secretion, which stimulates pancreatic acinar cells. Replacement therapy provides increased trypsin activity in the duodenum, which denatures CCK-releasing peptide, resulting in a reduction in endogenous CCK release and an attendant decrease in pancreatic stimulation and pain. Therapy is initiated with large doses of non–enteric-coated pancrelipases (i.e., pancreatic enzyme preparations) because the enteric-coated preparations theoretically release their enzymes further down the intestine, away from the stimulatory CCK enterocytes. Co-administration of acid suppressive therapy to prevent destruction of the enzymes by gastric acid may be helpful.

5. Neural transmission modification. Gabapentoids, including pregabalin, have been used effectively to treat neuropathic pain disorders, including diabetic neuropathy and neuropathic pain of central origin. Based on the finding that pancreatic pain is accompanied by similar alterations of central pain processing, studies suggest a benefit with pregabalin as an adjuvant treatment to decrease pain associated with chronic pancreatitis. Similarly, tricyclic antidepressants, selective serotonin reuptake inhibitors, and serotonin-norepinephrine reuptake inhibitors can be administered on a trial basis.
6. Antioxidants. Oxidative stress can cause direct pancreatic acinar cell damage through several pathways. Supplementation with antioxidants, such as selenium, vitamins C and E, and methionine, may relieve pain and reduce oxidative stress. In a randomized trial, the reduction in the number of painful days per month was higher for the patients who received antioxidants compared with those who received placebo (7.4 vs. 3.2 days). Patients who received antioxidants also were more likely to become pain free (32% vs. 13%).
7. Endoscopic decompression. Endoscopic decompression of the pancreatic duct is an option for obstruction of the main pancreatic duct caused by strictures, stones, or sphincter of Oddi dysfunction. Endoscopic therapies include pancreatic sphincterotomy, stricture dilation, stone removal with intracorporeal or extracorporeal shock wave lithotripsy, and temporary stent placement. Complete or partial pain relief is reported for approximately 50% to 80% of carefully selected patients during follow-up extending as long as 3 to 4 years.
8. Surgery. Surgical pancreatic ductal drainage, usually with lateral pancreaticojejunostomy (i.e., Puestow procedure), can be offered to those with a dilated (>6 mm in diameter) main pancreatic duct. Pain reduction is reported by approximately 80% of patients. This procedure is safe and has an operative mortality rate of less than 5%; however, only 35% to 60% of patients are free of pain at the 5-year follow-up. Individuals with nonobstructed, nondilated pancreatic ductal systems may be offered resection of focally diseased portions of the gland (i.e., Frey or Beger procedures) or total pancreatectomy with islet cell transplantation.

Management of Complications

The complications of chronic pancreatitis include pseudocysts, pancreatic fistulas, biliary obstruction, pancreatic cancer, small bowel bacterial overgrowth, and gastric varices due to splenic vein thrombosis.

Pancreatic Fistulas

Pancreatic fistulas occur as a result of duct disruption resulting in localized fluid collections, ascites, or pleural effusions. Treatment consists of bowel rest, endoscopic pancreatic duct stenting, and administration of a somatostatin analogue. Surgical intervention may be needed if this conservative approach is unsuccessful.

Vascular Complications

The splenic vein courses along the posterior surface of the pancreas, where it can be affected by inflammation from pancreatitis or malignancy that lead to thrombosis. Splenic vein thrombosis can result in isolated fundal gastric varices. Splenectomy is usually curative for patients who develop bleeding from gastric varices.

Pseudoaneurysm formation is a complication of acute and chronic pancreatitis. Affected vessels, including the hepatic, splenic, pancreaticoduodenal, and gastroduodenal arteries, lie close to the pancreas. CECT or MRI shows the pseudoaneurysm as a cystically dilated vascular structure in or adjacent to the pancreas. EUS with Doppler imaging can show blood flow within the pseudoaneurysm. Mesenteric angiography permits confirmation of the diagnosis and provides a means of therapy because selective embolization of the pseudoaneurysm can be accomplished during the procedure. Surgery for bleeding pseudoaneurysms is difficult and associated with high morbidity and mortality rates.

Biliary and Duodenal Obstruction

Symptomatic obstruction of the bile duct or duodenum, or both, develops in a few patients with chronic pancreatitis. Postprandial pain and early satiety are characteristic of duodenal obstruction, whereas pain and cholestasis (sometimes with resultant cholangitis) suggest a bile duct stricture. These complications most commonly result from inflammation or fibrosis in the head of the pancreas or an adjacent pseudocyst.

Endoscopic stenting may be attempted for bile duct strictures, but they are often refractory and typically require prolonged treatment. Endoscopic failures can be treated with surgical biliary decompression. The importance of decompression is underscored by the observation that it can reverse secondary biliary fibrosis associated with bile duct obstruction.

CARCINOMA OF THE PANCREAS

Definition and Epidemiology

Carcinoma of the pancreas is the fourth leading cause of cancer-related death in the United States, with approximately 43,000 new cases diagnosed annually. The peak incidence of pancreatic carcinoma occurs in the seventh decade of life. There is a slight male-to-female predominance (relative risk of 1.4 : 1), and blacks have a 30% to 40% higher incidence of pancreatic carcinoma than whites in the United States.

Many environmental factors have been implicated as increasing the risk for pancreatic cancer. Cigarette smoking is the most consistent factor, with the increased risk attributed to the