جامعة الملك سعود
King Saud University
1957

MED437
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Physiology of the Pancreas

Objectives:

- Functional Anatomy of Pancreas
- Major components of pancreatic juice
- Pancreatic Digestive Enzymes
- Cellular Mechanism of HCO3- Secretion
- Control of Pancreatic Secretion
- Release, Stimuli & Actions of Secretin
- Release, Stimuli & Actions of Cholecystokinin

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Colour index:
- Important
- Numbers
- Extra

وَأَن لَّيْسَ لِلْإِنسَانِ إِلَّا مَا سَعَىٰ

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:

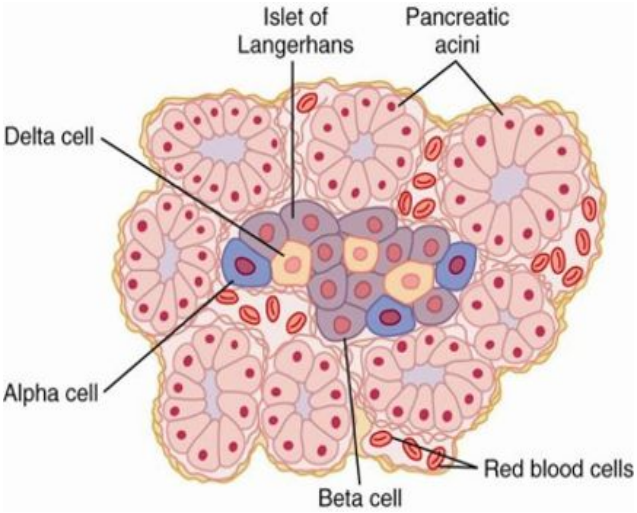
Endocrine portion (Islets of Langerhans)

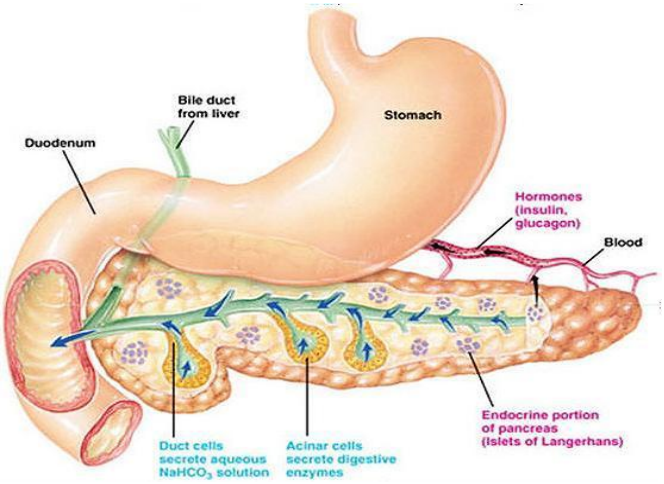
Secrete insulin (beta cells), glucagon (alpha cells) & somatostatin (delta cells).

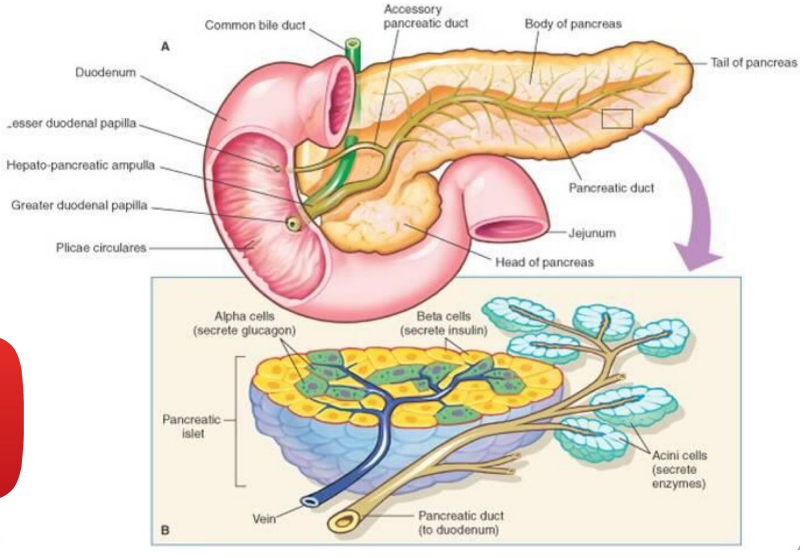
Exocrine portion (Acinar gland tissues)

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

Because it can secrete enzymes for digestion of all types of food







Pancreatic Secretion

Pancreatic juice Is secreted in response to the presence of certain type of chyme in the upper portions of the small intestine.

Major functions

- **Produce** enzymes involved in the digestion of carbohydrate, fat & protein.
- **Neutralize** the acids in the duodenal chyme. it's the main source of bicarbonate
- To **prevent** damage to duodenal mucosa by acid & pepsin. Stomach is strong acidic medium 2 PH it will damage duodenal epithelium

Characteristics

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

Composition of pancreatic secretion

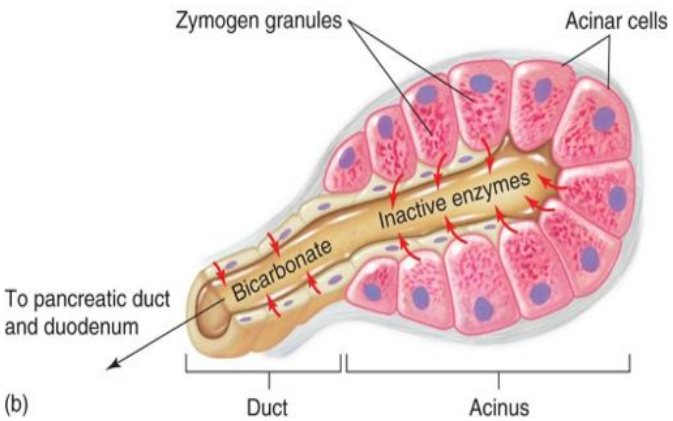
Organic materials (1-2 %)

- Mostly enzymes Secreted from acinar cells.

Inorganic materials (1%)

Electrolytes, produced from the centroacinar & intercalated duct cells.

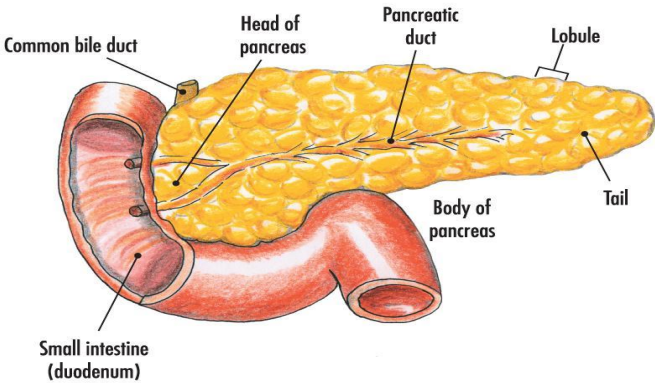
- Include Na^+, K^+, Ca^{++}, $HCO3^-$ and Cl^-, with greater bulk in the form of $NaHCO_3$.



Flow of Pancreatic Secretion into Duodenum

- The combined product of enzymes and $NaCO_3$ flows through a long pancreatic duct.

- Pancreatic duct joins the common bile duct immediately before it empties into the duodenum through the papilla of Vater, surrounded by the sphincter of Oddi.



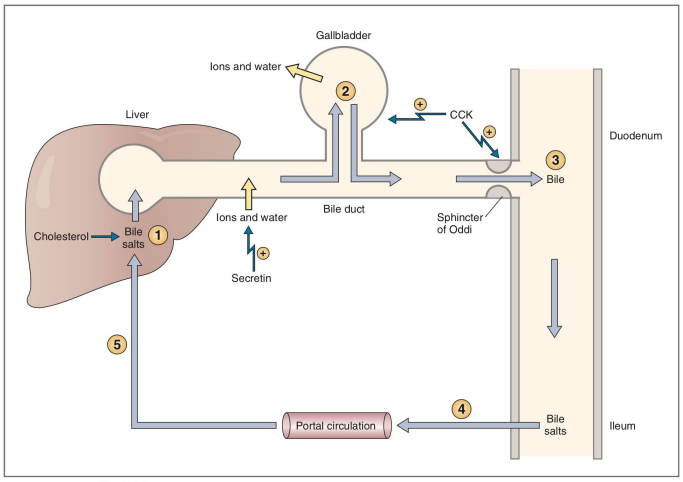
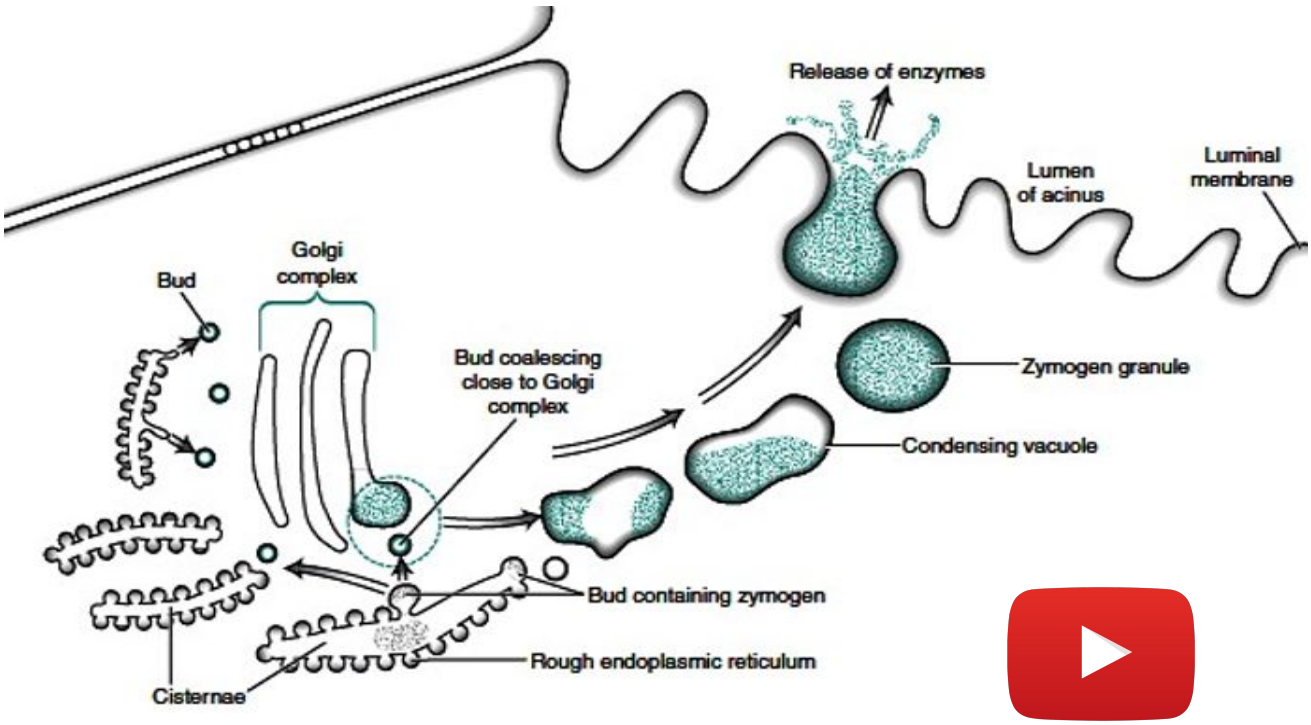


Fig. 8.24 **Secretion and enterohepatic circulation of bile salts.** *Light blue arrows* show the path of bile flow; *yellow arrows* show the movement of ions and water. *CCK*, Cholecystokinin.

Enzyme secretion by Acinar cells



Watch from 21:40 till 28:12

Pancreatic Digestive Enzymes

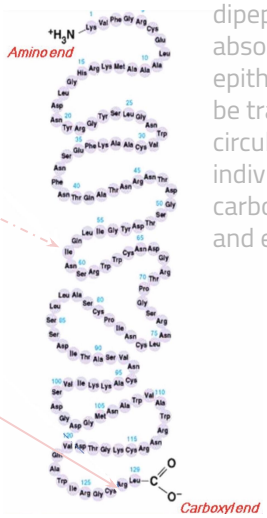
Protein Digestion	Carbohydrate Digestion	Fat Digestion
Trypsin Chymotrypsin Carboxypeptidase	Pancreatic Amylase	Pancreatic Lipase Cholesterol Esterase Phospholipase

Pancreatic Proteolytic Enzymes (proteases):

Trypsin, chymotrypsin and carboxypeptidase. +elastase

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.



Oligopeptides and dipeptides can be absorbed into the epithelium but cannot be transported to the circulation it must be individual by carboxypolypeptdases and enteropeptidase

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.

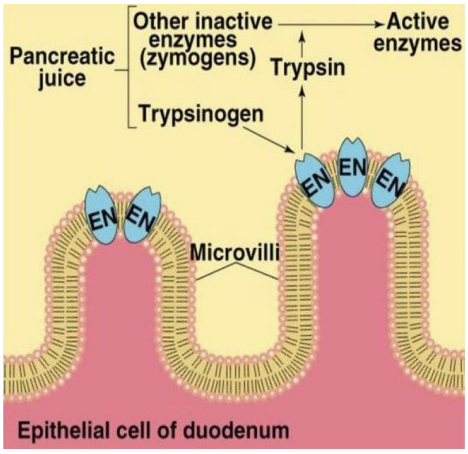
Trypsinogen is activated by:

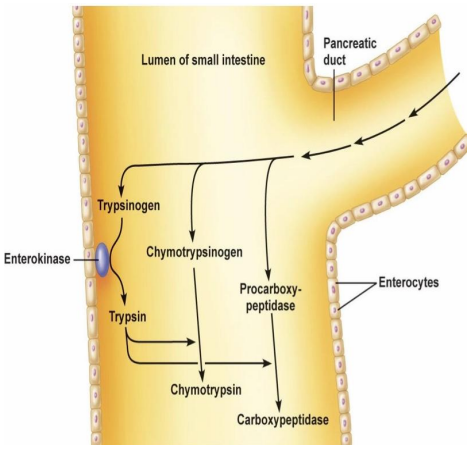
- Enteropeptidase (enterokinase), an enzyme secreted by the intestinal mucosa when chyme comes in contact with the mucosa. The chyme is the stimulus.
- Trypsinogen can be autocatalytically activated by trypsin formed from previously secreted trypsinogen.

Chymotrypsinogen and procarboxypolypeptidase are activated by:

- Trypsin to form chymotrypsin and carboxypolypeptidase.

Activation of Pancreatic proteolytic Enzymes:

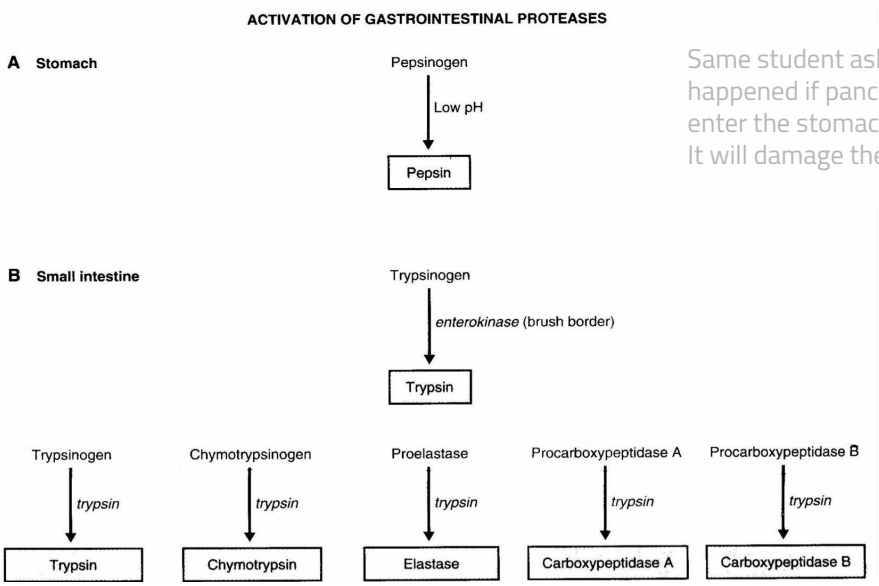




Trypsin Inhibitor:

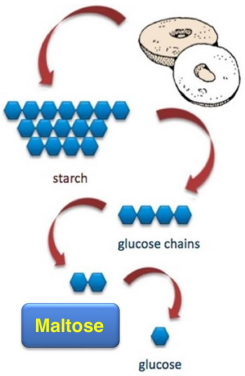
1	Pancreatic proteolytic enzymes do not become activated until after they have been secreted into the intestine because the trypsin and the other enzymes would digest the pancreas itself.
2	Trypsin inhibitor is formed in the cytoplasm of the glandular cells that secrete pancreatic proteolytic enzymes.
3	Trypsin inhibitor prevents activation of trypsin (and therefore other enzymes as well) inside the secretory cells of the acini and ducts of the pancreas.
4	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:



Same student asked: what happened if pancreatic enzymes enter the stomach?
It will damage the epithelium

2- Pancreatic Amylase



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

- Only monosaccharide can be absorbed
- Too much cellulose cause diarrhea

Why is the Pancreatic amylase is more important than the Salivary One ?
Both amylase have the same power, but the pancreatic has longer duration.

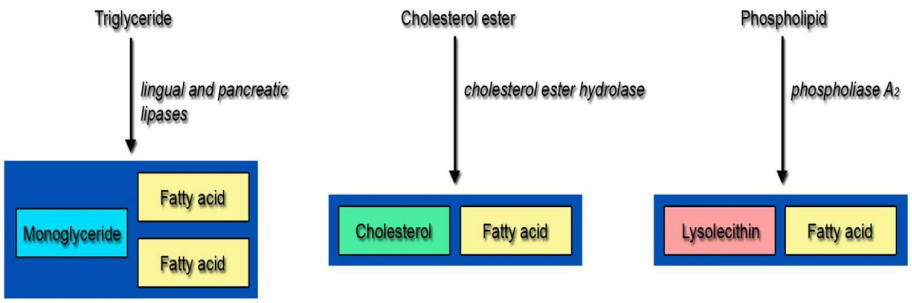
3- Pancreatic Enzymes for Fat Digestion

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

  Deficiency of pancreatic lipase → loss of fat in stool (steatorrhea)

- **Cholesterol esterase** which liberates cholesterol.
- **Phospholipase A_2** which splits phospholipids into lysolecithin & FA.

Small lipids can across the membrane passively and through the basolateral by chylomicron



End Products of Fat Digestion

Characteristics of Pancreatic Enzymes

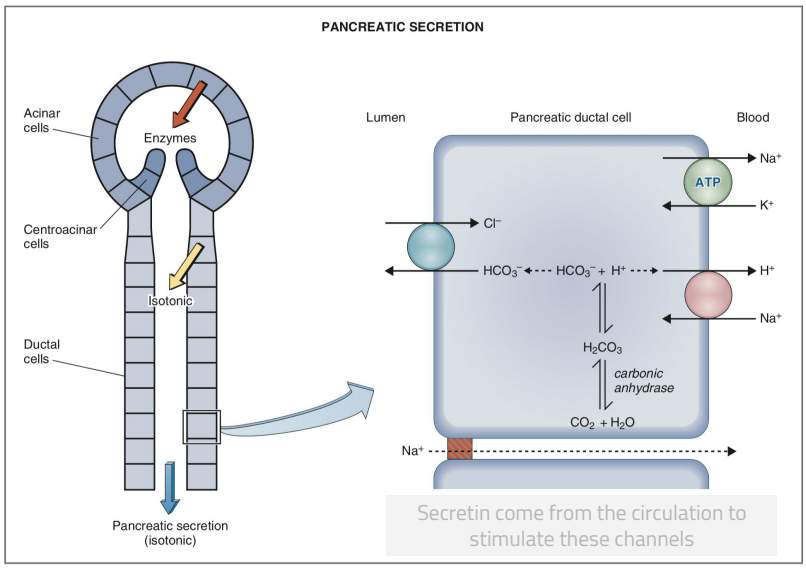
Enzyme	Specific Hydrolytic Activity
Proteolytic	
Endopeptidases	
Trypsin(ogen)	Cleaves peptide linkages in which the carboxyl group is either arginine or lysine
Chymotrypsin(ogen)	Cleaves peptides at the carboxyl end of hydrophobic amino acids, e.g., tyrosine or phynylalanine
(Pro)elastase	Cleaves peptide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

- NaHCO3 does not influence the osmolarity of the secretion but the NaCl does.

The ductal cells are permeable to water so we have isotonic secretion it works exactly as parietal cell but in the opposite side.



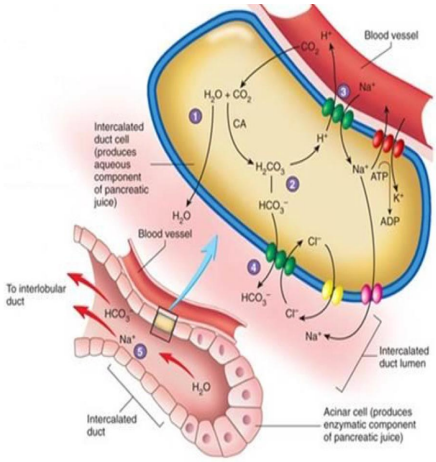
Acinar cell has direct communication with blood so they get the components and start to synthesize enzymes then store them in granules

Fig. 8.21 Mechanism of pancreatic secretion. The enzymatic component is produced by acinar cells, and the aqueous component is produced by centroacinar and ductal cells. *ATP*, Adenosine triphosphate.

Mechanism of HCO_3^- Secretion

1. CO_2 and H_2O combine in acinar cells to form H_2CO_3.
2. H_2CO_3 dissociates 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

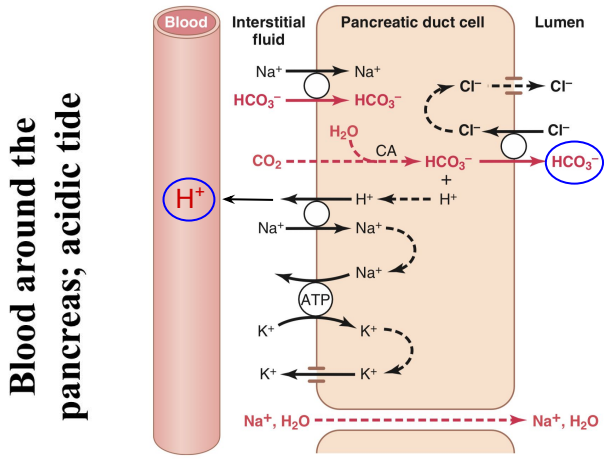


Figure 65-8. Secretion of isosmotic sodium bicarbonate solution by the pancreatic ductules and ducts. CA, carbonic anhydrase.

Flow Rate and Pancreatic Secretion

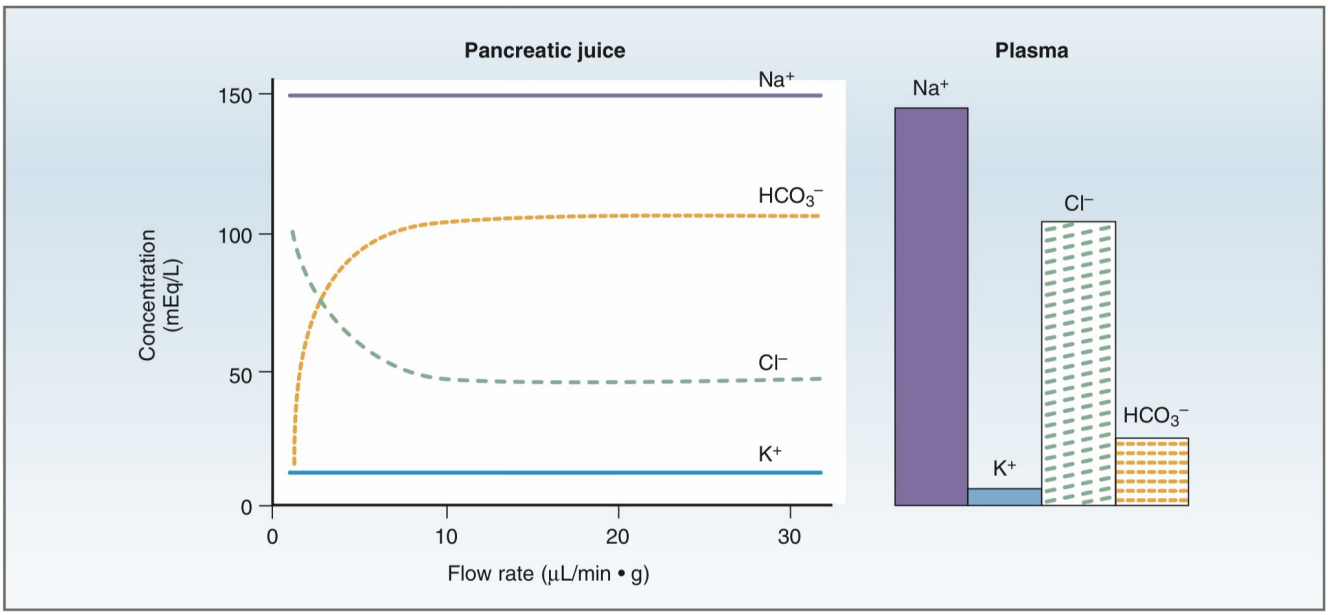


Fig. 8.22 Relationship between the composition of pancreatic juice and the pancreatic flow rate. The ionic composition of pancreatic juice is compared with that of plasma.

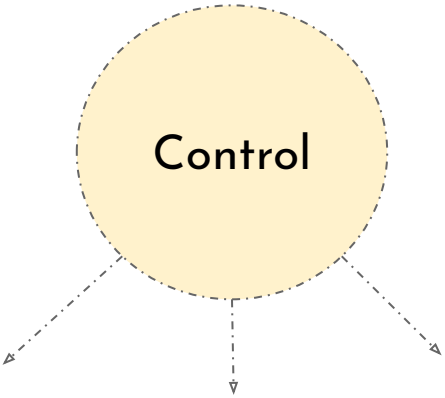
HCO_3^- concentration **increases** with increasing secretion rate

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



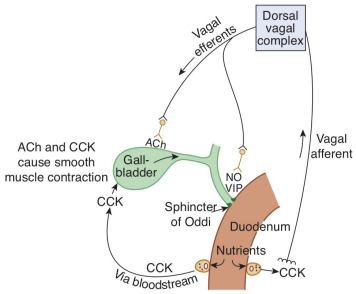


FIGURE 29–9 **Neurohumoral control of gallbladder contraction and biliary secretion.**

Parasympathetic

Stimulation through Ach on acinar cells) results in increase in enzyme secretion fluid and $HCO3^-$.

Secretin

Tends to stimulate a $HCO3^-$ - rich secretion by activating ductal cells.

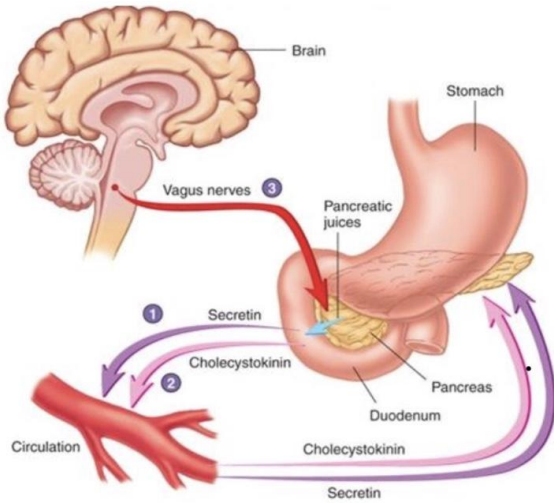
Ductal cells are really sensitive to secretin

Cholecystokinin

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

Both have the same action, but CCK is stronger than Ach.
Remember always Hormonal > Neural control

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.



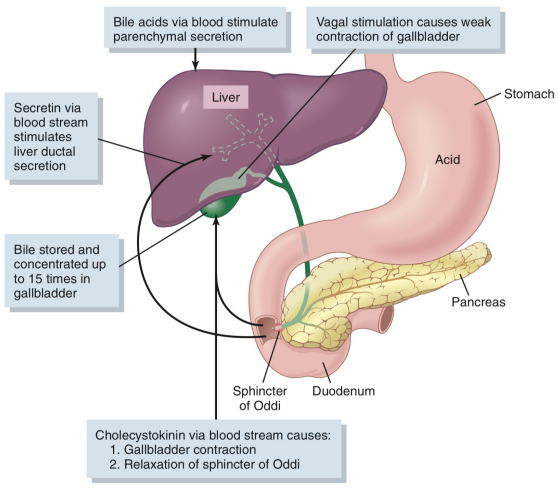


Figure 65-11. Liver secretion and gallbladder emptying.

Regulation of pancreatic secretion

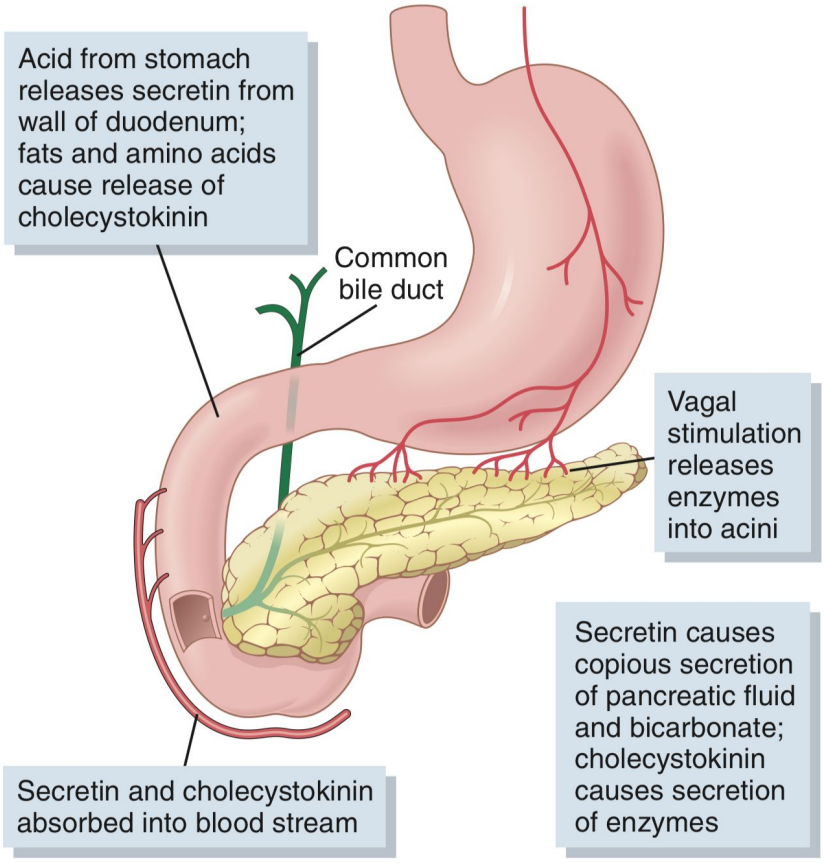


Figure 65-10. Regulation of pancreatic secretion.

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.

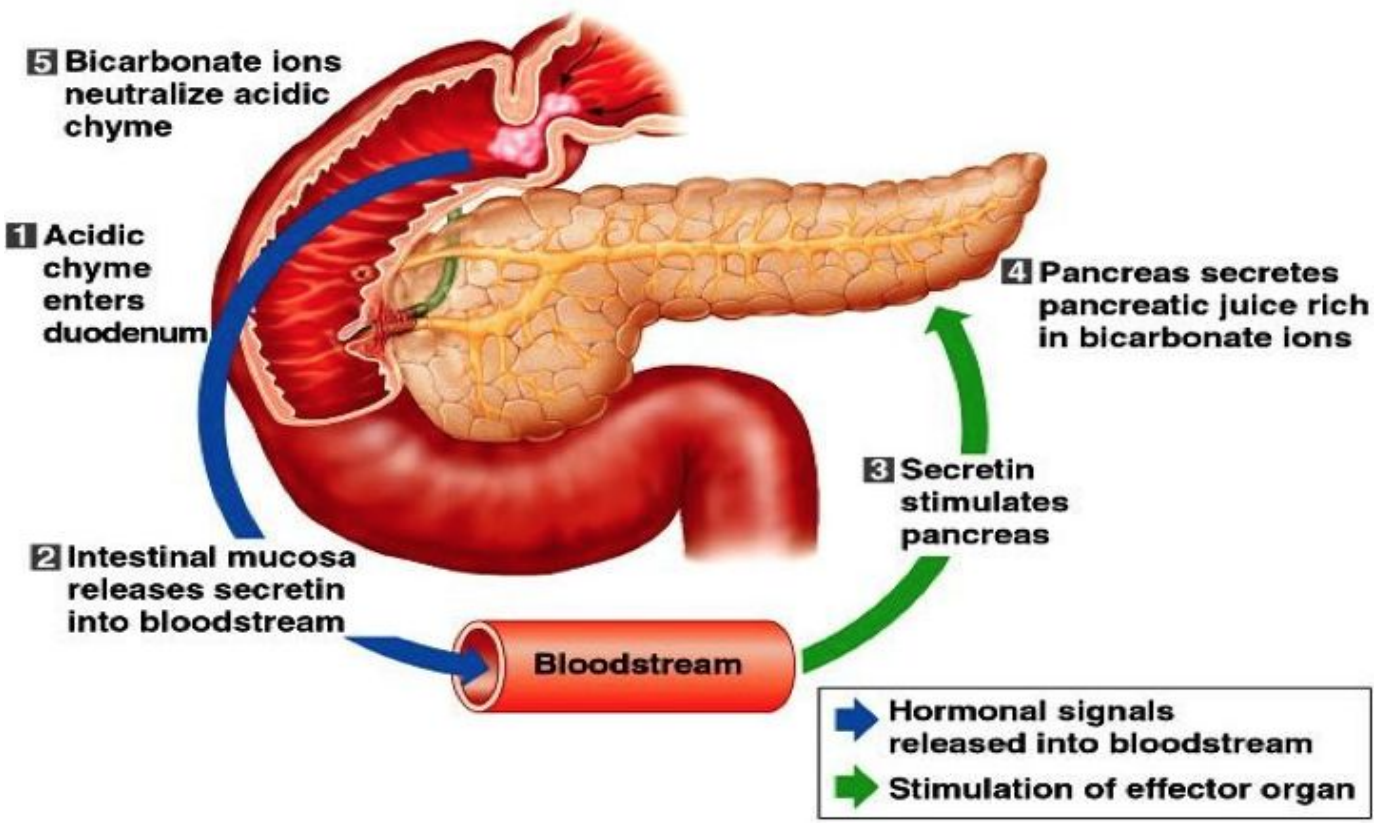
➥ **Stimulus**: Mainly proteoses, peptones and long-chain fatty acids in the chyme.

Function of secretin:

All of these inhibitions happen in the stomach

Stimulates	Augments	Stimulates	Inhibit	Inhibit	Inhibit
Pancreatic secretion rich in **HCO_3^-** and H_2O from duct cells.	stimulation of enzyme secretion by **CCK**.	hepatic bile flow and HCO_3^- secretion.	gastric acid secretion and gastrin release, but it stimulates pepsin secretion.	gastric motility, contracts pylorus and slows gastric emptying, relaxes LES	intestinal motility and contracts ileocecal sphincter.

Regulation of Pancreatic Secretion by Secretin

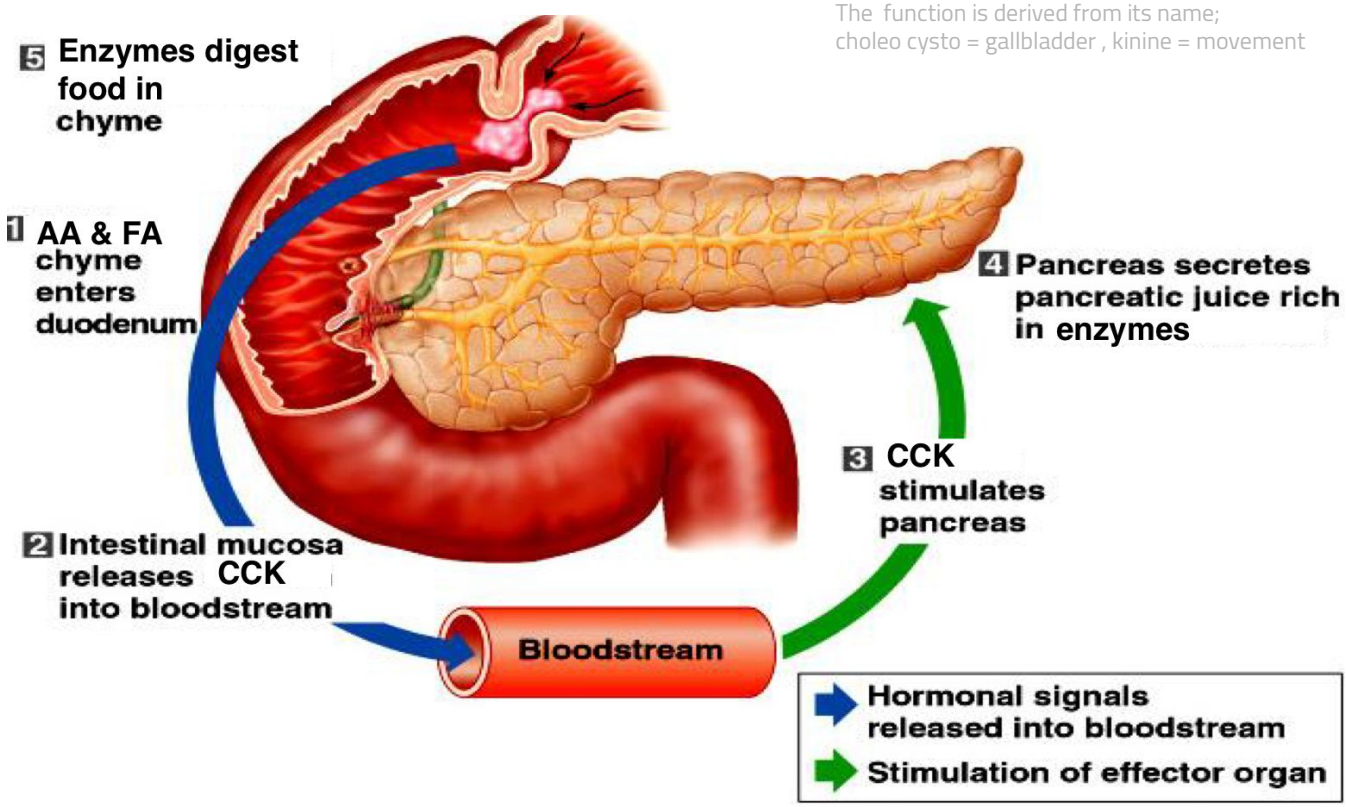


Function of cholecystokinin:

Stimulates	Augments	Contract	Has	Stimulates	Inhibits	In addition
Pancreatic enzyme secretion, accounting for 70-80% of total pancreatic digestive enzymes secretion after meal.	stimulation of H_2O and HCO_3^- secretion by secretin.	**Gall bladder,** relaxes sphincter of Oddi and causes bile discharge into intestine.	trophic effect on pancreas. Protect the mucosa.	intestinal motility and relaxes ileocecal sphincter.	stomach contraction moderately and slows its emptying.	it may be concerned with the mechanism of satiety.

Regulation of Pancreatic Secretion by CCK

The function is derived from its name;
choleo cysto = gallbladder , kinine = movement



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.

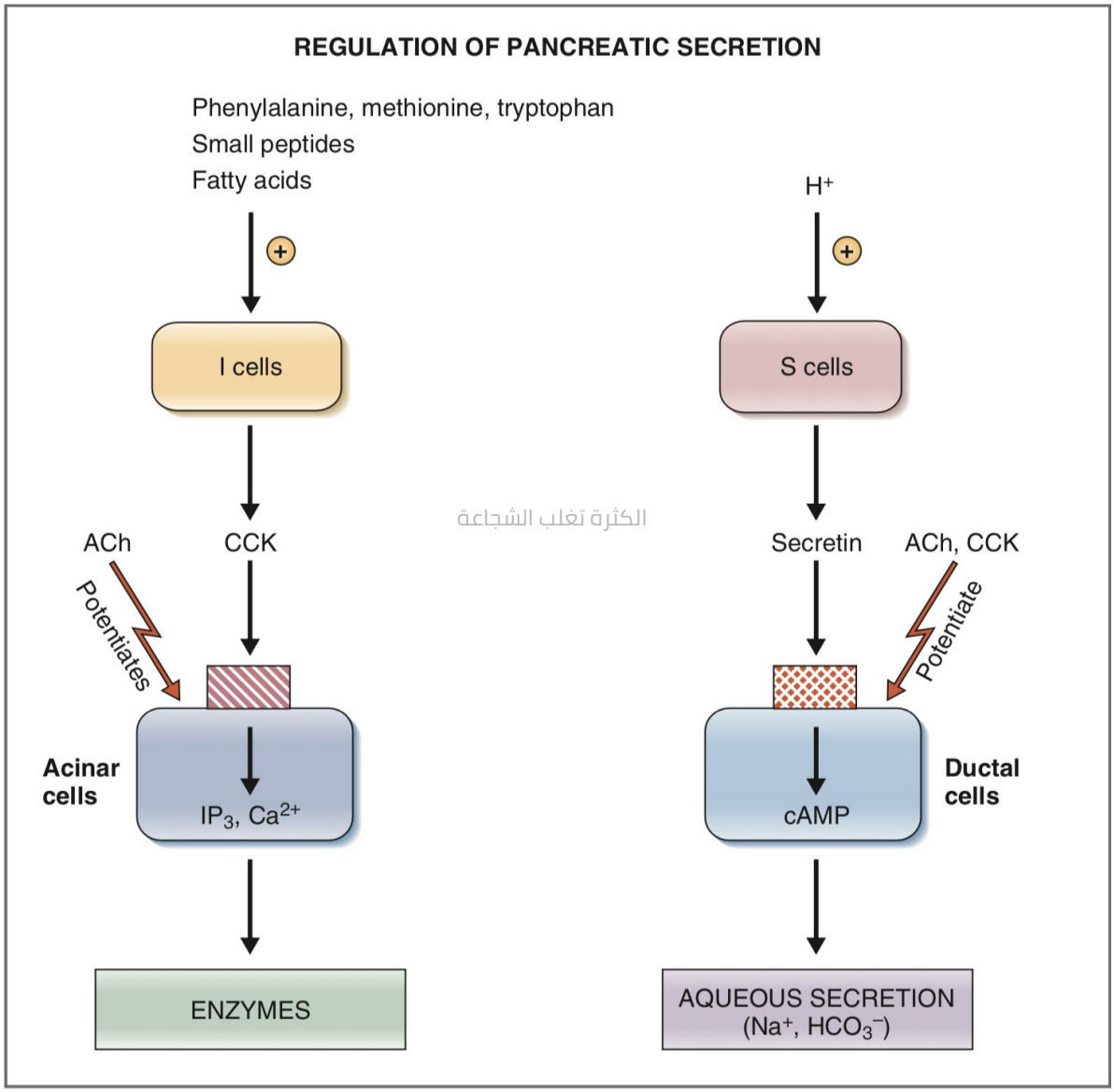
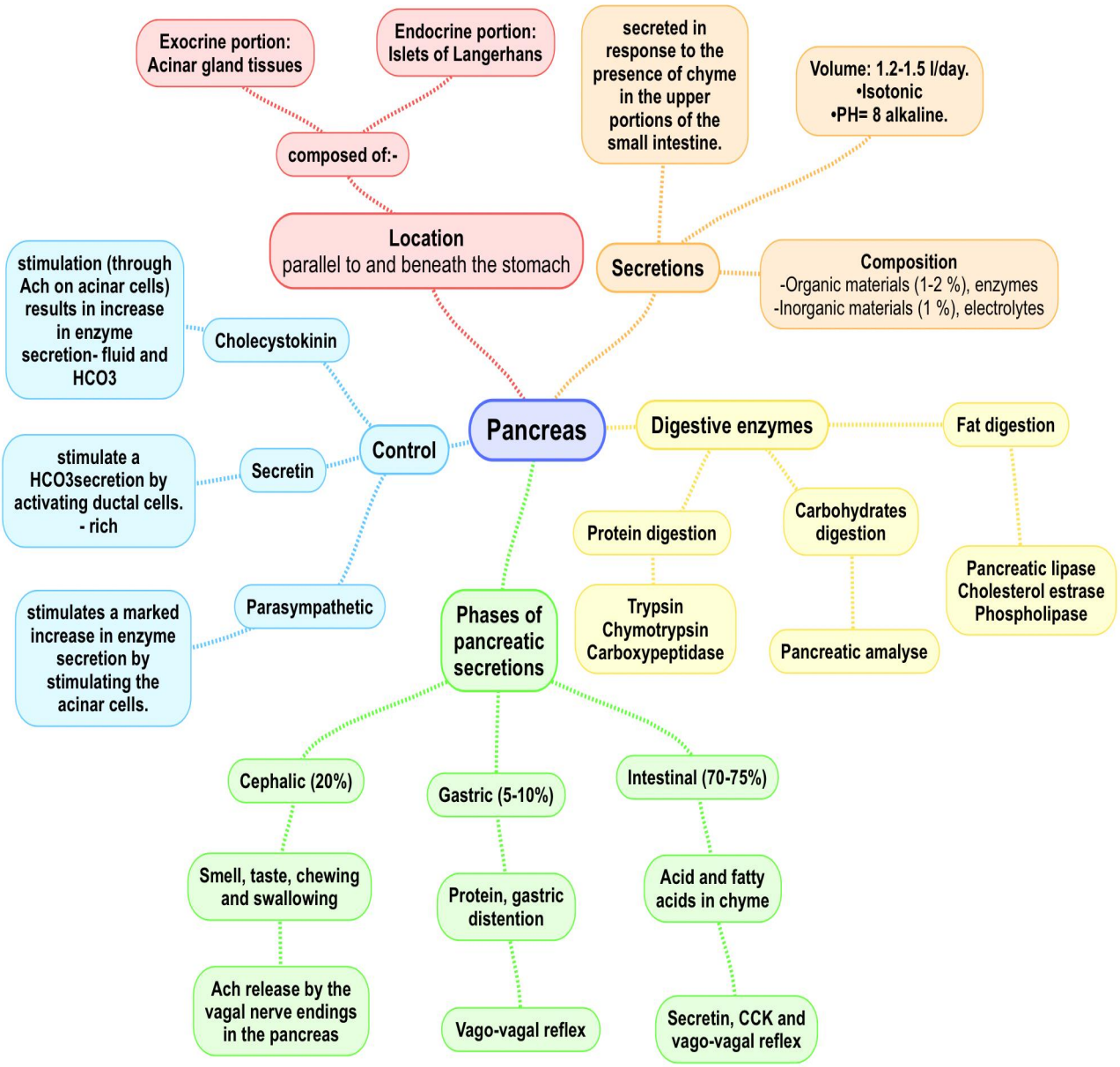


Fig. 8.23 Regulation of pancreatic secretion. *ACh,* Acetylcholine; *cAMP,* cyclic adenosine monophosphate; *CCK,* cholecystokinin; IP_3, inositol 1,4,5-triphosphate.

Summary


Exocrine portion: Acinar gland tissues
Endocrine portion: Islets of Langerhans
composed of:-
secreted in response to the presence of chyme in the upper portions of the small intestine.
Volume: 1.2-1.5 l/day.
•Isotonic
•PH= 8 alkaline.
Location
parallel to and beneath the stomach
Secretions
Composition
-Organic materials (1-2 %), enzymes
-Inorganic materials (1 %), electrolytes
stimulation (through Ach on acinar cells) results in increase in enzyme secretion- fluid and HCO3
Cholecystokinin
Pancreas
Digestive enzymes
Fat digestion
Control
Secretin
stimulate a HCO3secretion by activating ductal cells. - rich
Protein digestion
Carbohydrates digestion
Pancreatic lipase
Cholesterol estrase
Phospholipase
Parasympathetic
stimulates a marked increase in enzyme secretion by stimulating the acinar cells.
Phases of pancreatic secretions
Trypsin
Chymotrypsin
Carboxypeptidase
Pancreatic amalyse
Cephalic (20%)
Gastric (5-10%)
Intestinal (70-75%)
Smell, taste, chewing and swallowing
Protein, gastric distention
Acid and fatty acids in chyme
Ach release by the vagal nerve endings in the pancreas
Vago-vagal reflex
Secretin, CCK and vago-vagal reflex

MCQs

1) Pancreatic juice is released in response to:
A. Hypoglycemia.
B. Hyperglycemia.
C. Presence of chyme in small intestines.
D. Presence of chyme in stomach.

2. Which one of the following is an exopeptidase:
A. Trypsin
B. chymotrypsin
C. Elastase
D. Carboxypeptidase

3. Which one of the following activates proelastase into elastase:
A. Enteropeptidase
B. Trypsin
C. Pepsin
D. Secretin

4. The presence of long-chain fatty acids in the duodenum will stimulate which of the following?
A. I cells
B. S cells
C. C cells
D. G Cells

5. Increased HCO3 exchange with Cl occurs by:
A. Increased secretion of cholecystokinin
B. Decreased secretion of cholecystokinin
C. Increased secretion of secretin
D. Decreased secretion of secretin

6. Which one of The following pancreatic enzyme released for digesting carbohydrates :
A. a-Amylase
B. Trypsinogen
C. Ribonuclease
D. Non above

SAQ

What are the pancreatic enzymes involved in protein digestion?

Trypsin
Chymotrypsin
Carboxypeptidase

Answers:
1. C
2. D
3. B
4. A
5. C
6. A