

DISORDERS OF THE GALLBLADDER

❖ Cholelithiasis

- Very common health problem
- Two main types:
 - Cholesterol
 - Bile pigments

❖ Pathogenesis

- Cholesterol stones:
 - Cholesterol is water insoluble
 - Cholesterol is eliminated through the bile
 - Bile supersaturation
 - Nucleation
 - Formation of cholesterol Crystals

- Most are radiolucent

❖ Risk factors

- Cholesterol stones:
 - Demography
 - Age
 - Female gender
 - Oral contraceptive pills
 - Pregnancy
 - Obesity
 - rapid weight reduction
 - G.B. hypomotility



❖ Pathogenesis

- Pigment stones
 - Unconjugated bilirubin in the biliary tree
 - Precipitate as insoluble calcium bilirubinate salts
- Most are radiopaque

❖ Risk factors

- Pigment stones
 - Demography
 - Chronic hemolytic syndromes
 - Biliary infections

❖ Clinical features

- May be silent
- Pain : constant or colicky
- Complications :
 - Empyema
 - Perforation with abscess formation
 - Fistula formation/ peritonitis
 - Bacterial superinfection with cholangitis and sepsis
 - Pancreatitis
- ? More dangerous: large or small stones

Cholecystitis

- Inflammation of the gall bladder
 - Acute
 - Chronic
 - Acute superimposed on chronic
- Almost always associated with gall stones
- ❖ **Clinical features**
- Complications:
 - Bacterial superinfection with cholangitis or sepsis
 - Perforation and abscess formation
 - Rupture with peritonitis
 - Fistula formation

Cholecystitis

❖ **Acute calculous cholecystitis:**

- Acute inflammation & stones
- May be sudden and severe or mild and resolve spontaneously
- Precipitated by obstruction of the cystic duct → acute surgical emergency → emergency cholecystectomy
- Started as chemical irritation and inflammation due to bile flow obstruction → disruption of the mucosal lining → exposure to destructive effect of bile salts
- Might be superimposed by bacterial infections

❖ **Acute acalculous cholecystitis**

- Postoperatively after major surgeries
 - Severe trauma
 - Severe burns
 - Sepsis
- Multifactorial: dehydration, gallbladder stasis, vascular insufficiency, bacterial infections

❖ **Chronic cholecystitis**

- Almost always associated with stones
- Supersaturation of bile → both chronic inflammation and stone formation
- Microorganisms e.g. E.coli --- 30% of cases
- Symptomatic after long standing mild inflammation and presence of gall stones

Carcinoma of the Gall bladder

❖ **Carcinoma of the Gall bladder**

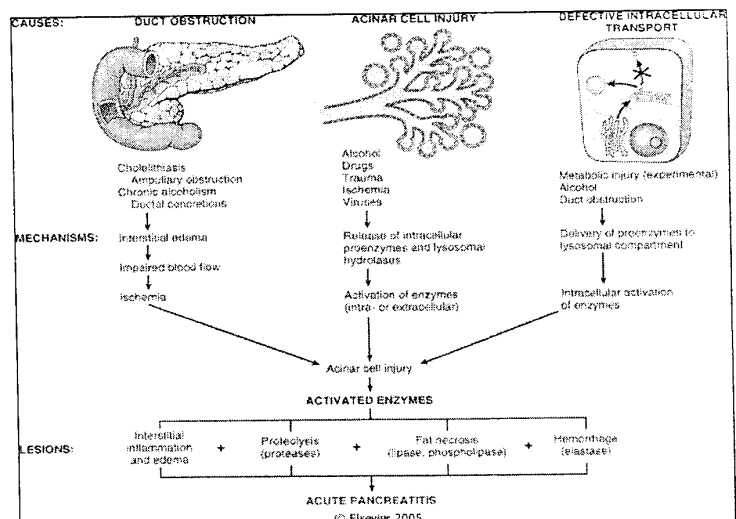
- Women > men
- Old age
- Mostly are adenocarcinoma
- Usually not resectable
- Up to 90% of cases has gall stones
- Parasitic diseases are involved in endemic areas

PANCREATITIS

- Inflammation of pancreas associated with acinar cell injury
 - Acute or chronic
- ❖ **Acute pancreatitis :**
 - Acute abdominal pain
 - Enzymatic necrosis and acute inflammation of the pancreas
 - Destruction of panc. parenchyma (protease)
 - Fat necrosis (lipase)
 - Vasculature damage (elastase)
- **Etiology :**
 - Metabolic:
 - Alcohol, drugs
 - Mechanical:
 - Gallstones, trauma
 - Vascular:
 - Shock, embolism
 - Infectious:
 - Mumps, coxsackievirus
- **Pathogenesis:** two fundamental events
 - Autodigestion of panc. substance by panc. enzymes
 - Cellular injury by cytokines

➤ Two main settings

- Pancreatic duct obstruction
- Direct injury to acinar cells



➤ Clinical features

- Abdominal pain
 - Mild to intolerable
 - Epigastric pain radiating to the back
- Medical emergency
- Shock
- High amylase (within first 12 hours) & lipase
- CT. scan
- Mortality rate 20% – 40% :
 - sepsis, shock, respiratory distress

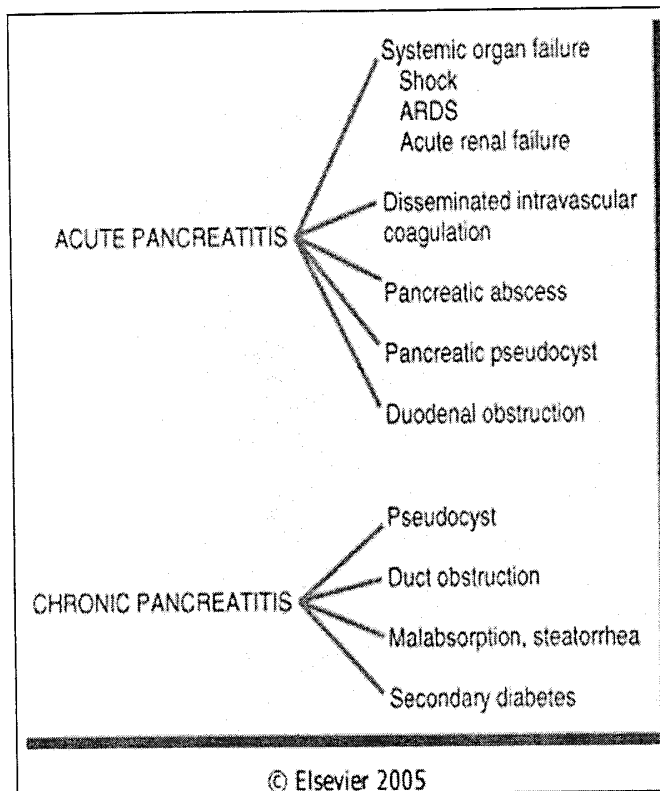
Chronic Pancreatitis

❖ Chronic Pancreatitis

- Repeated bouts of mild to moderate pancreatic inflammations with continued loss of pancreatic parenchyma and replacement by fibrous tissue.
- Mostly middle-aged men / alcoholic
- 50% of patients : idiopathic
- Pathogenesis is obscure
 - ? Hypersecretions of proteins → plugs → ?stones
 - ? Alcoholics → precipitations of ca → calcifications
 - In idiopathic ch. Panc. → mutations in CFTR

➤ **Clinical features:**

- Repeated attacks of pain
- Persistent abdominal and back pain
- Might be silent until pancreatic insufficiency and DM develop
- Mildly high amylase & lipase
- Radiology: calcifications, pseudocyst



DIABETES MELLITUS

❖ Diabetes Mellitus:

- Chronic disorder of metabolism
- Deficiency in insulin secretory response
- Impaired carbohydrate metabolism
- Hyperglycemia

Diabetes Mellitus

➤ Type 1

- Previously known as :
 - Insulin-dependent
 - Juvenile-onset
- Subtypes : 1A (autoimmune), 1B

➤ Type 2

- Previously known as:
 - Non-insulin dependent
 - Adult-onset

➤ Others

(see table 17-2)

Diabetes Mellitus

- Normal physiology
- Normal range 70 – 120 mg/dl
- Diagnosis :
 - Fasting blood glucose >126mg/dl more than once
 - Random blood glucose >200 mg/dl with clinical symptoms
 - Abnormal glucose tolerance test
- Pathogenesis
- Type 1A DM:
 - Autoimmune destruction of Beta cells
 - Usually in children and young adolescents
 - Insulin dependent for survival
 - Three mechanisms:
 - Genetic susceptibility
 - Autoimmunity
 - Environmental
- Genetic susceptibility
 - Related to class II MHC
 - Beta-cell autoantigen
 - Promote abnormal immunologic reaction
- Autoimmunity
 - Chronic autoimmune attacks
 - 90% of Beta cells destroyed before clinical manifestations
 - Lymphocytic infiltrate in the islets (insulinitis)
 - Mostly CD8+ T cells

- Beta-cells are selectively destroyed
- Autoantibodies
- Up to 20% have other autoimmune disorders

➤ **Environmental factors:**

- Work as triggers
- Viruses : Coxsackievirus, mumps, measles, rubella
- Mechanism of action is not clear

➤ **Pathogenesis**

➤ **Type 2 DM :**

- Less understood
- Two metabolic defects:
 - Insulin resistance
 - Derangement in secretion of Insulin
- Hyperglycemia → exhaustion of Beta-cells
- Life style & obesity
- Genetic factors
- No evidence of autoimmunity

➤ **Nonenzymatic glycosylation and formation of Advanced glycosylation end products (AGEs)**

- Degree of glycosylation is related directly to level of blood glucose
- Glycosylation of collagen and other proteins in blood vessels and interstitial tissues → AGEs
- AGEs formation on collagen → polypeptide cross-linking → trap of plasma and interstitial proteins → cholesterol deposition → acceleration of atherogenesis

- AGEs may affect structure and function of capillaries → leaky
 - AGEs binds to receptors on many cell types:
 - release of cytokines and growth factors
 - Increased endothelial permeability
 - Proliferation of fibroblasts and smooth muscle cells
 - and formation of extracellular matrix
- Intracellular hyperglycemia
 - In tissues that do not require insulin for glucose transport (BVs, nerves, lens, kidney)
 - Hyperglycemia → increased intracellular glucose → sorbitol → fructose
 - Increased intracellular osmolarity → influx of water → osmotic cell injury
 - E.g. lens opacity

❖ Morphology & complications

➤ Pancreas :

- Reduction in number and size of islets
- Infiltration of islets by leukocytes (insulitis) (DM1)
- Beta cell degranulation (EM)
- Amyloid deposition

➤ **Vascular system**

- Accelerated atherosclerosis
 - Myocardial infarction
 - Lower extremity gangrene

- Hyaline arteriosclerosis

➤ **Diabetic microangiopathy**

- Thickening of basement membranes
- Leaky capillaries

➤ **Nephropathy**

- Glomerular lesions
 - Capillary basement membrane thickening
 - Glomerulosclerosis (nodular/diffuse)
- Vascular lesions
 - Arteriosclerosis
 - Atherosclerosis
- pyelonephritis

➤ **Ocular complications**

- Retinopathy
 - Microangiopathy
 - Hemorrhages
 - Microaneurysms
 - neovascularizations

- Cataract formation

- **Neuropathy**

- Peripheral neuropathy of lower extremities
- Brain microangiopathy → stroke

- **Polyuria**

- **Polydipsia**

- **Polyphagia**

- **Wt. loss**

- **Features of complications**

- **Susceptibility to infections**

- **Diabetic ketoacidosis (DKA) – DM1**

TUMORS OF PANCREAS

- ❖ **Tumors of Pancreas**

- **Exocrine**

- Carcinoma of pancreas

- **Endocrine**

- Islet cell tumors
 - Functioning : insulinoma
 - Non-functioning

Tumors of Pancreas

➤ Ca of pancreas

- Arises in the exocrine portion of the pancreas
- 5 year survival < 5%
- more in smokers
- More risk with hereditary pancreatitis
- Mutations in K-RAS and CDKN2A
- Remain silent until advanced stage
 - Pain
 - Obstructive jaundice : tumors of head of pancreas

بالتوفيق للجميع...

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