REVIEW ARTICLES

MEDICAL PROGRESS

CHRONIC PANCREATITIS

MICHAEL L. STEER, M.D., IRVING WAXMAN, M.D., AND STEVEN FREEDMAN, M.D.

IN 1788 Cawley reported on a "free living young man" who had died of emaciation and diabetes and whose postmortem examination revealed multiple pancreatic calculi.[1] In the two centuries since that early description of chronic pancreatitis, literally thousands of reports dealing with this disease have been published, yet chronic pancreatitis remains an enigmatic process of uncertain pathogenesis, unpredictable clinical course, and unclear treatment.

Classification and Pathology

Acute and chronic pancreatitis are distinguished from each other on the basis of structural and functional criteria. In acute pancreatitis, the gland is normal before the attack and can return to normal after resolution of the attack, whereas in chronic pancreatitis, the gland is abnormal before or after the attack, or both.[2,3] This classification scheme does not depend on how rapidly symptoms appear or resolve, or on the severity of the symptoms. Thus, it may be impossible to distinguish an exacerbation of chronic pancreatitis from an attack of acute pancreatitis on clinical grounds alone.

The morphologic changes of chronic pancreatitis (Fig. 1) include varying degrees of edema, acute inflammation, and necrosis, superimposed on a background of chronic changes that include fibrosis, inflammation, and loss of exocrine tissue. Ductal elements may be dilated, and intraductal protein plugs, which may be calcified, can be seen.[2,3] Most investigators believe that acute pancreatitis does not lead to chronic pancreatitis unless complications, such as pseudocysts or ductal strictures, are present.[2]

Causes of Chronic Pancreatitis

In many patients, chronic pancreatitis is clinically silent. Similarly, many patients with unexplained abdominal pain may have chronic pancreatitis that eludes diagnosis. Thus, the true prevalence of the disease is not known, although estimates range from 0.04 to 5 percent.[4] In developed countries, 60 to 70 percent of patients with chronic pancreatitis have a long history (6 to 12 years) of heavy consumption of alcohol (150 to 175 g per day)[5] before the onset of clinically apparent disease.[4] A high-protein diet with either a very high or very low fat content may potentiate the injurious effects of alcohol.[6,7] Like alcoholism itself, alcohol-induced pancreatitis is most frequent among men, and it has its peak incidence between 35 and 45 years of age.

Obstruction of the pancreatic duct can also lead to chronic pancreatitis. The obstructing lesions that can cause pancreatitis include post-traumatic ductal strictures, pseudocysts, mechanical or structural changes of the pancreatic-duct sphincter, and periampullary tumors.[4] Pancreas divisum can also cause chronic pancreatitis, by creating a relative obstruction to the flow of pancreatic juice at the lesser papilla.[8] (Pancreas divisum is a developmental defect in which the head and body of the pancreas are separate glands.) In general, chronic pancreatitis caused by ductal obstruction is characterized by dilatation of the pancreatic duct and exocrine insufficiency. Intraductal plugs and stones are unusual.[4] Many of these changes may regress if the obstruction is relieved.

Tropical pancreatitis is a poorly characterized heterogeneous disease that occurs primarily in impoverished areas of Africa and Asia.[6] It typically appears in young people and is characterized by pancreatic insufficiency, diabetes mellitus, and recurrent attacks of pain. Pancreatic calcifications are common. It is not clear whether this disease is caused by protein deficiency or, what is more likely, by the ingestion of potentially toxic substances, such as the cyanogens in cassava root.[6,9]

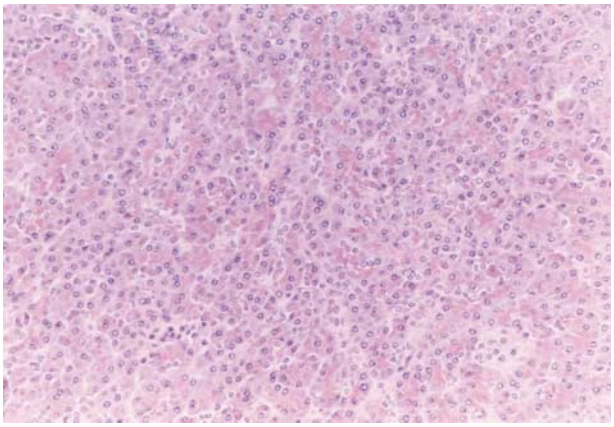
Chronic pancreatitis can occasionally occur in association with cystic fibrosis or hyperparathyroidism, or as a hereditary disease transmitted by an autosomal dominant gene with incomplete penetrance.[4]

Between 30 and 40 percent of patients with chronic pancreatitis have no apparent underlying cause of their disease. They are considered to have "idiopathic" chronic pancreatitis. Patients with idiopathic chronic pancreatitis have been noted to cluster in a younger group (peak incidence, 15 to 30 years of age) and an older group (peak incidence, 50 to 70 years of age). Patients in the younger group usually present with severe pain and subsequently have calcifications, exocrine insufficiency, and diabetes, whereas those in the older group frequently do not have pain.[10,11]

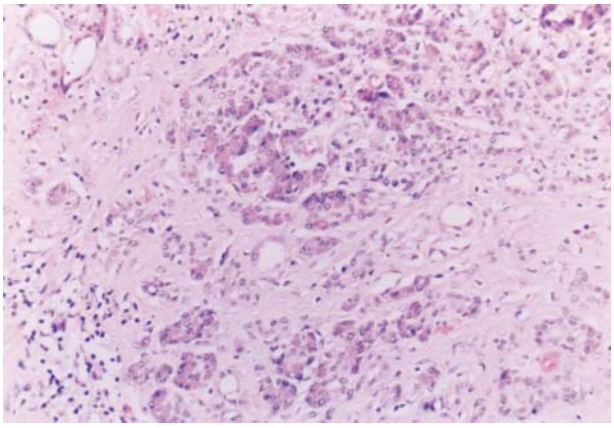
Pathogenesis

The hypersecretion of protein from acinar cells in the absence of increased fluid or bicarbonate secretion from duct cells is characteristic of chronic pancreatitis.[12] Plugs formed by the precipitation of protein within interlobular and intralobular ducts are an early finding.[13] Their importance is evidenced by the observation that endoscopic removal of the plugs may result in transient improvement in the pancreatitis.[14,15] Ductal plugs are initially composed of degenerating cells within a reticular network. They subsequently enlarge to form laminar aggregates through the acquisition of

From the Departments of Surgery (M.L.S.) and Medicine (I.W., S.F.) and the Pancreatico-Biliary Diseases Center, Beth Israel Hospital and Harvard Medical School, Boston. Address reprint requests to Dr. Steer at the Department of Surgery, Beth Israel Hospital, 330 Brookline Ave., Boston, MA 02215.



A



B

Figure 1. Photomicrographs of the Human Pancreas.
Panel A shows normal pancreatic tissue, and Panel B shows changes of chronic pancreatitis, characterized by a marked increase in interlobular fibrous tissue, atrophy of the acini, and chronic inflammatory infiltrate. (Hematoxylin and eosin, ×95.)

amorphous material. The plugs contain multiple proteins, including secreted digestive enzymes, glycoproteins, and acidic mucopolysaccharides.[16,17] The precipitation of calcium carbonate in the plugs results in the formation of intraductal stones. Ductal plugs can occur in all forms of chronic pancreatitis,[18] but stones are most commonly found in patients with either alcohol-induced or tropical (nutritional) pancreatitis.

Lithostathine (formerly called pancreatic-stone protein) is a 14,000-dalton protein that is secreted by acinar cells and is present in large amounts in pancreatic-juice precipitates, ductal plugs, and stones.[19] GP2, a homologue of the protein responsible for the formation of renal casts, is also secreted by acinar cells and is present within the precipitates and plugs.[18] The mechanisms responsible for the precipitation of these proteins and their potential role in causing chronic pancreatitis are not clear. The precipitation of lithostathine and GP2 is promoted by high hydrogen and altered salt concentrations. Whether premature digestive-enzyme activation leads to degradation of these proteins and a reduction in their solubility is not known.[20]

In vitro, lithostathine inhibits the precipitation of calcium carbonate from pancreatic juice,[21] and it was initially postulated that reduced lithostathine concentrations in pancreatic juice were responsible for the formation of stones in chronic pancreatitis.[22] However, the issue remains controversial.[23] Furthermore, the observation that lithostathine concentrations are lower in alcoholics without pancreatitis suggests that lithostathine may be only one of the factors preventing the precipitation of calcium carbonate.[24]

Patients with idiopathic chronic pancreatitis frequently have elevated pressure in the pancreatic duct, suggesting that ductal "hypertension" may play an important part in chronic pancreatitis.[25] The results of manometry of the sphincter of Oddi are usually normal under these conditions, suggesting that dysfunction of the sphincter is not the explanation for the elevated pressure. It is possible that papillary stenosis or ductal obstruction by plugs or stones could result in ductal hypertension, but the mechanisms by which these changes could lead to inflammation and fibrosis are not known.

Natural History

Chronic pancreatitis is usually characterized by a relentless and progressive loss of pancreatic parenchymal tissue.[26] After a subclinical phase of variable duration, recurrent attacks of abdominal pain are noted, and exocrine or endocrine insufficiency (or both) appears. In most cases, both exocrine and endocrine functions are lost, although the loss of endocrine function appears later in the disease.[27-31] Some investigators have suggested that the progressive loss of exocrine function leads to a decrease in or even complete resolution of the pain of chronic pancreatitis — that is, that the pancreatitis "burns itself out."[26] Others have not observed this phenomenon, and the issue remains highly controversial. The effects of abstinence from alcohol on the progression of chronic pancreatitis are also not clear.[27,28,31] Some reports have suggested that abstinence from alcohol may decrease the severity and frequency of painful attacks and the progressive loss of exocrine and endocrine function.[28,32-34] On the other hand, other reports indicate that, once established, the disease may progress without further alcohol abuse or may remain stable in spite of continued alcohol abuse.[31,35]

Chronic pancreatitis is associated with a mortality rate that approaches 50 percent within 20 to 25 years.[27,28,31,34] Approximately 15 to 20 percent of patients die of complications associated with attacks of pancreatitis,[27,29,31,34] and most of the remaining deaths are due to factors such as trauma, malnutrition, infection, or tobacco abuse, which are frequently present among chronic alcoholics.[27,28,31,34] A recent report indicates that pancreatic cancer develops in roughly 4 percent of patients within 20 years of a diagnosis of chronic pancreatitis.[36]

Medical History and Physical Examination

In developed countries, most patients with chronic pancreatitis have a history of prolonged and heavy alcohol use. They typically report recurrent attacks of

upper abdominal pain, which may radiate to the midback or scapula, increase after eating, and be relieved by either leaning forward or sitting upright. Their pain is usually associated with nausea or vomiting. Ten to 20 percent of patients have "painless pancreatitis."[29,37,38] They may present with diabetes, jaundice, or malabsorption. Steatorrhea with weight loss and diabetes are frequently present in the advanced stages of the disease, but many patients may be completely free of symptoms. Presumably, this reflects the fact that 80 to 90 percent of exocrine and endocrine tissue can be lost before malabsorption and diabetes are demonstrable. In one study, 45 percent of a group of alcoholics with no symptoms of pancreatitis had evidence of chronic pancreatitis on postmortem examination.[39]

Generally, few findings other than epigastric or upper abdominal tenderness are noted on physical examination. Fever or an epigastric mass should suggest the presence of a complication such as a pseudocyst.

Laboratory Tests

Serum amylase and lipase concentrations may be normal or only slightly elevated, particularly if the gland is already compromised by extensive fibrosis and is unable to synthesize digestive enzymes. The white-cell count and serum electrolyte concentrations are also usually normal unless fluids or electrolytes or both have been lost as a result of vomiting and diminished intake. In the presence of alcoholic liver disease, the results of liver-function tests may be abnormal. In 5 to 10 percent of patients with chronic pancreatitis, compression of the intrapancreatic portion of the bile duct, caused by either edema or fibrosis, leads to elevation of the serum bilirubin and alkaline phosphatase concentrations.[40] Malabsorption resulting from exocrine insufficiency may cause fecal fat excretion to be elevated. This can usually be detected by Sudan staining of feces and quantified by the measurement of fecal fat excretion while the patient eats a diet containing 100 g of fat per day (a normal diet contains $\leq$7 g per day).

Imaging Procedures

Pancreatic calcifications, pathognomonic of chronic pancreatitis, may be seen in up to 30 percent of plain abdominal radiographs (Fig. 2). The calcifications are located exclusively within the ductal system and are not present in the parenchyma of the gland. Ultrasonography may reveal pancreatic enlargement, ductal dilatation, or pseudocysts, with a reported sensitivity of 60 to 70 percent and a specificity of 80 to 90 percent.[41,42] Computed tomography has a reported sensitivity of 74 to 90 percent and a specificity of 85 percent in the diagnosis of chronic pancreatitis. It may reveal calcifications and cystic areas not noted on ultrasound or plain films[43] (Fig. 3). The preliminary results of endoscopic ultrasonography in the evaluation of this disease have been promising, but its specific diagnostic role has not yet been determined.[44,45] The role of magnetic resonance imaging in the diagnosis of chronic pancreatitis is also not clear.[46]

Endoscopic retrograde pancreatography is the gold-standard imaging procedure for diagnosing chronic pancreatitis and planning treatment (Fig. 4). Ductal changes detected by endoscopic retrograde pancreatography can be classified as mild, moderate, or severe on the basis of the severity and extent of the ductal changes, although the changes may not be closely related to the degree of pancreatic functional impairment.[47]

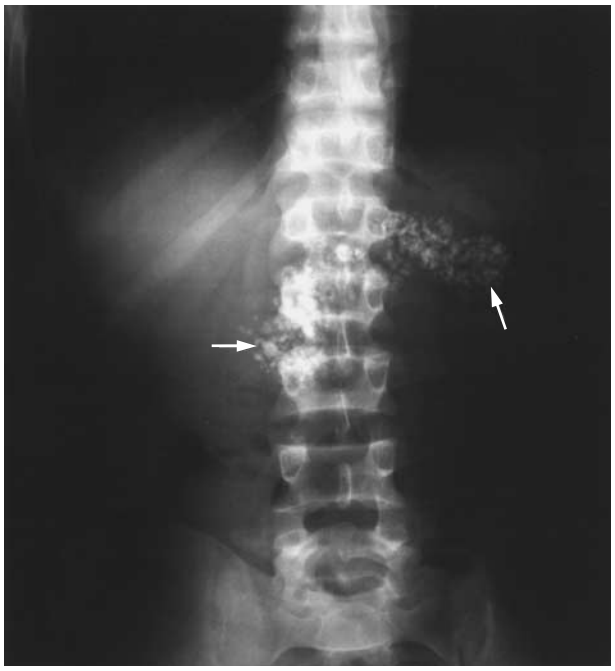


Figure 2. Plain Radiograph of the Abdomen Showing Diffuse Calcifications throughout the Pancreas (Arrows) in an Alcoholic Patient with Chronic Pancreatitis.

Pancreatic-Function Tests

Tests of pancreatic function may be particularly helpful in the diagnosis and treatment of patients who have recurrent pain and whose imaging studies and other tests are normal. The sensitivities and specificities of many of the tests of pancreatic function are listed in Table 1. The results reported often depend on the types of patients being studied and the severity of their pancreatic insufficiency. In practice, the choice of which, if any, test to use may depend on locally available expertise and resources. The principal problem with many of the pancreatic-function tests is their relative insensitivity, particularly during the first few years of the disease, when the changes may be mild. Therefore, a negative pancreatic-function test should not exclude the diagnosis of chronic pancreatitis.

The gold-standard pancreatic-function tests involve the collection of duodenal juice and the measurement of its volume and bicarbonate and protein concentrations after either the ingestion of a standard meal or the intravenous administration of secretin with or without pancreozymin (cholecystokinin). A simpler, albeit less sensitive and specific, approach involves the oral administration of substrates for pancreatic digestive enzymes and the measurement of their products

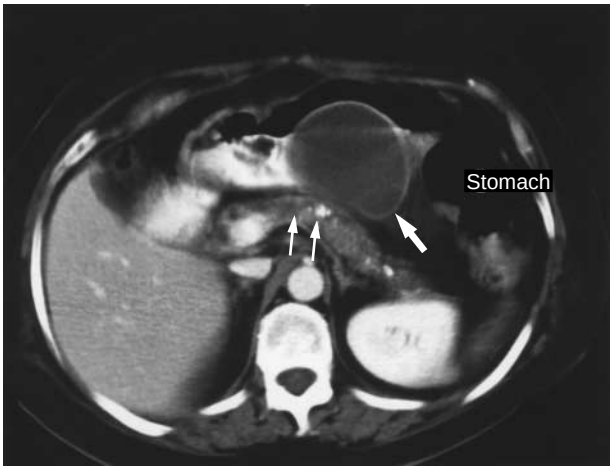


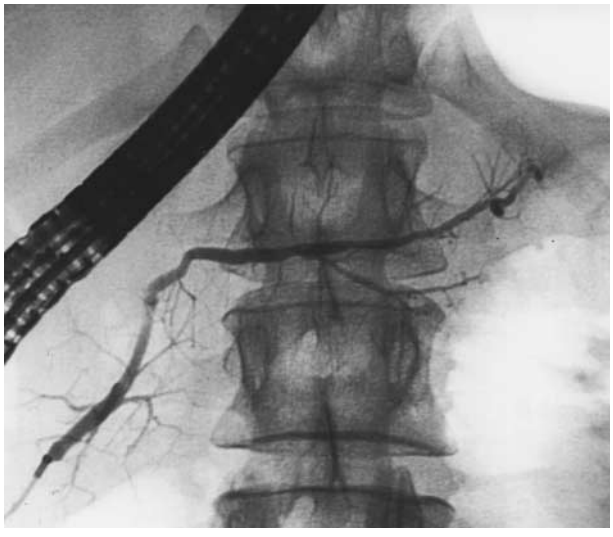
Figure 3. Dynamic Computed Tomographic Image Showing a Thin-Walled Pancreatic Pseudocyst (Thick Arrow) Compressing the Gastric Antrum and an Abnormal Pancreas with Ductal Dilatation and Calcifications (Thin Arrows).

of digestion. The two most commonly used of these so-called tubeless tests are the bentiromide test, in which *N*-benzoyl-L-tyrosyl-*p*-aminobenzoic acid (bentiromide) is administered, and the pancreolauryl test, in which fluorescein dilaurate is administered.[41] Chymotrypsin cleaves *N*-benzoyl-L-tyrosyl-*p*-aminobenzoic acid, yielding *p*-aminobenzoic acid, which is absorbed and can be measured in urine. In the pancreolauryl test, pancreatic esterases release fluorescein, which also is absorbed and can be measured in the urine. Liver disease, renal failure, and intestinal malabsorption can cause false positive results of these two tests.

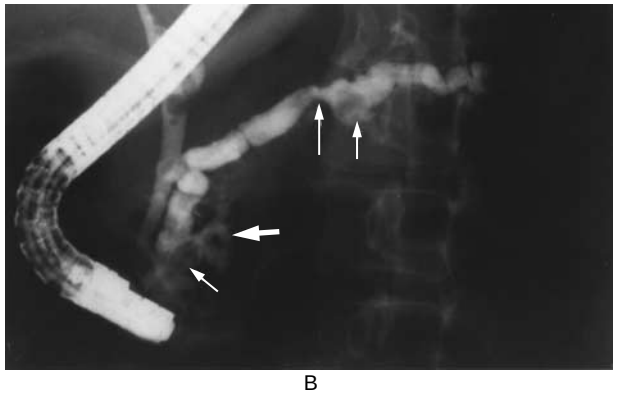
Other tests for the diagnosis of chronic pancreatitis include the measurement of chymotrypsin activity in the stool and trypsin-like immunoreactivity in serum. The former test has a lower sensitivity in cases of mild-to-moderate pancreatic insufficiency than either the bentiromide or the pancreolauryl test,[56] whereas the latter test is primarily of use in distinguishing pancreatic from nonpancreatic forms of fat malabsorption.[51] The administration of caerulein normally causes an increase in serum pancreatic polypeptide concentrations, but this response may be blunted in chronic pancreatitis.[52] The sensitivity and specificity of the last-mentioned test have not been clearly defined. Another test of pancreatic function involves modification of the standard Schilling test. In this test, dual-labeled R protein–vitamin B_{12} is given orally. Normally, this complex is hydrolyzed by pancreatic proteases and absorbed. Thus, the differential absorption of vitamin B_{12} and R protein, with and without the administration of exogenous pancreatic enzymes, can be used to identify patients with pancreatic insufficiency. The test results are abnormal in approximately 50 percent of patients with overt pancreatic exocrine insufficiency.[57]

In a general sense, pancreatic-function tests and imaging studies of duct morphology (i.e., endoscopic retrograde pancreatography) should be viewed as complementary diagnostic tests in chronic pancreatitis. In the majority of patients, the results of both tests are abnormal. However, approximately 10 to 15 percent of patients with normal pancreatograms have abnormal secretin–pancreozymin test results,[58,59] and about 25 percent of patients with abnormal pancreatograms have normal secretin–pancreozymin test results.[58,59] Finally, both tests are normal in 5 percent of patients with either pathologically documented chronic pancreatitis or a subsequent course that clearly establishes a diagnosis of chronic pancreatitis.

A major diagnostic problem is presented by the patient whose abdominal pain is caused by chronic pancreatitis but whose imaging studies are normal. Some have referred to such patients as having "minimal-change pancreatitis," which on histologic assessment can show severe morphologic changes.[60] These patients frequently have non–alcohol-related pancreatitis and



A



B

Figure 4. Endoscopic Retrograde Pancreatograms.

Panel A shows a normal subtraction endoscopic retrograde pancreatogram that reveals the filling of normal side branches and a smooth, nondilated main ductal system. Panel B shows an endoscopic retrograde pancreatogram in a patient with chronic pancreatitis, revealing a dilated, tortuous main duct that contains stones or protein plugs (lucencies in duct marked by short thin arrows). A stricture is visible in the midportion of the duct (long thin arrow). Note the dilatation of the uncinate-process branch (thick arrow).

Table 1. Pancreatic-Function Tests.*

TYPE	SENSITIVITY	SPECIFICITY	STUDY
	%		
Tubeless test			
Bentiromide	85	90	Niederau and Grendell,[41] Lang and Gyr[48]
Pancreolauryl	90	82	Niederau and Grendell,[41] Lankisch[49]
Fecal chymotrypsin	78	94	Adler and Weidenbach[50]
Trypsin radioimmunoassay	33–65	NR	Jacobson et al.[51]
Serum pancreatic polypeptide	48–76	86–93	Campbell et al.[52]
Dual-label Schilling	NR	NR	Brugge et al.[53]
Quantitative stool fat	NR	NR	—
Duodenal-intubation test			
Secretin–pancreozymin	75–90	80–90	Niederau and Grendell,[41] Gullo[54]
Lundh	66–94	NR	Mottaleb et al.,[55] Lankisch et al.[56]

*NR denotes not reported.

small-duct disease. Some have suggested that these patients can be identified by means of the secretin pancreatic-function test.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of chronic pancreatitis presents two major challenges. The first involves identifying the patients with abdominal pain who have chronic pancreatitis but the results of whose imaging procedures, including endoscopic retrograde pancreatography, reveal minimal or no morphologic changes. Pancreatic-function tests may be of value in these cases. The second challenge involves identifying the patients who have symptoms or findings suggestive of chronic pancreatitis but who in fact have pancreatic cancer. The diagnosis of pancreatic cancer in this setting may be difficult or even impossible.[61] Endoscopic retrograde pancreatography, in combination with brush cytology, may be of value in these cases. A pancreatic-duct stricture that is more than 10 mm long, in the absence of ectatic side branches, should suggest the presence of cancer.[61] The sensitivity of brush cytology is about 20 to 25 percent, with nearly 100 percent specificity.[62] Other potentially useful diagnostic tests include the cytologic examination of pancreatic-duct fluid, fine-needle aspiration biopsy of the pancreas, and the measurement of serum markers for pancreatic cancer, such as CA19-9 and carcinoembryonic antigen.[63-67] Unfortunately, the sensitivity and specificity of these tests in early, surgically curable, disease are not very good.

TREATMENT

Pain

Pain, either persistent or episodic, is the symptom that most often requires treatment. Noninvasive approaches include advising abstinence from alcohol or other causative agents, administering analgesic medications, and performing nerve blocks. Some investigators have suggested that pain can be relieved by blocking the stimulation of pancreatic secretion. Normally, the release of cholecystokinin from specific intestinal cells is regulated by a cholecystokinin-releasing peptide in the proximal small intestine that is luminally active and trypsin-sensitive.[70] In chronic pancreatitis, exocrine insufficiency may lead to increased cholecystokinin-mediated stimulation of the pancreas. Theoretically, this process could be interrupted by the administration of digestive enzymes, such as trypsin, cholecystokinin-receptor antagonists, or somatostatin.

The results of studies examining the use of pancreatic enzymes that are administered orally to treat the pain of chronic pancreatitis have been variable, in part because of a high placebo response rate (>35 percent), the potential for exogenously administered digestive enzymes to be inactivated by gastric acid and pancreatic proteases, and the lack of efficacy of enteric coated microsphere preparations.[69-73] In a placebo-controlled, double-blind, crossover study, pancrelipase (Viokase), in a dose of six tablets taken four times per day for one month, significantly reduced pain in 75 percent of patients with mild-to-moderate disease.[72] The best response was in young women with idiopathic chronic pancreatitis, whereas patients with advanced disease, including those with steatorrhea, had no response. Whether cholecystokinin-receptor antagonists or somatostatin analogues, such as octreotide, will be more effective in treating pain is not clear. In a recent multicenter pilot study, octreotide, in a dose of 200 μg administered subcutaneously three times per day for four weeks, reduced pain scores by 25 percent or more in 65 percent of patients with severe chronic pancreatitis,[74] whereas 35 percent responded to placebo. Clearly, the role of exogenous enzymes, cholecystokinin-receptor antagonists, and somatostatin in the treatment of pain in chronic pancreatitis remains uncertain, and further studies are needed before these therapies are widely adopted.

Patients whose pain persists in spite of aggressive noninvasive treatment should undergo endoscopic retrograde pancreatography to define the caliber and morphologic characteristics of their pancreatic ducts. Depending on the population being studied, up to half of these patients may have dilated ducts, frequently with areas of stricture — the "chain of lakes" or "string of pearls" appearance (Fig. 4); the remainder have either ducts of normal caliber (2 to 4 mm in diameter) or small ducts that may lack side branches — the "tree in winter" appearance.[75,76] Ducts larger than 8 mm in diameter can be successfully decompressed by an internal surgical-drainage procedure, such as a longitudinal pancreaticojejunostomy (the modified Peustow procedure[77,78]), but smaller ducts are not amenable to internal surgical drainage. The pain of "large duct" chronic pancreatitis can be relieved, in the short term, by pancreaticojejunostomy in 80 to 90 percent of patients, but five years after operation only 50 to 60 percent of patients remain pain-free.[75] Thus, although the operation is associated with very low morbidity and mortality, its long-term effect on pain control may be limited.

An alternative to surgical drainage involves the use

of endoprostheses or stents placed in the pancreatic duct endoscopically. Recent reports indicate that 30 to 76 percent of patients receiving such prostheses had symptomatic improvement over a period of 14 to 36 months of observation.[79-83] Cremer et al.,[79] for example, noted initial improvement of symptoms in 94 percent of patients who were so treated for pancreatic-duct strictures and upstream ductal dilatation. In that group of patients, 53 percent remained free of symptoms over a mean follow-up period of 36 months. Similarly, Grimm et al.[80] reported that 57 percent of their patients were symptomatically improved by this treatment over a mean follow-up period of 19 months. Although these results seem encouraging, it should be recognized that most of the data reported to date were from relatively short term, nonrandomized studies. The issue is further complicated by the fact that pancreatic-duct stents may not be entirely innocuous; for example, they may cause the pancreatic-duct changes of chronic pancreatitis.[84-86] To avoid this potential problem, some have suggested that endoscopically placed pancreatic-duct stents should be used only for relatively short periods and that the response to short-term endoscopic drainage can be used to identify the patients most likely to benefit from surgical drainage.[79,82,87] At present, endoscopically placed stents should be considered an unproved but potentially useful approach to the treatment of chronic pancreatitis.

The ideal treatment for patients with pancreatic-duct stones, dilated pancreatic ducts, and pain is not known. The stones can be easily removed coincidently with the performance of a surgical-drainage procedure, such as pancreaticojejunostomy. Alternatively, however, they can be fragmented by extracorporeal shock-wave lithotripsy and removed endoscopically after sphincterotomy of the pancreatic duct. Stones can be cleared by this approach in roughly 80 percent of patients, and approximately 50 percent of these have long-term relief of their symptoms.[88,89]

At present, the ultimate role of these various invasive approaches to the treatment of patients with large-duct, symptomatic chronic pancreatitis has not been established. Given the information available at the present time, most physicians recommend longitudinal pancreaticojejunostomy for patients with pain and dilated ducts. This operation may also retard the progression of exocrine and endocrine insufficiency.[90,91]

Patients with pain whose ducts are not dilated present a much greater challenge, since internal surgical drainage is not possible. Experience with endoscopically placed stents in this setting has been limited, but symptomatic improvement has been reported in up to 50 percent of patients.[81,82,92] For the most part, patients with pain and nondilated ducts are either continued on noninvasive treatments, which may include narcotics, or subjected to pancreatic resection. Percutaneous nerve blocks in the celiac plexus have been tried, but the results have been disappointing.[93-95] The small percentage of patients whose pancreatitis is due to posttraumatic ductal strictures usually have disease primarily in the tail of the pancreas, and they can be cured by distal pancreatectomy. In most patients, however, the disease is most severe in the head of the pancreas. Surgical options include the Whipple procedure (pancreaticoduodenectomy), with[96] or without[97] preservation of the pylorus; total pancreatectomy, with[98] or without autotransplantation; and partial resection of the pancreatic head, with preservation of the duodenum.[99,100] Since these procedures may result in the loss of functional pancreatic exocrine and endocrine tissue, they should be reserved for patients with small ducts and incapacitating pain.

Malabsorption

When more than 90 percent of exocrine pancreatic function is lost, clinically overt malabsorption occurs. Steatorrhea (fat malabsorption) is more problematic for the patient than azotorrhea (protein malabsorption), since the former is usually associated with diarrhea and bloating. Treatment consists of a low-fat diet. Medium-chain triglycerides may be useful because their absorption depends on minimal amounts of pancreatic enzymes and does not require the presence of bile salts. For persistent symptoms, pancreatic-enzyme replacement should be given orally just before meals. Neutralization of gastric acid with orally administered bicarbonate, inhibition of acid secretion, or enteric coating of enzyme preparations may prevent degradation of these enzymes as they traverse the stomach. Although there is variation in the lipase activity in the various enzyme preparations, no advantage has been demonstrated for preparations containing higher lipase activities.[101]

Pseudocysts

Pancreatic pseudocysts are collections of pancreatic secretions surrounded by non–epithelial-lined fibrous walls of granulation tissue. Pseudocysts develop in approximately 10 percent of patients with chronic pancreatitis, and in two thirds of them the cyst is in the body or tail of the gland. Most pseudocysts are asymptomatic and resolve spontaneously, but hemorrhage into a pseudocyst, rupture, or infection can occur. Small asymptomatic pseudocysts require no treatment, but treatment is indicated for those that persist for six weeks and are either enlarging or causing symptoms.[102] Treatment options include resection, external drainage, and internal drainage. Distal pancreatectomy is appropriate for cysts in the tail of the pancreas, but not for those whose resection would result in substantial loss of functional pancreatic tissue. External drainage, achieved either surgically or with a percutaneously placed catheter, is simple and safe but may result in a pancreatic fistula, which is often slow to heal and subject to repeated infection.[103] Internal drainage can be established either surgically or endoscopically. The surgical procedure of choice depends on the location of the cyst. Options include cystogastrostomy, cystoduodenostomy, and Roux-en-Y cystojejunostomy. Internal drainage can also be achieved en-

doscopically with the use of a transpapillary stent or, if the cyst bulges into either the stomach or duodenum, by means of an endoscopically created cystoenteric fistula. Reports of patients treated by endoscopic cyst drainage indicate a success rate of 80 percent and recurrence rates of 10 to 21 percent.[104,105] Complications have been reported in 11 percent of patients and a procedure-related mortality rate of 3 percent was noted.[82]

Pancreatic Ascites and Pleural Fistulas

Pancreatic juice can leak into the peritoneum from a ruptured duct or pseudocyst, resulting in pancreatic ascites, or it can track into the pleural space, causing a pancreaticopleural fistula. The diagnosis can be made if paracentesis or thoracentesis yields fluid rich in protein and amylase. Half the patients so affected can be cured by nonoperative methods, including repeated aspiration; the administration of diuretic agents, carbonic anhydrase inhibitors, or octreotide; and parenteral nutrition; but these methods may be associated with prolonged morbidity. Currently, most patients are treated surgically by anastomosis of a defunctionalized Roux-en-Y loop of jejunum to the site of the ductal rupture or, if the ductal communication is in the pancreatic tail, by distal pancreatectomy. Experience with the use of endoscopically placed stents to treat pancreatic-duct leaks is limited but suggests that, by bridging ductal disruptions with a transpapillary stent, surgeons can achieve short-term resolution in up to 90 percent of patients.[106] The long-term results, however, may still depend on the underlying ductal disease, and surgical intervention may be required for the long-term management of this problem.

Duodenal and Bile-Duct Obstruction

Symptomatic bile or duodenal obstruction, or both, develops in 5 to 10 percent of patients with chronic pancreatitis, usually those with large-duct disease. Obstruction may be caused by a pseudocyst in the head of the gland or by the chronic inflammation and fibrosis that is part of chronic pancreatitis. Treatment should be directed at relieving the obstruction either by decompression of the pseudocyst or by the creation of a gastrojejunostomy or choledochoenterostomy. Endoscopic stenting may provide an alternative approach to the treatment of symptomatic bile-duct strictures in patients who are not considered to be good candidates for surgery.[107,108]

We are indebted to Dr. Melissa Upton, Department of Pathology, Beth Israel Hospital, Boston, for providing Figure 1.

References

1. Marks IN, Bank S. Etiology, clinical aspects, and medical management. In: Berk JE, Haubrich WS, Kalser MH, Roth JLA, Schaffner F, eds. Bockus gastroenterology. 4th ed. Vol. 6. Philadelphia: W.B. Saunders, 1985:4020-40.
2. Singer MV, Gyr KE, Sarles H. Revised classification of pancreatitis: report of the Second International Symposium on the Classification of Pancreatitis in Marseille, France, March 28-30, 1984. Gastroenterology 1985;89:683-5.
3. Samer M, Cotton PB. Classification of pancreatitis. Gut 1984;25:756-9.
4. Owyang C, Levitt M. Chronic pancreatitis. In: Yamada T, Alpers DH, Owyang C, Powell DW, Silverstein FE, eds. Textbook of gastroenterology. Vol. 2. New York: J.B. Lippincott, 1991:1874-93.
5. Sarles H, Sahel J, Staub JL, Bourry J, Laugier R. Chronic pancreatitis. In: Howat HT, Sarles H, eds. The exocrine pancreas. Philadelphia: W.B. Saunders, 1979:402-39.
6. Pitchumoni CS. Role of nutrition in chronic pancreatitis. In: Beger HG, Büchler M, Ditschuneit H, Malfertheiner P, eds. Chronic pancreatitis: research and clinical management. Berlin, Germany: Springer-Verlag, 1990:15-25.
7. Durbec JP, Sarles H. Multicenter survey of the etiology of pancreatic diseases: relationship between the relative risk of developing chronic pancreatitis and alcohol, protein and lipid consumption. Digestion 1978;18:337-50.
8. Blair AJ III, Russell CG, Cotton PB. Resection for pancreatitis in patients with pancreas divisum. Ann Surg 1984;200:590-4.
9. Pitchumoni CS. Special problems of tropical pancreatitis. Clin Gastroenterol 1984;13:941-59.
10. Layer P, Singer MV. Non-alcohol-related etiologies in chronic pancreatitis. In: Beger HG, Büchler M, Ditschuneit H, Malfertheiner P, eds. Chronic pancreatitis: research and clinical management. Berlin, Germany: Springer-Verlag, 1990:35-40.
11. Ammann RW. Chronic pancreatitis in the elderly. Gastroenterol Clin North Am 1990;19:905-14.
12. Sachel J, Sarles H. Modifications of pure human pancreatic juice induced by chronic alcohol consumption. Dig Dis Sci 1979;24:897-905.
13. Nakamura K, Sarles H, Payan H. Three-dimensional reconstruction of the pancreatic ducts in chronic pancreatitis. Gastroenterology 1972;62:942-9.
14. Harada H, Miyake H, Miki T, Kobayashi T, Sasaki T, Kimura I. Role of endoscopic elimination of protein plugs in the treatment of chronic pancreatitis. Gastroenterol Japonica 1982;38:463-8.
15. Tsurumi T, Fujii M, Takeda M, Tanaka J, Harada H, Oka H. A case of chronic pancreatitis successfully treated by endoscopic removal of protein plugs. Acta Med Okayama 1984;38:169-74.
16. Harada H, Hayashi T, Miki H, et al. Histochemical studies on enzyme-digested protein plugs of patients with chronic pancreatitis: a preliminary report. Acta Med Okayama 1983;37:227-31.
17. Harada H, Ueda O, Yasuoka M, et al. Histochemical studies on protein plugs obtained by endoscopic retrograde catheterization of the papilla. Gastroenterol Japonica 1981;16:563-7.
18. Freedman SD, Sakamoto K, Venu RP. GP2, the homologue to the renal cast protein uromodulin, is a major component of intraductal plugs in chronic pancreatitis. J Clin Invest 1993;92:83-90.
19. Guy O, Robles-Diaz G, Adrich Z, Sahel J, Sarles H. Protein content of precipitates present in pancreatic juice of alcoholic subjects and patients with chronic calcifying pancreatitis. Gastroenterology 1983;84:102-7.
20. Allan J, White TT. An alternate mechanism for the formation of protein plugs in chronic calcifying pancreatitis. Digestion 1974;11:428-31.
21. Multigner L, De Caro A, Lombardo D, Campese D, Sarles H. Pancreatic stone protein, a phosphoprotein which inhibits calcium carbonate precipitation from human pancreatic juice. Biochem Biophys Res Commun 1983;110:69-74.
22. Multigner L, Sarles H, Lombardo D, De Caro A. Pancreatic stone protein. II. Implication in stone formation during the course of chronic calcifying pancreatitis. Gastroenterology 1985;89:387-91.
23. Schmiegel W, Burchert M, Kalthoff H, et al. Immunochemical characterization and quantitative distribution of pancreatic stone protein in sera and pancreatic secretions in pancreatic disorders. Gastroenterology 1990;99:1421-30.
24. Bernard JP, De Reggi M, Barthet M, Sahel J, Sarles H, Dagorn JC. Quantification of human lithostathine in pancreatic juice by high performance liquid chromatography. Gastroenterology 1993;104:Suppl:A295. abstract.
25. Okazaki K, Yamamoto Y, Nishimori I, et al. Motility of the sphincter of Oddi and pancreatic main ductal pressure in patients with alcoholic, gallstone-associated, and idiopathic chronic pancreatitis. Am J Gastroenterol 1988;83:820-6.
26. Kloppel G, Maillet B. The morphological basis for the evolution of acute pancreatitis into chronic pancreatitis. Virchows Arch A Pathol Anat Histopathol 1992;420:1-4.
27. Ammann RW, Akovbiantz A, Largiader F, Schueler G. Course and outcome of chronic pancreatitis: longitudinal study of a mixed medical-surgical series of 245 patients. Gastroenterology 1984;86:820-8.
28. Hayakawa T, Kondo T, Shibata T, Sugimoto Y, Kitagawa M. Chronic alcoholism and evolution of pain and prognosis in chronic pancreatitis. Dig Dis Sci 1989;34:33-8.
29. Layer P, Yamamoto H, Kalthoff L, Clain JE, Bakken LJ, DiMagno EP. The different courses of early- and late-onset idiopathic and alcoholic pancreatitis. Gastroenterology 1994;107:1481-7.
30. Warshaw AL. Pain in chronic pancreatitis: patients, patience, and the impatient surgeon. Gastroenterology 1984;86:987-9.
31. Lankisch PG, Lohr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis: pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. Digestion 1993;54:148-55.

32. Ammann RW, Buehler H, Muench R, Freiburghaus AW, Siegenthaler W. Differences in the natural history of idiopathic (nonalcoholic) and alcoholic pancreatitis: a comparative long-term study of 287 patients. Pancreas 1987; 2:368-77.
33. Gullo L, Barbara L, Labo G. Effect of cessation of alcohol use on the course of pancreatic dysfunction in alcoholic pancreatitis. Gastroenterology 1988;95:1063-8.
34. Miyake H, Harada H, Kunichika K, Ochi K, Kimura I. Clinical course and prognosis of chronic pancreatitis. Pancreas 1987;2:378-85.
35. Ammann RW, Muellhaupt B, Meyenberger C, Heitz PU. Alcoholic nonprogressive chronic pancreatitis: prospective long-term study of a large cohort with alcoholic acute pancreatitis (1976-1992). Pancreas 1994;9:365-73.
36. Lowenfels AB, Maisonneuve P, Cavallini G, et al. Pancreatitis and the risk of pancreatic cancer. N Engl J Med 1993;328:1433-7.
37. Marks IN, Bank S, Louw JH. Chronic pancreatitis in the Western Cape. Digestion 1973;9:447-53.
38. Ammann RW, Hammer B, Fumagalli I. Chronic pancreatitis in Zurich, 1963-1972: clinical findings and follow-up studies of 102 cases. Digestion 1973;9:404-15.
39. Clark E. Pancreatitis in acute and chronic alcoholism. Am J Dig Dis 1942; 9:428-31.
40. Littenberg G, Afroudakis A, Kaplowitz N. Common bile duct stenosis from chronic pancreatitis: a clinical and pathologic spectrum. Medicine 1979;58: 385-412.
41. Niederau C, Grendell JH. Diagnosis of chronic pancreatitis. Gastroenterology 1985;88:1973-95.
42. Bastid C, Sahel J, Filho M, Sarles H. Diameter of the main pancreatic duct in chronic calcifying pancreatitis: measurement by ultrasonography versus pancreatography. Pancreas 1990;5:524-7.
43. Luetmer PH, Stephens DH, Ward EM. Chronic pancreatitis: reassessment with current CT. Radiology 1989;171:353-7.
44. Zuccaro G Jr, Sivak MV Jr. Endoscopic ultrasonography in the diagnosis of chronic pancreatitis. Endoscopy 1992;24:Suppl 1:347-9.
45. Nattermann C, Goldschmidt AJ, Dancygier H. Endosonography in chronic pancreatitis — a comparison between endoscopic retrograde pancreatography and endoscopic ultrasonography. Endoscopy 1993;25:565-70.
46. Semelka RC, Kroeker MA, Shoenut JP, Kroeker R, Yaffe CS, Micflikier AB. Pancreatic disease: prospective comparison of CT, ERCP and 1.5-T MR imaging with dynamic gadolinium enhancement and fat suppression. Radiology 1991;181:785-91.
47. Axon ATR, Classen M, Cotton PB, Cremer M, Freeny PC, Lees WR. Pancreatography in chronic pancreatitis: international definitions. Gut 1984;25: 1107-12.
48. Lang C, Gyr K. Indirect pancreatic function test with NBT-PABA. In: Malfertheiner P, Ditschuneit H, eds. Diagnostic procedures in pancreatic disease. Berlin, Germany: Springer-Verlag, 1986:215-22.
49. Lankisch PG. The indirect pancreatic function test "pancreolauryl" in chronic pancreatitis. In: Malfertheiner P, Ditschuneit H, eds. Diagnostic procedures in pancreatic disease. Berlin, Germany: Springer-Verlag, 1986: 223-30.
50. Adler G, Weidenbach F. Fecal chymotrypsin in chronic pancreatitis disease. In: Malfertheiner P, Ditschuneit H, eds. Diagnostic procedures in pancreatic disease. Berlin, Germany: Springer-Verlag, 1986:231-7.
51. Jacobson DG, Curington C, Connery K, Toskes PP. Trypsin-like immunoreactivity as a test for pancreatic insufficiency. N Engl J Med 1984;310: 1307-9.
52. Campbell D, Slaff J, McGuigan J, DesJardin L, Toskes P. Integrated pancreatic polypeptide response in pancreatic diseases. Gastroenterology 1985;88:1341. abstract.
53. Brugge WR, Goff JS, Allen NC, Podell ER, Allen RH. Development of a dual label Schilling test for pancreatic exocrine function based on the differential absorption of cobalamin bound to intrinsic factor and R protein. Gastroenterology 1980;78:937-49.
54. Gullo L. Pancreatic function test by means of duodenal intubation. In: Malfertheiner P, Ditschuneit H, eds. Diagnostic procedures in pancreatic disease. Berlin, Germany: Springer-Verlag, 1986:201-7.
55. Mottaleb A, Kapp F, Noguera EC, Kellock TD, Wiggins HS, Waller SL. The Lundh test in the diagnosis of pancreatic disease: a review of five years' experience. Gut 1973;14:835-41.
56. Lankisch PG, Schreiber A, Otto J. Pancreolauryl test: evaluation of a tubeless pancreatic function test in comparison with other indirect and direct tests for exocrine pancreatic function. Dig Dis Sci 1983;28:490-3.
57. Toskes PP, Deren JJ. Vitamin B 12 absorption and malabsorption. Gastroenterology 1973;65:662-83.
58. Valentini M, Cavallini G, Vantini I, et al. A comparative evaluation of endoscopic retrograde cholangiopancreatography and the secretin-cholecystokinin test in the diagnosis of chronic pancreatitis: a multicentre study in 124 patients. Endoscopy 1981;13:64-7.
59. Lankisch PG, Seidensticker J, Otto J, et al. Secretin-pancreozymin test (SPT) and/or ERCP for diagnosing or excluding chronic pancreatitis? Pancreas 1993;8:760. abstract.
60. Walsh TN, Rode J, Theis BA, Russell RC. Minimal change chronic pancreatitis. Gut 1992;33:1566-71.
61. Shemesh E, Czerniak A, Nass S, Klein E. Role of endoscopic retrograde cholangiopancreatography in differentiating pancreatic cancer coexisting with chronic pancreatitis. Cancer 1990;65:893-6.
62. Wiersema MJ, Lehman GA. ERCP biopsy and cytology techniques. In: Barkin J, O'Phelan CA, eds. Advanced therapeutic endoscopy. 2nd ed. New York: Raven Press, 1994:291-8.
63. Del Favero G, Fabris C, Angonese C, et al. Cytology in the diagnosis of pancreatic cancer. Int J Pancreatol 1988;3:Suppl 1:S137-S141.
64. Sawada Y, Gonda H, Hayashida Y. Combined use of brushing cytology and endoscopic retrograde pancreatography for the early detection of pancreatic cancer. Acta Cytol 1989;33:870-4.
65. DelMaschio A, Vanzulli A, Sironi S, et al. Pancreatic cancer versus chronic pancreatitis: diagnosis with CA 19-9 assessment, US, CT, and CT-guided fine-needle biopsy. Radiology 1991;178:95-9.
66. Parsons L Jr, Palmer CH. How accurate is fine-needle biopsy in malignant neoplasia of the pancreas? Arch Surg 1989;124:681-3.
67. Steinberg W. The clinical utility of the CA 19-9 tumor-associated antigen. Am J Gastroenterol 1990;85:350-5.
68. Owyang C. Negative feedback control of exocrine pancreatic secretion: role of cholecystokinin and cholinergic pathway. J Nutr 1994;124:Suppl: 1321S-1326S.
69. Dobrilla G. Management of chronic pancreatitis: focus on enzyme replacement therapy. Int J Pancreatol 1989;5:Suppl:17-29.
70. Andren-Sandberg A. Theory and practice in the individualization of oral pancreatic enzyme administration for chronic pancreatitis. Int J Pancreatol 1989;5:Suppl:51-62.
71. Mossner J, Secknus R, Meyer J, Niederau C, Adler G. Treatment of pain with pancreatic extracts in chronic pancreatitis: results of a prospective placebo-controlled multicenter trial. Digestion 1992;53:54-66.
72. Slaff J, Jacobson D, Tillman CR, Curington C, Toskes P. Protease-specific suppression of pancreatic exocrine secretion. Gastroenterology 1984;87: 44-52.
73. Isaksson G, Ihse I. Pain reduction by an oral pancreatic enzyme preparation in chronic pancreatitis. Dig Dis Sci 1983;28:97-102.
74. Toskes PP, Forsmark CE, DeMeo MT, et al. A multicenter controlled trial of octreotide for the pain of chronic pancreatitis. Pancreas 1993;8:774. abstract.
75. Frey CF. Why and when to drain the pancreatic ductal system. In: Beger HG, Büchler M, Ditschuneit H, Malfertheiner P, eds. Chronic pancreatitis: research and clinical management. Berlin, Germany: Springer-Verlag, 1990:415-25.
76. Nagata A, Homma T, Tamai K, et al. A study of chronic pancreatitis by serial endoscopic pancreatography. Gastroenterology 1981;81:884-91.
77. Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. Arch Surg 1958;76:898-907.
78. Partington PF, Rochelle REL. Modified Puestow procedure for retrograde drainage of the pancreatic duct. Ann Surg 1960;152:1037-43.
79. Cremer M, Deviere J, Delhaye M, Baize M, Vandermeeren A. Stenting in severe chronic pancreatitis: results of medium-term follow-up in seventy-six patients. Endoscopy 1991;23:171-6.
80. Grimm H, Meyer WH, Nam VC, Soehendra N. New modalities for treating chronic pancreatitis. Endoscopy 1989;21:70-4.
81. Huibregtse K, Schneider B, Vrij AA, Tytgat GN. Endoscopic pancreatic drainage in chronic pancreatitis. Gastrointest Endosc 1988;34:9-15.
82. Geenen JE, Rolny P. Endoscopic therapy of acute and chronic pancreatitis. Gastrointest Endosc 1991;37:377-82.
83. Burdick JS, Hogan WJ. Chronic pancreatitis: selection of patients for endoscopic therapy. Endoscopy 1991;23:155-9.
84. Kozarek RA. Pancreatic stents can induce ductal changes consistent with chronic pancreatitis. Gastrointest Endosc 1990;36:93-5.
85. Gulliver DJ, Edmunds S, Baker ME, et al. Stent placement for benign pancreatic diseases: correlation between ERCP findings and clinical response. AJR Am J Roentgenol 1992;159:751-5.
86. Freedman SF, Venu RP. Can pancreatic stent placement lead to chronic pancreatitis. Gastroenterology 1993;104:Suppl:A304. abstract.
87. Siegel JH, Ben-Zvi JS, Pullano W, Cooperman A. Effectiveness of endoscopic drainage for pancreas divisum: endoscopic and surgical results in 31 patients. Endoscopy 1990;22:129-33.
88. Delhaye M, Vandermeeren A, Baize M, Cremer M. Extracorporeal shock-wave lithotripsy of pancreatic calculi. Gastroenterology 1992;102:610-20.
89. Neuhaus H. Fragmentation of pancreatic stones by extracorporeal shock wave lithotripsy. Endoscopy 1991;23:161-5.
90. Nealon WH, Townsend CM Jr, Thompson JC. Operative drainage of the pancreatic duct delays functional impairment in patients with chronic pancreatitis: a prospective analysis. Ann Surg 1988;208:321-9.
91. Nealon WH, Thompson JC. Progressive loss of pancreatic function in chronic pancreatitis is delayed by main pancreatic duct decompression: a longitudinal prospective analysis of the modified puestow procedure. Ann Surg 1993;217:458-66.
92. McCarthy J, Geenen JE, Hogan WJ. Preliminary experience with endoscopic stent placement in benign pancreatic diseases. Gastrointest Endosc 1988;34:16-8.

93. Leung JW, Bowen-Wright M, Aveling W, Shorvon PJ, Cotton PB. Coeliac plexus block for pain in pancreatic cancer and chronic pancreatitis. Br J Surg 1983;70:730-2.
94. Bengtsson M, Lofstrom JB. Nerve block in pancreatic pain. Acta Chir Scand 1990;156:285-91.
95. Imrie CW. Denervation procedures in the management of chronic pancreatitis. In: Beger HG, Büchler M, Ditschuneit H, Malfertheiner P, eds. Chronic pancreatitis: research and clinical management. Berlin, Germany: Springer-Verlag, 1990:411-4.
96. Traverso LW, Longmire WP Jr. Preservation of the pylorus in pancreaticoduodenectomy. Surg Gynecol Obstet 1978;146:959-62.
97. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg 1935;102:763-79.
98. Rossi RL, Rothschild J, Braasch JW, Munson JL, ReMine SG. Pancreatoduodenectomy in the management of chronic pancreatitis. Arch Surg 1987; 122:416-20.
99. Beger HG, Krautzberger W, Bittner R, Büchler M, Limmer J. Duodenum-preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. Surgery 1985;97:467-73.
100. Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. Pancreas 1987;2:701-7.
101. Opekun AR Jr, Klein PD, Sutton FM Jr, Trey G, Graham DY. Pancreatic enzyme enteric coated microspheres are now available with different lipase activities: does this result in improved therapy? Gastroenterology 1993; 104:Suppl:A326. abstract.
102. Vitas GJ, Sarr MG. Selected management of pancreatic pseudocysts: operative versus expectant management. Surgery 1992;111:123-30.
103. Criado E, De Stefano AA, Weiner TM, Jaques PF. Long term results of percutaneous catheter drainage of pancreatic pseudocysts. Surg Gynecol Obstet 1992;175:293-8.
104. Cremer M, Deviere J, Engelholm L. Endoscopic management of cysts and pseudocysts in chronic pancreatitis: long-term follow-up after 7 years of experience. Gastrointest Endosc 1989;35:1-9.
105. Sahel J. Endoscopic drainage of pancreatic cysts. Endoscopy 1991;23:181-4.
106. Kozarek RA, Ball TJ, Patterson DJ, Freeny PC, Ryan JA, Traverso LW. Endoscopic transpapillary therapy for disrupted pancreatic duct and peripancreatic fluid collections. Gastroenterology 1991;100:1362-70.
107. Deviere J, Devaere S, Baize M, Cremer M. Endoscopic biliary drainage in chronic pancreatitis. Gastrointest Endosc 1990;36:96-100.
108. Deviere J, Cremer M, Baize M, Love J, Sugai B, Vandermeeren A. Management of common bile duct stricture caused by chronic pancreatitis with metal mesh self expandable stents. Gut 1994;35:122-6.

IMAGES IN CLINICAL MEDICINE

Images in Clinical Medicine, a weekly *Journal* feature, presents clinically important visual images, emphasizing those a doctor might encounter in an average day at the office, the emergency department, or the hospital. If you have an original unpublished, high-quality color or black-and-white photograph representing such a typical image that you would like considered for publication, send it with a descriptive legend to Kim Eagle, M.D., University of Michigan Medical Center, Division of Cardiology, 3910 Taubman Center, Box 0366, 1500 East Medical Center Drive, Ann Arbor, MI 48109. For details about the size and labeling of the photographs, the requirements for the legend, and authorship, please contact Dr. Eagle at 313-936-5275 (phone) or 313-936-5256 (fax), or the *New England Journal of Medicine* at images@edit.nejm.org (e-mail).