D.Saria .N. Mohsin

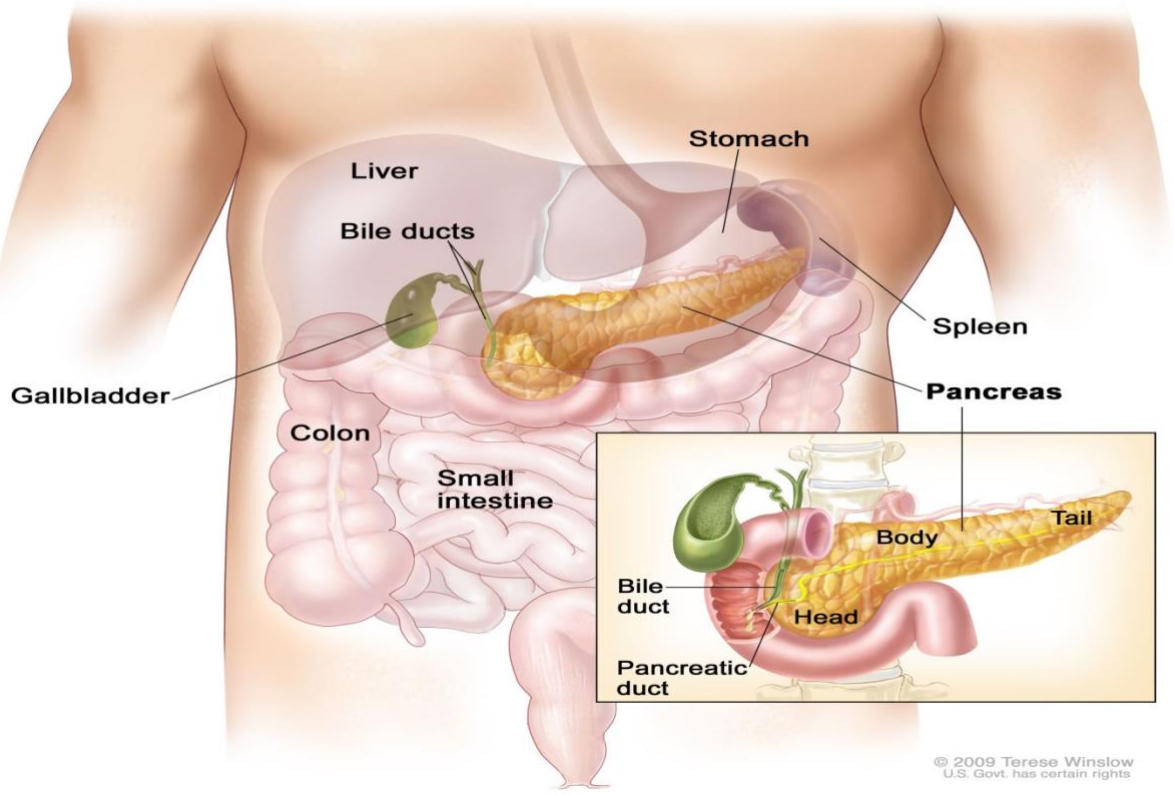
Pancreas

FUNCTIONAL ANATOMY AND NERVE SUPPLY OF PANCREAS

Pancreas is a dual organ having two functions, namely endocrine function and exocrine function. Endocrine function is concerned with the production of hormones (Chapter 69). The exocrine function is concerned with the secretion of digestive juice called pancreatic juice.

NERVE SUPPLY TO PANCREAS

Pancreas is supplied by both sympathetic and parasympathetic fibers. Sympathetic fibers are supplied through splanchnic nerve and parasympathetic fibers are supplied through vagus nerve.



PROPERTIES AND COMPOSITION OF PANCREATIC JUICE

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PROPERTIES OF PANCREATIC JUICE

Volume : 500 to 800 mL/day
Reaction : Highly alkaline with a pH of 8 to 8.3
Specific gravity : 1.010 to 1.018

COMPOSITION OF PANCREATIC JUICE

Pancreatic juice contains 99.5% of water and 0.5% of solids. The solids are the organic and inorganic substances. Composition of pancreatic juice is given in Fig. 39.1. Bicarbonate content is very high in pancreatic juice. It is about 110 to 150 mEq/ L, against the plasma level of 24 mEq/L. High bicarbonate content of pancreatic juice is important because of two reasons:

i. High bicarbonate content makes the pancreatic juice highly alkaline, so that it protects the intestinal mucosa from acid chyme by neutralizing it

ii. Bicarbonate ions provide the required pH (7 to 9) for the activation of pancreatic enzymes.

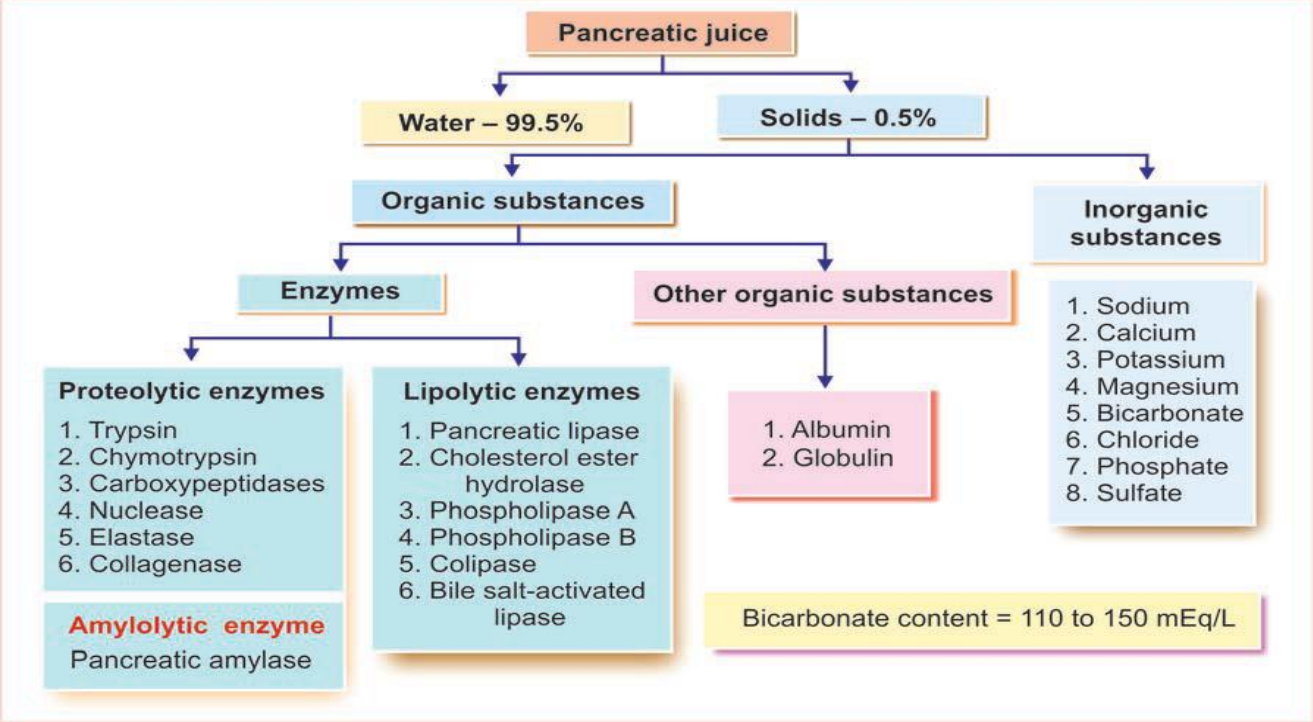

FIGURE 39.1: Composition of pancreatic juice

„ FUNCTIONS OF PANCREATIC JUICE

Pancreatic juice has digestive functions and neutralizing action.

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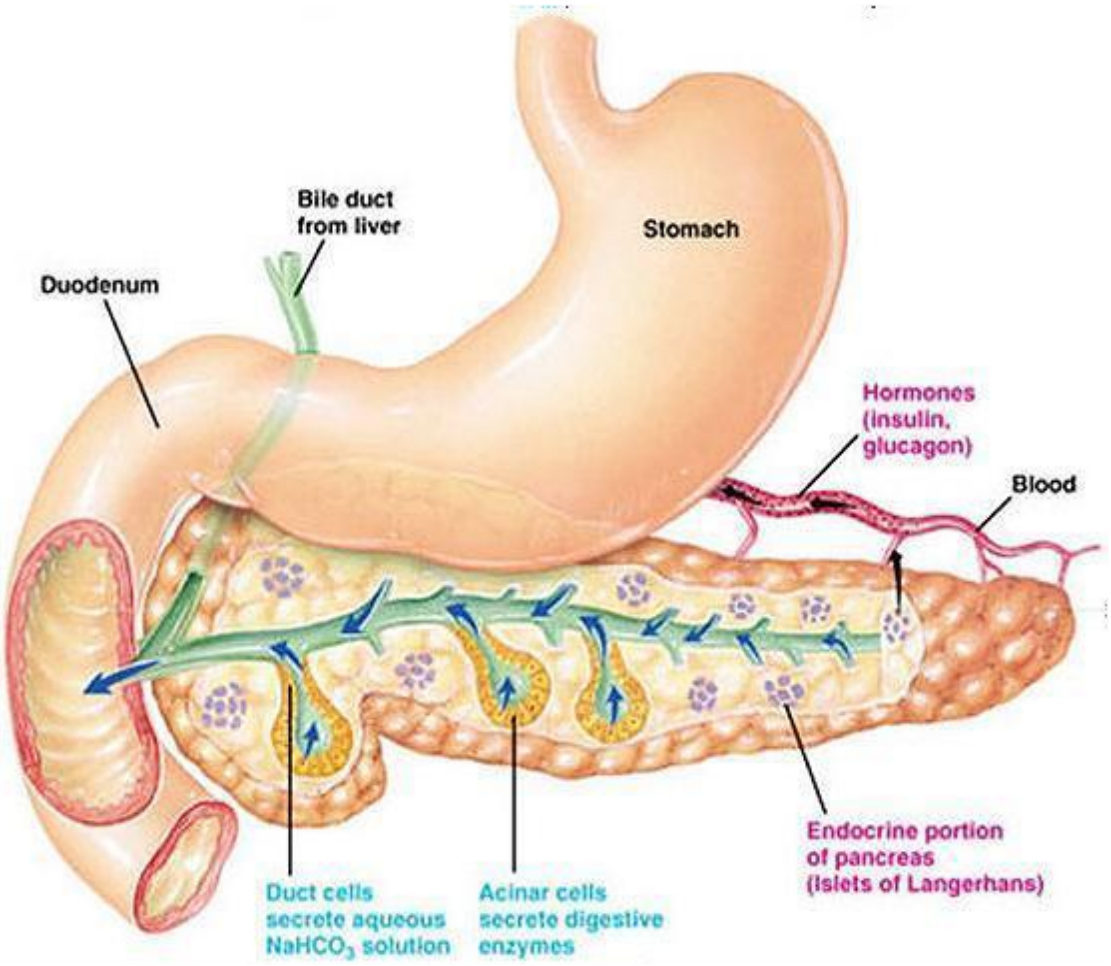
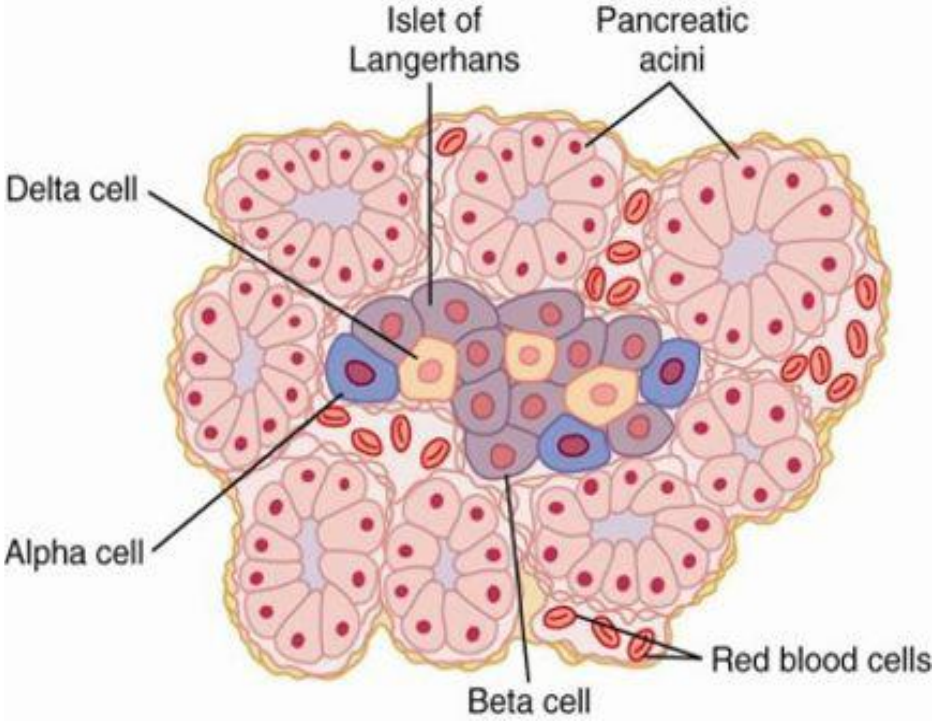
DIGESTIVE FUNCTIONS OF PANCREATIC JUICE

Pancreatic juice plays an important role in the digestion of proteins and lipids. It also has mild digestive action on carbohydrates.





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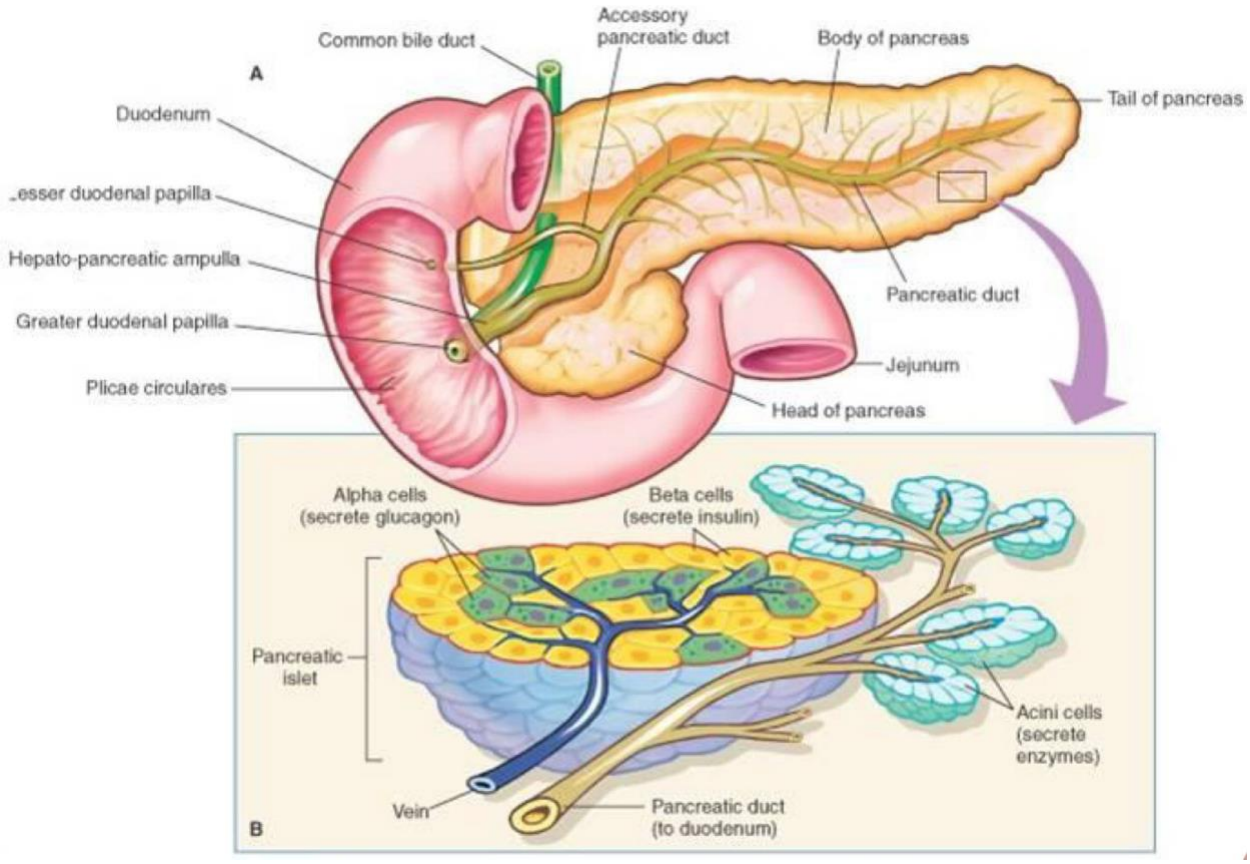
DIGESTION OF PROTEINS

Major proteolytic enzymes of pancreatic juice are try psin and chymotrypsin. Other proteolytic enzymes are carboxypeptidases, nuclease, elastase and collagenase.

1. Trypsin

Trypsin is a single polypeptide with a molecular weight of 25,000. It contains 229 amino acids.It is secreted as inactive trypsinogen, which is converted into active trypsin by enterokinase.Enterokinase is also called enteropeptidase and it is secreted by the brushbordered cells of duodenal mucus membrane. Once formed, trypsin itself activates trypsinogen by means of autocatalytic or autoactive action.



Trypsin inhibitor

Trypsinogen is activated only when it reaches the small intestine. If trypsin is activated when it is in pancreas, it may hydrolyze the pancreatic tissue proteins, resulting in pancreatic damage. But its activation in the secretory cells, acini and ducts of pancreas is prevented by an inhibitor protein called trypsin inhibitor. Any abnormality or deficiency of the trypsin inhibitor will result in unopposed trypsin activity, which damages the pancreas.

Actions of trypsin

i.) Digestion of proteins: Trypsin is the most powerful proteolytic enzyme. It is an endopeptidase and breaks the interior bonds of the protein molecules and converts proteins into proteoses and polypeptides
ii.) Curdling of milk: It converts caseinogen in the milk into casein
iii.)Blood clotting: It accelerates blood clotting
iv.) It activates the other enzymes of pancreatic juice, viz.

a. Chymotrypsinogen into chymotrypsin
b. Procarboxypeptidases into carboxypeptidases
c. Proelastase into elastase
d. Procolipase into colipase
v. Trypsin also activates collagenase, phospholipase A and phospholipase B
vi. Autocatalytic action: Once formed, trypsin itself converts trypsinogen into trypsin.

2. Chymotrypsin

Chymotrypsin is a polypeptide with a molecular weight of 25,700 and 246 amino acids. It is secreted as inactive chymotrypsinogen, which is activated into chymotrypsin by trypsin.

Actions of chymotrypsin

i. Digestion of proteins: Chymotrypsin is also an endopeptidase and it converts proteins into polypeptides
ii. Digestion of milk: Chymotrypsin digests caseinogen faster than trypsin. Combination of both enzymes causes rapid digestion of milk
iii. On blood clotting: No action.

3. Carboxypeptidases

Carboxypeptidases are carboxypeptidase A and carboxypeptidase B. Carboxypeptidase A is derived from the precursor procarboxypeptidase A. Carboxypeptidase B is derived from procarboxypeptidase B. Procarboxypeptidasesare activated into carboxypeptidases by trypsin.

Actions of carboxypeptidases

Carboxypeptidases are exopeptidases and break the terminal bond of protein molecules. Exopeptidases split the polypeptides and other proteins into amino acids. Carboxypeptidase A splits the proteins into amino acids having aromatic or aliphatic side chains. Carboxypeptidase B converts the proteins into aminoacids having basic side chains.

4. Nucleases

Nucleases of pancreatic juice are ribonuclease and deoxyribonuclease, which are responsible for the digestion of nucleic acids. These enzymes convert the ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) into mononucleotides.

5. Elastase

Elastase is secreted as inactive proelastase, which is activated into elastase by trypsin. Elastase digests the elastic fibers.

6. Collagenase

Collagenase is secreted as inactive procollagenase, which is activated into collagenase by trypsin. It digests collagen.

„ DIGESTION OF LIPIDS

Lipolytic enzymes present in pancreatic juice are pancreatic lipase, cholesterol ester hydrolase, phospholipase A, phospholipase B, colipase and bilesaltactivated lipase.

1. Pancreatic lipase

Pancreatic lipase is a powerful lipolytic enzyme. It digests triglycerides into monoglycerides and fatty acids. Activity of pancreatic lipase is accelerated in the presence of bile. Optimum pH required for activity of this enzyme is 7 to 9. Digestion of fat by pancreatic lipase requires two more factors:

i.)Bile salts, which are responsible for the emulsification of fat, prior to their digestion

ii.) Colipase, which is a coenzyme necessary for the pancreatic lipase to digest the dietary lipids. About 80% of the fat is digested by pancreatic lipase. Deficiency or absence of this enzyme leads to excretion of undigested fat in feces (steatorrhea; see below).

2. Cholesterol ester hydrolase

Cholesterol ester hydrolase or cholesterol esteraseconverts cholesterol ester into free cholesterol and fatty acid by hydrolysis.

3. Phospholipase A

Phospholipase A is activated by trypsin. Phospholipase A digests phospholipids, namely lecithin and cephalin and converts them into lysophospholipids. It converts lecithin into lysolecithin and cephalin into lysocephalin.

4. Phospholipase B

Phospholipase B is also activated by trypsin. It converts lysophospholipids (lysolecithin and lysocephalin) tophosphoryl choline and free fatty acids.

5. Colipase

Colipase is a small coenzyme, secreted as inactive procoli pase. Procolipase is activated into colipase by trypsin. Colipase facilitates digestive action of pancreatic lipase on fats.

6. Bile-salt-activated lipase

Bilesaltactivated lipase is the lipolytic enzyme activatedby bile salt. It is also called carboxyl ester lipase or cholesterol esterase. This enzyme has a weak lipolyticaction than pancreatic lipase. But it hydrolyses a varietyof lipids such as phospholipids, cholesterol esters and triglycerides. Human milk contains an enzyme similar tobile-salt-activated lipase (Table 39.1).

TABLE 39.1: Digestive enzymes of pancreatic juice

Enzyme	Activator	Substrate	End products
Trypsin	Enterokinase Trypsin	Proteins	Proteoses and polypeptides
Chymotrypsin	Trypsin	Proteins	Polypeptides
Carboxypeptidases	Trypsin	Polypeptides	Amino acids
Nucleases	Trypsin		Mononucleotides
Elastase	Trypsin	Elastin	Amino acids
Collagenase	Trypsin	Collagen	Amino acids
Pancreatic lipase	Alkaline medium	Triglycerides	Monoglycerides and fatty acids
Cholesterol ester hydrolase	Alkaline medium	Cholesterol ester	Cholesterol and fatty acids

Phospholipase A	Trypsin	Phospholipids	Lysophospholipids
Phospholipase B	Trypsin	Lysophospholipids	Phosphoryl choline and free fatty acids
Colipase	Trypsin	Facilitates action of pancreatic lipase	————
Bilesaltactivated lipase	Trypsin	Phospholipids/ Cholesterol esters/ Triglycerides	Lysophospholipids/ Cholesterol and fatty acids/ Monoglycerides and fatty acids
Pancreatic amylase	————	Starch	Dextrin and maltose

DIGESTION OF CARBOHYDRATES

Pancreatic amylase is the amylolytic enzyme present in pancreatic juice. Like salivary amylase, the pancreatic amylase also converts starch into dextrin and maltose.

NEUTRALIZING ACTION OF PANCREATIC JUICE

When acid chyme enters intestine from stomach, pancreatic juice with large quantity of bicarbonate is released into intestine. Presence of large quantity of bicarbonate ions makes the pancreatic juice highly alkaline. This alkaline pancreatic juice neutralizes acidity of chyme in the intestine.

Neutralizing action is an important function of pancreatic juice because it protects the intestine from the destructive action of acid in the chyme.

MECHANISM OF PANCREATIC SECRETION

SECRETION OF PANCREATIC ENZYMES

Pancreatic enzymes are synthesized in ribosomes,which are attached to the endoplasmic reticulum of acinar cells in pancreas. The raw materials for the synthesis of pancreatic enzymes are the amino acids,

which are derived from the blood. After synthesis, the enzymes are packed into different zymogen granules by Golgi apparatus and stored in cytoplasm. When stimulated, the acinar cells release zymogen granules into the pancreatic duct. From the granules, the enzymes are liberated into intestine.

SECRETION OF BICARBONATE IONS

Bicarbonate ions of pancreatic juice are secreted from the cells of pancreatic ductules and released into the pancreatic duct.

Mechanism of bicarbonate secretion

1. Carbon dioxide derived from blood or metabolic pro cess combines with water inside the cell to form carbonic acid in the presence of carbonic anhydrase
2. Carbonic acid dissociates into hydrogen and bicarbonate ions
3. Bicarbonate ions are actively transported out of the cell into the lumen
4. Hydrogen ion is actively transported into blood in exchange for sodium ion.
5. Sodium ion from the cell is transported into the lumen, where it combines with bicarbonate to form sodium bicarbonate .
6. Because of the loss of sodium and bicarbonate ions from the blood, there is some disturbance inthe osmotic equilibrium of the blood. To maintain the osmotic equilibrium, water leaves the blood and enters the lumen of pancreatic duct by osmosis.
7. In the lumen, bicarbonate combines with water forming the solution of bicarbonate.

REGULATION OF PANCREATIC SECRETION

Secretion of pancreatic juice is regulated by both nervous and hormonal factors.

STAGES OF PANCREATIC SECRETION

Pancreatic juice is secreted in three stages (Fig. 39.2)

like the gastric juice:
1. Cephalic phase
2. Gastric phase
3. Intestinal phase.

These three phases of pancreatic secretion correspond with the three phases of gastric secretion.

„ 1. CEPHALIC PHASE

As in case of gastric secretion, cephalic phase is regulatedby nervous mechanism through reflex action. Two types of reflexes occur:
1. Unconditioned reflex
2. Conditioned reflex.

Unconditioned Reflex

Unconditioned reflex is the inborn reflex. When food is placed in the mouth, salivary secretion (Chapter 37) and gastric secretion (Chapter 38) are induced. Simultaneously, pancreatic secretion also occurs.

Stages of reflex action:

i. Presence of food in the mouth stimulates the taste buds and other receptors in the mouth
ii. Sensory (afferent) impulses from mouth reach dorsal nucleus of vagus and efferent impulses reach pancreatic acini via vagal efferent nerve fibers
iii. Vagal efferent nerve endings secrete acetylcholine, which stimulates pancreatic secretion.

Conditioned Reflex

Conditioned reflex is the reflex response acquired by previous experience (Chapter 162). Presence of food in the mouth is not necessary to elicit this reflex. The sight, smell, hearing or thought of food, which induce salivary secretion and gastric secretion induce pancreatic secretion also.

Stages of reflex action:

i.) Impulses from the special sensory organs (eye,

ear and nose) pass through afferent fibers of neural circuits to the cerebral cortex. Thinking of food stimulates the cerebral cortex directly.
ii.0 From cerebral cortex, the impulses pass through dorsal nucleus of vagus and vagal efferents and reach pancreatic acini
iii.) Vagal nerve endings secrete acetylcholine, which stimulates pancreatic secretion.

2. GASTRIC PHASE

Secretion of pancreatic juice when food enters the stomach is known as gastric phase. This phase of pancreatic secretion is under hormonal control. The hormone involved is gastrin.

When food enters the stomach, gastrin is secreted from stomach (Chapter 39). When gastrin is transported to pancreas through blood, it stimulates the pancreatic secretion. The pancreatic juice secreted during gastric
phase is rich in enzymes.

„ 3. INTESTINAL PHASE

Intestinal phase is the secretion of pancreatic juice when the chyme enters the intestine. This phase is also under hormonal control.

When chyme enters the intestine, many hormones are released. Some hormones stimulate the pancreatic secretion and some hormones inhibit the pancreatic secretion.

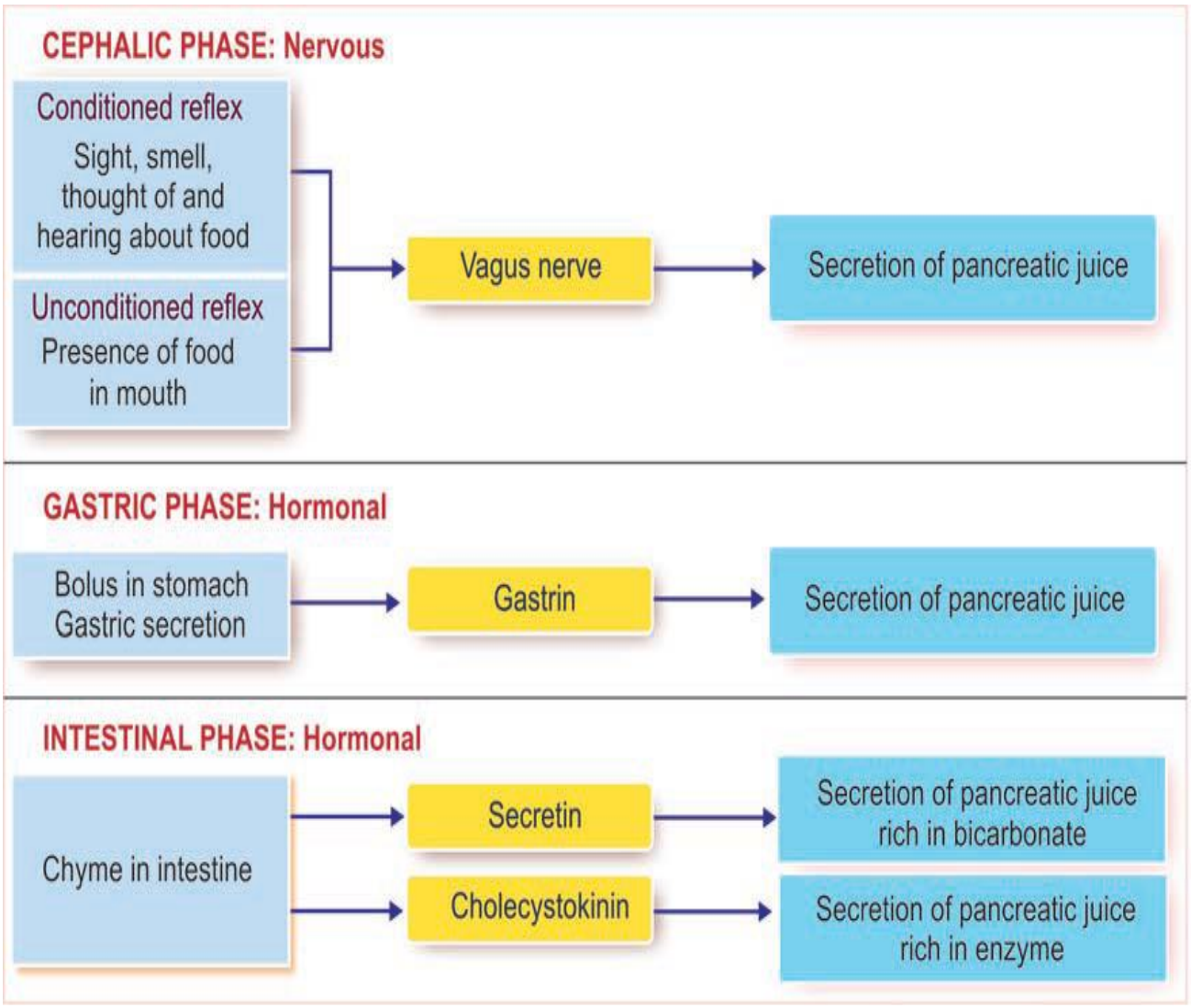


FIGURE 39.2: Schematic diagram showing the regulation of pancreatic secretion

Hormones Stimulating Pancreatic Secretion

i. Secretin

ii. Cholecystokinin.

Secretin

Secretin is produced by S cells of mucous membrane in duodenum and jejunum. It is secreted as inactive prosecretin, which is activated into secretin by acid chyme.

The stimulant for the release and activation of prosecretin is the acid chyme entering intestine.Products of protein digestion also stimulate the hormonal secretion.

Action of secretin

Secretin stimulates the secretion of watery juice which is rich in of bicarbonate ion and high in volume. It increases the pancreactic secretion by acting on pancreatic ductules via cyclic AMP (messenger). Other actions of secretin are explained in Chapter 44.

Cholecystokinin

Cholecystokinin (CCK) is also called cholecystokininpancreozymin (CCKPZ). It is secreted by I cells in duodenal and jejunal mucosa. The stimulant for the release of this hormone is the chyme containing digestive products such as fatty acids, peptides and amino acids.

Action of cholecystokinin

Cholecystokinin stimulates the secretion of pancreatic juice which is rich in enzyme and low in volume, by acting on pancreatic acinar cells via inosine triphosphate (second messenger). The other actions of cholecystokinin are described in Chapter 44.

Hormones Inhibiting Pancreatic Secretion

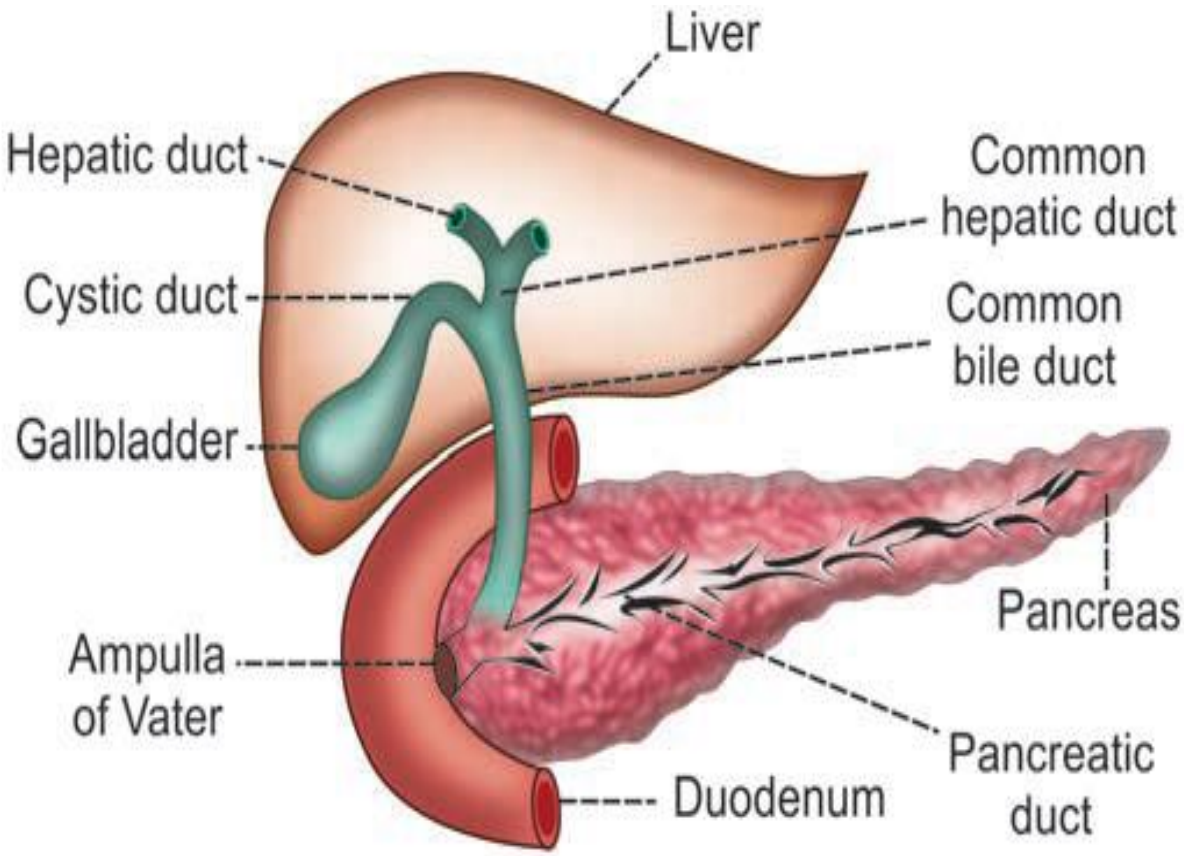
i. Pancreatic polypeptide (PP) secreted by PP cells in islets of Langerhans of pancreas.

ii. Somatostatin secreted by D cells in islets of Langerhans of pancreas.

iii. Peptide YY secreted by intestinal mucosa.

iv. Peptides like ghrelin and leptin.

Refer Chapter 44 for details of these hormones.


Liver
Hepatic duct
Common hepatic duct
Cystic duct
Common bile duct
Gallbladder
Pancreas
Ampulla of Vater
Pancreatic duct
Duodenum