Pathology Lectures

Gastro-esophageal reflux disease

Peptic Ulcer Disease

Pancreatitis

Diarrhea

Malabsorption

Inflammatory bowel disease-1

Inflammatory bowel disease-2

Colonic polyps and carcinoma-1

Colonic polyps and carcinoma-2

Cirrhosis

Cirrhosis

Cholecystitis

Tumors of liver and pancreas

Pathology and pathogenesis of pancreatitis

Objectives

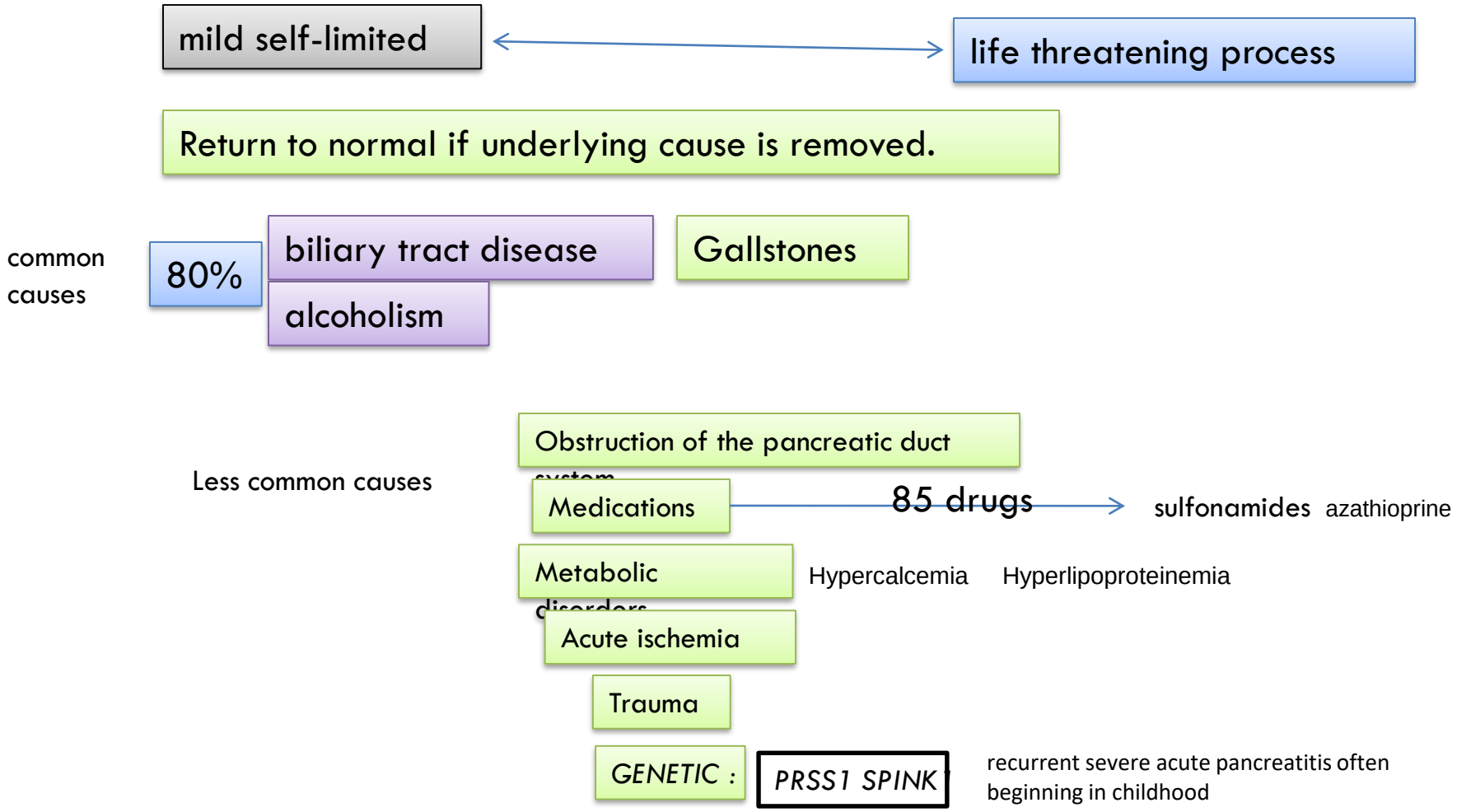
1. Describe the pathology of acute and chronic pancreatitis
2. Understand the pathogenesis of acute and chronic pancreatitis
3. Describe the clinical features and possible complications of acute and chronic pancreatitis.

- The pancreas is in reality two organs in one.

1. 90% ……exocrine (digestion of food).
2. 10% ……endocrine (hormones).

Pancreatitis is	inflammation of the pancreas.

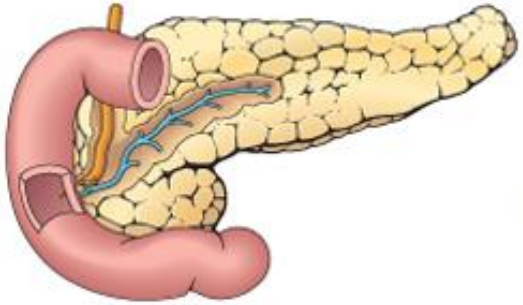
Acute Pancreatitis



Pathogenesis

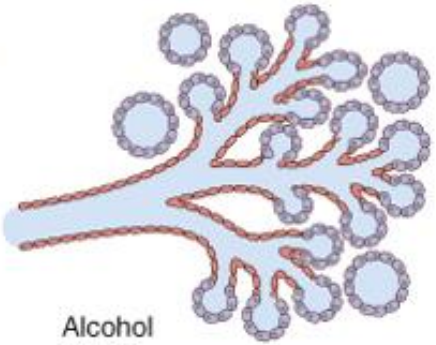
CAUSES:

DUCT OBSTRUCTION



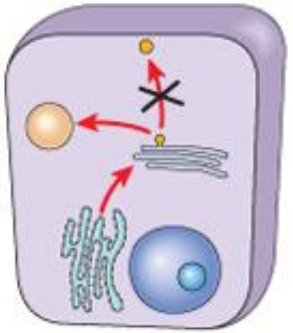
Cholelithiasis
Ampullary obstruction
Chronic alcoholism
Ductal concretions

ACINAR CELL INJURY



Alcohol
Drugs
Trauma
Ischemia
Viruses

DEFECTIVE INTRACELLULAR TRANSPORT



Metabolic injury (experimental)
Alcohol
Duct obstruction

MECHANISMS:

Interstitial edema
↓
Impaired blood flow
↓
Ischemia

Release of intracellular proenzymes and lysosomal hydrolases
↓
Activation of enzymes (intra- or extracellular)

Delivery of proenzymes to lysosomal compartment
↓
Intracellular activation of enzymes

Acinar cell injury
↓
ACTIVATED ENZYMES

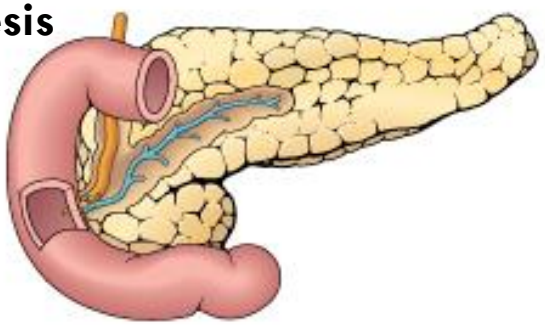
LESIONS:

Interstitial inflammation and edema + Proteolysis (proteases) + Fat necrosis (lipase, phospholipase) + Hemorrhage (elastase)

↓

ACUTE PANCREATITIS

Pathogenesis

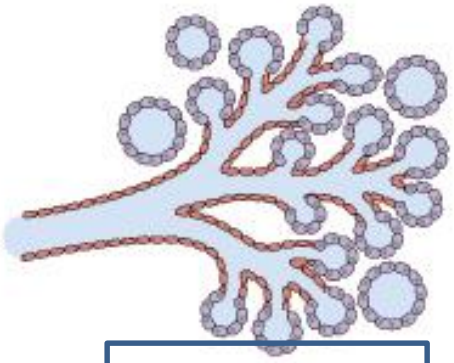


DUCT OBSTRUCTION

Cholelithiasis
Ampullary obstruction
Chronic alcoholism
Ductal concretions
↓
Interstitial edema
↓
Impaired blood flow
↓
Ischemia

ACINAR CELL INJURY

Alcohol
Drugs
Trauma
Viruses
Ischemia



HEREDITARY PANCREATITIS

Mutations in cationic trypsinogen

Intracellular activation of trypsinogen

Intracellular activation and retention of other proenzymes

Acinar cell injury

Proteolysis (proteases) + Fat necrosis (lipase, phospholipase) + Hemorrhage (elastase)

Acinar cell injury response

Interstitial inflammation

ACUTE PANCREATITIS

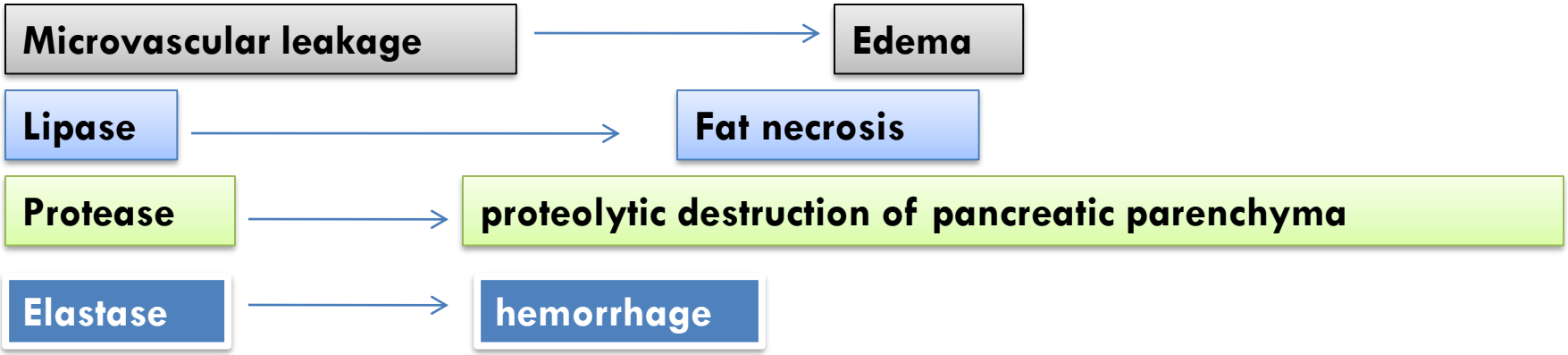
The pancreas is normally protected from autodigestion by synthesis of pancreatic enzymes in the acinar cell in the proenzyme form

Pathogenesis. *autodigestion of the pancreatic substance by inappropriately activated pancreatic enzymes.* Thus, *activation of trypsinogen is an important triggering event in acute pancreatitis.*

Acute pancreatitis: Morphology

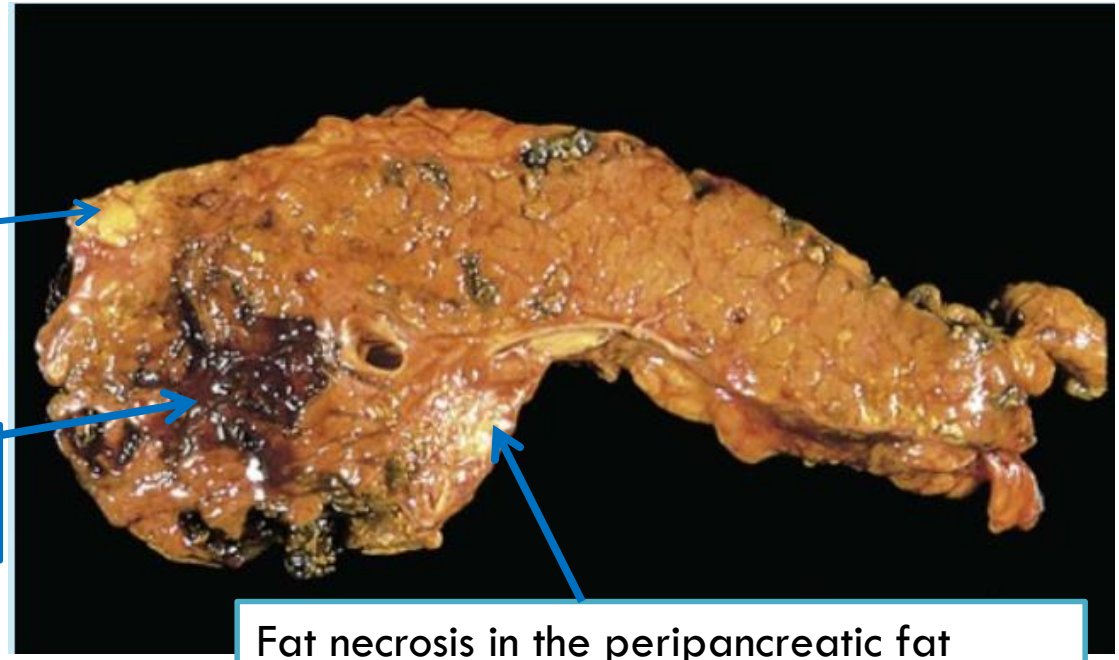
Mild

Severe



Fat necrosis results from enzymatic destruction of fat cells; the released fatty acids combine with calcium to form insoluble salts that precipitate in situ.

Acute pancreatitis: Morphology



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

Acute pancreatitis

Morphology

The morphology of acute pancreatitis ranges from inflammation and edema to severe extensive necrosis and hemorrhage

The basic alterations are:

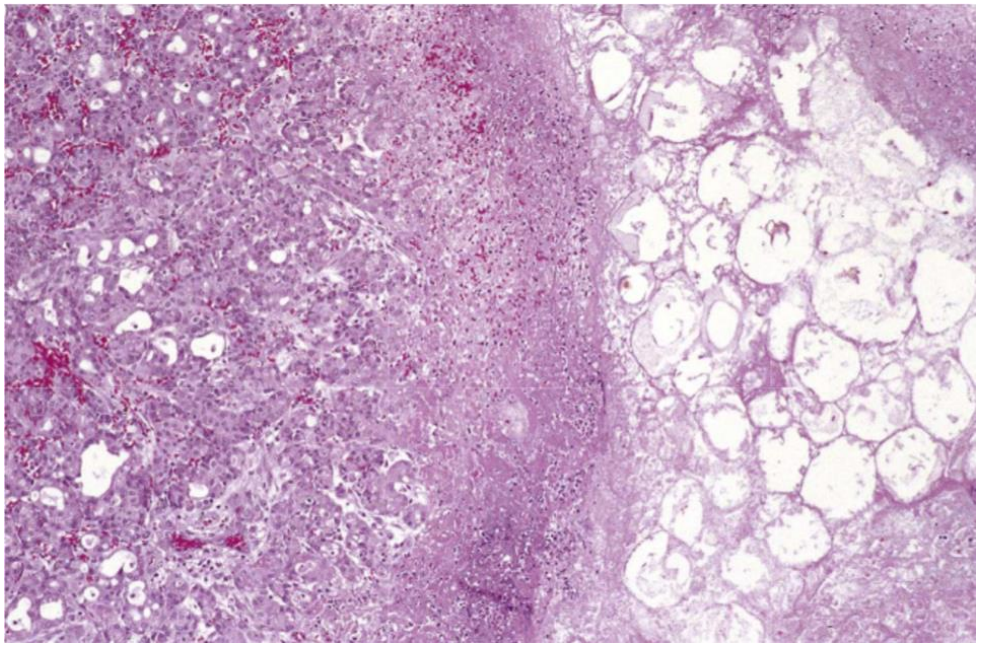
(1) microvascular leakage causing edema

(2) necrosis of fat by lipolytic enzymes

(3) an acute inflammatory reaction

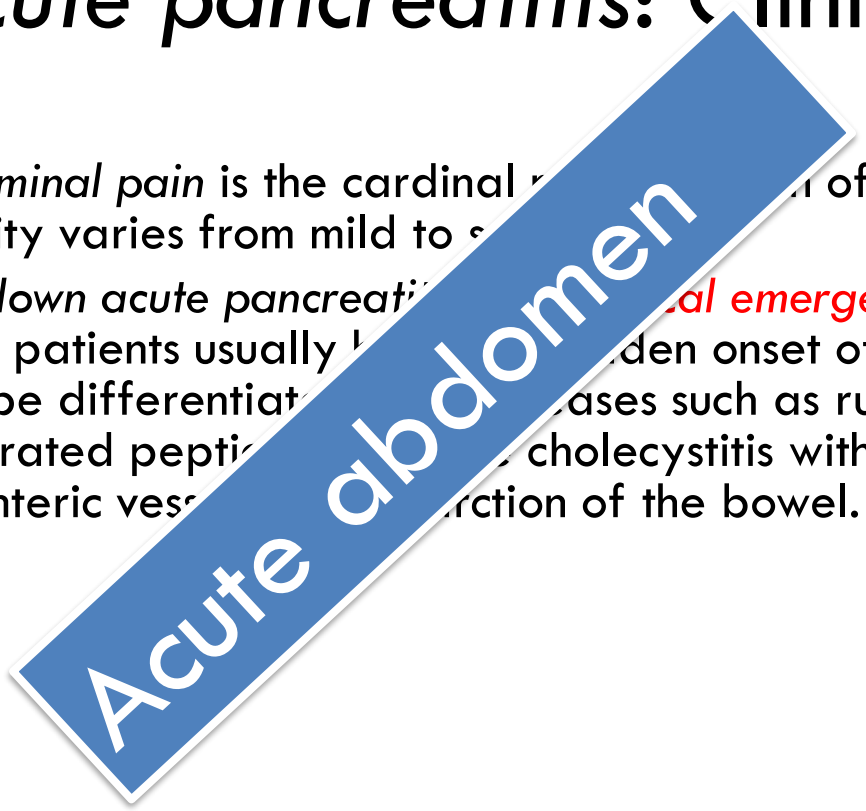
(4) proteolytic destruction of pancreatic parenchyma

(5) destruction of blood vessels with subsequent interstitial hemorrhage.



Acute pancreatitis: Clinical Features.

- *Abdominal pain* is the cardinal [illegible] of acute pancreatitis. Its severity varies from mild to [illegible]
- *Full-blown acute pancreati[illegible]al emergency of the first magnitude*. These patients usually [illegible]den onset of an "acute abdomen" that must be differentiat[illegible]ases such as ruptured acute appendicitis, perforated pepti[illegible] cholecystitis with rupture, and occlusion of mesenteric ves[illegible]rction of the bowel.



Acute pancreatitis: Clinical Features.

Often referred to the upper back

leukocytosis, hemolysis, disseminated intravascular coagulation, acute respiratory distress syndrome

shock with acute renal tubular necrosis may occur Due to peripancreatic collection of fluid

Acute pancreatitis

- *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.

Case study

- A 42-year-old obese woman presents with severe abdominal pain that radiates to the back. The blood pressure is 90/45 mm Hg, Physical examination shows abdominal tenderness, guarding, and rigidity. An X-ray film of the chest shows a left pleural effusion. Laboratory studies reveal elevated serum amylase (850 U/L) and lipase (675 U/L), and hypocalcemia (7.8 mg/dL).

Acute pancreatitis

Acute pancreatitis treatment and prognosis

- The key to the management is "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 include a sterile *pancreatic abscess* and a *pancreatic pseudocyst*.

Chronic pancreatitis

- Chronic pancreatitis is characterized by inflammation of the pancreas with destruction of exocrine parenchyma, fibrosis, and, 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.

Chronic pancreatitis

Chronic pancreatitis

- There is significant overlap in the causes of acute and chronic pancreatitis. By far *the most common cause of chronic pancreatitis is long-term alcohol abuse and biliary tract disease*, and these patients are usually middle-aged males.

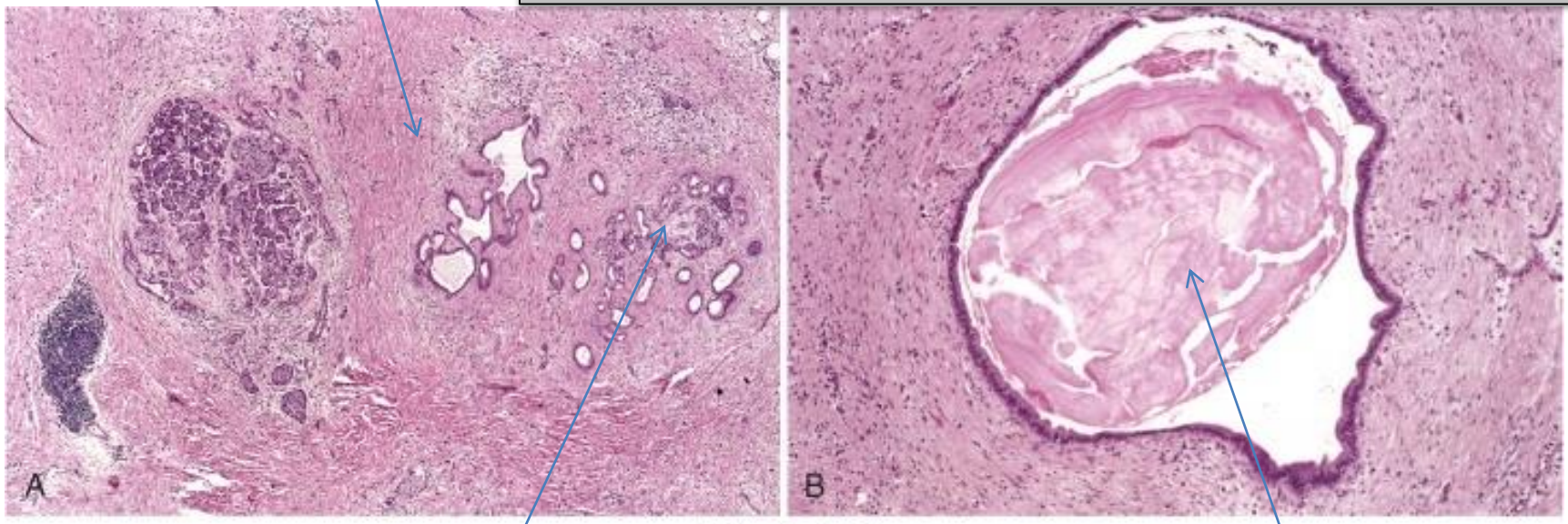
Chronic pancreatitis

Less common causes of chronic pancreatitis include the following:

- Hypercalcemia, hyperlipidemia.
- Long-standing o*bstruction* of the pancreatic duct by pseudocysts, calculi, trauma, neoplasms, or pancreas divisum.
- *Tropical pancreatitis*, which is a poorly characterized disease seen in Africa and Asia. It has been attributed to malnutrition.
- *Hereditary pancreatitis* (*PRSS1* mutations)
- *Idiopathic chronic pancreatitis*.

parenchymal fibrosis

relative sparing of the islets of Langerhans,



Acinar atrophy

Ducts dilatation

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), or the use of opiates and other drugs.

Chronic pancreatitis: Clinical Features

- 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 malabsorption, *diabetes mellitus* (due to destruction of islets of Langerhans),and p*ancreatic pseudocysts.*

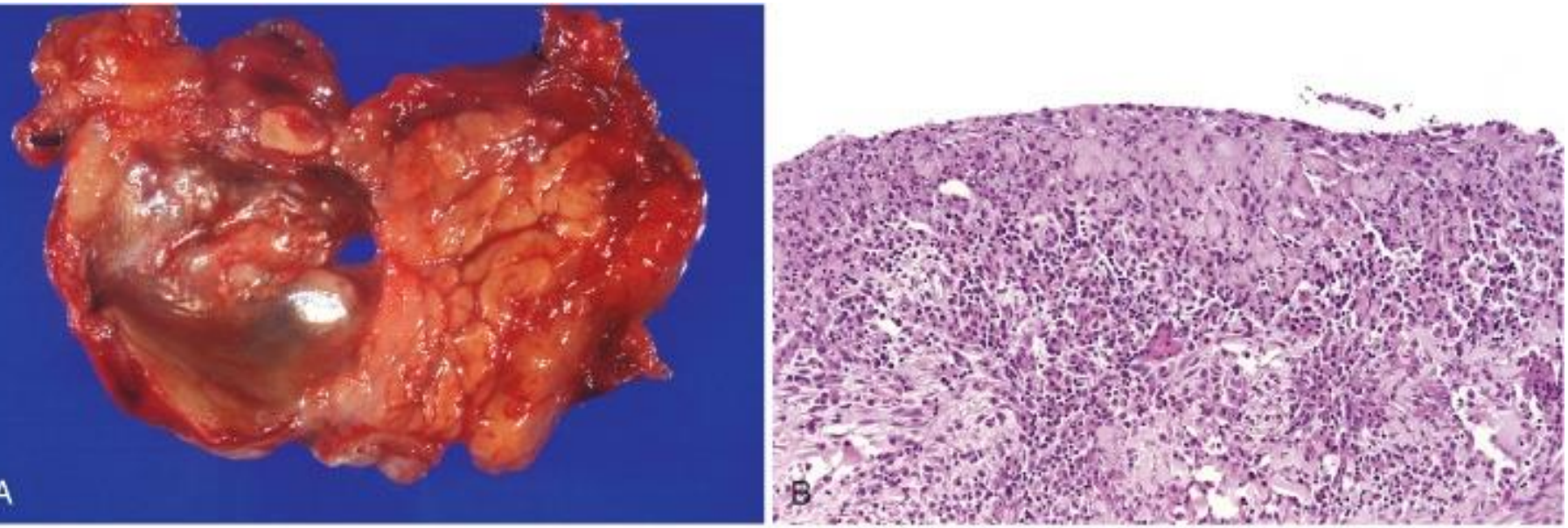
PSEUDOCYSTS OF PANCREAS

- 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.
- Traumatic injury to the abdomen can also give rise to pseudocysts

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



Objectives

- Describe the pathology of acute and chronic pancreatitis
- Understand the pathogenesis of acute and chronic pancreatitis
- Describe the clinical features and possible complications of acute and chronic panreatitis.

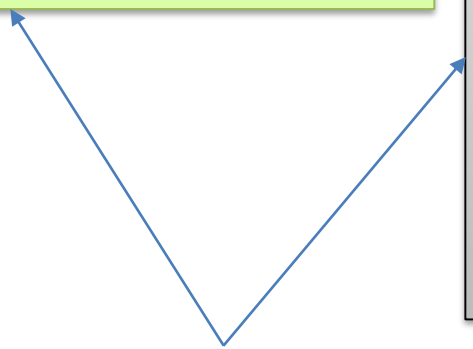
Summary

acute pancreatitis

- Gallstone alcohol others,
- *Activation of trypsinogen*
- Fat necrosis, hemorrhage
- Acute abdomen
- serum amylase

chronic pancreatitis

- *long-term alcohol abuse and biliary tract disease*
- abdominal pain
- Fibrosis, Acinar atrophy
- serum amylase mild ↑
- irreversible impairment in pancreatic function, chronic malabsorption, *diabetes mellitus*



PSEUDOCYSTS

Case study

- A 42-year-old obese woman (BMI = 32 kg/m2) presents
- with severe abdominal pain that radiates to the back. There is no history of alcohol or drug abuse. The blood pressure is 90/45 mm Hg. An X-ray film of the chest shows a left pleural effusion. Laboratory studies reveal elevated serum amylase (850 U/L) and lipase (675 U/L), and hypocalcemia (7.8 mg/dL). Which of the following is the most likely diagnosis?
- (A) Acute cholecystitis
- (B) Acute pancreatitis
- (C) Alcoholic hepatitis
- (D) Chronic calcifying pancreatitis
- (E) Dissecting aortic aneurysm

- **The answer is B: Acute pancreatitis. Acute pancreatitis is**
- defined as an inflammatory condition of the exocrine pancreas
- that results from injury to acinar cells. The disease presents
- with a spectrum of signs and symptoms. Severe forms are
- characterized by the sudden onset of abdominal pain, often
- accompanied by signs of shock (hypotension, tachypnea,
- and tachycardia). The release of amylase and lipase from the
- injured pancreas into the serum provides a sensitive marker
- for monitoring injury to acinar cells. Left pleural effusion is
- a common finding in patients with acute pancreatitis due to
- local irritation below the diaphragm. The other choices do
- not feature increases in serum amylase and lipase.
- **Diagnosis: Pancreatitis, acute**

- Which of the following is most likely associated with the pathogenesis of the condition of the patient described in previous Question ?
- (A) Carcinoid syndrome
- (B) Cholelithiasis
- (C) Insulinoma
- (D) Pancreatic adenocarcinoma
- (E) Portal hypertension

Approximately 80% of acute pancreatitis cases are attributable to either biliary tract disease or alcoholism

- **The answer is B: Cholelithiasis. Some 45% of all patients** with acute pancreatitis also have cholelithiasis, and the risk of developing acute pancreatitis in patients with gallstones is 25 times higher than that in the general population.
- Chronic alcoholism accounts for approximately one third of the cases of acute pancreatitis. Other causes include obstruction of the pancreatic duct by gallstones, intake of drugs, and viral infections. The other choices do not cause acute pancreatitis.
- **Diagnosis: Pancreatitis, acute; cholelithiasis**

- 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
- (E) Miliary tuberculosis

- **The answer is B: Chronic pancreatitis. Chronic pancreatitis is**
- characterized by the progressive destruction of the pancreas,
- with accompanying irregular fibrosis and chronic inflammation.
- Calcification and intraductal calculi often develop.
- Pancreatic insufficiency results in malabsorption syndrome.
- Chronic pancreatitis is most commonly seen in patients with a
- history of alcohol abuse (70% of cases). The other choices are
- not associated with pancreatic calcifications. Although islets
- may be affected by chronic pancreatitis, hypoglycemia is an
- uncommon and late feature of the disease.
- **Diagnosis: Pancreatitis, chronic**

- Which of the following findings is most likely to be encountered in the patient described in previous Question ?
- (A) Achlorhydria
- (B) Hypoglycemia
- (C) Melena
- (D) Pernicious anemia
- (E) Steatorrhea

- **The answer is E: Steatorrhea.**
- **Fat malabsorption in the** setting of chronic pancreatitis is most often associated with steatorrhea. In patients with steatorrhea, the fecal matter is foul smelling and floats because of a high fat content. Longstanding malabsorptive disease is accompanied by nutritional deficiency, including weight loss, anemia, osteomalacia, and a tendency to bleed. Hypoglycemia (choice B) is incorrect because loss of pancreatic islet cells would be associated with hyperglycemia.
- **Diagnosis: Pancreatitis, chronic; steatorrhea**

- A 50-year-old woman complains of persistent abdominal pain,
- anorexia, and abdominal distention. Her past medical history
- is significant for a previous hospitalization for acute pancreatitis.
- Physical examination shows jaundice and a nonpulsatile
- abdominal mass. Laboratory studies reveal normal serum
- levels of bilirubin, AST, and ALT. A CT scan of the abdomen
- shows a fluid-filled cavity in the head of the pancreas. What is
- the most likely diagnosis?
- (A) Acute hemorrhagic pancreatitis
- (B) Insulinoma
- (C) Pancreatic cystadenoma
- (D) Pancreatic islet cell tumor
- (E) Pancreatic pseudocyst

- **The answer is E: Pancreatic pseudocyst. Pancreatic**
- pseudocyst is a late complication of acute pancreatitis, in
- which necrotic pancreatic tissue is liquefi ed through the
- action of pancreatic enzymes (e.g., peptidases, lipases, and
- amylase). The necrotic tissue becomes encapsulated by granulation
- tissue, which then develops into a fi brous capsule.
- Pseudocysts may enlarge to compress and even obstruct the
- duodenum. They may become secondarily infected and form
- an abscess. Choices B, C, and D are not consequences of
- acute pancreatitis.
- **Diagnosis: Pancreatic pseudocyst**