

Pathology & Pathogenesis of the **Pancreas**

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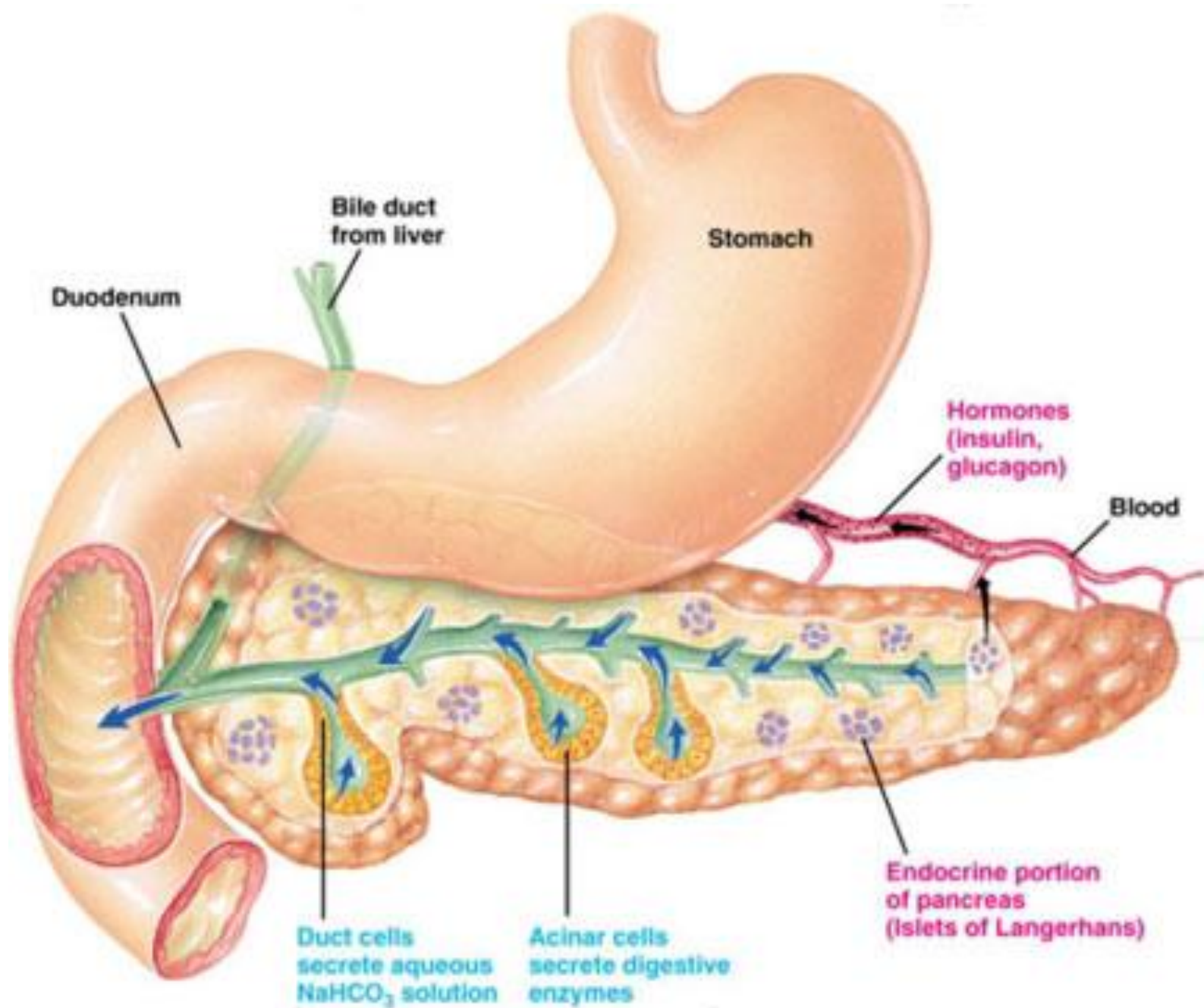
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Pancreatitis

- Inflammation of the pancreas.
- The clinical manifestations can range in severity from a mild, self-limited disease to a lifethreatening acute inflammatory process
- The duration of the disease can range from a transient attack to an irreversible loss of function.

Pancreatitis

- Acute or chronic
- In **acute pancreatitis**, the pancreas gland can **return to normal** if underlying cause of the pancreatitis is removed.
- By contrast, **chronic pancreatitis** is defined by **irreversible** destruction of exocrine pancreatic parenchyma.

Remember: a complication

chronic → fibrosis → irreversible → destruction of Islets of Langerhans → decreased insulin → DM (diabetes mellitus)

Acute pancreatitis

- A group of **reversible** lesions characterized by inflammation of the pancreas ranging in severity from *edema and fat necrosis* to *parenchymal necrosis with severe hemorrhage*.
- Most of cases are associated with one of two conditions:
 - Biliary tract disease
 - Alcoholism
 - Gallstones are present in 35% to 60% of cases.

Causes

Metabolic

Alcoholism

Hyperliporoteinemia

Drugs: thiazide diuretics

Genetic

Mechanical

Trauma

Gallstones

Iatrogenic injury

Perioperative injury

Endoscopic procedures with dye injection

Vascular

Shock

Atheroembolism

Polyarthritits nodosa

Infectious

Mumps

Coxsackievirus

Mycoplasma pneumoniae

Terminology:

Iatrogenic Injury: an injury caused by a medical procedure.

Perioperative Injury: an injury caused during the time of injury.

Atheroembolism: obstruction of a blood vessel by an atherosclerotic embolism.

Polyarthrititis nodosa: is a vasculitis of medium-sized arteries (systemic vasculitis), which become swollen and damaged from attack by rogue immune cells.

Causes

- **Obstruction of the pancreatic duct system**
 - eg. periampullary tumors, congenital cystic dilatation of the common bile duct, biliary "sludge" (mud-like tumors), and parasites (particularly *Ascariasis lumbricoides* and *Clonorchis sinensis* organisms)
- **Medication**
 - More than 85 drugs have been reported to cause acute pancreatitis. e.g . thiazide diuretics, estrogens, etc
- **Metabolic disorders**
 - Including hypertriglyceridemia (due to of sweets and alcohol together), hyperparathyroidism, and other hypercalcemic states
- **Acute ischemia**
 - Vascular thrombosis, embolism, vasculitis and shock.
- **Trauma:**
 - Blunt trauma
 - Iatrogenic injury during surgery or endoscopic retrograde cholangiopancreatography

Pathogenesis

Simply:

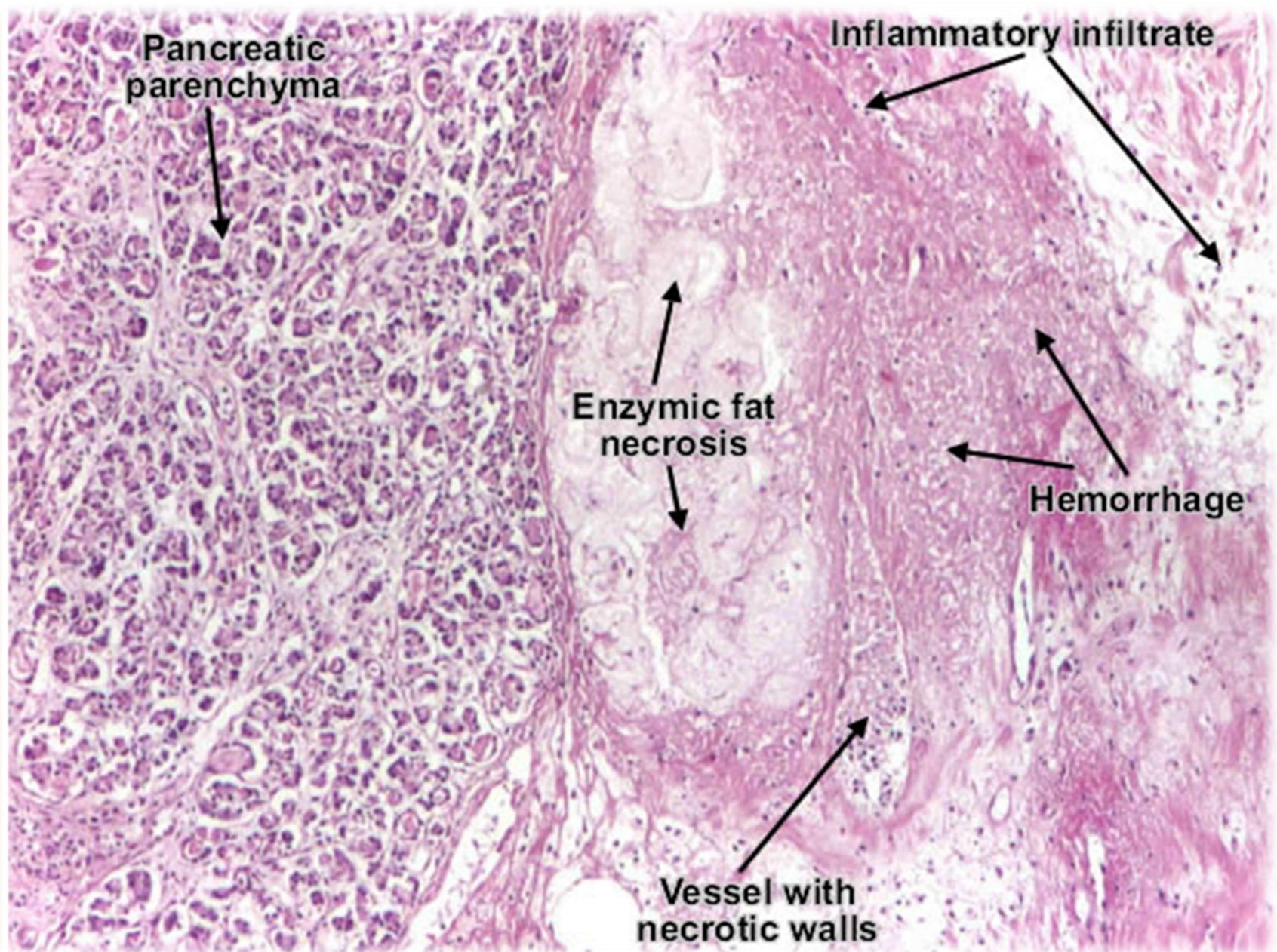
autodigestion of the pancreatic substance by inappropriately activated pancreatic enzymes.

24. In pancreatitis:

- ① a. the tissue damage likely results from release of pancreatic enzymes.
- b. high cholesterol intake is causative.
- c. diabetes is uncommon in chronic pancreatitis.
- d. bacterial infection is the etiological cause.

Morphology

- The basic alterations are
 - (1) microvascular leakage causing **edema**
 - (2) **necrosis** of fat by lipolytic enzymes
 - (3) an acute **inflammatory** reaction
 - (4) proteolytic destruction of pancreatic parenchyma
 - (5) destruction of blood vessels with subsequent interstitial hemorrhage, due to:
Dissemination intervacular coagulation (DIC)
a pathological activation to “coagulation mechanisms” in response to a variety of diseases.
- **Fat necrosis** results from enzymatic destruction of fat cells
→ The released fatty acids combine with calcium to form insoluble salts that precipitate = “**dystrophic calcification**”



Clinical Features.

- **Abdominal pain** is the cardinal (main) manifestation of acute pancreatitis.
- Full-blown acute pancreatitis is a **medical emergency**. These patients usually have the sudden onset of an "acute abdomen" .
- Characteristically, **the pain** is constant and intense and is often referred to the upper back.
- There is
 - leukocytosis
 - hemolysis (blood loosing)
 - disseminated intravascular coagulation
 - fluid sequestration (prevention)
 - acute respiratory distress syndrome
 - diffuse fat necrosis.
- Peripheral vascular collapse and shock with acute renal tubular necrosis may occur

Laboratory Findings

- marked elevation of:
 - **serum amylase levels** during the first 24 hours
 - followed within 72 to 96 hours by a rising **serum lipase level**.

Management

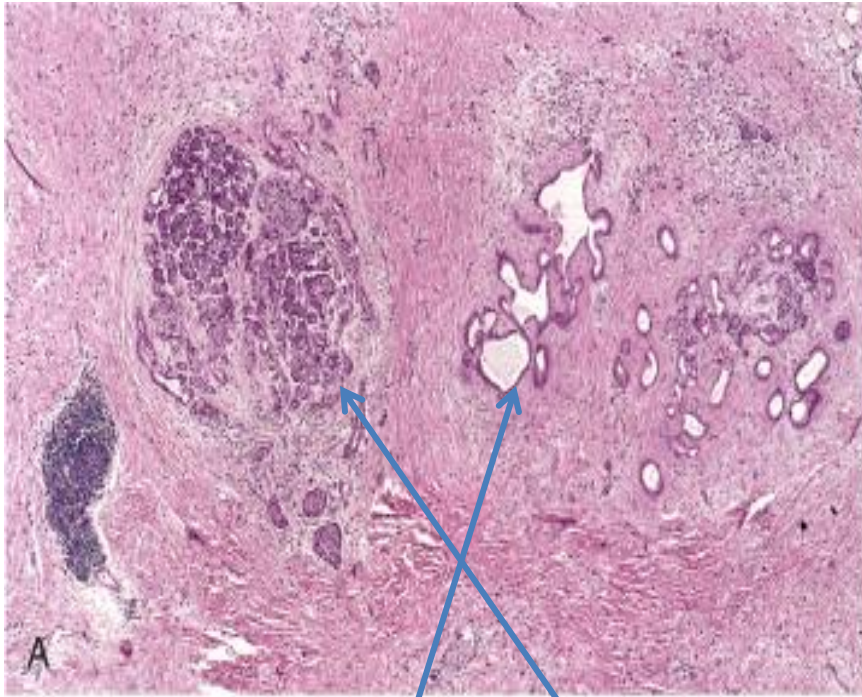
“Resting” the pancreas by total restriction of food and fluids and by supportive therapy.

- Most patients recover fully. About 5% die from shock during the first week of illness. Acute respiratory distress syndrome and acute renal failure are fatal complications.
- In surviving patients, sequelae (consequences) include:
 - a **sterile pancreatic abscess**
 - a **pancreatic pseudocyst** (will be described)

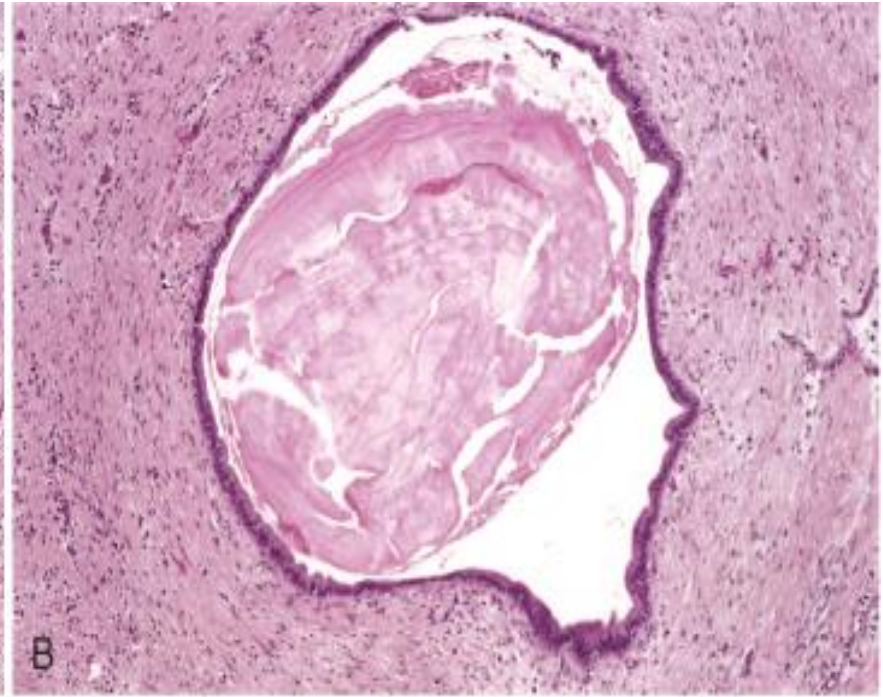
Chronic pancreatitis

- **Chronic pancreatitis is characterized by :**
inflammation of the pancreas with destruction of exocrine parenchyma → **fibrosis** → in the late stages, the destruction of endocrine parenchyma.
- The chief distinction between acute and chronic pancreatitis is **the irreversible impairment in pancreatic function** that is characteristic of chronic pancreatitis.

Morphology



Extensive fibrosis and atrophy has left only residual islets (**left**) and ducts (**right**), with a sprinkling of **chronic inflammatory** cells and acinar tissue.



A higher-power view demonstrating dilated ducts with inspissated eosinophilic ductal concretions in a patient with alcoholic chronic pancreatitis.

Causes

There is significant overlap in the causes of acute and chronic pancreatitis.

The most common cause of chronic pancreatitis is:

- long-term alcohol abuse**
- biliary tract disease**

and these patients are usually middle-aged males.

Causes

Less common causes of chronic pancreatitis include the following:

- Hypercalcemia, hyperlipidemia.
- Long-standing *obstruction* of the pancreatic duct by pseudocysts, calculi (**stones**), trauma, neoplasm, or pancreas divisum.
- *Tropical pancreatitis*, which is a poorly characterized disease seen in Africa and Asia. It has been attributed to malnutrition.
- *Hereditary pancreatitis*
- *Idiopathic chronic pancreatitis*.

Pseudocyst : abnormal sac that resembles a cyst but has no epithelial lining, but true cyst has epithelial lining

The mechanism of formation of this pseudocyst is = inflammation

→ necrosis of this inflamed region → then it becomes a sac

Morphology

- **Chronic pancreatitis is characterized by:**
 - **parenchymal fibrosis**
 - **reduced number and size of acini with relative sparing of the islets of Langerhans**
 - **and variable dilation of the pancreatic ducts**
- **These changes are usually accompanied by a chronic inflammatory infiltrate around lobules and ducts.**
- **Grossly: gland is hard, sometimes with extremely dilated ducts and visible calcification**

Clinical Features

- Silent or repeated attacks of abdominal pain or persistent abdominal and back pain.
- Attacks may be precipitated by alcohol abuse, overeating , or the use of opiates and other drugs.
- During an attack of abdominal pain, there may be mild fever and mild-to-moderate elevations of serum amylase.
- Calcifications can be seen within the pancreas by CT scan and ultrasonography.

Complications

- Severe *pancreatic exocrine insufficiency*
- Chronic mal-absorption
 - *Diabetes mellitus* (due to destruction of islets of Langerhans “insulin”)
 - *Severe chronic pain*
 - *Pancreatic pseudocysts*

Pseudocyst : abnormal sac that resembles a cyst but has no epithelial lining, but true cyst has epithelial lining

The mechanism of formation of this pseudocyst is =
inflammation → necrosis of this inflamed region → then it
become a sac

PSEUDOCYSTS OF PANCREAS

- Pseudocysts are localized collections of necrotic-hemorrhagic material rich in pancreatic enzymes. Such cysts lack an epithelial lining (hence the prefix "pseudo"), and they account for majority of cysts in the pancreas.
- Pseudocysts usually arise after an episode of acute pancreatitis, or of chronic alcoholic pancreatitis.

A pancreatic cyst is a collection of fluid that pools within the pancreas. When the cyst is a true cyst, the pool of fluid is surrounded by a layer of cells (**epithelium**) that secrete fluid into the interior of the cyst.

By contrast, pseudocysts, which are the most common type of cyst, are not surrounded by this cell layer.

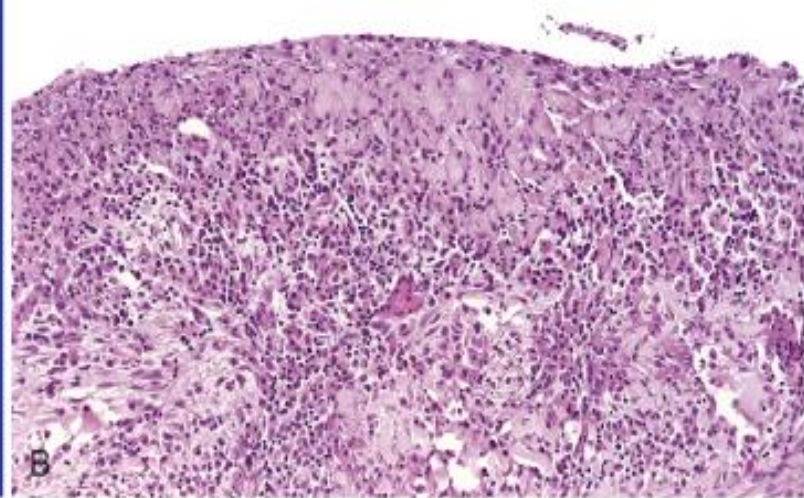
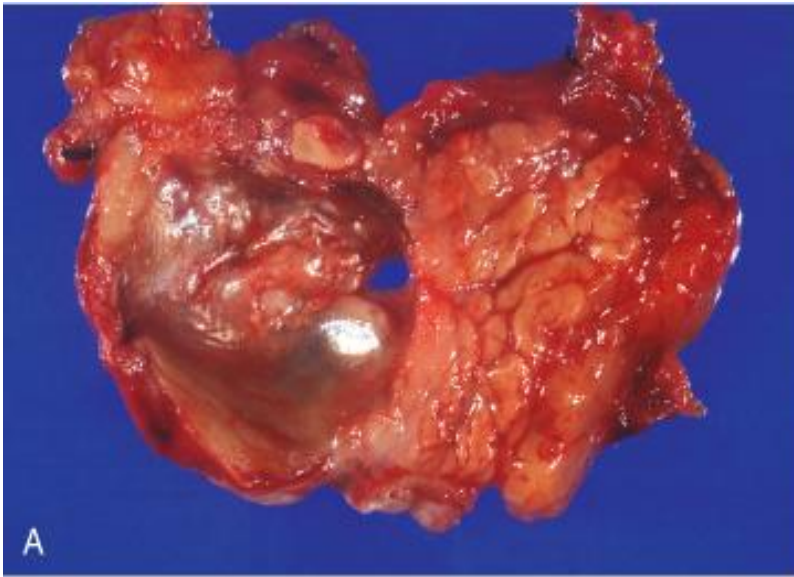
- **True cyst = has epithelium lining**
- **pseudocyst = has no epithelial lining**

PSEUDOCYSTS OF PANCREAS

Morphology:

- Pseudocysts are usually **solitary**
- Pseudocysts can range in size from 2 to 30 cm in diameter.
- While many pseudocysts spontaneously resolve, they may become secondarily infected, and larger pseudocysts may compress or even perforate into adjacent structures.
- They can produce abdominal pain and predispose to intraperitoneal hemorrhage or peritonitis.

PSEUDOCYSTS OF PANCREAS



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Cross-section through this previously bisected lesion revealing a poorly defined cyst with a necrotic brown-black wall.

Histologically, the cyst lacks a true epithelial lining and instead is lined by fibrin and granulation tissue