Approach to the Patient with Pancreatic Disease

Chapter 358 | Part 10: Disorders of the Gastrointestinal System

KEY CLINICAL POINTS

1. Diagnosis of acute pancreatitis requires serum lipase or amylase ≥3x upper limit of normal (ULN) combined with characteristic abdominal pain.
2. Serum lipase is the preferred enzyme for diagnosis in patients with renal disease; amylase may be falsely normal in hypertriglyceridemia.
3. Fecal elastase <100 µg/g indicates exocrine pancreatic insufficiency (EPI); false positives occur with nonformed stools.
4. Chronic pancreatitis (CP) diagnosis requires imaging criteria (calcification, atrophy, duct dilation) or functional testing (peak bicarbonate <80 mEq/L).
5. Endoscopic ultrasonography (EUS) is the preferred modality for evaluating pancreatic cystic lesions and detecting CP (≥5 of 9 criteria).
6. Intraductal papillary mucinous neoplasm (IPMN) is a precancerous mucinous cyst; mucinous cystic neoplasms (MCNs) occur almost exclusively in women.
7. Serous cystadenomas have a negligible risk of progression to malignancy.
8. CT with intravenous contrast is the best imaging study for complications of acute pancreatitis; multiphasic CT is preferred for staging cancer.
9. EUS is preferred over ERCP for diagnostic assessment of the pancreatic duct and is increasingly preferred for management of choledocholithiasis.
10. Hyperamylasemia has numerous non-pancreatic causes (e.g., renal insufficiency, salivary gland lesions, COVID-19 infection).

DEFINITION & OVERVIEW

- **Acute Pancreatitis:** One of the most common reasons for hospitalizations in gastroenterology; associated with potential complications including diabetes, exocrine pancreatic insufficiency (EPI), and chronic pancreatitis.
- **Clinical Significance:** In elderly patients, acute pancreatitis may serve as an early symptom of pancreatic cancer.
- **Chronic Pancreatitis (CP):** An irreversible disease of the pancreas associated with poor quality of life due to abdominal pain and exocrine insufficiency; established risk factor for pancreatic cancer.
- **Pancreatic Cysts:** Often incidentally detected on cross-sectional imaging; range from benign to precancerous.

Key Cyst Classifications:

  – **Intraductal papillary mucinous neoplasm (IPMN):** A precancerous mucinous cyst; radiographic surveillance is typically recommended in the absence of high-risk features.

- **Mucinous cystic neoplasms (MCNs):** Less common; occur almost exclusively in women.
- **Serous cystadenomas:** Neoplastic cysts with a negligible risk of progression to malignancy.
- **Pseudocysts:** The most commonly encountered benign cyst, occurring in patients with a history of acute or chronic pancreatitis.

EPIDEMIOLOGY

- **Acute Pancreatitis (US):** ~300,000 hospitalizations annually.
- **Chronic Pancreatitis (US):** ~13,000 admissions per year; annual prevalence of 42–73 cases per 100,000 adults.
- **Economic Impact:** Acute and chronic pancreatic disease costs an estimated $3 billion annually in US healthcare.
- **Global Incidence:**
  - Acute: ~33.7 cases (95% CI, 23.3–48.8) per 100,000 person-years; 1.16 deaths.
  - Chronic: ~9.6 cases (95% CI, 7.9–11.8) per 100,000 person-years; 0.09 deaths.
- **Cancer:** Incidence of pancreatic adenocarcinoma is increasing; it is the third most common cancer death in the US.

ETIOLOGY & PATHOPHYSIOLOGY

- **Primary Causes:** Biliary tract disease, alcohol abuse.
- **Other Causes:** Medications, genetic mutations, and trauma.
- **Undetermined Etiology:** ~30% of patients with acute pancreatitis and 25–40% of patients with chronic pancreatitis have initially unexplained causes.

CLINICAL FEATURES

- **Chronic Pancreatitis Symptoms:** Abdominal pain, nausea, weight loss, steatorrhea, malabsorption, history of alcohol abuse, recurrent pancreatitis, fatty-food intolerance.
- **Exocrine Pancreatic Insufficiency (EPI):**
  - Maldigestion of fat and protein becomes evident only when >90% of the pancreas is functionally damaged or obstructed.
- **Enzyme Kinetics:**
  - Serum amylase and lipase typically elevated within 24h of onset; remain elevated for 3–7 days.
  - Levels return to normal within 7 days unless there is ductal disruption, obstruction, or pseudocyst formation.
  - ~85% of patients with acute pancreatitis have ≥3x elevation of lipase and amylase.
- **Factors causing low/normal enzyme levels in acute cases:**
  - Delay (2–5 days) before blood sampling.
  - Underlying condition is chronic rather than acute.
  - Presence of hypertriglyceridemia (causes spuriously low levels).
- **Ascitic Fluid Amylase:** Elevated in acute pancreatitis, but also in intestinal obstruction, infarction, or perforated peptic ulcer.
- **Pleural Fluid Amylase:** Elevated in acute/chronic pancreatitis, lung cancer, and esophageal perforation.

DIFFERENTIAL DIAGNOSIS

- **Causes of Hyperamylasemia (Table 358-2):**
  - **Pancreatic Disease:** Acute/Chronic pancreatitis, complications (pseudocyst, ascites, necrosis), trauma, adenocarcinoma.
  - **Nonpancreatic Disorders:** Renal insufficiency, Salivary gland lesions (Mumps, Calculus, Irradiation sialadenitis, Maxillofacial surgery), Tumor hyperamylasemia (Lung, esophagus, breast, ovary), Macroamylasemia, Burns, Diabetes mellitus (especially with ketoacidosis), Pregnancy, Renal transplantation, COVID-19 infection, Cerebral trauma, Drugs (opiates).
  - **Other Abdominal Disorders:** Biliary tract disease (cholecystitis, choledocholithiasis), Intraabdominal disease (Perforated/penetrating peptic ulcer, Intestinal obstruction/inflammation, Ruptured ectopic pregnancy, Peritonitis, Aortic aneurysm, Postoperative hyperamylasemia).

INVESTIGATIONS & DIAGNOSIS

1. **Laboratory Assessment:**
   - **Serum Lipase:** Enzyme measurement of choice for acute pancreatitis; increased specificity if level is ≥3x ULN.
   - **Amylase:** Simple test; increased specificity if >3x ULN; may be falsely normal in hypertriglyceridemia.
   - **Fecal Elastase:** Used to assess exocrine function; value <100 µg/g indicates insufficiency (highest accuracy when pretest probability is high).
   - **Macroamylasemia:** If serum amylase is <500 IU/L without evidence of acute pancreatitis, consider macroamylasemia.
2. **Imaging Modalities:**
   - **CT with IV Contrast:** Best for assessing complications (necrosis, pseudocysts) and staging cancer.
   - **MRI/MRCP:** Superior to CT for detecting mild pancreatitis, necrosis, choledocholithiasis, and cystic neoplasms; T2-weighted MRI differentiates necrotic debris from fluid.
   - **EUS:** High resolution; preferred for evaluating pancreatic parenchyma, ductal anatomy, and identifying small cysts (based on ≥5 of 9 criteria in Table 358-3).
3. **Functional Testing:**
   - **Secretin Test:** Sensitive to detect occult disease; rarely performed.
   - **Endoscopic Pancreas Function Test (ePFT):** High negative predictive value for chronic pancreatitis.
   - **EUS-ePFT:** Combines endosonographic evaluation of structure and endoscopic collection of juice.
   - **Secretin-stimulated MRCP:** Noninvasive; improved visualization of ductal anatomy; less accurate than ePFT for functional assessment.

Diagnostic Algorithm for Chronic Pancreatitis (Figure 358-2)

1. **Initial Assessment:** Clinical suspicion → Physical exam, labs, and fecal elastase.

2. **Step 1 (CT):** Perform Contrast-enhanced CT scan →

→ **If** "calcifications in combination with atrophy and/or dilated duct" are present → **Diagnosis Met**;

→ **Else** (Inconclusive) → Proceed to Step 2.

3. **Step 2 (MRI/MRCP):** Perform MRI and MRCP (sMRCP) →

→ **If** "Cambridge III, dilated duct, atrophy of gland, filling defects" are present → **Diagnosis Met**;

→ **Else** (Inconclusive) → Proceed to Step 3.

4. **Step 3 (EUS):** Perform EUS with quantification →

→ **If** ≥5 EUS criteria met → **Diagnosis Met**;

→ **Else** (Inconclusive) → Proceed to Step 4.

5. **Step 4 (ePFT):** Perform endoscopic Pancreas function test (ePFT) →

→ **If** peak [bicarbonate] <80 mEq/L → **Diagnosis Met**;

→ **Else** (Inconclusive) → Monitor symptoms and repeat testing in 6 months – 1 year.

MANAGEMENT & TREATMENT

1. **Acute Pancreatitis Management:**
   - **CT Timing:** Not recommended in the first 3 days if diagnosis is confirmed by serology/physical exam (to avoid contrast-induced nephropathy).
2. **Choledocholithiasis Management:**
   - **EUS vs. ERCP:** EUS is preferred over ERCP for diagnostic assessment of the pancreatic duct and is increasingly preferred for management of choledocholithiasis in acute pancreatitis and pancreatic neoplasm with biliary obstruction.
3. **Chronic Pancreatitis Pain Management:**
   - **Interventional Procedures:** EUS can facilitate delivery of nerve-blocking agents (celiac plexus block) or neurolysis.

KEY PEARLS & CLINICAL TRAPS

- **Lipase vs. Amylase:** Lipase is more specific for acute pancreatitis; amylase can be elevated in many non-pancreatic tissues (salivary, lung, etc.).
- **Macroamylasemia:** If serum amylase is <500 IU/L without evidence of acute pancreatitis, consider macroamylasemia to avoid unnecessary tests.
- **Fecal Elastase Pitfalls:** False positives occur with nonformed stools; accuracy is highest when pretest probability is high.
- **EUS Timing:** Not beneficial during acute pancreatitis; perform after resolution (e.g., ~4 weeks) to detect underlying causes like malignancy or stones.
- **Cyst Differentiation:**
  - **IPMN:** Predominantly mucinous, precancerous.
  - **MCN:** Mucinous, almost exclusively in women.
  - **Serous Cystadenoma:** Benign, negligible risk of malignancy.

REFERENCE TABLES

TABLE 358-1

Tests Useful in the Diagnosis of Acute and Chronic Pancreatitis and Pancreatic Neoplasms TEST Pancreatic Enzymes in...

TEST	PRINCIPLE	COMMENT
Pancreatic Enzymes in Body Fluids		

TEST	PRINCIPLE	COMMENT
Serum lipase	Pancreatic inflammation leads to increased serum enzyme levels	Enzyme measurement of choice for the diagnosis of acute pancreatitis; increased specificity if the level is more than three times the upper limit of normal (3× ULN)
Amylase		
1. Serum	Pancreatic inflammation leads to increased serum enzyme levels	Simple; increased specificity if the level is >3× ULN; may be falsely normal in patients with hypertriglyceridemic pancreatitis
2. Urine	Renal clearance of amylase is increased in acute pancreatitis	Infrequently used
3. Ascitic fluid	Disruption of gland or main pancreatic duct leads to increased amylase concentration	Can help establish source of ascites; false positives occur with intestinal obstruction and perforated ulcer; can also measure lipase
4. Pleural fluid	Exudative pleural effusion with pancreatitis	False positives occur with carcinoma of the lung and esophageal perforation
Studies Pertaining to Pancreatic Structure		
Tests of Exocrine Pancreatic Function		
Direct stimulation of the pancreas with analysis of duodenal contents		
1. Secretin test	Secretin leads to increased output of pancreatic juice and HCO_3^-; pancreatic secretory response is 3 related to the functional mass of pancreatic tissue; involves duodenal intubation and fluoroscopic placement of gastroduodenal tube	Sensitive to detect occult disease; poorly defined normal enzyme response; large secretory reserve capacity of the pancreas; rarely performed
2. Endoscopic pancreatic function test (ePFT)	Secretin-stimulated collection of pancreatic juice performed during upper endoscopy; replaces need for tube placement in the duodenum	Sensitive to detect occult disease; high negative predictive value for chronic pancreatitis; requires sedation
3. EUS-ePFT	Combines endosonographic evaluation of the pancreas and endoscopic collection of pancreatic juice	Single endoscopic evaluation of pancreatic structure and function

TEST	PRINCIPLE	COMMENT
4. Secretin-stimulated MRCP	Combines imaging evaluation of the pancreas and a semiquantitative estimation of pancreatic juice output in the duodenum	Improved visualization of pancreatic ductal anatomy; functional evaluation is less accurate than ePFT; noninvasive
Measurement of intraluminal digestion products		
1. Stool fat determination	Lack of lipolytic enzymes brings about impaired fat digestion; quantitative 72-h stool collection and estimation are more reliable than qualitative analysis of a random stool sample	Reliable reference standard for defining severity of fat malabsorption; does not distinguish between pancreatic and nonpancreatic cause of malabsorption
Measurement of pancreatic enzymes in feces		
1. Fecal elastase	Pancreatic secretion of proteolytic enzymes; not degraded in intestine	Diagnostic accuracy is highest when the pretest probability is high and the value is <100 μg/g; false positives will occur in patients with nonformed stools

TABLE 358-2

Causes of Hyperamylasemia Pancreatic Disease I. Pancreatitis

- Pancreatic Disease
- I. Pancreatitis A. Acute B. Chronic: ductal obstruction C. Complications of pancreatitis 1. Pancreatic pseudocyst 2. Ascites caused by pancreatic duct disruption 3. Pancreatic necrosis II. Pancreatic trauma III. Pancreatic adenocarcinoma
- Nonpancreatic Disorders
- I. Renal insufficiency II. Salivary gland lesions A. Mumps B. Calculus C. Irradiation sialadenitis D. Maxillofacial surgery III. "Tumor" hyperamylasemia A. Carcinoma of the lung, esophagus, breast, or ovary IV. Macroamylasemia V. Burns VI. Diabetes mellitus, particularly when ketoacidosis is present VII. Pregnancy VIII. Renal transplantation IX. COVID-19 infection X. Cerebral trauma XI. Drugs: opiates
- Other Abdominal Disorders
- I. Biliary tract disease: cholecystitis, choledocholithiasis II. Intraabdominal disease A. Perforated or penetrating peptic ulcer B. Intestinal obstruction or inflammation C. Ruptured ectopic pregnancy D. Peritonitis E. Aortic aneurysm F. Postoperative hyperamylasemia

TABLE 358-3

Endoscopic Ultrasonographic Criteria for Chronic Pancreatitis (Total Criteria = 9) DUCTAL Stones Hyperechoic main duct...

DUCTAL	PARENCHYMAL
Stones	Echogenic strands
Main duct irregularity	Lobular contour
Visible side branches	