PATHOLOGY TEAM

Pathology and pathogenesis of

Pancreatitis

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Pancreatitis:

Pancreatitis encompasses a group of disorders characterized by inflammation of the pancreas. The clinical manifestations can range in severity from a mild, self-limited disease to a life threatening acute inflammatory process, and the duration of the disease can range from a transient attack to an irreversible loss of function.

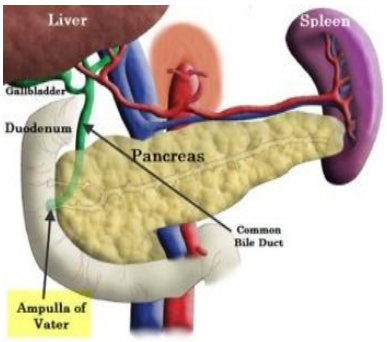
Types:

- In *acute pancreatitis*: gland can return to normal if underlying cause of the pancreatitis is removed.
- In *chronic pancreatitis*: irreversible destruction of exocrine pancreatic parenchyma.

- Acute pancreatitis: inflammation, neutrophils.
- Chronic pancreatitis: fibrosis, lymphocytes.
- What is different about pancreatitis? That there are enzymes in the cells of pancreas, so when it is destructed by inflammation, the enzymes (especially proteolytic enzymes)will diffuse outside .

Acute pancreatitis:

Acute pancreatitis is a group of reversible lesions characterized by inflammation of the pancreas ranging in severity from edema and fat necrosis (because the pancreas is covered by fat) *to parenchymal necrosis with severe hemorrhage.*



Necrosis will lead to calcification.

✓ Causes:

- 80% of cases in Western countries are associated with one of two conditions: biliary tract disease or alcoholism (chronic paccreatitis).
- Gallstones are present in 35% to 60% of cases of acute pancreatitis.

✓ Less common causes of acute pancreatitis include the following:

- Obstruction of the pancreatic duct system eg. periampullary tumors, congenital cystic dilatation of the common bile duct, biliary "sludge," and parasites (particularly *Ascariasis lumbricoides*(people who eat row meat) and *Clonorchis sinensis* organisms).

The **ampulla of Vater**, also known as the **hepatopancreatic ampulla**, is formed by the union of the pancreatic duct and the common bile duct.

- Medications. More than 85 drugs have been reported to cause acute pancreatitis. These include thiazide diuretics, azathioprine , estrogens, etc
- Metabolic disorders, including hypertriglyceridemia (alcohol) , hyperparathyroidism, and other hypercalcemic states
- Acute ischemia induced by vascular thrombosis, embolism, vasculitis and shock
- Trauma, both blunt trauma and iatrogenic injury during surgery or endoscopic retrograde cholangiopancreatography

Etiologic factors in acute pancreatitis

- Metabolic:

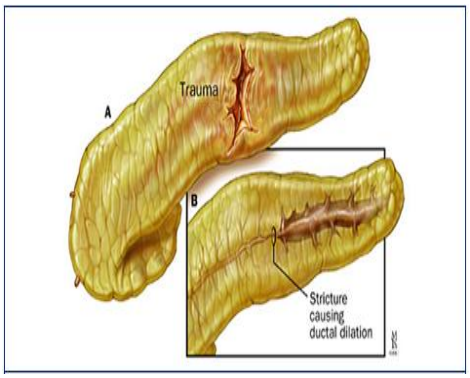
1. Alcoholism
2. Hyperlipoproteinemia
3. Hypercalcemia

hypercalcemia causes stimulation of the acinar cell, increases calcium secretion, and alters the diffusion barrier between the pancreatic duct lumen and the interstitial space.

4. Drugs(e.g.,thiazidediuretics)
5. Genetic.

- Mechanical:

1. Trauma
2. Gallstones (small stones)
3. Iatrogenic injury
4. Perioperative injury
5. Endoscopic procedures with dye injection



- Vascular:

1. Shock
2. Atheroembolism
3. Polyarteritis nodosa

- Infectious:

1. Mumps
2. Coxsackievirus
3. Mycoplasma Pneumonia

Acute Pancreatitis: Morphology

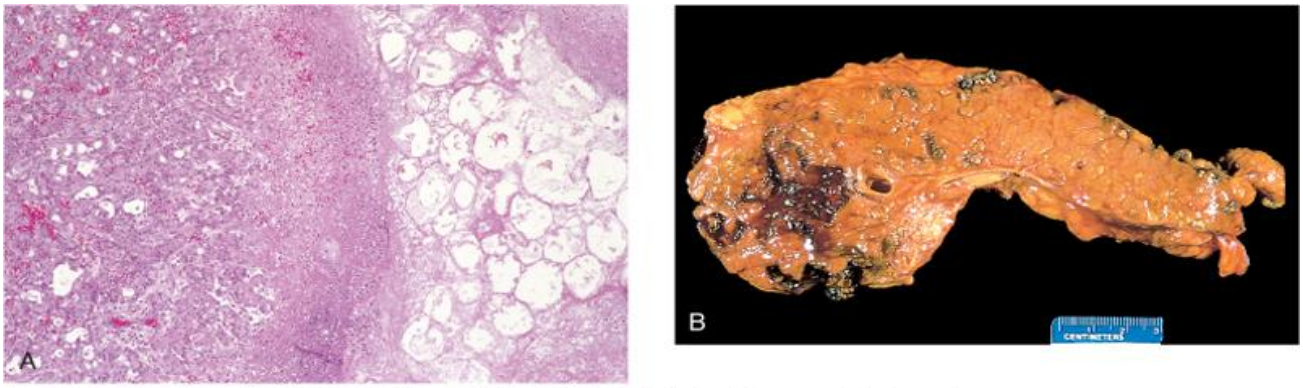
- The morphology of acute pancreatitis ranges from inflammation and edema to severe extensive necrosis and hemorrhage.

Bleeding is because of the digestion of the blood vessels by the enzyme (

- 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.

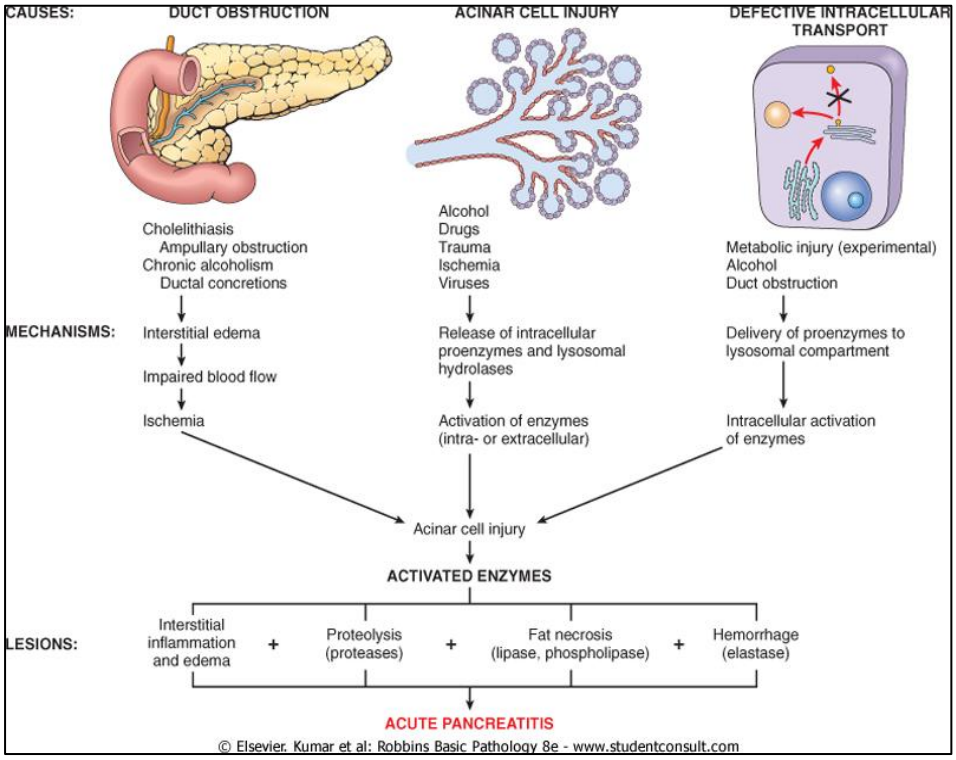
Fat necrosis, as we have seen, results from enzymatic destruction of fat cells. The released fatty acids combine with calcium to form insoluble salts that precipitate in situ.(dystrophic calcification).



Pathogenesis of Acute Pancreatitis

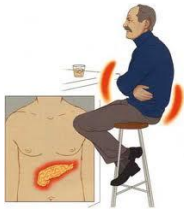
- *autodigestion of the pancreatic substance by inappropriately activated pancreatic enzymes*. Thus, *activation of trypsinogen is an important triggering event in acute pancreatitis*.

Trypsinogen is the precursor form or zymogen of the pancreatic enzyme trypsin.it is required for protein digestion.



Clinical features

- *Abdominal pain* is the cardinal manifestation of acute pancreatitis. Its severity varies from mild to severe.



- *Full-blown acute pancreatitis is a medical emergency of the first magnitude*. These patients usually have the sudden onset of an "acute abdomen" that must be differentiated from diseases such as ruptured acute appendicitis, perforated peptic ulcer, acute cholecystitis with

rupture, and occlusion of mesenteric vessels with infarction of the bowel.

- Characteristically, the pain is constant and intense and is often referred to the upper back referred To the upper back (because It is a retroperitoneal organ). There is *leukocytosis*, *hemolysis*, *disseminated intravascular coagulation*, *fluid sequestration, acute respiratory distress syndrome*, *and diffuse fat necrosis*. *Peripheral vascular collapse and shock with acute renal tubular necrosis may occur* .

Laboratory findings

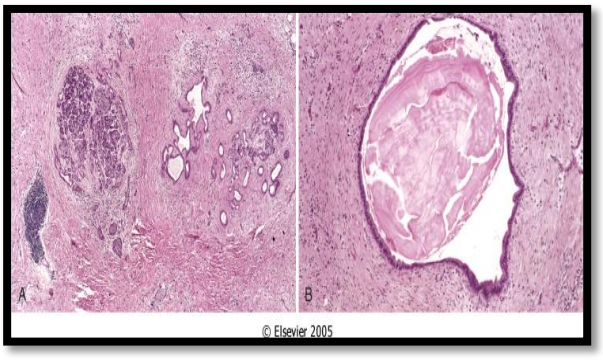
marked elevation of serum amylase levels during the first 24 hours, followed within 72 to 96 hours by a rising serum lipase level.

Management

- The key to the management is "resting" the pancreas by total restriction of food and fluids and by supportive therapy.
- A naso-gastric tube may be implanted so it can suck any secretion.
- IV fluids for nutrition,antibiotics,and morphine are also given as management
- 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

- 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. *A*, Extensive fibrosis and atrophy has left only residual islets (*left*) and ducts (*right*), with a sprinkling of chronic inflammatory cells and acinar tissue. *B*, A higher-power view demonstrating dilated ducts with inspissated eosinophilic ductal concretions in a patient with alcoholic chronic pancreatitis.

How to differentiate it with malignant tumor ?

By desmoplastic reaction:**desmoplasia** is the growth of fibrous or connective tissue causing dense fibrosis around the tumor.[1]

- 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.
- 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.

Less common causes of chronic pancreatitis include the following:

- Hypercalcemia, hyperlipidemia.
- Long-standing *obstruction* 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.*
- *Idiopathic chronic pancreatitis*. (autoimmune)

Chronic Pancreatitis: Morphology

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:

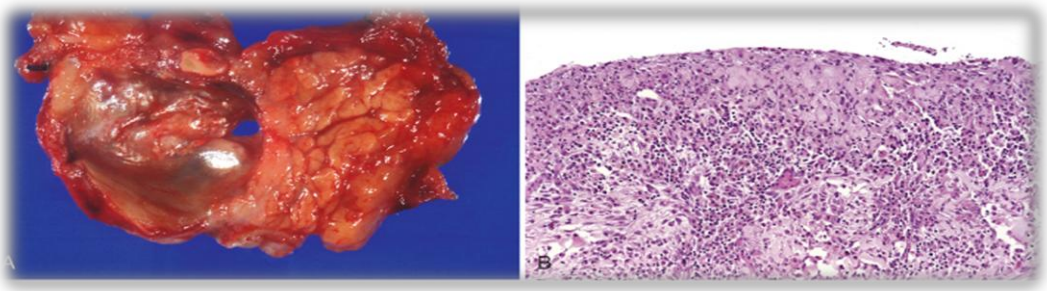
- During an attack of abdominal pain, there may be mild fever and mild-to-moderate elevations of serum amylase.
- Calcifications can be seen within the pancreas by CT scan and ultrasonography.
- Complications: Severe *pancreatic exocrine insufficiency,* chronic malabsorption, *diabetes mellitus* (due to destruction of islets of Langerhans), *severe chronic pain* 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.

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.



Pancreatic pseudocyst. *A*, Cross-section through this previously bisected lesion revealing a poorly defined cyst with a necrotic brown-black wall. *B*, Histologically, the cyst lacks a true epithelial lining and instead is lined by fibrin and granulation tissue.

SUMMARY

Acute pancreatitis is characterized by inflammation and reversible parenchymal damage with lesions ranging from focal edema and fat necrosis to widespread parenchymal necrosis and hemorrhage; clinical manifestations vary from mild abdominal pain to a rapidly fatal vascular collapse.

Chronic pancreatitis is characterized by irreversible parenchymal damage and scar formation; clinical manifestations include chronic malabsorption (due to pancreatic exocrine insufficiency) and diabetes mellitus (due to islet cell loss).

Both entities share similar pathogenic mechanism, and indeed recurrent acute pancreatitis can result in chronic pancreatitis.

Ductal obstruction and alcohol are the most common causes of both forms. Inappropriate activation of pancreatic digestive enzymes (due to mutations in genes encoding trypsinogen or trypsin inhibitors) and primary acinar injury (due to toxins, infections, ischemia, or trauma) also cause pancreatitis.

Questions

1_ Ali came to the emergency department after an accident, complaining of severe abdominal pain, after investigation the pathology department reported; fat necrosis and inflammation.

So the doctor suspected:

A. Acute pancreatitis.
B. Tuberculosis.
C. Cancer.

2_ The most common cause of chronic pancreatitis is:

A. Hypertension.
B. Cancer.
C. Alcohol.