ACUTE AND CHRONIC PANCREATITIS WITH ASSOCIATED COMPLICATIONS

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RICHARD C. STAAB MEMORIAL SYMPOSIUM – APRIL 10, 2021
OVERVIEW

- Epidemiology
- Etiology
- Severity Scoring System
- Diagnosis
- Treatment
- Complications
  - Chronic Pancreatitis
  - Pancreatic Fluid Collections
EPIDEMIOLOGY

- Third most common reason for hospitalization with a gastrointestinal condition.
- Annual costs exceeding $2.5 billion.
- Admissions have increased by at least 20% over the past 10 years.
- World wide incidence ranges between 5 and 80 per 100,000 population with highest incidence recorded in United States and Finland.
- This increased risk of pancreatitis tracks with the worldwide obesity epidemic and increasing rates of gallstones.
- Approximately 80% of patients admitted with acute pancreatitis have mild, self-limited disease and are discharged within several days.
- Severe disease seen in elderly, those with more numerous and more severe coexisting conditions (particularly obesity).

### Table 1. Causes of Acute Pancreatitis.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Approximate Frequency</th>
<th>Diagnostic Clues</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallstones</td>
<td>40%</td>
<td>Gallbladder stones or sludge, abnormal liver-enzyme levels</td>
<td>Endoscopic ultrasonography can reveal very small gallbladder or duct stones.</td>
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<tr>
<td>Alcohol</td>
<td>30%</td>
<td>Acute flares superimposed on underlying chronic pancreatitis</td>
<td>Diagnosis rests on history, obtained with CAGE questions. †</td>
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<tr>
<td>Hypertriglyceridemia</td>
<td>2–5%</td>
<td>Fasting triglycerides &gt;1000 mg/dl (11.3 mmol per liter)</td>
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<tr>
<td>Genetic causes</td>
<td>Not known</td>
<td>Recurrent acute pancreatitis and chronic pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td>&lt;5%</td>
<td>Other evidence of drug allergy (e.g., rash) only in rare cases</td>
<td></td>
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<tr>
<td>Autoimmune cause</td>
<td>&lt;1%</td>
<td>Type 1: obstructive jaundice, elevated serum IgG4 levels, response to glucocorticoids; type 2: possible presentation as acute pancreatitis; occurrence in younger patients; no IgG4 elevation; response to glucocorticoids</td>
<td>Type 1 is a systemic disease affecting the pancreas, salivary glands, and kidneys; in type 2, only the pancreas is affected.</td>
</tr>
<tr>
<td>ERCP</td>
<td>5–10% (among patients undergoing ERCP)</td>
<td></td>
<td>The symptoms can be reduced with rectal NSAIDS (diclofenac or indomethacin) or temporary placement of a stent in the pancreatic duct.</td>
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<tr>
<td>Trauma</td>
<td>&lt;1%</td>
<td>Blunt or penetrating trauma, particularly in midbody of pancreas as it crosses spine</td>
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<tr>
<td>Infection</td>
<td>&lt;1%</td>
<td>Viruses: CMV, mumps, and EBV most common; parasites: ascaris and clonorchis</td>
<td></td>
</tr>
<tr>
<td>Surgical complication</td>
<td>5–10% (among patients undergoing cardiopulmonary bypass)</td>
<td>The condition is probably due to pancreatic ischemia; pancreatitis may be severe.</td>
<td></td>
</tr>
<tr>
<td>Obstruction</td>
<td>Rare</td>
<td>Celiac disease and Crohn's disease, pancreas divisum (controversial), and sphincter of Oddi dysfunction (very controversial)</td>
<td>On rare occasions, malignant pancreatic duct or ampullary obstruction is seen.</td>
</tr>
<tr>
<td>Associated conditions</td>
<td>Common</td>
<td>Diabetes, obesity, and smoking</td>
<td></td>
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</tbody>
</table>

* CMV denotes cytomegalovirus, EBV Epstein–Barr virus, ERCP endoscopic retrograde cholangiopancreatography, and NSAIDs nonsteroidal antiinflammatory drugs.

† CAGE is an acronym for the following questions: Have you ever felt you should cut down on your drinking? Have people annoyed you by criticizing your drinking? Have you ever felt bad or guilty about your drinking? Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?
GALLSTONES

- Gallstones are the most common cause
- Migrating gallstones cause transient obstruction of the pancreatic duct, a mechanism shared by other recognized causes (e.g., endoscopic retrograde cholangiopancreatography [ERCP]), as well as purported causes (i.e., pancreas divisum and sphincter of Oddi dysfunction).
- A recent trial failed to show that sphincter of Oddi dysfunction contributed to post-cholecystectomy biliary pain, and there are no convincing data from controlled trials that either pancreatic sphincter of Oddi dysfunction or pancreas divisum plays a role in acute pancreatitis.

Côté GA, Imperiale TF, Schmidt SE, et al. Similar efficacies of biliary, with or without pancreatic, sphincterotomy in treatment of idiopathic recurrent acute pancreatitis. Gastroenterology 2012;143:1502-1509.e1
Alcohol is the second most common cause of acute pancreatitis.

Prolonged alcohol use (four to five drinks daily over a period of more than 5 years) is required for alcohol-associated pancreatitis.

In most cases, chronic pancreatitis has already developed and the acute clinical presentation represents a flare superimposed on chronic pancreatitis.

The risk is higher for men than for women, perhaps reflecting differences in alcohol intake or genetic background.

The mechanisms by which alcohol causes acute (or chronic) pancreatitis are complex and include both direct toxicity and immunologic mechanisms.

The type of alcohol ingested does not affect risk, and binge drinking in the absence of long-term, heavy alcohol use does not appear to precipitate acute pancreatitis.

DRUGS

- Drugs appear to cause less than 5% of all cases of acute pancreatitis, although hundreds of drugs have been implicated.
- The drugs most strongly associated with the disorder are azathioprine, 6-mercaptopurine, didanosine, valproic acid, angiotensin-converting-enzyme inhibitors, and mesalamine.
- Pancreatitis caused by drugs is usually mild.
- Recent data do not support a role for glucagon-like peptide 1 mimetics in causing pancreatitis.
- It is common for patients to be taking one of the many drugs associated with pancreatitis when they are admitted to the hospital with acute pancreatitis, but it is exceedingly difficult to determine whether the drug is responsible.

Forsmark CE. Incretins, diabetes, pancreatitis and pancreatic cancer: what the GI specialist needs to know. Panreatology 2016;16:10-13a
Mutations and polymorphisms in a number of genes are associated with acute (and chronic) pancreatitis, including mutations in the genes encoding cationic trypsinogen (PRSS1), serine protease inhibitor Kazal type 1 (SPINK1), cystic fibrosis transmembrane conductance regulator (CFTR), chymotrypsin C, calcium-sensing receptor, and claudin-2.

These mutations may serve as cofactors, interacting with other causes; for example, claudin-2 mutations work synergistically with alcohol.

Whitcomb DC. Genetic risk factors for pancreatic disorders. Gastroenterology 2013;144:1292-1302
TYPE 1 AIP has been associated with other immune-mediated diseases, including immunoglobulin (Ig) G4–associated cholangitis (IAC), salivary gland disorders, mediastinal fibrosis, retroperitoneal fibrosis, tubulointerstitial disease and inflammatory bowel disease, and increased levels of IgG4, both in tissue plasma cells and in the serum, thus terming this collection of disease processes IgG4-related systemic disease.

TYPE 2 AIP – Also known as idiopathic duct-centric pancreatitis.
- Without IgG4 involvement
- Associated with inflammatory bowel disease
- Exclusion of pancreatic adenocarcinoma must be confirmed before pursuing AIP as a diagnosis
- Corticosteroid therapy has been accepted as the mainstay of therapy for AIP, both in terms of improving symptoms and preventing long-term consequences.

Kamraan Madhani, James J. Farrell, Autoimmune Pancreatitis: An Update on Diagnosis and Management, Gastroenterology Clinics of North America.
The cause of acute pancreatitis often cannot be established, and the proportion of persons who are considered to have idiopathic acute pancreatitis increases with age.

A number of potential factors might contribute to unexplained pancreatitis, including unidentified genetic polymorphisms, exposure to smoking and other environmental toxins, and effects of coexisting diseases that are commonly associated with acute pancreatitis (e.g., obesity and diabetes).

Morbid obesity is a risk factor for acute pancreatitis and for severe acute pancreatitis.

Type 2 diabetes increases the risk of acute pancreatitis by a factor of 2 or 3.

Both obesity and diabetes are also risk factors for chronic pancreatitis and pancreatic cancer.

Hong S, Qiwen B, Ying J, Wei A, Chaoyang T. Body mass index and the risk and prognosis of acute pancreatitis: a meta-analysis. Eur J Gastroenterol Hepatol 2011;23:1136-1143

Several scoring systems have been developed to incorporate clinical, radiographic, and laboratory findings in various combinations: Acute Physiology and Chronic Health Evaluation II (APACHE II), APACHE combined with scoring for obesity (APACHE-O), the Glasgow scoring system, the Harmless Acute Pancreatitis Score (HAPS), PANC 3, the Japanese Severity Score (JSS), Pancreatitis Outcome Prediction (POP), and the Bedside Index for Severity in Acute Pancreatitis (BISAP).

A number of predictive systems use CT findings, but CT evidence of severe acute pancreatitis lags behind clinical findings, and an early CT study can underestimate the severity of the disorder.

These scoring systems all have a high false positive rate (i.e., in many patients with high scores, severe pancreatitis does not develop), which is an unavoidable consequence of the fact that in most patients, severe disease does not develop.

The scoring systems are complex and cumbersome and not routinely used.
SEVERITY SCORING SYSTEM

- The most useful predictors are elevated blood urea nitrogen and creatinine levels and an elevated hematocrit, particularly if they do not return to the normal range with fluid resuscitation.

- The degree of elevation of the serum amylase or lipase level has no prognostic value.

- SIRS can be diagnosed on the basis of four routine clinical measurements, with findings of two or more of the following values: temperature, below 36°C or above 38°C; pulse, greater than 90 beats per minute; respiratory rate, greater than 20 breaths per minute (or partial pressure of arterial carbon dioxide, <32 mm Hg); and white-cell count, lower than 4000 or higher than 12,000 per cubic millimeter.

- SIRS that persists for 48 hours or more after the onset of symptoms is indicative of a poor prognosis.

- During the first 48 to 72 hours, a rising hematocrit or blood urea nitrogen or creatinine level, persistent SIRS after adequate fluid resuscitation, or the presence of pancreatic or peripancreatic necrosis on cross-sectional imaging constitutes evidence of evolving severe pancreatitis.
On the basis of retrospective studies suggesting that aggressive fluid administration during the first 24 hours reduces morbidity and mortality, current guidelines provide directions for early and vigorous fluid administration.

Vigorous fluid therapy is most important during the first 12 to 24 hours after the onset of symptoms and is of little value after 24 hours.

Administration of a balanced crystalloid solution has been recommended at a rate of 200 to 500 ml per hour, or 5 to 10 ml per kilogram of body weight per hour, which usually amounts to 2500 to 4000 ml within the first 24 hours.

One trial suggested the superiority of Ringer’s lactate as compared with normal saline in reducing inflammatory markers.

The main risk of fluid therapy is volume overload. Excessive fluid administration results in increased risks of the abdominal compartment syndrome, sepsis, need for intubation, and death.

Fluid therapy needs to be tailored to the degree of intravascular volume depletion and the cardiopulmonary reserve that is available to handle the fluid.

In patients with mild acute pancreatitis who do not have organ failure or necrosis, there is no need for complete resolution of pain or normalization of pancreatic enzyme levels before oral feeding is started.

A low-fat soft or solid diet is safe and associated with shorter hospital stays than is a clear-liquid diet with slow advancement to solid foods.

Most patients with mild acute pancreatitis can be started on a low-fat diet soon after admission, in the absence of severe pain, nausea, vomiting, and ileus (all of which are unusual in mild cases of acute pancreatitis).
A need for artificial enteral feeding may be predicted by day 5, on the basis of symptoms that continue to be severe or an inability to tolerate attempts at oral feeding.

Although nasojejunal tube feeding is best for minimizing pancreatic secretion, randomized trials and a meta-analysis have shown that nasogastric or nasoduodenal feeding is clinically equivalent.

Simple tube feeding has replaced total parenteral nutrition and feeding through complex, deeply placed intestinal tubes.
Total parenteral nutrition should be reserved for the rare cases in which enteral nutrition is not tolerated or nutritional goals are not met.

In a prospective randomized study, Petrov et al demonstrated that patients receiving total enteral nutrition (TEN) had significantly lower rates of pancreatic infectious complications (20% vs 47%), multiorgan failure (20% vs 50%), and death (6% vs 35%) compared to patients receiving TPN.

Similarly, Wu et al demonstrated that TEN was associated with significantly lower rates of organ failure (21% vs 80%), multiorgan failure (15% vs 65%), need for surgery (22% vs 80%), septic pancreatic necrosis (23% vs 72%), and mortality (11% vs 43%) compared to TPN.

M.S. Petrov, M.V. Kukosh, N.V. Emelyanov A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition

Address nutrition in the first 24–72 hours

Nausea, vomiting, ileus, or bowel obstruction

Yes

No

Immediately oral diet

Patient unable to tolerate

Total enteral nutrition

GOO, delayed gastric emptying, high aspiration risk

NG tube

NJ tube

Retrial oral feeds when clinically appropriate

Nasal irritation or prolonged TEN anticipated

Endoscopic feeding tube placement

Tolerates NG?

Yes

No

PEG

GOO, delayed gastric emptying, aspiration risk

Needs gastric decompression

Yes

No

PEG-J

Direct PEJ

Cannot tolerate oral or nasoenteric feeds and not a candidate for percutaneous feeding tube
Although the development of infected pancreatic necrosis confers a significant risk of death, well-designed trials and meta-analyses have shown no benefit of prophylactic antibiotics.

Prophylaxis with antibiotic therapy is not recommended for any type of acute pancreatitis unless infection is suspected or has been confirmed.

Infected necrosis should be suspected when cross-sectional imaging demonstrates gas in a pancreatic or peripancreatic collection.

Other factors that may be indicative of infected necrosis include the presence of fevers, bacteremia, worsening leukocytosis, persistent unwellness, or clinical deterioration.

When infected necrosis is suspected, initiation of broad-spectrum intravenous antibiotics with good penetration into the pancreas is recommended.

These include carbapenems, quinolones, metronidazole, and third- or higher-generation cephalosporins.

Computed tomography–guided percutaneous biopsies of necrotic collections with samples sent for Gram stain and cultures can be performed to confirm the presence of infection – however this is unnecessary in a majority of cases as false-negative results are possible and risk of contaminating a sterile collection.

One scenario where computed tomography–guided biopsy/aspiration may help is for guidance in antibiotic selection, for example, in a patient with suspected infected necrosis but continued deterioration despite antibiotic administration.
ERCP is used primarily in patients with gallstone pancreatitis and is indicated in those who have evidence of cholangitis superimposed on gallstone pancreatitis.

This procedure is also a reasonable treatment in patients with documented choledocholithiasis on imaging or findings strongly suggestive of a persistent bile duct stone.

ERCP is not beneficial in the absence of these features, in mild cases of acute gallstone pancreatitis, or as a diagnostic test before cholecystectomy.
## ENDOSCOPIC THERAPY

### Predictors of choledocholithiasis

**Very strong**
- CBD stone on transabdominal US
- Clinical ascending cholangitis
- Bilirubin >4 mg/dL

**Strong**
- Dilated CBD on US (6 mm with gallbladder in situ)
- Bilirubin level 1.8-4 mg/dL

**Moderate**
- Abnormal liver biochemical test other than bilirubin
- Age >55 years
- Clinical gallstone pancreatitis

### Assigning a likelihood of choledocholithiasis based on clinical predictors

| Presence of any very strong predictor | High |
| Presence of both strong predictors | High |
| No predictors present | Low |
| All other patients | Intermediate |

*ASGE, American Society of Gastrointestinal Endoscopy; CBD, common bile duct; US, ultrasound examination*

- High likelihood → ERCP
- Intermediate likelihood → Pre-operative MRCP or EUS
- Low likelihood → Proceed with cholecystectomy
## Pancreatic Fluid Collections

<table>
<thead>
<tr>
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<th>Interstitial Edematous Pancreatitis</th>
<th>Necrotizing Pancreatitis</th>
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<tbody>
<tr>
<td><strong>&lt; 4 weeks</strong></td>
<td>Acute (peri)pancreatic fluid collection</td>
<td>Acute necrotic collection</td>
</tr>
<tr>
<td></td>
<td>Homogenous fluid adjacent to pancreas without a recognizable wall</td>
<td>Intra and/or extra pancreatic necrotic collection without a well-defined wall</td>
</tr>
<tr>
<td><strong>≥ 4 weeks</strong></td>
<td>Pancreatic pseudocyst</td>
<td>Walled off necrosis</td>
</tr>
<tr>
<td></td>
<td>An encapsulated, well-defined, usually extrapancreatic fluid collection with minimal solids</td>
<td>Intra and/or extra pancreatic necrotic collection with a well-defined wall</td>
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</table>
In the initial Atlanta criteria, PFCs were recommended for drainage based on the presence of symptoms and/or complications such as abdominal pain, gastrointestinal obstruction, vascular compression, biliary obstruction, or infection, as well as on the size of the collection.

However, in the revised criteria, size alone does not necessitate treatment; only symptomatic PFCs are recommended for drainage.
Percutaneous drainage can provide a rapid and effective means for source control in patients with infected pancreatic necrosis who are too ill to undergo endoscopic transmural drainage.

Percutaneous drainage monotherapy may provide definitive therapy for a subset of patients.

Advantages:

- For patients in the early phase of acute necrotizing pancreatitis (<2–4 weeks) who have suspected or confirmed infected necrosis—without the presence of a walled-off collection—and are failing conservative medical management.
- In cases where necrosis extends into one or both paracolic gutters and/or into the pelvis.
- Catheter tract can act as an entry portal for other minimally invasive debridement methods, such as video-assisted retroperitoneal debridement or endoscopic sinus tract debridement.
- Major downside - risk of pancreatocutaneous fistula formation.
- One large prospective study comparing endoscopic drainage approaches to a combined percutaneous/VARD approach showed the rate of pancreatic fistula formation was significantly higher in the percutaneous/VARD group (32% vs 5%; \( P < .01 \)).
While large randomized trials of endoscopic ultrasound (EUS) and non-EUS transmural drainage are lacking, most experts agree that EUS-guided transmural entry is safer, particularly with regard to avoidance of bleeding.

Options include plastic stents, self-expandable metal stents (SEMS) or lumen-apposing metal stents (LAMS).
Debridement of necrotic tissue can be in the form of irrigation through endoscopically placed nasocystic tubes or percutaneously placed drains, or by way of passing an endoscope into the cavity with mechanical removal, which is referred to as direct endoscopic necrosectomy (DEN).

The need for debridement, especially when large-diameter SEMS are placed, is likely dependent on the degree of solid material present within the walled-off necrotic cavity.

DEN carries risks for severe adverse events that include air embolism, intracavitary bleeding, and perforation.

While data have emerged that endoscopic step-up therapy and DEN starting at <4 weeks are clinically possible when indicated, patients who could clinically wait ≥4 weeks before endoscopic intervention had decreased mortality.
In patients with infected pancreatic necrosis or those with sterile pancreatic necrosis who have persistent organ dysfunction or failure to thrive, operative debridement should be considered.

Timing of intervention is important - as debridement during the early phase of acute pancreatitis (within 2–4 weeks of onset), carries a significantly higher mortality rate.

The goals of operative debridement are to control the source of infection and decrease the burden of necrosis, while minimizing the pro-inflammatory insult of the intervention itself on the debilitated patient.

There are multiple approaches to operative debridement, including VARD ("step-up"), laparoscopic and open transgastric debridement, and open operative debridement.

H.C. van Santvoort, M.G. Besselink, O.J. Bakker, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis
The tract formed from the previously placed drain is utilized to access the retroperitoneal space for an intracavitary videoscopic necrosectomy, employing traditional laparoscopic instrumentation under direct visualization with the laparoscope.

Drains are left in the cavity for postoperative lavage and fistula control, if needed.

The Dutch Pancreatitis Study Group compared the step-up approach to open necrosectomy in a prospective randomized multicenter trial (PANTER) and found equivalent mortality between the groups, but a higher rate of new-onset multiple-organ failure in the open necrosectomy group (40% vs 12%), as well as a higher rate of new-onset diabetes (38% vs 16%) and hernias (24% vs 7%).
TRANSGASTRIC DEBRIDEMENT

- Involves an anterior gastrostomy to access the posterior wall of the stomach for transmural access to the necrosis cavity.
- The variety of available surgical instrumentation allows for an easy, short, single debridement procedure, in contrast to the endoscopic approach.
- The transgastric approaches are best suited to the patient with centrally located necrosis, and extension of the necrosis burden into either paracolic gutter can lead to incomplete debridement.
OPEN DEBRIDEMENT

- Open debridement entails a laparotomy with entry into the lesser sac and gentle blunt debridement of necrotic tissue.
- Concurrent cholecystectomy can be performed in cases of biliary pancreatitis.
- Comparative studies with the exception of randomized trials should be interpreted with caution, given the often-higher severity of disease in patients undergoing open debridement in the current era.
Walled-off pancreatic necrosis
Sterile with severe symptoms or infected?

Central component of sufficient size and accessible transmurally?

Yes

EUS-guided placement of LAMS for drainage

*Large amount of solid debris?

Yes

Direct endoscopic necrosectomy until resolution

No

Remove LAMS after resolution or DEN for failure of LAMS

No

Large paracolic gutter extension?

Aggressive percutaneous drainage
Severe acute pancreatitis with necrosis

**Acute phase (<2–4 weeks)**
- Management of systemic inflammatory response
- Supportive care of associated organ dysfunction
- Nutritional optimization (enteral preferred)
- Avoidance of prophylactic antibiotics
- If concern for infection during acute phase (i.e., retroperitoneal air), consider image-guided percutaneous drainage
- Intra-abdominal hypertension common; clinical abdominal compartment syndrome unusual

**Late phase (≥2–4 weeks)**
- Continue supportive care of organ dysfunction
- Continue to optimize nutrition (enteral)
- Drainage and debridement indicated when evidence of infection (air in peripancreatic necrosis)
- Consider intervention on necrosis in patient with persistent nutritional failure or organ dysfunction

**Approach to debridement**
Dependent on pattern of necrosis and institutional expertise
- **Central retrogastric collection:**
  - Endoscopic transgastric or laparoscopic transgastric approach
- **Retrogastric with paracolic gutter extension:**
  - Percutaneous drainage with step-up to videoendoscopic retroperitoneal debridement or endoscopic debridement with addition of percutaneous drain as needed
- **Retrogastric collection with extension to the right of the mesenteric vessels:**
  - Endoscopic or laparoscopic transgastric; may need open debridement
In a subset of patients with severe acute pancreatitis, necrosis and disruption of the main pancreatic duct can result in a lack of continuity between the duct in the left-sided pancreas (body/tail) and the luminal gastrointestinal tract.

This disconnected pancreatic duct syndrome (DPDS) can produce a persistent pancreatic fistula, most often presenting as a peripancreatic fluid collection.

Recognition of this condition is important for therapeutic decision-making.

Standard treatment for DPDS is operative resection of the disconnected pancreas.
Disconnected Left Pancreatic Remnant
Demonstrated on CT imaging

MRCP to confirm ductal anatomy, consider ERCP if noninvasive imaging non-diagnostic

Early phase <2-4 weeks
- Supportive care of systemic inflammatory response and organ dysfunction
- Enteral nutrition
- No prophylactic antibiotics

Concern for infection (Gas in peripancreatic fluid collection)?
- No
  - Percutaneous drain
- Yes

Late phase ≥2-4 weeks
- Supportive care of systemic inflammatory response and organ dysfunction
- Enteral nutrition
- No prophylactic antibiotics

Good operative candidate? (Young, good physiology, few major comorbidities)
- Yes
  - Distal pancreatectomy
- No
  - Consider long-term transgastric endoscopic stenting
NEED FOR MULTIDISCIPLINARY APPROACH

- Management of patients with pancreatic necrosis is most effective at a specialized referral center with nutritionists, medical intensivists, procedural radiologists, advanced endoscopists, and pancreatic surgeons who have expertise in caring for this complex patient population.
- Percutaneous drainage remains an important adjunctive or definitive therapy in the early stage of the disease.
- Similarly, EUS-guided drainage and DEN when required for WON, particularly in the era of LAMS, and a step-up approach that utilizes minimally invasive and open surgical approaches for debridement are important and effective interventions.
CHRONIC PANCREATITIS
CHRONIC PANCREATITIS

- The Mechanistic Definition affirms the characteristics of end-stage disease in individuals with genetic, environmental, and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress:
  - pancreatic atrophy,
  - fibrosis,
  - duct distortion and strictures,
  - calcifications,
  - pancreatic exocrine dysfunction,
  - pancreatic endocrine dysfunction,
Computed tomography (CT) or MRI are recommended for the diagnosis of CP. Either test should be the first choice for the diagnosis of CP.

Endoscopic ultrasonography (EUS), because of its invasiveness and lack of specificity, should be used only if the diagnosis is in question after cross-sectional imaging is performed.

If cross-sectional imaging and EUS are not diagnostic of CP, s-MRCP can be used to identify subtle ductal abnormalities such as dilated branches or an ectatic duct, which may indicate morphologic changes consistent with imaging criteria for CP.

However, the diagnosis of CP should not be made solely on s-MRCP findings or other imaging modalities.
Pancreatic function testing is an important means of diagnosing EPI; however, its role in establishing the diagnosis of CP is complementary.

Although a 72-hour fecal fat measurement might be considered the gold standard for complete failure, most studies use either clinical steatorrhea or reduced levels of fecal elastase as the primary diagnostic test.

The accuracy of fecal elastase to detect EPI depends on the cutoff chosen.

Some studies have used levels of <200 [μg/g stool], but this level has a high false-positive rate. Lowering the cutoff to <100 [μg/g stool] improves specificity but lowers sensitivity.

### ETIOLOGY

#### TIGAR-O CLASSIFICATION

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
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<tbody>
<tr>
<td>Toxic</td>
<td>Alcohol</td>
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<tr>
<td></td>
<td>Cigarette smoking</td>
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<td></td>
<td>Hypercalcemia, hyperparathyroidism</td>
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<tr>
<td></td>
<td>Hypertriglyceridemia</td>
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<td></td>
<td>Chronic renal failure</td>
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<tr>
<td>Idiopathic</td>
<td>Early onset &lt; 35 years</td>
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<tr>
<td></td>
<td>Late onset &gt; 35 years</td>
</tr>
<tr>
<td>Genetic</td>
<td>PRSS1, CFTR, and SPINK1 mutations</td>
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<tr>
<td>Autoimmune</td>
<td>Type I: IgG4-related disease</td>
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<td></td>
<td>Type II: IgG4-negative</td>
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<tr>
<td>Severe acute pancreatitis-associated</td>
<td>Pancreas divisum</td>
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<tr>
<td>Obstructive</td>
<td>Pancreatic duct scars</td>
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<td>Groove pancreatitis</td>
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- Genetic testing is recommended in patients with clinical evidence of a pancreatitis-associated disorder or possible CP in which the etiology is unclear, especially in younger patients.

- This is important in because therapies (such as CFTR-modulating drugs) can target mechanism, and knowing the mechanism allows the most appropriate drug and/or therapy to be selected.

- In most instances, patients should be referred to a genetic counselor for evaluation.

- At minimum, patients with idiopathic CP should be evaluated for PRSSI, SPINK1, CFTR, and CTRC gene mutation analysis, although more extended panels with over a dozen susceptibility and modifier genes, hypertriglyceridemia genes, and pharmacogenetics are available.
Although the evidence is low quality, strict alcohol avoidance should be a cornerstone of any treatment program for patients with CP. There is a randomized trial, demonstrating that alcohol cessation counseling in patients admitted with an attack of acute alcoholic pancreatitis can limit further hospitalizations and pain attacks.

Strict smoking avoidance should be a cornerstone of any treatment program for patients with CP, recognizing however that the long-term success rate of smoking cessation is low.

No definitive benefit to screen patients with CP for pancreatic ductal adenocarcinoma. This is based on the invasive and costly nature of testing and the inherent difficulty in screening given the structural changes of CP.

New-onset DM with weight loss is potentially also an indicator of pancreatic ductal adenocarcinoma.
Patients with CP often experience pain in the setting of pancreatic duct obstruction – pancreatic duct stones or stricture.

Endoscopic decompressive procedures include ERCP with pancreatic sphincterotomy, stone clearance, stricture dilation, and pancreatic duct stenting.

Other endoscopic options include interventional EUS procedures that usually involve placement of a transluminal stent to allow for pancreatic duct decompression.

Several surgical decompressive procedures exist (Puestow, Frey, and Beger procedures) that may also include a component of partial pancreatectomy.

Although surgical approaches to pancreatic duct decompression have been shown to provide better long-term pain relief than endoscopic approaches, they are rarely first-line therapies.
- Antioxidant therapy appears to be safe and may reduce pain and can be considered for clinical use, especially early in the course of disease. The type of antioxidants used has widely varied in clinical practice, but clinical trials generally include at least selenium, ascorbic acid, [beta]-carotene, and methionine.

- Co-analgesics such as antidepressants and anticonvulsants (eg, gabapentin, pregabalin) have shown effectiveness in treating chronic visceral and neuropathic pain in chronic pancreatitis, and can reduce the need for opioids.

- If opioids are necessary, they should be given in a long-acting oral form.

- Pancreatic enzyme therapy should not be used as a form of pain control in patients with CP given their expense and general lack of clinical efficacy.
Celiac plexus blockade refers to the injection of pharmaceuticals into and/or around the region of the celiac ganglia. The most common celiac plexus ingredients are a combination of a local anesthetic and a steroid, i.e., bupivacaine and triamcinolone. Celiac plexus blockade can be performed through endoscopy, interventional radiology, or surgical approaches.

Advantages of celiac plexus blockade include the fact that a single treatment can potentially provide pain reduction or relief for 3-6 months, may reduce or eliminate the need for oral analgesia, and can be performed quickly and repeated as needed. Disadvantages of celiac plexus blockade include the risks of the procedure itself (bleeding, allergic reaction, etc.)
TREATMENT OF EPI

- EPI should be suspected in those with long-standing CP or in those with CP and weight loss, malnutrition, diarrhea, steatorrhea, osteoporosis, or osteopenia.
- An abnormal fecal elastase is the most easily available diagnostic test.
- Therapy should include an adequate dosage (at least 40,000-50,000 USP units of lipase with each meal) administered during the meal. Usual starting dose is 500 units/kg/meal
- If needed, proton pump inhibitors increase the efficacy of treatment.
Periodic evaluation of fat-soluble vitamin and zinc deficiency should be considered in patients with CP given their higher fracture risk and overall increased incidence of malnutrition.

- Recommend small, frequent meals without fat restriction

Future?? Immune-modulating therapies for treating sterile inflammation have been approved, and computer modelling in chronic pancreatitis suggests that similar therapeutics might be effective for chronic pancreatitis.
THANK YOU!

QUESTIONS?