Chronic pancreatitis: Management

AUTHORS: Steven D Freedman, MD, PhD, Christopher E Forsmark, MD
SECTION EDITOR: Douglas G Adler, MD, FACG, AGAF, FASGE
DEPUTY EDITOR: Shilpa Grover, MD, MPH, AGAF

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **Sep 13, 2023.**

INTRODUCTION

Chronic pancreatitis can produce a variety of symptoms and complications that require therapy [1]. Abdominal pain is the most common clinical feature, the most common reason for intervention, and has the most negative impact on quality of life. As chronic pancreatitis progresses, patients may develop exocrine pancreatic insufficiency (steatorrhea, maldigestion) as well as diabetes due to destruction of pancreatic islet cells. Patients with chronic pancreatitis can develop a variety of complications, including pancreatic pseudocyst, bile duct or duodenal obstruction, visceral artery pseudoaneurysm, pancreatic ascites and pancreatic pleural effusions, gastric varices due to thrombosis of the splenic vein, and pancreatic malignancy. The avoidance of environmental toxins such as tobacco and alcohol are the only measures that can prevent progression of chronic pancreatitis. All other therapies are directed at managing abdominal pain, maldigestion, pancreatogenic diabetes, or the other complications of chronic pancreatitis. This topic will review the treatment of abdominal pain, pancreatic exocrine insufficiency, and pancreatogenic diabetes. The clinical manifestations of chronic pancreatitis and management of complications of chronic pancreatitis are discussed in detail separately. (See "Overview of the complications of chronic pancreatitis" and "Etiology and pathogenesis of chronic pancreatitis in adults" and "Causes and contributing risk factors for chronic pancreatitis in children and adolescents" and "Chronic pancreatitis: Clinical manifestations and diagnosis in adults" and "Clinical manifestations and diagnosis of chronic and acute recurrent pancreatitis in children".)

GENERAL MEASURES

Cessation of alcohol and tobacco — We advise alcohol and smoking cessation in patients with chronic pancreatitis. Cessation of alcohol (if this is the etiology of the chronic pancreatitis) and tobacco delay progression of chronic pancreatitis, and, in the case of tobacco, reduce the likelihood of subsequent pancreatic carcinoma. Their impact on pain is variable; some patients will experience some degree of pain relief with abstinence.

Diet and supplements — Patients with chronic pancreatitis are advised to consume low-fat meals, small meals, and avoid dehydration. While these recommendations are reasonable and often most tolerable to patients, they are not supported by any data. Many patients with chronic pancreatitis may also have some degree of gastroparesis, and smaller meals may minimize symptoms as well as consideration of prokinetic medications. Very low-fat diets are to be avoided due to increased risk for fat-soluble vitamin deficiencies (A, E, D, and K). Vitamin supplementation is often required, and vitamin D and calcium supplementation should be nearly universal. More specialized nutritional supplementation (eg, medium-chain triglyceride oil, elemental diets) are rarely, if ever, necessary.

MANAGEMENT OF PAIN ASSOCIATED WITH CHRONIC PANCREATITIS

Evaluation to rule out other etiologies — Pain is the most common symptom of chronic pancreatitis and is responsible for the most negative impact on quality of life [2-4]. However, pain is not universal and some patients with chronic pancreatitis may present with exocrine insufficiency or diabetes rather than pain.

Prior to initiating therapy in a patient with chronic pancreatitis who presents with abdominal pain, it is necessary to confirm that the symptoms are in fact due to chronic pancreatitis and not an alternative etiology. This is particularly challenging in the early stages of chronic pancreatitis when abdominal pain may be significant, but characteristic and diagnostic imaging features may be absent. (See "Chronic pancreatitis: Clinical manifestations and diagnosis in adults" and "Clinical manifestations and diagnosis of chronic and acute recurrent pancreatitis in children".)

Initial evaluation should include a detailed history to assess for the presence of abdominal pain associated with chronic pancreatitis at baseline, the character of pain (constant or intermittent, usual triggers for pain), severity, and impact on their quality of life. Patients with established chronic pancreatitis may develop worsening abdominal pain for many other reasons (peptic ulcer disease, superimposed pancreatic carcinoma, narcotic bowel, gastroparesis, pancreatic pseudocyst, duodenal or biliary obstruction). While there is no single pathognomonic

characteristic of pain associated with chronic pancreatitis, it is most commonly epigastric, boring with radiation to the back, and is alleviated by leaning forward. Typically, the pain is worse within 5 to 10 minutes of eating as a result of stimulating the inflamed gland. Pain may initially be episodic and tends to become more continuous over time. During the initial phases, elevations in amylase and lipase are common with painful flares, but as the disease progresses, pancreatic enzymes are often not elevated during painful flares.

To identify alternative causes of pain we perform high-quality computed tomography (CT) or magnetic resonance imaging (MRI). Imaging can also determine the anatomy and diameter of the pancreatic duct, which is useful when considering possible endoscopic or surgical therapy for pain. The appearance of the pancreatic duct, and of the pancreas itself, on imaging studies does not predict symptoms. Patients with a very dilated pancreatic duct and an obstructing stone in the head of the pancreas or with diffuse pancreatic calcifications may have no pain, while those with a non-dilated duct and few or no calcifications may have severe pain. (See 'Subsequent approach' below.)

Initial non-invasive approach — The mechanisms of pain in patients with chronic pancreatitis are complex and involve both injury of the pancreas and alterations in visceral nociceptive signaling [5,6]. Unfortunately, and perhaps due to, these complex mechanisms, strategies for treatment of pain have limited efficacy.

Analgesics — The majority of patients with painful chronic pancreatitis require analgesics [7,8]. Efforts should be made to minimize opioids, especially chronic narcotic use. We begin with nonsteroidal antiinflammatory drugs (NSAIDs) and acetaminophen and suggest the use of opioid agents only if non-narcotic agents fail. Patients should be seen frequently and counseled that pain control, rather than total absence of pain, is the realistic goal. In patients who require opioid analgesia, we initially use lower-potency opioid agents like tramadol. Tramadol, a dual-action analgesic, with mu-opioid agonistic and monoaminergic properties, has been studied in painful chronic pancreatitis and has similar efficacy as stronger opioids. In any patient with pain requiring opioid therapy, we add adjunctive agents including tricyclic antidepressants, serotonin reuptake inhibitors (SSRIs), and combined serotonin and norepinephrine reuptake inhibitors (eg, duloxetine) or gabapentoids (pregabalin or gabapentin). These should continue for several weeks or even a few months, prior to considering increasing the dose of potency of opioid therapy. Referral to a pain clinic is often of benefit. Our approach is consistent with The World Health Organization (WHO) analgesic ladder, which was developed to guide treatment of cancer pain in adults, and suggests initial treatment of chronic pain with nonopioid medications [9].

Adjunctive agents — In patients with pain requiring opioid therapy, we use adjunctive agents to minimize the use of opioid analgesia. Adjunctive agents including tricyclic antidepressants,

SSRIs, and combined serotonin and norepinephrine reuptake inhibitors (eg, duloxetine) or gabapentoids (pregabalin or gabapentin) may allow opioid dose to be minimized and treat co-existent depression, which is highly prevalent in patients with chronic pancreatitis.

Antioxidants and other therapies — Antioxidant therapy can be utilized for initial management of abdominal pain due to chronic pancreatitis, although the benefit of pain reduction is likely small. Results from randomized trials of antioxidant supplements for treatment of pain associated with chronic pancreatitis have been conflicting [10,11]. It is not clear what might explain these different results, but it may be due to differences in the population studied (particularly the nutritional status prior to antioxidant therapy or etiology of chronic pancreatitis). In a 2014 meta-analysis that included nine randomized trials, antioxidants appeared to reduce pain but the effect size was small [12]. Adverse events occurred in 16 percent of participants and were mostly mild (eg, headache, gastrointestinal complaints), but resulted in cessation of antioxidant use by trial participants. We generally use a combination of vitamin E (200 international units [IU]), vitamin C (500 mg), beta-carotene (5000 IU), selenium (500 mcg), and methionine (1000 mg).

Pancreatic enzyme supplementation (table 1) may reduce pain due to abdominal cramping and diarrhea due to exocrine pancreatic insufficiency in selected patients. However, it is unclear whether enzyme supplementation treats pain secondary to pancreatic inflammation or ductal stones. The rationale for using pancreatic enzyme supplementation was that delivering high doses of pancreatic proteases to the duodenum would reduce cholecystokinin (CCK) levels, which would reduce the stimulation of the pancreas by CCK. However, only the non-enteric preparations release the majority of their proteases in the duodenum, and these agents are not easily available. Randomized trials using a non-enteric-coated tablet demonstrated some reduction in pain, while several trials using enteric-coated capsules had no effect. A meta-analysis of these trials was not able to demonstrate a benefit [13], although these agents are still commonly utilized in an attempt to reduce pain (see 'Exocrine pancreatitis insufficiency' below).

The use of medical marijuana and nontraditional approaches (acupuncture, acupressure, cognitive behavioral therapy, mindfulness, meditation) are not well studied in patients with chronic pancreatitis [14].

Subsequent approach — In patients with pain due to chronic pancreatitis who fail to respond to medical management alone, the subsequent management depends on pancreatic ductal anatomy and the available expertise. Patients should be managed by a multidisciplinary team and should have surgical consultation at this point. In those with a non-dilated pancreatic duct, continued medical therapy is appropriate, with consideration of celiac plexus block. Surgical

management in patients with a nondilated main pancreatic duct (<6 to 7 mm) involves resection of the involved pancreas.

Patients with non-dilated pancreatic duct

Celiac plexus block — Celiac plexus blockade is an option for pain relief in patients with refractory pain due to chronic pancreatitis. Advantages of celiac plexus blockade include the fact that a single treatment can potentially provide pain reduction or relief, may reduce or eliminate the need for oral analgesia, and can be performed quickly and repeated as needed. However, it is unclear which patients will derive the most benefit and the pain relief is transient, lasting for three to six months. Celiac plexus blockade can be repeated on an "as-needed" basis, generally separating procedures by three months or more if the patient has had clinical benefit from the initial celiac intervention.

The celiac nerve plexus transmits nociceptive signals from the pancreas, with transmission through several splanchnic nerves. Blocking of the pain signal by injection of an anesthetic (typically bupivacaine), sometimes with a steroid, into the celiac plexus could induce temporary pain relief. Celiac plexus block can be administered by computed tomography (CT) guidance, or by endoscopic ultrasound (EUS) guidance, which is safer and more effective than CT. The benefit of EUS-guided celiac plexus block in chronic pancreatitis is not well studied [15].

Celiac plexus neurolysis, an attempt to destroy the nerve fibers within the plexus, either with injection of absolute alcohol or sectioning the splanchnic nerves in the thorax, is not appropriate for chronic pancreatitis and is reserved for pancreatic malignancy.

Surgical resection — In patients with a small-diameter main pancreatic duct (<6 to 7 mm) with refractory pain, resection, rather than drainage of the fibrotic and poorly drained parenchyma, is performed. Directed partial resection is performed based on whether the disease is head-dominant (pancreaticoduodenectomy) or tail-dominant (distal pancreatectomy). Patients with diffuse parenchymal involvement may require a total pancreatectomy, ideally with islet autotransplantation. All of these operations are uncommonly performed for chronic pancreatitis. Surgery has largely focused on the pancreatic head in those with an inflammatory mass in the head of the pancreas obstructing the duodenum or the bile duct. (See "Surgery for chronic pancreatitis" and "Total pancreatectomy" and "Pancreas and islet transplantation in diabetes mellitus".)

- **Pancreatoduodenectomy (Whipple operation)** – This operation, to remove the entire pancreatic head and duodenum, creates a pancreaticojejunostomy and choledochojejunostomy, and can be performed with antrectomy or with pylorus-sparing reconstruction (figure 1). It is most commonly performed for chronic pancreatitis with a

large inflammatory mass in the head of the pancreas, and particularly in those in whom pancreatic cancer cannot be ruled out. Mortality from this operation is less than 3 percent in the most experienced centers, but substantially more in centers doing less than 10 such procedures yearly. (See "Surgery for chronic pancreatitis", section on 'Pancreaticoduodenectomy'.)

- **Duodenum-preserving pancreatic head resection (DPPHR)** – Several procedures have been developed to allow resection of the pancreatic head while leaving in place the duodenum, in an effort to reduce postoperative morbidity (figure 2A-B and figure 1). In the Beger operation, the pancreatic head is formally resected, and a Roux-anastomosis is created to drain the remaining pancreatic remnant and bile duct. In the Frey operation, only the anterior surface of the pancreatic head is cored out and a longitudinal incision is performed over the remaining pancreatic duct in the body and tail of the pancreas, again with a Roux reconstruction. Other variants on this surgical approach also exist. (See "Surgery for chronic pancreatitis", section on 'Duodenal-preserving pancreatic head resection'.)

  A number of randomized trials have compared these resective procedures, comparing a Whipple operation with one of the DPPHR approaches. In short-term follow-up, the results are comparable in relieving pain and in operative complications, mortality, and quality of life [16]. More postoperative diabetes is seen in the patients undergoing Whipple surgery. Exocrine insufficiency and diabetes are more frequent in those undergoing these resective procedures compared with those undergoing a simple drainage operation.

- **Total pancreatectomy with islet cell autotransplantation (TPIAT)** — This procedure involves complete resection of the pancreas with subsequent digestion of the resected gland to obtain pancreatic islets and reinfusion of these islets in the portal vein to prevent or attenuate the development of diabetes (figure 3) [17,18]. It is only performed in a few centers and is most appropriate to consider in younger patients with intractable pain, with idiopathic or genetic forms of chronic pancreatitis. Diabetes is common after this procedure, and exocrine insufficiency is universal. (See "Surgery for chronic pancreatitis" and "Total pancreatectomy".)

Patients with dilated pancreatic duct — Patients with refractory pain due to chronic pancreatitis and a dilated pancreatic duct may require drainage if the pancreatic duct is obstructed. This may be performed endoscopically or surgically.

Choice of treatment — We suggest endoscopic drainage procedures in patients with a symptomatic, obstructed pancreatic duct as first-line therapy. We reserve surgery for patients

who fail endoscopic treatment or are unable or unwilling to undergo endoscopic treatment. Emerging data suggest that surgical therapy is more effective and more durable than endoscopic approaches. However, in practice, many patients still choose endoscopic therapy due to a reluctance to undergo surgery, and many surgeons only operate once endoscopic approaches to pancreatic drainage have been exhausted or unsuccessful. (See "Surgery for chronic pancreatitis", section on 'Endoscopy versus surgery'.)

Randomized trials have compared endoscopic with surgical therapy for painful chronic pancreatitis. One trial randomized 72 patients to either endoscopic or surgical therapy and noted similar rates of pain relief at one year of follow-up, but better rates of long-term pain relief in the surgical group [19]. A second randomized trial was stopped early, after only 39 subjects had been randomized, due to better outcomes in the surgical group [20,21]. Higher rates of complete or partial pain relief were observed in the surgical group as compared with patients who received initial endoscopic therapy at two years of follow-up (75 versus 32 percent) and in a subsequent study with five years of follow-up (80 versus 38 percent).

However, endoscopic techniques for drainage have continued to improve since these initial trials. There are limited data on the optimal timing of surgery. A randomized trial of initial surgery, versus an approach of utilizing endoscopic techniques first followed by subsequent surgery if needed for pain control, included 88 patients with a dilated pancreatic duct on prescribed opioids for severe pain (strong opioids for ≤2 months or weak opioids for ≤6 months) [22]. In this study, pain relief as measured by differences in pain scores was better in the initial surgery group over 18 months, and the surgical group required fewer interventions over follow-up (median one versus three). However, there was no difference in rates of complete or partial pain relief at end of follow-up in the early surgery or endoscopy-first approach group (58 versus 39 percent). There was no difference in complications, hospital admissions, pancreatic function, or quality of life between the two groups. These results need replication and studies are needed to determine if these differences in pain relief are sustained over time.

Endoscopic therapy — The primary goal of endoscopic therapy is to improve the flow through the pancreatic duct by eliminating obstructing ductal strictures or ductal stones. Endoscopic intervention requires a high degree of technical skill, but also requires careful patient selection. As the goal is to improve ductal drainage, the pancreatic ductal anatomy is the paramount feature for patient selection.

Those patients most amenable for endoscopic therapy are those with clear-cut evidence of ductal obstruction, including a dilated main pancreatic duct with an obstructing stricture or stone in the head of the pancreas (close enough to the tip of the endoscope to allow effective therapy). Endoscopic therapy alone is generally less feasible for stones or strictures in the body

of the pancreas and impossible if the obstruction is in the tail of the pancreas. Accessory devices are often required, including lithotripsy for stones. Endoscopic therapy for pain usually involves a pancreatic sphincterotomy, pancreatic stone removal, and pancreatic duct stents. Stones that are impacted require extracorporeal or intraductal lithotripsy. Intraductal lithotripsy, using endoscopic retrograde cholangiopancreatography (ERCP) scopes and small pancreatoscopy scopes, is most widely available. Multiple endoscopic procedures are usually necessary to achieve ductal clearance and resolution of strictures. (See "Extracorporeal shock wave lithotripsy for pancreatic stones".)

The largest report with long-term follow-up included 1018 patients treated at eight expert centers and followed for an average of five years. This series included patients with appropriate ductal anatomy and included a mixture of pancreatic duct strictures and stones. In this study, approximately one-fourth of patients ultimately underwent surgery for failure of endoscopic therapy to relieve pain, and pain relief was seen in two-thirds of patients based on intention-to-treat analysis [23]. This study includes a highly selected population referred to expert centers for endoscopic therapy and likely represents better results than would be seen with less selected patients. (See "Extracorporeal shock wave lithotripsy for pancreatic stones" and "Pancreatic stenting at endoscopic retrograde cholangiopancreatography (ERCP): Indications, techniques, and complications" and "Endoscopic ultrasound-guided celiac plexus interventions for pain related to pancreatic disease" and "Intraductal ultrasound for evaluating the pancreaticobiliary ductal system".)

Surgical drainage procedure — Like endoscopic therapy, surgical therapy can be directed at improving pancreatic ductal flow. Patients who would be candidates for these types of operations generally require a dilated pancreatic duct (similar to endoscopic therapies), with a size of at least 5 to 6 mm so that the duct can be readily identified at surgery. The most common operation historically has been the modified Puestow operation, in which the pancreatic duct and overlying pancreas is incised along its length, and stones are removed and strictures are incised. This exposed duct is overlaid with a Roux limb for drainage (figure 4). This procedure is the least technically demanding surgical approach and preserves the maximum amount of pancreatic parenchyma. In many case series, approximately three-quarters of patients will experience pain improvement or relief, although this drops to approximately one-half over more prolonged follow-up. Pancreatic exocrine and endocrine function are generally unaffected by this procedure as no parenchyma is resected, but these continue to deteriorate as in nonsurgical patients.

Patients with a dilated main pancreatic duct (≥6 to 7 mm) and pain are candidates for a drainage procedure, such as lateral pancreaticojejunostomy (LPJ), or Frey procedure (LPJ with added local

head resection to address fibrotic parenchyma that drains poorly and peripancreatic neural damage in the pancreatic head). These procedures are not commonly performed, and surgical expertise in these procedures is not widely available.

MANAGEMENT OF PANCREATIC INSUFFICIENCY

Exocrine pancreatitis insufficiency — Exocrine pancreatic insufficiency is a late manifestation of chronic pancreatitis, usually occurring after more than five years of disease. Patients with mild exocrine pancreatic insufficiency may be asymptomatic or have mild abdominal discomfort and bloating with normal-appearing bowel movements. Advanced exocrine pancreatic insufficiency results in maldigestion of fat and protein and weight loss. Overt steatorrhea does not occur until approximately 90 percent of glandular function has been lost. Patients with steatorrhea report loose, greasy, foul-smelling stools that are difficult to flush. Other symptoms include bloating, cramping, and increased flatulence. Deficiencies of vitamins (especially fat-soluble vitamins A, D, E, K) are common. In particular, vitamin D deficiency and subsequent osteopenia and osteoporosis are exceedingly common (40 and 25 percent, respectively), with an increased rate of nontraumatic bone fracture [24,25]. (See "Exocrine pancreatic insufficiency", section on 'Clinical manifestations' and "Exocrine pancreatic insufficiency", section on 'Laboratory findings'.)

Nutritional assessment — Prior to initiating pancreatic enzyme replacement therapy, anthropometric (body mass index, muscle mass or strength) and nutritional assessment, and laboratory testing for vitamin deficiency should be performed at baseline and annually thereafter. In addition, we perform a baseline dual-energy X-ray absorptiometry (DEXA) scan.

Laboratory evaluation should include the following:

- Serum retinol and retinol-binding protein
- Serum 25-hydroxyvitamin D (25[OH]D)
- Serum alpha-tocopherol levels
- International normalized ratio (INR)
- Prealbumin
- B12
- HgBA1c annually to assess for concomitant pancreatogenic diabetes

Pancreatic enzyme replacement therapy

- **Initial dose** — A reasonable starting dose for pancreatic enzyme supplementation is 40,000 to 50,000 USP units taken with the first bite of each main meal, and one-half that

amount with snacks. Commercial pancreatic enzyme products range from 3000 to 40,000 USP units of lipase per capsule or tablet. In the United States, one product is available in tablet (non-enteric-coated) form; the rest are enteric-coated capsules.

Patients should be advised that the enzymes should be taken with the first bite of a meal but, if consuming a meal takes more than 20 minutes, to instead take half the number of capsules with the first bite and the other half in the middle of the meal to maximize digestion. If the non-enteric-coated preparation is chosen, suppression of gastric acid with a histamine-2 (H2) receptor antagonist or proton pump inhibitor is required to avoid acid denaturation of lipase. Although it is estimated that delivery of 10 percent of normal pancreatic lipase output (approximately 90,000 USP units with each meal) can theoretically correct steatorrhea and maldigestion, in practice enzyme replacement therapy only rarely leads to normalization of digestion [26]. The full 90,000 USP units (10 percent of normal pancreatic enzyme output) may not be needed, as the remaining pancreas may still have some function and gastric lipase may compensate, but some patients may need more than 90,000 USP units.

- **Assessment of response** — The effectiveness of enzyme supplementation is generally gauged clinically by an improvement in stool consistency, loss of visible fat in the stool, improvement in fat-soluble vitamin levels, and gain in muscle strength and body weight.

- **Refractory symptoms** — Failure of enzyme therapy can be due to several different etiologies including:

  - Inadequate dose
  - Noncompliance due to the number of pills or cost
  - Acid denaturation of enzymes
  - Alternative cause of maldigestion or malabsorption

Patients with refractory symptoms should be advised to eat more frequent, smaller meals. It is occasionally useful to change from one formulation to another (eg, changing from enteric-coated preparations to a combination of a non-enteric-coated preparation plus an agent to suppress acid) or to raise the dose higher than 90,000 USP units of lipase per meal. If all these measures fail to improve signs and symptoms of malabsorption, it is important to evaluate patients for alternative causes, such as small intestinal bacterial overgrowth. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Diagnosis'.)

Endocrine insufficiency (pancreatogenic diabetes) — Patients with chronic pancreatitis may suffer from type 2 diabetes mellitus but are also prone to a particular type of diabetes from destruction of pancreatic islets from the chronic pancreatitis. This type of diabetes, termed type

3c diabetes, is characterized by loss of insulin as well as loss of other counter-regulatory islet hormones (glucagon, pancreatic polypeptide) [27]. This can produce a brittle diabetes, with a high risk of treatment-induced hypoglycemia.

Metformin is the preferred oral hypoglycemic agent as there is circumstantial evidence that it may lower the risk of secondary pancreatic carcinoma [28]. However, insulin is often needed. Patients with chronic pancreatitis tend to have lower insulin requirements than patients with type 1 diabetes mellitus. Vigorous attempts at tight control of blood glucose value may be associated with disastrous complications of treatment-induced hypoglycemia. Glucagon-like peptide (GLP)-1 analogues and dipeptidyl peptidase-4 (DPP4) inhibitors have not been well studied in patients with chronic pancreatitis and are generally avoided due to their risk of acute pancreatitis. (See "Overview of the complications of chronic pancreatitis", section on 'Pancreatic diabetes' and "Initial management of hyperglycemia in adults with type 2 diabetes mellitus".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Chronic pancreatitis and pancreatic exocrine insufficiency".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Chronic pancreatitis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Chronic pancreatitis is an ongoing process of pathologic response to pancreatic injury. Abdominal pain is the most common clinical symptom. As chronic pancreatitis progresses, patients may develop exocrine pancreatic insufficiency (steatorrhea, maldigestion) and diabetes. Complications of chronic pancreatitis include pancreatic pseudocyst, bile duct or duodenal obstruction, visceral artery pseudoaneurysm, pancreatic ascites and pancreatic pleural effusions, gastric varices due to thrombosis of the splenic vein, and pancreatic malignancy. (See 'Introduction' above and "Chronic pancreatitis: Clinical manifestations and diagnosis in adults", section on 'Clinical presentation' and "Overview of the complications of chronic pancreatitis".)

- We screen patients with chronic pancreatitis for smoking and alcohol use and encourage vigorous efforts at cessation. In addition, patients with chronic pancreatitis are advised to consume low-fat meals, small meals, and avoid dehydration. (See 'General measures' above.)

- Prior to initiating therapy in a patient with chronic pancreatitis who presents with abdominal pain, it is necessary to confirm that the symptoms are in fact due to chronic pancreatitis and not an alternative etiology. Initial evaluation should include a detailed history to assess for the presence of abdominal pain at baseline, the character of pain, severity, and impact on quality of life. To identify alternative reversible causes of abdominal pain, we perform high-quality computed tomography (CT) or magnetic resonance imaging (MRI). (See 'Evaluation to rule out other etiologies' above.)

- The majority of patients with pain due to chronic pancreatitis require analgesics. We use a stepwise approach to treatment with the goal of avoiding high-dose opioids for pain control. We begin with acetaminophen and/or nonsteroidal anti-inflammatory drugs (NSAIDs) for initial management of abdominal pain due to chronic pancreatitis. In patients with pain requiring opioid therapy, we use suggestive adjunctive agents to minimize the use of opioid analgesia and treat coexisting depression. Adjunctive agents including tricyclic antidepressants, serotonin reuptake inhibitors (SSRIs), and combined serotonin and norepinephrine reuptake inhibitors (eg, duloxetine) or gabapentoids (pregabalin or gabapentin). (See 'Antioxidants and other therapies' above and 'Analgesics' above.)

- In patients with pain due to chronic pancreatitis who fail to respond to initial medical management alone, subsequent management is individualized depending on pancreatic ductal anatomy, available expertise, and patient preference.

- Patients with a non-dilated pancreatic duct who prefer nonoperative therapy may continue medical therapy with a celiac plexus block. Surgical management in patients with a non-dilated main pancreatic duct (<6 to 7 mm) involves resection of the involved pancreas. (See 'Patients with non-dilated pancreatic duct' above and "Surgery for chronic pancreatitis", section on 'Nondilated pancreatic duct'.)

- In patients with refractory pain due to chronic pancreatitis and an obstructed, dilated pancreatic duct, we suggest initial endoscopic drainage rather than surgical therapy (**Grade 2C**). Emerging data suggest that surgical therapy is more effective and more durable than endoscopic approaches. However, in practice, many patients still choose endoscopic therapy due to a reluctance to undergo surgery, and many surgeons only operate once endoscopic approaches to pancreatic drainage have been exhausted or unsuccessful. (See 'Patients with dilated pancreatic duct' above and "Surgery for chronic pancreatitis", section on 'Dilated pancreatic duct'.)

- Patients with exocrine pancreatic insufficiency require pancreatic enzyme supplementation. A reasonable starting dose for pancreatic enzyme supplementation in patients with exocrine pancreatic insufficiency is 40,000 to 50,000 USP units with each meal, and one-half that amount with snacks. The effectiveness of enzyme supplementation is generally gauged clinically by an improvement in stool consistency, loss of visible fat in the stool, improvement in fat-soluble vitamin levels, and gain in muscle strength and body weight. (See 'Exocrine pancreatitis insufficiency' above.)

- Patients with chronic pancreatitis may suffer from type 2 diabetes mellitus, but are also prone to diabetes from destruction of pancreatic islets from the chronic pancreatitis (type 3c diabetes). This can produce a brittle diabetes, with a high risk of treatment-induced hypoglycemia. Metformin may lower the risk of secondary pancreatic carcinoma in these patients. However, insulin is often needed to control diabetes. (See 'Endocrine insufficiency (pancreatogenic diabetes)' above.)

REFERENCES

1. Vege SS, Chari ST. Chronic Pancreatitis. N Engl J Med 2022; 386:869.
2. Yadav D, Askew RL, Palermo T, et al. Association of Chronic Pancreatitis Pain Features With Physical, Mental, and Social Health. Clin Gastroenterol Hepatol 2023; 21:1781.

3. Kempeneers MA, Issa Y, Verdonk RC, et al. Pain patterns in chronic pancreatitis: a nationwide longitudinal cohort study. Gut 2021; 70:1724.
4. Tuck NL, Teo K, Kuhlmann L, et al. Pain patterns in chronic pancreatitis and chronic primary pain. Pancreatology 2022; 22:572.
5. Drewes AM, Bouwense SAW, Campbell CM, et al. Guidelines for the understanding and management of pain in chronic pancreatitis. Pancreatology 2017; 17:720.
6. Anderson MA, Akshintala V, Albers KM, et al. Mechanism, assessment and management of pain in chronic pancreatitis: Recommendations of a multidisciplinary study group. Pancreatology 2016; 16:83.
7. Nusrat S, Yadav D, Bielefeldt K. Pain and opioid use in chronic pancreatitis. Pancreas 2012; 41:264.
8. Shah I, Bocchino R, Yakah W, et al. Evaluating Outcomes and Misuse in Opioid-Dependent Chronic Pancreatitis Using a State-Mandated Monitoring System. Dig Dis Sci 2022; 67:5493.
9. World Health Organization. Cancer pain relief: with a guide to opioid availability, 2nd ed, Geneva 1996.
10. Bhardwaj P, Garg PK, Maulik SK, et al. A randomized controlled trial of antioxidant supplementation for pain relief in patients with chronic pancreatitis. Gastroenterology 2009; 136:149.
11. Siriwardena AK, Mason JM, Sheen AJ, et al. Antioxidant therapy does not reduce pain in patients with chronic pancreatitis: the ANTICIPATE study. Gastroenterology 2012; 143:655.
12. Ahmed Ali U, Jens S, Busch OR, et al. Antioxidants for pain in chronic pancreatitis. Cochrane Database Syst Rev 2014; :CD008945.
13. Winstead NS, Wilcox CM. Clinical trials of pancreatic enzyme replacement for painful chronic pancreatitis--a review. Pancreatology 2009; 9:344.
14. Yadav D, Palermo TM, Phillips AE, et al. Painful chronic pancreatitis - new approaches for evaluation and management. Curr Opin Gastroenterol 2021; 37:504.
15. Gardner TB, Adler DG, Forsmark CE, et al. ACG Clinical Guideline: Chronic Pancreatitis. Am J Gastroenterol 2020; 115:322.
16. Zhao X, Cui N, Wang X, Cui Y. Surgical strategies in the treatment of chronic pancreatitis: An updated systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2017; 96:e6220.
17. Bellin MD, Freeman ML, Gelrud A, et al. Total pancreatectomy and islet autotransplantation in chronic pancreatitis: recommendations from PancreasFest. Pancreatology 2014; 14:27.

18. Khazaaleh S, Babar S, Alomari M, et al. Outcomes of total pancreatectomy with islet autotransplantation: A systematic review and meta-analysis. World J Transplant 2023; 13:10.
19. Díte P, Ruzicka M, Zboril V, Novotný I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. Endoscopy 2003; 35:553.
20. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. N Engl J Med 2007; 356:676.
21. Cahen DL, Gouma DJ, Laramée P, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. Gastroenterology 2011; 141:1690.
22. Issa Y, Kempeneers MA, Bruno MJ, et al. Effect of Early Surgery vs Endoscopy-First Approach on Pain in Patients With Chronic Pancreatitis: The ESCAPE Randomized Clinical Trial. JAMA 2020; 323:237.
23. Rösch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy 2002; 34:765.
24. Duggan SN, Smyth ND, Murphy A, et al. High prevalence of osteoporosis in patients with chronic pancreatitis: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2014; 12:219.
25. Tignor AS, Wu BU, Whitlock TL, et al. High prevalence of low-trauma fracture in chronic pancreatitis. Am J Gastroenterol 2010; 105:2680.
26. De la Iglesia-Garcia D, Huang W, Szatmary P, et al. Efficacy of pancreatic enzyme replaceme nt therapy in chronic pancreatitis: systematic review and meta-analysis. Gut 2017; 66:1474.
27. Hart PA, Bellin MD, Andersen DK, et al. Type 3c (pancreatogenic) diabetes mellitus secondary to chronic pancreatitis and pancreatic cancer. Lancet Gastroenterol Hepatol 2016; 1:226.
28. Gong J, Robbins LA, Lugea A, et al. Diabetes, pancreatic cancer, and metformin therapy. Front Physiol 2014; 5:426.

Topic 5647 Version 33.0

GRAPHICS

Oral preparations for pancreatic enzyme replacement therapy (PERT)

Pancrelipase preparations (United States trade name)	Description and United States manufacturer (see NOTE)	Administration	Lipase (USP units)	Amylase (USP units)	Protease (USP units)
Pancreaze 2600	Delayed-release capsule containing enteric-coated microtablets, porcine origin. (Janssen Pharmaceuticals, Inc)	Applies to Pancreaze, Creon, Zenpep: Preparation is suitable for use in adults, children, and infants. Swallow capsules whole or sprinkle capsule contents on small amount of acidic, soft food with pH of 4.5 or less (eg, applesauce, yogurt, commercially prepared bananas or pears). Consume immediately and follow with water, juice, or other liquid. Do not crush or chew capsule shell or contents. For infants, contents of the capsule may also be administered directly into the mouth, followed by breast milk or formula*.	2600	10,850	6200
Pancreaze 4200			4200	24,600	14,200
Pancreaze 10,500			10,500	61,500	35,500
Pancreaze 16,800			16,800	98,400	56,800
Pancreaze 21,000			21,000	83,900	54,700
Creon 3	Delayed-release capsule containing enteric-coated minimicrospheres, porcine origin. (AbbVie, Inc)		3000	15,000	9500
Creon 6			6000	30,000	19,000
Creon 12			12,000	60,000	38,000
Creon 24			24,000	120,000	76,000
Creon 36			36,000	180,000	114,00
Zenpep 3	Delayed-release capsule containing enteric-coated beads, porcine origin. (Nestlé Healthcare Nutrition, Inc)		3000	14,000	10,000
Zenpep 5			5000	24,000	17,000
Zenpep 10			10,000	42,000	32,000
Zenpep 15			15,000	63,000	47,000
Zenpep 20			20,000	84,000	63,000
Zenpep 25			25,000	105,000	79,000
Zenpep 40			40,000	168,000	126,000
Viokace 10,440	Regular-release (non-enteric-	Only indicated for use in adult patients	10,440	39,150	39,150

	coated) tablet, porcine origin. (Nestlé Healthcare Nutrition, Inc)	also treated with a proton pump inhibitor. Swallow tablets whole with sufficient liquid. Do not crush or chew. Preparation is not suited for infants or children who do not readily swallow whole pills.			
Viokace 20,880			20,880	78,300	78,300
Pertzye 4	Delayed-release capsule containing bicarbonate-buffered, enteric-coated microspheres, porcine origin. (Digestive Care, Inc)	Preparation is suitable for use in adults, children, and infants. Swallow capsules whole or sprinkle capsule contents on small amount of acidic, soft food with pH of 4.5 or less (eg, applesauce, yogurt, commercially prepared bananas or pears). Consume immediately and follow with water, juice, formula, or breast milk as appropriate. Do not crush or chew capsule shell or contents. Do not mix contents of capsule in formula or breast milk. Pertzye 24 is indicated for children over 12 months of age and adults.	4000	15,125	14,375
Pertzye 8			8000	30,250	28,750
Pertzye 16			16,000	60,500	57,500
Pertzye 24			24,000	90,750	86,250

This table shows USP units of enzyme activity for product brands available in the United States. Individual product contents, preparation type, and units of activity vary by country. The units of

activity used in other countries are not equivalent to the USP units shown in this table (unless the data are specifically given as USP units). Consult local prescribing information before use or changing products.

NOTE: Products are not equivalent to one another and are not automatically interchangeable with any other pancreatic enzyme replacement product.

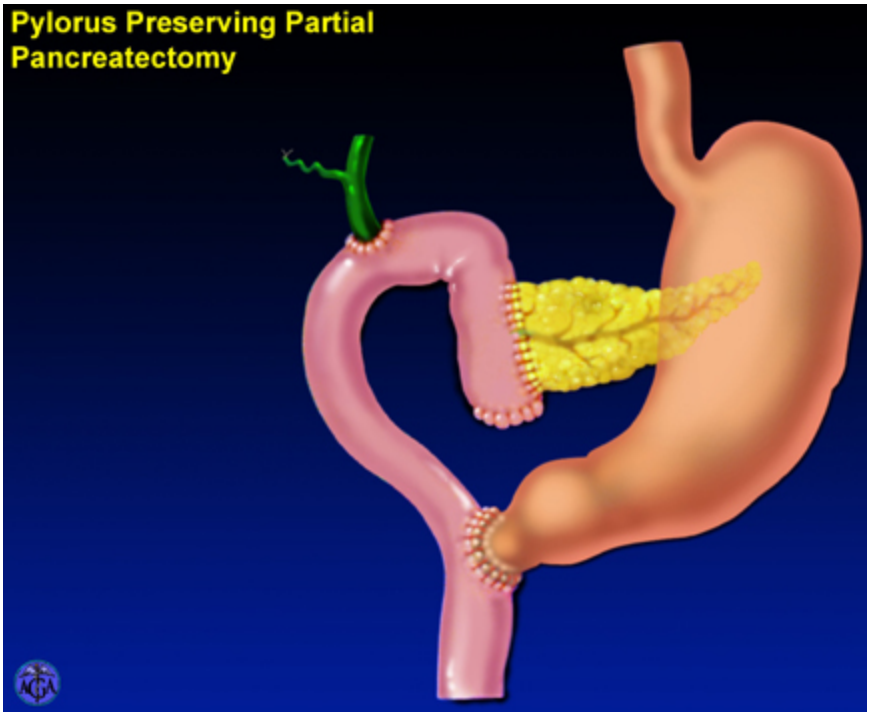
USP: United States Pharmacopeial.

* Care should be taken to be sure that the capsule contents (pellets) are not crushed or retained in the mouth, to avoid irritation of the oral mucosa. Do not mix directly into infant formula or breast milk, as this may diminish efficacy.

Data from: US licensed prescribing information. Available at: https://dailymed.nlm.nih.gov/dailymed/index.cfm (Accessed on May 13, 2020).

Graphic 57416 Version 29.0

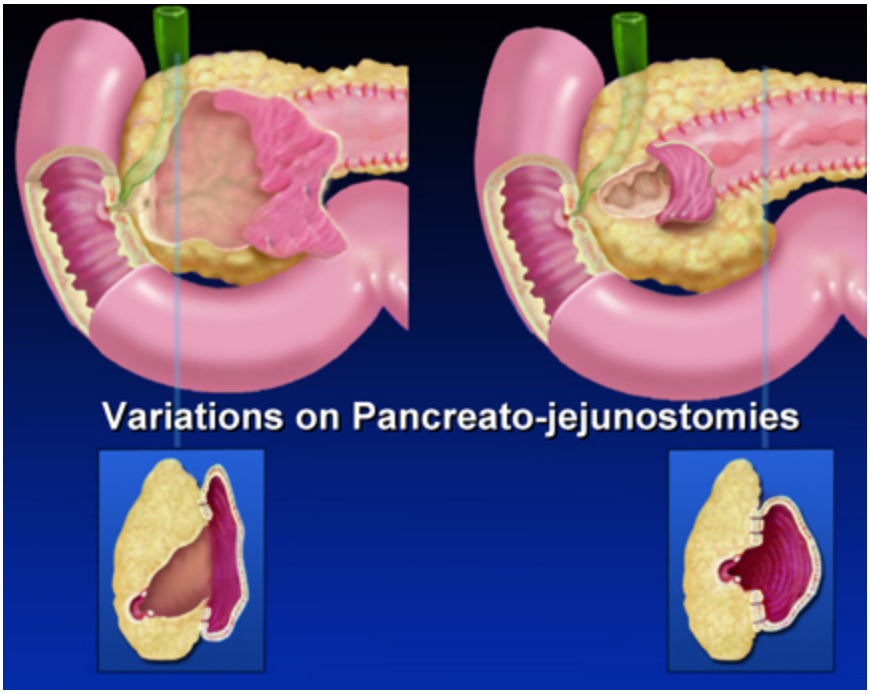
Pylorus preserving Whipple



Reproduced with permission from: American Gastroenterological Association (AGA) GTP slide set (2003), Pancreatic Disease. Authors: Gorelick F, Pandol S, Topazian M. Artist: Schoendorf J. Copyright © 2003 American Gastroenterological Association.

Graphic 59715 Version 4.0

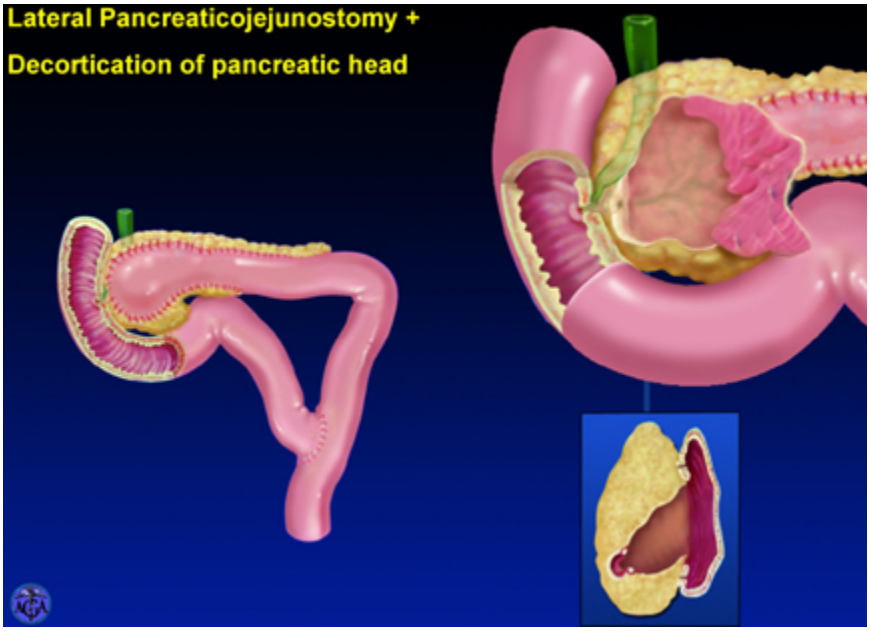
Variations on pancreatojejunostomies



Reproduced with permission from: American Gastroenterological Association (AGA) GTP slide set (2003), Pancreatic Disease. Authors: Gorelick F, Pandol S, Topazian M. Artist: Schoendorf J. Copyright © 2003 American Gastroenterological Association.

Graphic 61669 Version 3.0

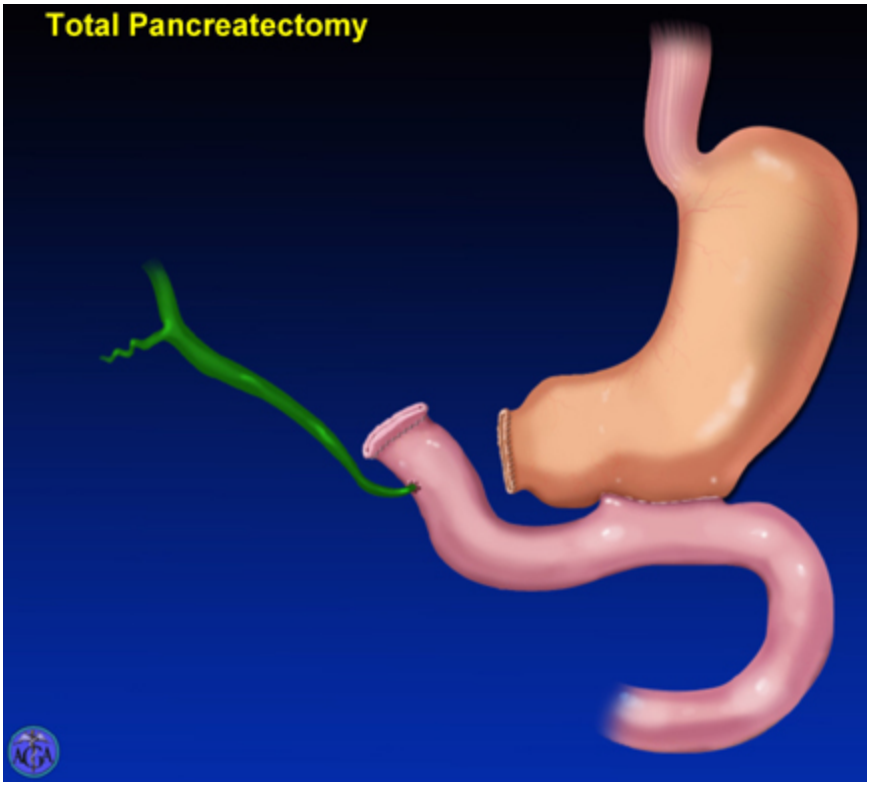
Pancreatic decortication AGA



Reproduced with permission from: American Gastroenterological Association (AGA) GTP slide set (2003), Pancreatic Disease. Authors: Gorelick F, Pandol S, Topazian M. Artist: Schoendorf J. Copyright © 2003 American Gastroenterological Association.

Graphic 50008 Version 3.0

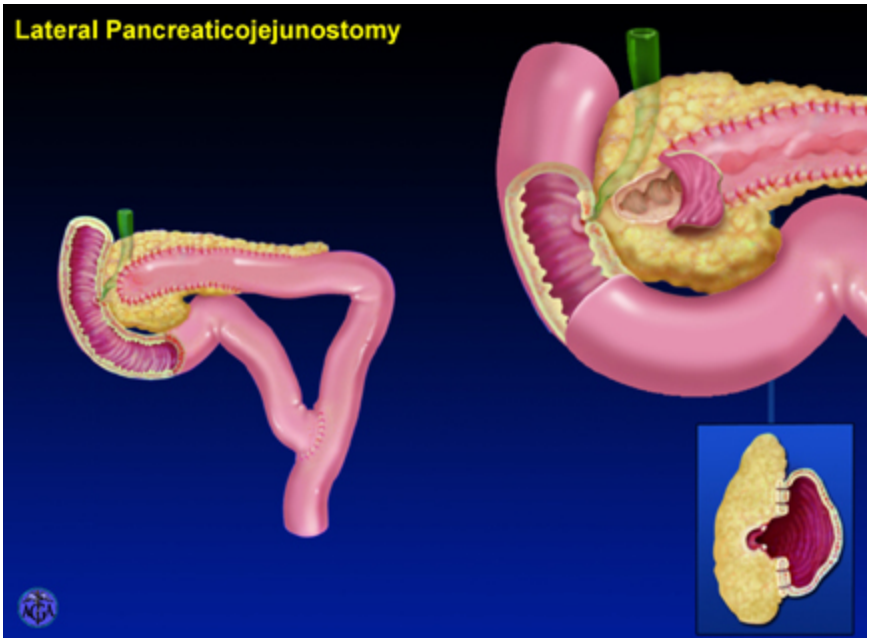
Total pancreatectomy



Reproduced with permission from: American Gastroenterological Association (AGA) GTP slide set (2003), Pancreatic Disease. Authors: Gorelick F, Pandol S, Topazian M. Artist: Schoendorf J. Copyright © 2003 American Gastroenterological Association.

Graphic 68307 Version 4.0

Lateral pancreaticojejunostomy



Reproduced with permission from: American Gastroenterological Association (AGA) GTP slide set (2003), Pancreatic Disease. Authors: Gorelick F, Pandol S, Topazian M. Artist: Schoendorf J. Copyright © 2003 American Gastroenterological Association.

Graphic 67361 Version 3.0

Contributor Disclosures

Steven D Freedman, MD, PhD No relevant financial relationship(s) with ineligible companies to disclose. **Christopher E Forsmark, MD** Grant/Research/Clinical Trial Support: Abbvie - Protocol M16-142 [exocrine pancreatic insufficiency in pancreatic cancer subjects]; NIDDK and NCI through RFA-DK-14-027 - Consortium for the study of chronic pancreatitis, diabetes, and pancreatic cancer clinical centers (UO1) - UF PI and co-Chair consortium [Pancreatitis, diabetes, and pancreatic cancer]; NIH through RFA-DK-19-023 – Consortium for the study of Type 1 Diabetes After Acute Pancreatitis – Clinical Centers (UO1) – UF PI [Type 1 Diabetes after acute Pancreatitis]. Consultant/Advisory Boards: Nestlé Healthcare Nutrition [Exocrine Pancreatic Insufficiency]. All of the relevant financial relationships listed have been mitigated. **Douglas G Adler, MD, FACG, AGAF, FASGE** Consultant/Advisory Boards: Abbvie [Endoscopy]; Boston Scientific [Endoscopy]; Endorotor [Endoscopy]; Merit [Endoscopy]; Olympus [Endoscopy]. Speaker's Bureau: Abbvie [Pancreatology, general GI]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→