Pancreas Diseases. Acute and Chronic Pancreatitis. Pancreatic Tumors.
Acute Pancreatitis

• ESSENTIALS OF DIAGNOSIS
• Gallstone disease and alcohol are the most common causes of acute pancreatitis; other causes include hypertriglyceridemia, drugs, and specific disorders of the biliary tree and pancreas.
• Diagnosis is usually made based on a history of acute abdominal pain; a threefold elevation in serum amylase or lipase, or both; or an abnormal abdominal computed tomography (CT) scan showing changes of acute pancreatitis.
• Severe necrotizing acute pancreatitis is characterized by persistent (> 48 hours) systemic inflammatory response syndrome (SIRS), hemoconcentration, and organ failure (systemic blood pressure < 90 mm Hg, PaO2 < 60 mm Hg, creatinine > 2.0 mg/dL).
• Diagnosis of necrotizing pancreatitis is confirmed by abdominal CT scan.
• **General Considerations**

  • Acute pancreatitis is an acute inflammatory disorder of the pancreas that involves the pancreas and peripancreatic tissues but can sometimes affect other organ systems.

  • The initial evaluation of patients with acute pancreatitis involves determining the cause and assessing the severity of disease since this guides subsequent management.
• **A. Incidence**

• Acute pancreatitis is the third most common inpatient gastrointestinal diagnosis in Western world.

• The incidence rate of acute pancreatitis appears to be increasing without any changes in the short-term or long-term case fatality rates.
• **B. Causes and Risk Factors**

• The most common causes of acute pancreatitis are gallstones and alcohol abuse, accounting for 70–80% of cases.

• Other causes, including hypertriglyceridemia, drug reactions, iatrogenic causes (eg, postsurgical or endoscopic retrograde cholangiopancreatography [ERCP]), hereditary factors, and idiopathic causes.
- **Causes of acute pancreatitis.**
- Alcohol
- Autoimmune
- Biliary (eg, gallstones, gallbladder microlithiasis/sludge)
- Drug-induced
- Iatrogenic
  - Surgery (eg, common bile duct exploration, sphincterotomy, splenectomy, distal gastrectomy)
  - ERCP
- Idiopathic
- Infectious (eg, ascariasis, clonorchiasis, mumps, toxoplasmosis, coxsackievirus, cytomegalovirus, tuberculosis, Mycobacterium avium complex)
- Inherited
  - CFTR (cystic fibrosis transmembrane conductance regulator) mutations
  - SPINK1 (serine protease inhibitor Kazal type 1) mutations
  - PRSS1 (cationic trypsinogen) mutations
Causes of acute pancreatitis.

- Metabolic (e.g., hypercalcemia, hypertriglyceridemia)
- Neoplastic (e.g., pancreatic or ampullary tumors)
- Structural (e.g., pancreatic divisum, annular pancreas, sphincter of Oddi dysfunction, periampullary diverticula, duodenal duplication cysts, choledochoccele, anomalous pancreaticobiliary junction, regional enteritis)
- Toxic (e.g., organophosphates, scorpion venom)
- Traumatic (especially motor vehicle accidents)
- Vascular
• **Drugs implicated in acute pancreatitis**
  • Class IA: α-Methyldopa, Arabinoside, Azodisalicylate, Bezafibrate, Cannabis, Carbimazole, Codeine, Cytosine, Dapsone, Enalapril, Furosemide, Isoniazid, Mesalamine, Metronidazole, Pentamidine, Pravastatin, Procainamide, Pyritinol, Simvastatin, Stibogluconate, Sulfamethoxazole, Sulindac, Tetracycline, Valproic acid
  • Class IB: All-transretinoic acid, Amiodarone, Azathioprine, Clomiphene, Dexamethasone, Ifosfamide, Lamivudine, Losartan, Lynestrenol/methoxyethinylestradiol, 6-mercaptopurine, Meglumine, Methimazole, Nelfinavir, Norethindronate/mestranol, Omeprazole, Premarin, Sulfamethoxazole, Trimethoprim–sulfamethoxazole
  • Class II: Acetaminophen, Chlorothiazide, Clozapine, Dideoxyinosine (DDI), Erythromycin, Estrogen, L-Asparaginase, Pegasparaginase, Propofol, Tamoxifen
• **Pathogenesis**

• Acute pancreatitis develops in response to premature activation of intracellular trypsinogen (which causes acinar cell injury) and the release of chemokines and cytokines.

• The exact mechanisms leading to alcoholic and biliary acute pancreatitis remain to be defined.

• Biliary pancreatitis is most commonly caused by the passage of a stone from the gallbladder through the cystic duct into the common bile duct.
Clinical Findings

A. Symptoms and Signs

Abdominal pain is the most common symptom in patients presenting with acute pancreatitis.

The pain is typically epigastric and radiates to the back.

Patients also often present with nausea and vomiting.

In patients with severe acute pancreatitis, signs and symptoms parallel the presence of a systemic inflammatory response and organ dysfunction.

Cullen sign (periumbilical ecchymoses) and Grey Turner sign (flank ecchymoses) are rare but can be seen in cases of acute pancreatitis with hemorrhage and are associated with increased mortality.
• **B. Laboratory Findings**

• Serum amylase and lipase are the principle serologic data that aid in the diagnosis of acute pancreatitis.

• Elevations greater than three times the upper limit of normal are typically used to diagnose acute pancreatitis.

• Serum lipase is a more sensitive and specific indicator than amylase.
• C. Imaging Studies
  
  • Contrast-enhanced CT is the single most important test in diagnosing acute pancreatitis, determining its severity, and assessing for complications.
  
  • Although ultrasonography is useful for specifically evaluating biliary etiologies and excluding acute cholecystitis or hepatic abscesses, it has limited utility in diagnosing and determining other etiologies of acute pancreatitis.
  
  • Magnetic resonance cholangiopancreatography (MRCP) is equivalent to CT in its ability to detect necrosis and determine severity of acute pancreatitis.
• **D. Diagnostic Approach**

• **1. Confirmation of the diagnosis**—The diagnosis of acute pancreatitis is usually made when there is a history of acute abdominal pain and a threefold elevation in serum amylase or lipase, or both, or an abnormal abdominal CT scan demonstrating changes consistent with acute pancreatitis.

• **2. Indications for more extensive evaluation**—Patients older than 40 years are thought to have an increased risk of pancreatic malignancy. Therefore, a contrast-enhanced CT scan should be part of the initial evaluation.

• Secondary evaluation of ductal anatomy is a combination of MRCP and endoscopic ultrasound
3. Criteria for assessing severity in acute pancreatitis—The criteria for severe acute pancreatitis were defined as organ failure of at least one organ system (systolic blood pressure < 90 mm Hg, PaO2 < 60 mm Hg, creatinine > 2.0 mg/dL after rehydration, and gastrointestinal bleeding > 500 mL/24 h) and the presence of local complications such as necrosis, pseudocyst, and abscess.

Risk factors for severe acute pancreatitis on admission include older age (> 55 years), obesity (basal metabolic index ≥ 30), and comorbid disease.

At admission, predictors of severity in acute pancreatitis include APACHE II scores, SIRS, hemoconcentration, presence of pleural effusions, and organ failure.
• It should be noted that necrotizing pancreatitis is uncommon (10–20% of all patients with acute pancreatitis) and the far greater proportion of patients presenting in clinical practice have interstitial pancreatitis.
• **Differential Diagnosis**
• Perforated viscus
• Cholecystitis
• Bowel obstruction
• Vascular occlusion (especially mesentery venous disease)
• Renal colic
• Inferior myocardial infarction
• Pneumonia
• Diabetic ketoacidosis
• Duodenal ulcer
• **Complications**
  • Commonly seen complications include pancreatic pseudocyst, abscess formation, and pancreatic ascites from pancreas duct disruption.
  • Pancreatic pseudocyst should only be drained if it causes symptoms such as abdominal pain or gastric obstruction. Drainage can safely be performed endoscopically or surgically.
  • Pancreatic abscess formation usually requires surgical drainage and intravenous antibiotics.
  • Pancreatic ascites can be managed conservatively with endoscopic therapy if the disruption can be “bridged” with a pancreatic stent.
  • Bleeding complications from esophagogastric varices can occur from splenic vein obstruction.
  • Less commonly seen complications include pancreatic encephalopathy, subcutaneous fat necrosis, or splenic complications such as a subcapsular hematoma.
Treatment

A. Mild Acute Pancreatitis

The majority of patients with mild acute pancreatitis respond to simple supportive care measures that form the hallmark of treatment in acute pancreatitis: bowel rest, intravenous hydration with crystalloid, and analgesia.

Patients with gallstone pancreatitis are at increased risk of recurrence.

Therefore, following recovery from mild pancreatitis, consideration should be given to performing a laparoscopic cholecystectomy during the same admission.

An alternative for patients who are not surgical candidates would be to perform an endoscopic biliary sphincterotomy.
• **B. Severe Acute Pancreatitis**
  • It is recommended that vigorous fluid resuscitation be initiated.
  • Once it is clear that a patient will not be able to tolerate oral feeding, enteral nutrition (rather than total parenteral nutrition) should be considered.
  • Enteral nutrition that bypasses the stomach and duodenum is believed to stimulate pancreatic secretions less, and this supports the use of the nasojejunal route.
  • There is currently no role for prophylactic antibiotics in either interstitial or necrotizing pancreatitis.
  • It is reasonable to start antibiotics in a patient who appears septic while awaiting the results of cultures.
  • Once the diagnosis of infected necrosis is established, appropriate antibiotics should be initiated and surgical debridement should be undertaken.
• Urgent ERCP (within 24 hours) is indicated in patients who have severe acute biliary pancreatitis with organ failure or cholangitis, or both.
• Elective ERCP with sphincterotomy can be considered in patients with persistent or incipient biliary obstruction, those deemed to be poor candidates for cholecystectomy, and those in whom there is strong suspicion of bile duct stones after cholecystectomy
• ERCP also is indicated for pancreatic ductal disruptions that occur as part of the inflammatory process and result in peripancreatic fluid collections.
Chronic Pancreatitis

• ESSENTIALS OF DIAGNOSIS
• Diagnosis relies on a combination of clinical findings, imaging tests, and pancreatic function testing.
• Pancreatic calcifications, dilated pancreatic ducts, diabetes mellitus, and maldigestion characterize advanced disease.
• Early–stage diagnosis remains a clinical challenge, especially in patients with chronic or episodic abdominal pain and no imaging abnormalities.
• **General Considerations**

• Among established risk factors, alcohol ingestion is associated with up to 60–70% of cases of chronic pancreatitis.

• In addition, ductal obstruction, autoimmune disease, tropical disease, and an association with further systemic illnesses such as scleroderma and hypertriglycerideridemia have been described.

• The most widely accepted system of etiologic classification for chronic pancreatitis is the TIGAR-O system.
TIGAR-O classification of chronic pancreatitis.

- Toxic-Metabolic
- Alcoholic
- Tobacco smoking
- Hypercalcemia (hyperparathyroidism)
- Hyperlipidemia (rare and controversial)
- Chronic renal failure
TIGAR-O classification of chronic pancreatitis.

- **Idiopathic**
- Cause unknown, likely genetic origin
- Tropical
- **Genetic**
- Autosomal dominant
- Cationic trypsinogen
- Autosomal recessive/modifier genes
- CFTR mutations
- SPINK1 mutations
- $\alpha_1$-Antitrypsin deficiency (possible)
TIGAR-O classification of chronic pancreatitis.

• **Autoimmune**
  • Isolated autoimmune chronic pancreatitis
  • Associated with:
    • Primary sclerosing cholangitis
    • Sjögren syndrome
    • Primary biliary cirrhosis
    • Type 1 diabetes mellitus
• **Recurrent and Severe Acute Pancreatitis**
  • Postnecrotic (severe acute pancreatitis)
  • Vascular diseases/ischemia
  • Postradiation exposure
TIGAR-O classification of chronic pancreatitis.

- **Obstructive**
- Pancreas divisum (controversial)
- Sphincter of Oddi dysfunction (controversial)
- Duct obstruction (tumors, post-traumatic)
• **Pathogenesis**

- Morphologic changes associated with chronic pancreatitis include both ductal and parenchymal changes.
- Pancreatic ducts may become dilated, irregular, or strictured.
- The glandular tissue itself is often characterized by irregular and patchy replacement of normal acinar cell architecture with fibrosis.
• **Pathogenesis**
  
  • The oxidative-stress hypothesis attributes pancreatic damage to reflux of bile rich in reactive oxidation byproducts.
  
  • The toxic-metabolic theory involves direct damage to pancreatic acinar cells from noxious stimuli such as alcohol.
  
  • The obstructive theory attributes the majority of injury to pancreatic ductal injury resulting from obstruction related to increased lithogenicity, the latter, in turn, caused by either genetic or environmental exposures (eg, alcohol).
  
  • The necrosis-fibrosis hypothesis describes chronic pancreatitis as a continuum that is initiated early on by an attack of acute pancreatitis.
• Clinical Findings
• A. Symptoms and Signs
• The hallmark features of chronic pancreatitis are abdominal pain and pancreatic insufficiency.
• Advanced disease can also be associated with weight loss and diabetes.
• History include post-prandial pain triggered by high-fat or protein-rich meals.
1. Abdominal pain—

- The pain associated with chronic pancreatitis is classically described as epigastric, often with radiation to the back.
- Pain may be post-prandial, associated with nausea and vomiting.
- Pain may become continuous.
- 20–45% of patients may not have pain.
2. Pancreatic insufficiency—

- Pancreatic exocrine and endocrine dysfunction with advanced disease.
- Clinically significant protein malabsorption and fat deficiency does not occur until over 90% of pancreatic function is lost.
- Steatorrhea precedes the onset of protein malabsorption.
- Pancreatic endocrine insufficiency presenting as diabetes is a distinctly late occurrence.
• **B. Laboratory Findings**

• Amylase and lipase are often elevated during acute pain episodes early in the natural history of the disease.

• Fecal pancreatic elastase-1 (FPE-1) levels less than 100 mcg/g of stool correlate with severe exocrine pancreatic insufficiency.

• Pancreatic enzyme supplementation does not interfere with interpretation of test results.

• Additional tests that may be useful in evaluating chronic pancreatitis include hemoglobin A1c (to investigate glucose intolerance) and markers of autoimmune chronic pancreatitis, including immunoglobulin G4, rheumatoid factor, and antinuclear antibody.
- **C. Imaging Studies**
- Plain abdominal radiographs may reveal calcifications within the pancreas.
- Transabdominal ultrasound has been associated with low sensitivity in diagnosing chronic pancreatitis except in patients with severe disease.
- Contrast enhanced computed tomography (CT) and magnetic resonance imaging (MRI) offer enhanced visualization of the pancreas and adjoining structures.
• 1. Endoscopic ultrasound (EUS)—
  • EUS appears to be particularly beneficial
• 2. Endoscopic retrograde cholangiopancreatography (ERCP)—
  • ERCP is generally reserved for situations in which intervention is likely.
**D. Special Tests**

- Hereditary and idiopathic forms of chronic pancreatitis account for up to 20–30% of cases.
- Genetic alterations associated with chronic pancreatitis include mutations in the cationic trypsinogen gene *PRSS1* (*carriers bear a markedly increased lifetime risk of pancreatic cancer*), the cystic fibrosis transmembrane conductance regulator (*CFTR*, an apical membrane chloride channel), and the serine protease inhibitor, Kazal type 1 (*SPINK1*).
• **2. Pancreatic function testing**—

• Sampling of secretin stimulated pancreatic fluid from duodenal aspirates theoretically allows detection of impaired pancreatic function prior to the onset of structural abnormalities.

• The most widespread technique consists of aspiration of duodenal juice through a dual lumen (Dreiling tube) every 15 minutes for a total of 60 minutes following administration of secretin.

• A peak bicarbonate concentration less than 80mEq/L is consistent with the diagnosis of chronic pancreatitis.
3. Mixed triglyceride breath test—

Recently, the 13Cmixed triglyceride breath test (MTG) has been evaluated as a potential tool for evaluating the effect of enzyme therapy on fat digestion in chronic pancreatitis.
• Differential Diagnosis
• peptic ulcer disease
• inflammatory bowel disease
• gastric dysmotility
• Irritable bowel syndrome
• celiac disease
• Complications
• Pseudocyst
• biliary ductal or duodenal obstruction
• Pancreatic ascites or pleural effusion
• splenic vein thrombosis
• Pancreatic fistulae
• Pseudoaneurysms
• increased risk of pancreatic cancer.
• **Treatment:** lifestyle modifications
• cessation of alcohol
• consumption of smaller low-fat meals
• quitting smoking
• A. Pain

• 1. Inflammation and pancreatic pressure—

• Methods of reducing pancreatic pressure include suppression of secretion via administration of a proton pump inhibitor, pancreatic enzymes, and potentially octreotide.

• In the rare but now increasingly recognized instance where autoimmune pancreatitis is suspected, therapy with corticosteroids has also been found to be beneficial
2. Obstruction—

- If ductal obstruction is present due to stricture, stone, or pseudocyst with mass effect, invasive therapy may be necessary.

- In the case of ductal stones, endoscopic clearance, surgical therapy, or extracorporeal shock wave lithotripsy may be attempted.

- Symptomatic pseudocysts may be drained percutaneously, endoscopically, or surgically.

- Surgical options for chronic pancreatitis include lateral pancreaticojejunostomy for decompression of a dilated main duct, removal of localized disease by either a Whipple procedure or tail resection, and, finally, total pancreatectomy.
3. Modification of neural transmission—
- EUS-guided celiac plexus block
- Bilateral thorascopic splanchnicectomy
- transcranial magnetic stimulation
• B. Exocrine Insufficiency
• Pancreatic enzyme supplementation
• These enzymes should be given with each meal
• **Course & Prognosis**

• The natural history of chronic pancreatitis remains illdefined in part because of its highly variable nature.
Autoimmune Pancreatitis

• ESSENTIALS OF DIAGNOSIS
• Presentation with obstructive jaundice.
• Diffuse swelling and enlargement of the pancreas, especially the head, the latter mimicking carcinoma of the pancreas.
• Diffuse irregular narrowing of the pancreatic duct on ERCP or MRCP.
• Elevated serum IgG4 level.
• Extrapancreatic bile duct changes (ie, stricture of the common bile duct and intrahepatic ducts) mimicking primary sclerosing cholangitis.
• Resolution or marked improvement in pancreatic and extrapancreatic manifestations after corticosteroid treatment.
• **General Considerations**

• Autoimmune pancreatitis is a rare disorder of presumed autoimmune causation with characteristic chemical, histologic, and morphologic findings.

• Autoimmune pancreatitis has been described as a primary pancreatic disorder and is also associated with other disorders of presumed autoimmune etiology, including primary sclerosing cholangitis, primary biliary sclerosis, retroperitoneal fibrosis, rheumatoid arthritis, and Sjögren syndrome.
• Clinical Findings
• A. Symptoms and Signs
• Mild symptoms, usually abdominal pain, are present but attacks of acute pancreatitis are unusual.
• Three quarters of patients with autoimmune pancreatitis present with obstructive jaundice.
• Weight loss and new onset of diabetes may also occur.
• Sjögren syndrome, rheumatoid arthritis, retroperitoneal fibrosis, ulcerative colitis, and mediastinal adenopathy have all been reported in patients with autoimmune pancreatitis
• **B. Laboratory Findings**
  
• An obstructive pattern on liver tests is common
  
• Elevated serum levels of immunoglobulin G4 (IgG4) provide a marker for the disease
• C. Imaging Studies

• diffuse enlargement of pancreas
• focal enlargement
• distinct enlargement at the head of the pancreas
• enlarged pancreatic lymph nodes
• ERCP or magnetic resonance pancreatography (MRCP) reveals strictures in the bile duct
• Narrowing of the pancreatic bile duct
Autoimmune pancreatitis: diffuse narrowed pancreatic duct.
• D. Histopathologic Findings

• Characteristic findings include extensive lymphoplasmacytic infiltrates with dense fibrosis, and infiltration of polymorphic leukocytes

• Varying degrees of pancreatic parenchymal atrophy may be present

• Pancreatic ducts exhibit no calcification or plugging but are slitlike or star shaped.
• **Treatment**
• **Corticosteroid Therapy**
• Corticosteroids have shown efficacy in alleviating symptoms, decreasing the size of the pancreas, and reversing histopathologic features in patients with autoimmune pancreatitis.
• Prednisone is usually administered at an initial dose of 40 mg/day
• The median duration of treatment is 12 weeks.
• Maintenance treatment with prednisone at a dosage of 5–10 mg/day.
Tumors of the Pancreas

- ESSENTIALS OF DIAGNOSIS
- Elevated CA 19-9 in ~80% of patients.
- Helical pancreatic protocol computed tomography (PPCT) is generally the best initial modality for diagnosis and staging.
- Endoscopic ultrasound (EUS) is superior to CT in diagnosing small tumors, and portal and splenic vein invasion.
- Less than 15% of tumors are resectable at the time of diagnosis.
• General Considerations
• Pancreatic cancer is the second most common gastrointestinal malignancy, and the fourth leading cause of cancer related deaths in Western world.
• Less than 4% of patients are alive 5 years after diagnosis.
• The disease is more common in men than in women (1.3:1)
• **Pathogenesis & Risk Factors**

• Most pancreatic neoplasms arise from the three different types of the epithelial cells found in the pancreas.

• Acinar cells account for 80% of the volume of the gland but constitute 1% of exocrine tumors.

• Ductal cells constitute 10–15% of the volume but give rise to 90% of all tumors.

• Endocrine cells are 1–2% of volume and account for 1–2% of the tumors.

• Approximately 70% of ductal tumors are localized to the head of the pancreas, 5–10% to the body, and 10–15% to the tail.
• **A. Molecular Pathogenesis**

• **1. Activation of oncogenes**—Mutations of the *K-ras oncogene* are seen in 90% of tumors and are the hallmark of pancreatic adenocarcinoma.

• **2. Inactivation of tumor suppressor genes**—The genes most frequently involved are *CDKN2A* (95%), *P53* (60%), *DPC4* (50%), *BRCA2*, and *STK11*.

• **3. Defect of DNA mismatch repair gene**—Mutations of mismatch repair genes, such as *MLH1 and MSH2*, have been found in 4% of pancreatic tumors.
• **B. Hereditary Risk Factors**

• **1. Family history of pancreatic cancer**—

• Genetic predisposition is the greatest risk factor for the development of pancreatic cancer.

• About 8–10% of patients with pancreatic cancer have a first-degree relative with the disease.
2. Hereditary chronic pancreatitis—

- This autosomal dominant condition is strongly associated with pancreatic cancer.
- The risk of an affected family member developing cancer is as high as 40% by age 70 and is highest among those who smoke.
• 3. Other conditions—

• The risk of pancreatic cancer is also increased in patients with certain familial cancer syndromes such as Peutz-Jeghers syndrome, ataxia–telangiectasia, familial adenomatous polyposis, and Lynch syndrome II.
C. Environmental Risk Factors

- The best-established environmental risk factor associated with pancreatic cancer is cigarette smoking.
- The relative risk of pancreatic cancer among current smokers is 2.5.
- Diets high in fat and meat appear to be linked to the development of pancreatic cancer, while consumption of fruits and vegetables seem to have a protective effect.
- Obesity significantly increased the risk of pancreatic cancer.
• D. Nonhereditary Risk Factors

• The risk of pancreatic adenocarcinoma is about 4% in patients with nonhereditary chronic pancreatitis 20 years after disease onset.
Clinical Findings

A. Symptoms and Signs

Most patients with pancreatic tumors present late in the course of the disease.

Less than 15% of tumors are resectable at the time of diagnosis.

Patients may present with vague, low-intensity, dull abdominal discomfort or pain that radiates to the back and may be associated with weight loss, anorexia, weakness, diarrhea, and vomiting.

Tumors of the head of the pancreas produce symptoms early, and painless jaundice is seen in more than 50% of cases.

Obstruction of the bile duct by pancreatic neoplasm is accompanied by a palpable, nontender gallbladder referred to as Courvoisier sign.

Tumors of the body and tail are either “asymptomatic” or manifest with nonspecific symptoms, such as abdominal discomfort.
• Obstruction of the pancreatic duct may lead to pancreatic exocrine insufficiency in the form of steatorrhea and malabsorption.
• New-onset diabetes mellitus after the age of 50 years has been associated with the development of pancreatic cancer.
• Other uncommon manifestations of pancreatic neoplasm include acute pancreatitis in the elderly without any obvious cause, thrombophlebitis, psychiatric disturbances, pruritus due to cholestasis, signs and symptoms of gastrointestinal bleeding, and obstruction due to erosion and growth of the pancreatic neoplasm into the duodenal lumen.
B. Laboratory Findings

1. Tumor markers—CA 19-9 is a sialylated Lewis antigen that has been found to be clinically useful in both diagnosis and monitoring of the treatment response.

- Biliary tract obstruction with cholangitis due to a nonmalignant cause can result in high levels of CA 19-9.
• C. Imaging and Other Diagnostic Studies
• 1. Computed tomography (CT) scan—

• A correct diagnosis of pancreatic cancer is made in more than 90% of cases.

• In addition to detecting metastasis, based on the involvement adjacent organs, and vascular invasion, the helical CT scan can predict unresectability with more than 90% accuracy.
• 2. Endoscopic ultrasound (EUS)—
  
  • EUS has a diagnostic sensitivity similar to helical CT scan but may be superior in diagnosing small pancreatic tumors, and portal and splenic vein invasion.
  
  • EUS-guided fine needle aspiration (EUS–FNA) has a diagnostic sensitivity of about 85–90%.
3. Endoscopic retrograde cholangiopancreatography (ERCP)—

- Pancreatic tumors appear as strictures of the pancreatic duct or the bile duct on ERCP.
- This stricturing of both the bile duct and the pancreatic duct is referred to as the “double duct sign.”
- Advances in pancreatic imaging such as helical CT have made ERCP unnecessary as an initial test.
• **4. Magnetic resonance imaging (MRI)—**
  • Accuracy of MRI appears comparable to the dualphase helical CT scan.
  • MRCP is as sensitive as ERCP in the diagnosis of pancreatic tumors.

• **5. Positron emission tomography (PET)—**
  • PET scanning is not routinely used in diagnosis of pancreatic cancers.
  • It can be useful in diagnosing tumor reoccurrence after pancreatic resection.
6. Laparoscopy—

Studies have shown that standard preoperative imaging modalities, including CT scan in 15–40% cases, are unable to detect small peritoneal and liver metastasis.

In select patients, staging laparoscopy along with peritoneal cytologic examination can detect unsuspected metastasis and prevent unwarranted surgery.
• **Differential Diagnosis**

• Pancreatic adenocarcinoma must be differentiated from the following conditions of the pancreas that can mimic its symptoms:
  • autoimmune pancreatitis
  • chronic pancreatitis
  • pancreatic lymphoma
  • neuroendocrine tumors of the pancreas
  • cystic lesions of the pancreas.
• **Treatment**

• Patients with pancreatic cancer can be subdivided into three categories based on the extent of tumor spread:
  
  • (1) tumor confined to the pancreas (resectable disease at diagnosis), representing approximately 15–20% of patients;
  
  • (2) locally advanced disease (unresectable), 40%
  
  • (3) metastatic disease, 40%.
A. Resectable Disease

Surgical resection is the only curative treatment for pancreatic cancer.

The most common surgery is the Whipple pancreaticoduodenectomy.

Even after surgical resection with negative margins, patients have a 5-year survival rate of only 10–25%.

Surgical resection of tumors located on the body and the tail consists of distal subtotal pancreatectomy along with splenectomy.
• **B. Locally Advanced Disease**

• The combination of chemotherapy and radiation is associated with modest improvements in median survival but may produce significant side effects. 5-Fluorouracil, gemcitabine, and paclitaxel are some of the common chemotherapeutic agents used with radiotherapy.
Symptom palliation is an essential component of care for patients with locally advanced disease.

1. **Obstructive jaundice**—Endoscopic stent placement is the most effective approach to relieve malignant bile duct obstruction.

2. **Gastric outlet obstruction**—Obstruction of the gastric outlet is caused by extension of the pancreatic cancer and can be treated by gastrojejunostomy or by endoscopically placed expanding metal stents.

3. **Pain**—Narcotic medications are usually required to control pain associated with pancreatic cancers. Celiac plexus block (chemical neurolysis) can be achieved though a percutaneous approach, or the block can be performed using EUS. Radiation can be used to control intractable pain.
• C. Metastatic Disease

• Chemotherapy is used for palliation and results in slight survival benefits.

• Gemcitabine-based combination therapy is the treatment of choice and associated with better pain control, decreased weight loss, and improvement in performance status.