# PATHOLOGY OF THE

# PANCREAS

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# ANATOMY & HISTOLOGY OF THE P A N C R E A S

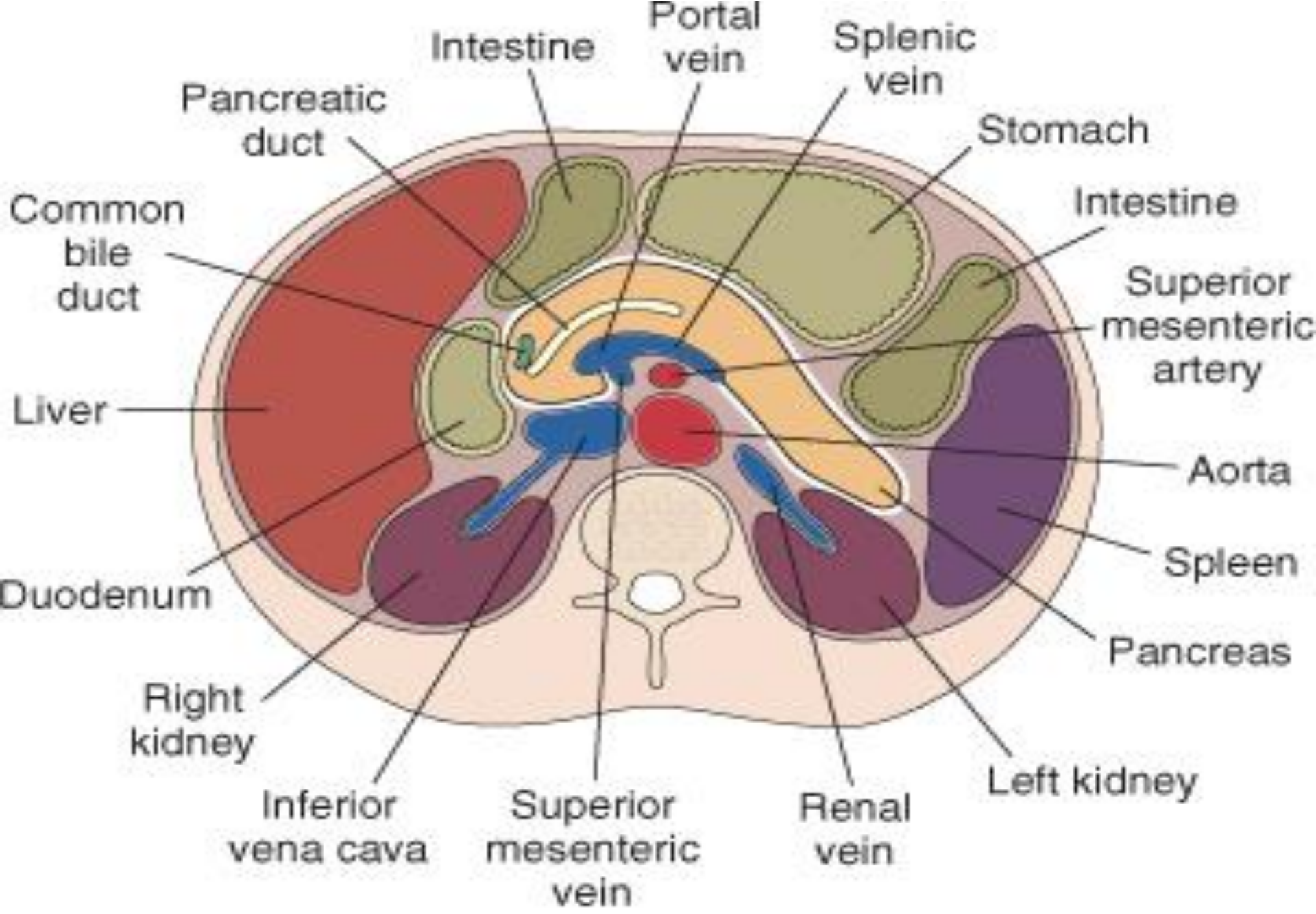
- **15 cm in length, 60-140 gm, consists of head, body & tail; pancreatic duct empty into duodenum or common bile duct .**
- **Histologically, consists of 2 components:**

**1) Exocrine: 80-85%, consists of numerous glands (acini) lined by columnar basophilic cells containing zymogen granules, which form lobules; ductal system .**

- **Trypsin, chemotrypsin, aminopeptidase, amylase**

**2) Endocrine: islets of Langerhans, which are invaded by capillaries. Islets consist of:**

- **4 main cell types: B (insulin), A (glucagon), D (somatostatin), PP cells (pancreatic polypeptide)**
- **2 minor cell types: D1 (VIP) & enterochromaffin cells (serotonin)**

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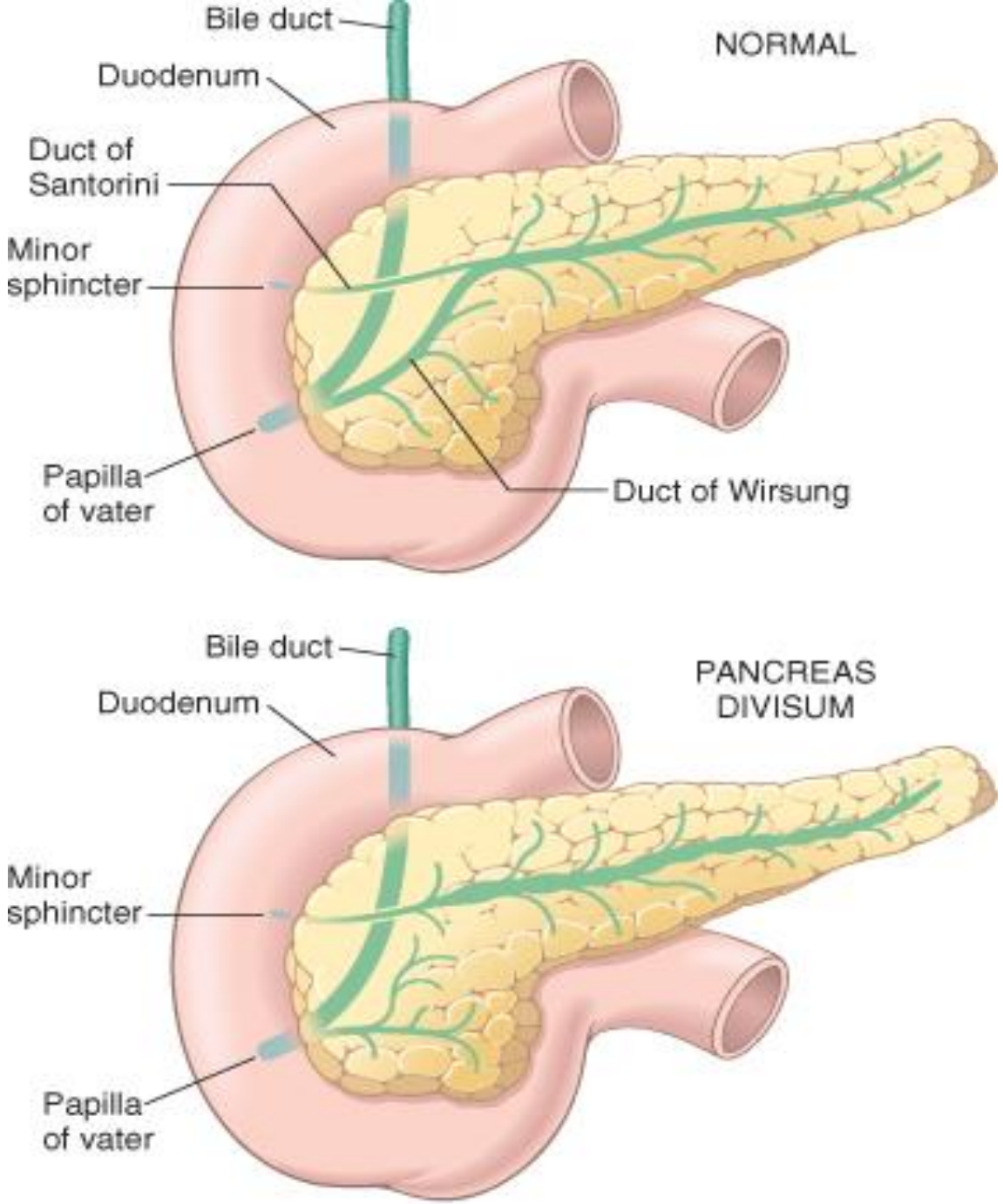


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# DISEASES OF THE PANCREAS

- **Congenital anomalies:**
  - **Agenesis, hypoplasia, ectopia, duct anomalies**
- **Exocrine pancreas:**
  - **Cystic fibrosis**
  - **Acute pancreatitis**
  - **Chronic pancreatitis**
  - **Carcinoma of the pancreas**
- **Endocrine pancreas:**
  - **Diabetes mellitus**
  - **Islet cell tumors**

# CONGENITAL ANOMALIES OF THE PANCREAS

- **Agenesis: usually associated with widespread severe malformations that are incompatible with life .**
- **Hypoplasia: both endocrine & exocrine elements may be involved .**
- **Annular pancreas: pancreas head encircle duodenum & may cause obstruction**
- **Aberrant (ectopic) pancreas: 2%; mostly in stomach, duodenum, jejunum, Meckel's diverticulum & ileum**
- **Ducts anomalies: duct of Wirsung may drain into common bile duct or an orifice high in the duodenum**

# DISEASES OF THE EXOCRINE PANCREAS

# CYSTIC FIBROSIS

- **CF is the most common lethal genetic disease that affects white populations (1 in 2000 live births) .**
- **Characterized by abnormally viscid mucous secretions that block airways & pancreatic ducts & are responsible for:**
  - **1) Recurrent chronic pulmonary infections .**
  - **2) Pancreatic insufficiency .**
- **High level of NaCl in sweat .**
- **Pathogenesis:**
- **Due to primary defect in transport of $Cl^-$ across epithelia.**
- **The cAMP-dependent $Cl^-$ channels (CF trans membrane conductance regulator [CFTR]) are defective.**

# CYSTIC FIBROSIS

- **CF gene is located on chromosome 7 with up to 300 mutations identified in this gene so far.**

- **Pancreatic pathology: abnormalities are seen in 85% of patients:**
  - **Mucus accumulation .**
  - **Duct dilation & plugging .**
  - **Exocrine gland atrophy. Islets usually spared.**
  - **Ducts may be converted into cysts separated only by islets of Langerhans & fibrous stroma (fibrocystic disease of pancreas) .**
  - **Malabsorption syndrome: particularly fat .**
  - **Squamous metaplasia of duct lining.**

- **Meconium ileus (GIT ), Pulmonary problems (Resp) .**

- **Rx: gene therapy**

# DISEASES OF THE EXOCRINE PANCREAS

# ACUTE PANCREATITIS

- **Inflammation of the pancreas, which is almost always associated with acinar cell injury .**
- **A clinical & histological spectrum of severity & duration**
- **Etiologic factors:**
  1. **Metabolic: alcohol, hyperlipoproteinemia, hypercalcemia, drugs (e.g. thiazides), genetic .**
  2. **Mechanical: gallstones, traumatic & perioperative injury .**
  3. **Vascular: shock, atheroembolism, polyarteritis nodosa**
  4. **Infections: Mumps, Coxsackie virus, Mycoplasma**
  5. **Idiopathic : 10-20% ; ? Genetic basis**

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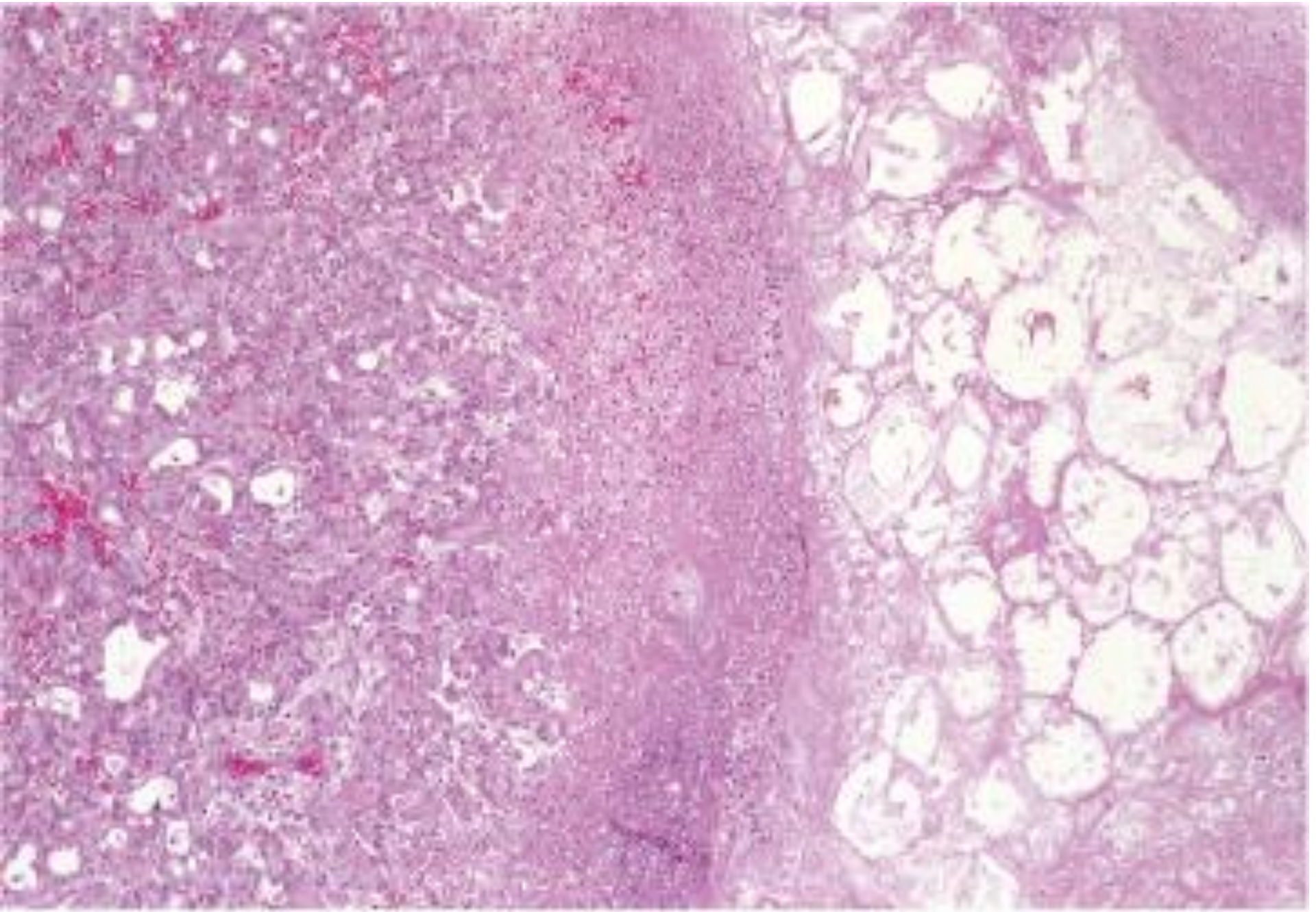

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# DISEASES OF THE EXOCRINE PANCREAS

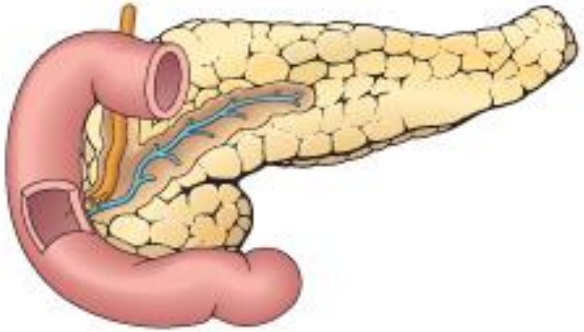
# ACUTE PANCREATITIS

- **Pathogenesis:**
  - **Auto digestion of pancreatic tissue by inappropriately activated pancreatic enzymes .**
  - **Trypsin has a major role:**
    1. **Activates other proenzymes (proelastase ,prophospholipase )**
    2. **Converts prekallikrein to kallikrein (Kinin system)**
    3. **Hageman factor is activated**

  - **Mechanisms of pancreatic enzyme activation:**
    - **1) Pancreatic duct obstruction (Stone) .**
    - **2) Primary acinar cell injury (Alcohol ) .**
    - **3) Defective intracellular transport of proenzymes within acinar cells .**

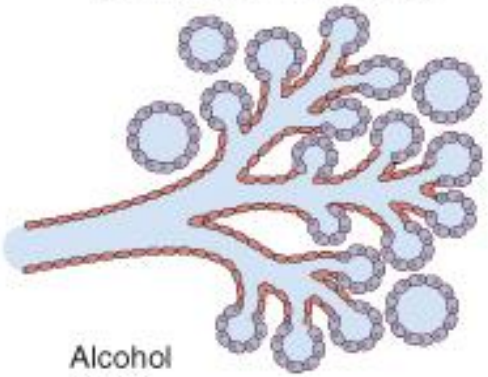
**CAUSES:**

**DUCT OBSTRUCTION**



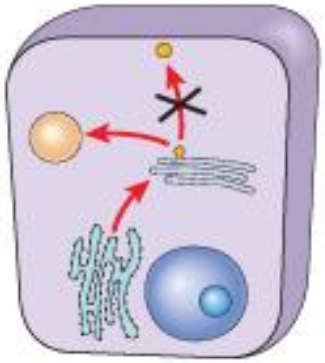
Cholelithiasis
Ampullary obstruction
Chronic alcoholism
Ductal concretions

**ACINAR CELL INJURY**



Alcohol
Drugs
Trauma
Ischemia
Viruses

**DEFECTIVE INTRACELLULAR TRANSPORT**



Metabolic injury (experimental)
Alcohol
Duct obstruction

**MECHANISMS:**

Interstitial edema → Impaired blood flow → Ischemia

Release of intracellular proenzymes and lysosomal hydrolases → Activation of enzymes (intra- or extracellular)

Delivery of proenzymes to lysosomal compartment → Intracellular activation of enzymes

Acinar cell injury

**ACTIVATED ENZYMES**

**LESIONS:**

Interstitial inflammation and edema + Proteolysis (proteases) + Fat necrosis (lipase, phospholipase) + Hemorrhage (elastase)

**ACUTE PANCREATITIS**

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# DISEASES OF THE EXOCRINE PANCREAS

# ACUTE PANCREATITIS

- **Pathology:**
  - 4 basic alterations:
    1. Proteolytic destruction of pancreatic substance .
    2. Necrosis of blood vessels & interstitial hemorrhage
    3. Fat necrosis by lipolytic enzymes
    4. Associated acute inflammatory reaction

    - **Pathologic lesions:**
    - a. Acute pancreatic necrosis .
    - b. Acute hemorrhagic pancreatitis .
    - c. Suppurative peritonitis .
    - d. Pancreatic pseudocysts .

# DISEASES OF THE EXOCRINE PANCREAS

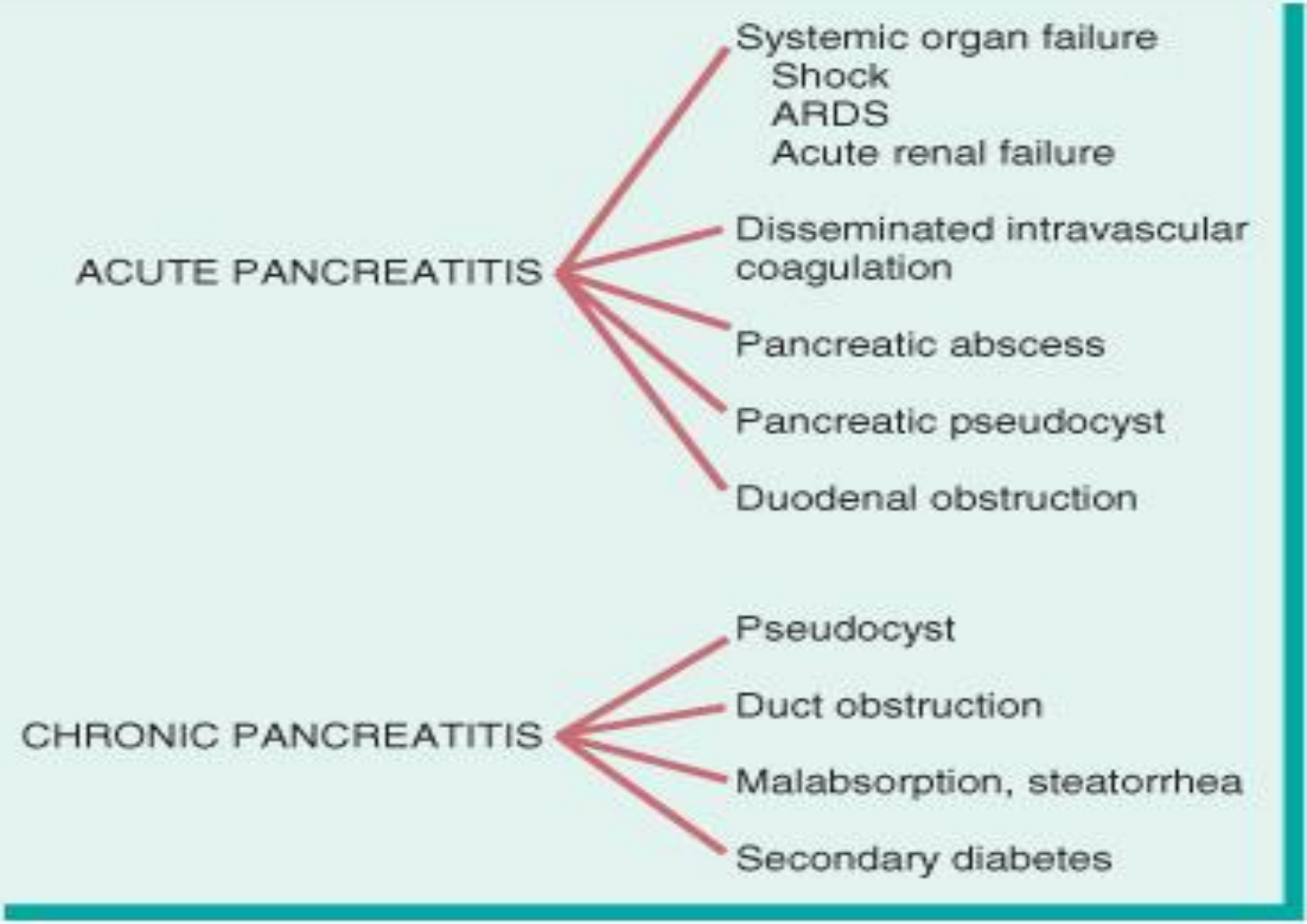
# ACUTE PANCREATITIS

- **Clinical features:**
  - **Abdominal pain is the cardinal manifestation: epigastric, radiating to back, variable in severity**
  - **Shock: due to pancreatic hemorrhage & release of vasodilator agents (BK & PGs) .**
- **Lab: ↑ serum amylase and lipase , ↓ Ca**
  **↑ bilirubin, ↑ glucose & glycosuria**
- **CT scan: inflammation, pseudocysts .**
- **Px: severe cases have high mortality rate (20-40%)**
- **Death due to: 1) shock, 2) secondary abdominal sepsis, 3) adult respiratory distress syndrome**

# DISEASES OF THE EXOCRINE PANCREAS

# CHRONIC PANCREATITIS

- **Repeated bouts of mild to moderate pancreatic inflammation, with continued loss of pancreatic parenchyma & replacement by fibrous tissue .**
- **Distinction from acute pancreatitis may be difficult; distinction is made if there is evidence of previous attacks .**
- **Middle-aged men, mostly in alcoholics but may due to billiary tract disease, hyperlipoproteinemia & hypercalcemia; no apparent cause in 50% of cases .**
- **Pathogenesis:**
  - **Protein hypersecretion from acinar cells .**
  - **Precipitation of proteins forming ductal plugs .**
  - **Plugs enlarge forming laminar aggregates .**

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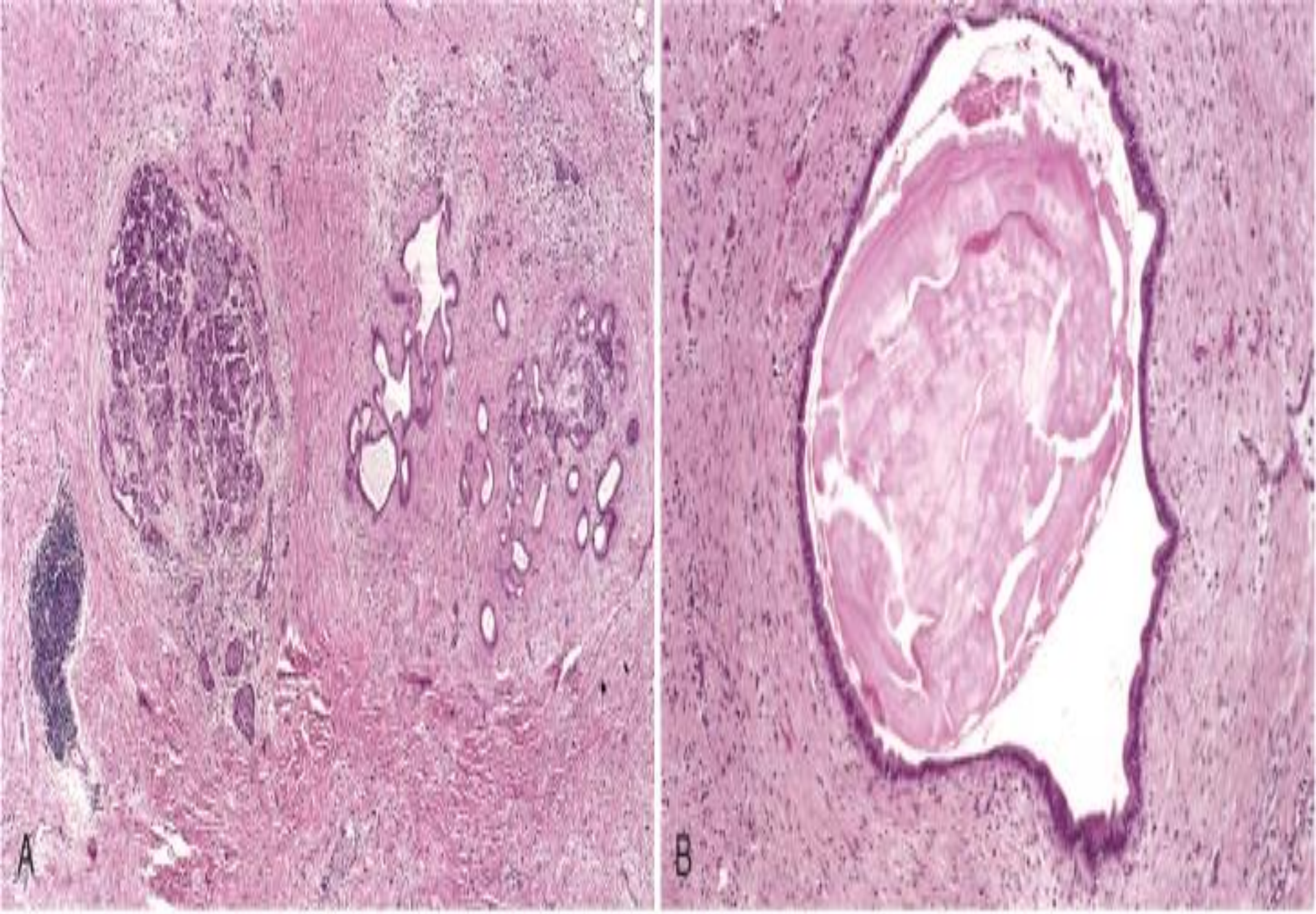
# CHRONIC PANCREATITIS

- **Pathology**:
  - Hard organ with dilated ducts & calcified concretions .
  - Fibrosis , chronic inflammatory cells .
  - Obstruction of ducts by protein plugs .
  - Extensive atrophy of exocrine glands .
  - Pseudocysts .
- **Clinical features** :
  - Repeated attacks of abdominal pain or may be silent .
- **Dx**: Clinical suspicion, lab ( Amyelase) & CT
- **Px**: Chronic disabling disease due to its major complications: pancreatic insufficiency & diabetes mellitus .

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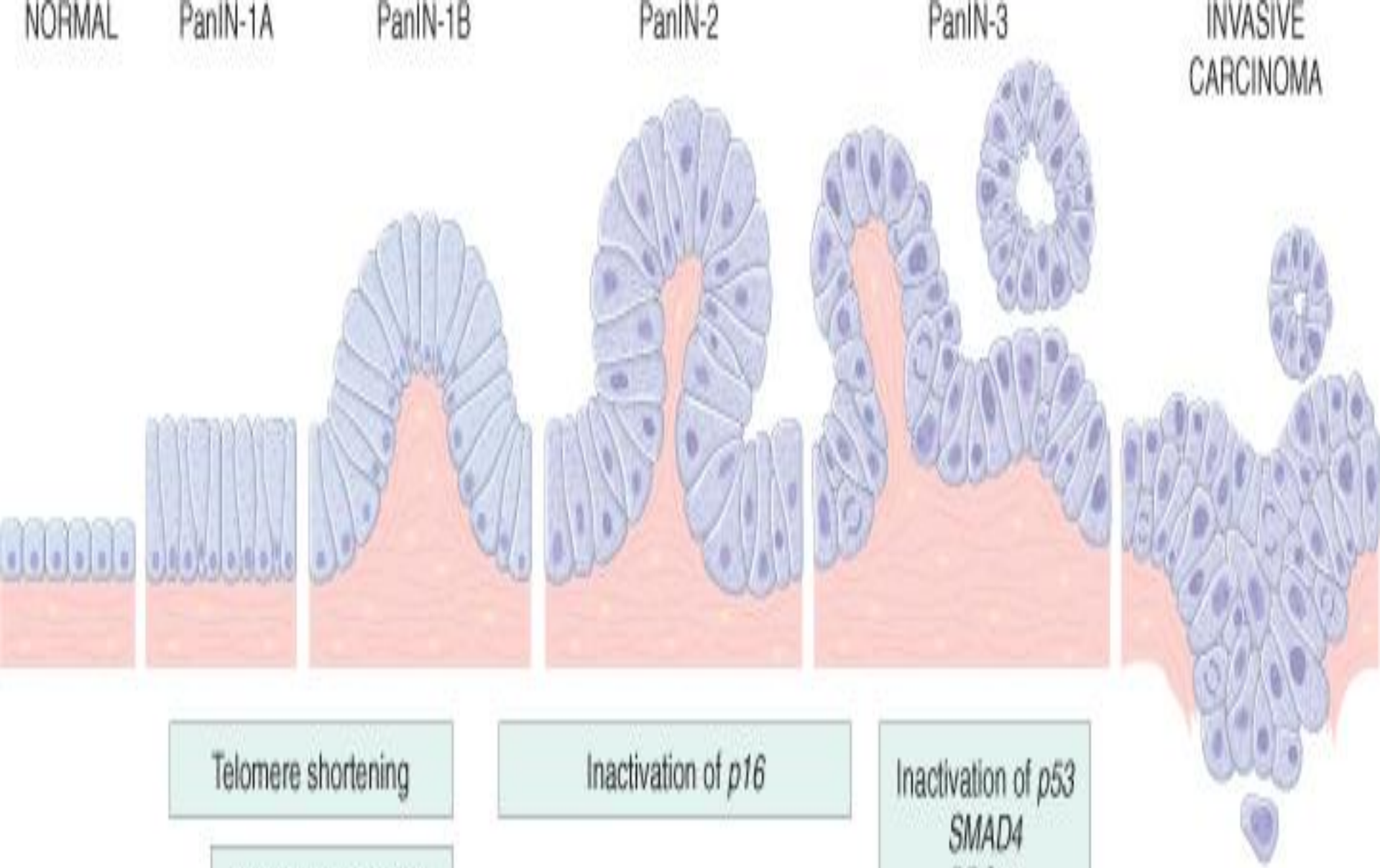
# DISEASES OF THE EXOCRINE PANCREAS

# PANCREATIC CARCINOMA

- Malignant epithelial neoplasm of exocrine portion of pancreas
- 5th most frequent cause of death from cancer
- Increasing in incidence in the West
- Peak incidence: 60 - 80 years
- Cause is unknown; more frequent in smokers
- Location:
  - Head of pancreas 60%
  - Body of pancreas 15%
  - Tail of pancreas 5%
  - Diffuse involvement 20%

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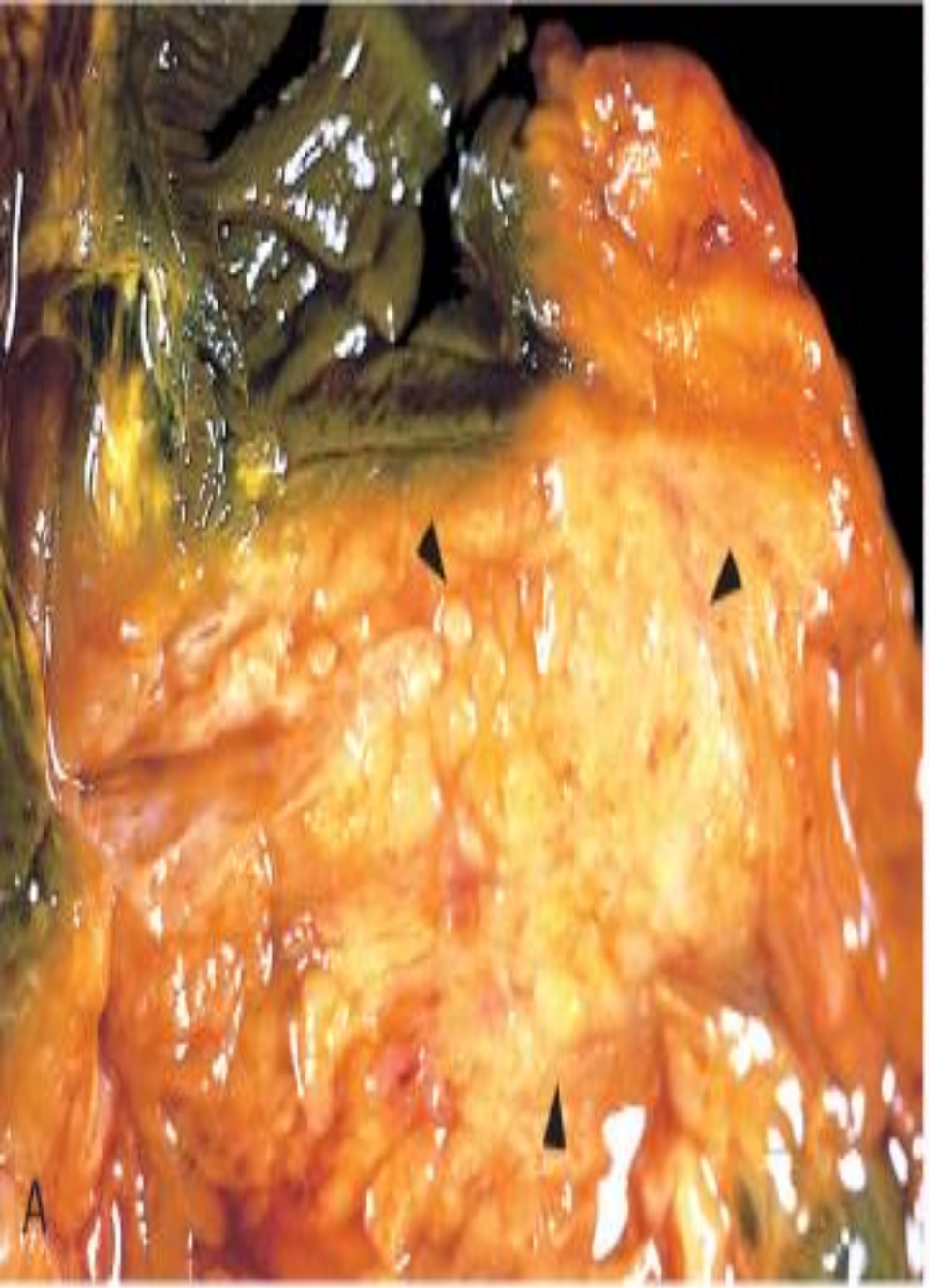
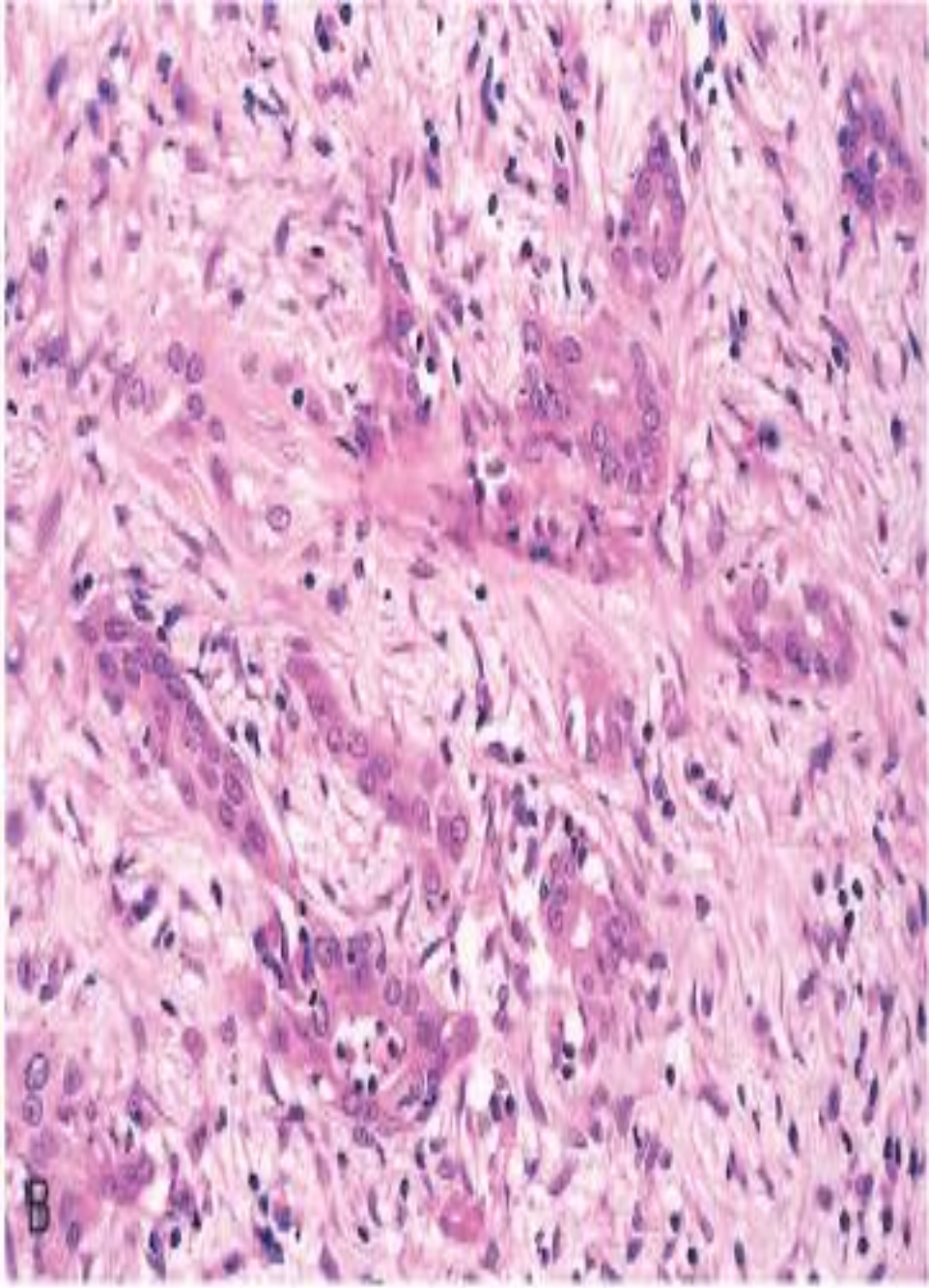
# DISEASES OF THE EXOCRINE PANCREAS

## PANCREATIC CARCINOMA

- **Gross :Gritty gray hard masses**
- **M/E: Vast majority are adenocarcinomas, with poorly formed glands and densely fibrous stroma**
- **Carcinoma of pancreatic head: invasion of ampullary region with bile outflow obstruction, & distension of biliary tree**
- **Carcinoma of body & tail: no impingement on biliary tract & remain silent for longer periods**
- **Extends into retroperitoneal spaces, infiltrate nerves, abdominal organs & lymph nodes**
- **Distant metastasis to lungs, bone, ..**

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# DISEASES OF THE EXOCRINE PANCREAS

# PANCREATIC CARCINOMA

- **Clinical features:**
  - **Usually silent until its extension impinges on other structures .**
  - **Pain is usually the first symptom .**
  - **Obstructive jaundice .**
  - **Trousseau's syndrome: Migratory thrombophlebitis (phlebothrombosis) .**
- **Lab: tumor markers, e.g. CEA, CA19-9 Ag are nonspecific .**
- **Dx: CT scan & percutaneous biopsy .**
- **Px: 1 year survival is 10%; 5 yr survival is 2.5%**