ACUTE PANCREATITIS

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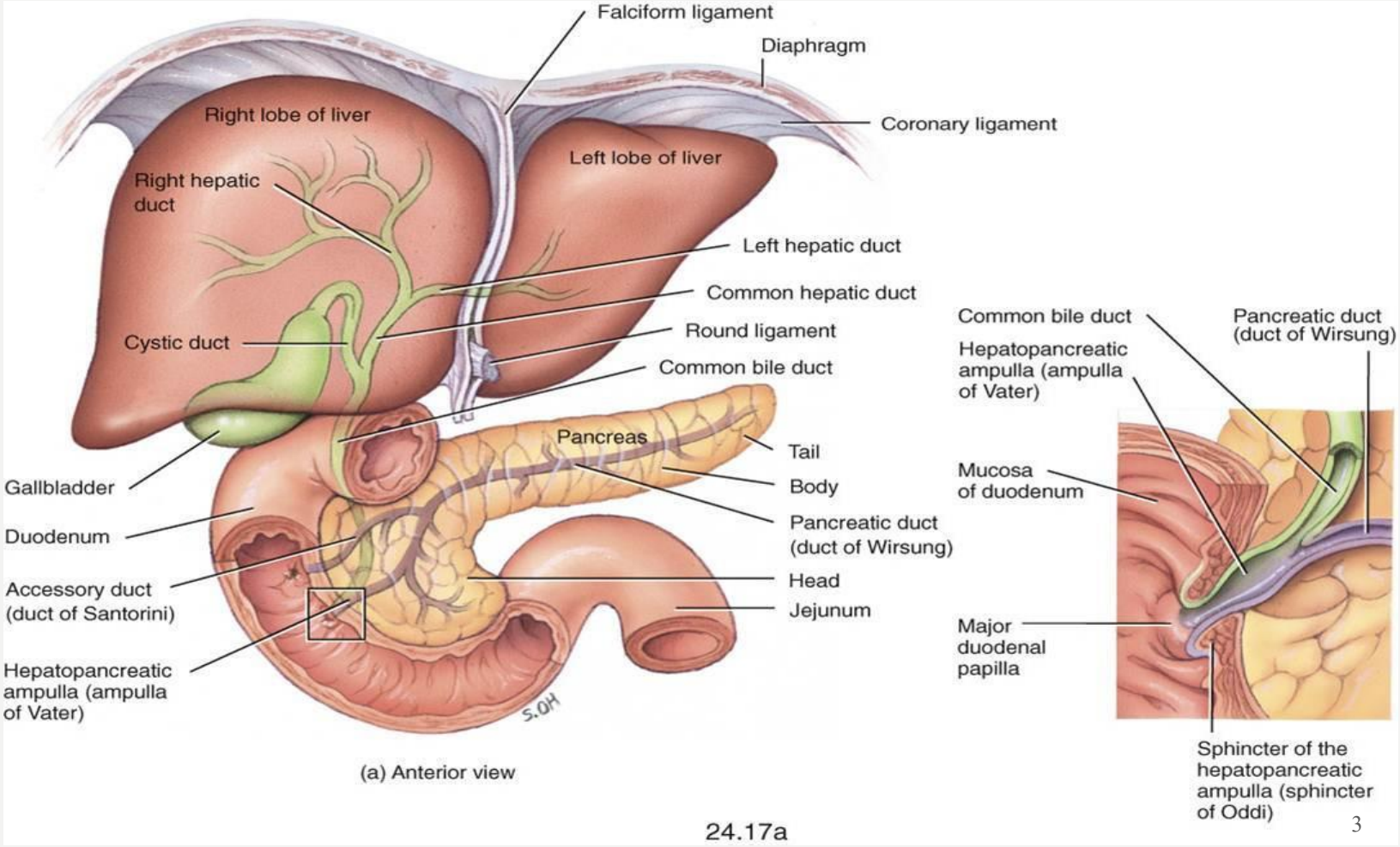
1. Definition
2. Etiology
3. Pathophysiology
4. History / Symptoms
5. Physical Examination / Signs
6. Investigation
7. Differential Diagnosis
8. Management
9. Complications
10. Clinical Scenarios

ACUTE PANCREATITIS: DEFINITION

- **Autodigestion of the pancreas by its escaped enzymes**
- **Inflammation of the pancreas by enzyme-mediated autodigestion**



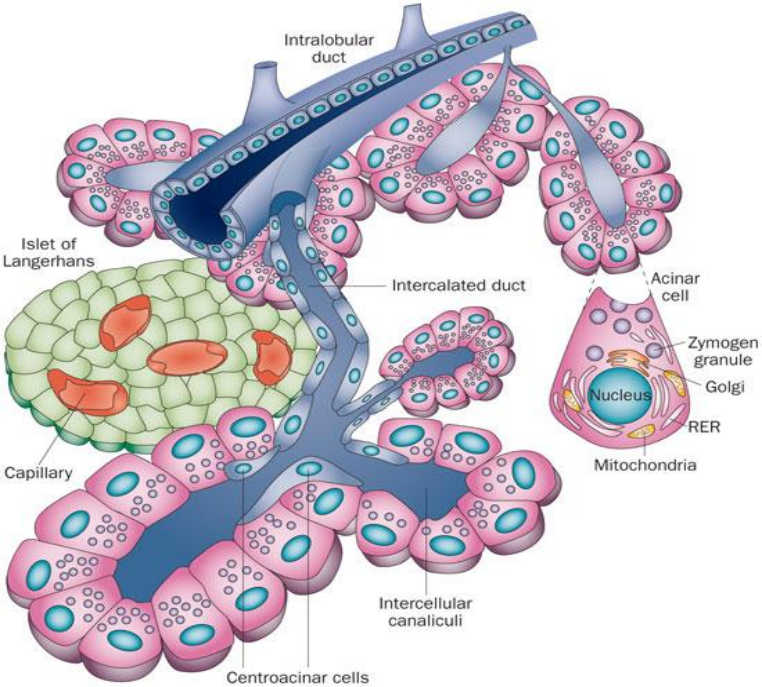
	Etiological Factor	Discussion
1	**Gallstones / Biliary tract disease**	It is one of the most common causes of acute pancreatitis accounting for approximately 40% of cases. Gallstone passing into the bile duct and temporarily lodging at the Sphincter of Oddi causes acinar cell injury secondary to increase in pancreatic duct pressure. **Idiopathic Pancreatitis** are mainly due to microlithiasis.
2	**Alcohol**	It accounts for approximately 35% of cases. Ethanol **increases the permeability of ductules**, allowing enzymes to reach the parenchyma and causing pancreatic damage. It also causes the formation of **protein plugs** that block pancreatic outflow.
3	**ERCP**	It is the third most common cause of acute pancreatitis.
4	**Trauma**	Pancreatic injury occurs more often after penetrating injury to the abdomen. Blunt injury to the abdomen or back may crush the gland across the spine, leading to a ductal injury. Operative trauma.
5	**Drugs**	Common drugs associated with acute pancreatitis: **Azathioprine**, **Sulfonamides**, **Tetracycline**, **Valproic acid**, **Methyldopa**, **Estrogens**, **Furosemide**, **Thiazide diuretics** , **6-Mercaptopurine**, **5-ASA**, **Corticosteroids**, **Octreotide**, **H_2 antagonist**, L-asparaginase, Ethacrynic acid, Phenformin, Procainamide, Clonidine, Dideoxyinosine, and Pentamidine
6	**Infections**	**Viral causes**: **mumps**, **coxsackie**, cytomegalovirus, hepatitis virus, Epstein-Barr virus, echovirus, varicella-zoster virus, measles, and rubella. **Bacterial causes** (Rare): Mycoplasma pneumoniae, Salmonella, Campylobacter, and Mycobacterium tuberculosis. **Ascaris**: is a recognized cause of pancreatitis resulting from the migration of worms in and out of the duodenal papillae
7	**Developmental abnormalities of pancreas**	Pancreatic divisum & annular pancreas
8	**Duodenal obstruction & Tumors**	Obstruction of pancreatic ductal system due to tumors. Ampullary stenosis, Sphincter of Oddi dysfunction
9	**Toxins**	**Scorpion venom**, Organophosphate insecticides, and snake bites
10	**Metabolic**	**Hypercalcemia**, **Hypertriglyceridemia**, Hyperthyroidism
11	**Surgical procedures / Ischemia**	Abdominal surgeries or CABG may cause pancreatitis due to ischemia. Hypotension, Vasculitis, Atheroembolism
12	**Hereditary / Familial Pancreatitis**	is a genetic condition characterized by recurrent episodes of pancreatitis.
13	**Autoimmune**	very rare cause

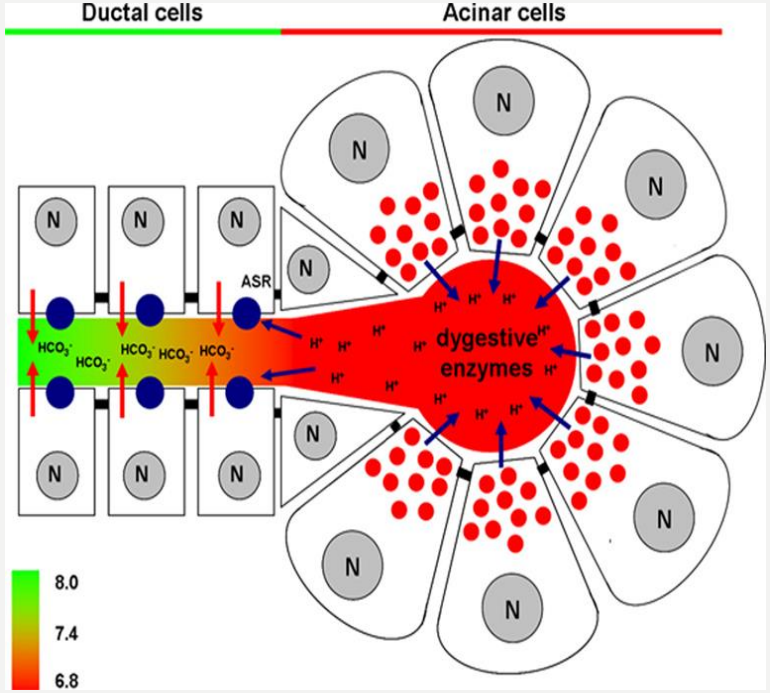
ETIOLOGY- I GET SMASHED

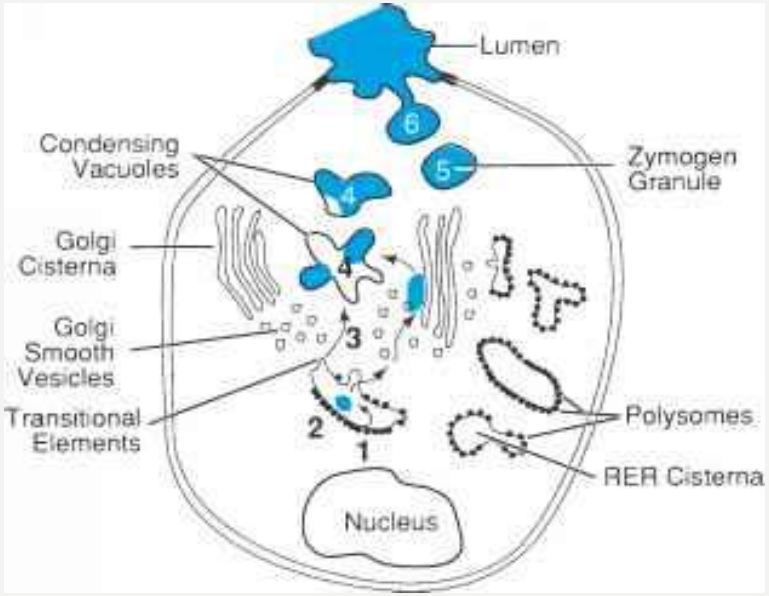
- Idiopathic
- Gallstones
- Ethanol
- Trauma
- Steroids
- Mumps
- Autoimmune
- Scorpion venom
- Hypercalcemia, Hyperlipidemia
- ERCP
- Drugs

PANCREATIC DIVISUM

- Is a congenital anomaly in the anatomy of the ducts of the pancreas in which a single pancreatic duct is not formed, but rather remains as two distinct dorsal and ventral ducts.
- Causes: The human embryo begins life with two ducts in the pancreas, the ventral duct and the dorsal duct. Normally, the two ducts will fuse together to form one main pancreatic duct; this occurs in more than 90% of embryos. In approximately 10% of embryos the ventral and dorsal ducts fail to fuse together, resulting in pancreas divisum.
- In utero, the majority of the pancreas is drained by the dorsal duct which opens up into the minor duodenal papilla. The ventral duct drains the minority of the pancreas and opens into the major duodenal papilla. In adults however, this situation is reversed whereby 70% of the pancreas is drained by the ventral duct. Therefore in pancreas divisum, where fusion of the ducts does not occur, the major drainage of the pancreas is done by the dorsal duct which opens up into the minor papilla.
- Most individuals with pancreas divisum remain without symptoms or complications. A minority of people with pancreatic divisum may develop episodes of abdominal pain, nausea or vomiting due to acute or chronic pancreatitis.
- The presence of pancreas divisum is usually identified with cross sectional diagnostic imaging, such as MRI or CT imaging. In some cases, ERCP is performed, revealing the diagnosis of pancreas divisum. If no symptoms or complications are present, then treatment is not necessary. However, if there is recurrent pancreatitis, then a sphincterotomy of the minor papilla may be indicated.


Intralobular duct
Islet of Langerhans
Intercalated duct
Acinar cell
Zymogen granule
Golgi
Nucleus
RER
Mitochondria
Capillary
Intercellular canaliculi
Centroacinar cells


Ductal cells
Acinar cells
N
ASR
HCO_3^-
H^+
dygestive enzymes
8.0
7.4
6.8

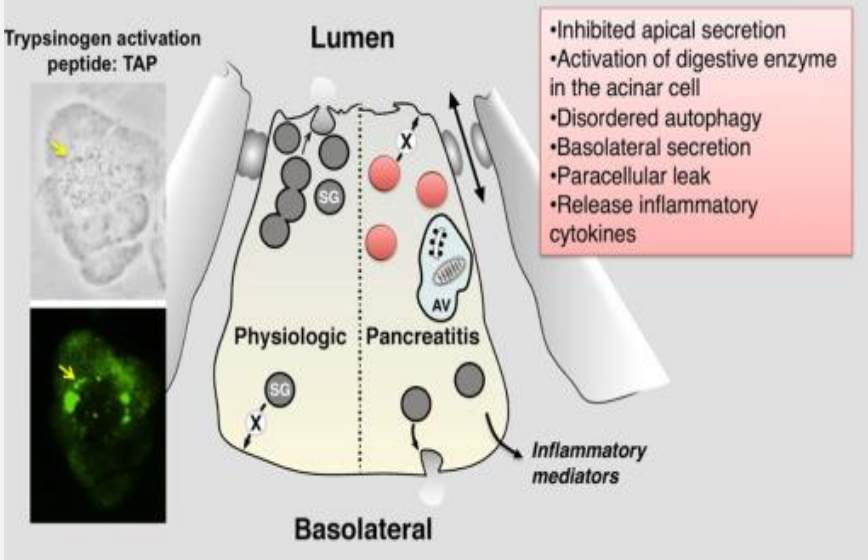

Lumen
Condensing Vacuoles
Zymogen Granule
Golgi Cisterna
Golgi Smooth Vesicles
Transitional Elements
Polysomes
RER Cisterna
Nucleus
1
2
3
4
5
6

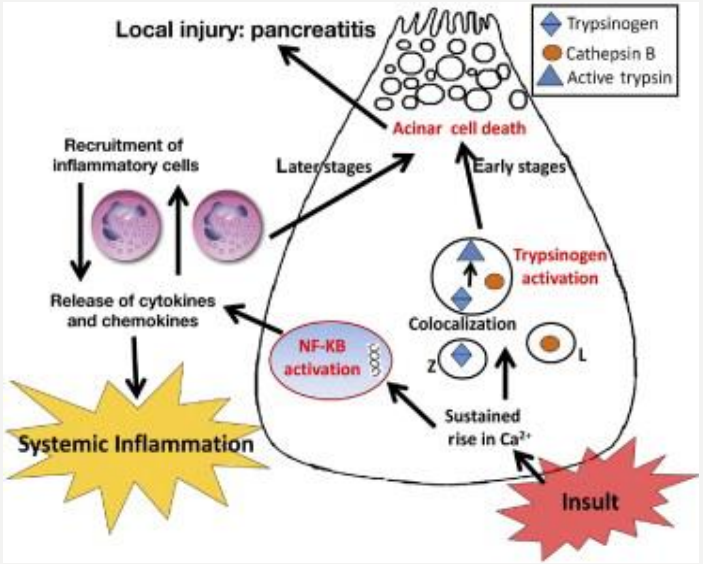
PATHOPHYSIOGY

- Acute pancreatitis occurs when factors involved in maintaining cellular homeostasis are out of balance. The initiating event may be anything that **injures the acinar cell** and **impairs the secretion of zymogen granules**; examples include alcohol use, gallstones, and certain drugs.
- Both extracellular factors (e.g., neural and vascular response) and intracellular factors (e.g., intracellular digestive enzyme activation, increased calcium signaling, and heat shock protein activation) play a role.
- Once a cellular injury pattern has been initiated:
  - Lysosomal and zymogen granule compartments fuse, enabling **activation of trypsinogen to trypsin**
  - Intracellular trypsin triggers the entire zymogen activation cascade
  - Secretory vesicles are extruded across the basolateral membrane into the interstitium, where molecular fragments act as chemoattractants for inflammatory cells.
- The **mediators of inflammation** (TNF alpha, IL6, IL 8) cause an increased pancreatic vascular permeability, leading to hemorrhage, edema, and eventually pancreatic necrosis.
- As the mediators are excreted into the circulation, **systemic complications** can arise, such as bacteremia due to gut flora translocation, acute respiratory distress syndrome (ARDS), pleural effusions, GI hemorrhage, and renal failure.
- The **systemic inflammatory response syndrome** (SIRS) can also develop, leading to the development of systemic shock. Eventually, the mediators of inflammation can become so overwhelming to the body that hemodynamic instability and death ensue.
- In acute pancreatitis, parenchymal edema and peripancreatic fat necrosis occur first; this is known as **acute edematous pancreatitis**. When necrosis involves the parenchyma, accompanied by hemorrhage and dysfunction of the gland, the inflammation evolves into **hemorrhagic or necrotizing pancreatitis**.
- **Pseudocysts** and **pancreatic abscesses** can result from necrotizing pancreatitis because enzymes can be walled off by granulation tissue (pseudocyst formation) or via bacterial seeding of pancreatic or peripancreatic tissue (pancreatic abscess formation).

PATHOPHYSIOGY

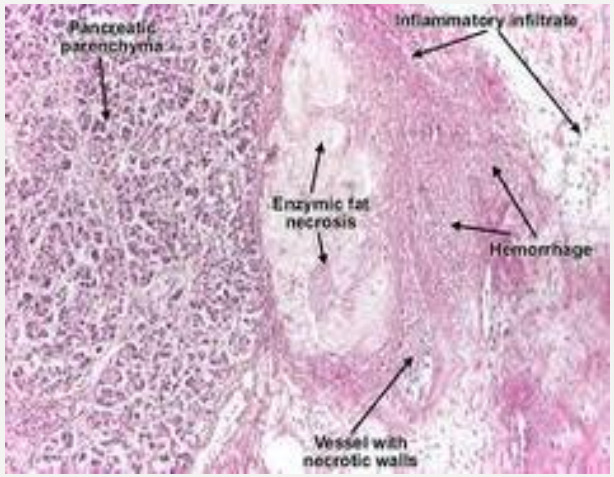
- **Atlanta classification**: pancreatitis is divided into:
  1. Acute interstitial edematous pancreatitis (IEP) and
  2. Necrotizing pancreatitis (NP), based on the presence of pancreatic tissue necrosis.
- The fluid collections associated with these two "types" of pancreatitis are also differentiated:
  1. Early (4 weeks) fluid collections in IEP are called pancreatic pseudocysts, and
  2. In NP, they are called walled-off pancreatic necrosis (WOPN).



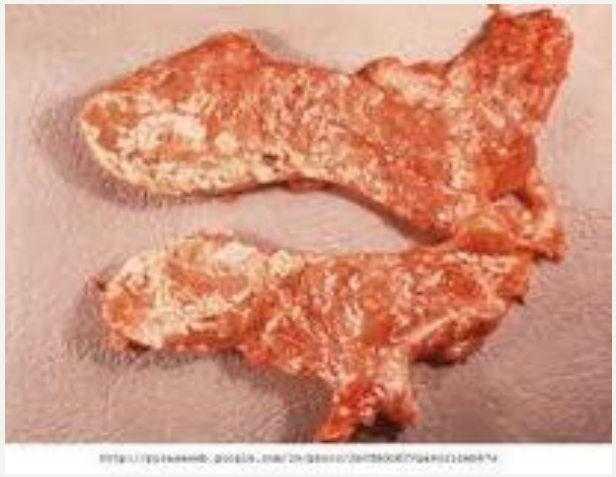


PATHOPHYSIOGY

- Acute pancreatitis represents a broad spectrum of disease. Although the disease course may smolder, typically an initial inciting event results in organ injury, which sets into play the evolving clinical course.
- The early phase of disease is marked by the inflammatory mediators from damaged pancreatic tissue, resulting in variable degrees of systemic inflammatory response.
- The later phase is determined by the morphology of organ injury, specifically with regard to tissue ischemia and necrosis. The outcome of this later phase is often impacted by local or systemic infection.
- Peripancreatic fluid collections can occur in both the early and the late phases of disease. They presumably occur from injury to or ischemia of the main pancreatic duct or a side branch duct, although some, particularly early on, may be the result of third-space edema fluid.
- Peripancreatic fluid collections represent a heterogeneous entity. Definition of peripancreatic fluid collections is essential in determination of clinical decision making



Acute Hemorrhagic Pancreatitis



Enzymatic Fat Necrosis

SURGICAL PATHOLOGY

1. Edema
2. Exudation
3. Hemorrhage
4. Suppuration / Pancreatic phlegmon & Abscess
5. Necrosis
6. Fat necrosis (combination of liberated fatty acids from hydrolized fat with calcium)
7. Fluid loss → Hypovolemia
8. Pseudocyst

HISTORY / SYMPTOMS

1. **Abdominal Pain**:
   - A. Cardinal Symptom of acute pancreatitis.
   - B. Typically dull and boring.
   - C. Usually intense, continuous (increase in Crescendo fashion), and sudden in onset.
   - D. Localized to upper abdomen, usually in the epigastric region, but it may be perceived more on the left or right side, depending on which portion of the pancreas is involved
   - E. Radiates directly through the abdomen to the back in 50% of cases
   - F. Is worse when the patient is supine
   - G. Food usually worsens the pain and bending forwards ameliorates the pain
   - H. bizarre position of the patient / **Hunchback position**

2. **Anorexia, Nausea and Vomiting**. Nausea and nonfeculent vomiting are present in 75-90% of patients
3. There can be **history** of recent operative or other invasive procedures (e.g. ERCP) or family history of hypertriglyceridemia. Patients frequently have a history of previous biliary colic and binge alcohol consumption.

PHYSICAL EXAMINATION / SIGNS

General	Local
Shock (↓BP, ↑PR). ↓Urine output. Patient is pale, diaphoretic (sweating heavily), and listless	Peritonitis: Tenderness + guarding +distension
Fever (76%)	Gastric, jejunal and splenic flexure colonic paralytic ileus ↓ bowel sounds
Jaundice (28%)	Abdominal mass (Pseudocyst or abscess)
Left pleural effusion: basilar rales (crackles), especially in the left lung	Skin Signs: (1) Grey-Turner's sign (2) Cullen's sign (3) Fox's sign (4) Walzel's sign
Acute pulmonary failure, ARDS Dyspnea, tachypnea	
Subcutaneous necrosis: **Erythematous skin nodules**	
In severe cases, hemodynamic instability is evident (10%) and hematemesis or melena sometimes develops (5%);	
Cerebral abnormalities/ hypoxia	
Occasionally, in the extremities, muscular spasm may be noted secondary to hypocalcemia.	

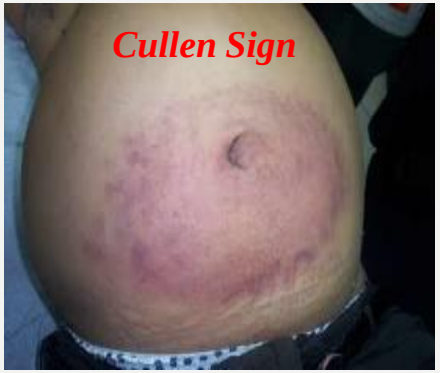
PHYSICAL EXAMINATION

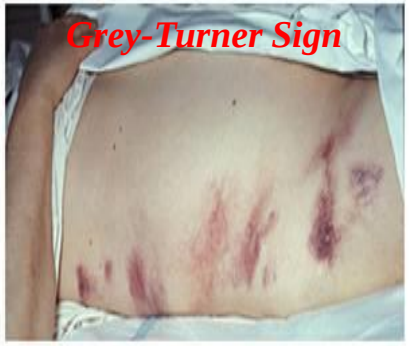
A few uncommon physical findings are associated with severe necrotizing pancreatitis:

•The ***Cullen Sign*** is a bluish discoloration around the umbilicus resulting from hemoperitoneum.

•The ***Grey-Turner Sign*** is a reddish-brown discoloration along the flanks resulting from retroperitoneal blood dissecting along tissue planes; more commonly, patients may have a ruddy erythema in the flanks secondary to extravasated pancreatic exudate.

•**Erythematous skin nodules** may result from focal subcutaneous fat necrosis; these are usually not more than 1 cm in size and are typically located on extensor skin surfaces; in addition, polyarthritis is occasionally seen.

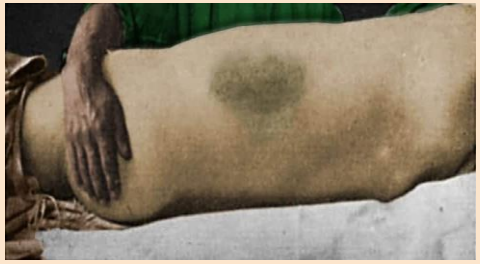
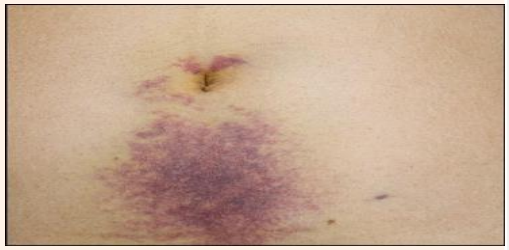
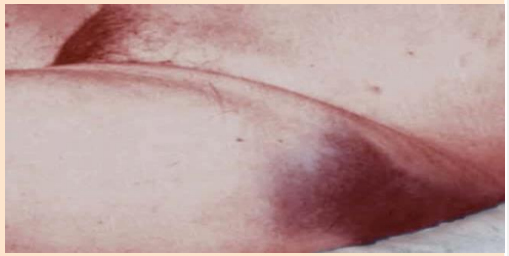




Causes	References
Acute Pancreatitis	Bosmann et al[9]
Bilateral acute salpingitis in the presence of intrauterine pregnancy	Orient and Sapira[10]
Cirrhosis with portal hypertension	Orient and Sapira[10]
Hemorrhaging ascites from hepatic tumor	Mabin and Gelfand[11], Dalal and Mace[12]
Hepatocellular carcinoma	Orient and Sapira[10]
Hypothyroid myopathy	Orient and Sapira[10]
Ischemic and gangrenous bowel	Kelley[13]
Ovarian cyst hemorrhage	Orient and Sapira[10]
Percutaneous liver biopsy	Capron et al[14]
Perforated duodenal ulcer	Evans[15]
Retroperitoneal necrotizing fasciitis	Pryor et al[16]
Ruptured abdominal aortic aneurysm	Armour et al[17]
Renal sarcoma metastatic to the peritoneum	Orient and Sapira[10]
Rectus sheath hematoma	Guthrie and Stanley[18]
Splenic rupture	Chung et al[19]
Strangulation of ileum with hemorrhage	Orient and Sapira[10]
Strangulated umbilical hernia	Orient and Sapira[10]

Causes of Cullen's Sign

SKIN SIGNS IN ACUTE PANCREATITIS

Sign	Description	Photo
Grey-Turner's sign	Is produced by spread from the anterior pararenal space between the two leaves of the posterior renal fascia and subsequently to the lateral edge of the quadratus lumborum muscle. Communication may be established to the posterior pararenal space and to the structures of the flank wall. The lumbar triangle, a site of anatomical weakness on the flank wall, may serve as a structural predisposing factor	
Cullen's sign	Can be seen following the tracking of liberated pancreatic enzymes to the anterior abdominal wall from the inflamed gastrohepatic ligament and across the falciform ligament. Another more direct pathway may be extension from inflammatory changes of the small mesentery or greater omentum to the round ligament, and from there to properitoneal fat deep to the umbilicus.	
Fox's sign	Is believed to be produced by tracking of the fluid extraperitoneally along the fascia of psoas and iliacus beneath the inguinal ligament until it becomes subcutaneous in the upper thigh.	
Walzel's sign	Livedo reticularis on the abdomen and / or chest and thighs, is believed to be because of trypsin-induced damage of the subcutaneous venous network.	

These skin signs have been considered rare and thought to indicate an unfavorable prognosis.

INVESTIGATION

General	Laboratory Tests	Radiology
CBC	S. amylase	Chest X-ray
S. Electrolytes + BUN/EUC	S. amylase isoenzymes (P+S types)	Abdominal X-ray
Lft	Urinary amylase	US
S. Ca^{+2}	Amylase-creatinine clearance ratio	CT scan
Blood glucose	S. lipase	MRI
C-reactive protein	S. methemalbumin	ERCP
S. Triglyceride + cholesterol	Peritoneal fluid analysis	
Arterial blood gas		

INTRA-ABDOMINAL DISORDERS ASSOCIATED WITH HYPERAMYLASEMIA

Pancreatic disorders	Non pancreatic disorders
Acute pancreatitis	Ruptured aortic aneurysm
Chronic pancreatitis	Ruptured ectopic pregnancy
Trauma	Intestinal obstruction
Carcinoma	Acute appendicitis
Pseudocyst pancreatic ascites	Perforated peptic ulcer
Abscess	Biliary tract disease
	Mesenteric infarction
	Afferent loop syndrome

EXTRA-ABDOMINAL DISORDERS ASSOCIATED WITH HYPERAMYLASEMIA

Salivary gland disorders + Impaired amylase excretion	+Miscellaneous
Mumps	Pneumonia
Parotitis	Pancreatic pleural effusion
Trauma	Mediastinal pseudocyst
Calculi	Cerebral trauma
Irradiation sialadenitis	Severe burns
Renal failure	Diabetic ketoacidosis
Macroamylasemia	Pregnancy
	Drugs
	bisalbuminemia

INVESTIGATION-LABORATORY TESTS

In addition to confirming the diagnosis, laboratory tests are helpful in defining an etiology and looking for complications.

•Serum ***amylase*** and ***lipase*** levels are typically elevated in persons with acute pancreatitis.

•**Amylase** or **lipase** levels at least 3 times above the reference range are generally considered diagnostic of acute pancreatitis.

•Serum **amylase** is however, not specific for pancreatitis. The serum half-life of amylase is short, and elevations generally return to reference ranges within a few days.

•**Lipase** has a slightly longer half-life and abnormalities may support the diagnosis if a delay occurs between the pain episode and the time the patient seeks medical attention. Elevated lipase levels are more specific to the pancreas than elevated amylase levels. Lipase levels remain high for 12 days. In patients with chronic pancreatitis (usually caused by alcohol abuse), lipase levels may be elevated in the presence of a normal serum amylase level.

•Elevated ***alkaline phosphatase***, ***total bilirubin***, ***aspartate aminotransferase (AST)***, and ***alanine aminotransferase (ALT)*** provide evidence of gallstone pancreatitis.

•***C-reactive protein (CRP)*** is an acute-phase reactant that is not specific for pancreatitis. A value can be obtained 24-48 hours after presentation to provide some indication of prognosis. Higher levels have been shown to correlate with a propensity toward organ failure.

•Measurement of ***blood urea nitrogen (BUN)***, ***creatine, and electrolytes*** should be done as a great disturbance in the electrolyte balance is usually found, secondary to third space loss of fluids.

•Blood ***glucose*** level may be elevated from B-cell injury in the pancreas.

•Measurement of ***calcium***, ***cholesterol, and triglyceride*** levels should be done to search for an etiology of pancreatitis (e.g., hypercalcemia or hyperlipidemia) or complications of pancreatitis (e.g., hypocalcemia resulting from saponification of fats in the retroperitoneum).

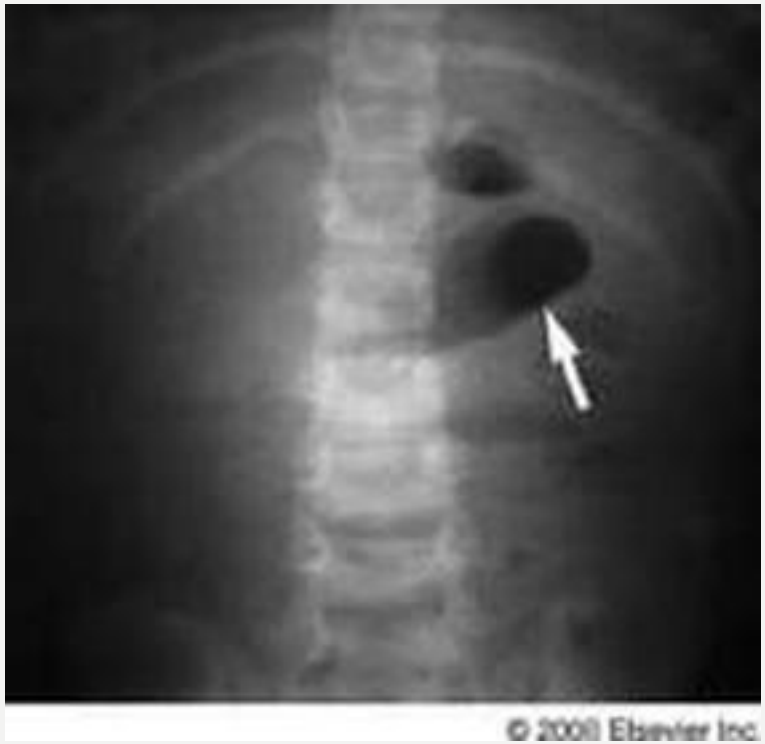
INVESTIGATION - IMAGING

- ***Abdominal & chest X ray***: not useful in diagnosing acute pancreatitis. They may be used to exclude perforation peritonitis. In some cases, the inflammatory process may damage peripancreatic structures, resulting in a sentinel loop sign or ileus. The presence of calcifications within or around the pancreas may indicate chronic pancreatitis. **CXR** may show left pleural effusion or atelectasis.
- ***Abdominal Ultrasound***: is the most useful initial test in determining the etiology of pancreatitis and is the technique of choice for detecting gallstones and ductal dilation. In the setting of acute pancreatitis, sensitivity is reduced to 70-80%.
- ***Abdominal CT scan***: is generally not indicated for mild pancreatitis unless diagnosis in uncertain. It is always indicated in patients with severe acute pancreatitis and is the imaging study of choice for assessing complications. Scans are seldom needed within the first 72 hours after symptom onset unless the diagnosis is uncertain, because inflammatory changes are often not radiographically present until this time. Abdominal CT scans also provide prognostic information based on the following grading scale developed by *Balthazar et al*.

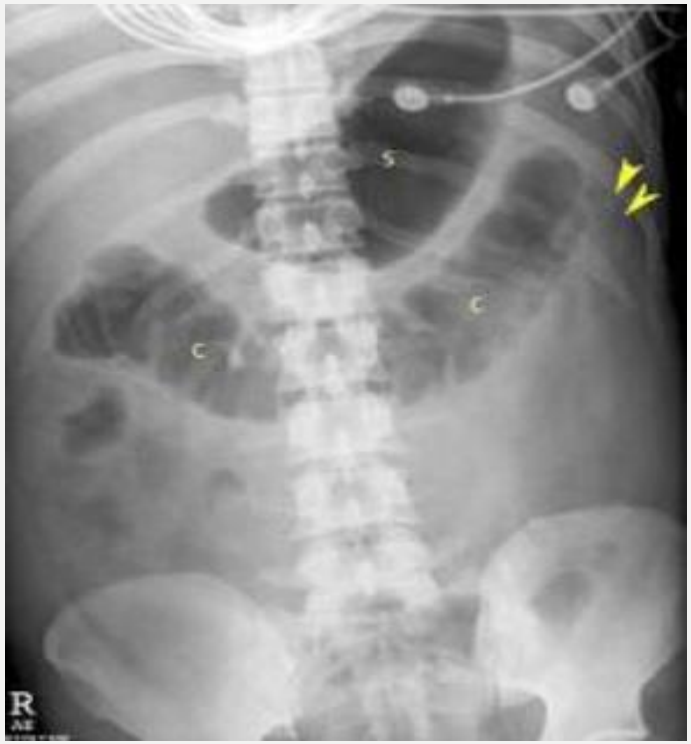
Grade A	Normal pancreas
Grade B	Focal or diffuse gland enlargement
Grade C	Intrinsic gland abnormality recognized by haziness on the scan
Grade D	Single ill-defined collection or phlegmon
Grade E	Two or more ill-defined collections or the presence of gas in or nearby the pancreas

- **MRCP**
- **ERCP**: (Diagnostic & therapeutic), used to evaluate the biliary and pancreatic ductal system and is indicated in a subset of patients with acute pancreatitis. It should be performed only in the following situations:
    1. The patient has severe acute pancreatitis that is believed, and is seen on other radiographic studies, to be secondary to choledocholithiasis
    2. The patient has biliary pancreatitis and is experiencing worsening jaundice and clinical deterioration despite maximal supportive therapy.
- When combined with sphincterotomy and stone extraction, ERCP may reduce the length of hospital stay, the complication rate, and, possibly, mortality.

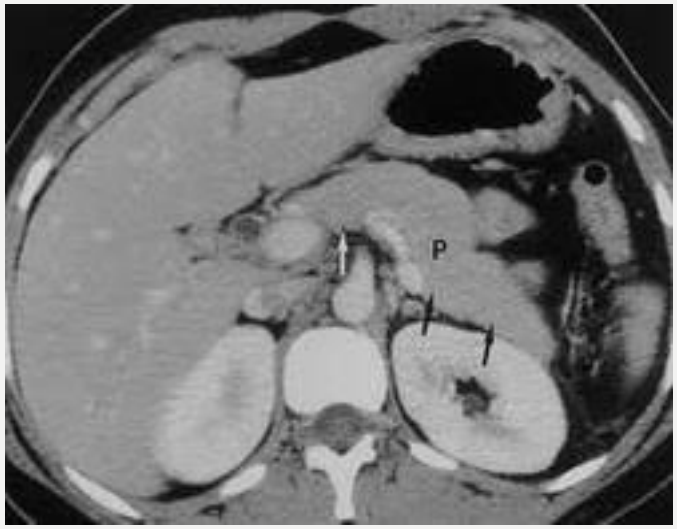
Abdominal X ray findings in Acute Pancreatitis



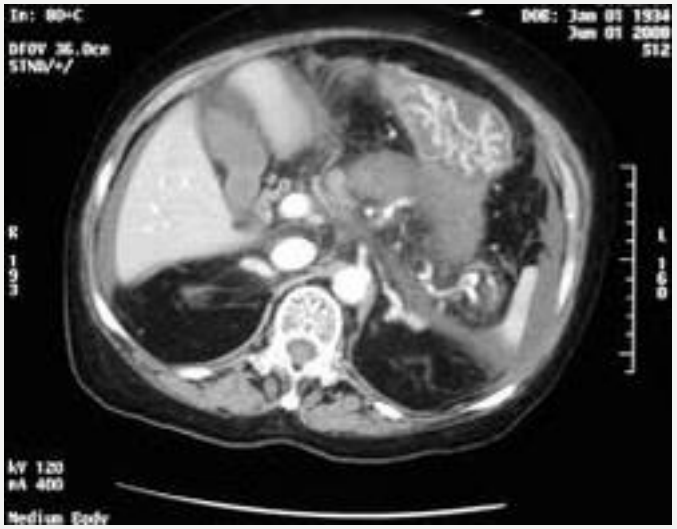
Sentinel Loop Sign



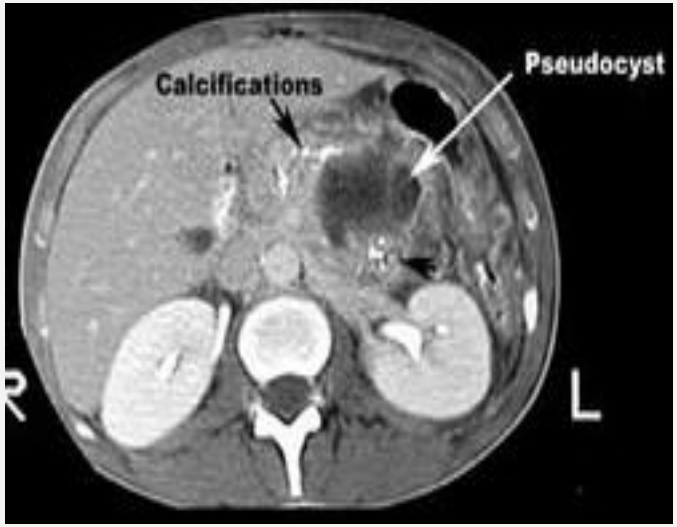
Colon Cut off sign



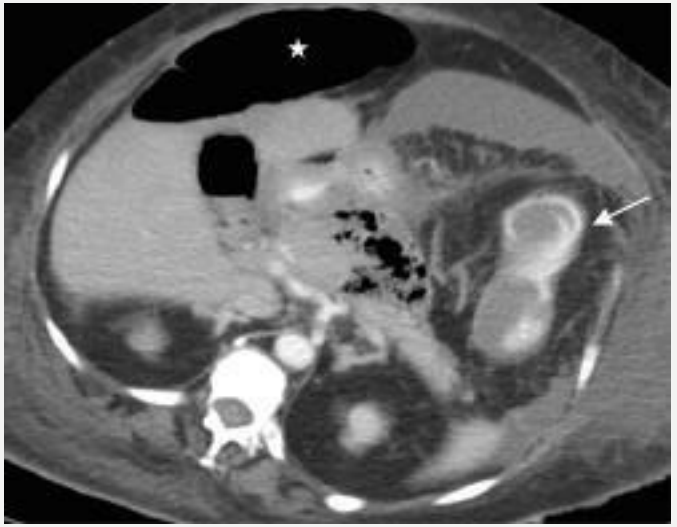
Gallstone induced pancreatitis



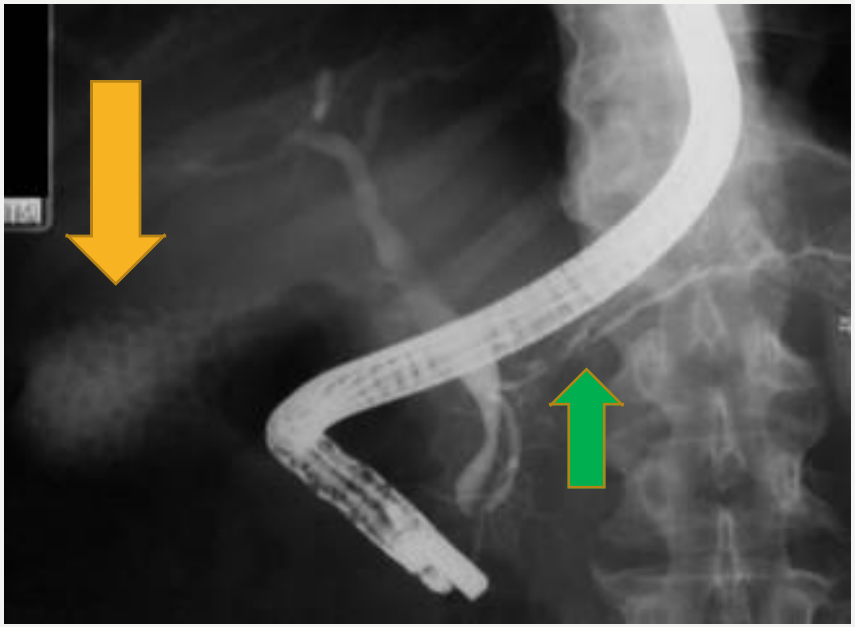
Early Necrotizing Pancreatitis



Pancreatic Pseudocyst



Severe Acute pancreatitis and infected necrosis of body



ERCP: Acute Gallstone Induced Pancreatitis

Cholangiogram shows no stones in common bile duct and multiple small stones in gallbladder. Pancreatogram shows narrowing of pancreatic duct in area of genu, resulting from extrinsic compression of ductal system by inflammatory changes in pancreas.

DIFFERENTIAL DIAGNOSIS

Recognizing patients with severe acute pancreatitis as soon as possible is critical for achieving optimal outcomes. It can be difficult occasionally to differentiate pancreatitis from the following conditions but repeated examinations and investigations are helpful.

1. Perforated peptic ulcer / Perforation Peritonitis
2. Gastritis
3. Acute Cholecystitis
4. Mesenteric Ischemia
5. Myocardial Infarction

MORTALITY AND PROGNOSIS

- **Mortality rate is 6-20%**
- **Causes of death:**
  1. Hypovolemic shock
  2. Electrolyte disturbances / hypocalcemia
  3. Toxemia
  4. Renal failure
  5. Respiratory failure (collapse, consolidation, effusion)

RANSON'S CRITERIA

At admission	At 48 hours
Age > 55	Hematocrit fall > 10%
WBC > 16000 cells/mm3	BUN rise 5mg /dl (BUN increase ≥ 1.8 mmol/ L)
Glucose > 200 mg/dl (10 mmol/L)	Ca^{+2} < 8 mg/dl (2 mmol/L)
Serum AST > 250 IU/L	PO2 < 60 mm Hg
Serum LDH > 350 IU/L	Base deficit > 4 mEq/L
	Fluid sequestration > 6 L

Ranson's Score ≥ 3 indicates severe pancreatitis

- <2 → no mortality
- 3-4 → 15% mortality
- 5-6 → 50% mortality
- ≥ 7 → test the limits of modern medicine

MODIFIED GLASGOW CRITERIA

- Glasgow prognostic score: (Note PANCREAS Acronym)
  1. **P**aO2 < 8kPa (60mmhg)
  2. **A**ge > 55 years
  3. **N**eutrophils: WBC >15 x109/l
  4. **C**alcium < 2mmol/l
  5. **R**enal function: Urea > 16 mmol/l
  6. **E**nzymes: AST/ALT > 200 IU/L or LDH > 600 iu/L
  7. **A**lbumin < 32 g/l
  8. **S**ugar: Glucose >10mmol/L

- Score ≥ 3 indicates severe pancreatitis

APACHE II

- The APACHE score has the advantage of being able to assess the patient at any point during the illness; however, it is very cumbersome for routine clinical use.
- Attempts have been made to make this evaluation user friendly (e.g., with APACHE II, the Simplified Acute Physiology Score [SAPS], and the Imrie score), but it remains cumbersome.
- The sensitivity is 77%, and the specificity is 84%.

TREATMENT (WHEN DIAGNOSIS CERTAIN)

Rest the patient (Relief pain)	Pethidine 100mg/4hr + antispasmodic Or low dose ketamine or fentanyl
Rest the pancreas	NPO, IV fluid (Ringer lactate), electrolytes replacement + enteral or parenteral feeding
Rest the bowel	NG tube
Resuscitation	Replacement therapy, urinary output monitoring
Resist enzymatic activity	Protease inhibitors, Trasylol , H_2 antagonist, glucagon ?
Resist infection	Antibiotics → only if there is infection (infected pseudocyst or infected necrosis). Carbapenems (e.g. Imipenem)
Repeated examination	General features, abdominal signs, fluid balance. Hourly BP, PR & Urine output
Repeated serum estimations	Daily CBC, amylase, EUC, Ca^{+2}, fibrinogen, methemalbumin, Mg^{+2}
Respiratory support	O_2 , assisted respiration
Relate to underlying causes	E.g. ERCP stone extraction + sphincterotomy + CCY Treatment of hyperglyceridemia (insulin drip, fibrate, apheresis)

MANAGEMENT

Fluid resuscitation:

•Patients with acute pancreatitis lose a large amount of fluids to third space into the retroperitoneum and intra-abdominal area. Accordingly, they require prompt IV hydration within the first 24 hours. Especially in the early phase of the illness, aggressive fluid resuscitation is critically important.

Nutritional support:

•In patients with mild uncomplicated pancreatitis, no benefit is observed from nutritional support, and the energy (caloric) intake received with IV dextrose 5% in water (D5W) suffices; oral feedings should be initiated once the patient's pain and anorexia resolve.

•In patients with moderate-to-severe pancreatitis, begin nutritional support early in the course of management, as soon as stabilization of fluid and hemodynamic parameters permits; optimally, nasojejunal feedings with a low-fat formulation should be initiated at admission

•Total parenteral nutrition (TPN) may be required when patients cannot meet their caloric needs with enteral nutrition or when adequate jejunal access cannot be maintained; the TPN solution should include fat emulsions in amounts sufficient to prevent essential fatty acid deficiency.

•If surgery is required for diagnosis or complications of the disease, place a feeding jejunostomy at the time of the operation; use a low-fat formula

•Begin oral feedings once abdominal pain has resolved and the patient regains appetite; the diet should be low in fat and protein.

MANAGEMENT

- **Analgesics**:
- **Antibiotics**: usually drugs of the imipenem class, should be used in any case of pancreatitis complicated by infected pancreatic necrosis. However, they should not be given routinely for fever, especially early in the disease course, because this symptom is almost universally secondary to the inflammatory response and typically does not reflect an infectious process.
- For patients with gallstone pancreatitis, **cholecystectomy** should be performed during the same admission
- Patients with severe acute pancreatitis require intensive care. Within hours to days, a number of complications (e.g., shock, pulmonary failure, renal failure, GI bleeding, or multiorgan system failure) may develop. The goals of medical management are to provide **aggressive supportive care**, to decrease inflammation, to limit infection or superinfection, and to identify and treat complications as appropriate.
- **Surgical intervention**, whether by minimally invasive or conventional open techniques, is indicated when an anatomic complication amenable to a mechanical solution is present (e.g., acute necrotizing pancreatitis in which the necrotic phlegmon is excised to limit the source of sepsis or hemorrhagic pancreatitis in which surgical control of bleeding is warranted). Depending on the situation and local expertise, this may require the talents of an interventional radiologist, an interventional endoscopist, or surgeon (individually or in combination).
- When diagnosis is uncertain: Laparotomy + Peritoneal lavage may be needed.
- Toxic patient, abdominal mass or persistent high gastric aspiration indicate complications had occurred.

COMPLICATIONS

1. MOF
2. Pseudocyst formation
3. Intra-abdominal infection & Abscess formation
4. Pancreatic Necrosis
5. Recurrent acute attacks
6. Chronic pancreatitis

Other Complications:

1. **Hemorrhage** into the GI tract, retroperitoneum or the peritoneal cavity is possible because of erosion of large vessels.
2. **Intestinal obstruction or necrosis** may occur.
3. **Common bile duct obstruction** may be caused by a pancreatic abscess, pseudocyst, or biliary stone that caused the pancreatitis.
4. **Internal pancreatic fistula** from pancreatic duct disruption or a leaking pancreatic pseudocyst may occur.

PANCREATIC PSEUDOCYST

- Collection of pancreatic secretions contained within a fibrous sac comprised of chronic inflammatory cells and fibroblasts in and adjacent to the pancreas contained by surrounding structures (a fibrous sac filled with pancreatic fluid).
- It represents a sleeping tiger, which though frequently harmless, still can rise up unexpectedly and attack with its enzymatic claws into adjacent visceral and vascular structures and cause life-threatening complications.
- ***Acute Pseudocyst***: This is a collection of pancreatic fluid that is walled off by granulation tissue after an episode of acute pancreatitis; it requires 4 or more weeks to develop. Although pseudocysts are sometimes palpable on physical examination, they are usually detected with abdominal ultrasonography or computed tomography (CT).
- Most pancreatic cystic masses encountered in clinical practice are postinflammatory pseudocysts.
- Pancreatic pseudocysts are defined as: Localized enzymes-rich fluid collections located within the pancreatic tissue or adjacent to the pancreas and surrounded by a fibrous wall that does not possess an epithelial lining.
- The CT finding: a round or oval fluid collection with a thin, barely perceptible wall or thick wall that shows evidence of contrast enhancement.
- They develop most often as a complication of acute or chronic pancreatitis and may develop secondary to pancreatic trauma or surgery.

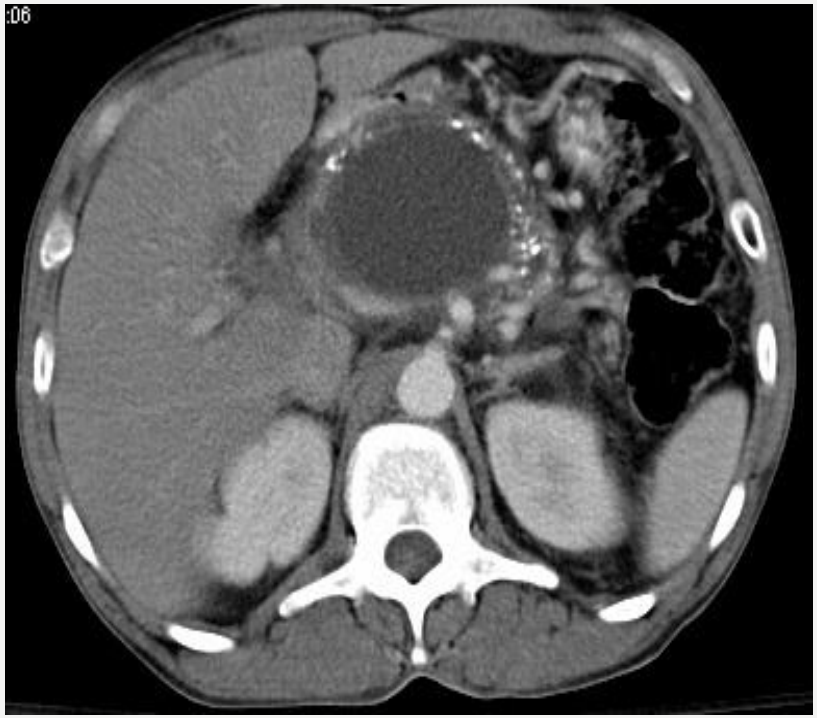
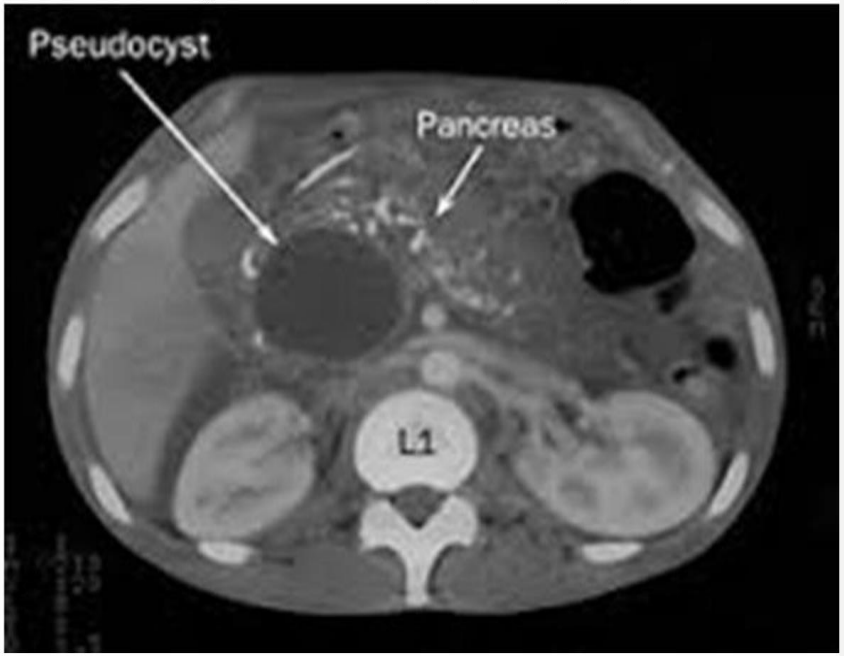


Figure 1: It shows the CT image of pancreatic pseudocyst.



JSS was performed in 40 patients (100%) and CT scan in 30 patients (75%). The size and location of the

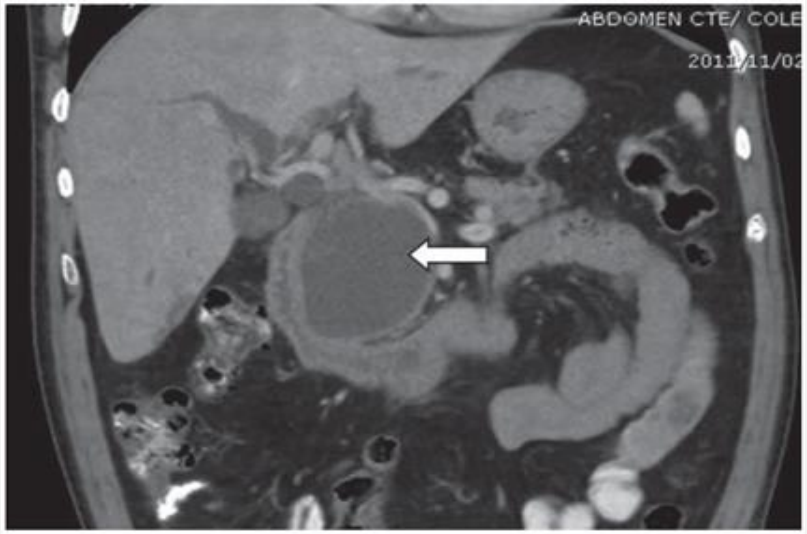
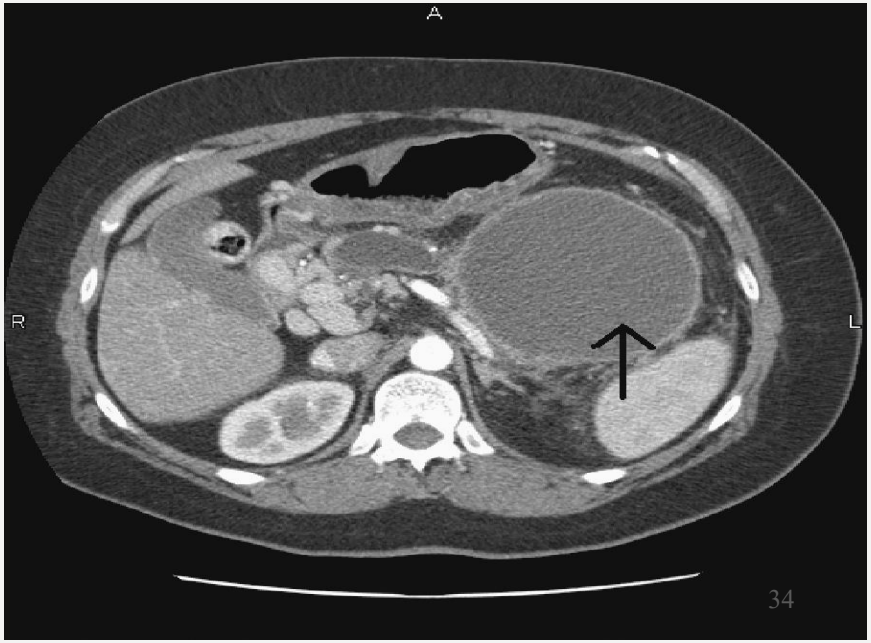


Figure 3. Patient with pancreatic pseudocyst. The image shows a hypodense lesion in the pancreatic head.



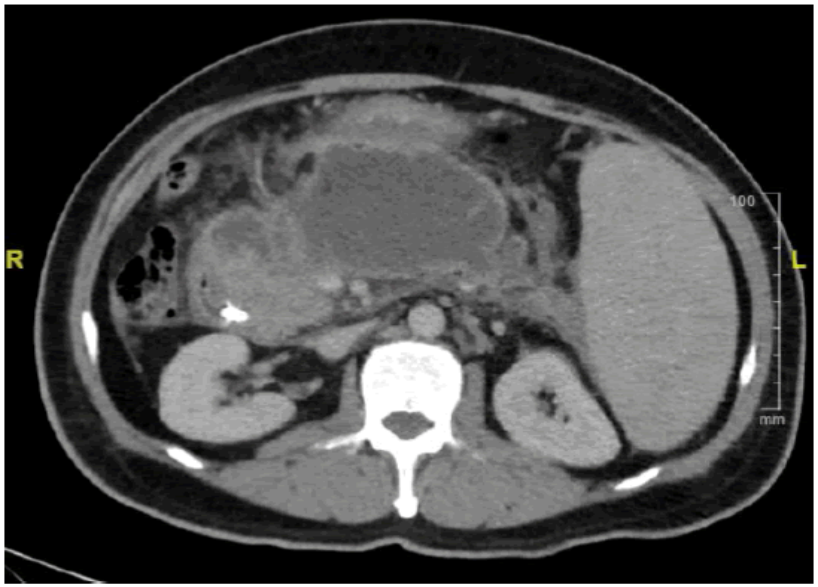
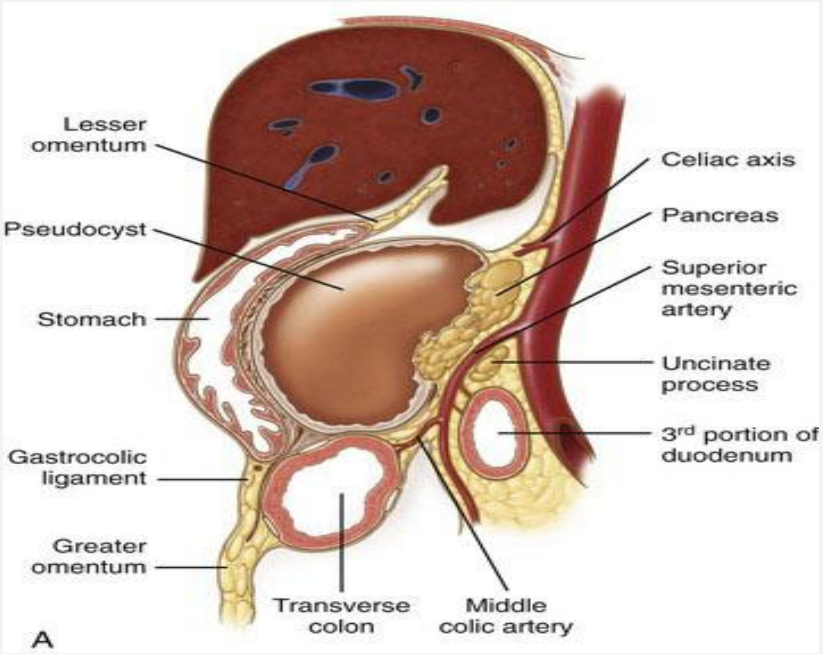
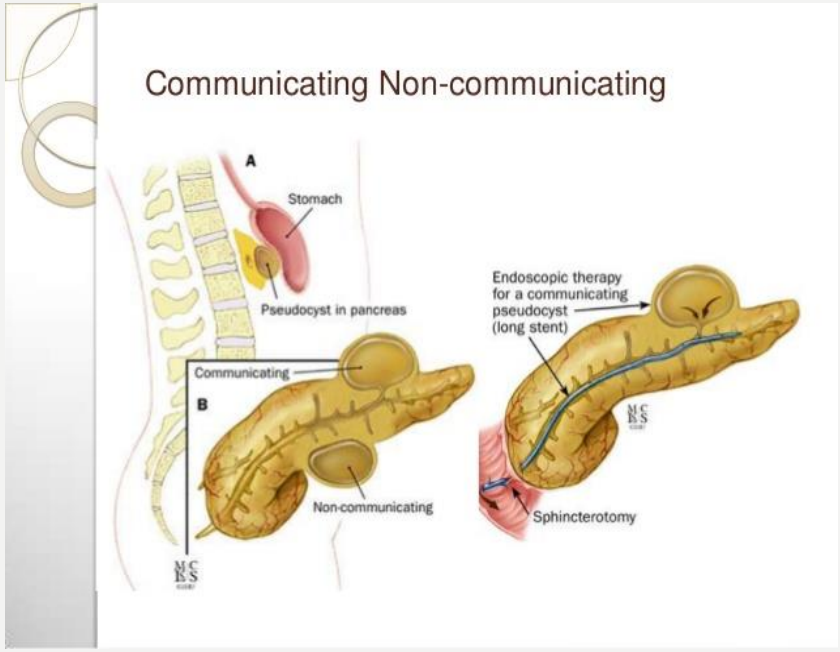


Figure 1. Pancreatic pseudocyst.





MANAGEMENT OF PSEUDOCYST (1)

- The goal of therapy is avoidance of complications. Note the following:
- Most pseudocysts resolve without interference and only require supportive care.
- About 10% of pseudocysts become **infected**.
- Pseudocysts can also **rupture**.
  - A controlled rupture into an enteric organ can sometimes cause GI bleeding.
  - A free rupture into the peritoneal cavity produces abdominal pain and, rarely, peritonitis or even death.
- The **size of the cyst** and the **length of time the cyst** has been present are poor predictors of complications. In general, larger cysts are more likely to become symptomatic or cause complications. However, some patients with larger collections do well; therefore, the size of the pseudocyst alone is not an indication for drainage.
- Indications for drainage include the following:

  (1) Complications (2) Symptoms (3) Concern about possible malignancy (4) Enlarging cysts > 5-6 cm in size ?

MANAGEMENT OF PSEUDOCYST (2)

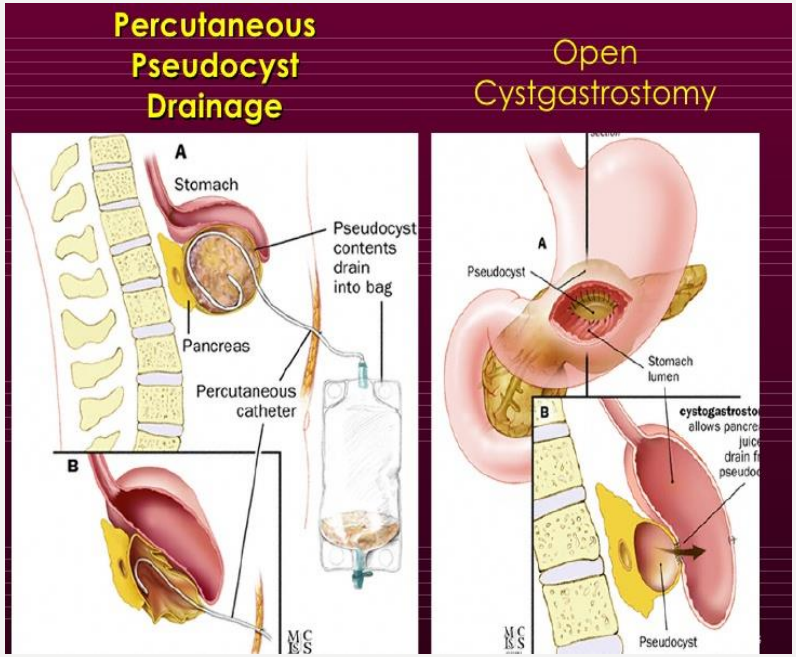
- Management of pseudocysts requires a team approach. Gastroenterologists, surgeons, and invasive radiologists must work together to determine the necessity, timing, and method of intervention.
- If **nonsurgical drainage** is contemplated, it is important to elucidate the anatomy of the pancreatic duct beforehand. This may be done via ERCP or MRI. A large number of patients who fail or have complications with nonsurgical drainage have disruption or stenosis of the pancreatic duct.
- **Diet and activity:** Patients may eat a low-fat diet as tolerated. Patients in whom eating causes abdominal pain need parenteral or enteral nutrition through a percutaneously or endoscopically placed jejunal tube.
- Patients may engage in activities as tolerated.
- **Outpatient monitoring**
- Patients who have endoscopically placed stents must be monitored via serial CT scans to observe resolution of the cyst. Stents may then be endoscopically removed after resolution.
- Closely monitor patients with percutaneous drains for pain, infection, or catheter migration. Remove the drain when drainage ceases.

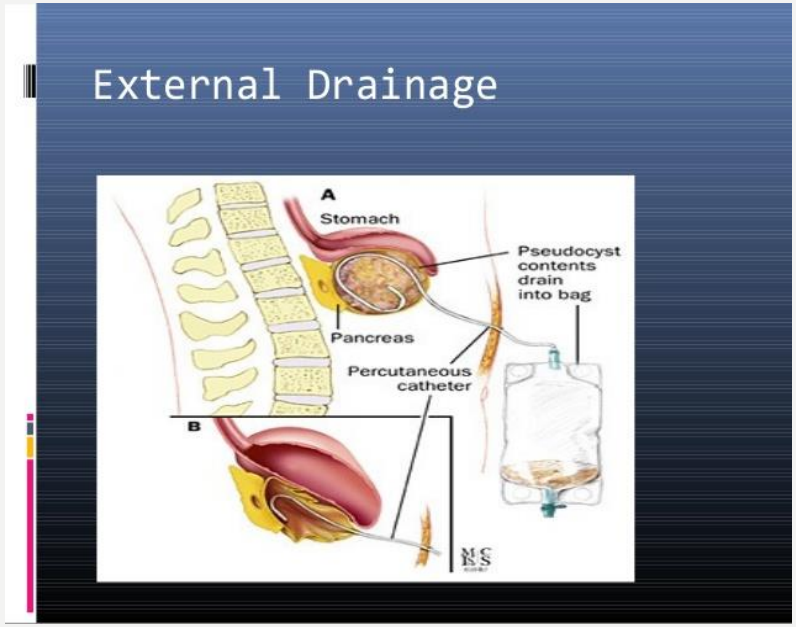
CYSTO-GASTROSTOMY OR CYSTO-JEJUNOSTOMY

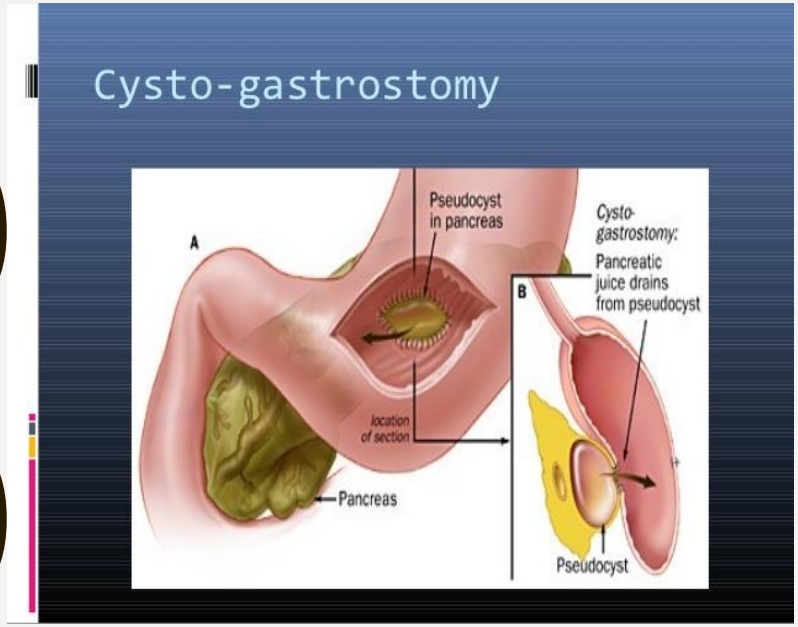
- Open surgical intervention for treatment of simple pancreatic pseudocyst (PP) has a high success rate and has been the historical gold standard. Open surgical intervention, however, confers significant morbidity and mortality, which has spurred the development of less invasive techniques.
- Laparoscopic approaches are feasible with the potential for lower complication rates and length of stay.
- The endoscopic approach has the appeal of potentially shorter hospitalization length of stays and does not require general anesthesia.
- Ultrasonography-guided percutaneous catheter drainage (US-PCD).
- Complicated PPs or those that arise in the setting of chronic pancreatitis warrant additional workup and special consideration.

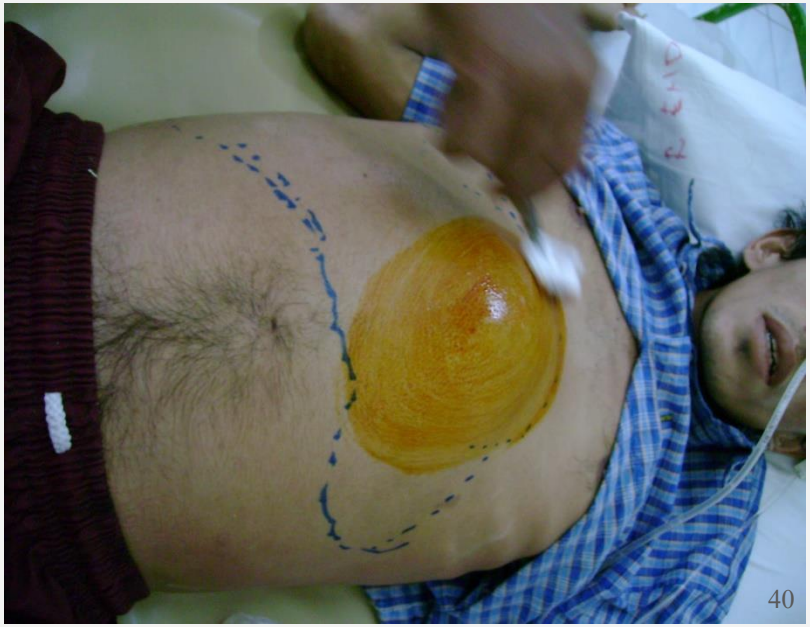
APPROACH

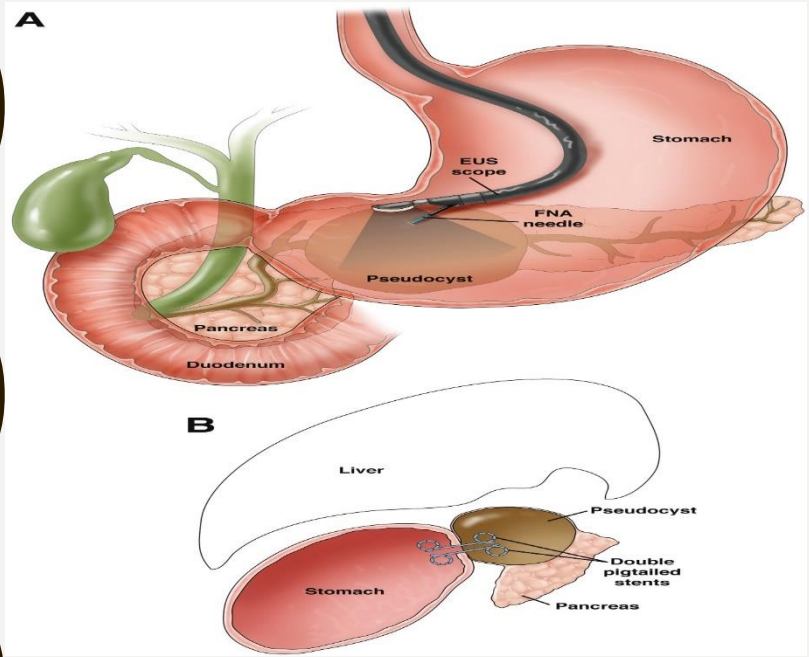
- **External Drainage**:
- **Endoscopic Drainage**:
- **Internal Drainage** (laparotomy or Laparoscopy):
  1. Cystogastrostomy.
  2. Cystojejunostomy: permanent resolution
  3. Cystoduodenostomy: can be complicated by duodenal fistula and bleeding at anastomotic site.
- **Surgical Excision**:
  1. Pancreatic tail & along with proximal strictures → Distal pancreatectomy + splenectomy.
  2. Pancreatic head with strictures of pancreatic or bile ducts → Pancreaticoduodenectomy.

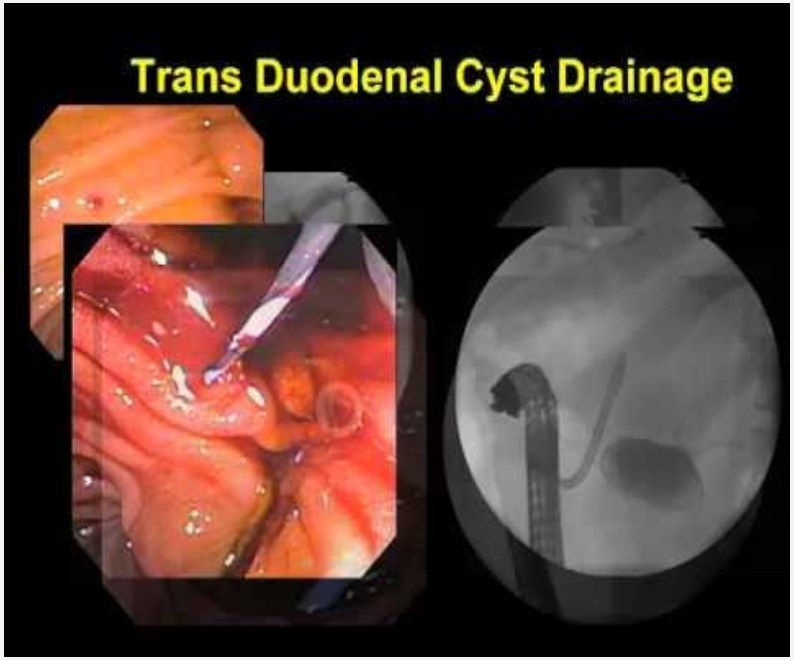

Percutaneous Pseudocyst Drainage
Open Cystgastrostomy
A
Stomach
Pseudocyst contents drain into bag
Pancreas
Percutaneous catheter
B
Pseudocyst
Stomach lumen
Pseudocyst

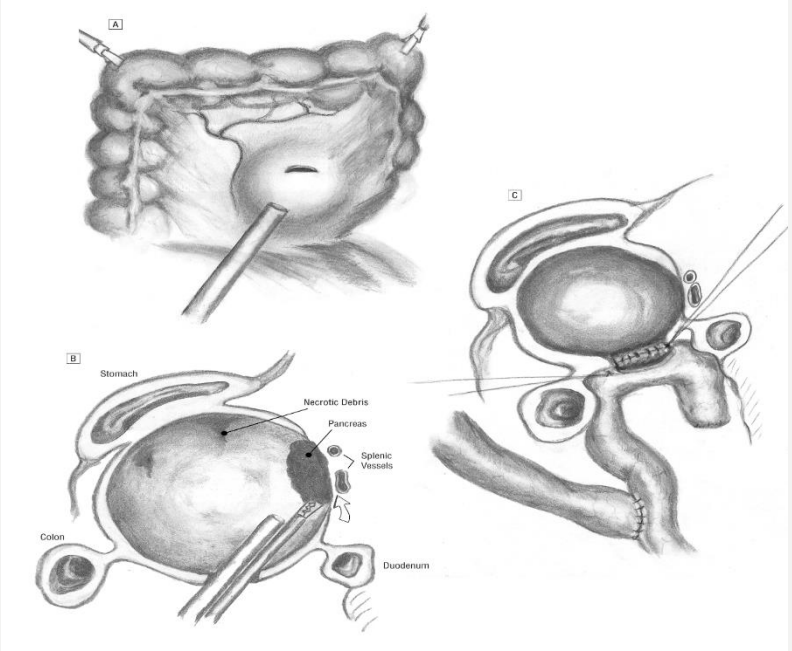

External Drainage
A
Stomach
Pseudocyst contents drain into bag
Pancreas
Percutaneous catheter
B


Cysto-gastrostomy
A
Pseudocyst in pancreas
Cysto-gastrostomy:
Pancreatic juice drains from pseudocyst
B
location of section
Pancreas
Pseudocyst

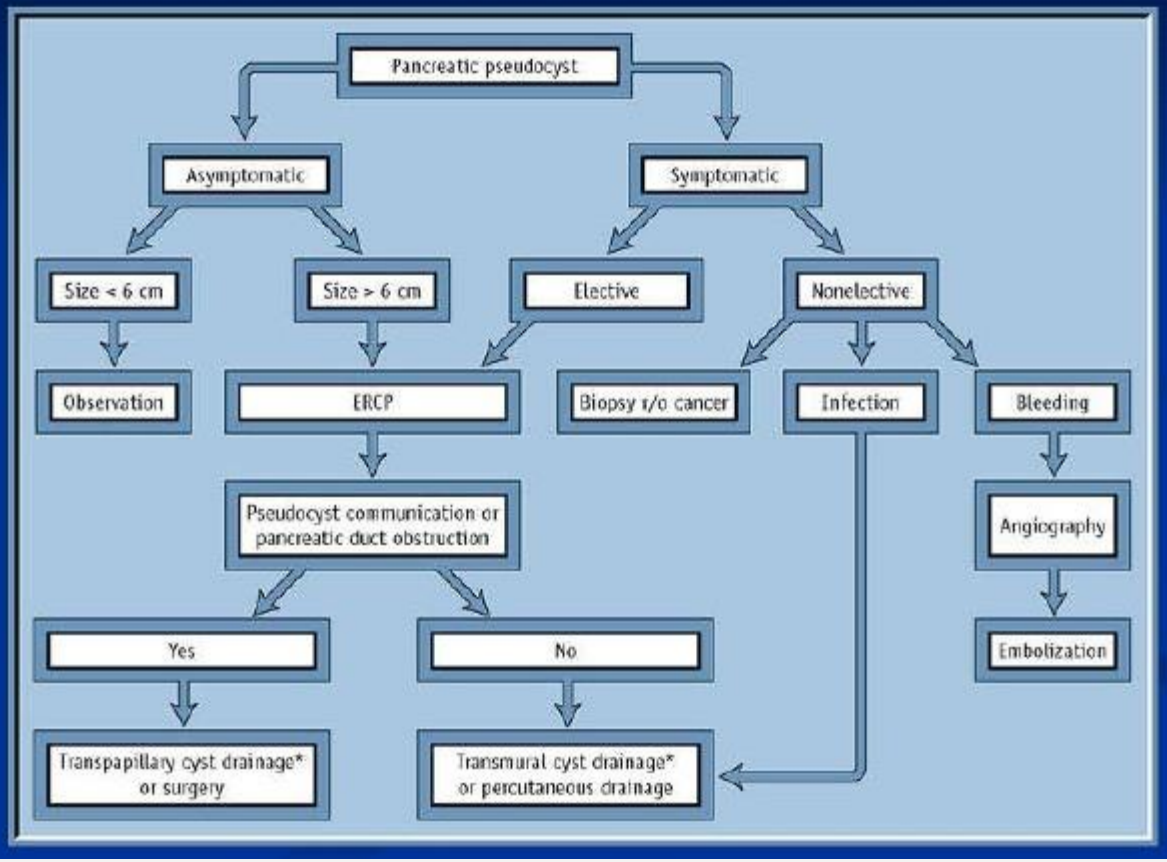


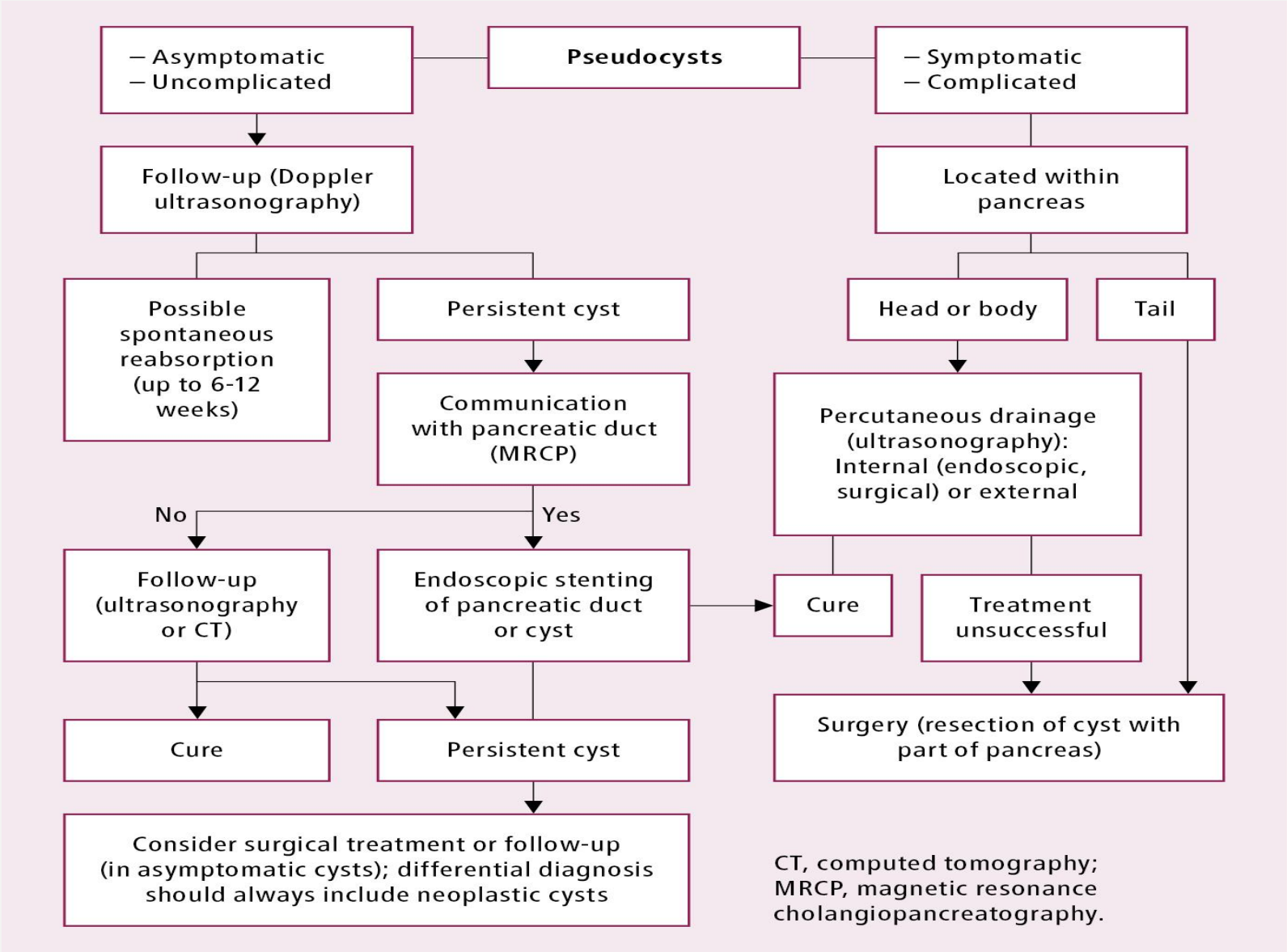

A
Stomach
EUS scope
FNA needle
Pseudocyst
Pancreas
Duodenum
B
Liver
Pseudocyst
Double pigtailed stents
Stomach
Pancreas

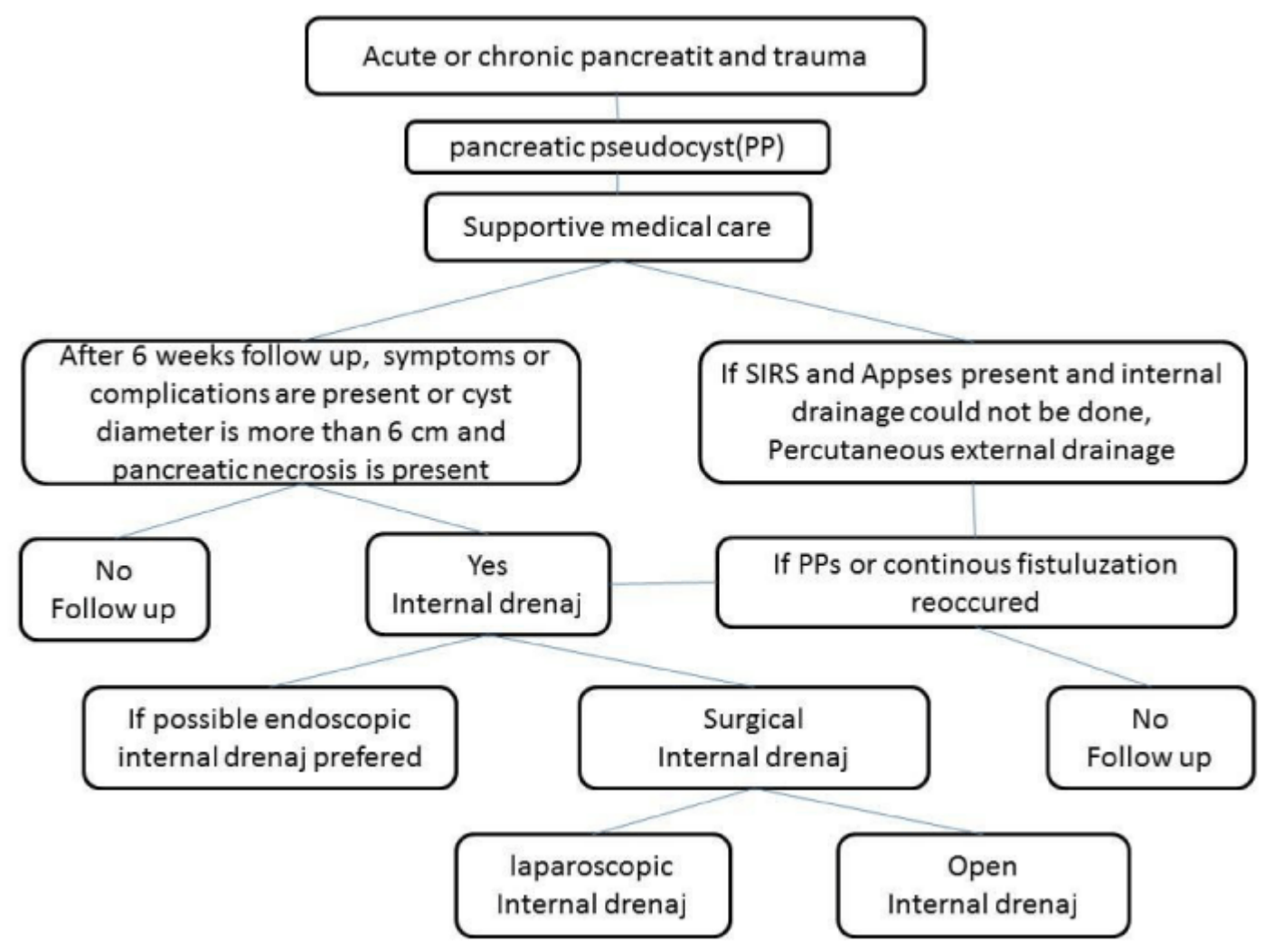

Trans Duodenal Cyst Drainage


A
B
Stomach
Necrotic Debris
Pancreas
Splenic Vessels
Colon
Duodenum
C

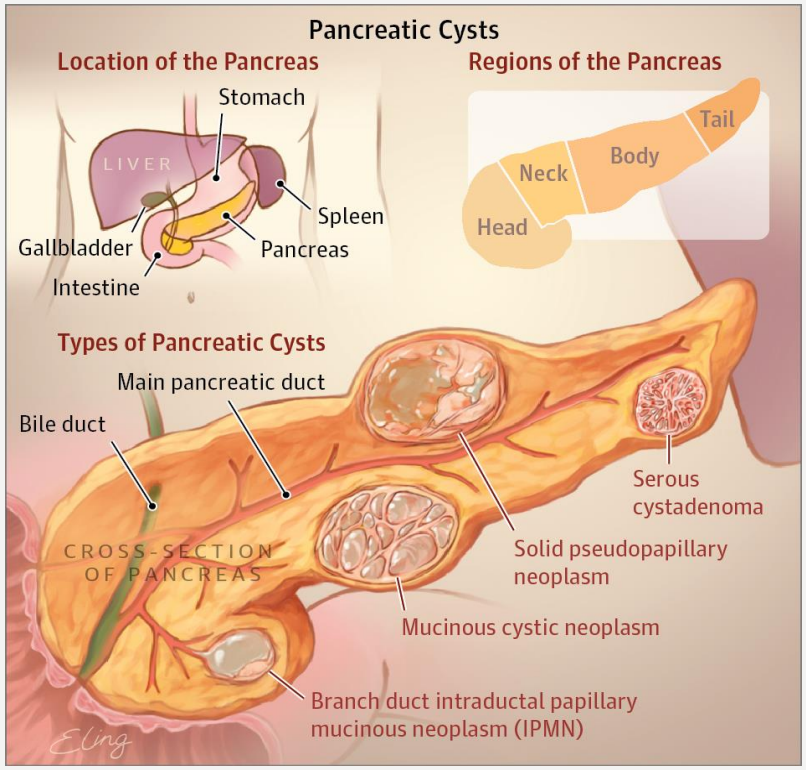
ERCP–based algorithm for management of pancreatic pseudocysts




Pseudocysts
– Asymptomatic
– Uncomplicated
– Symptomatic
– Complicated
Follow-up (Doppler ultrasonography)
Located within pancreas
Possible spontaneous reabsorption (up to 6-12 weeks)
Persistent cyst
Head or body
Tail
Communication with pancreatic duct (MRCP)
Percutaneous drainage (ultrasonography): Internal (endoscopic, surgical) or external
No
Yes
Follow-up (ultrasonography or CT)
Endoscopic stenting of pancreatic duct or cyst
Cure
Treatment unsuccessful
Cure
Persistent cyst
Surgery (resection of cyst with part of pancreas)
Consider surgical treatment or follow-up (in asymptomatic cysts); differential diagnosis should always include neoplastic cysts
CT, computed tomography;
MRCP, magnetic resonance cholangiopancreatography.


Acute or chronic pancreatit and trauma
pancreatic pseudocyst(PP)
Supportive medical care
After 6 weeks follow up, symptoms or complications are present or cyst diameter is more than 6 cm and pancreatic necrosis is present
If SIRS and Appses present and internal drainage could not be done, Percutaneous external drainage
No Follow up
Yes Internal drenaj
If PPs or continous fistuluzation reoccured
If possible endoscopic internal drenaj prefered
Surgical Internal drenaj
No Follow up
laparoscopic Internal drenaj
Open Internal drenaj

DIFFERENTIAL DX OF PANCREATIC CYSTS



INTRA ABDOMINAL INFECTIONS

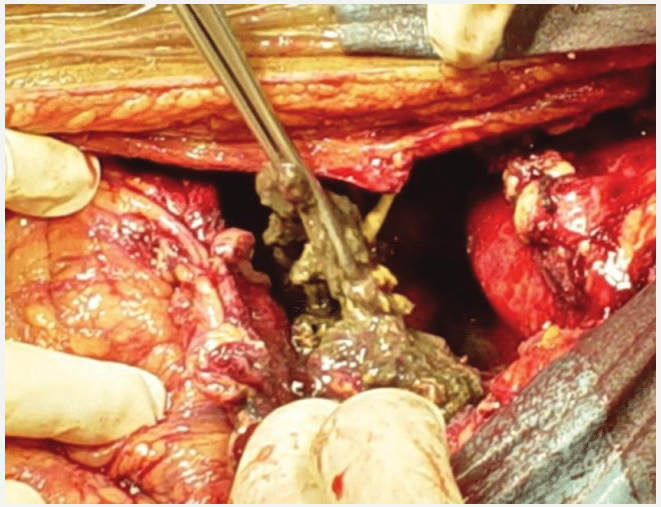
- Within the first 1-3 weeks, fluid collections or pancreatic necrosis can become infected and jeopardize clinical outcome.
- From 3 to 6 weeks, pseudocysts may become infected or a pancreatic abscess may develop.
- The intestinal flora is the predominant source of bacteria causing the infection. The usual suspects are Escherichia coli (26%), Pseudomonas species (16%), Staphylococcus species (15%), Klebsiella species (10%), Proteus species (10%), Streptococcus species (4%), Enterobacter species (3%), and anaerobic organisms (16%).
- Fungal superinfections may occur weeks or months into the course of severe necrotizing pancreatitis.

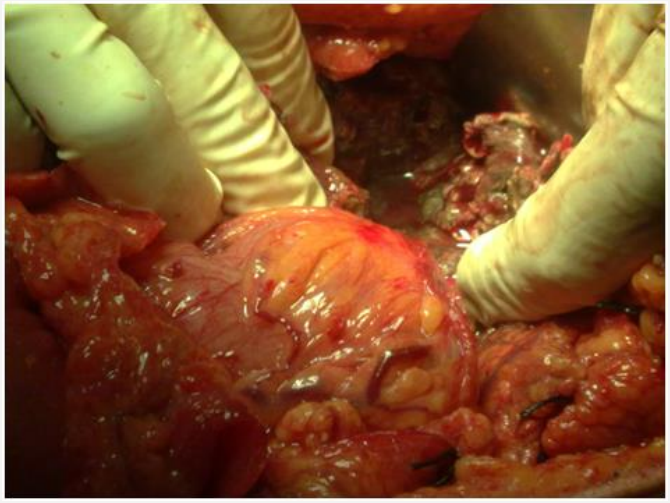
PANCREATIC NECROSIS

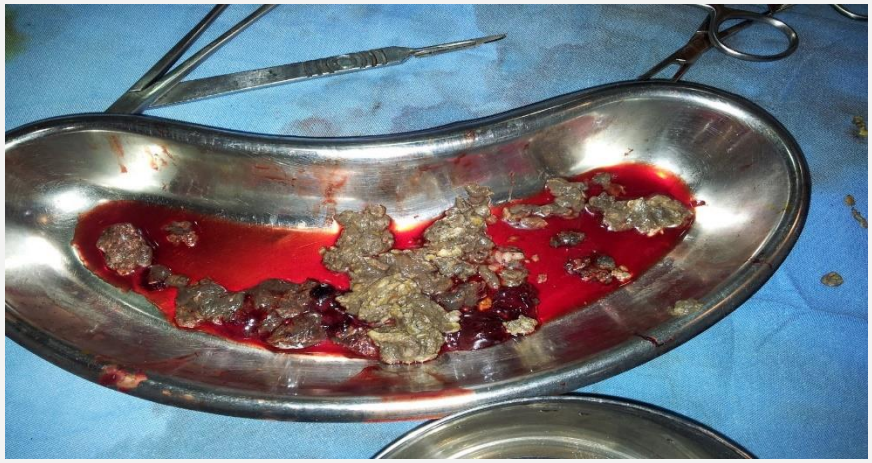
- Is a nonviable area of pancreatic parenchyma that is often associated with peripancreatic fat necrosis and is principally diagnosed with the aid of dynamic spiral CT scans.
- Distinguishing between infected and sterile pancreatic necrosis is an ongoing clinical challenge. Sterile pancreatic necrosis is usually treated with aggressive medical management, whereas almost all patients with infected pancreatic necrosis require surgical debridement or percutaneous drainage if they are to survive.

MANAGEMENT OF PANCREATIC NECROSIS

- Laparostomy + Peritoneal Lavage + Pancreatic necrosectomy (Debridement)







ENDOSCOPIC TRANSGASTRIC NECROSECTOMY

Endoscopic transgastric necrosectomy is a natural orifice transluminal endoscopic surgery technique for treatment of infected necrotizing pancreatitis.

CLINICAL SCENARIOS: COMPLICATIONS OF ACUTE PANCREATITIS

1. A 72 year old woman is admitted with severe acute pancreatitis (modified Glasgow score of 4). Her urine output in the past 24 hours is 400 ml. She has a hemoglobin of 11.5g/dl, a creatinine of 201 µmol/l and is hypoxic with a PaO2 of 7.9 kPa.
2. A 39 year old alcoholic man is in ICU with organ failure due to severe acute pancreatitis. He is on ionotropes, intubated and ventilated and is being fed enterally via a nasogastric tube. His fluid balance for the past 24 hours reads.

Fluids In		Fluids out	
IV fluids	4200 ml	Urine output	2100 ml
Inotrope Infusion	200 ml	NG aspirate	1500 ml
NG tube feed	2160 ml	Vomit	500 ml

3. A 46 year old man attends the outpatient clinic following a recent admission with acute pancreatitis. He reports intermittent upper abdominal pain and vomiting. On examination there is a large not tender mass in the epigastrium.

CLINICAL SCENARIOS: CONT

For each of the scenarios, select the best answer from the list of options given below:

- Acute renal failure
- Acute respiratory distress syndrome
- Chronic pancreatitis
- Foregut obstruction
- Hemorrhage
- Hypovolemia
- Infected pancreatic necrosis
- Multi-organ failure
- Pancreatic abscess
- Pancreatic duct stricture
- Pancreatic necrosis
- Pseudocyst formation

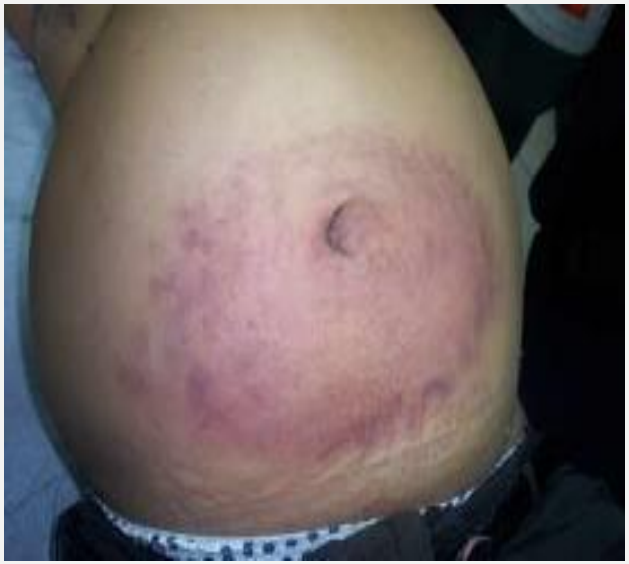
CLINICAL SCENARIOS: ANSWERS

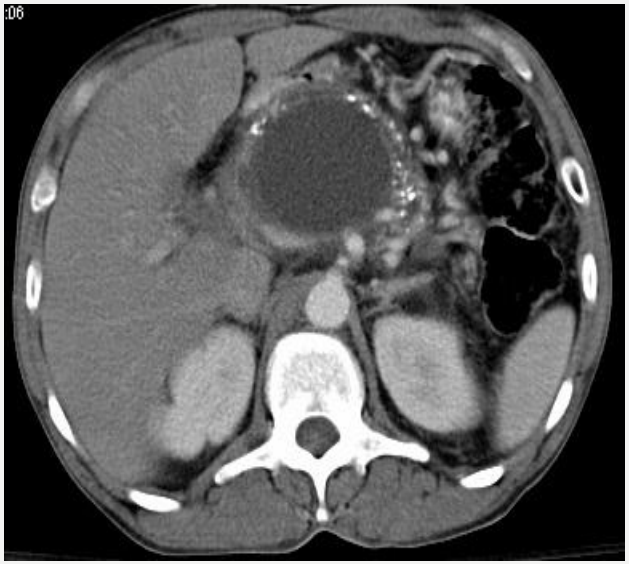
Answers to clinical scenarios 1 to 3

1. Multi-organ failure
2. Foregut obstruction: High NG tube aspirate and vomiting confirm foregut obstruction secondary to peri pancreatic inflammation/edema causing external obstruction.
3. Pseudocyst formation

A 45 year old male patient presented to the emergency Room complaining of sudden, intense, dull and boring abdominal pain. The pain is continuous (increase in Crescendo fashion), localized to the epigastric region and radiates directly through the abdomen to the back. The pain is worse when the patient is supine, and bending forwards ameliorates the pain. The patient gave a history of previous attacks of biliary colic.

A. What is your Diagnosis
B. Name 2 prognosticators on admission
C. Name the sign seen on abdominal inspection (see photo)
D. Name the complication seen on Abdominal CT scan (see CT image)





ANSWERS

A. What is your Diagnosis: **Acute Pancreatitis**

B. Name 2 prognosticators on admission:

1. **Age > 55**
2. **WBC > 16000 cells/mm3**
3. **Glucose > 200 mg/dl (10 mmol/L)**
4. **Serum AST > 250 IU/L**
5. **Serum LDH > 350 IU/L**

C. Name the sign seen on abdominal inspection (see photo):

- **Cullen's sign**

D. Name the complication seen on Abdominal CT scan (see CT image):

- **Pancreatic Pseudocyst**