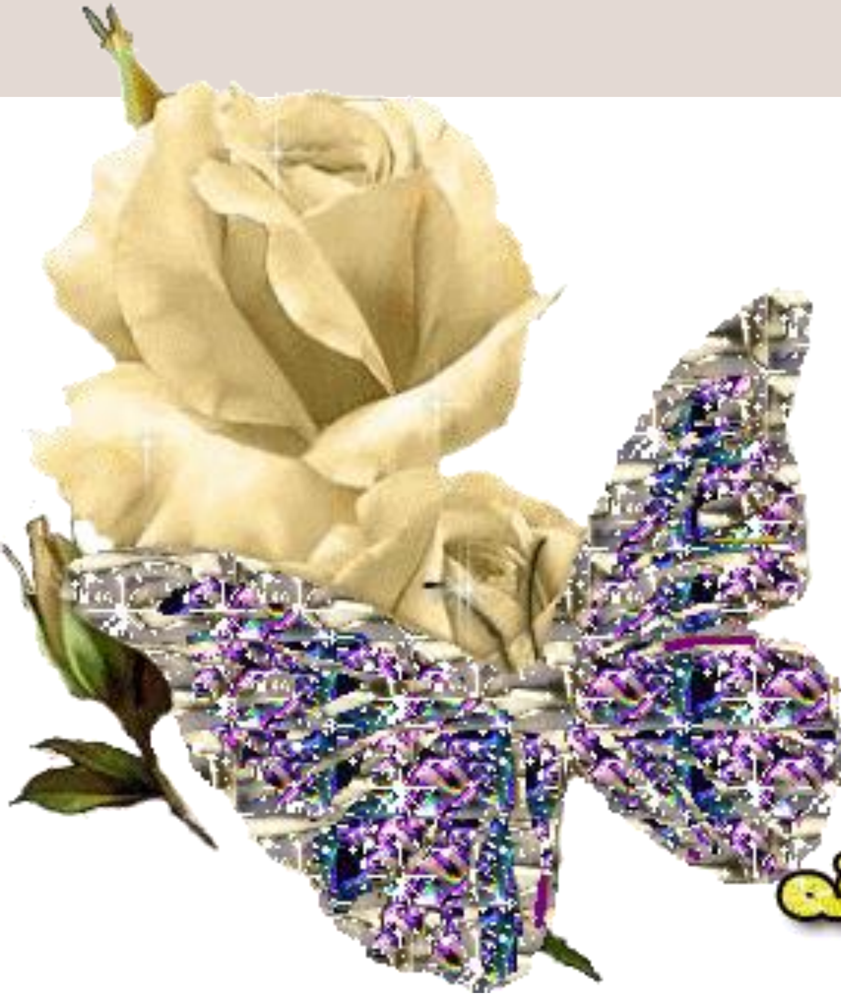

بسم الله الرحمن الرحيم

السلام عليكم ورحمة الله وبركاته

Gastrointestinal Physiology

Lecture 4

Physiology of the Pancreas

Chapter 65; Pages: 825-827

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Learning Objectives

- Functional Anatomy of Pancreas
- Major components of pancreatic juice
- Pancreatic Digestive Enzymes
- Cellular Mechanism of HCO_3^- Secretion
- Control of Pancreatic Secretion
- Release, Stimuli & Actions of Secretin
- Release, Stimuli & Actions of Cholecystokinin

The Pancreas

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

Endocrine portion

Islets of Langerhans

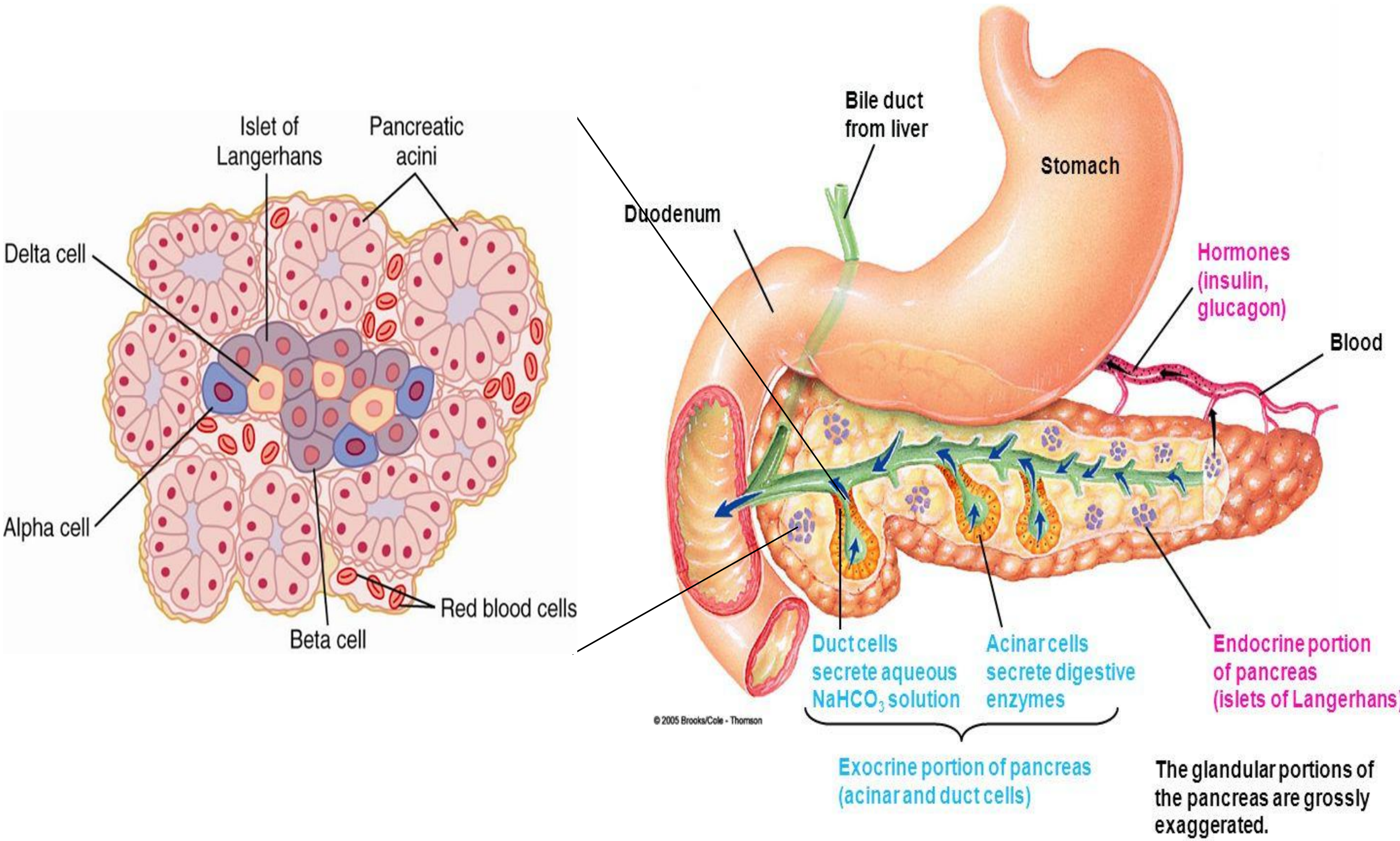
- **Secrete insulin (beta cells), glucagon (alpha cells) and somatostatin (delta cells).**

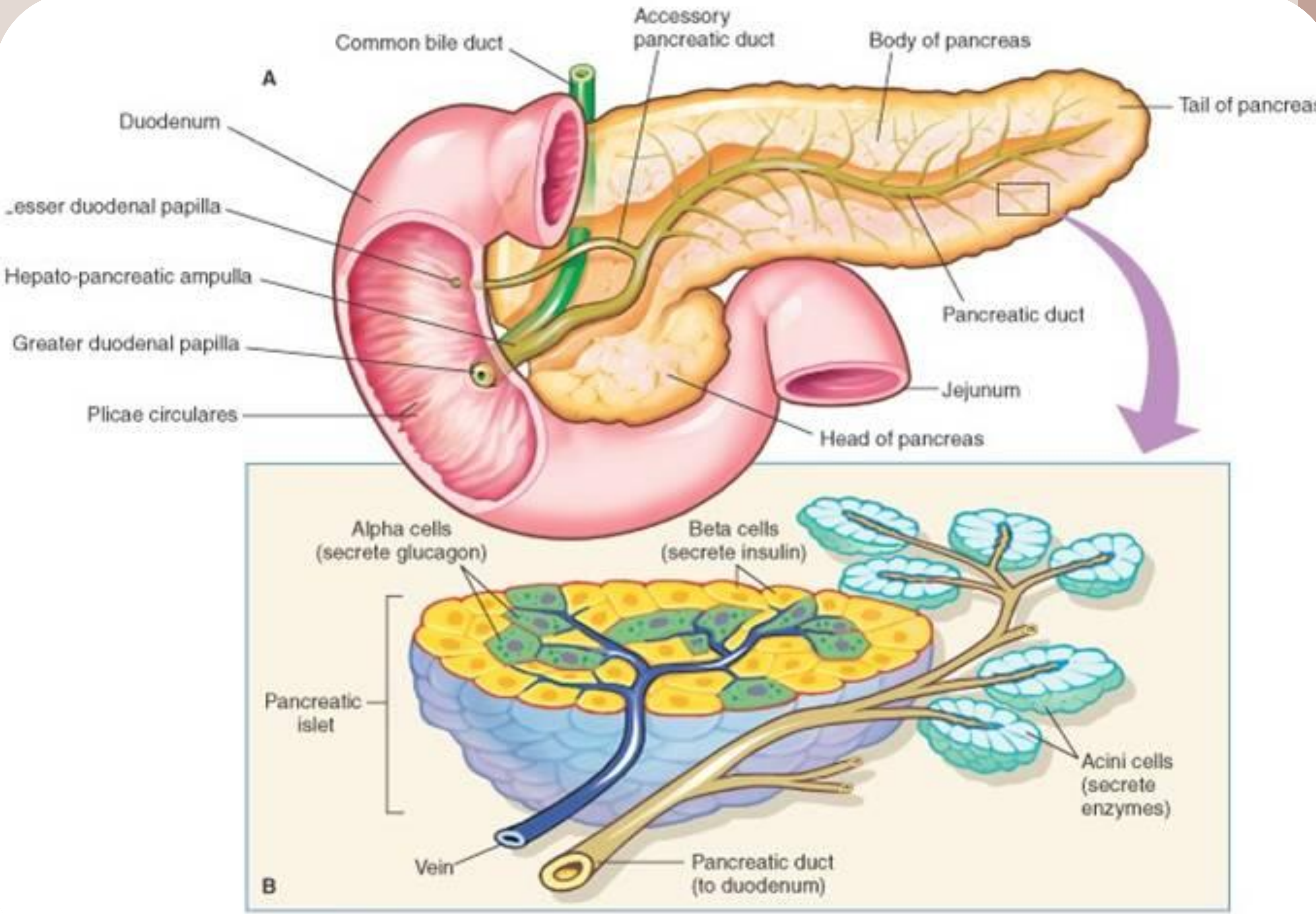
Exocrine portion

Acinar gland tissues

- **The cells lining the acini are serous cells containing zymogen granules, the precursors of pancreatic enzymes (the main source of digestive enzymes).**

The Endocrine & Exocrine Pancreas




A
Common bile duct
Accessory pancreatic duct
Body of pancreas
Tail of pancreas
Duodenum
Lesser duodenal papilla
Hepato-pancreatic ampulla
Greater duodenal papilla
Plicae circulares
Pancreatic duct
Jejunum
Head of pancreas
Alpha cells (secrete glucagon)
Beta cells (secrete insulin)
Pancreatic islet
Acini cells (secrete enzymes)
Vein
Pancreatic duct (to duodenum)
B

Pancreatic Secretion

Pancreatic juice

- Is secreted in response to the presence of chyme in the upper portions of the small intestine.

Major functions

- Neutralize the acids in the duodenal chyme.
- To prevent damage to duodenal mucosa by acid & pepsin.
- Produce enzymes involved in the digestion of carbohydrate, fat & protein.

Characteristics

- Volume: 1.2-1.5 l/day.
- Isotonic, similar to plasma
- PH= 8 alkaline.

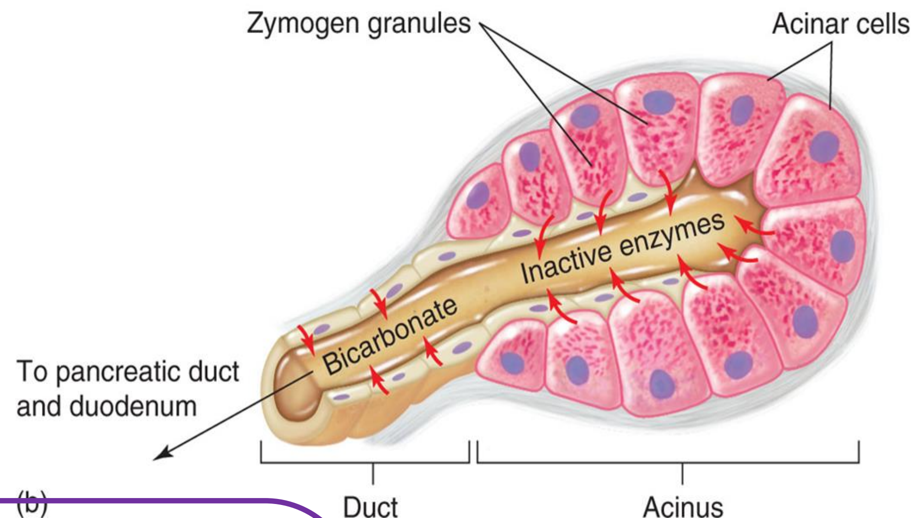
Composition of Pancreatic Secretion

Organic materials (1-2 %)

- Mostly enzymes
- Secreted from acinar cells.

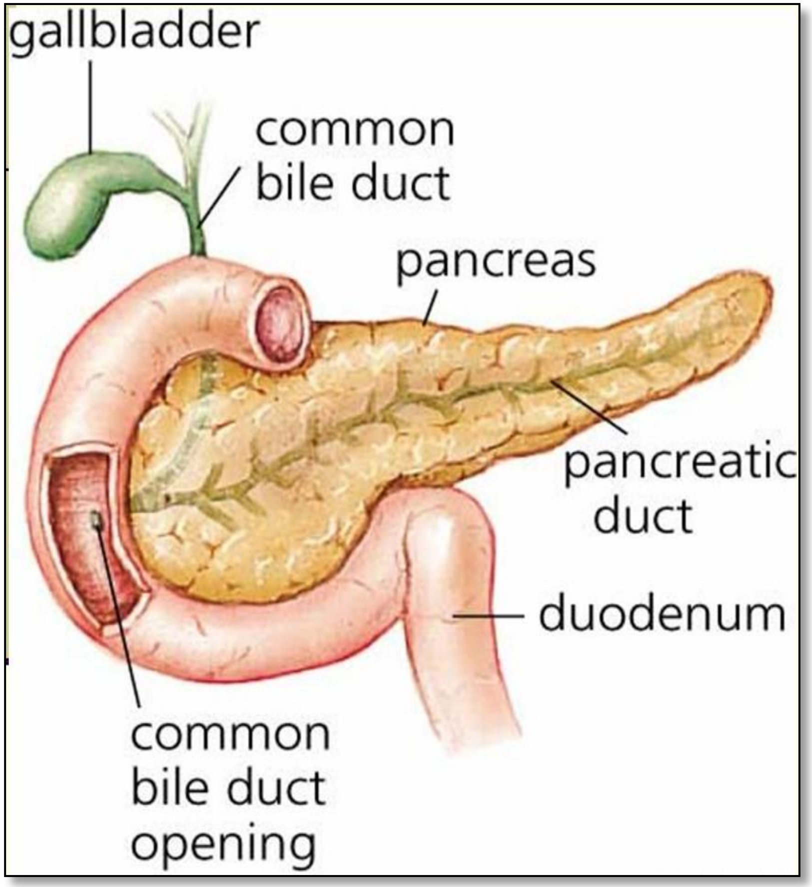
Inorganic materials (1 %)

- Eelectrolytes, produced from the centroacinar & intercalated duct cells.
- Include Na^{+}, K^{+}, Ca^{++}, HCO_3^{-} and Cl^{-}, with greater bulk in the form of $NaHCO_3$.

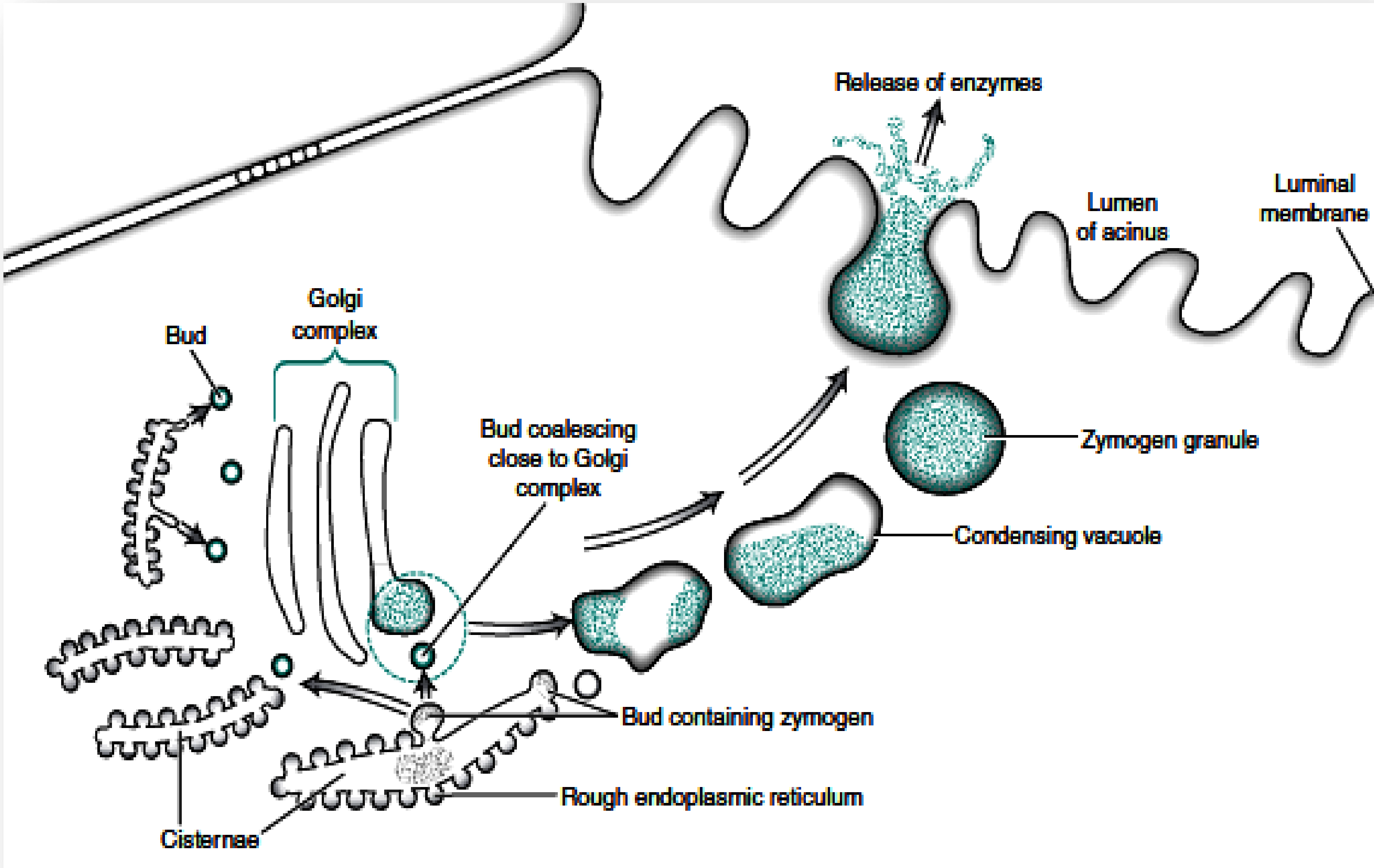


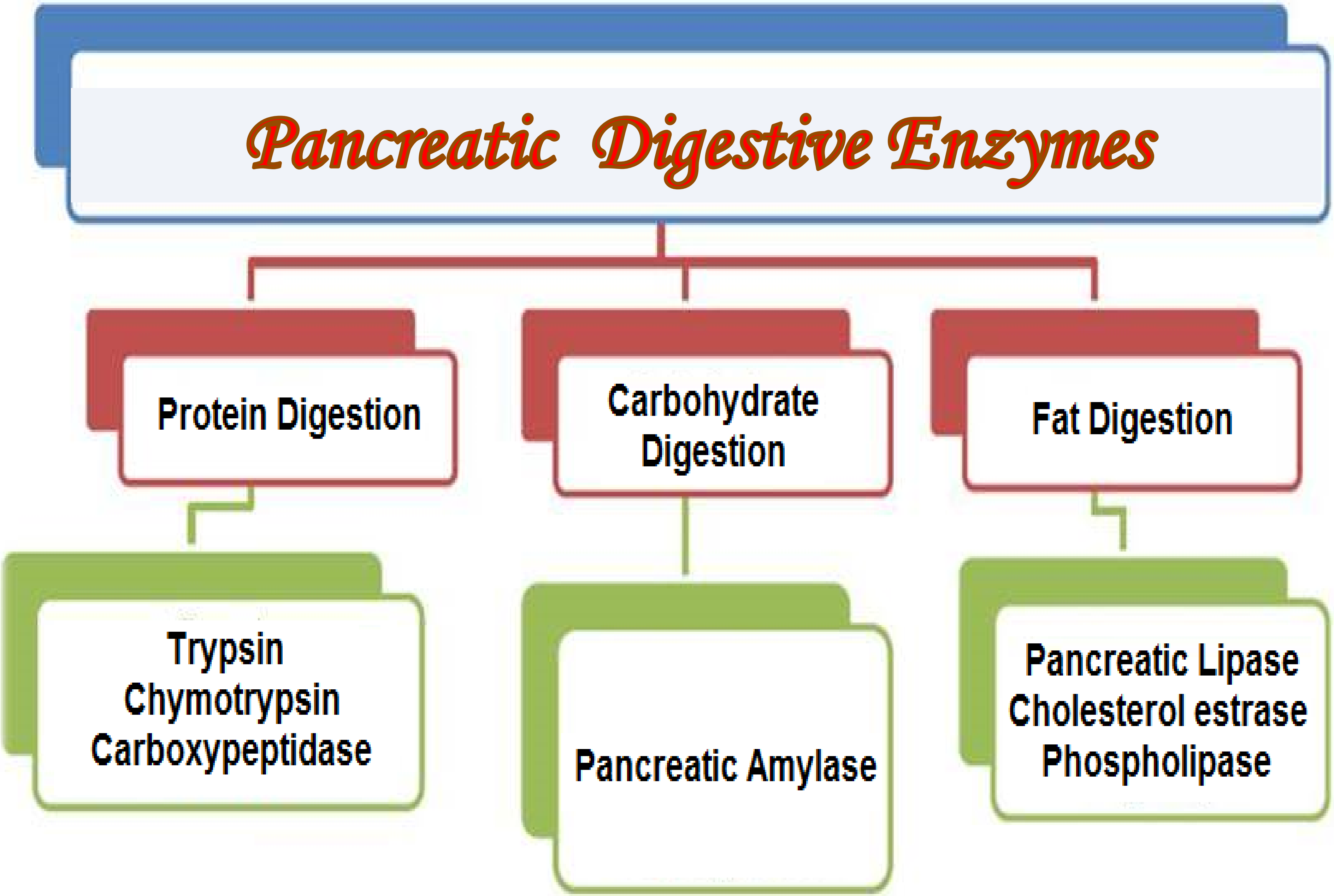
Flow of Pancreatic Secretion into Duodenum

- 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.



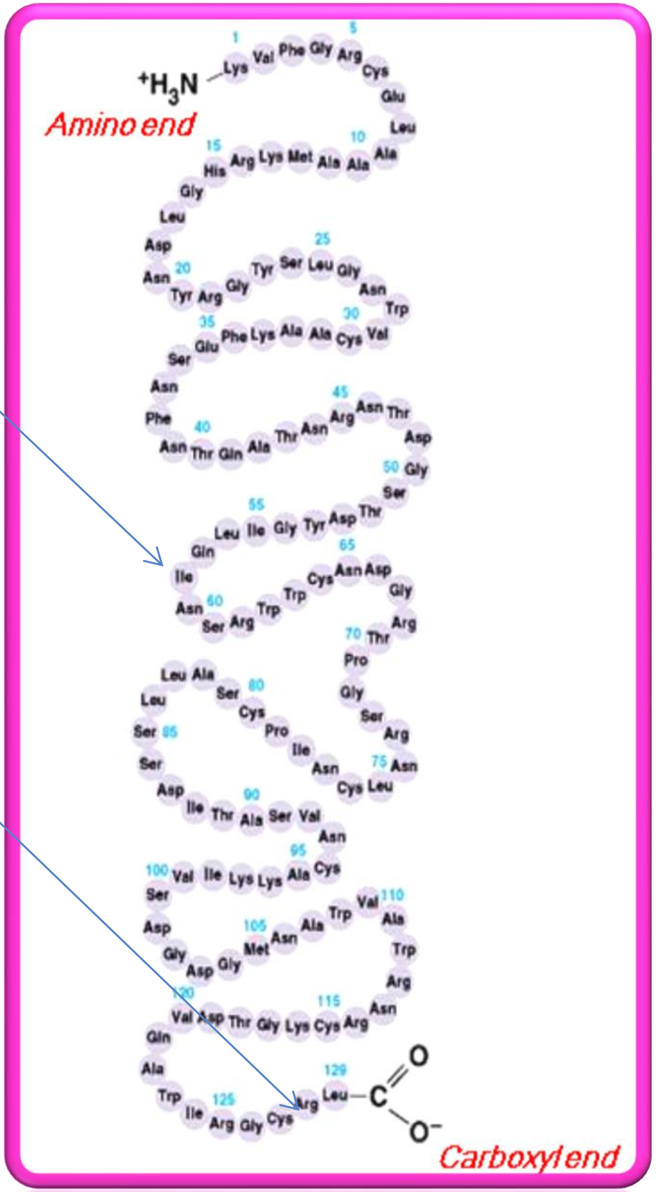
Enzyme Secretion by Acinar Cells




Pancreatic Digestive Enzymes
Protein Digestion
Carbohydrate Digestion
Fat Digestion
Trypsin
Chymotrypsin
Carboxypeptidase
Pancreatic Amylase
Pancreatic Lipase
Cholesterol estrase
Phospholipase

1- Pancreatic proteolytic enzymes (proteases)

- Trypsin, chymotrypsin and carboxypeptidase.
- Trypsin, chymotrypsin are endopeptidases, splitting into peptides of various sizes but do not cause release of individual amino acids.
- Carboxypeptidase is an exopeptidase which splits off amino acids at the carboxyl terminus of the peptide.



Pancreatic Proteolytic Enzymes (Cont.)

When first synthesized in the pancreatic cells, the proteolytic digestive enzymes are in the inactive forms: trypsinogen, chymotrypsinogen and procarboxypolypeptidase
These enzymes become activated only after they are secreted into the intestinal tract.

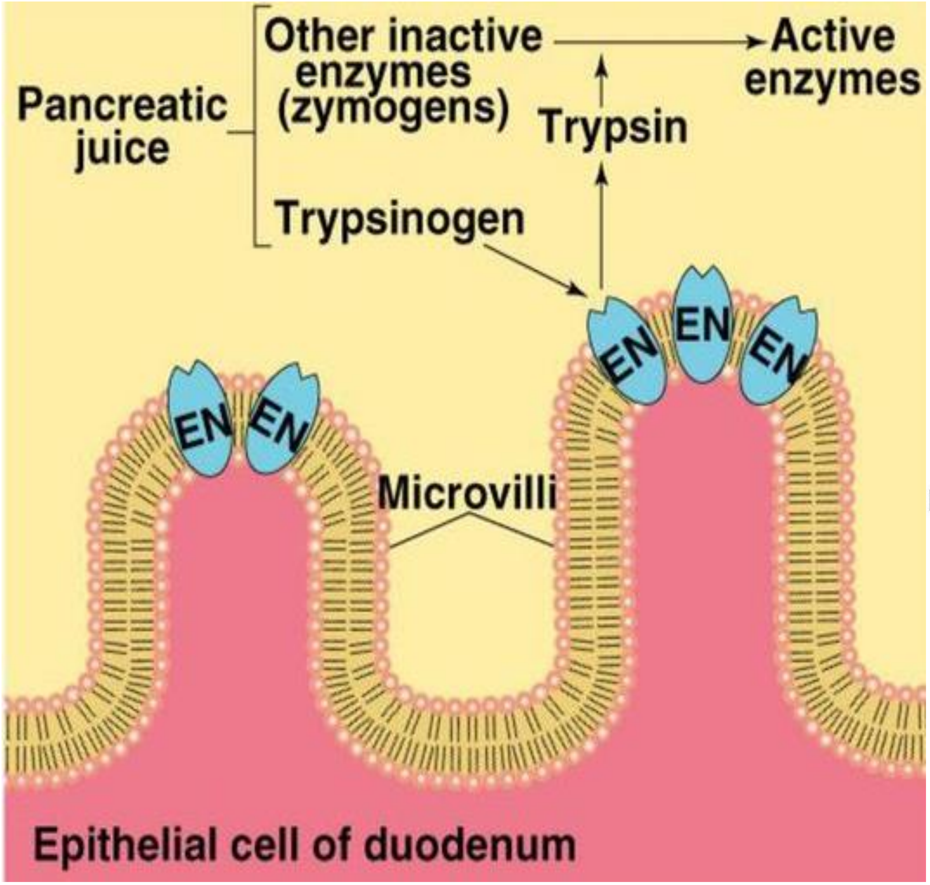
- **Trypsinogen is activated by:**

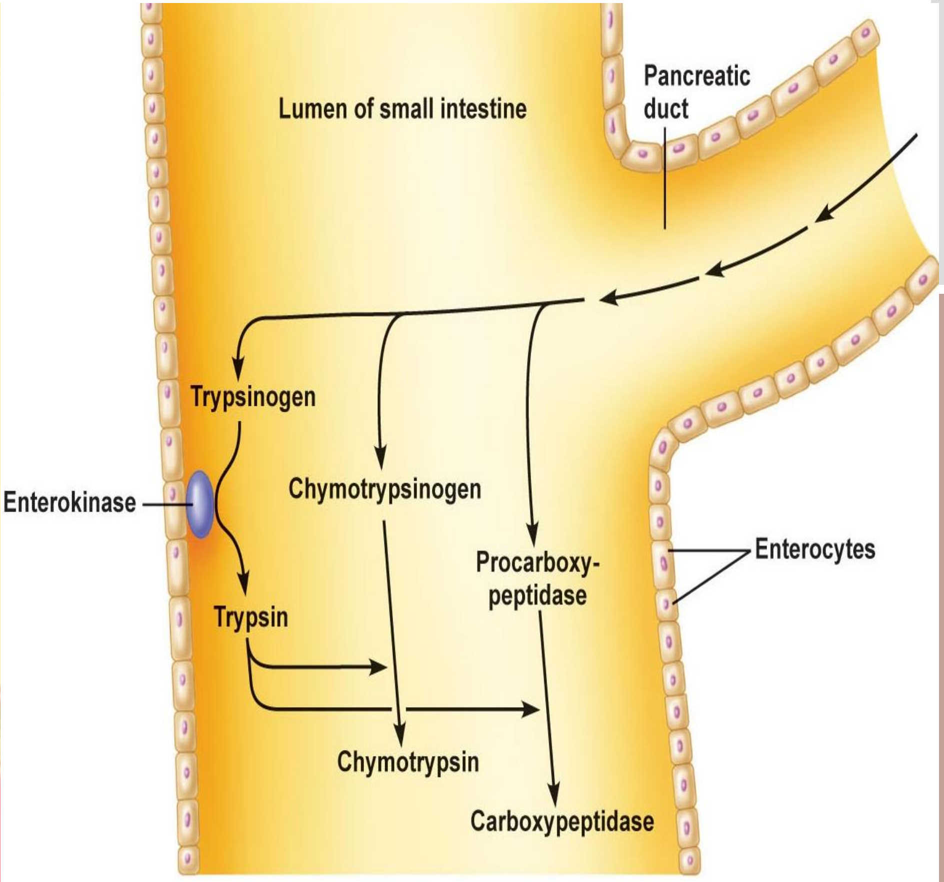
• Enteropeptidase (enterokinase), an enzyme secreted by the intestinal mucosa when chyme comes in contact with the mucosa.

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

- **Chymotrypsinogen and procarboxypolypeptidase are activated by trypsin to form chymotrypsin and carboxypolypeptidase.**

Activation of Pancreatic Proteolytic Enzymes





Trypsin Inhibitor

01

Pancreatic proteolytic enzymes 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.

02

Trypsin inhibitor is formed in the cytoplasm of the glandular cells that secrete pancreatic proteolytic enzymes.

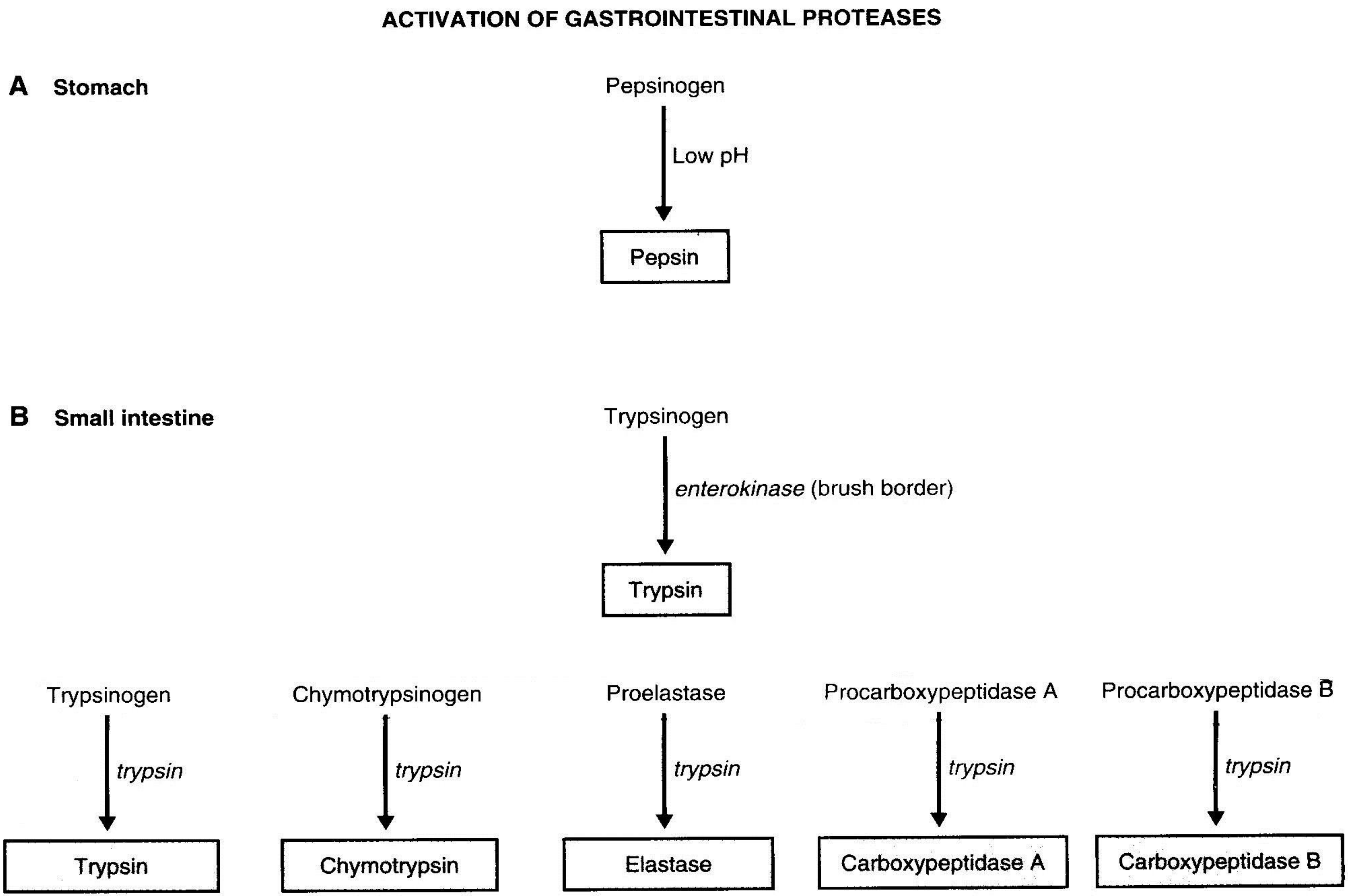
03

Trypsin inhibitor prevents activation of trypsin (and therefore other enzymes as well) inside the secretory cells of the acini and ducts of the pancreas.

04

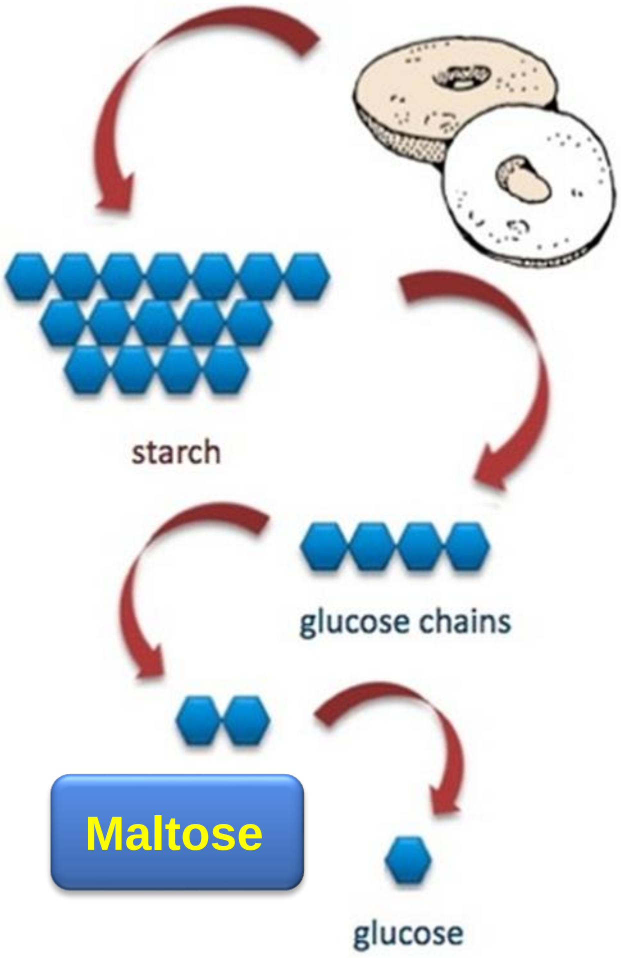
When a duct is blocked, trypsin inhibitor can not inhibit activation of accumulated enzymes which will be activated and digest the pancreas in few hours.

Activation of Gastrointestinal Proteases



2- Pancreatic Amylase

It hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides (maltose) and a few tri-saccharides.

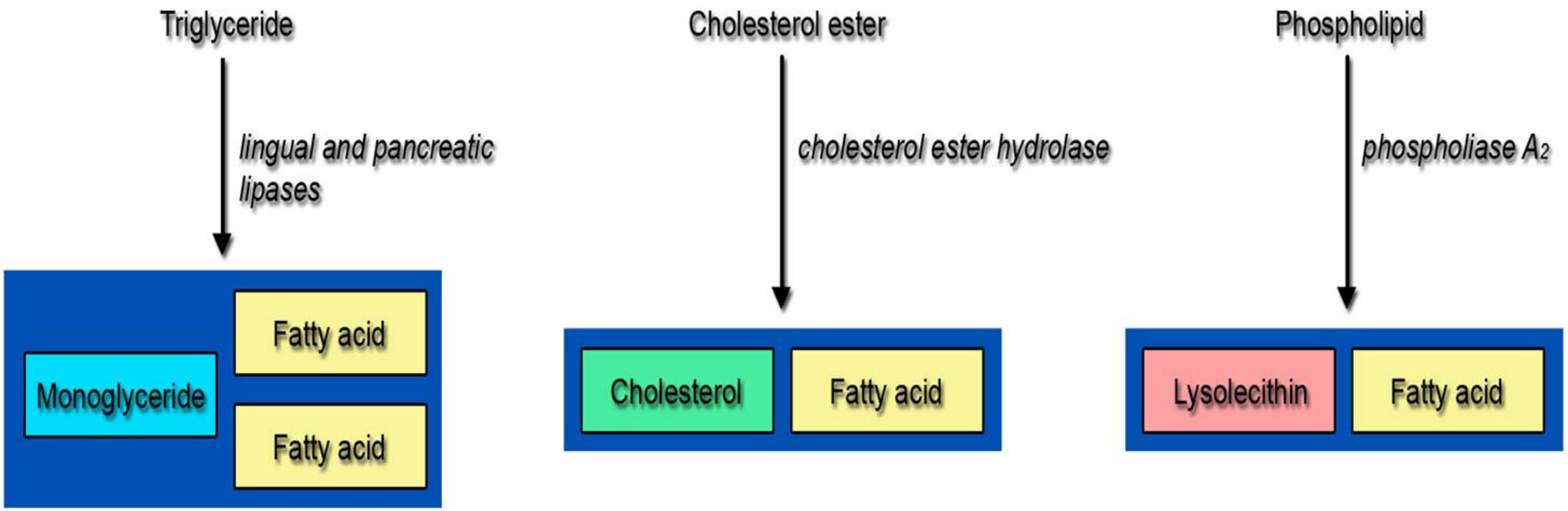


3- Pancreatic Enzymes for Fat Digestion

a. **Pancreatic lipase** is the most important fat splitting enzyme. It breaks TG into MG and FA in the presence of bile salts and colipase.

b. **Cholesterol esterase** which liberates cholesterol.

c. **Phospholipase A_2** which splits phospholipids into lysolecithin & FA.



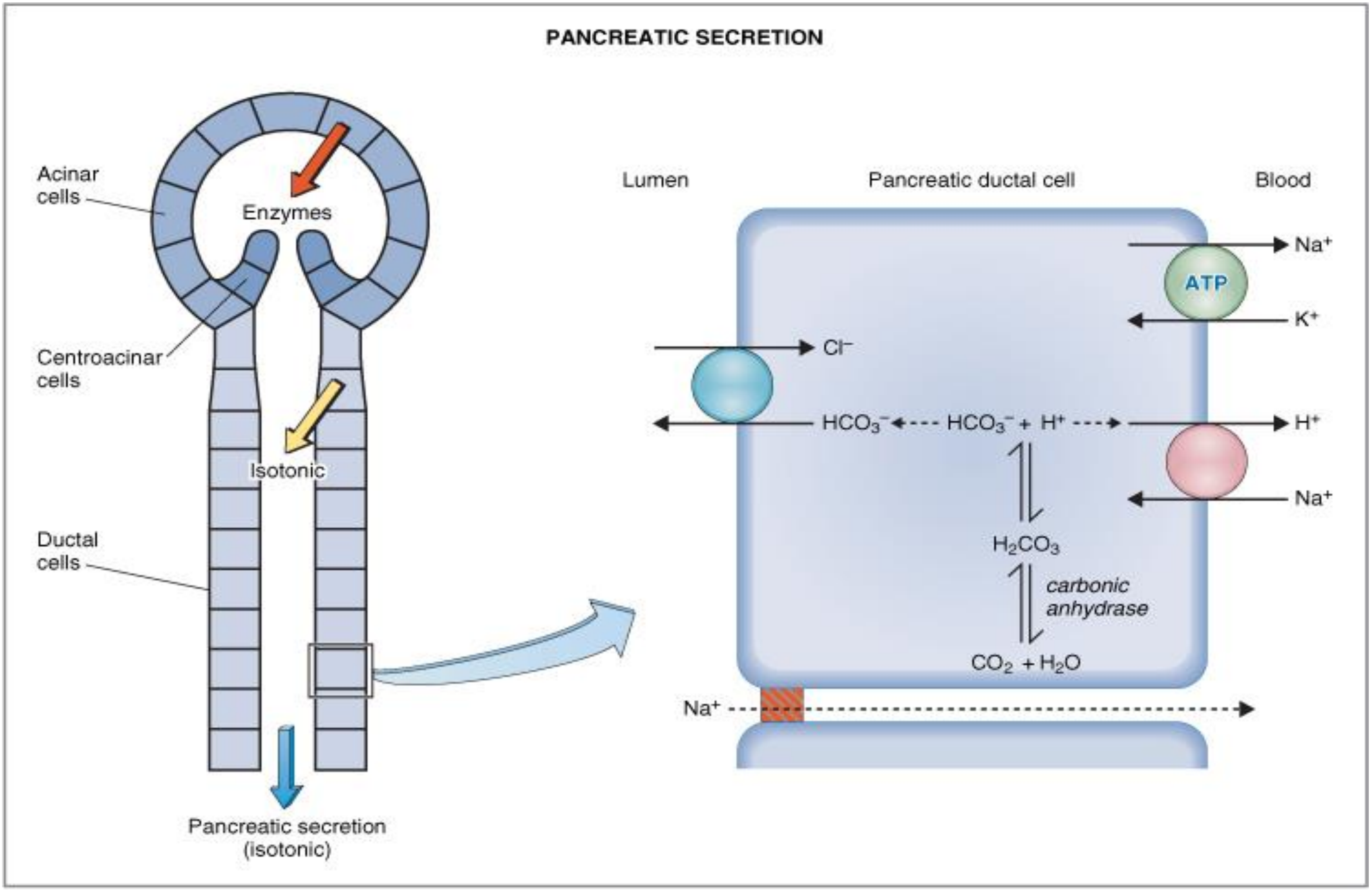
End Products of Fat Digestion

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 phynylalanine
(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

Secretion of Isosmotic Sodium Bicarbonate Solution.



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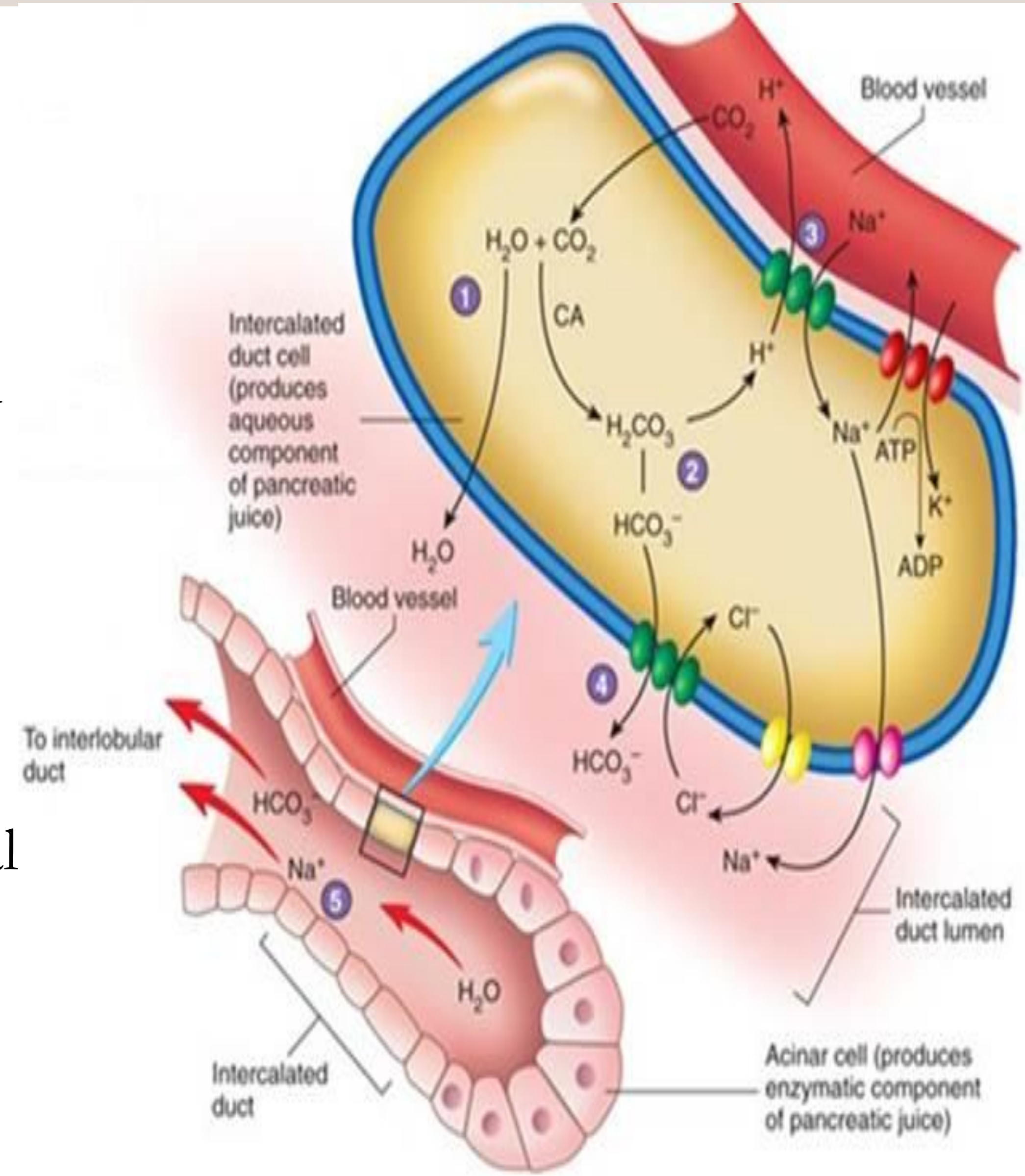
Mechanism of HCO_3^- Secretion

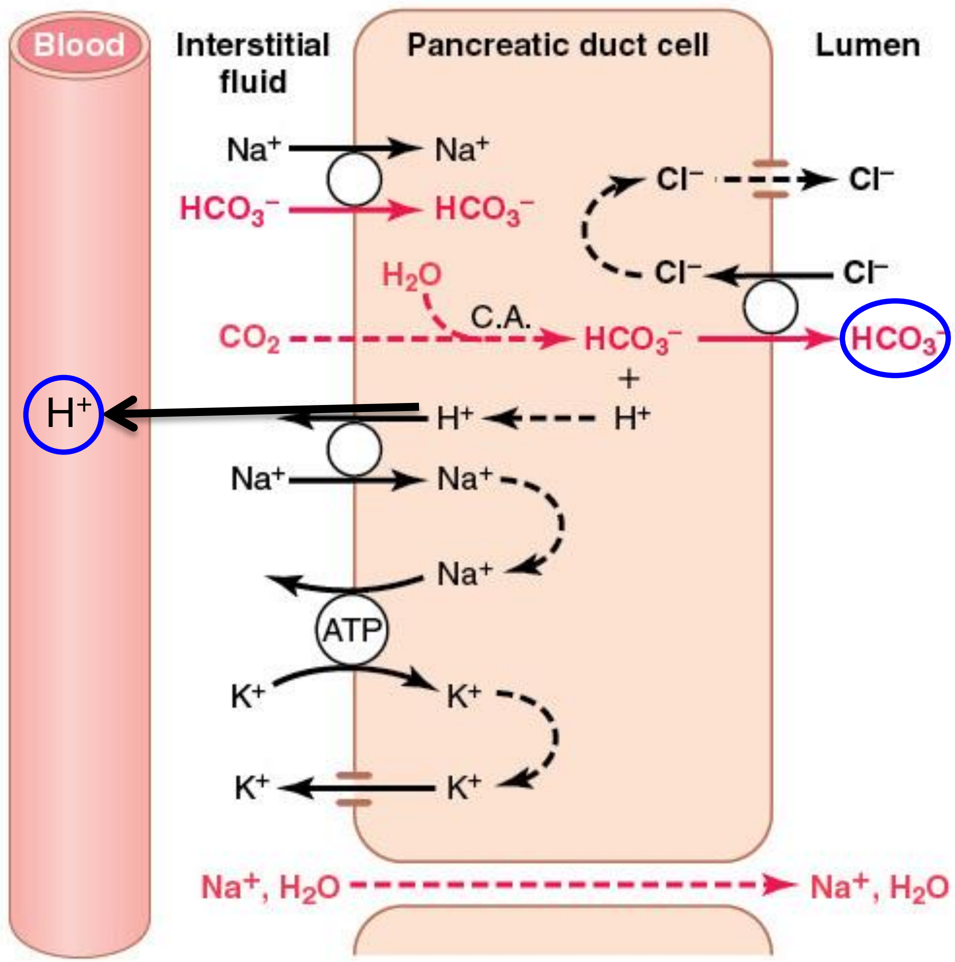
1. CO_2 and H_2O combine in acinar cells to form H_2CO_3
2. H_2CO_3 dissociated into H^+ and HCO_3^-
3. H^+ is transported into blood by Na^+-H^+ exchanger at basolateral membrane of ductal cells
4. HCO_3^- is secreted into pancreatic juice by Cl^--HCO_3^- exchanger at apical membrane of ductal cells

- Absorption of H^+ causes acidification of pancreatic venous blood

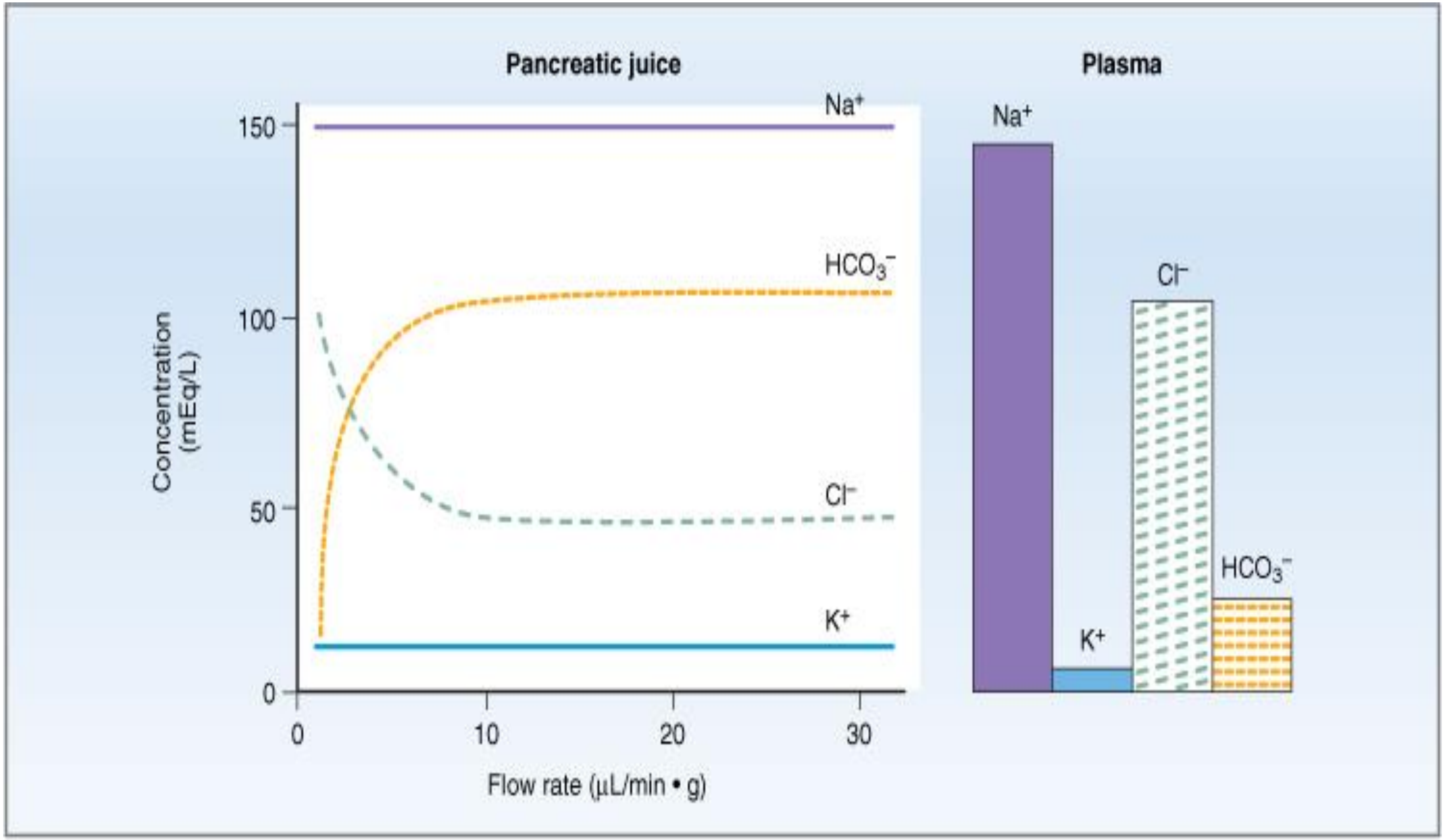


Secretion of Bicarbonate Ions From Pancreatic Ductal cell

Blood around the pancreas; acidic tide



Flow Rate & Pancreatic Secretion



HCO_3 concentration increases with increasing secretion rate

Phases of Pancreatic Secretion

- Pancreatic secretion is under neural and hormonal control.
- It normally results from the combined effects of the multiple basic stimuli which potentiate each other.

Phase	Cephalic (20%)	Gastric (5-10%)	Intestinal (70-75%)
Stimulus	Smell, taste, chewing and swallowing	Protein, gastric distention	Acid and fatty acids in chyme
Mediator	Ach release by the vagal nerve endings in the pancreas	Vago-vagal reflex	Secretin, CCK and vago-vagal reflex

Pancreatic Secretion is Under Neural and Hormonal Control

Control

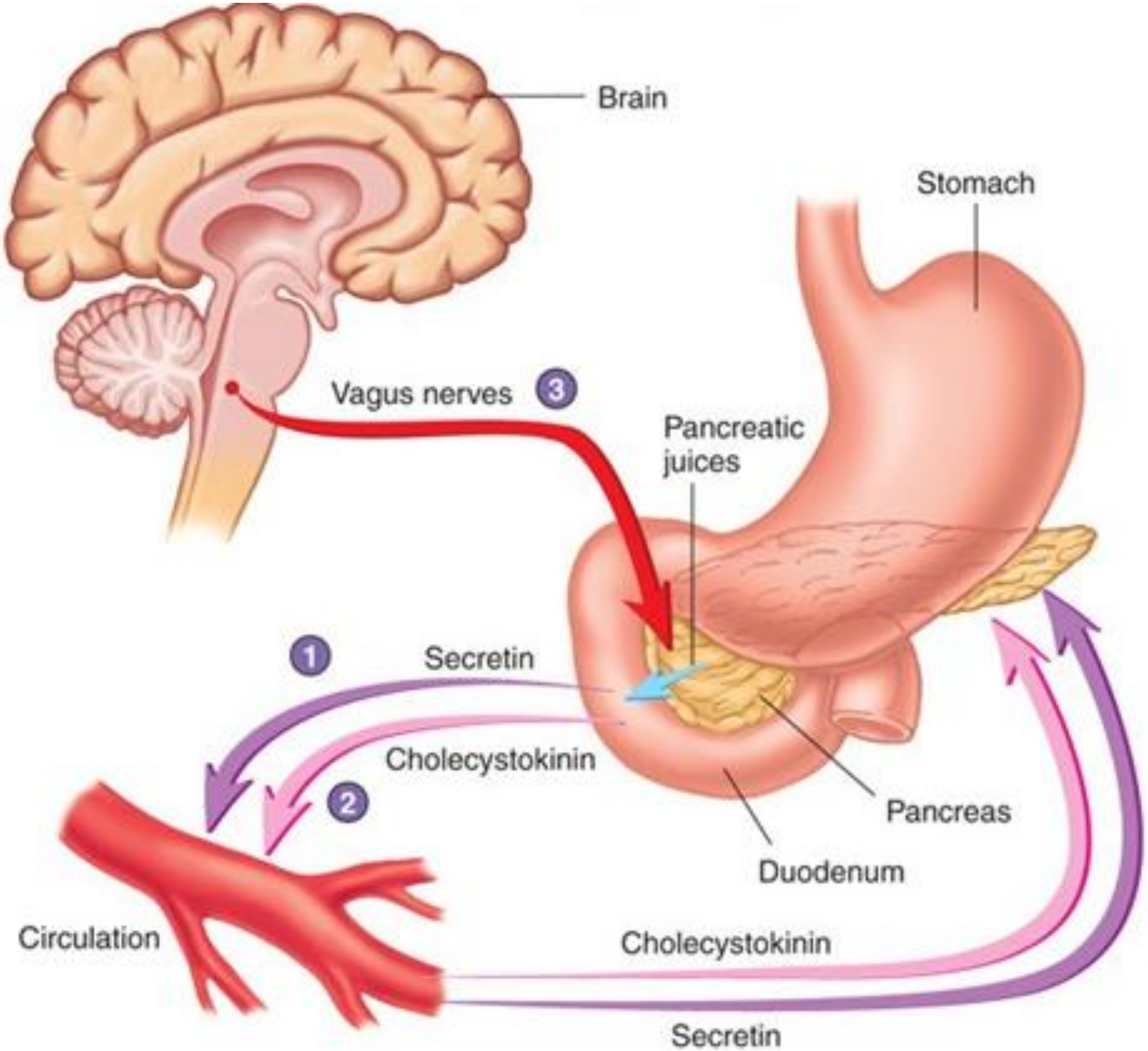
Parasympathetic stimulation (through Ach on acinar cells) results in increase in enzyme secretion- fluid and HCO_3^-

Secretin tends to stimulate a HCO_3^- rich secretion by activating ductal cells.

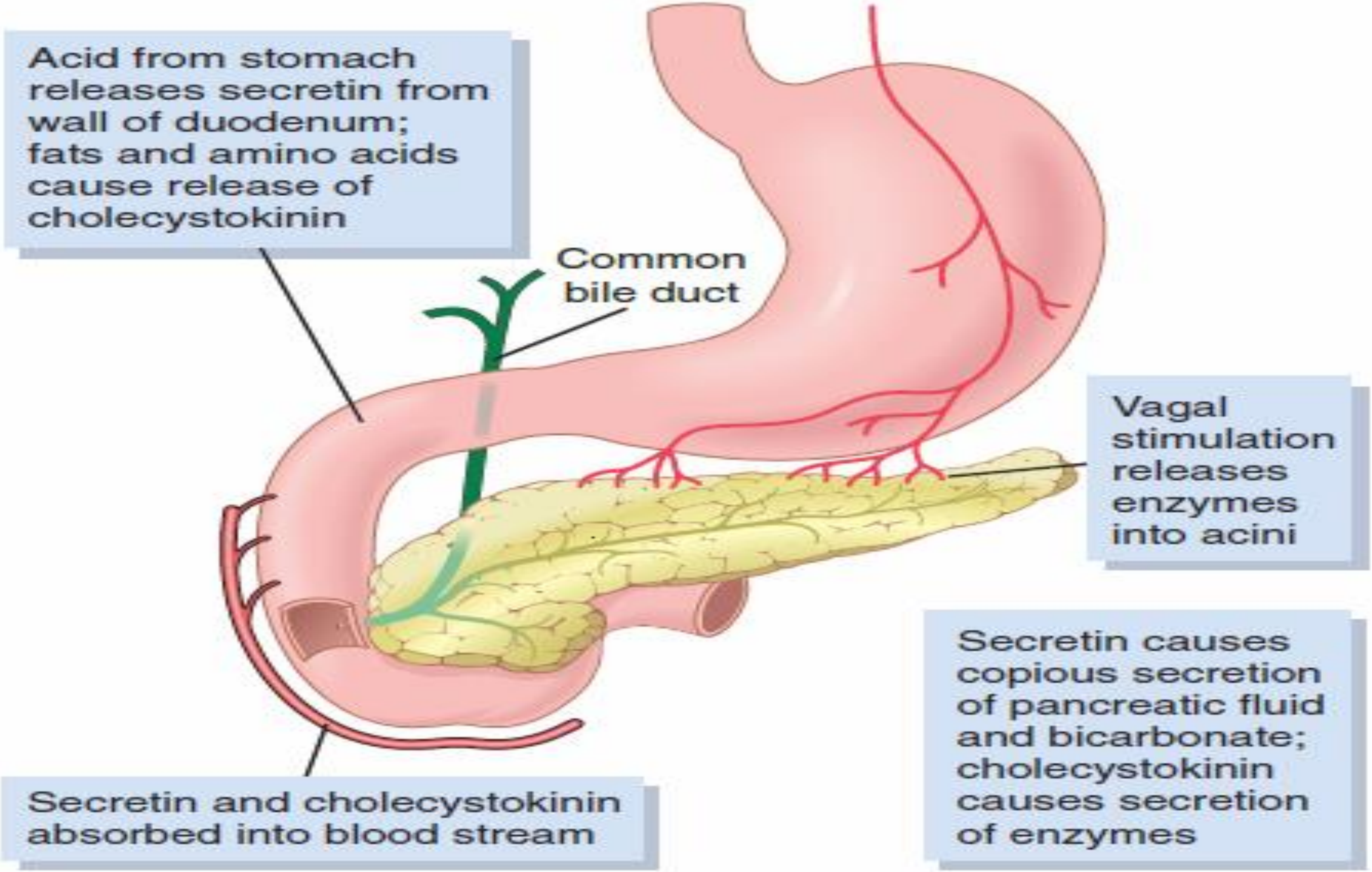
Cholecystokinin stimulates a marked increase in enzyme secretion by stimulating the acinar cells.

Neural and Hormonal Control of Pancreatic Secretion

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.



Regulation of Pancreatic Secretion



Hormonal Regulation of Pancreatic Secretion

1

Secretin

Release: From “S” cells in the mucosa of the duodenum and jejunum (present as presecretin) .

Stimulus: Mainly acid chyme with pH less than 4.5-5.0 in the duodenum

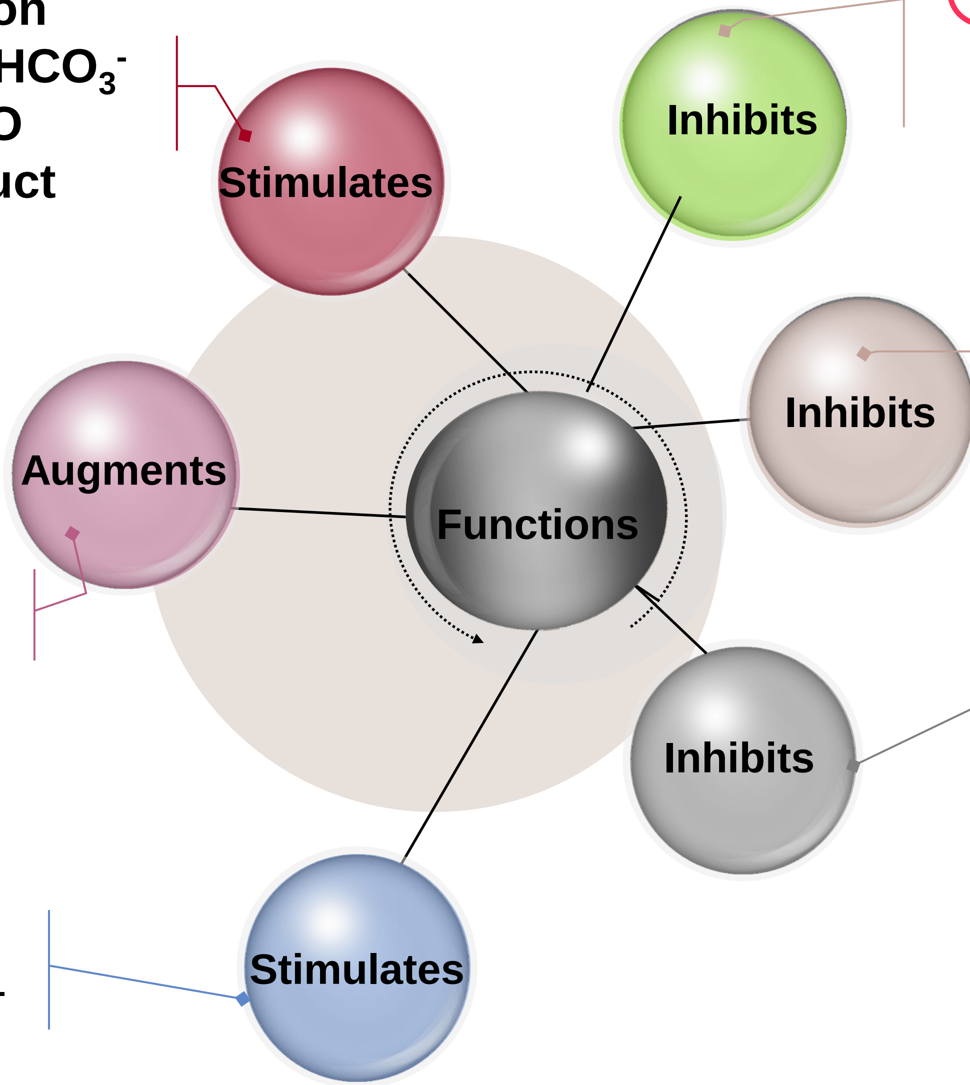
2

Cholecystokinin

Release: From “I” cells in the mucosa of the duodenum and upper jejunum.

Stimulus: Mainly proteoses, peptones and long-chain fatty acids in the chyme

Functions of Secretin



1. pancreatic secretion rich in HCO_3^- and H_2O from duct cells.

2. stimulation of enzyme secretion by CCK.

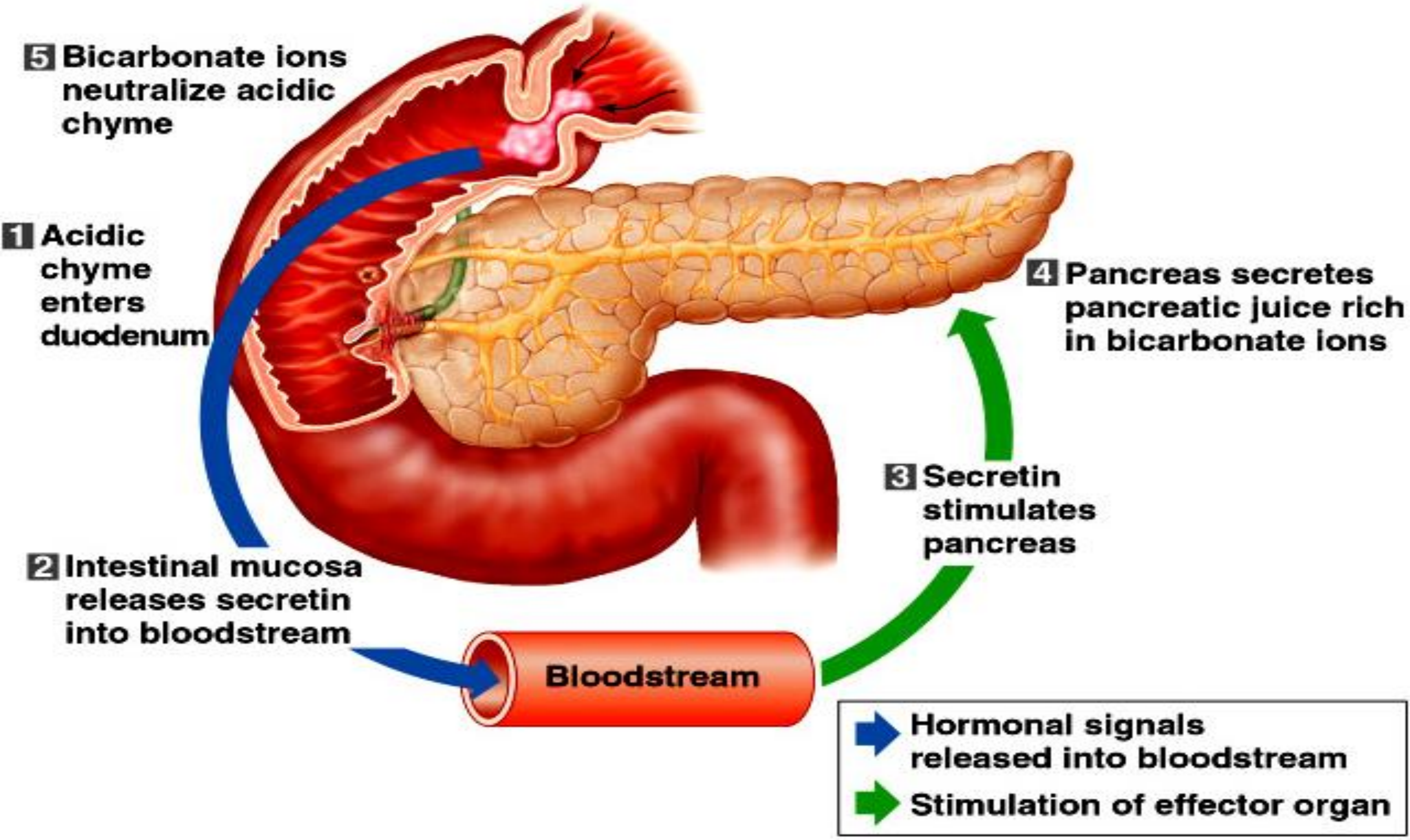
3. hepatic bile flow and HCO_3^- secretion.

4. gastric acid secretion and gastrin release, but it stimulates pepsin secretion.

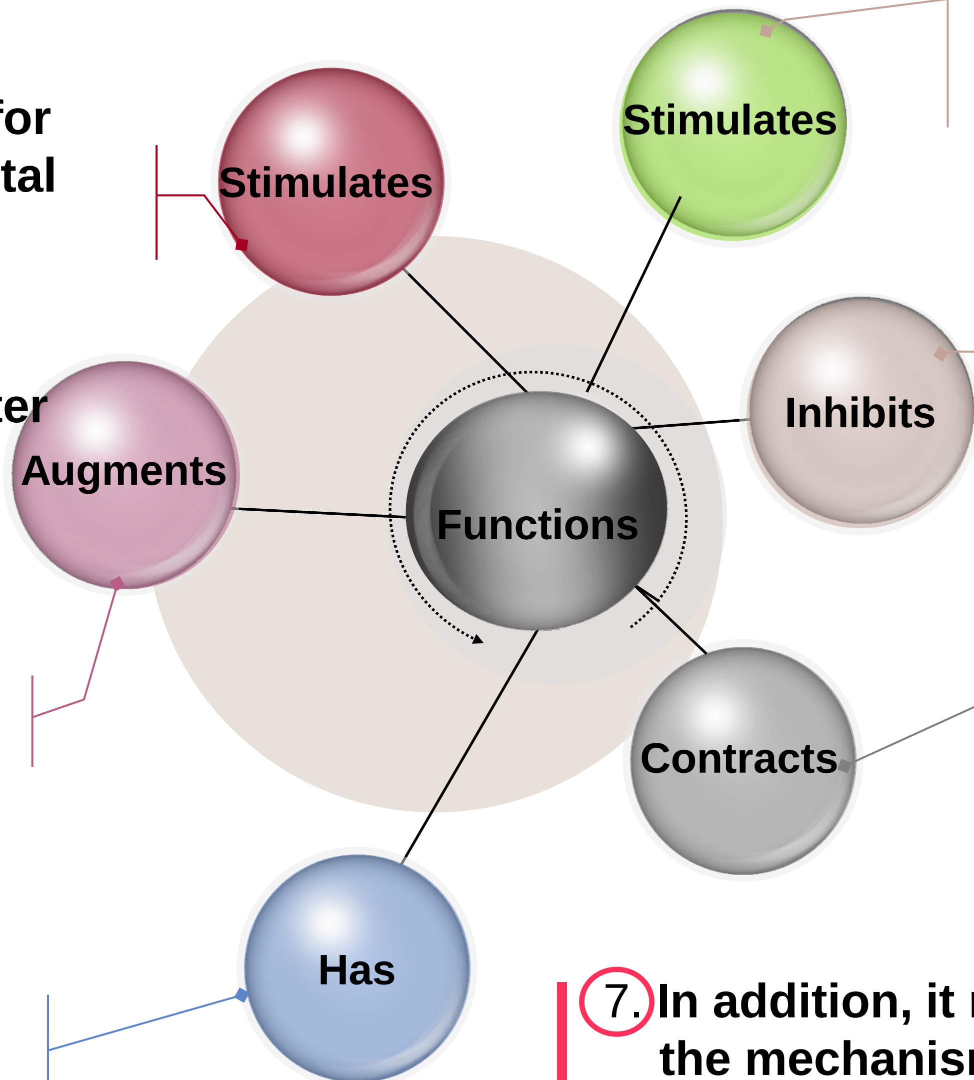
5. gastric motility, contracts pylorus and slows gastric emptying, relaxes LES

6. intestinal motility and contracts ileocecal sphincter.

Regulation of Pancreatic Secretion by Secretin

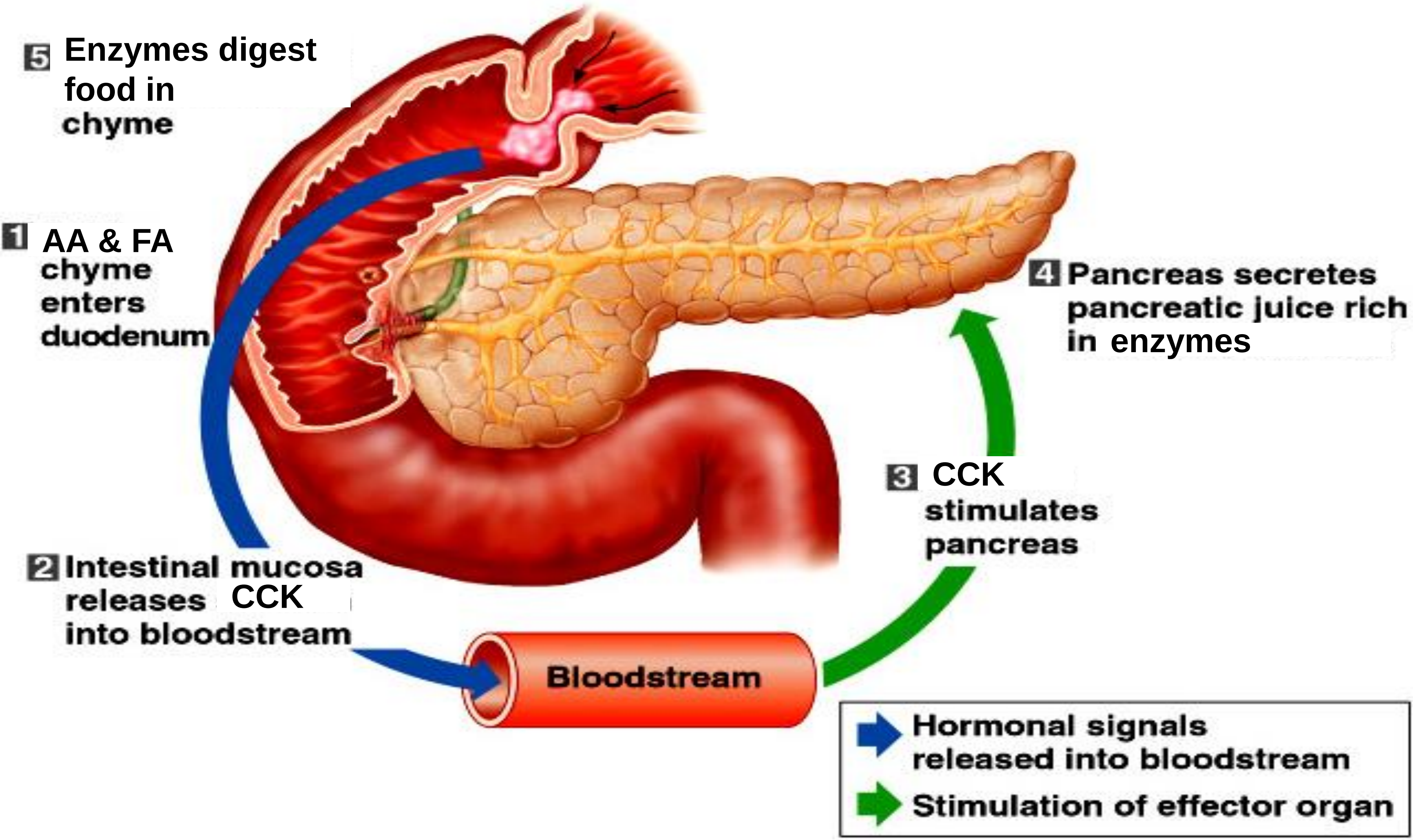


Functions of Cholecystokinin



1. pancreatic enzyme secretion, accounting for 70-80% of total pancreatic digestive enzymes secretion after a meal.
2. stimulation of H_2O and HCO_3^- secretion by secretin.
3. trophic effect on pancreas.
4. gall bladder, relaxes sphincter of Oddi and causes bile discharge into intestine.
5. stomach contraction moderately and slows its emptying.
6. intestinal motility and relaxes ileocecal sphincter.
7. In addition, it may be concerned with the mechanism of satiety.

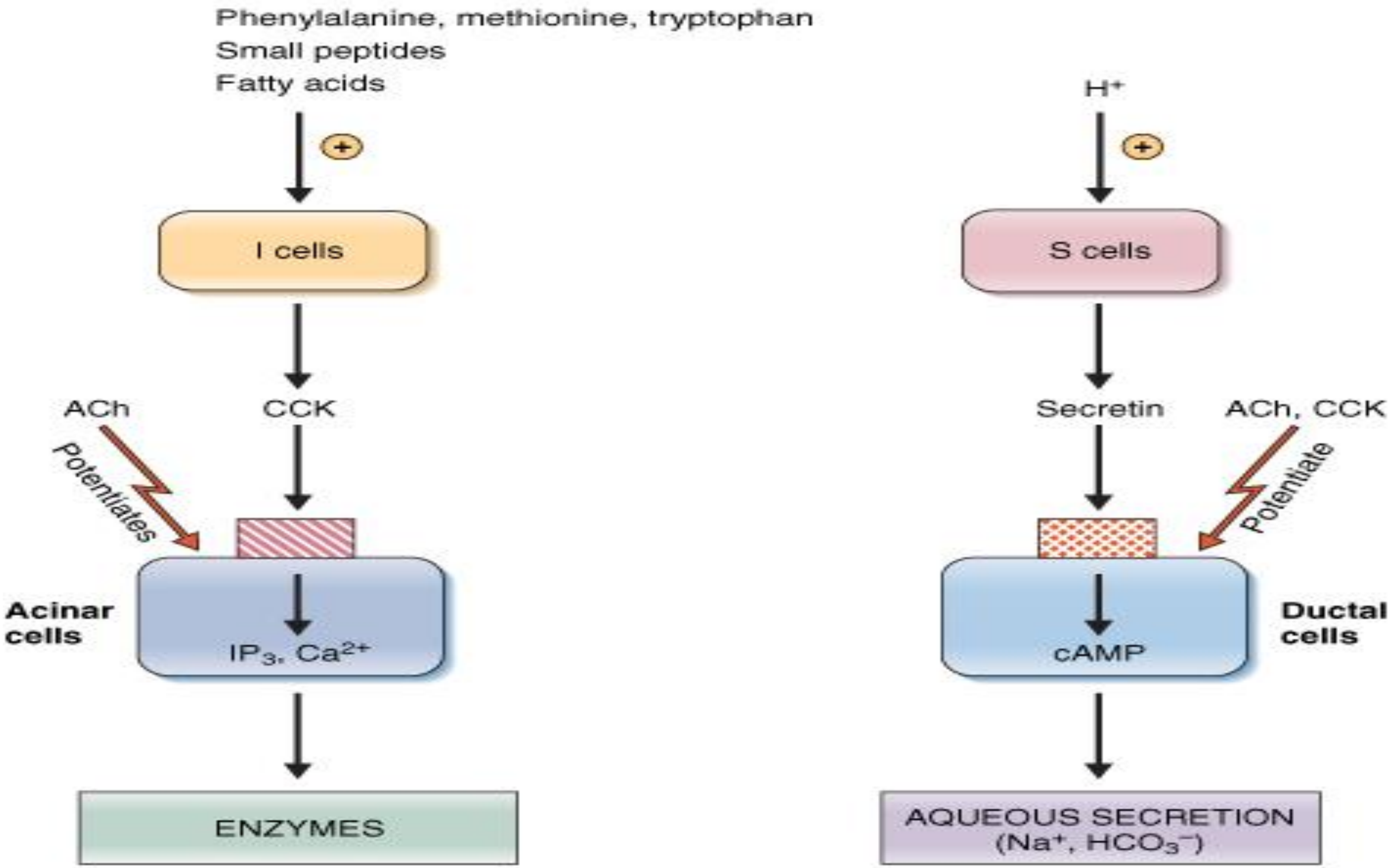
Regulation of Pancreatic Secretion by CCK



Multiplicative or Potentiation Effects of Different Pancreatic Secretion Stimuli

- Usually, pancreatic secretions are the result of multiple basic stimuli (Ach, cholecystokinin, and secretin) rather than one stimulus alone.
- When all these different stimuli of pancreatic secretion 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.

Multiplicative or Potentiation Effects of Different Pancreatic Secretion Stimuli (Cont.)




Thank You