5 Physiology of Pancreas

MED 433 Teams

GIT

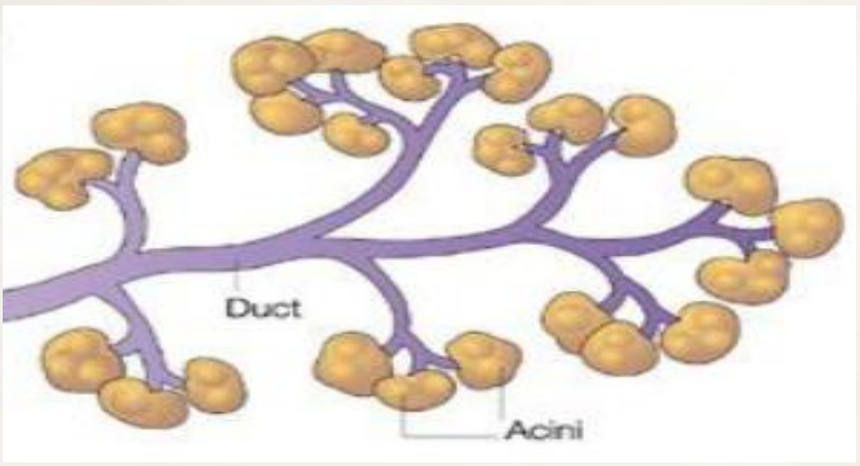
1. Functional Anatomy

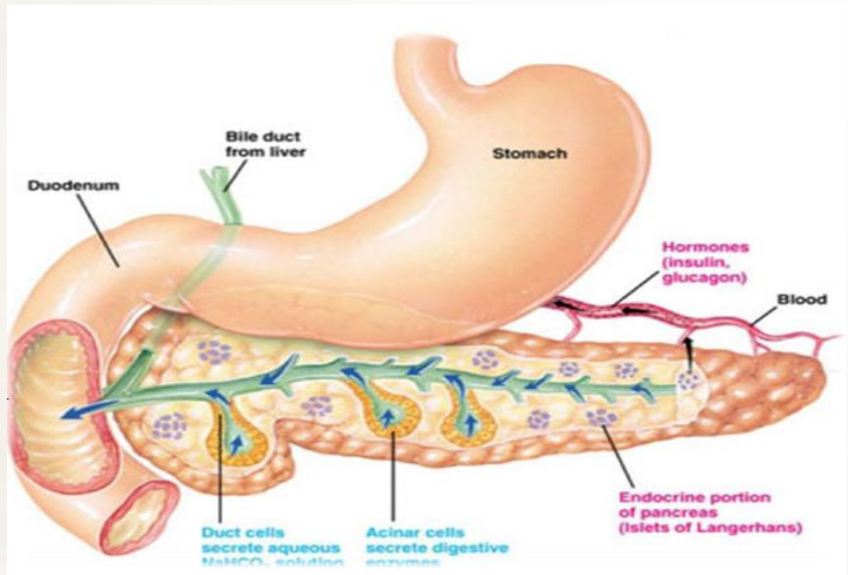
- **The pancreas which lies parallel to and beneath the stomach is composed of:**
  1. **The endocrine islets of Langerhans which secrete:**

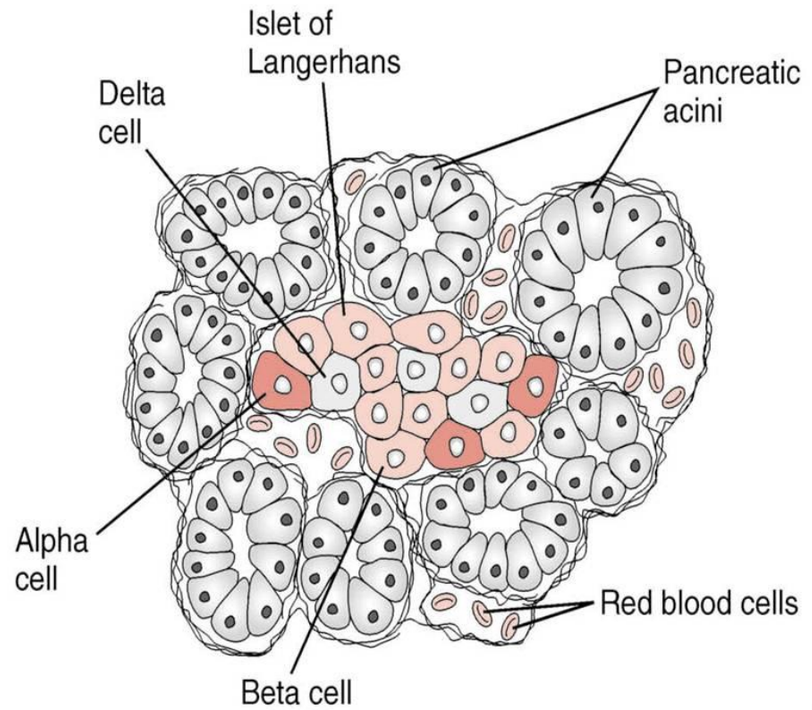
Hormone	Type of cell	% of secretion
Insulin	**Beta cells**	**60%**
Glucagon	**Alpha cells**	**~25%**
Somatostatin	delta cells	~10%

} crucial for normal regulation of glucose, lipid & protein metabolism

  1. **Acinar gland tissues which produce pancreatic juice (the main source of digestive enzymes).**
- **The pancreatic digestive enzymes are secreted by pancreatic acini.**
- **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.**







2. Major Components of Pancreatic Secretion and Their Physiologic Roles & 5. Activation of Pancreatic Enzymes

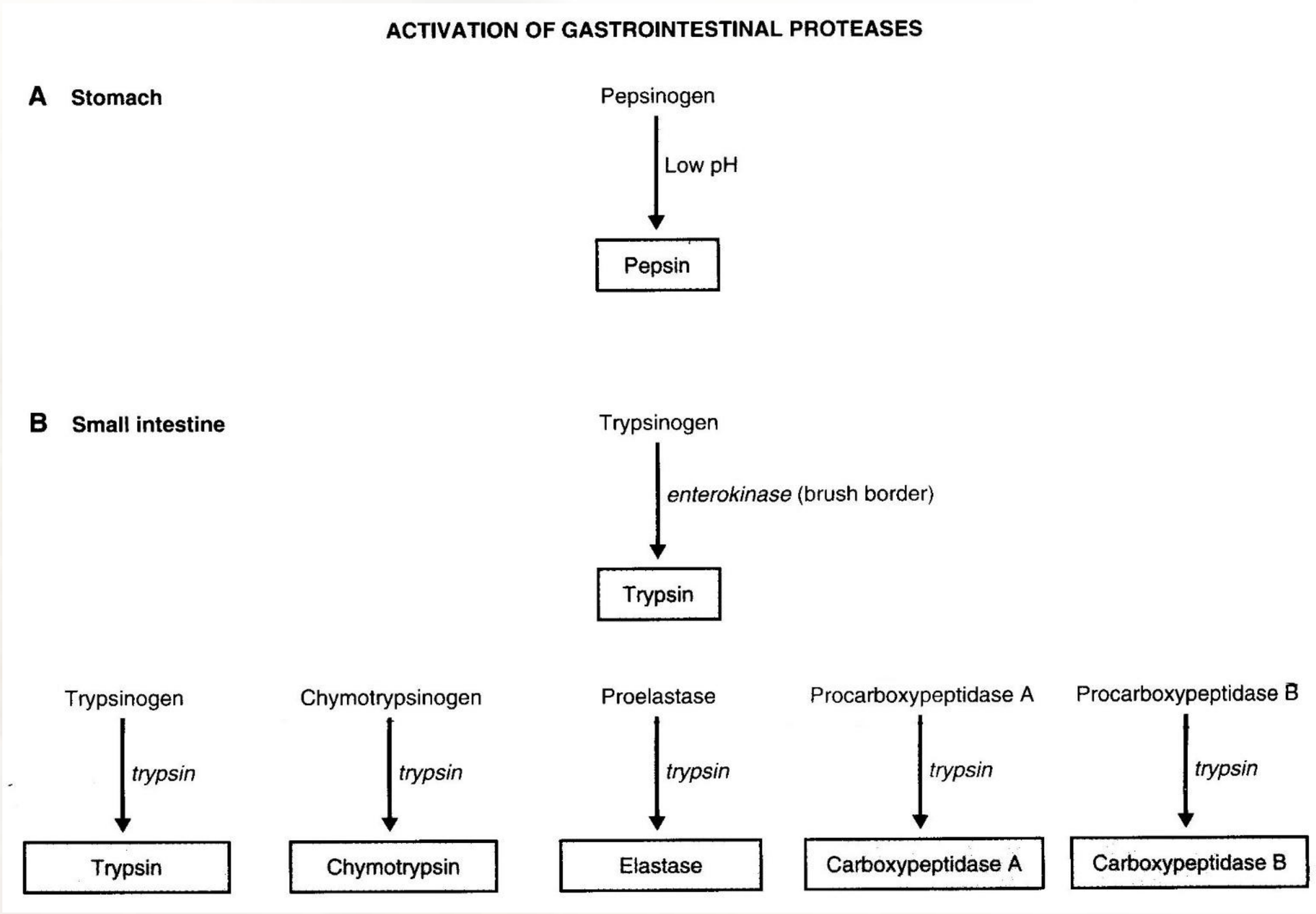
- **The major functions of pancreatic secretion:**
  1. **To neutralize the acids in the duodenal chyme to optimum range (pH= 7.0-8.0) for activity of pancreatic enzymes.**
  2. **To prevent damage to duodenal mucosa by acid & pepsin.**
  3. **To produce enzymes involved in the digestion of dietary carbohydrate,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

Pancreatic Enzymes: The pancreas secrests enzymes that act on all major types of food stuffs.

1. Pancreatic Proteolytic Enzymes (Trypsin, Chymotrypsin, Carboxypolypeptidase, Elastase)

- **Trypsin & 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.**
- **When first synthesized in the pancreatic cells, digestive enzymes are in the <u>inactive</u> forms; these enzymes become <u>activated</u> 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.**
  - **It can be autocatalytically activated by trypsin formed from previously secreted trypsinogen.**
- **Chymotrypsinogen to Chymotrypsin**
- **Procarboxypolypeptidase to Carboxypolypeptidase** } **activated by trypsin**
- **Proelastase to Elastase**

Activation of Trypsinogen in Duodenal Lumen:

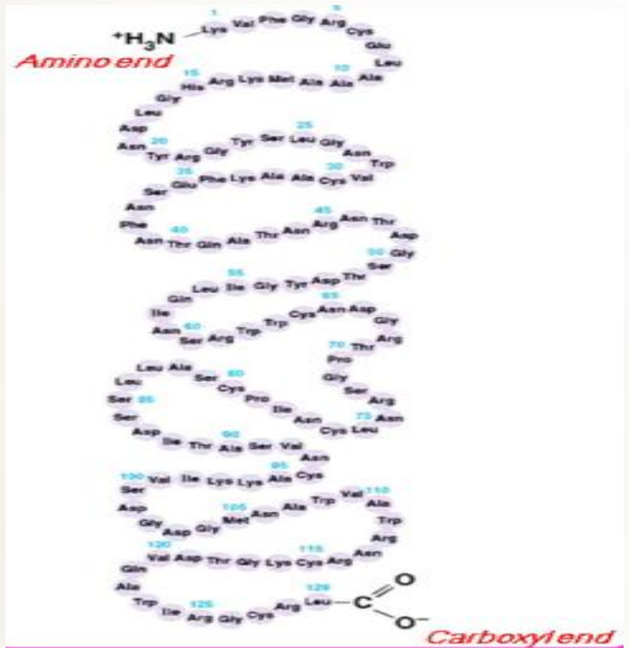


Trypsin Inhibitor:

- **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.**

Note:

- ✓ **Trypsin, chymotrypsin and elastase are endopeptidases,** splitting protein into shorter peptide chains.
- ✓ **Carboxypeptidase is an exopeptidase**; splits off amino acids at the carboxyl terminus of the peptide.
- ✓ **Endopeptidase** break peptide bonds of nonterminal amino acids, in contrast to **exopeptidases**, which break peptide bonds from their end-pieces. For this reason, endopeptidases cannot break down peptides into monomers while exopeptidases can.



2. Major Components of Pancreatic Secretion and Their Physiologic Roles & 5. Activation of Pancreatic Enzymes

Pancreatic Enzymes:

2. Pancreatic Amylase:

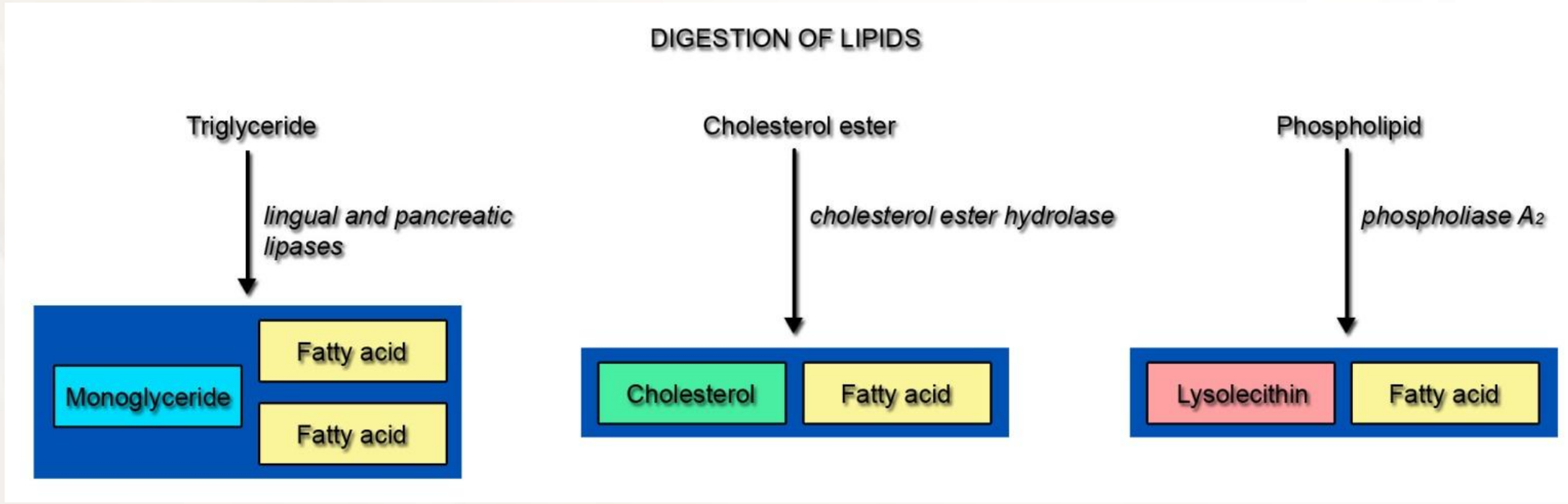
- **The pancreatic enzyme for digesting carbohydrates is pancreatic amylase, which hydrolyzes starches, glycogen, and most other carbohydrates (except cellulose) to form mostly disaccharides and a few trisaccharides. (maltose, multitriose)**

3. 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: liberates cholesterol & FA.

C. Phospholipase A2: splits phospholipids into lysophospholipids & FA.



Pancreatic enzymes for digestion

- **Protein digestion**
  - Trypsin
  - Chymotrypsin
  - Carboxypolypeptidase
- **Carbohydrate digestion**
  - Pancreatic amylase, which hyrolyzes starches, glycogen, and most other carbohydrates
- **Fat digestion**
  - Pancreatic lipase
  - Cholesterol esterase
  - Phospholipase

Characteristics of Pancreatic Enzymes

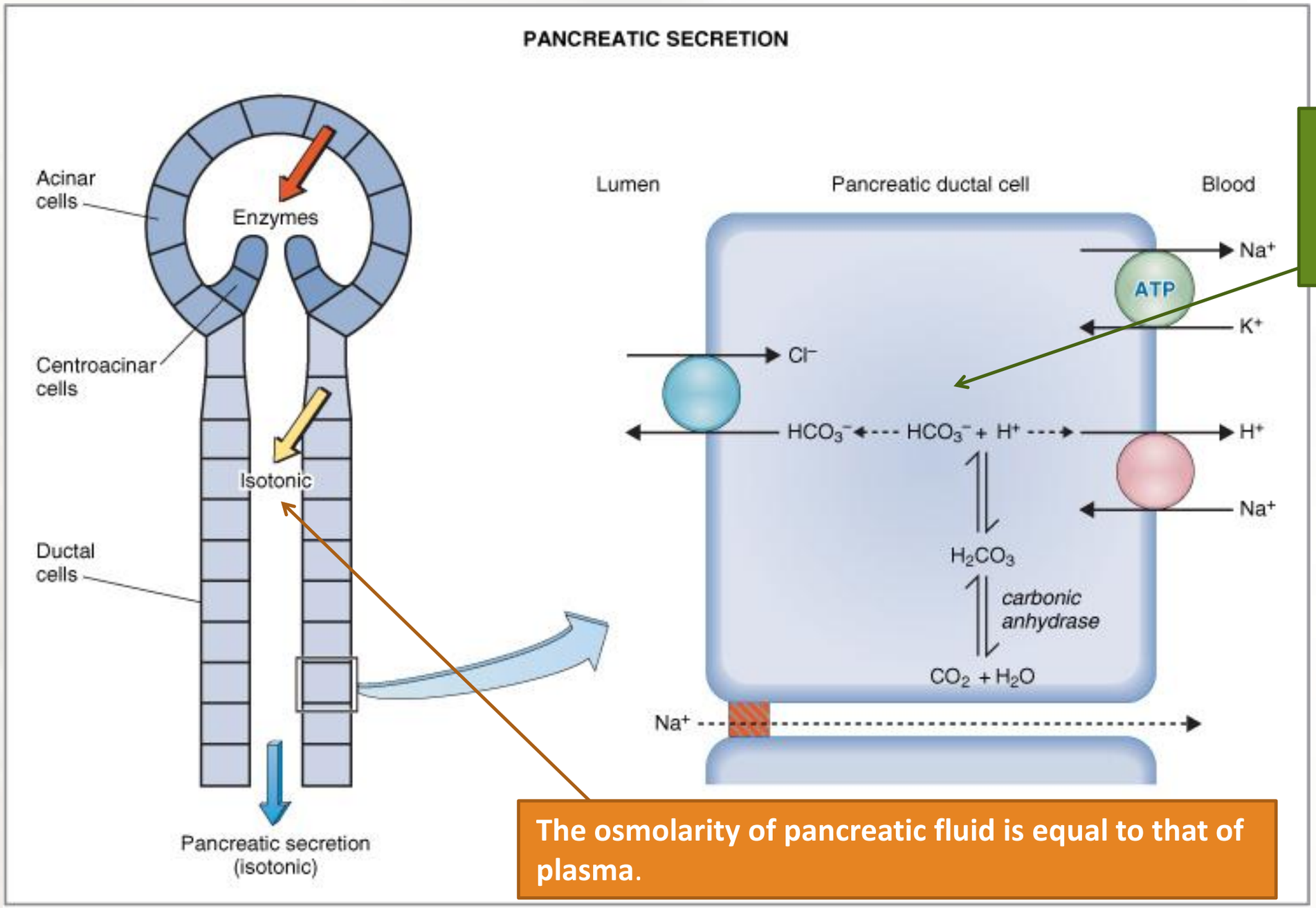
Enzyme	Specific Hydrolytic Activity
Proteolytic	
Endopeptidases	
Trypsin(ogen)	Cleaves peptide linkages in which the carboxyl group is either arginine or lysine
Chymotrypsin(ogen)	Cleaves peptides at the carboxyl end of hydrophobic amino acids, e.g., tyrosine or phynylalanine
(Pro)elastase	Cleaves peptide 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

important

Doctor said not important

Cellular Mechanisms of Bicarbonate Secretion .٣

Secretion of Isosmotic Sodium Bicarbonate Solution



The pancreas secrets about 1 L/day of HCO_3–rich fluid from the epithelial cells of the ductules and ducts.

*HCO3 concentration increases with increasing secretion rate.

The osmolarity of pancreatic fluid is equal to that of plasma.

6. Hormonal & Neural Regulation of Pancreatic Secretion

Mediator	Stimulation leads to:	Secreted from:	When it released :
Acetylcholine	Parasympathatic stimulation of the acinar cells of pancreas, causing increase in enzyme rich-fluid + HCO_3 secretion.	- Parasympathetic vagus nerve ending. - Cholinergic nerve in enteric nervous system .	
Secretin	Activating ductual epithelium of pancreas, causing an increase in HCO_3 rich secretion.	Dudunal and jeujenal mucosa (S cell).	When highly acidic chyme enter to small Intestine. (so, it works as neutralization of Acidic Stomach Chyme by bicarbonate)
CCK (cholecystokinin)	Stimulaton of the acinar cells of pancreas , causing marked increase in enzymatic secretion.	Duodenal and upper jejunal mucosa (I cell) when food enter small Intestine.	When food enter small Intestine , especially of precence of proteoses and peptones and long-chain fatty acids in the chyme.

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

- ✓ **Theses mediators (potentiate each other) to get a huge amount of pancreatic juices , far greater than if they stimulate individually.**
  i.e. they multiplied by each other not summation to each other.
- ✓ **Usually, pancreatic secretions are the result of multiple stimuli rather than one stimulus.**

Note:

- ✓ **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, stimulates secretion of large quantities of H_2O and $NaHCO_3$ solution by the pancreatic ductal epithelium**

Stimuli for Pancreatic Secretion

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

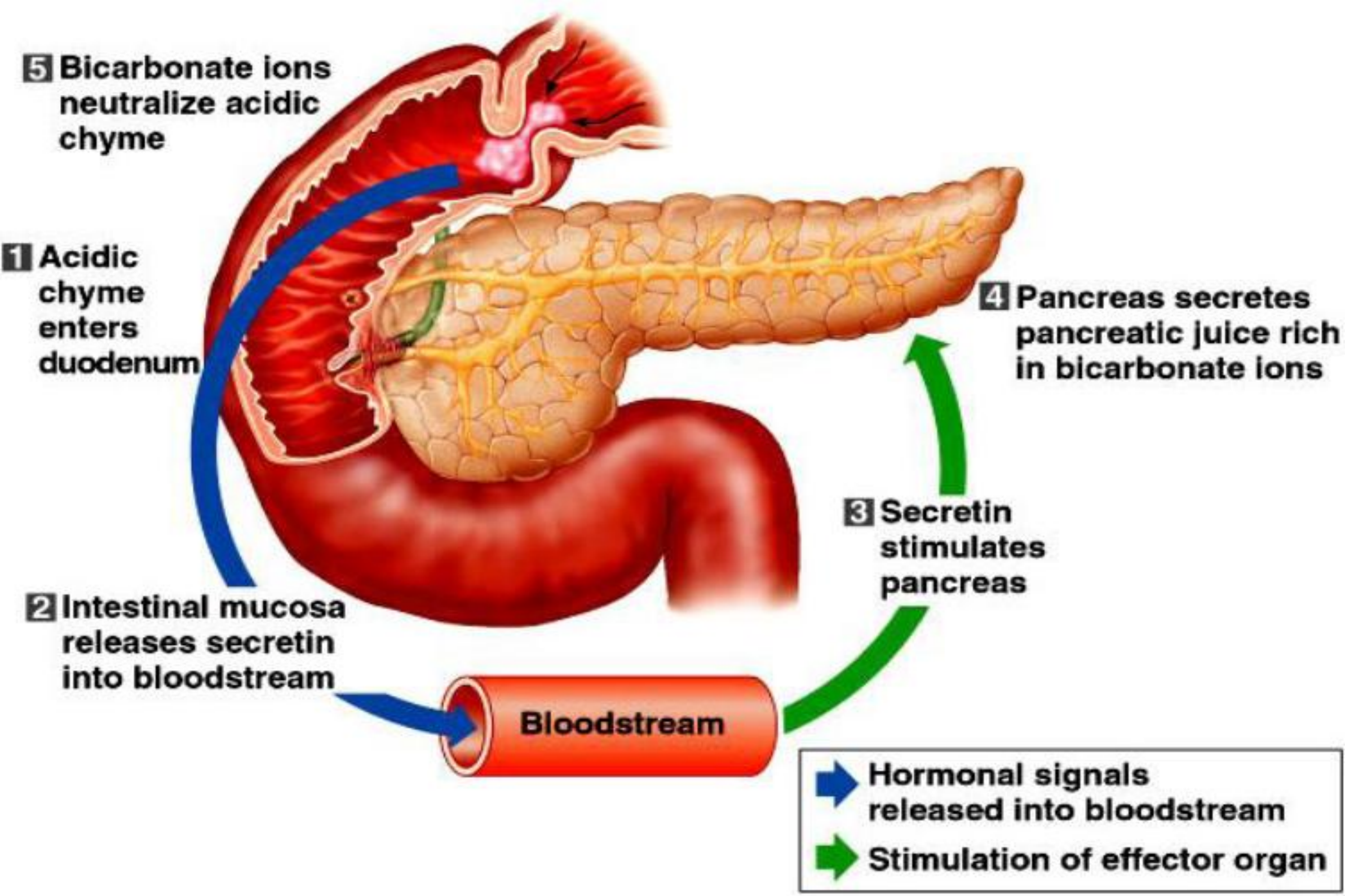
- **Secretin is present in an inactive form, prosecretin (in S cells in the mucosa of the duodenum and jejunum).**
- **When acid chyme with pH less than 4.5-5.0 enters the duodenum from the stomach, it causes duodenal mucosal release and activation of secretin, which is then absorbed into the blood.**
- **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^-.**

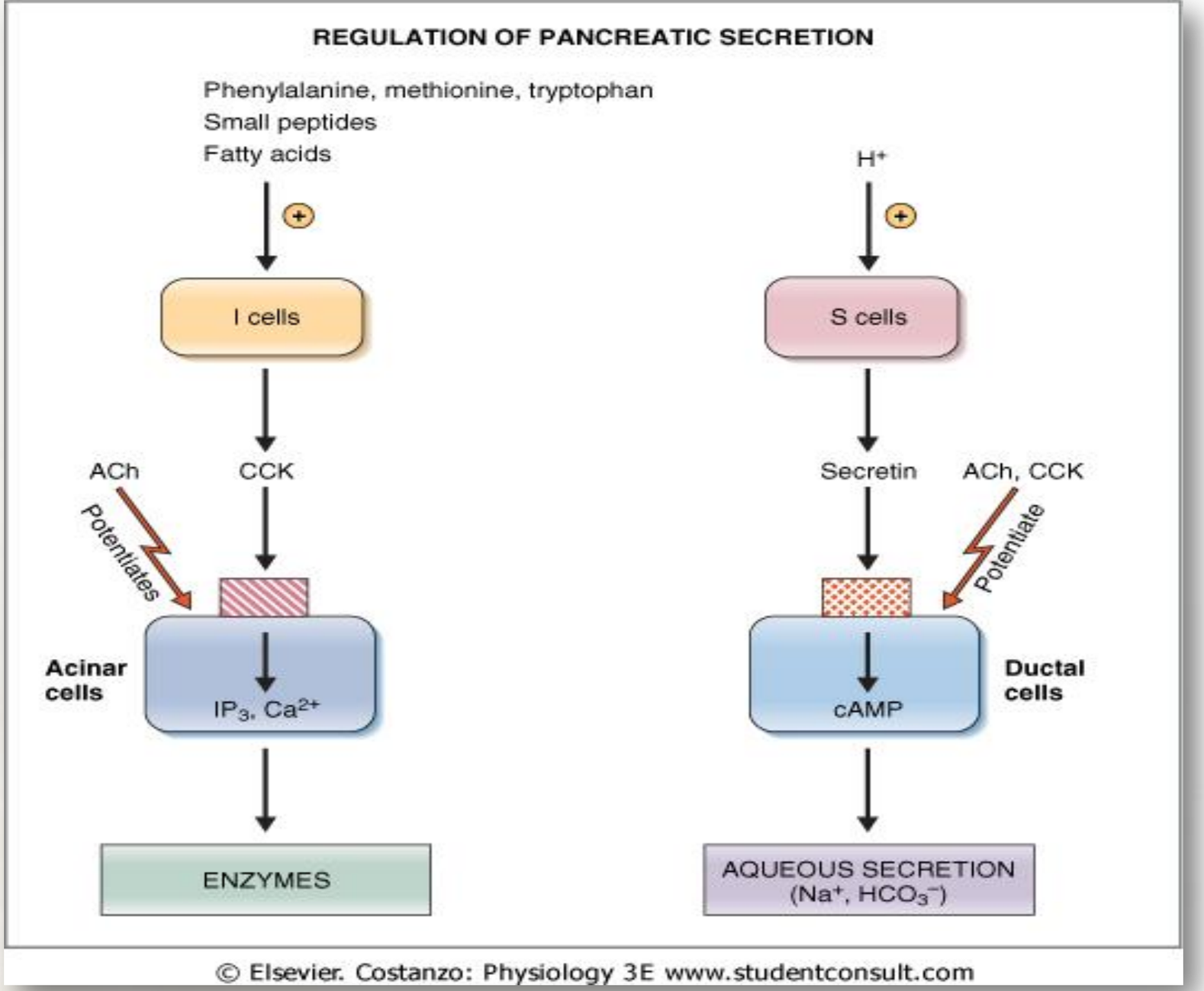
$$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$$

- **H_2CO_3 dissociates into CO_2 and H_2O.**

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.**


5 Bicarbonate ions neutralize acidic chyme
1 Acidic chyme enters duodenum
4 Pancreas secretes pancreatic juice rich in bicarbonate ions
3 Secretin stimulates pancreas
2 Intestinal mucosa releases secretin into bloodstream
Bloodstream
Hormonal signals released into bloodstream
Stimulation of effector organ



1. Present of food -> I cells activation -> CCK secretion -> stimulate acinar cells -> causing enzymes secretions.
2. Present of highly acid chyme (H+) -> S cells activation -> Secretin secretion -> stimulate ductal cells -> causing Bicarbonate secretions (to neutralized the acidity) .

- Both are happens with potentiate of Ach from parasympathetic effect .

Phases of Pancreatic Secretion

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

Summary

- The pancreas secretes tow important hormones **Insulin,Glucagon.**
- Pancreatic juice is secreted in Response to the presence of Chyme in the upper portions of the small intestine.
- Trypsinogen is activated into trypsin by enzyme **Enteropeptidase (enterokinase)**, if Chyme comes in contact with the mucosa.
- Trypsin, chymotrypsin and elastase are **endopeptidases**, while Carboxypeptidase is an **Exopeptidase.**
- Secretion of Trypsin Inhibitor prevents digestion of The Pancreas Itself.
- The pancreatic enzyme for digesting carbohydrates is **pancreatic amylase**, for fat Digesting is **pancreatic lipase** which is the most important fat enzyme.
- The osmolarity of pancreatic fluid is equal to that of plasma.
- Ach, Secretin, CCK mediators (potentiate each other) to get a huge amount of pancreatic juices.

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GOOD LUCK