pancreas

- **Pancreas composed of 2 parts:**
- **1- exocrine gland**
- **2- endocrine gland**

Acute pancreatitis

- **Inflammation of the pancreas associated with acinar cell injury**

- Clinical features:
- **1-abdominal pain**

  cardinal sign

  mild-severe

  epigastric in location with

  radiation to the back

- **2-shock**

-It is due to:

-Pancreatic hemorrhage

-Release of vasodilating agents as bradykinin & PGs

-It results in electrolyte imbalance , loss of blood volume & toxemia

- **<u>3- increased serum amylase level</u>**

-It inceases within the first 12 hrs & back to normal within 48-72 hrs

- **<u>Other conditions associated with increase in amylase serum level are:</u>**

1-perforated gastric ulcer

2-pancreatic carcinoma

3-intestinal obstruction

4-perotinitis

5-secondary pancreatic disease

- **4-increase serum lipase level**

-It increases within 72-96 hrs & lasts for 7-10 days

- It is highly sensitive & specific for acute pancreatitis

- **5-hypocalcemia**

- Calcium binds fatty acids released from lipolysis of fat in the abdomen

- **6-Jaundice ,hyperglycemia & glycosuria occur in less than 50% of cases**
- **7-ARDS & acute renal failure**

Causes of acute pancreatitis

1-pancreatic duct obstruction (35-60 %)

a.gall bladder stones (25X increase risk)

b.cystic fibrosis

c.tumors

d.edema

e.parasites e.g Ascaris

2-direct injury of acinar cells of pancreas

a.ethanol

b.viruses

c.drugs as diuretics

d.trauma

e.acute ischemia , shock,vasculitis -----

f.hypercalcemia

g.hyperlipidemia

h.obesity

3- idiopathic

10-20% of the cases

4-hereditary pancreatitis

Aut. Dominant trait

Mutation in PRSS1 gene →typsonigen &trypsin become resistant to inactivation

Pathogenesis

1- autodigestion of pancreatic tissue by activated pancreatic enzymes (chemotrypsinogen,proelastase, prophospholipase& trypsinogen)

2-cellular injury response mediated by proinflammatory cytokines

3-defective I.C transport of proenzymes within acinar cells

- normally pancreatic enzymes are present in acinar cells as proenzyme forms (zymogen granules) & confind to membrane-bound compartment before secrtion

-zymogen granules release their enzymes into the apical lumen for delivery via the pancreatic duct to the duodenal lumen

-trypsin is a major activator of other proenzymes which is synthesized by acinar as proenzyme trypsinogen

- **in acute pancreatitis proenzymes are activated & released from zymogen granules within the acinar cells →dammage of acinar cells & fatty tissue in & around the pancreas → damage of elastic tissue of blood vessels → hemorrhage**

-premature activation of proenzymes esp.trypsinogen is the key step & it is favoured by:

1-low pH

2-increased I.C calcium

3-cathepsin B within lysosomes

Activated trypsin →

Prekallikrin → active form
→stimulate kinin system,Hagman factor(factor XII) & clotting & complement factors → small vessels thrombosis → rupture
→hemorrhage

- damaged acinar cells release potent cytokines →attraction of neutrophils & macrophages →release of more cytokines as IL-1,NO,PAF →inflammation & pancreatic damage

Mrphology of acute pancreatitis

-It is related to duration & severity

-features:

1-proteolytic destruction of pancreatic substance

2-necrosis of blood vessels & interstitial hemorrhage

3-necrosis of fat by lipase

4-acute inflammatory reaction

-Fat necrosis is most characteristic

Fat hydrolysis→ glycerol →reabsorbed

FFA

↓

combine with Ca++ (saponification)

insoluble salts(calcification)

-Pancreatic pseudocyst are formed in 50% of the cases

-suppurative appendicitis

-obstruction of duodenum

-abscess formation

-hemorrhages

Prognosis:

-mortality is high 20-40%

-death is usually due to:-

1-shock

2-abdominal sepsis

3-ARDS

Chronic pancreatitis

- **Repeated bouts of mild-moderate pancreatic inflammation with progressive loss of pancreatic parenchyma & fibrosis.**

Predisposing factors

1-alcoholism
2-hypercalcemia
3-hyperlipoproteinemia
4-long standing obstruction of pancreatic duct
5-biliary tract disease
6-hereditary
7-hemochromatosis
8-cystic fibrosis
9-idiopathic (40% of cases)

Pathogenesis

-increased secretion of proteins from acinar cells in the absence increased fluid secretion →percipitation of proteins →admixture with cellular debris →ductal plugs →ductal stones

-decreased acinar proteins that inhibits percipitation of Ca++ →calcification →

obstruction of small ducts →atrophy

-iflammation→toxic metabolites →oxidative stress

-necrosis and fibrosis

Morphology

-Atrophy of exocrine gland

-fibrosis

-chronic inflammation

-destruction of pancreatic ducts

-ductal protein plugs

-calcifications

-pseudocysts

Clinical features

-asymptomatic

-attacks of abdominal pain

-recurrent attacks of jaundice

-indigestion

-diabetes mellitus

-weight loss

-malabsorption

diagnosis

-increased amylase & lipase in the serum

-calcifications in the pancreas on x-ray or CT scan

-presence of pseudocysts

Pancreatic carcinoma

-Peak incidence 60-80 yr

<u>-Predisposing factors:</u>

1-smoking

2-hereditary pancreatitis (increase risk 40X)

3-genetic mutations

- **K-RAS gene mutation (80-90%)**
- **CDKN2A (P16) mutation (95%)**
- **SMAD (55%)**
- **T_{53} gene mutation (>50-70%)**
- **HER2/NEU amplification (>50% of the cases)**
- **BRCA2 gene mutation**

epidemiology

-M : F = 3 : 1 in youngs

1 : 1 in olds (>60yrs)

-blacks > whites

Risk factors

1-smoking icreases the risk by 2-3X

2-chemical carcinogens

3-meat & fat-rich diet

4-D.M

5-chronic pancreatitis

-location:

60-70%	head of the pancreas
10-15%	body
5%	tail
20%	diffuse infiltration

General features :

-adenocarcinoma

-desmoplastic reaction

-ulceration of duodenal mucosa

-dilatation of biliary tree

-involvement of adjacent organs as spleen, adrenal, vertebra, colon, stomach---

-perineural invasion

Metastesis

-liver & regional lymph nodes

-lung ,bones , adrenals , peritoneum

Clinical presentation

-silent

-pain

-weight loss

-obstructive jaundice

-migratory thrombophlebitis (Trousseau sign)
in 10% of the cases

-acute painless dilatation of GB & jaundice (Courvoisie sign)

-increased CEA & CA 19.9 Ag in the serum

Prognosis

-50% of cases die within 6 months

-5-yr survival is < 1%