Digestive System
Physiology of the pancreas

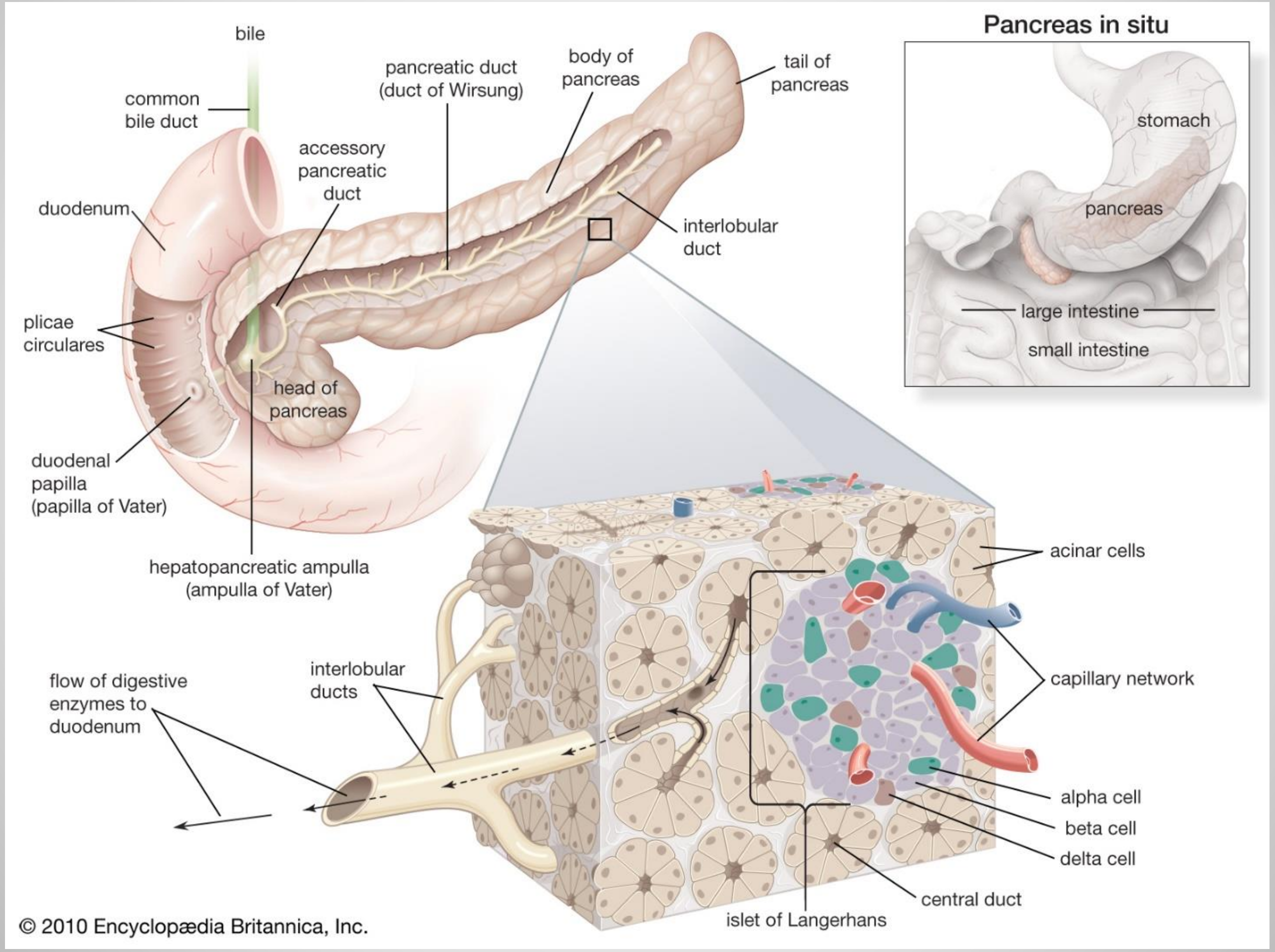
Dr. Hana Alzamil

Objectives

- Pancreatic acini
- Pancreatic secretion
- Pancreatic enzymes
- Control of pancreatic secretion
  - Neural
  - Hormonal
    - Secretin
    - Cholecystokinin

What are the types of glands?

Anatomy of pancreas



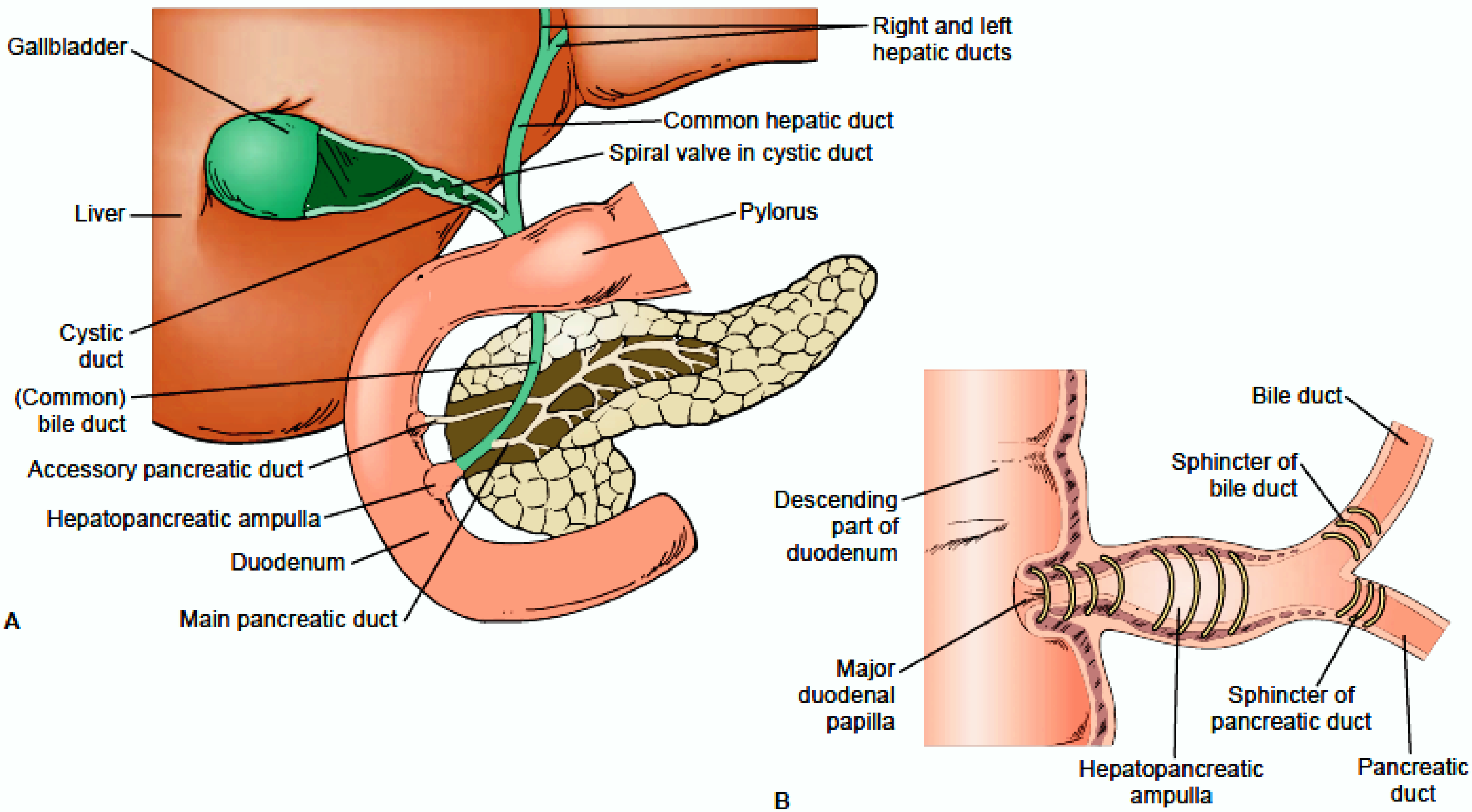


FIGURE 40-18 (**A**) Extrahepatic bile passages, gall bladder, and pancreatic ducts. (**B**) Entry of bile duct and pancreatic duct into the hepatopancreatic ampulla, which opens into the duodenum.

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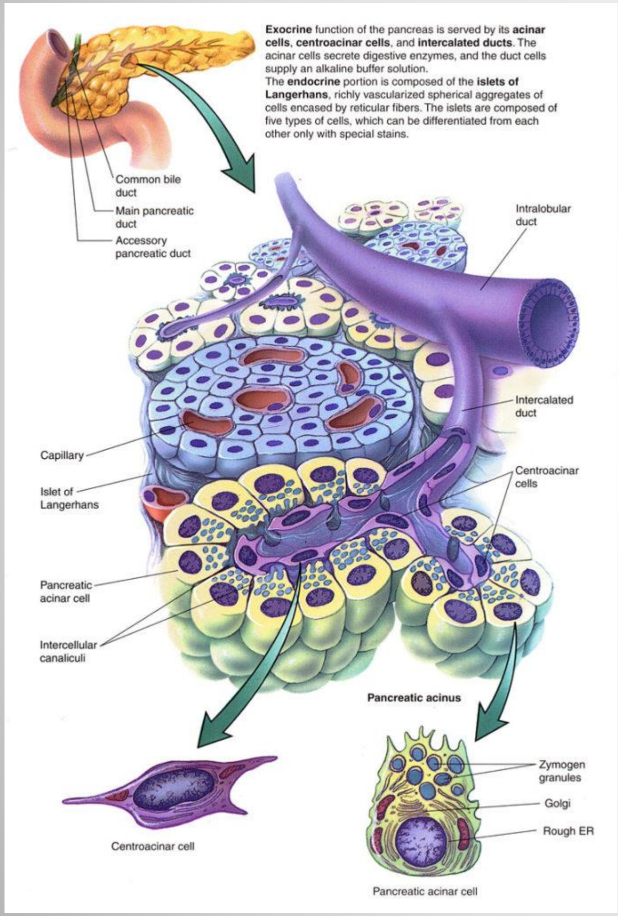
Histology of the Pancreas



- Acini
  - Exocrine
  - 99% of gland
- Islets of Langerhans
  - Endocrine
  - 1% of gland

Secretory function of pancreas

- Acinar and ductal cells in the exocrine pancreas form a close functional unit.
- Pancreatic acini secrete the pancreatic digestive enzymes.
- The ductal cells secrete large volumes of sodium bicarbonate solution
- The combined product of enzymes and sodium bicarbonate solution then flows through a long pancreatic duct
- Pancreatic duct joins the common hepatic duct to form hepatopancreatic ampulla
- The ampulla empties its content through papilla of vater which is surrounded by sphincter of oddi

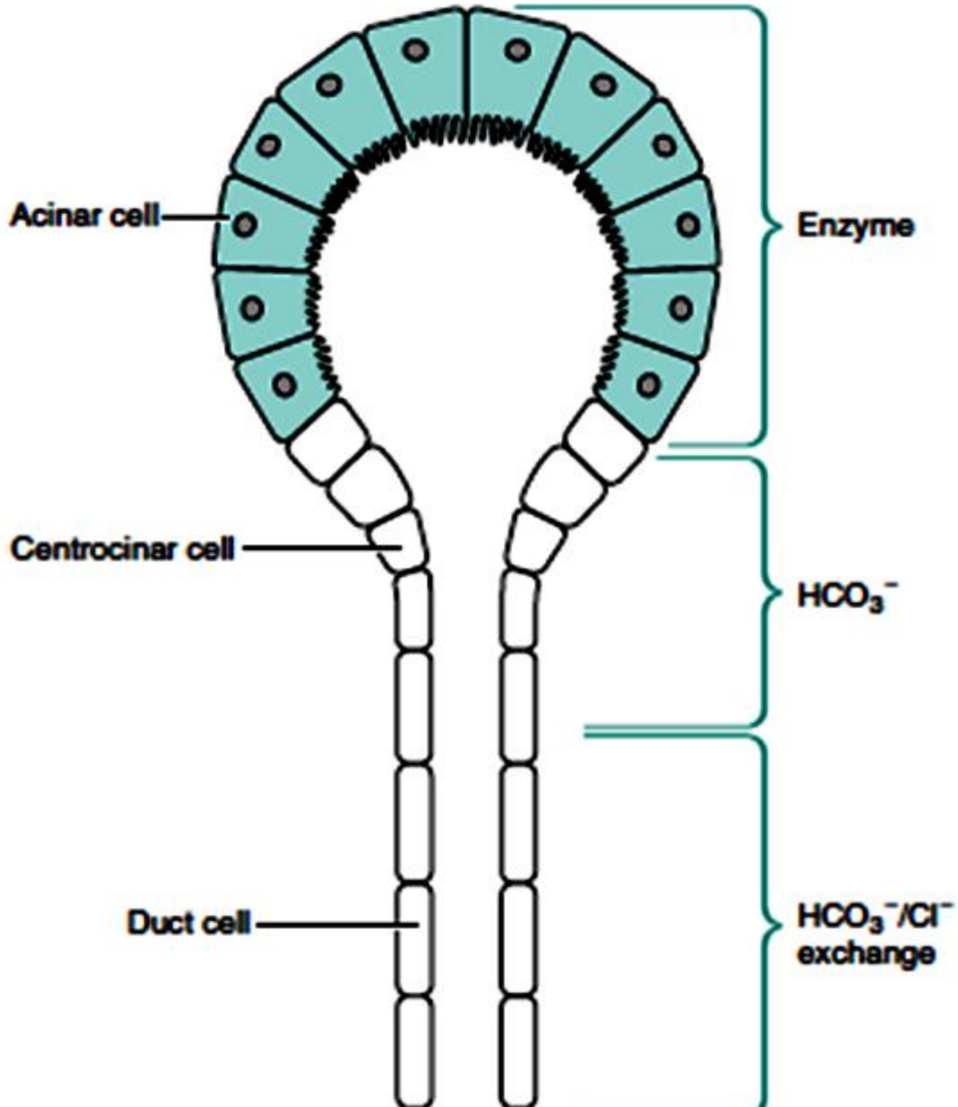


Fig. 5.4
Secretory unit showing the cellular locations of the different secretions.

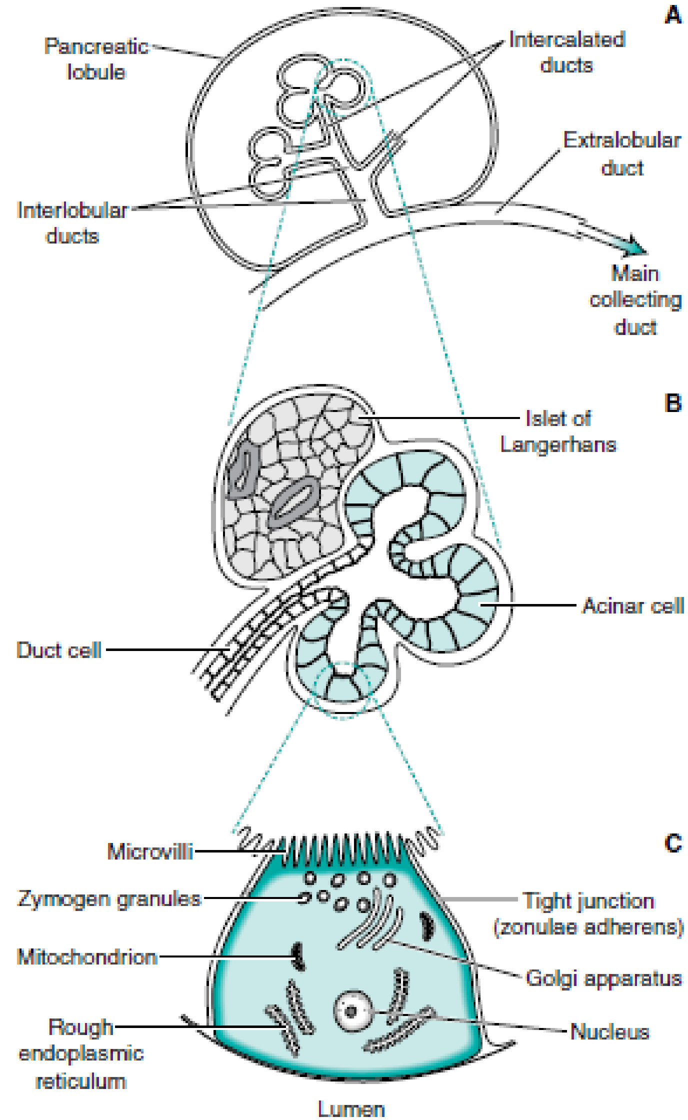


Fig. 5.3
(A) A lobule of the pancreas indicating the duct system, (B) the relationship of an exocrine unit and an islet of Langerhans, (C) an acinar cell.

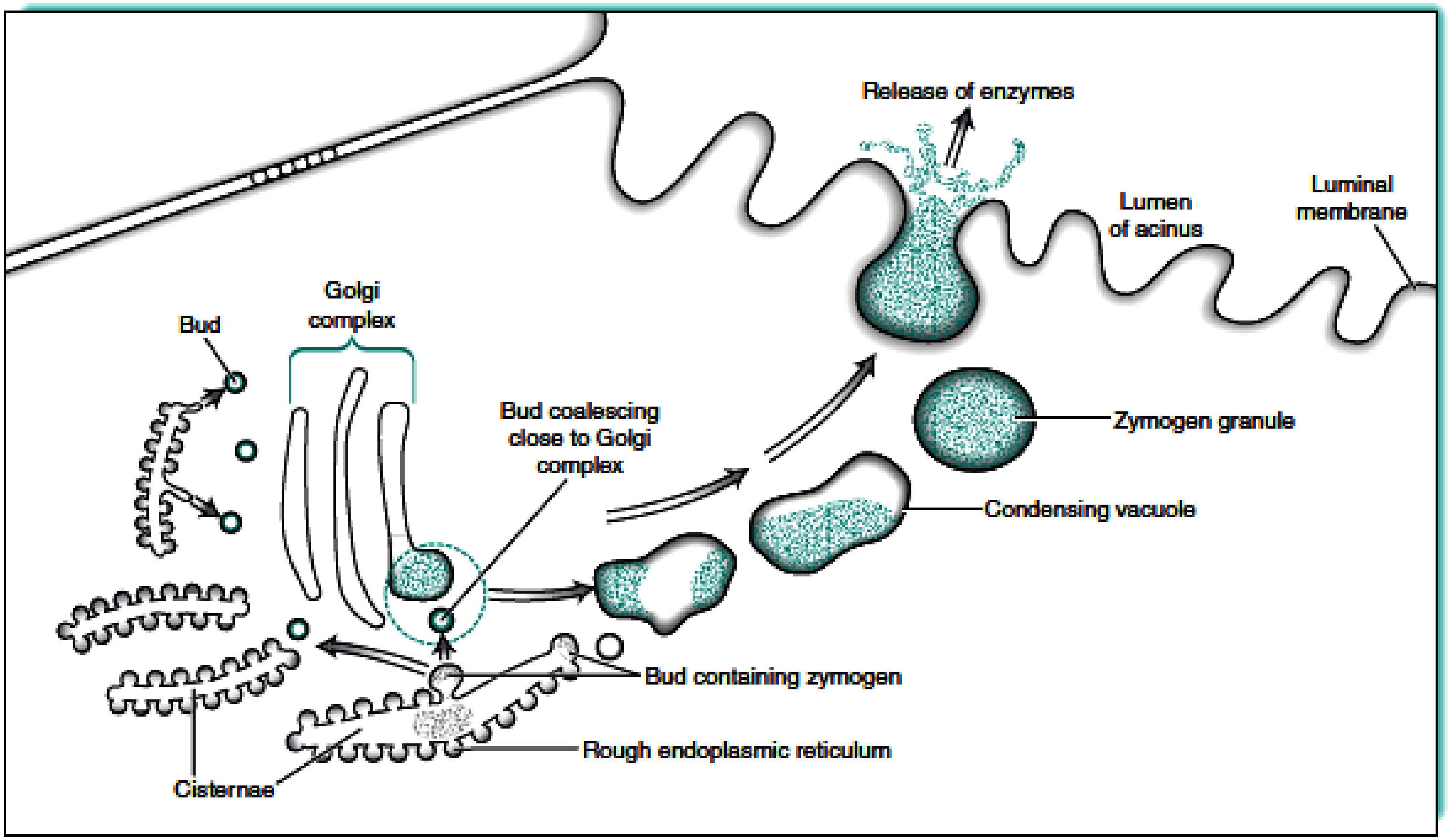


Fig. 5.9
Mechanism of enzyme secretion in the acinar cell.

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Composition of Pancreatic Juice

- Contains
  - Water
  - Sodium bicarbonate
  - Digestive enzymes
    - Pancreatic amylase
    - pancreatic lipase
    - Pancreatic nucleases
    - Pancreatic proteases

Functions of pancreatic secretion

- Fluid (pH from 7.6 to 9.0)
  - acts as a vehicle to carry inactive proteolytic enzymes to the duodenal lumen
  - Neutralizes acidic gastric secretion
- Enzymes
  - Digestion of
    - Proteins
    - Lipids
    - Starch

Physiology – Exocrine Pancreas

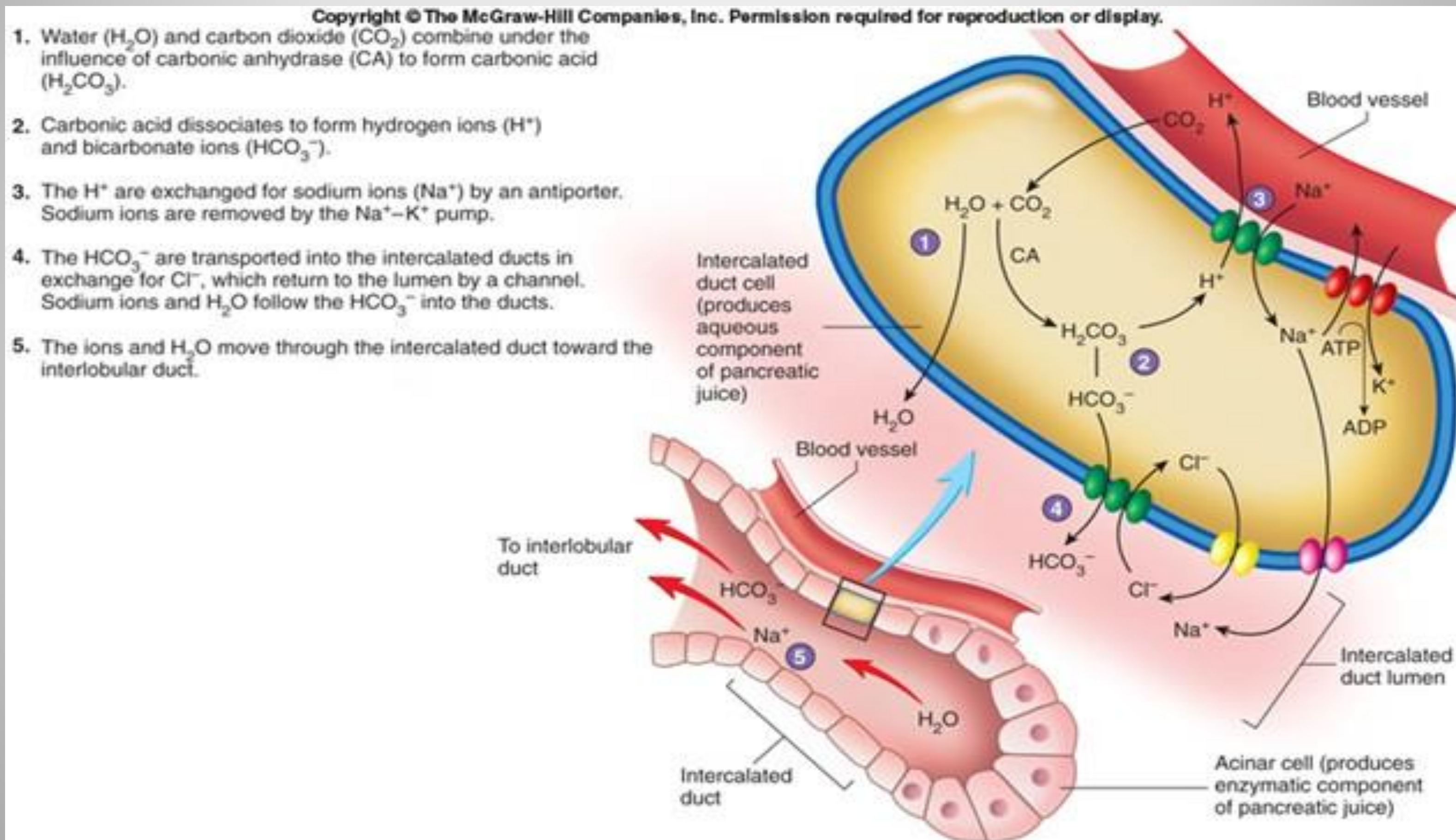
- Pancreatic enzymes originate in the acinar cells
- Secretion of water and electrolytes originates in the centroacinar and intercalated duct cells
- Final product is a colorless, odorless, and isosmotic **alkaline** fluid that contains digestive enzymes (amylase, lipase, chymotrypsinogen and trypsinogen)

Mechanism of $HCO3^-$ Secretion

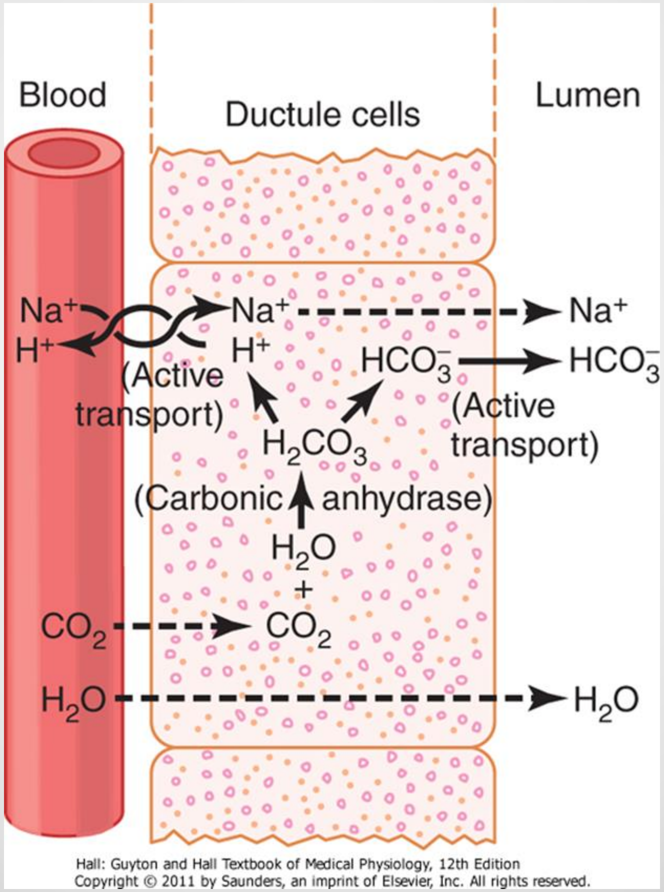
- Apical membrane of ductal cells contains a Cl^--HCO_3^- exchanger
- Basolateral membrane contains Na^+-K^+ ATPase and a Na^+-H^+ exchanger

1. CO_2 and H_2O combine in cells to form H+ and HCO_3^-
2. HCO_3^- is secreted into pancreatic juice by Cl^--HCO_3^- exchanger
3. H^+ is transported into blood by Na^+-H^+ exchanger
    - Absorption of H^+ causes acidification of pancreatic venous blood

Mechanism of HCO3 secretion



Mechanism of HCO3 secretion



Phases of pancreatic secretion

- Cephalic phase:
  - Through vagus nerve
  - 20% of pancreatic enzymes
- Gastric phase
  - Through vagus nerve
  - 5-10 % of pancreatic enzymes
- Intestinal phase
  - Through hormonal stimulation (secretin & CCK)
  - 70-75 % of pancreatic enzymes & fluid

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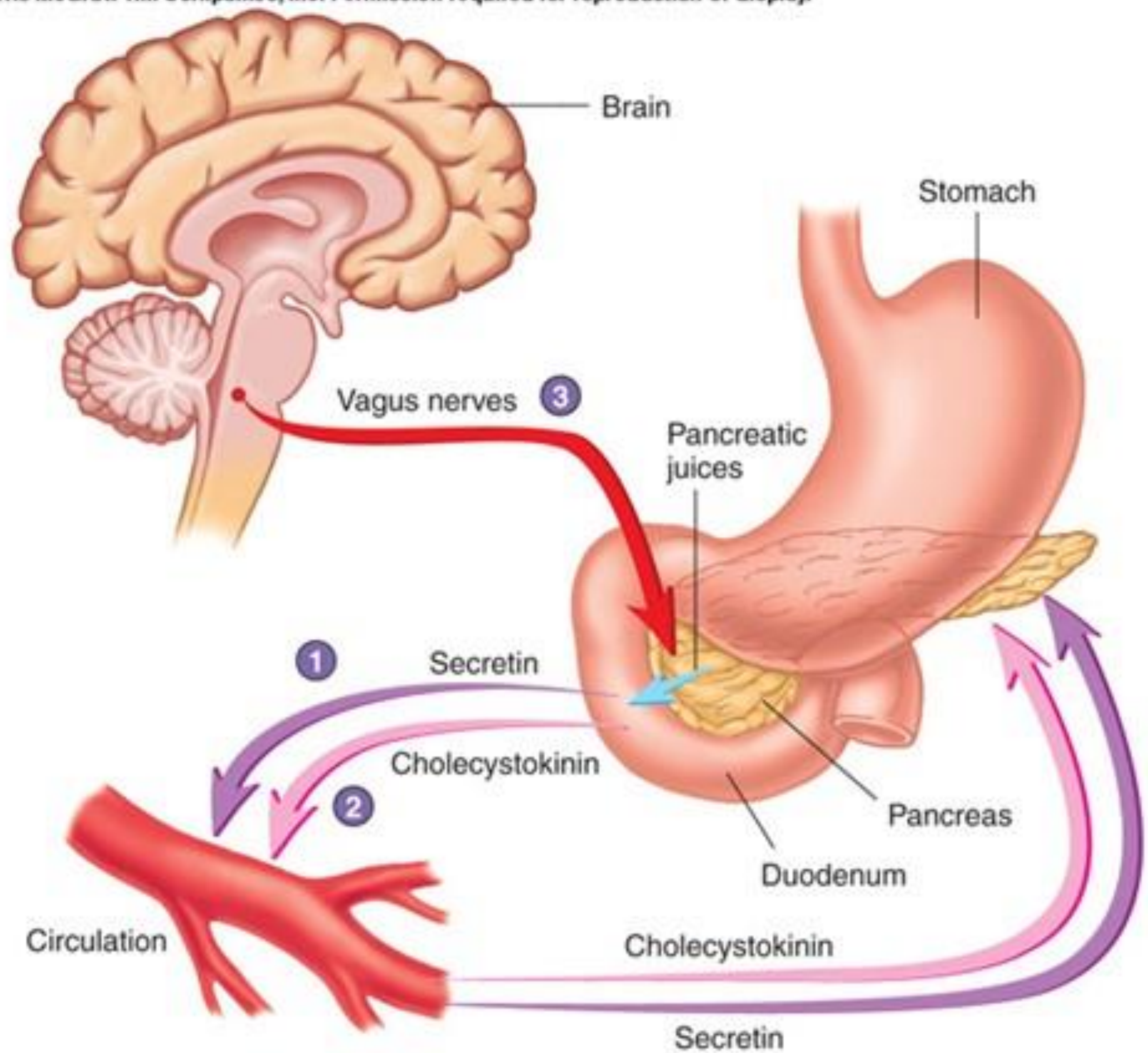
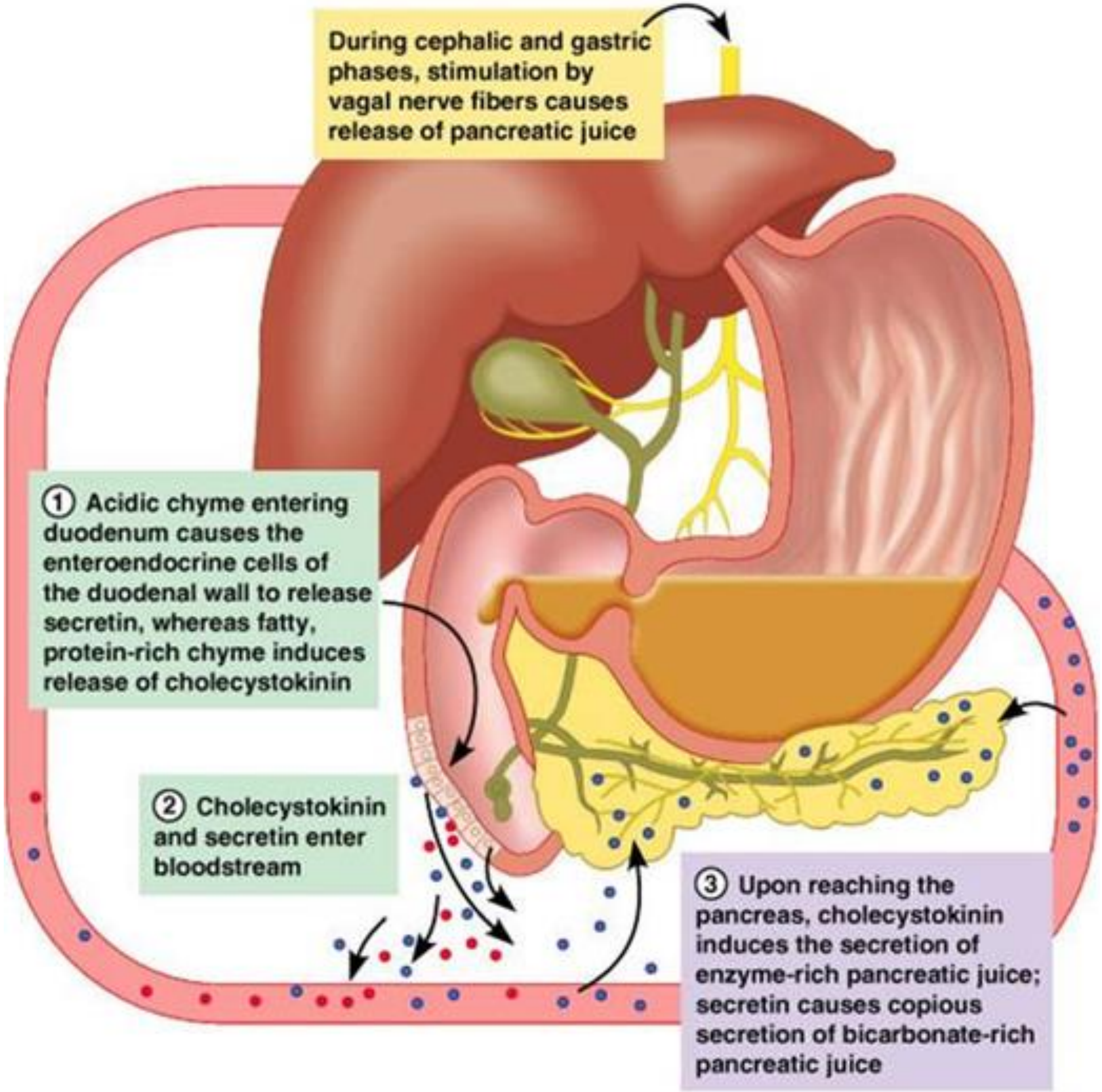
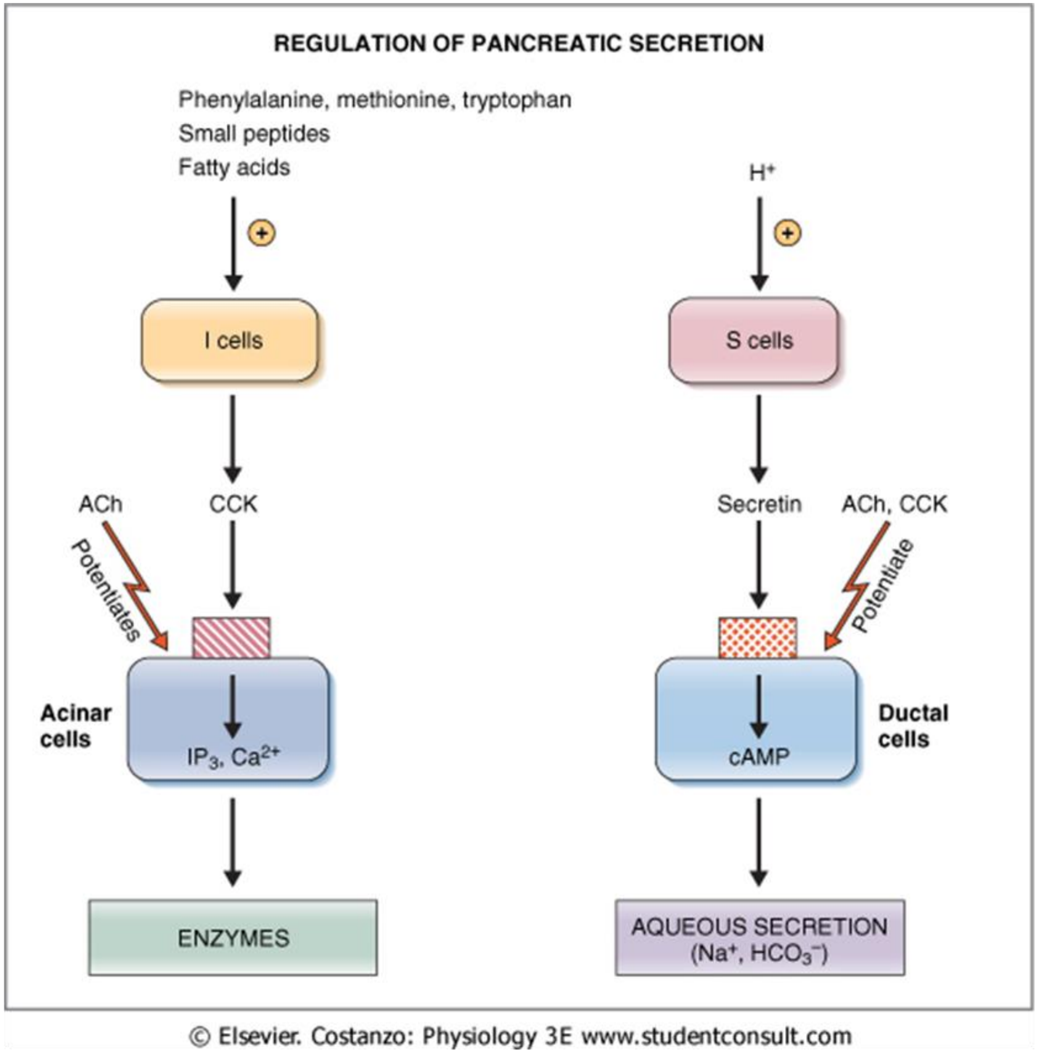
Control of Pancreatic Secretion

- **Acinar cells (enzymatic secretion)**
  - Receptors for CCK and muscarinic receptors for ACh
  - **CCK** is most important stimulant
    - I cells secrete CCK in presence of amino acids and fatty acids in intestinal lumen
  - **ACh** also stimulates enzyme secretion
- **Ductal cells (aqueous secretion of HCO_3^-)**
  - Receptors for CCK, ACh, and secretin
  - **Secretin** (from S cells of duodenum) is major stimulant
    - Secreted in response to H^+ in intestine
  - Effects of secretin are potentiated by both CCK and ACh

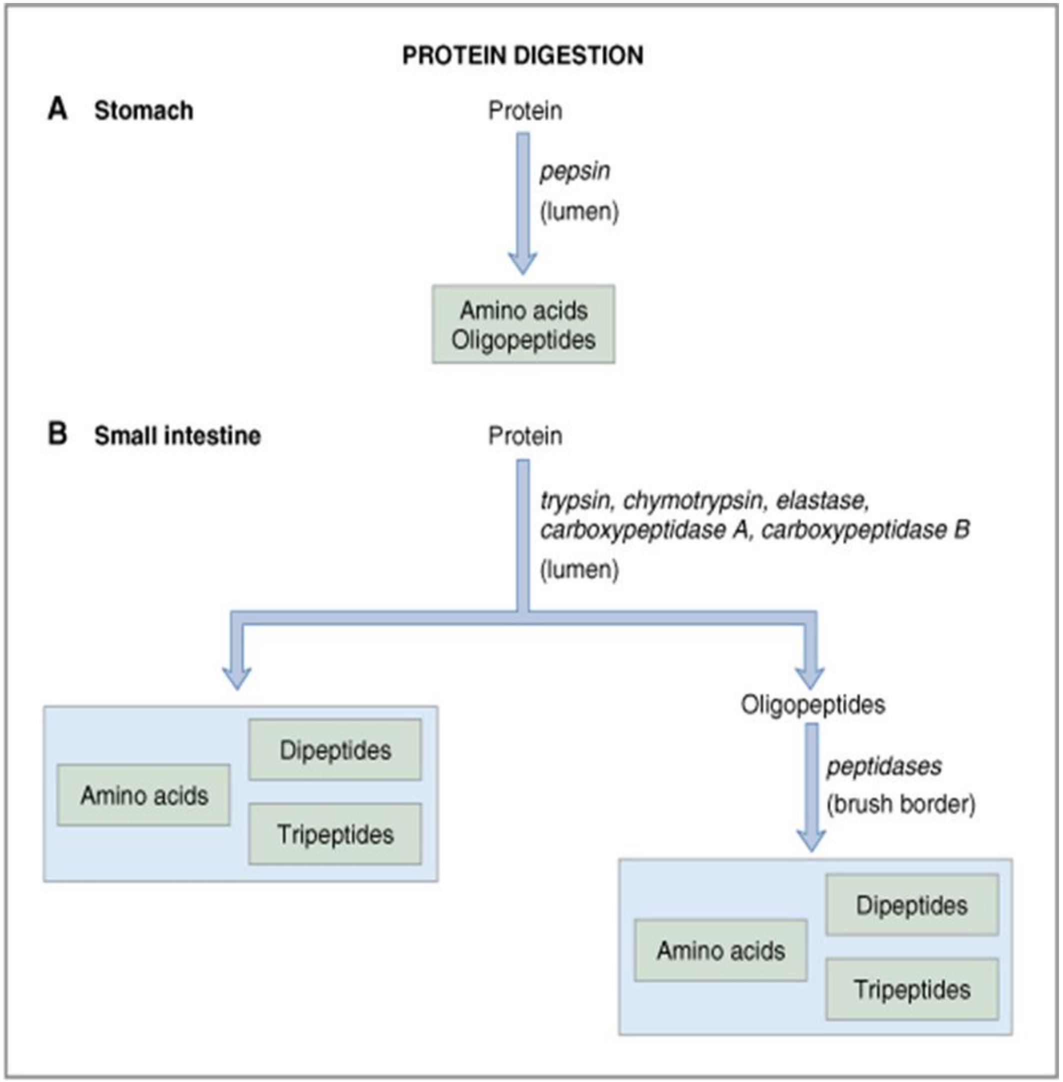
1. Secretin (*purple arrows*) released from the duodenum stimulates the pancreas to release a watery secretion rich in HCO_3^-.
2. Cholecystokinin (*pink arrows*) released from the duodenum causes the pancreas to release a secretion rich in digestive enzymes.
3. Parasympathetic stimulation from the vagus nerve (*red arrow*) causes the pancreas to release a secretion rich in digestive enzymes.




During cephalic and gastric phases, stimulation by vagal nerve fibers causes release of pancreatic juice
① Acidic chyme entering duodenum causes the enteroendocrine cells of the duodenal wall to release secretin, whereas fatty, protein-rich chyme induces release of cholecystokinin
② Cholecystokinin and secretin enter bloodstream
③ Upon reaching the pancreas, cholecystokinin induces the secretion of enzyme-rich pancreatic juice; secretin causes copious secretion of bicarbonate-rich pancreatic juice

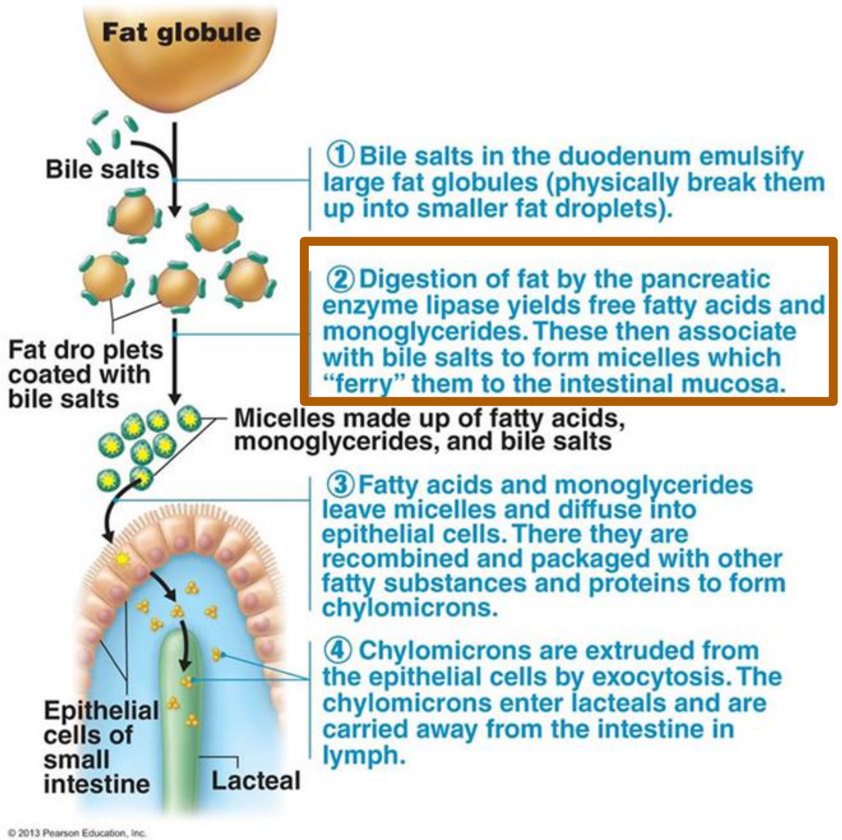


Regulation of pancreatic secretion. ACh, Acetylcholine; cAMP, cyclic adenosine monophosphate; CCK, cholecystokinin; IP_3, inositol 1,4,5-triphosphate



Digestion of proteins in the stomach (A) and small intestine (B).

Hormone	Stimuli for Secretion	Site of Secretion	Actions
Gastrin	Protein Distention Nerve *(Acid inhibits release)*	G cells of the antrum, duodenum, and jejunum	Stimulates Gastric acid secretion Mucosal growth
Cholecystokinin	Protein Fat Acid	I cells of the duodenum, jejunum, and ileum	Stimulates Pancreatic enzyme secretion Pancreatic bicarbonate secretion Gallbladder contraction Growth of exocrine pancreas Inhibits Gastric emptying
Secretin	Acid Fat	S cells of the duodenum, jejunum, and ileum	Stimulates Pepsin secretion Pancreatic bicarbonate secretion Biliary bicarbonate secretion Growth of exocrine pancreas Inhibits Gastric acid secretion
Gastric inhibitory peptide	Protein Fat Carbohydrate	K cells of the duodenum and jejunum	Stimulates Insulin release Inhibits Gastric acid secretion
Motilin	Fat Acid Nerve	M cells of the duodenum and jejunum	Stimulates Gastric motility Intestinal motility


Fat globule
Bile salts
Fat dro plets coated with bile salts
Micelles made up of fatty acids, monoglycerides, and bile salts
Epithelial cells of small intestine
Lacteal
① Bile salts in the duodenum emulsify large fat globules (physically break them up into smaller fat droplets).
② Digestion of fat by the pancreatic enzyme lipase yields free fatty acids and monoglycerides. These then associate with bile salts to form micelles which "ferry" them to the intestinal mucosa.
③ Fatty acids and monoglycerides leave micelles and diffuse into epithelial cells. There they are recombined and packaged with other fatty substances and proteins to form chylomicrons.
④ Chylomicrons are extruded from the epithelial cells by exocytosis. The chylomicrons enter lacteals and are carried away from the intestine in lymph.
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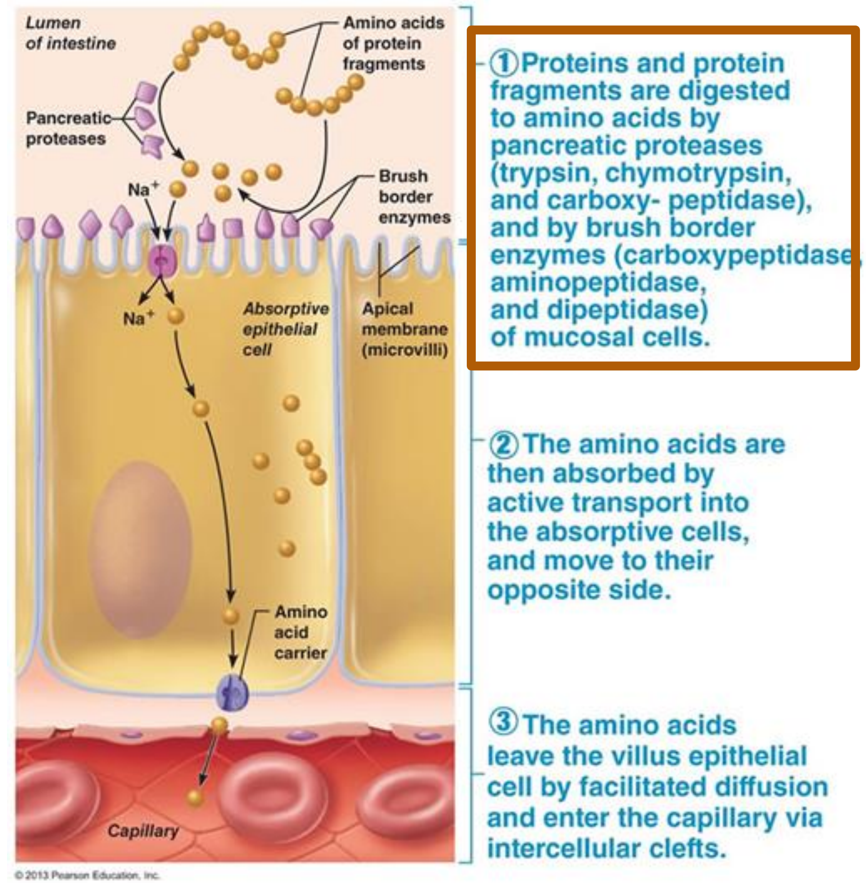
Lumen of intestine
Amino acids of protein fragments
Pancreatic proteases
Brush border enzymes
Na+
Na+
Absorptive epithelial cell
Apical membrane (microvilli)
Amino acid carrier
Capillary
① Proteins and protein fragments are digested to amino acids by pancreatic proteases (trypsin, chymotrypsin, and carboxy- peptidase), and by brush border enzymes (carboxypeptidase, aminopeptidase, and dipeptidase) of mucosal cells.
② The amino acids are then absorbed by active transport into the absorptive cells, and move to their opposite side.
③ The amino acids leave the villus epithelial cell by facilitated diffusion and enter the capillary via intercellular clefts.
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What protect pancreas from digestion by its enzymes

- Pancreatic enzymes are secreted in inactive form: trypsinogen, chymotrypsinogen, procarboxypolypeptidase.
- They will be activated by **enterokinase** enzyme in small intestine to their active forms.
- The acinar cells that secrete the enzymes secretes **trypsin inhibitor** which prevent activation of trypsin inside acini and ducts.
- When a duct is blocked the trypsin inhibitor **can not inhibit activation** of accumulated enzymes which will be activated and digest the pancreas in few hours.

Table 5.1
Activation of enzyme precursors in the small intestine

Precursor		*Active enzyme*
Trypsinogen	*enterokinase, trypsin* →	trypsin + peptide
Chymotrypsinogen	*trypsin* →	chymotrypsin + peptide
Proelastase	*trypsin* →	elastase + peptide
Procarboxypeptidase	*trypsin* →	carboxypeptidase + peptide
Prophospholipase A	*trypsin* →	phospholipase A + peptide

Enterokinase is an enzyme that is secreted by brush border of small intestine and activate pancreatic enzymes.
Trypsin inhibitor is secreted by acinar cells to prevent activation of the enzymes inside the cells, in the acini and in the ducts.

Group activity

Flipped classroom

- Divide into 6 groups
- Prepare presentation about
  - Enteric nervous system
  - Swallowing
  - Function of saliva
  - Motor function of the stomach
  - Secretory functions of the stomach
  - Mechanism of HCL secretion

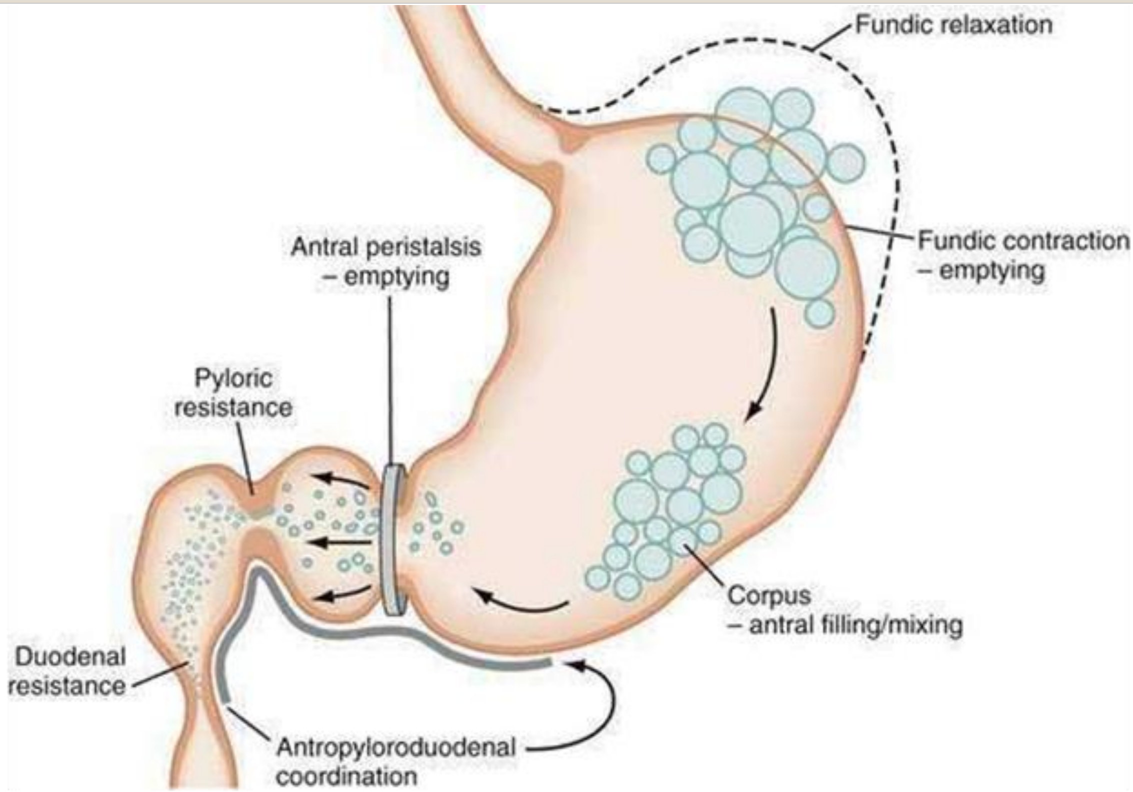

Figure 48-8. Spectrum of gastric neuromuscular work after ingestion of a solid meal. To receive the ingested solid foods and accommodate the volume of food without increasing intragastric pressure, the fundic smooth muscle relaxes (receptive relaxation). The fundus then contracts to empty the ingested food into the corpus and antrum for trituration and emptying. Recurrent corpus-antral peristaltic waves mill the solids into chyme, which is composed of 1- to 2-mm solid particles suspended in gastric juice. Antral peristaltic waves, indicated by the ring-like indentation in the antrum, empty 2 to 4 mL of the chyme through the pylorus and into the duodenal bulb at the slow wave frequency of three peristaltic contractions per minute. Antropyloroduodenal coordination indicates efficient emptying of chyme through the pylorus, which modulates flow of the chyme by varying sphincter resistance. Contractions in the duodenum also provide resistance to emptying.
(Modified from Koch KL. Physiological basis of electrogastrography. In: Koch KL, Stern RM, editors. Handbook of Electrogastrography.New York, NY: Oxford Press; 2004. pp 37-67.)