Acute and Chronic Pancreatitis

objectives

- Describe the definition, epidemiology, pathogenesis, morphology, and clinical findings of acute and chronic pancreatitis.

Black: original content
Red: Important
Green: only found in males slides

Orange: Doctor notes
Grey: Extra/Robbins
Purple: Only found in females slides

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Editing File

Acute Pancreatitis

Pancreatitis

- Is a group of disorders characterized by inflammation of the pancreas, divided into acute and chronic forms.
- Range in severity from a mild, self-limited disease to a life-threatening acute inflammatory process.

Acute pancreatitis

- **Reversible** pancreatic parenchymal injury associated with inflammation.
- Glands can return to normal if underlying cause of the pancreatitis is removed.

Epidemiology

1) The annual incidence in Western countries is 10 to 20 cases per 100,000 people.

2) 80% of cases in Western countries are associated with one of two conditions:
1. biliary tract disease
2. Alcoholism.

3) Gallstones are present in 35% to 60% of cases of acute pancreatitis.

4) The male-to-female ratio is 1 : 3 in the group with **biliary tract disease**
6 : 1 in those with **alcoholism**.

Etiologic Factors

- 10% to 20% of cases of acute pancreatitis are **idiopathic** pancreatitis

Metabolic

1. Alcoholism
2. Hyperlipoproteinemia
3. Hypercalcemia
4. Drugs (e.g. azathioprine).

Genetic

Mutations in the cationic trypsinogen (**PRSS1**) and trypsin inhibitor (**SPINK1**) genes causing Dysregulation of trypsinogen inactivation.
In these conditions recurrent severe acute pancreatitis often beginning in **childhood**.

Mechanical

1. Gallstones
2. Trauma (seat belt trauma, posterior penetration of duodenal ulcer)
4. Iatrogenic injury:
I. Operative injury
II. Endoscopic procedures with dye injection

Vascular

1. Shock
2. Atheroembolism
3. Vasculitis

Infectious

1. Mumps
2. Coxsackievirus
3. Mycoplasma pneumoniae

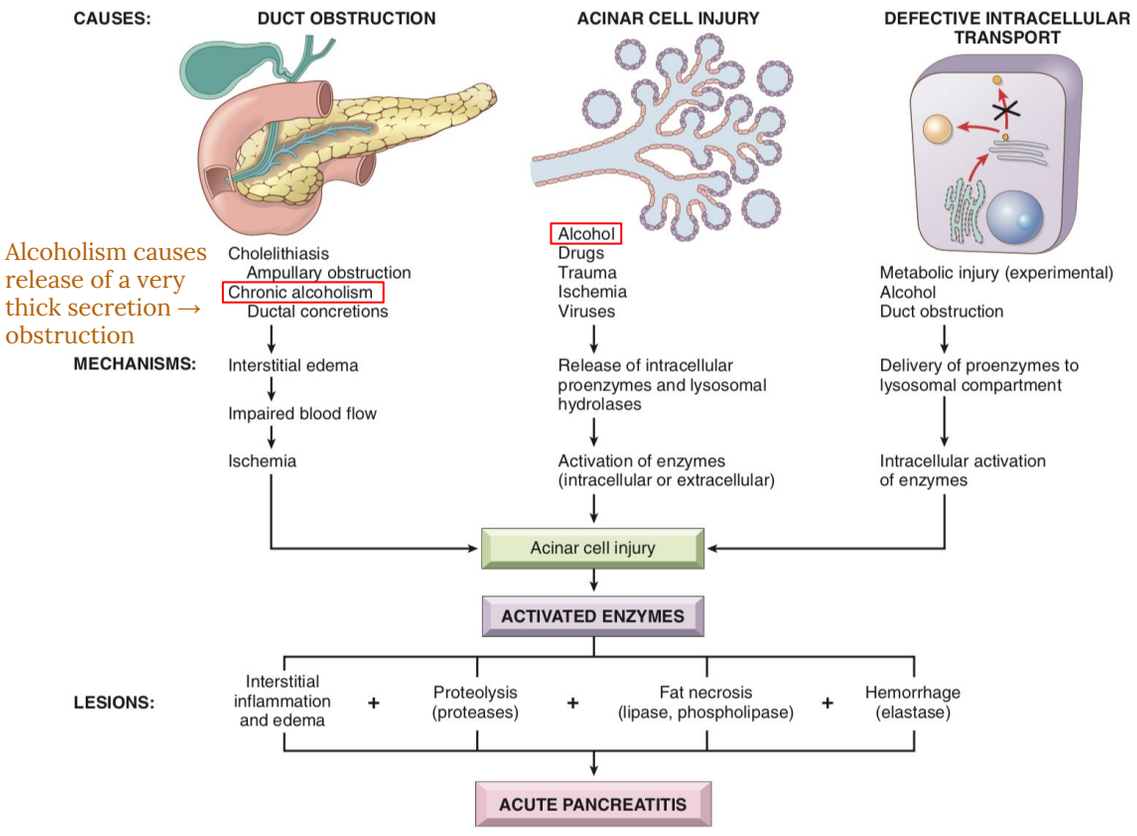
Acute Pancreatitis

Pathogenesis

- Autodigestion of the pancreatic substance by **inappropriately activated pancreatic enzymes.**
- Mechanisms protect the pancreas from enzymatic self digestion:

1. Most digestive enzymes are synthesized as inactive proenzymes (zymogens), which are packaged within secretory granules.
2. Most proenzymes are activated by trypsin, which itself is activated by duodenal enteropeptidase (enterokinase) in the small bowel.
3. Acinar and ductal cells secrete trypsin inhibitors, including serine protease inhibitor Kazal type l (SPINK1) which further limit intrapancreatic trypsin activity.

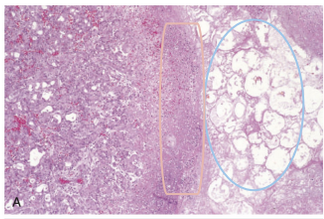
- Actions of activated pancreatic enzymes (**trypsinogen activation**):
  - **Proteases damage acinar cell** structure.
  - **Lipases** and phospholipases produce enzymatic **fat necrosis.**
  - **Elastases** damage vessel walls and induce **hemorrhage**
  - Activated enzymes also circulate in the blood.



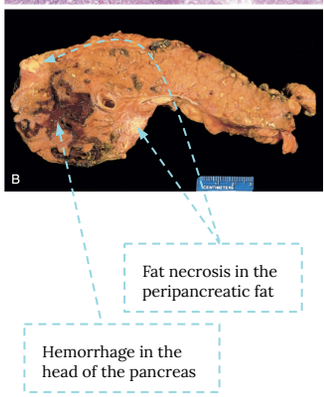
Acute Pancreatitis

Morphology

- The morphology of acute pancreatitis ranges from inflammation and edema to severe extensive necrosis and hemorrhage.
  - **Pic A:**



01	02	03	04
Acute inflammatory reaction with **edema caused by microvascular leakage**	**Fat necrosis** by lipolytic enzymes	Proteolytic destruction of pancreatic parenchyma	Destruction of blood vessels with subsequent interstitial **hemorrhage**



  - **Pic B:** Fat necrosis results from enzymatic destruction of fat cells. The released fatty acids combine with calcium to form insoluble salts (saponification) that precipitate in situ (appear as foci of yellow-white, chalky material)

Clinical Features

Full-blown acute pancreatitis is a medical emergency.

- Fever, nausea, and vomiting.
- **Abdominal pain** the cardinal manifestation. varies from mild to severe.
  - Severe, boring (**knife-like**) midepigastric pain with **radiation into the back.**
- **Hypovolemic shock** Due to peripancreatic collection of fluid.
- **Hypoxemia** circulating phospholipase destroys surfactant.
- Hemorrhage
- **Disseminated intravascular coagulation** Due to activation of prothrombin by trypsin.
- **Tetany** muscle spasm

Calcium binds to fatty acids, which decreases ionized calcium → **hypocalcemia**. The worse the inflammation, the lower the calcium level. **If persistent, it is a poor prognostic sign.**

Acute Pancreatitis

Laboratory findings

Amylase: Not specific for pancreatitis
Initial increase occurs at 2 to 12 hours; peaks over 12 to 30 hours
Returns to normal in 2 to 4 days, **Present in urine** for 1 to 14 days.

Serum lipase: More specific for pancreatitis
Initial increase occurs in 3 to 6 hours; peaks in 12 to 30 hours;
returns to normal over 7 to 14 days, It is **not excreted in urine.**

Serum immunoreactive trypsin Increases 5 to 10 times normal
Remains increased for 4 to 5 days.

Management and Prognosis

The key to the management is resting the pancreas by **total restriction of food** and fluids and by supportive therapy (intravenous fluids and **nasogastric suction**).

Most patients recover fully

About 5% die from:
1. Shock (during the first week of illness).
2. Acute respiratory distress syndrome
3. Acute renal failure

Complications

- In surviving patients:
  - Sterile pancreatic abscess
  - Pancreatic pseudocyst Cyst lacks epithelial cells and lined by fibrous tissue.
- Chronic pancreatitis due to Repeated episodes of pancreatitis.
- Hereditary pancreatitis have a 40% lifetime risk of developing pancreatic cancer (adenocarcinoma).

Chronic Pancreatitis

- Prolonged inflammation of the pancreas with **irreversible** destruction of exocrine parenchyma, and fibrosis.
- In the late stages, the destruction of endocrine parenchyma occur.

Epidemiology

- The prevalence ranges between 0.04% and 5%.
- Most affected patients are middle-aged males.

Causes

- **Repeated bouts of acute pancreatitis**, Long-standing obstruction of the pancreatic duct by calculi or neoplasms.
- **Chronic alcohol abuse** (the most common cause)
- **Hereditary pancreatitis:** Germline mutations in genes such as **CFTR** (the gene encoding the transporter that is defective in cystic fibrosis), particularly when combined with environmental stressors (up to 25% of chronic pancreatitis has a genetic basis)
- Autoimmune injury to the gland (IgG-related disease)

Pathogenesis

- Most often follows repeated episodes of acute pancreatitis.
- Chronic pancreatic injury leads to local **production of inflammatory mediators** that promote fibrosis and acinar cell loss.
  - e.g. transforming growth factor β (TGF-β) and platelet derived growth factor (PDGF).
  - Induce the activation and proliferation of periacinar myofibroblasts (pancreatic stellate cells), **resulting in the deposition of collagen and fibrosis.**

Morphology

characterized by:

1. Parenchymal **fibrosis**
2. **Reduced number and size** of acini with relative sparing of the islets of Langerhans
3. Variable **dilation of the pancreatic ducts.**

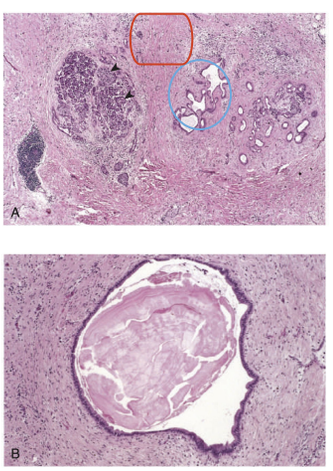
Grossly:

Gland is:

- Hard.
- Dilated ducts.
- Visible calcification.

Microscopically:

Pic A: **Fibrosis** and **atrophy** has left only residual islets and ducts, with **chronic inflammatory cells and acinar loss.**
Pic B: **Dilated ducts** with inspissated eosinophilic ductal concretions in alcoholic chronic pancreatitis.



Chronic Pancreatitis

Clinical Features

- Silent or repeated attacks of abdominal pain, or persistent abdominal and back pain.
- Attacks may be precipitated by:
  - Alcohol abuse.
  - Overeating (which increases demand on the pancreas).
  - The use of opiates and other drugs.
- May be entirely silent until:
  - Pancreatic insufficiency.
  - Diabetes mellitus develop.

  due to **destruction of the exocrine and endocrine pancreas.**

Diagnosis

- Requires a high degree of suspicion.
- Gallstone-induced obstruction may be evident as **jaundice or elevations in serum levels of alkaline phosphatase.**
- Serum amylase is variable and less reliable than in acute disease.
- Lipase in chronic pancreatitis is not clinically useful.
- **Serum immunoreactive trypsin:** Decease concentration.
- **Calcifications** within the pancreas by CT and ultrasonography.

Prognosis

01 - Not an immediately life-threatening condition.
- The long-term outlook for individuals with chronic pancreatitis is poor, with a 20- to 25-year mortality rate of 50%.

02 Pancreatic exocrine insufficiency, chronic malabsorption, and diabetes mellitus can all lead to significant morbidity and contribute to mortality.

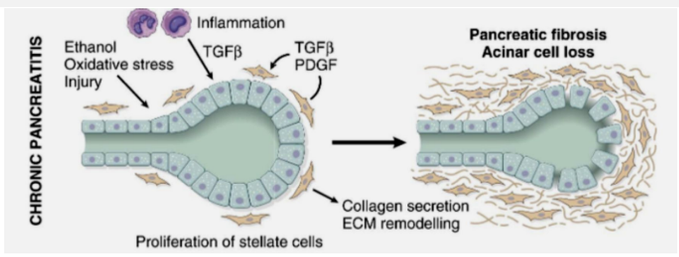
03 - In other patients severe chronic pain is a dominant problem.
- **Pancreatic pseudocysts:** in about 10% of patient.

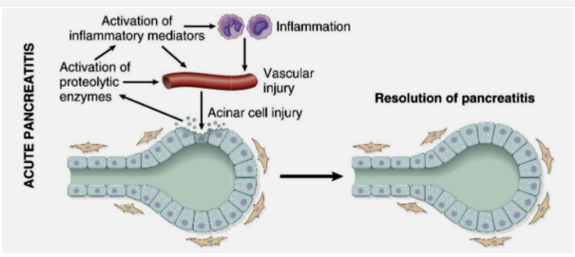
04 Patients with hereditary pancreatitis, have a 40% lifetime risk of developing pancreatic cancer

Summary

Pancreatitis

Chronic	Acute
Irreversible injury of the pancreas leading to fibrosis, loss of pancreatic parenchyma, loss of exocrine and endocrine function, and high risk of developing pseudocysts.	**Reversible** pancreatic parenchymal injury associated with inflammation.
• Idiopathic or caused by: 1. Repeated bouts of acute pancreatitis 2. Chronic alcohol abuse 3. Germline mutations in genes such as CFTR 4. Malnutrition (most common cause in developing countries) 5. Autoimmune disorder 6. Long-standing obstruction of the pancreatic duct by calculi or neoplasms.	• Caused by: 1. Excessive alcohol intake 2. Pancreatic duct obstruction (e.g., gallstones) 3. Genetic factors (e.g., PRSS1, SPINK1). 4. Traumatic injuries 5. Medications 6. Infections (e.g., mumps). 7. Metabolic disorders leading to hypercalcemia. 8. Ischemia All of these causes promote **the inappropriate activation of digestive enzymes** within the substance of the pancreas
Clinical features intermittent or persistent abdominal pain, intestinal malabsorption and diabetes.	**Clinical features** acute abdominal pain, systemic inflammatory response syndrome, and elevated serum lipase and amylase levels
Pathogenesis Repeated episodes of acinar cell injury leads to the production of TGF-β and PDGF, resulting in proliferation of myofibroblasts, secretion of collagen and irreversible loss of acinar cell mass, fibrosis, and pancreatic insufficiency.	**Pathogenesis** Acinar injury results in release of proteolytic enzymes, leading to activation of the clotting cascade, acute inflammation, vascular injury, and edema. - In most patients, complete resolution of the acute injury occurs with restoration of acinar cell mass.





Quiz

Q1: In acute pancreatitis, inflammation of the pancreas occurs when:

- **A)** Repeated alcohol intake forms protein plugs in ducts
- **B)** Pancreatic enzymes are inappropriately activated and start digesting the pancreatic substance
- **C)** Gallstones cause local production of inflammatory mediators that promote fibrosis and acinar cell loss
- **D)** Massive amounts of fluid accumulate in the peritoneal cavity

Q2: Which of the following is the most common laboratory finding in acute pancreatitis?

- **A)** Elevated alkaline phosphate serum levels
- **B)** Normal serum amylase levels with rising serum lipase level
- **C)** Elevated serum amylase with normal serum lipase level
- **D)** elevated serum amylase levels followed by rising serum lipase level

Q3: Mutations in which of the following genes is associated with acute pancreatitis?

- **A)** PRSS1, SPINK1
- **B)** p53
- **C)** CFTR
- **D)** NF2

Q4: Which of the following is NOT seen in acute pancreatitis?

- **A)** Fat necrosis
- **B)** Destruction of blood vessels leading to interstitial hemorrhage
- **C)** Eosinophils
- **D)** Edema

Q5: Which of the following would be seen in chronic pancreatitis?

- **A)** Interstitial hemorrhage
- **B)** Dilated ducts
- **C)** Neutrophils
- **D)** Fat necrosis

Q6: what is the most common known cause of chronic pancreatitis

- **A)** Alcoholism
- **B)** Gallstones
- **C)** Autoimmune disorders
- **D)** Cystic fibrosis

Q7: Which of the following is NOT a complication of chronic pancreatitis?

- **A)** Malabsorption
- **B)** Type 1 diabetes mellitus
- **C)** Acute ischemia
- **D)** Pancreatic pseudocysts

Q8: Serum amylase levels are increased and reliable to diagnose chronic pancreatitis

- **A)** True
- **B)** False

Q9: A 60-year-old alcoholic man presents with a 6-month history of recurrent epigastric pain, progressive weight loss, and foul- smelling diarrhea. The abdominal pain is now almost constant and intractable. An X-ray film of the abdomen reveals multiple areas of calcification in the mid-abdomen. Which of the following is the most likely diagnosis?

- A) Carcinoid syndrome
- B) Chronic pancreatitis
- C) Crohn disease
- D) Insulinoma

1-B 2-D 3-A 4-C 5-B 6-A 7-C 8-B 9-B

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THANK YOU