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
• **3- increased serum amylase level**

- It increases within the first 12 hrs & back to normal within 48-72 hrs
Other conditions associated with increase in amylase serum level are:

1. perforated gastric ulcer
2. pancreatic carcinoma
3. intestinal obstruction
4. peritonitis
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 secretion
-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 → damage 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
Morphology 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 $\rightarrow$ glycerol $\rightarrow$ reabsorbed FFA

$\downarrow$

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 $\rightarrow$ precipitation of proteins $\rightarrow$ admixture with cellular debris $\rightarrow$ ductal plugs $\rightarrow$ ductal stones

-decreased acinar proteins that inhibits precipitation of Ca++ $\rightarrow$ calcification $\rightarrow$ obstruction of small ducts $\rightarrow$ atrophy
- inflammation $\rightarrow$ toxic metabolites $\rightarrow$ 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
-Predisposing factors:
  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 increases 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
**Metastasis**

- 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%