

**(Chapter 65; Pages 825-827;
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Pancreatic Secretion

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Required Textbook

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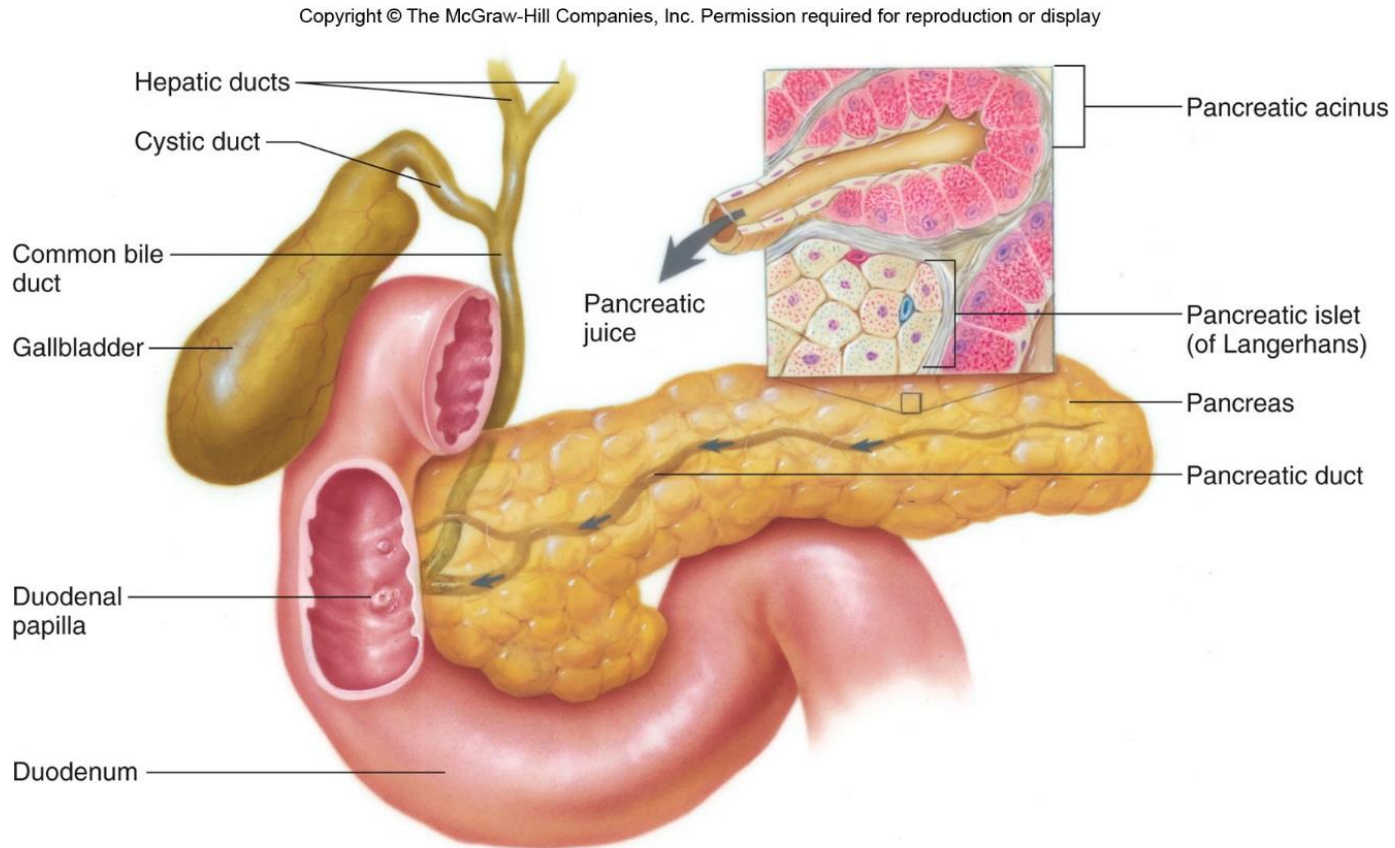
Pancreatic Secretion (Exocrine)

Objectives:

- 1. Functional Anatomy**
- 2. Major components of pancreatic juice and their physiologic roles**
- 3. Cellular mechanisms of bicarbonate secretion**
- 4. Cellular mechanisms of enzyme secretion**
- 5. Activation of pancreatic enzymes**
- 6. Hormonal & neural regulation of pancreatic secretion**
- 7. Potentiation of the secretory response**

Functional Anatomy

- 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



Islet of Langerhans in the pancreas.

The pancreas, in addition to its digestive functions, secretes two important hormones:

1. Insulin (Beta cells; 60%).
2. Glucagon (Alpha cells; ~25%).

that are crucial for normal regulation of glucose, lipid, and protein metabolism.

Also Somatostatin is secreted by delta cells (form ~10% of islets's cells).

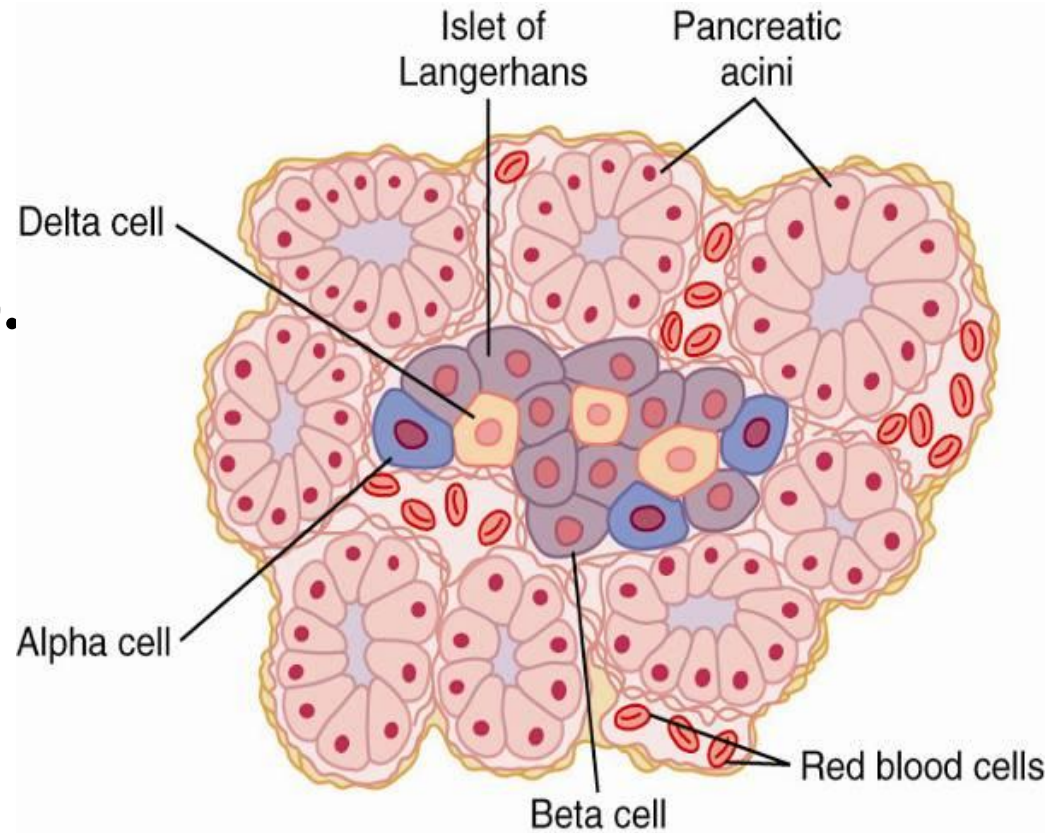
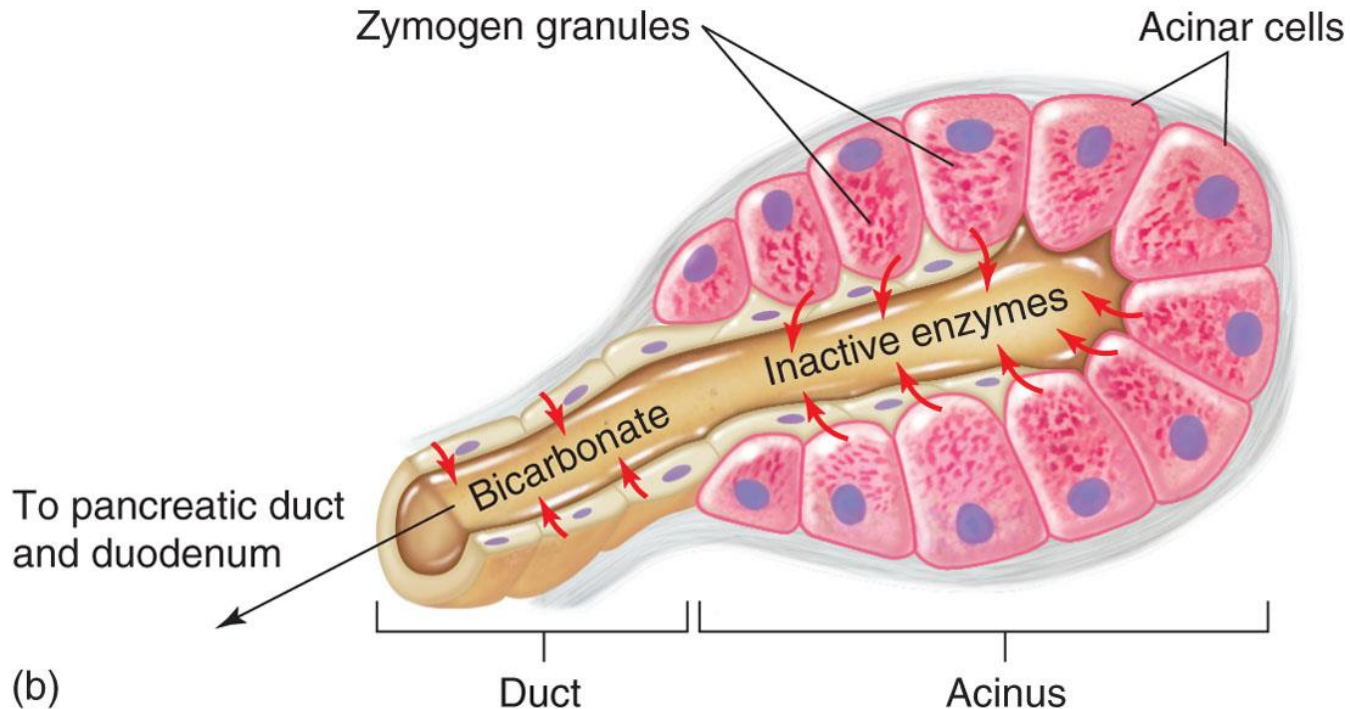


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Functional Anatomy (cont.)

- 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.
- Pancreatic juice is secreted in response to the presence of chyme in the upper portions of the small intestine.

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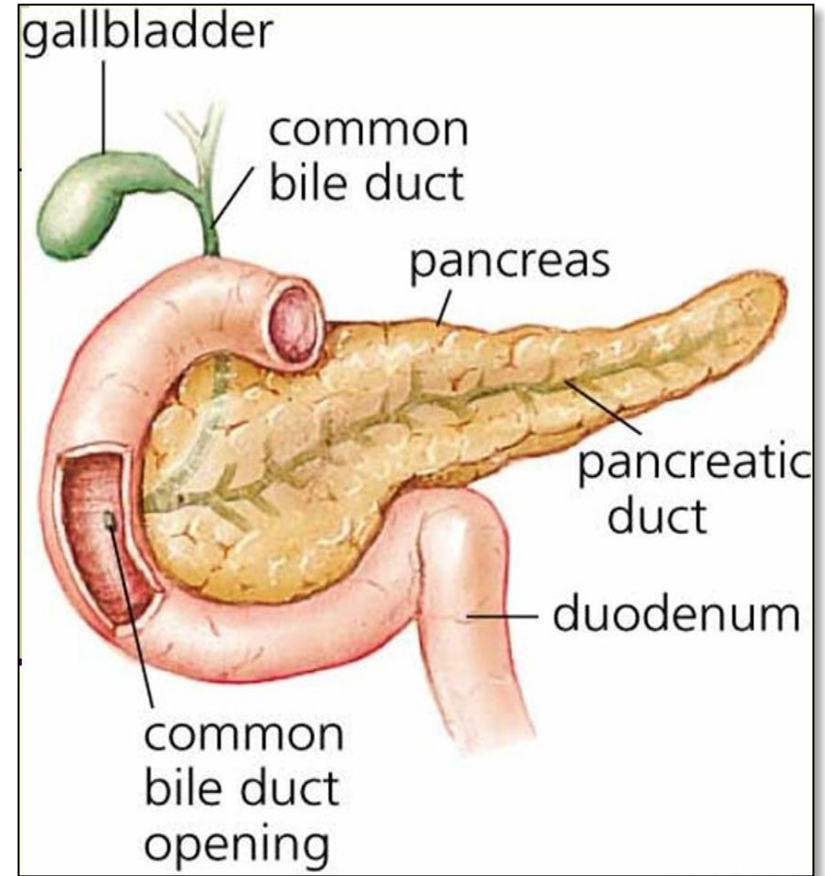


Pancreatic Secretion

- **The major functions of pancreatic secretion:**
 1. **To neutralize the acids in the duodenal chyme to optimum range (pH= 7.0-8.0) for activity of pancreatic enzymes.**
 2. **To prevent damage to duodenal mucosa by acid & pepsin.**
 3. **To produce enzymes involved in the digestion of dietary carbohydrate, fat, and protein.**

Flow of Pancreatic Secretion into Duodenum

- **The combined product of enzymes and NaCO_3 flows through a long pancreatic duct.**
- **Pancreatic duct joins the hepatic duct immediately before it empties into the duodenum through the papilla of Vater, surrounded by the sphincter of Oddi.**



Pancreatic secretion (continued)

- **Pancreatic secretions contain many enzymes for digesting proteins, carbohydrates, and fats, and large quantities of HCO_3 ions.**
- **The most important pancreatic enzymes for digesting proteins are:**
 - 1. *Trypsin.***
 - 2. *Chymotrypsin.***
 - 3. *Carboxypolypeptidase.***
- **Trypsin and chymotrypsin split whole and partially digested proteins into peptides of various sizes but do not cause release of individual amino acids.**
- **Carboxypolypeptidase splits some peptides into individual amino acids, thus completing digestion of some proteins to amino acids.**

Pancreatic Enzymes (continued)

When first synthesized in the pancreatic cells, the proteolytic digestive enzymes are in the inactive forms:

- 1. Trypsinogen**
- 2. Chymotrypsinogen**
- 3. Procarboxypolypeptidase**

These enzymes become activated only after they are secreted into the intestinal tract.

1. Trypsinogen is activated by:

- Enteropeptidase (enterokinase), an enzyme secreted by the intestinal mucosa when chyme comes in contact with the mucosa.**

- Trypsinogen can be autocatalytically activated by trypsin formed from previously secreted trypsinogen.**

2 & 3. Chymotrypsinogen and procarboxypolypeptidase are activated by trypsin to form chymotrypsin and carboxypolypeptidase.

Trypsin Inhibitor

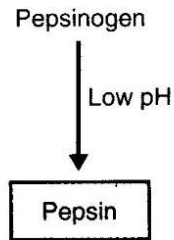
Secretion of Trypsin Inhibitor Prevents Digestion of the Pancreas Itself.

- **Proteolytic enzymes of the pancreatic juice do not become activated until after they have been secreted into the intestine because the trypsin and the other enzymes would digest the pancreas itself.**
- **The same cells that secrete proteolytic enzymes into the acini of the pancreas secrete another substance called trypsin inhibitor, which is formed in the cytoplasm of the glandular cells, and it prevents activation of trypsin both inside the secretory cells and in the acini and ducts of the pancreas.**
- **Because trypsin activates the other pancreatic proteolytic enzymes, therefore trypsin inhibitor prevents activation of the other enzymes as well.**

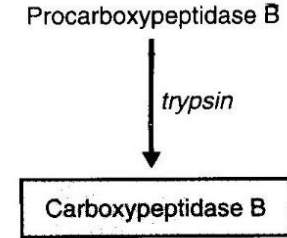
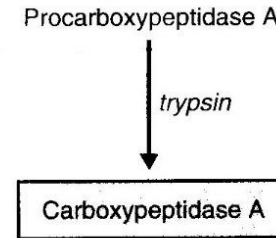
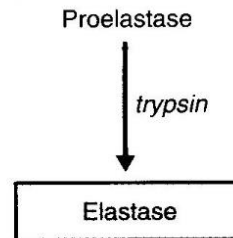
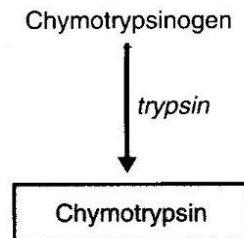
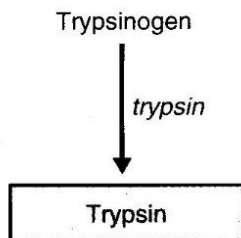
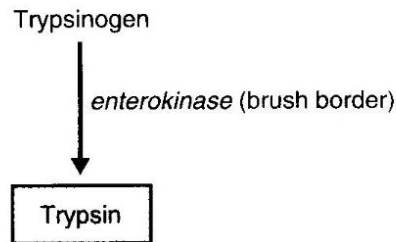
Activation of Trypsinogen in duodenal Lumen

ACTIVATION OF GASTROINTESTINAL PROTEASES

A Stomach

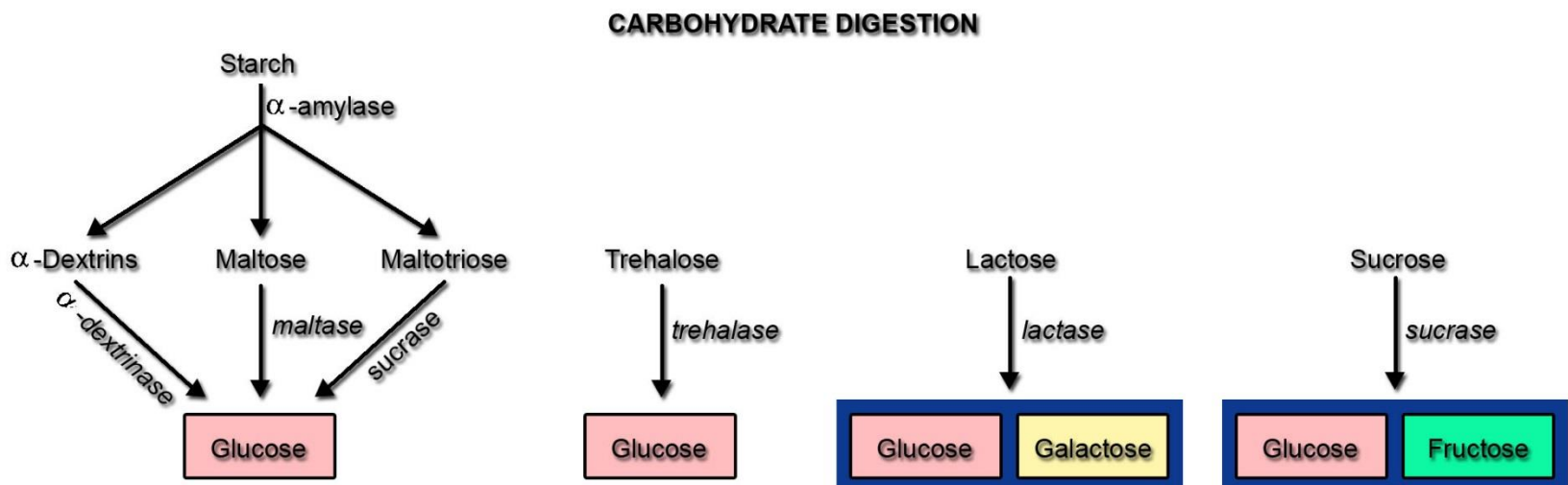


B Small intestine



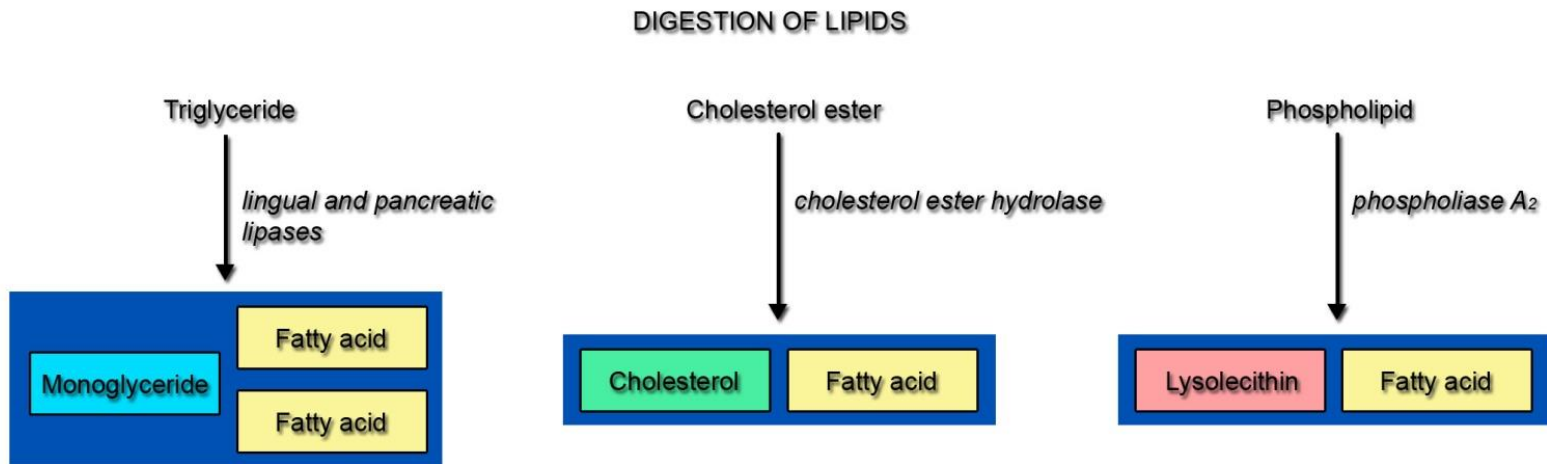
Pancreatic secretion (continued)

- The pancreatic enzyme for digesting carbohydrates is *pancreatic amylase*, which *hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few tri-saccharides.*



Pancreatic secretion (continued)

- The main enzymes for fat digestion are:
 - (1) *Pancreatic lipase*
 - (2) *Cholesterol esterase*
 - (3) *Phospholipase*



Characteristics of Pancreatic Enzymes

Enzyme

Specific Hydrolytic Activity

Proteolytic

Endopeptidases

Trypsin(ogen)

Chymotrypsin(ogen)

(Pro)elastase

Exopeptidase

(Pro)carboxypeptidase

Amylolytic

α -Amylase

Lipases

Lipase

(Pro)phospholipase A₂

Carboxylester hydrolase

(cholesterol esterase)

Nucleolytic

Ribonuclease

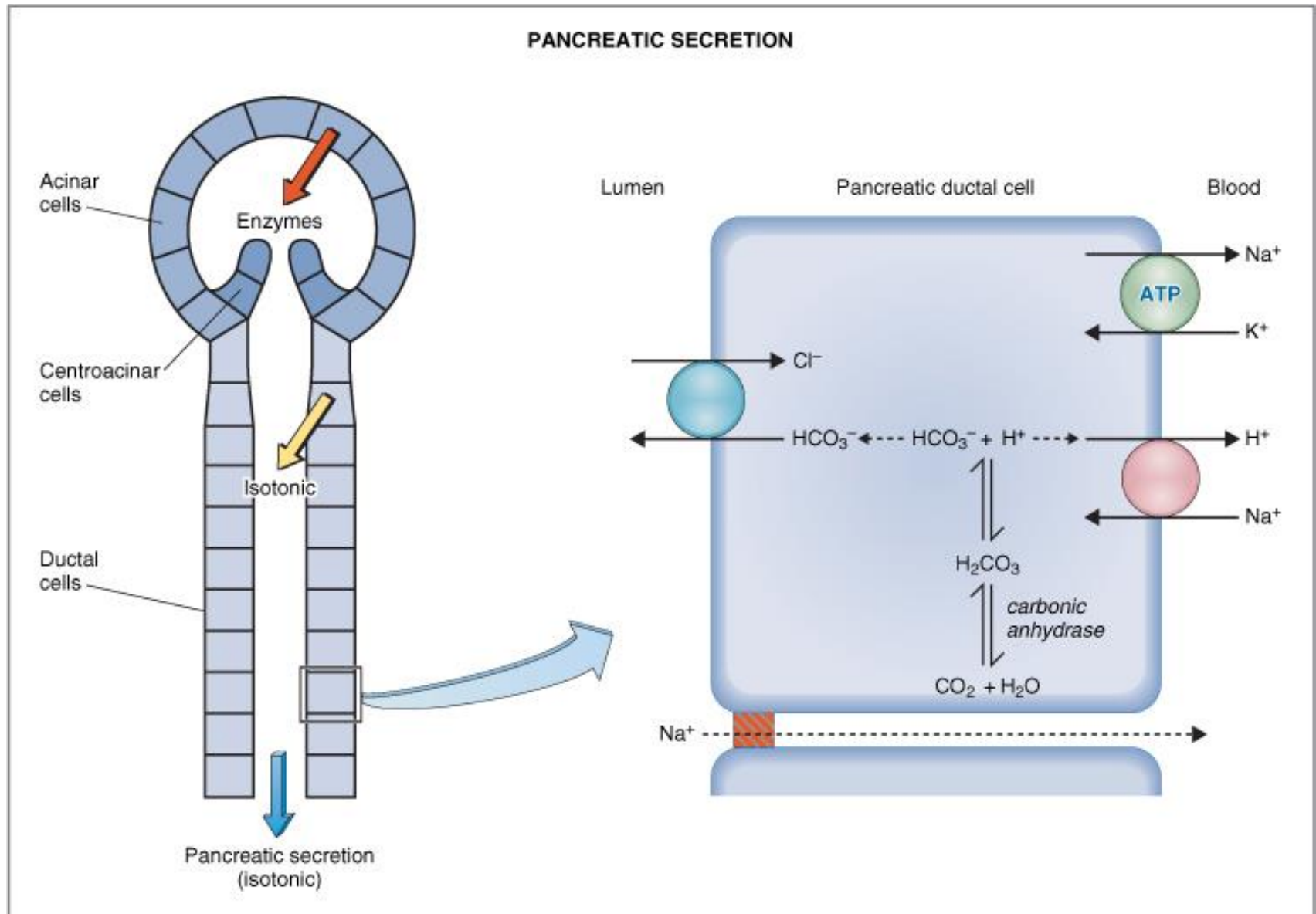
Deoxyribonuclease

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

Pancreatic secretions are rich in bicarbonate ions

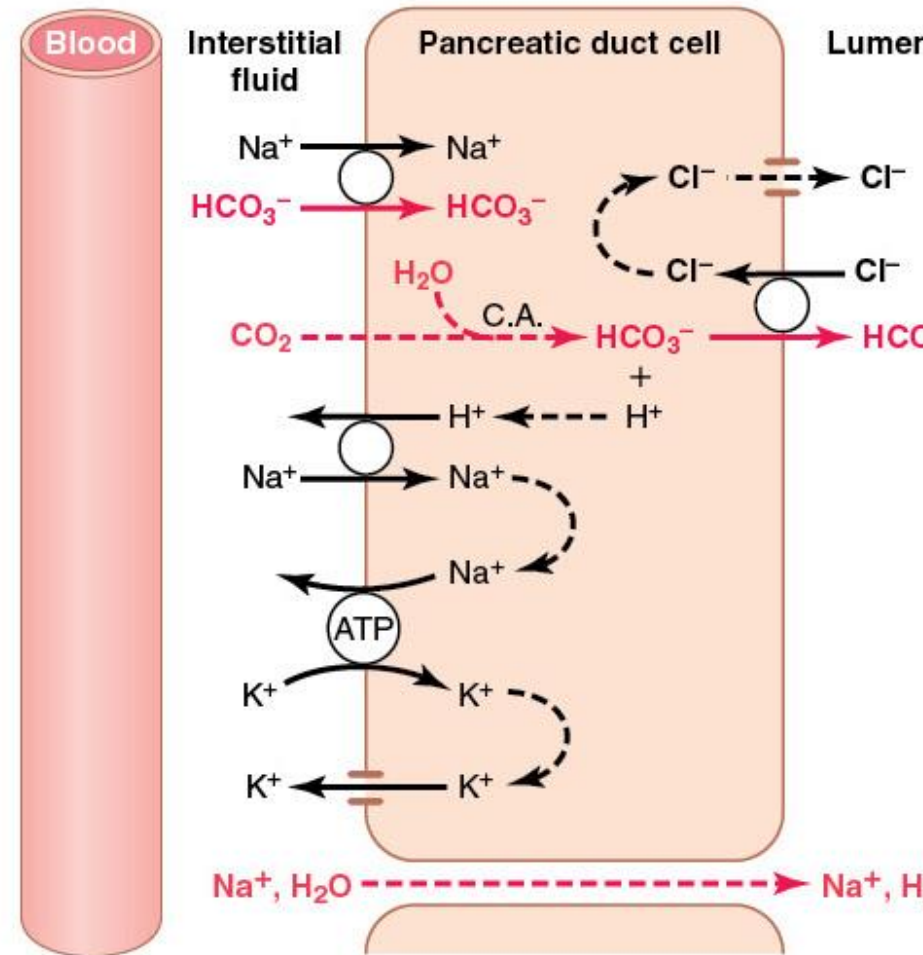
- **The pancreas secretes about 1 L/day of HCO_3^- -rich fluid from the epithelial cells of the ductules and ducts.**
- **The osmolarity of pancreatic fluid is equal to that of plasma.**
- **HCO_3^- concentration increases with increasing secretion rate.**

Secretion of Isosmotic Sodium Bicarbonate Solution.

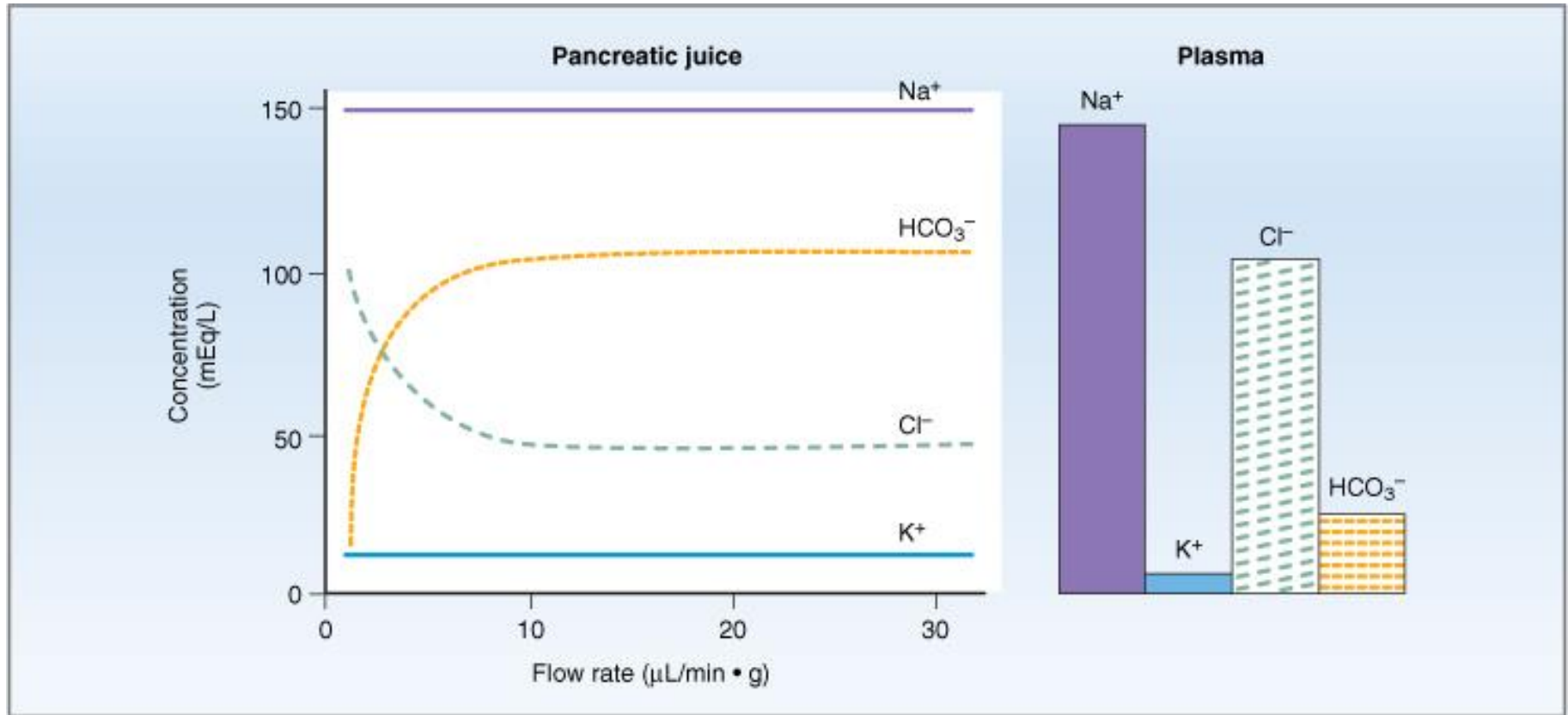


Mechanism of HCO_3^- Secretion From Pancreatic Ductal cell

1. CO_2 and H_2O combine in ductal cells to form H_2CO_3
 2. H_2CO_3 dissociated into H^+ and HCO_3^-
 3. H^+ is transported into blood by $\text{Na}^+ - \text{H}^+$ exchanger at basolateral membrane of ductal cells
 4. HCO_3^- is secreted into pancreatic juice by $\text{Cl}^- - \text{HCO}_3^-$ exchanger at apical membrane of ductal cells
- **Absorption of H^+ causes acidification of pancreatic venous blood**



Flow Rate and pancreatic secretion



Pancreatic Secretion is Under Neural and Hormonal Control

- Parasympathetic stimulation (through Ach on acinar cells) results in an increase in enzyme secretion-fluid and HCO_3^- .
- Secretin tends to stimulate a HCO_3^- rich secretion by activating ductal cells.
- CCK stimulates a marked increase in enzyme secretion by stimulating the acinar cells.
- Pancreatic secretion normally results from the combined effects of the multiple basic stimuli, not from one alone (potentiate each other).

Stimuli for Pancreatic Secretion

1. **Acetylcholine:** released from the parasympathetic vagus nerve endings and from other cholinergic nerves in the enteric nervous system.
2. **Cholecystokinin:** secreted by the duodenal and upper jejunal mucosa (I cells) when food enters the small intestine.
3. **Secretin:** also secreted by the duodenal and jejunal mucosa (S cells) when highly acidic chyme enters the small intestine.

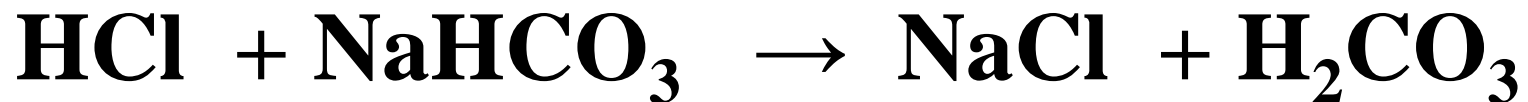
Acetylcholine and cholecystokinin stimulate the acinar cells of the pancreas, causing production of large quantities of pancreatic digestive enzymes but relatively small quantities of water and electrolytes to go with the enzymes.

Secretin, in contrast to the first two basic stimuli, stimulates secretion of large quantities of H₂O and NaHCO₃ solution by the pancreatic ductal epithelium.

Stimuli for Pancreatic Secretion (continued)

Secretin Stimulates Secretion of Copious Quantities of Bicarbonate Ions—Neutralization of Acidic Stomach Chyme.

- Secretin is present in an inactive form, **prosecretin** (in S cells in the mucosa of the duodenum and jejunum).
- When acid chyme with pH less than 4.5-5.0 enters the duodenum from the stomach, it causes duodenal mucosal release and activation of secretin, which is then absorbed into the blood.
- Secretin causes the pancreas to secrete large quantities of fluid containing a high concentration of HCO_3^- (up to 145 mEq/L = ~5X normal) but a low concentration of Cl^- .



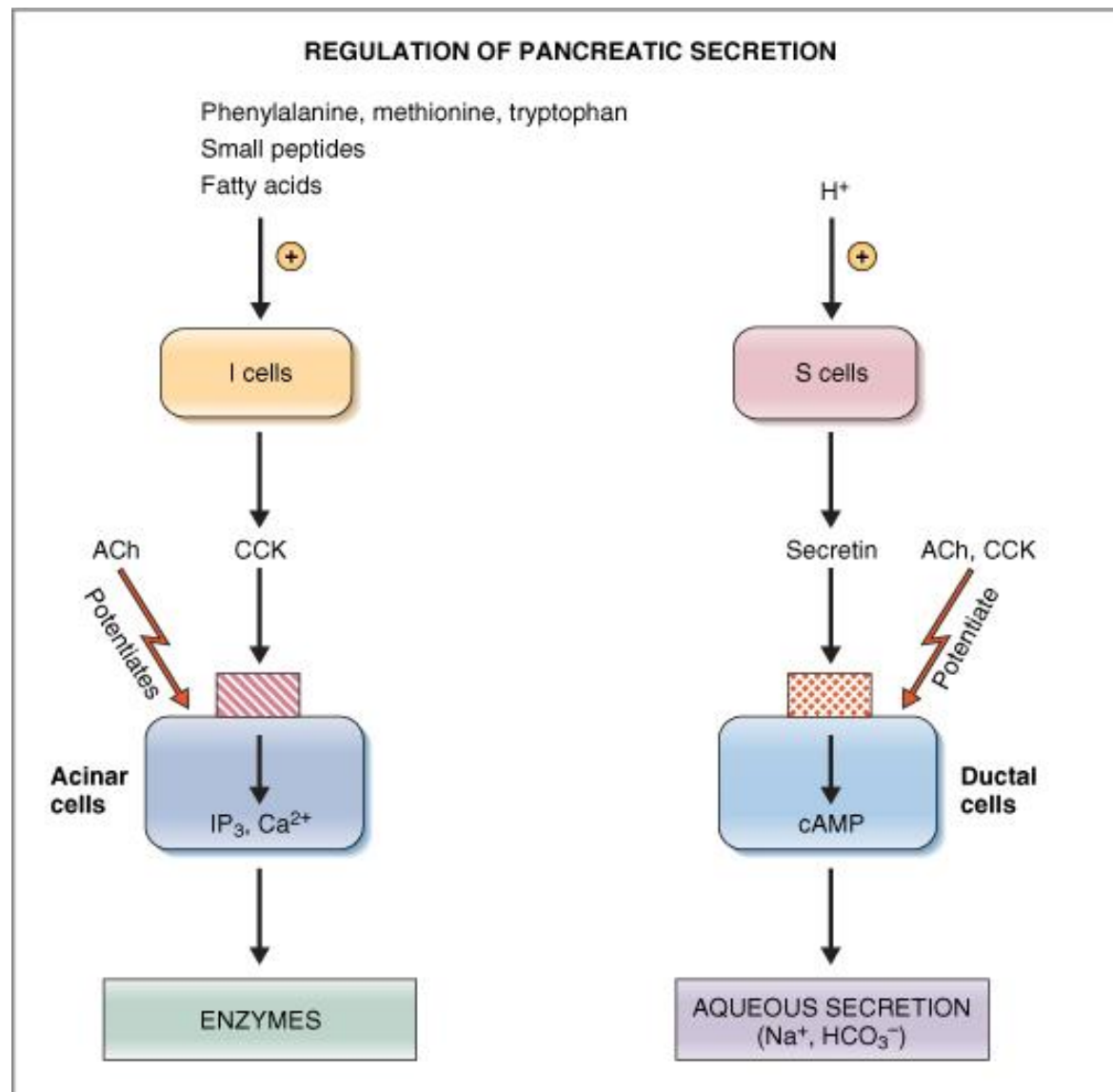
H_2CO_3 dissociates into CO_2 and H_2O .

Stimuli for Pancreatic Secretion (continued)

Cholecystokinin—Its Contribution to Control of Digestive Enzyme Secretion by the Pancreas.

- The presence of food in the upper small intestine causes cholecystokinin to be released from the I cells in the mucosa of the duodenum and upper jejunum.
- Release of cholecystokinin results especially from the presence of proteoses and peptones (products of partial protein digestion) and long-chain fatty acids in the chyme.
- Cholecystokinin, like secretin, passes by way of the blood to the pancreas and causes secretion of pancreatic digestive enzymes by the acinar cells.
- This effect is similar to that caused by vagal stimulation but even more pronounced, accounting for 70-80% of the total secretion of the pancreatic digestive enzymes after a meal.

Regulation of Pancreatic Secretion



Multiplicative or Potentiation Effects of Different Pancreatic Secretion Stimuli

- **When all different stimuli of pancreatic secretion (acetylcholine, cholecystokinin, and secretin) occur at once, then the total secretion is far greater than the sum of the secretions caused by each stimulus separately. The stimuli are said to “multiply” or “potentiate” one another.**
- **Usually, pancreatic secretions are the result of multiple stimuli rather than one stimulus.**

Pancreatic secretion is phasic

Phase	Stimulus	Mediators
Cephalic phase	Smell, taste, chewing and swallowing	Release of Ach by the vagal nerve
Gastric phase	Protein, gastric distention	Release of Ach by the vagal nerve
Intestinal phase	Acid in chyme, fatty acids	Mainly in response to Secretin

The End