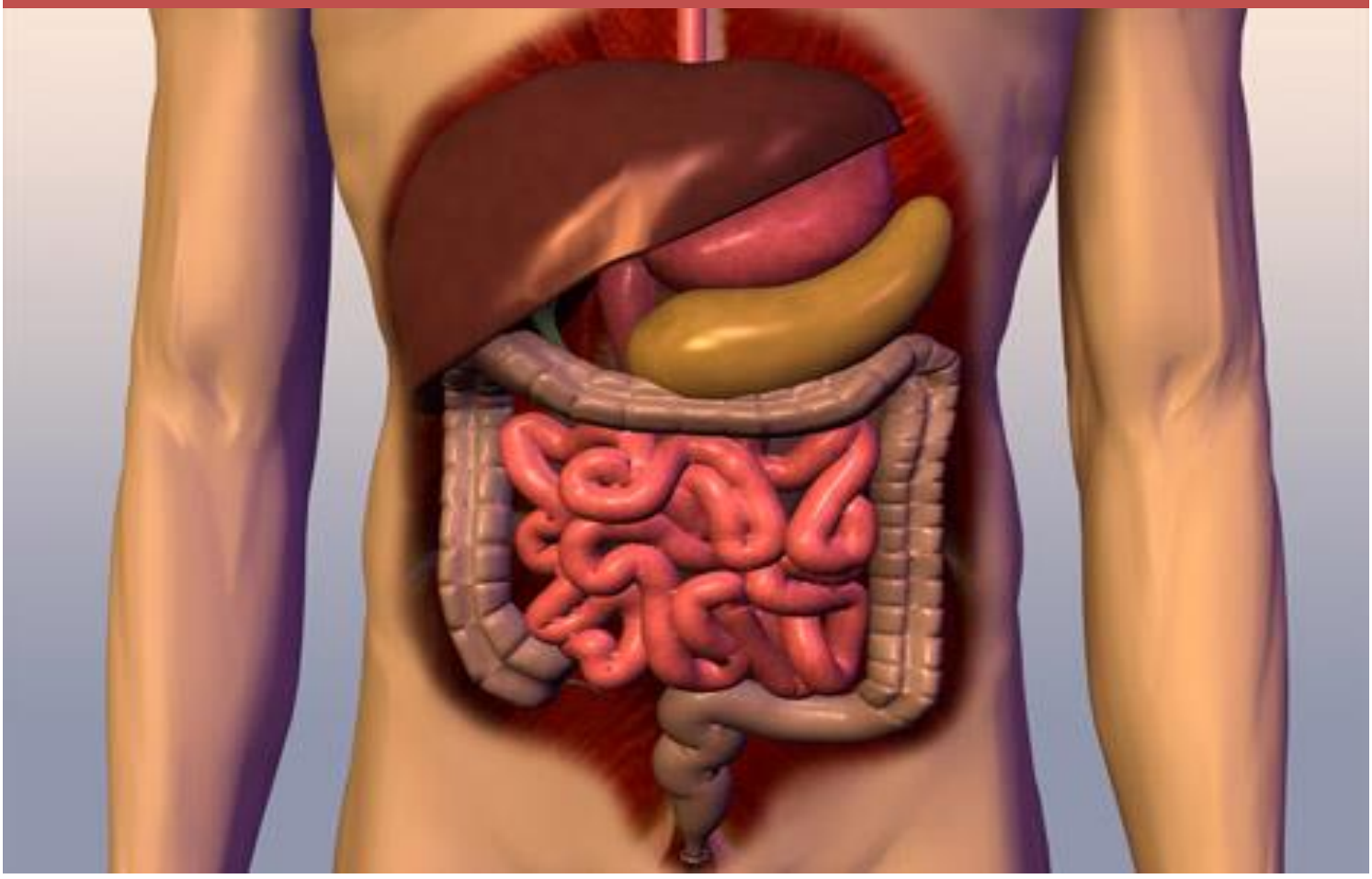

Lecture Four **Pathology and pathogenesis of**

Pancreatitis

*432 **Pathology** Team*

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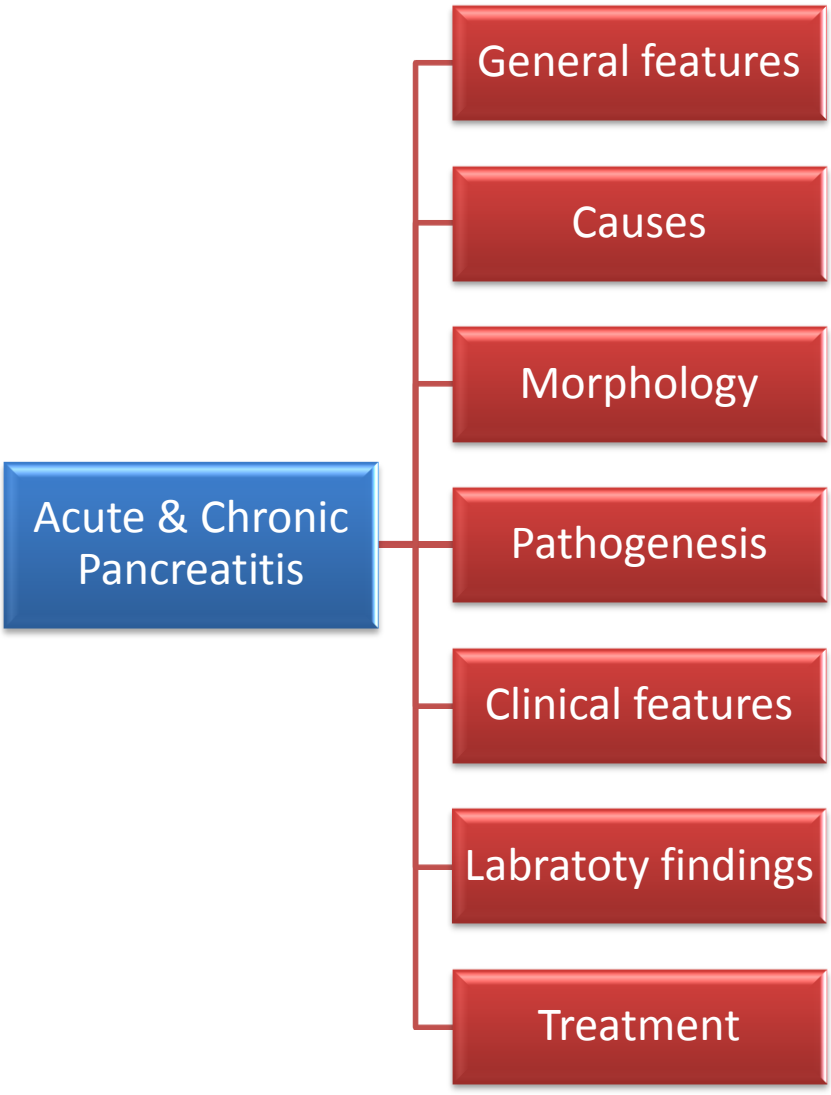
GIT Block

Color Index: female notes are in Green. Male notes are in Blue. Red is important. Orange is explanation.

Pathology and pathogenesis of pancreatitis

Mind Map:



Pancreatitis

Definition:

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.

1- Acute pancreatitis (*Reversible*):

The gland can return to normal if underlying cause of the pancreatitis is removed. The inflammation of the pancreas is ranging in severity from edema and fat necrosis to parenchymal necrosis with severe hemorrhage.

Causes:

Common

1- Biliary tract disease (gallbladder stones) (mainly in the acute) Small stones can travel through the biliary track and block it while large stones are more likely the cause of cancer.
2- Alcoholism (mainly in the chronic).

Less common

1- Obstruction of the pancreatic duct system e.g. periampullary tumors*, congenital cystic dilatation of the common bile duct, biliary sludge**, and parasites (particularly Ascarasis lumbricoides and Clonorchis sinensis organisms)
2- Medications. More than 85 drugs have been reported to cause acute pancreatitis. These include thiazide diuretics, azathioprine , estrogens, etc
3- Metabolic disorders, including hypertriglyceridemia, hyperparathyroidism, hyperlipoproteinemia and other hypercalcemic states (lead to calcification then stone)
4- Acute ischemia induced by vascular thrombosis, embolism, vasculitis and shock
5- Trauma, perioperative injury, both blunt trauma and iatrogenic injury during surgery or endoscopic retrograde cholangiopancreatography***
6- Genetic
(Autosomal dominant mutation in (PRSS1) gene which encodes for trypsinogen which results in hyperactivity of trypsin and autolysis. or mutation in (SPINK1) gene which encodes a trypsin inhibitor).
7- Infection: Such as Coxackievirus (causes DM type 1), Mumps and Mycoplasma pneumonia.

NOTE: * Periampullary cancer is a cancer that forms near the ampulla of Vater, an enlargement of the ducts from the liver and pancreas where they join and enter the small intestine, It presents with painless jaundice which may be intermittent in nature because of the sloughing of the tumor tissue relieving the obstruction intermittently.

** Biliary sludge is a mixture of particulate matter and mucous that forms in bile (eg: cholesterol crystals and calcium salts)

*** Endoscopic retrograde cholangiopancreatography is a procedure that combines upper gastrointestinal (GI) endoscopy and x rays to treat problems of the bile and pancreatic ducts.

Morphology:

(1) **Microvascular leakage causing edema.**

(2) **Necrosis of fat by lipolytic enzymes** (Fat necrosis, results from enzymatic destruction of fat cells. The released fatty acids combine with calcium to form insoluble salts that precipitate in situ.)

(3) **An acute inflammatory reaction.**

(4) **Proteolytic destruction of pancreatic parenchyma.**

(5) **Destruction of blood vessels with subsequent interstitial haemorrhage.**

Pathogenesis:

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

Clinical features:

1- Abdominal pain (epigastric pain) is the cardinal manifestation of acute pancreatitis. Its severity varies from mild to severe.
2- 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.
3- Characteristically, the pain is constant and intense and is often referred to the upper back. There is leukocytosis, hemolysis, disseminated intravascular coagulation (serious complication) , fluid sequestration, acute respiratory distress syndrome, and diffuse fat necrosis. Peripheral vascular collapse and shock with acute renal tubular necrosis may occur.
4- If it is very severe we may see petechiae.

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. Coagulation may be disturbed (Clots formation and haemorrhage).

Treatment:

- The key to the management is **"resting"** the pancreas by total restriction of food and fluids and by supportive therapy (NPO)*.
- 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

NOTE: *NPO = Nothing Per Os (mouth) is a medical instruction meaning to withhold oral food and fluids from a patient to decrease secretions in the GI. We put a nasogastric tube (Ng tube) to aspirate secretions of stomach instead of going to the duodenum.

2- Chronic pancreatitis (*Usually in middle aged men*):

Irreversible destruction of exocrine pancreatic parenchyma
(Can occur without an acute attack)

- 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.➔If these occur will lead to diabetes.

- The chief distinction between acute and chronic pancreatitis is the irreversible impairment in pancreatic function that is characteristic of chronic pancreatitis.

Causes:

Common

1- Biliary tract disease (gallbladder stones) (mainly in the acute) Small stones can travel through the biliary track and block it while large stones are more likely the cause of cancer.
2- Alcoholism (mainly in the chronic)

Less common

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

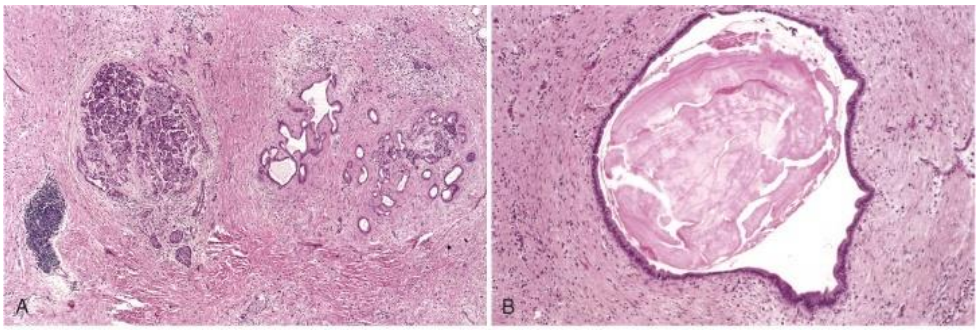
Morphology:

(1) 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

(2) 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 (Dystrophic calcification).

Microscopically:



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.

Pathogenesis:

Although the pathogenesis of chronic pancreatitis is not well defined, several hypotheses are proposed.

- ***Ductal obstruction by concertion.*** Many of inciting agents in chronic pancreatitis (e.g. alcohol) increase the protein concentration of pancreatic secretion, and these proteins can form **Ductal plugs.**
- ***Toxic- metabolic.*** Include alcohol and its metabolites, can exert a direct toxic effect on **Acinar cells,** leading to lipid accumulation, acinar cells loss, and eventually parenchymal fibrosis.
- ***Oxidative stress.*** Alcohol-induce oxidative stress may generate free radical in **acinar cells,** leading to membrane damage.

NOTE: **Duct obstruction which causes increased intraductal pressure which causes accumulation of enzymes including lipase leading to fat necrosis**

Clinical features:

1- 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.

2- 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.

3- Complications: Severe pancreatic exocrine insufficiency, chronic malabsorption, diabetes mellitus (due to destruction of islets of Langerhans), severe chronic pain and pancreatic pseudocysts.

Laboratory findings:

In end-stage, acinar destruction may be so advanced that enzyme elevations are absent.

NOTE: **It is hard to differentiate between chronic pancreatitis and pancreatic neoplasm; chronic pancreatitis shows atipia and is hard when palpated.**

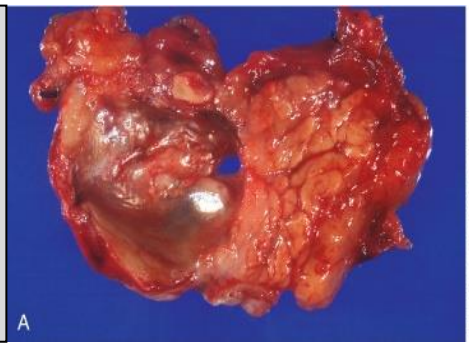
Pseudocysts of Pancreas:

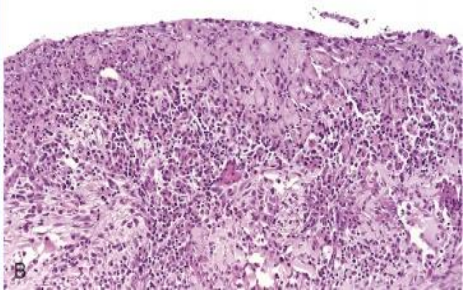
- Pseudocysts are localized collections of necrotic-haemorrhagic material rich in pancreatic enzymes. Such cysts lack an epithelial lining (hence the prefix "pseudo"), and they account for majority of cysts in the pancreas.
- Pseudocysts usually arise after an episode of acute pancreatitis, or of chronic alcoholic pancreatitis.
- Traumatic injury to the abdomen can also give rise to pseudocysts.
- 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 haemorrhage or peritonitis.

Morphology of Pseudocysts:

Pseudocysts are usually solitary. Pseudocysts can range in size from 2 to 30 cm in diameter.

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.





A Pancreas is transplanted in the arm under the skin in diabetic patients because the location is easily accessible

Summary (from Robbins Basic Pathology)

Pancreatitis

- **Acute pancreatitis is characterized by inflammation and reversible parenchymal damage that ranges from focal edema and fat necrosis to widespread parenchymal necrosis and hemorrhage; the clinical presentation varies widely, from mild abdominal pain to rapidly fatal vascular collapse.**
- **Chronic pancreatitis is characterized by irreversible parenchymal damage and scar formation; clinical presentations include chronic malabsorption(due to pancreatic exocrine insufficiency) and diabetes mellitus (due to islet cell loss)**
- **Both entities share similar pathogenic mechanisms, and indeed recurrent acute pancreatitis can result in chronic pancreatitis. Ductal obstruction and long term alcohol abuse are the most common causes of both forms. Inappropriate activation of pancreatic digestive enzymes (due to mutation in genes encoding trypsinogen or trypsin inhibitors) and primary acinar injury (due to toxins, infections, ischemia or trauma) also can cause pancreatitis.**

Helpful Videos:

Click control then click the link if you cannot click it directly

Anatomy and Role of The Pancreas

Acute Pancreatitis

Management and Treatment of Acute Pancreatitis

Chronic Pancreatitis

Questions

1/ A 42-year-old obese woman (BMI = 32kg/m2) presents with severe abdominal pain that radiates to the back. There is no history of alcohol or drug abuse. The blood pressure is 90/45mmHg, respirations are 32 per minute, and pulse is 100 per minute. 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 (850U/L) and lipase (675U/L), and hypocalcemia (7.8mg/dL). Which of the following is the most likely diagnosis?

(A) Acute cholecystitis
(B) Acute pancreatitis
(C) Alcoholic hepatitis
(D) Chronic calcifying pancreatitis

2/ 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 fol- lowing is the most likely diagnosis?

(A) Carcinoid syndrome
(B) Chronic pancreatitis
(C) Crohn disease
(D) Miliary tuberculosis

3/ which of the following findings is most likely to be encountered in the patient described in Question above?

(A) Achlorhydria
(B) Hypoglycemia
(C) Melena
(D) Steatorrhea

4/ A 52 year old male present to the accident and emergency complaining of a severe abdominal pain radiating to the back. The patient is known alcoholic . He is found to have increased serum amylase. What is the most likely diagnosis in this case?

(A) Chronic pancreatitis
(B) Acute pancreatitis
(C) Perforated colon
(D) Acute appendicitis

5/ A 67 year old male is operated for removal of a pancreatic lesion. The patient history includes an episode of acute pancreatitis 2years ago. The most likely histological feature on microscopic examination is the presence of a:

(A) Serous cyst
(B) Mucinous cyst
(C) Pancreatic pseudocyst
(D) Choledocal cyst

6/ Fibrosis, cystic dilatation of the ducts, loss of the pancreatic acini and lymphocytic infiltration of the pancreas are most likely seen in:

(A) Chronic pancreatitis
(B) Infiltrating ductal carcinoma of the pancreas
(C) Acute pancreatitis
(D) Solid pseudopapillary tumor of the pancreas

7/ Patients with acute pancreatitis may develop:

(A) Loss of the islets of Langerhans and the onset of diabetes.
(B) Acinar cell carcinoma secondary to the inflammation
(C) Cushing syndrome with hypercortisolemia
(D) Solid pseudopapillary tumor of the pancreas

8/ The most frequent cause of acute pancreatitis is:

(A) Ascariasis lumbricoides
(B) Periampullary tumor
(C) Gallbladder stones
(D) Medications

9/ what are the most frequent laboratory findings in patients with acute pancreatitis?

(A) Elevation of serum lipase followed by elevation of amylase.
(B) Normal amylase level with elevation of lipase level only.
(C) Normal lipase level with elevation of amylase level only
(D) Elevation of amylase levels followed by a rising of lipase.

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

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*Good Luck ^_^*