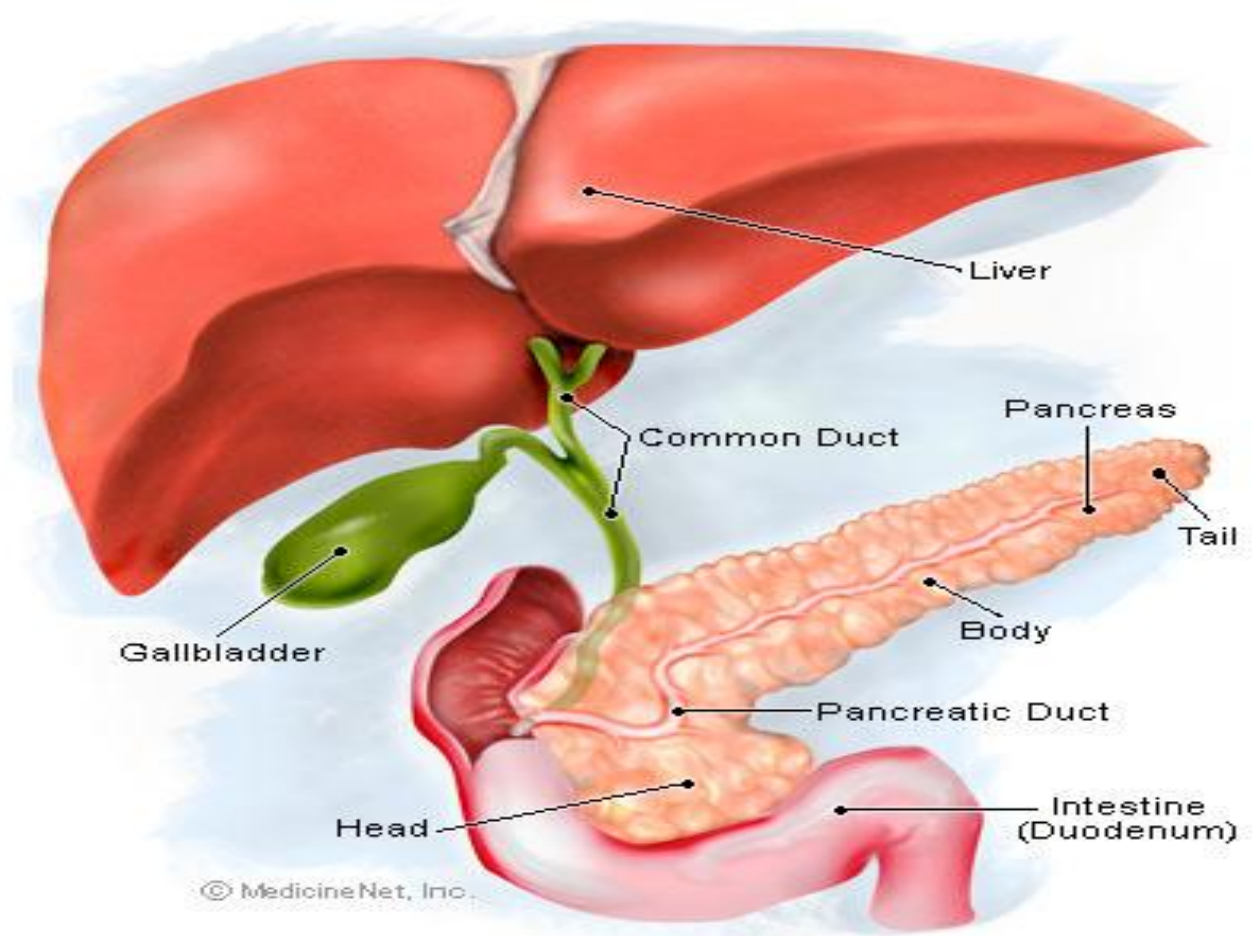


6th Lecture

Physiology of the pancreas



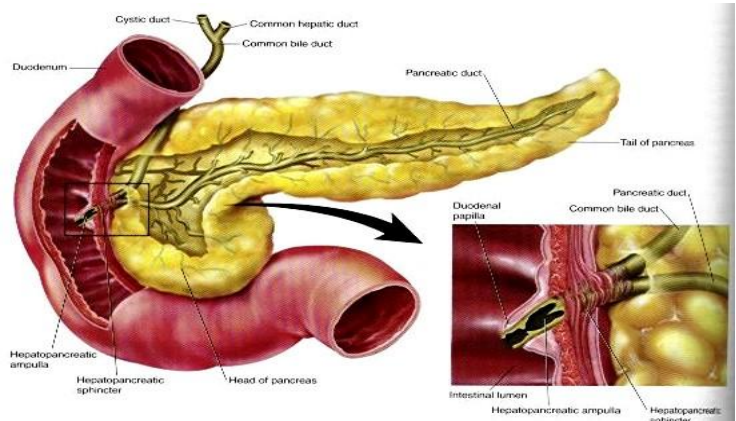
PHYSIOLOGY TEAM - 430

This Lecture is done by :

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Pancreas

- The pancreas, which lies parallel to and beneath the stomach is a large compound gland with most of its internal structure similar to that of the salivary glands



- **Innervation of pancreas:**

- Preganglionic parasympathetic fibers arise in vagus nerve to synapse with ganglion cells around the large ducts
- Postganglionic fibers supply the acini
- The sympathetic fibers accompany the blood vessels

- **The pancreas is composed of:**

1. The endocrine islets of Langerhans which secrete insulin, glucagone and somatostatin
2. Acinar gland tissues which produce pancreatic juice (the main source of digestive

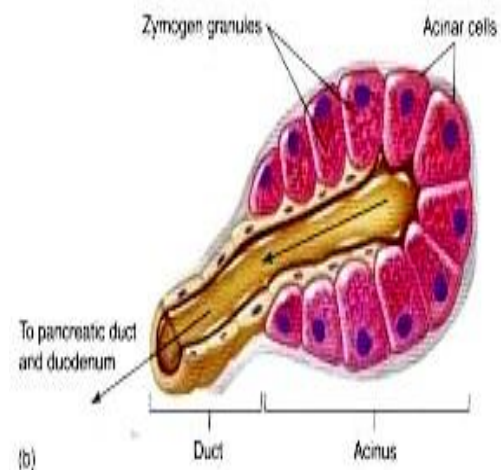
Note:

The cells lining the acini are serous cells containing zymogen granules (the precursors of pancreatic enzymes). The acini drain into intracalated ducts. These join to form intralobular (striated) ducts which lead to interlobular ducts that drain into the main pancreatic duct which join into the bile duct at ampulla of vater that is surrounded by sphincter of Oddi → duodenum

enzymes)

- **Pancreatic secretions:**

- The pancreatic digestive enzymes are secreted by pancreatic acini, and large volumes of sodium bicarbonate solution are secreted by the small ductules and larger ducts leading from the acini.



Note:

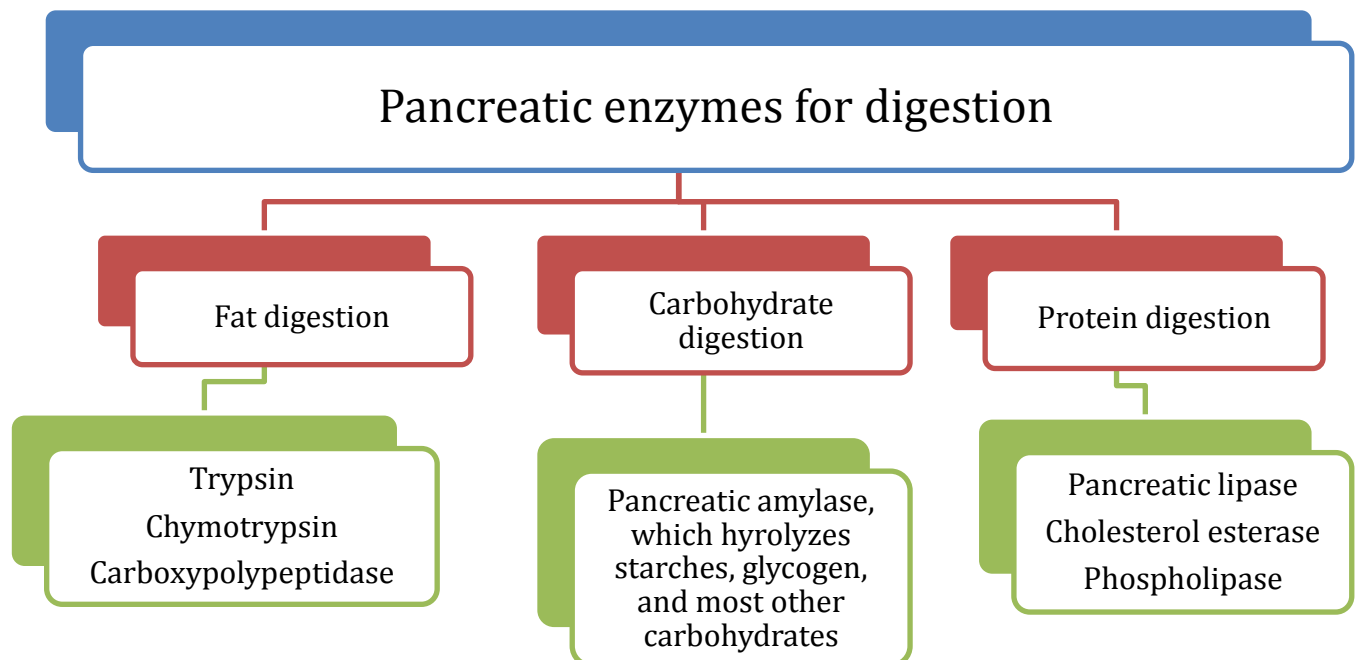
The presence of chyme in the upper portions of the small intestine leads to the secretion of pancreatic juice.

- **Pancreatic juice:**

- Volume: 1.2-1.5 l/day.
- Specific gravity: 1008-1030. It is isotonic.
- PH: 8 alkaline.
- Composition: 1 % inorganic materials (electrolytes)
- 1-2 % organic materials mostly enzymes.

- **The major functions of pancreatic secretion:**

- To neutralize the acids in the chyme
- To produce enzymes involved in the digestion of dietary carbohydrate, fat, and protein



- The same cells that secrete proteolytic enzymes (glandular cells) into the acini secrete another substance called trypsin inhibitor
- Secretion of Trypsin Inhibitor Prevents Digestion of the Pancreas Itself

Characteristics of Pancreatic Enzymes

Enzyme	Specific Hydrolytic Activity
Proteolytic	
Endopeptidases	
Trypsin(ogen)	Cleaves peptide linkages in which the carboxyl group is either arginine or lysine
Chymotrypsin(ogen)	Cleaves peptides at the carboxyl end of hydrophobic amino acids, e.g., tyrosine or phenylalanine
(Pro)elastase	Cleaves peptide bonds at the carboxyl terminal of aliphatic amino acids
Exopeptidase	
(Pro)carboxypeptidase	Cleaves amino acids from the carboxyl end of the peptide
Amylolytic	
α -Amylase	Cleaves α -1,4-glycosidic linkages of glucose polymers
Lipases	
Lipase	Cleaves the ester bond at the 1 and 3 positions of triglycerides, producing free fatty acids and 2-monoglyceride
(Pro)phospholipase A ₂	Cleaves the ester bond at the 2 position of phospholipids
Carboxylesterhydrolase (cholesterol esterase)	Cleaves cholesteryl ester to free cholesterol
Nucleolytic	
Ribonuclease	Cleaves ribonucleic acids into mononucleotides
Deoxyribonuclease	Cleaves deoxyribonucleic acids into mononucleotides

The suffix -ogen or prefix pro- indicates the enzyme is secreted in an inactive form

• Pancreatic juice consist of:

1) The electrolytes:

- They are produced by duct cells and include cations Na⁺, K⁺, Ca⁺⁺ and anions HCO₃⁻ and Cl⁻
- The greater bulk of electrolytes are in the form of NaHCO₃. It makes a major contribution to neutralization of acid chyme along with bile and duodenal secretion in order to create a suitable medium for the action of pancreatic enzymes

2) The enzymes:

- The pancreas secretes enzymes that act on all major types of food stuffs

1. Pancreatic proteolytic enzymes:

- Trypsin, chymotrypsin, elastase, carboxypeptidase, ribonuclease and deoxyribonuclease. They are secreted in inactive form which is activated in intestinal lumen. Trypsinogen is activated into trypsin by the enzyme enteropeptidase (enterokinase), secreted by duodenal mucosal cells. Once trypsin is produced, it acts to activate chymotrypsinogen to chymotrypsin, proelastase to elastase and procarboxypeptidase into carboxypeptidase.
- Activation of trypsinogen by enterpeptidase is the key to activation of pancreatic proteases. Enteropeptidase is considered the most important intestinal enzyme.

- chymotrypsin and elastase are endopeptidases, splitting protein into shorter peptide chains. Carboxypeptidase is an exopeptidase which splits off amino acids at the carboxyl terminus of the peptide.
- Trypsin inhibitor is present in cytoplasm of glandular cells. It inhibits activation of trypsin in acini and ducts of the pancreas.

2. Pancreatic amylase:

- It splits starch to maltose, maltotriose and dextrins.

3. Enzymes for fat digestion:

- Pancreatic lipase is the most important fat splitting enzyme. It breaks TG into MG and FA in the presence of bile salts and colipase.
- Cholesterol esterase, which liberates cholesterol.
- Phospholipase A2 that splits phospholipids into lysophospholipids & FA.

- The pancreas secretes about 1 L/day of HCO_3^- -rich fluid from the epithelial cells of the ductules and ducts.
- The osmolarity of pancreatic fluid is equal to that of plasma
- HCO_3^- concentration increases with increasing secretion rate

• Control of pancreatic secretion:

- It is regulated by neurohormonal mechanisms. Hormonal regulation is the most important. It includes three phases

1. Cephalic phase:

- It is mediated by vagus nerve through non-conditioned and conditioned reflexes. Vagus nerve stimulates secretion of pancreatic juice with enzymes forming greater portion.

2. Gastric phase:

- When food reaches stomach, it activates both neural and hormonal mechanisms.
- Gastric distension stimulates pancreas through long vagovagal reflex and local gastropancreatic reflex.
- Gastrin is released from antrum by distension and presence of peptides and amino acids bathing the antral lumen.

3. Intestinal phase:

- It is the main phase of pancreatic secretion; it is mainly mediated by two hormones released from the upper intestine, secretin and cholecystokinin-pancreozymin (CCK).

A. Secretin hormone:

- It is a peptide released into the blood from S cells in upper intestinal mucosa.
- Stimuli for its release:
Mainly acids (pH 4 or less) and to a less extent AA and FA.
- **Functions:**
 - 1) It acts on pancreatic duct cells to stimulate secretion of HCO_3^- and H_2O .
 - 2) It acts on biliary duct cells to stimulate hepatic bile flow and HCO_3^- secretion.
 - 3) It augments the action of CCK in stimulating pancreatic enzyme secretion.
 - 4) It inhibits gastric acid secretion and gastrin release, but it stimulates pepsin secretion.
 - 5) It inhibits gastric motility, contracts pylorus and slows gastric emptying.
 - 6) It relaxes LES.
 - 7) It inhibits intestinal motility and contracts ileocecal sphincter.

B. CCK:

- It is a peptide released from I cells in the upper intestine.
- Stimuli of release:-Mainly by AA and FA and to a lesser extent by HCl.
- **Functions:**
 - 1) It acts on pancreatic acinar cells to stimulate enzyme secretion. It also augments stimulation of H_2O and HCO_3^- secretion by secretin.
 - 2) It has trophic effect on pancreas.
 - 3) It contracts gall bladder, relaxes sphincter of Oddi and causes discharge of bile into the intestine.
 - 4) In small dose it stimulates gastric acid secretion.
 - 5) It stimulates gastric motility, contracts pylorus thus slows gastric emptying.
 - 6) It relaxes LES.
 - 7) It stimulates intestinal motility.

8) It may be concerned with the mechanism of satiety.

- **Summary of pancreatic secretion phases:**

Phase	stimulus	Mediators
Cephalic phase	Smell, taste, chewing and swallowing	Release of Ach and gastrin
Gastric phase	Protein, gastric distention	Vago-vagal reflex
Intestinal phase	Acid in chyme, fatty acids	Secretin, CCK and vago-vagal reflex