiencies of fat-soluble vitamins are surprisingly uncommon. Physical findings in these patients are usually unimpressive, so that there is a disparity between the severity of abdominal pain and the physical signs that usually consist of some mild tenderness.

The diagnosis of early or mild chronic pancreatitis can be challenging because there is no biomarker for the disease. In contrast to acute pancreatitis, the serum amylase and lipase levels are usually not strikingly elevated in chronic pancreatitis. Elevation of serum bilirubin and alkaline phosphatase may indicate cholestasis secondary to common bile duct stricture caused by chronic inflammation. Many patients have impaired glucose tolerance with elevated fasting blood glucose levels. The fecal elastase-1 and small-bowel biopsy are useful in the evaluation of patients with suspected pancreatic steatorrhea. The fecal elastase level will be abnormal and small-bowel histology will be normal in such patients. A decrease of fecal elastase level to <100 μg per gram of stool strongly suggests severe pancreatic exocrine insufficiency.

The radiographic evaluation of a patient with suspected chronic pancreatitis usually proceeds from a noninvasive to more invasive approach. Abdominal CT imaging (Fig. 371-4*A*,*B*) is the initial modality of choice, followed by MRI (Fig. 371-4*C*), endoscopic ultrasound, and pancreas function testing. In addition to excluding a