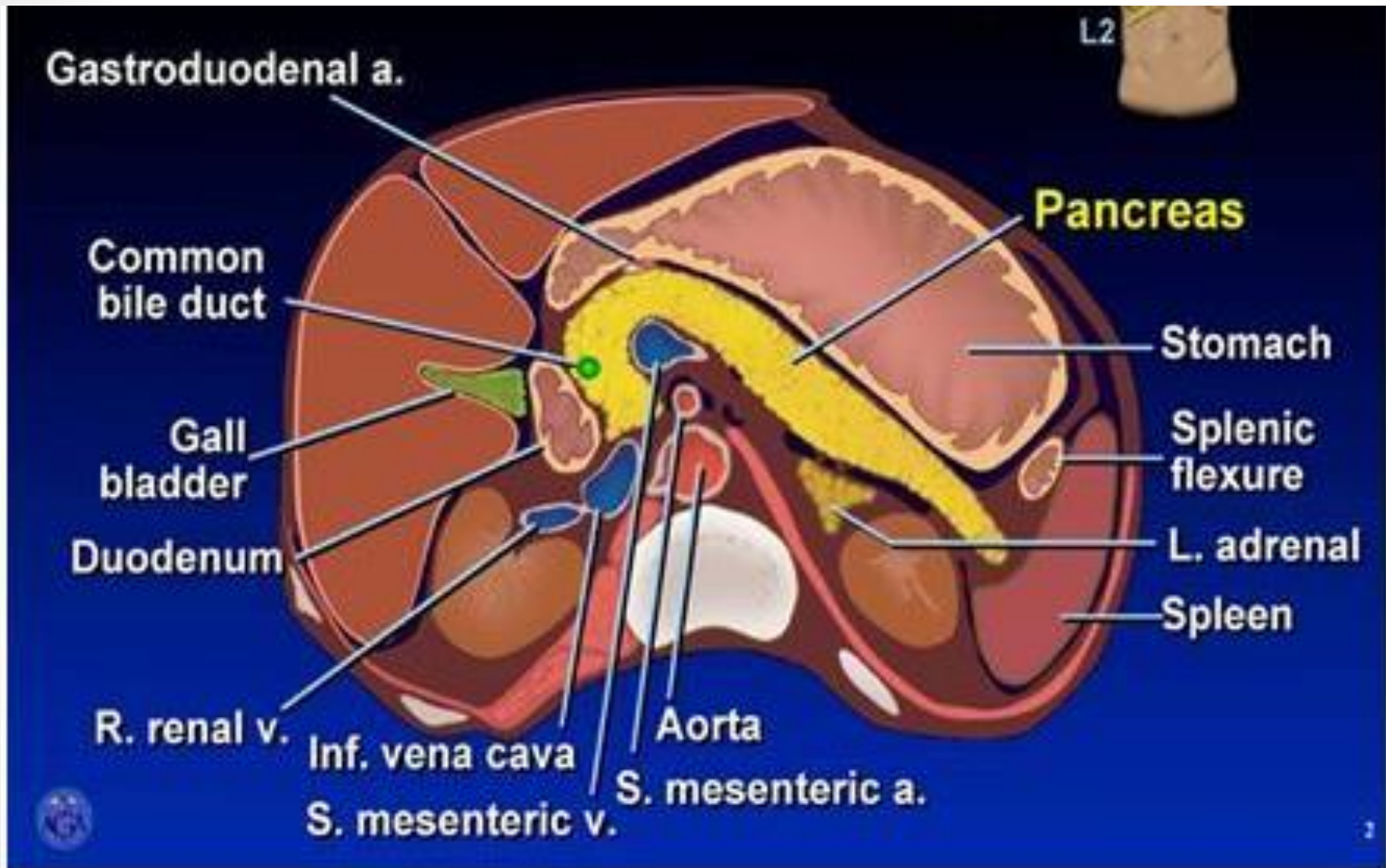


Pathology and Function of Pancreas

- Location of pancreas
- Anatomy of pancreas
- Role of pancreas in Hormonal secretion
- Digestive role of Pancreas
- Pathology of pancreas
 - Pancreatitis
 - Cystic fibrosis
 - Diabetes mellitus
 - Carcinoma of pancreas
 - Islet Cells Tumor

Location of pancreas



Structure of pancreas

Pancreas actually '2 glands in 1'

Endocrine portion:

this makes 1-2% of pancreatic mass

consists of islets of Langerhans

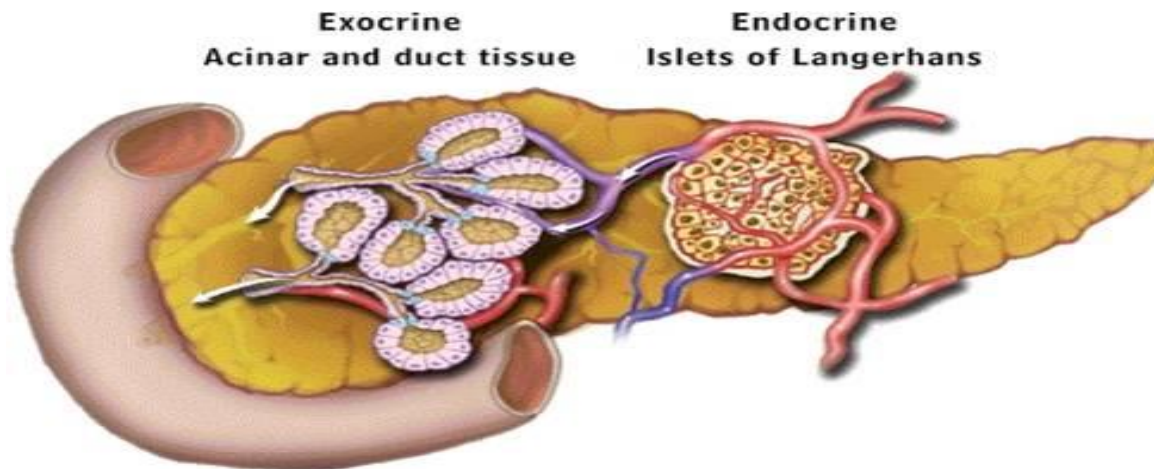
which secrete hormones such as insulin and glucagon

Exocrine portion:

comprise of 80-90% of pancreas

composed of acinar cells and ducts

secrete digestive enzymes



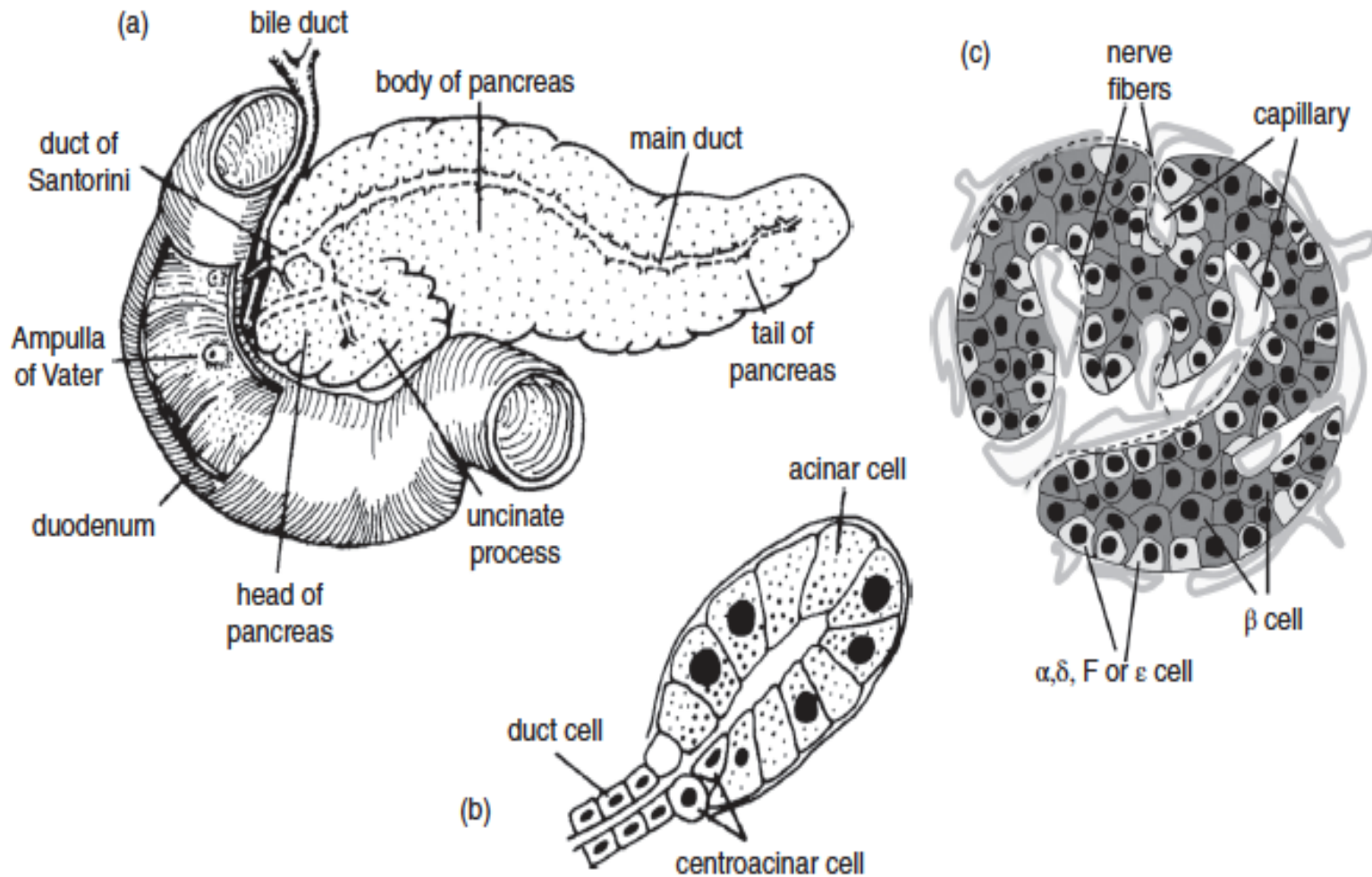
Endocrine pancreas

Histologically, the islets consist of four major cell types:

- 1. Alpha cells**, which are the source of glucagon and consist of 25% of islet mass
- 2. Beta cells**, which consist of 60% of islet mass that synthesize and secrete insulin
- 3. Delta cells**, which make up 10% of islet mass and produce somatostatin
- 4. F cells**, secrete pancreatic polypeptide, which plays important role in reducing appetite and food intake

The remaining 4% of islet mass consists of connective tissue, blood vessels and nerves.

Exocrine and endocrine portion of pancreas



Ghrelin cells:

- Ghrelin is produced in a population of endocrine cells in the gastric mucosa, but expression in intestine, hypothalamus and testis also found
- The cells were few, but regularly seen in adults as single cells at the islet periphery, in exocrine tissue, in ducts, and in pancreatic ganglia

Function of ghrelin:

- Ghrelin affects insulin secretion and plays a direct role in metabolic regulation and energy balance
- Involve in the developing pancreas might be to locally promote cell growth and maturation, and perhaps also, by hormonal actions, promote growth at distant sites

Exocrine pancreas

Exocrine pancreas have 2 types of cells i.e., acinar and ductal cells

Acinar cells:

- synthesize, store, and secrete digestive enzymes into a lumen space that is connected to the ductal system
- have receptors for hormones and neurotransmitters that regulate the secretion of digestive enzymes
- Beneath lumen are zymogen granules, the storage depot of digestive enzymes

Digestive enzymes

Three types of enzymes that are secreted by exocrine pancreas:

1. Proteolytic enzymes

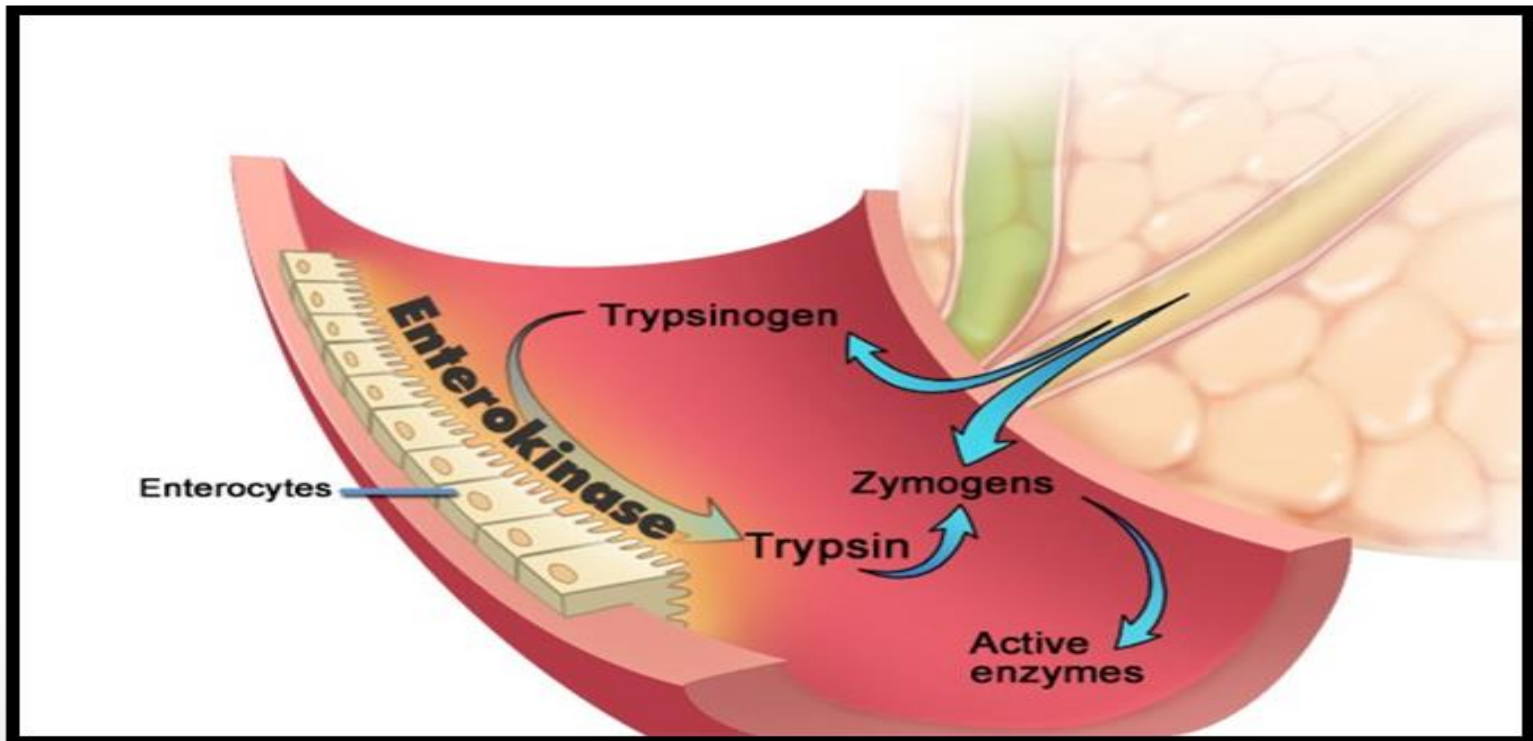
2. Pancreatic amylase

3. Pancreatic lipase

Proteolytic Enzymes

- ❖ Involve in protein digestion
- ❖ Examples are trypsinogen, chymotrypsinogen, and procarboxypeptidase each of which is secreted in an inactive form

- Once trypsinogen convert into its active form trypsin by enterokinase enzyme embedded in luminal membrane line the duodenal mucosa
- Remaining proteolytic enzymes, are converted by trypsin to their active forms, within the duodenal lumen



Pancreatic amylase

- It is also secreted in active form
- carbohydrate digestion by converting polysaccharides into disaccharide maltose.

Pancreatic lipase

- Secreted in active form
- hydrolyzes dietary triglycerides(fat) into monoglycerides and free fatty acids
- Both these are secreted in inactive form because there is no risk of pancreatic self- digestion

Ductal cells of exocrine:

- Secrete an aqueous alkaline solution that line pancreatic ducts
- This solution is rich in sodium bicarbonate ions
- contain abundant mitochondria necessary for energy products (ATP) needed for ion transport
- **Two other types** of cells i.e., centroacinar cell and stellate cell also present
- Centroacinar cells have ductal cell characteristics
- are also likely stem cells for populating the different cell types for the pancreas.

Pancreatic stellate cells:

- Pancreatic stellate cell (PaSC) is important because of its role in pathologic states
- Stellate cell is a very slender star shaped that drapes itself around the acini, ducts and the Islets of Langerhans
- In normal function PaSCs are involved in directing proper formation of the epithelial structures
- In pathologic states such as chronic pancreatitis and pancreatic cancer the PaSC is transformed into a proliferating myofibroblastic cell type

Regulation of pancreatic secretion

1 **Neural stimulation:** vagus nerve

2 **Humoral factors:** Secretin and cholecystokinin from the duodenum

Secretin stimulates water and bicarbonate secretion from the duct cells

Cholecystokinin promotes discharge of the digestive enzymes from the acinar cells

Pancreatitis

- Inflammation of the pancreas associated with acinar cell injury = pancreatitis
- Occurs along a spectrum of severity
- and a spectrum of duration
- **Mechanism:** Autodigestion by inappropriately activated pancreatic enzymes

Acute Pancreatitis

Characterized by intra-acinar cell activation of digestive enzymes

A subsequent systemic inflammatory response by the release of proinflammatory cytokines.

Pathogenesis:

Two main factors that cause acute pancreatitis

- Gallstone
- Excessive alcohol consumption
- less common cause is obstruction in ducts

- **Clinical manifestation:** Abdominal pain and tenderness

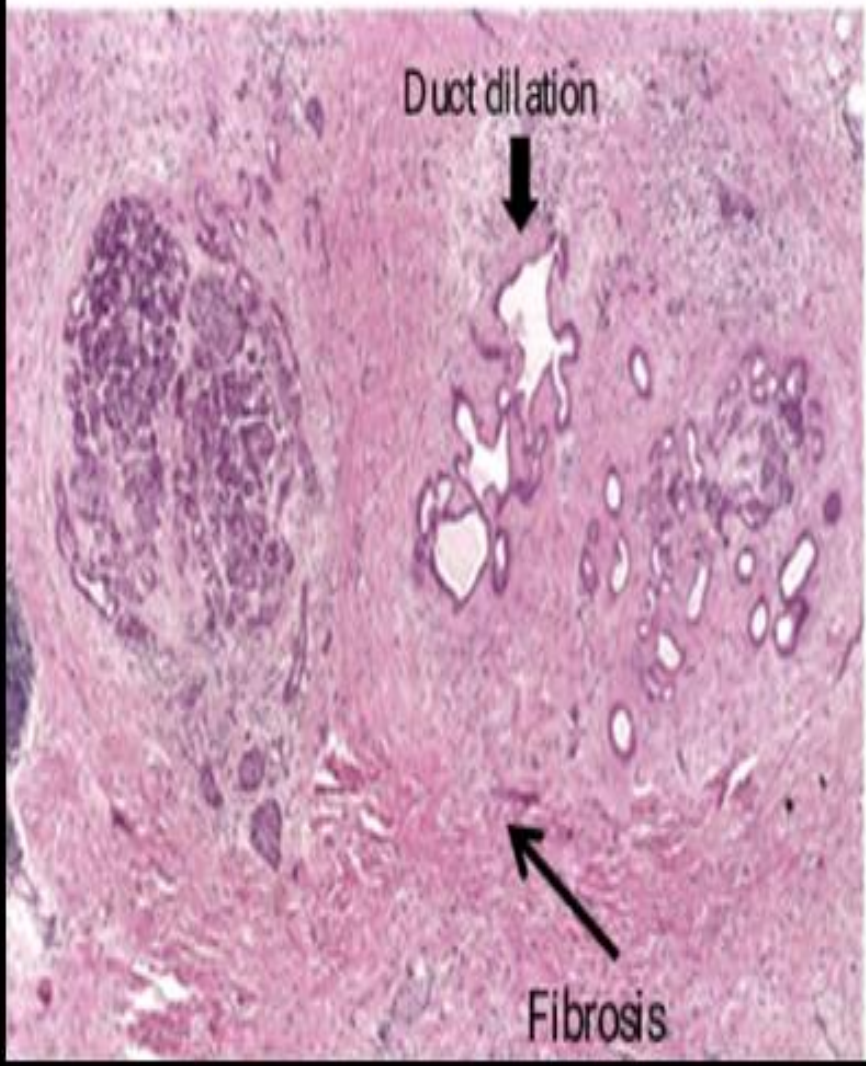
Varies from mild to severe

- Activated digestive enzymes not only destroy pancreas but also blood vessels
- This condition is called acute hemorrhagic pancreatitis
- Fat and parenchymal necrosis also occur

Chronic pancreatitis

- Persistent interstitial pancreatitis may lead to interstitial fibrosis and atrophy of acinar tissue
- Further process in destruction of acinar cells and scarring
- Then cause loss of acinar cells that persistent duct obstruction
- These cause permanent change in pancreas called acute pancreatitis
- As result, malnutrition and diabetes(islets cells destruction) also occur

Pancreatic duct is very dilated and full of concretions



Cystic fibrosis

CF is a genetically determined and inherited autosomal recessive systemic disease

in which mucinous secretions are abnormally viscous

Manifest in infancy and childhood

Infrequent in black people than white

Etiology:

- Mutation of gene CFTR, that cause defective transport across cell membranes of chlorine, sodium, and water molecules
- That cause mucus thickening, in respiratory tract, pancreatic duct, bronchioles and bile duct
- form dense plug that obstruct pancreatic duct, bronchi and bronchioles, and bile duct

Diabetes Mellitus

- Heterogeneous group of chronic disorders involving metabolic disturbance
- Absolute or relative deficiency in insulin
- Hereditary also influence
- Long term complications of DM can involve many organs systems with resultant high morbidity
- Atherosclerosis, peripheral vascular disease, peripheral neuropathy, microangiopathy and cerebrovascular infarcts and hemorrhages

Types of Diabetes

Type I or Insulin Dependent DM

Also called juvenile onset diabetes

Autoimmune disease, autoantibodies against beta cells

Less amount of insulin and marked hyperglycemia

Exogenous factor like viral infection

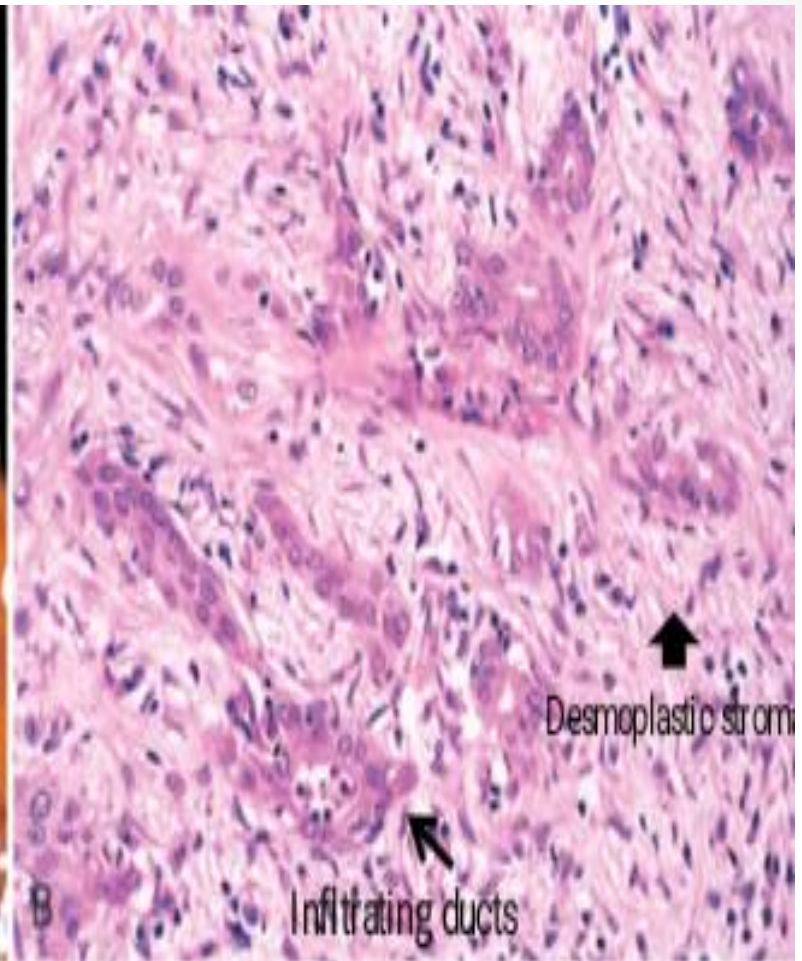
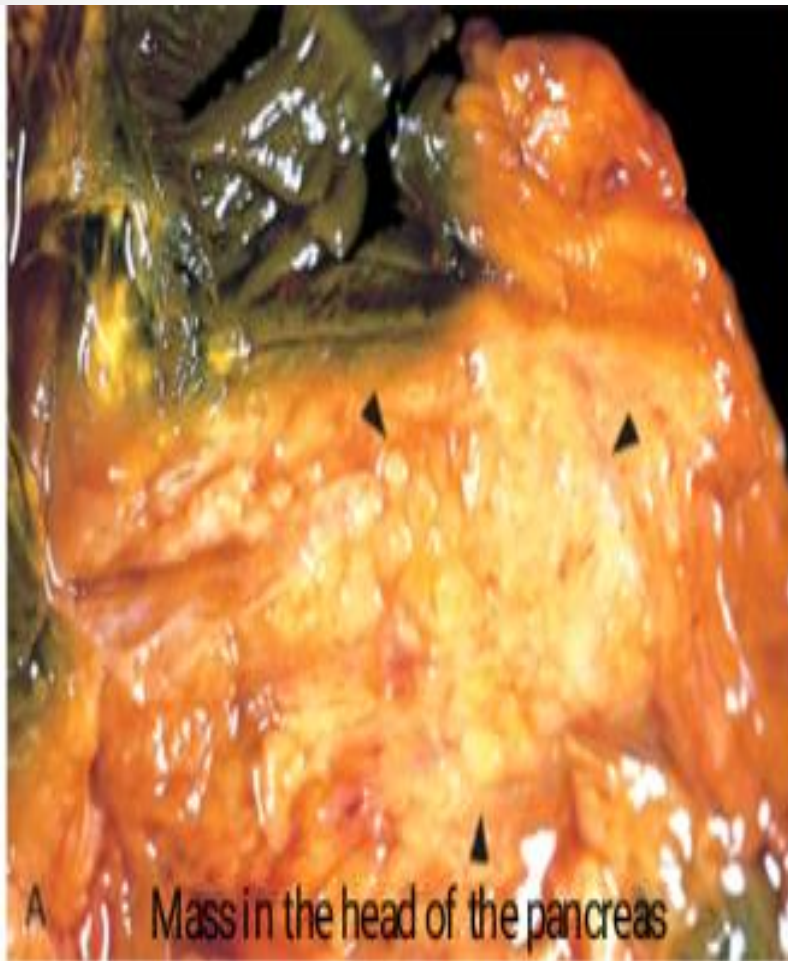
Type II or Insulin Independent DM

Also called adult onset diabetes (90 to 95%)

Normal to high insulin level

Carcinoma of pancreas

- Pancreatic carcinoma may arise from duct cells, acinar cells, or islet cells
- Carcinoma of the pancreas usually refers to **neoplasms** arising in the exocrine pancreas
- Whereas neoplasms arising in the endocrine pancreas are collectively termed **islet cell tumors**
- Incidence is rising and ranks fifth among cancers in the United States



Carcinoma of pancreas

Occurrence

89% of cancers are of ductal origin, like ductal cell adenocarcinomas while 1 % indicated as being of acinar cell origin

Pancreatic head cancer:

- The average size of ductal adenocarcinomas found in the head of the pancreas was 5 cm in a large series

Pancreatic tail cancer:

- located in the body or tail averaged 10 cm diameter in size
- not cause early symptoms and typically are not discovered
- until there has been a local extension to retroperitoneal nerves,
- causing pain or metastasis,
- Metastases involve liver, regional nodes, peritoneum, lungs, and pleura

Islet cells tumor

- Rare compared to adenocarcinoma

Clinical presentation

May present with symptoms related to increased hormone secretion

Hyperinsulinemia causing hypoglycemia

- Hypergastrinemia causing increased gastric acid production and severe ulcers .

May present as a non-functional (non-secreting) mass

- This is the most common