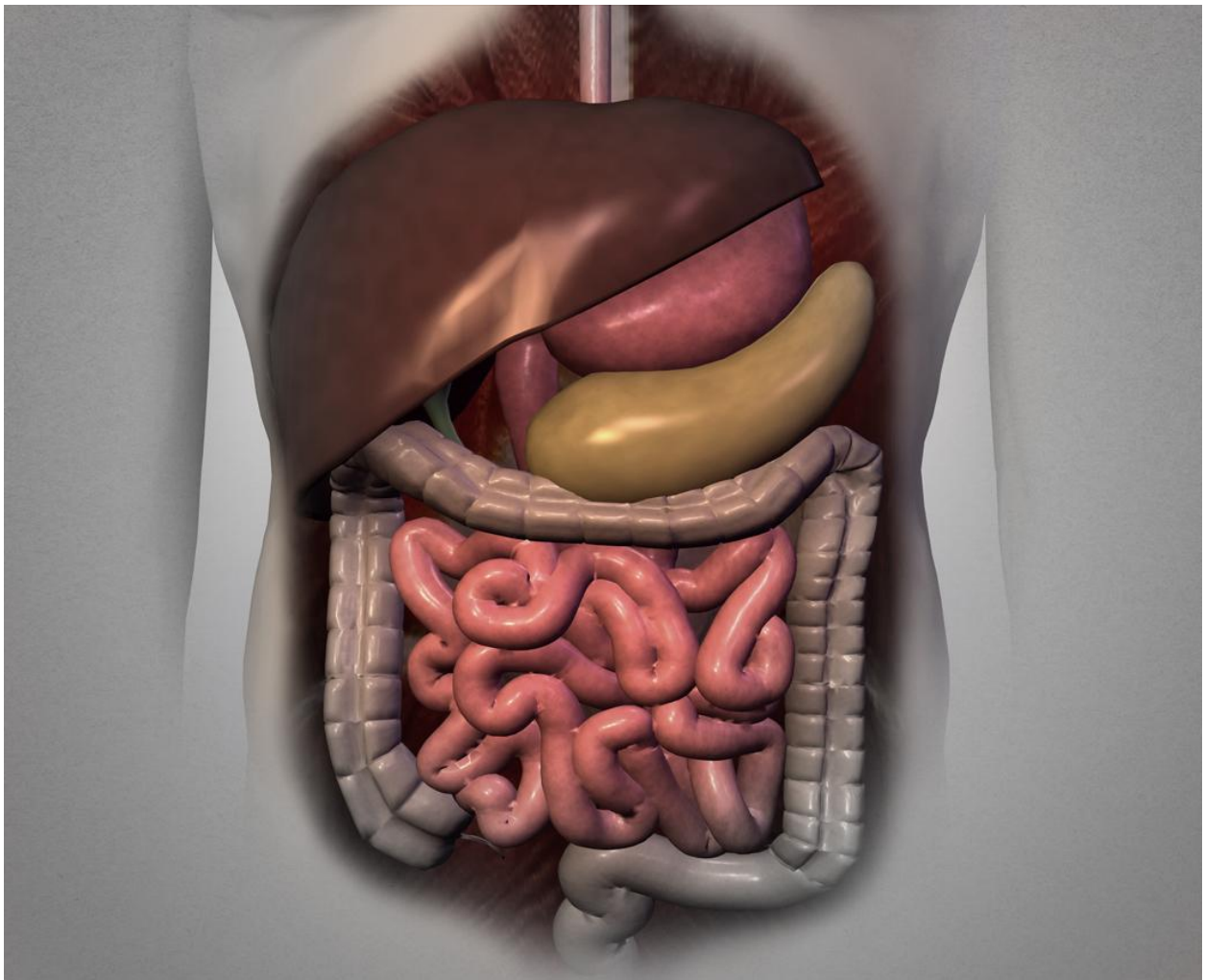

GIT Block

Physiology Team 431

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Revised by : Nour Al-Khawajah & Mohmmed Asiri

- Extra information.
- Important.
- Female's doctor's notes.
- Male's doctor's notes

PHYSIOLOGY OF PANCREAS

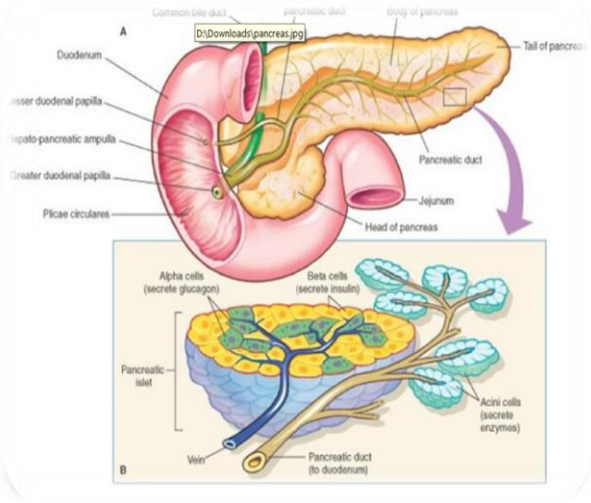
The exocrine pancreas

The pancreas, which lies parallel to and beneath the stomach, is composed of:

1) The endocrine islets of Langerhans which secrete insulin, glucagon and somatostatin.

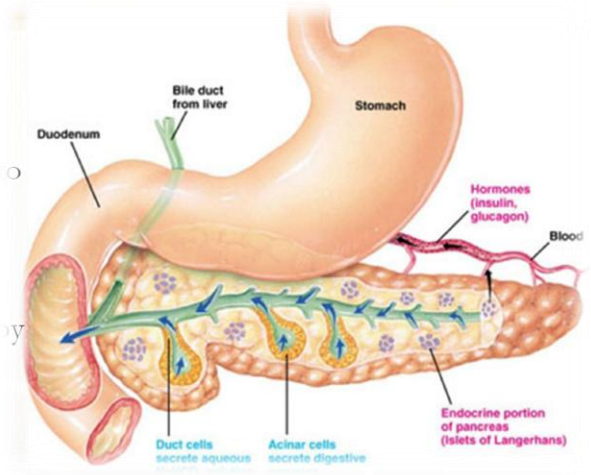
2) Acinar gland tissues which produce pancreatic juice (the main source of digestive enzymes).

The cells lining the acini are serous cells containing zymogen granules.

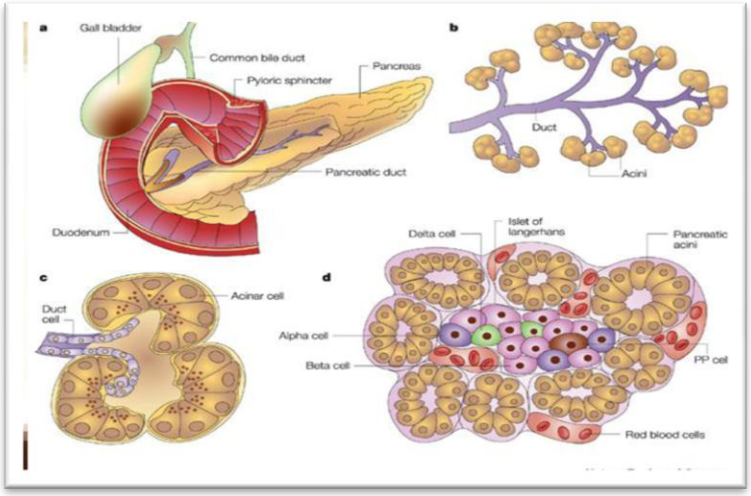


Zymogen granules are the precursors of pancreatic enzymes.

The acini drain into intracalated ducts. These join to form intralobular (striated) ducts which lead to interlobular ducts that drain into the main pancreatic duct.



The main pancreatic duct joins into bile duct at ampulla of vater that is surrounded by sphincter of Oddi.



Pancreas secretion

- Pancreatic juice is secreted in response to the presence of chyme in the upper portions of the small intestine.
- The major functions of pancreatic secretion:
  - To neutralize the acids in the chyme.
  - To produce enzymes involved in the digestion of dietary carbohydrate, fat, and protein.

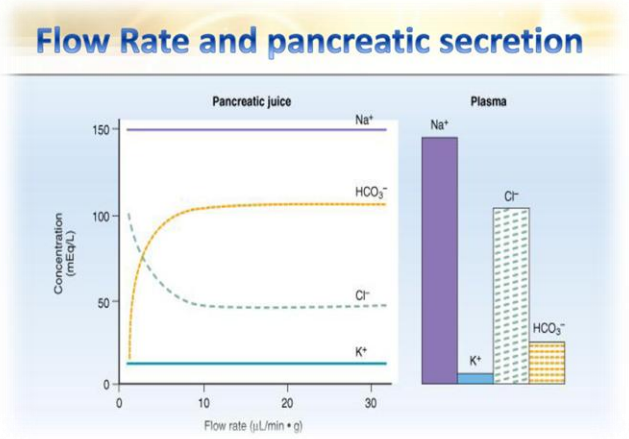
Because it is the main source of HCO3

Pancreas secretion is alkaline.
The neutralization is important for:
- To other enzymes to work in intestine.
- To protect the intestinal mucosa from the acids carried by the chyme.

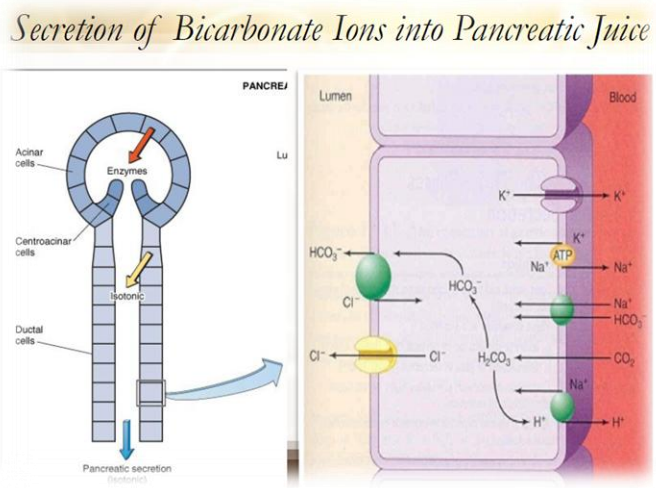
Pancreatic secretion is able to digest all kinds of food: carbohydrates, proteins, fats, DNA and RNA.

Volume: 1.2-1.5 l/day.
The osmolarity of pancreatic fluid is equal to that of plasma (isotonic)
PH = 8 alkaline.
Composition: **In addition to water:** 1 % inorganic materials (electrolytes), 1-2 % organic materials mostly enzymes.
The electrolytes:

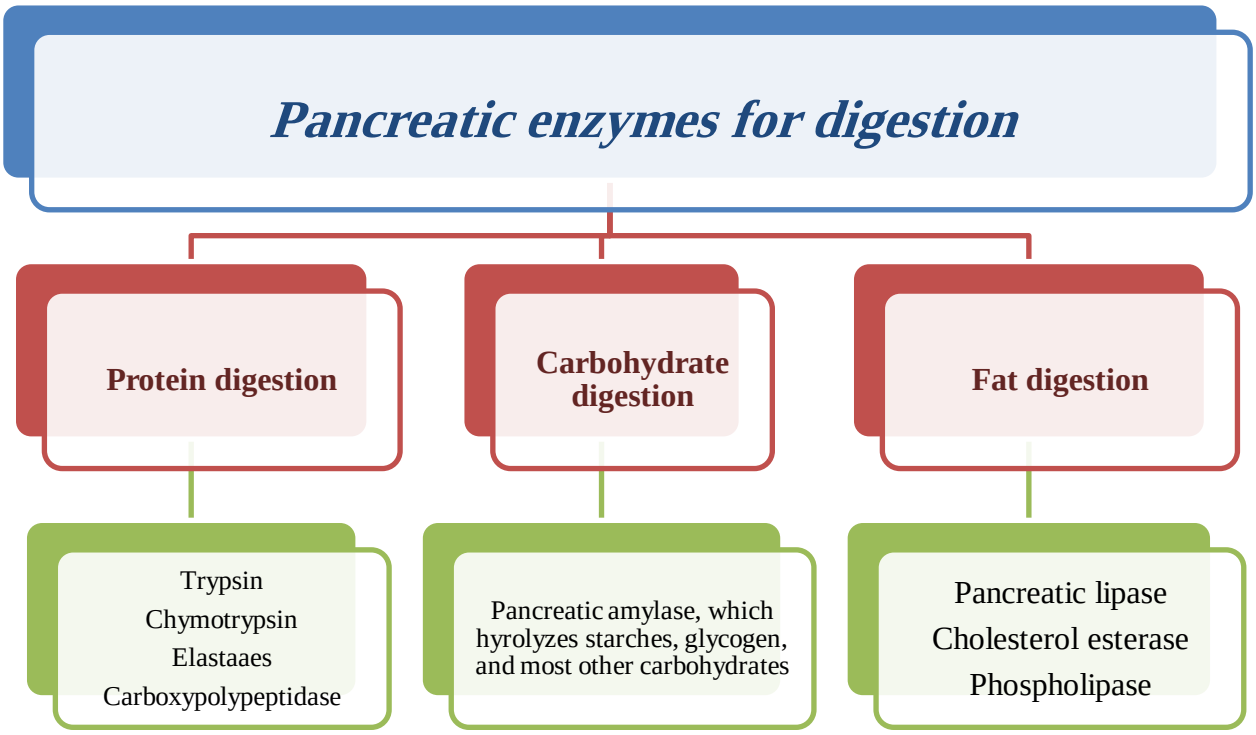
- Are produced from the epithelial cells of the ductules and ducts and include cations Na^+, K^+, Ca^{++} and anions HCO_3^- and Cl^- → HCO_3^- is a characteristic of pancreas secretion, which gives it its alkaline pH.
- The greater bulk of electrolytes is in the form of $NaHCO_3$.
- HCO3 concentration increases with increasing secretion rate.



With increasing secretion rate ***Na, K unaffected and Cl decrease***



Bicarbonate is secreted by duct cells not by acinar cells in to the lumen, acinar cells secrete the enzymes.

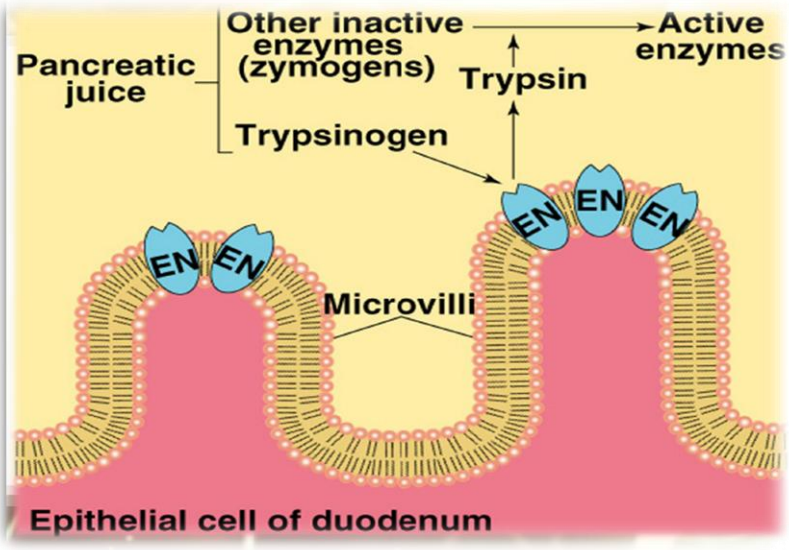


Pancreatic enzymes

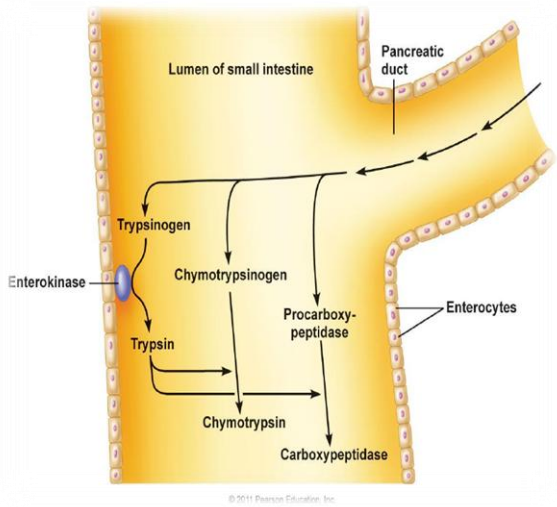
The pancreas secrets enzymes that act on all major types of food stuffs.

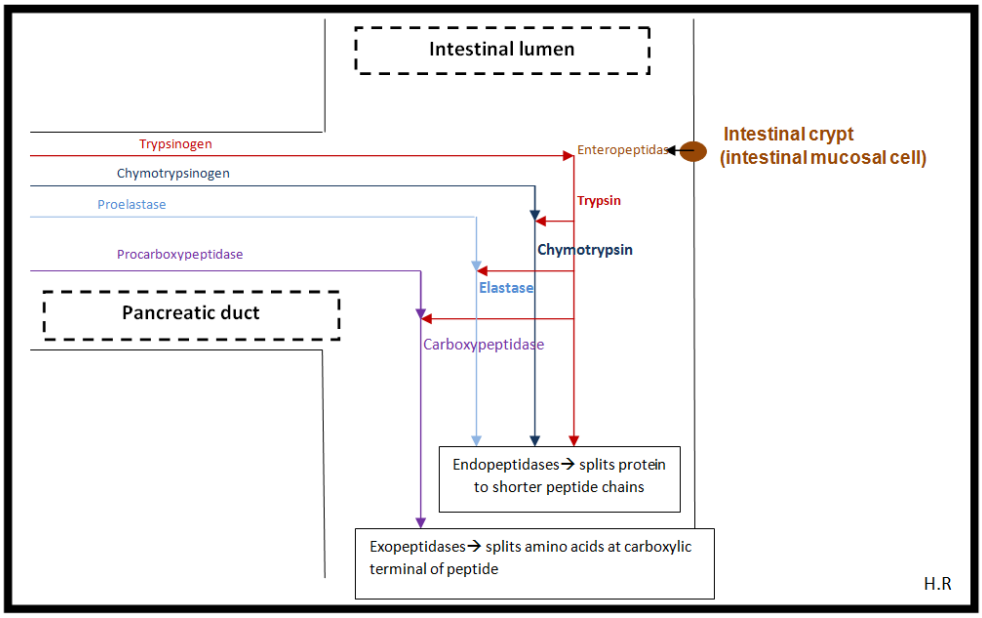
1- Pancreatic proteolytic enzymes (proteases)

- Trypsin, chymotrypsin, elastase, carboxypeptidase.
- They are secreted in inactive form and activated in intestinal lumen.
  → If it is active, it could auto digest the pancreatic tissue.
- Trypsinogen is activated into trypsin by the enzyme enteropeptidase (enterokinase), secreted by duodenal mucosal cells.



- Trypsin activates chymotrypsinogen to chymotrypsin, proelastase to elastase and procarboxypeptidase into carboxypeptidase.
- Trypsin, chymotrypsin and elastase are endopeptidases, splitting protein into shorter peptide chains.
- Carboxypeptidase is an exopeptidase which splits off amino acids at the carboxyl terminus of the peptide.
- Trypsin inhibitor is present in cytoplasm of glandular cells. It inhibits activation of trypsin in acini and ducts of the pancreas. → Protection of pancreas tissue (since trypsin is proteolytic it could digest pancreas which is basically protein).





Endopeptidases: are proteolytic peptidases that break peptide bonds of non-terminal amino acids (i.e. within the molecule).

Exopeptidases: are proteolytic peptidases that break peptide bonds of terminal amino acids (i.e. within the molecule).

2- Pancreatic amylase

Splits starch to maltose, maltotriose and dextrin.

It is more important than the one in saliva cause it stays for longer duration in intestine.

3- Enzymes for fat digestion

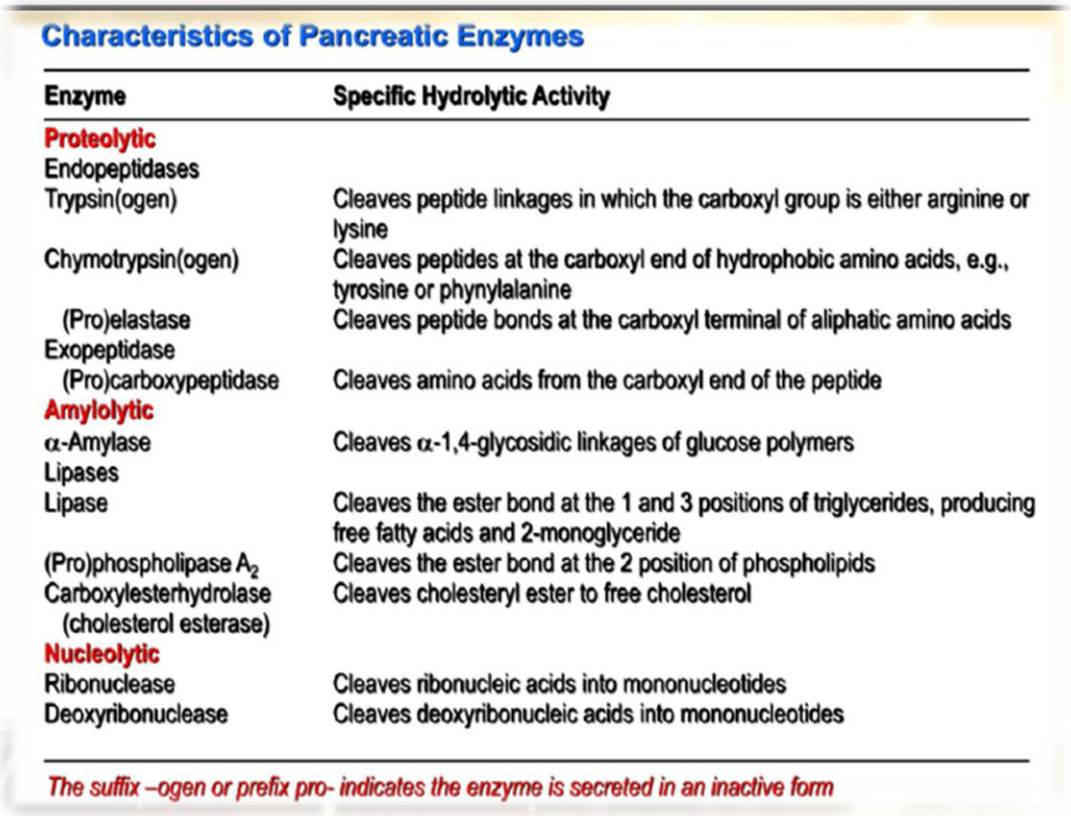
a. Pancreatic lipase is the most important fat splitting enzyme. It breaks TG into MG and FA in the presence of bile salts and colipase.
b. Cholesterol esterase which liberates cholesterol in addition to fatty acids from cholesterol esters.
c. Phospholipase A2 which splits phospholipids into lysophospholipids & FA.

TG= Triglyceride.

Mg= Monoglyceride

FA= Fatty Acids

4- Nucleolytic enzyme: digest DNA and RNA to mono nucleotides.



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

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Pancreatic secretion is under neural and hormonal control

It is regulated by neurohormonal mechanisms. Hormonal regulation is the most important. It includes three phases

1. Cephalic phase:

- it is stimulated by presence of food in the mouth and/ or psychic stimulation. It is mediated by gastrin hormone and vagus nerve through non-conditioned and conditioned reflexes. Vagus nerve stimulates secretion of pancreatic juice with enzymes forming greater portion.

Phases of Pancreatic secretion

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

2. Gastric phase:

- When food reaches stomach, it activates both neural and hormonal mechanisms.

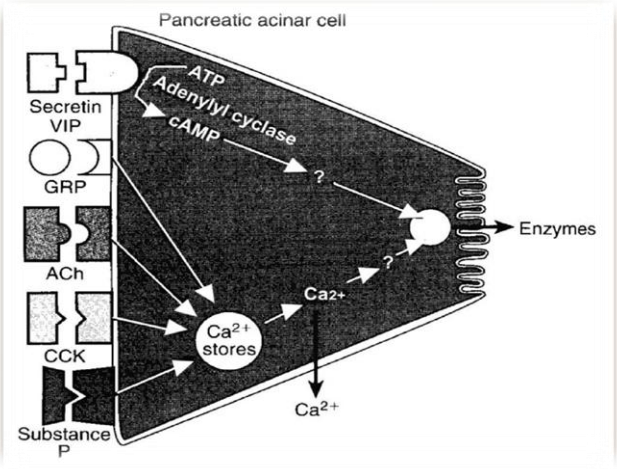
- Gastric distension stimulates pancreas through long vagovagal reflex and local gastropancreatic reflex.

- Gastrin is released from antrum by distension and presence of peptides and amino acids bathing the antral lumen.

3. Intestinal phase:

-it is stimulated by the presence of chyme in the intestines due to presence of fatty asids.
- It is the main phase of pancreatic secretion; it is mainly mediated by two hormones released from the upper intestine, secretin and cholecystokinin-pancreozymin (CCK).

- 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.
- Cholecystokinin (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).



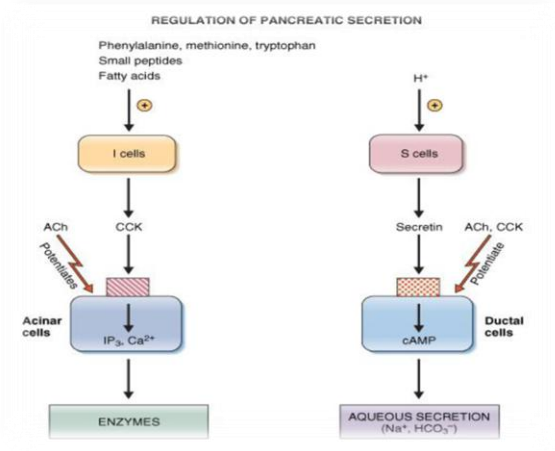
Secretin hormone

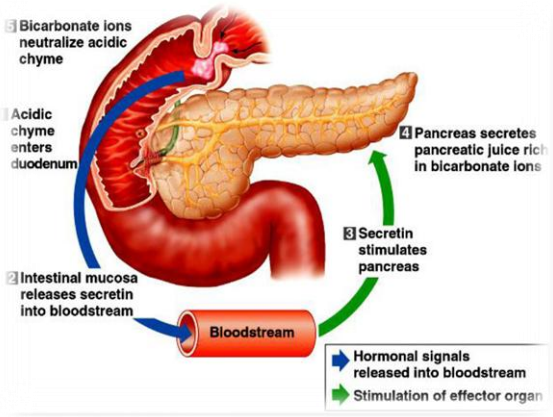
- It is a peptide released into the blood from S cells in upper intestinal mucosa.
- Stimuli for its release: Mainly acids (pH 4 or less) and to a less extent AA and FA.
- Functions:
    - It acts on pancreatic duct cells to stimulate secretion of HCO_3^- and H_2O.
    - It acts on biliary duct cells to stimulate hepatic bile flow and HCO_3^- secretion.
    - It augments the action of CCK in stimulating pancreatic enzyme secretion.

AA= Amino Acids

LES= Lower esophageal sphincter

- It inhibits gastric acid secretion and gastrin release, but it stimulates pepsin secretion.
- It inhibits gastric motility, contracts pylorus and slows gastric emptying.
- It relaxes LES.
- It inhibits intestinal motility and contracts ileocecal sphincter (like sympathetic).

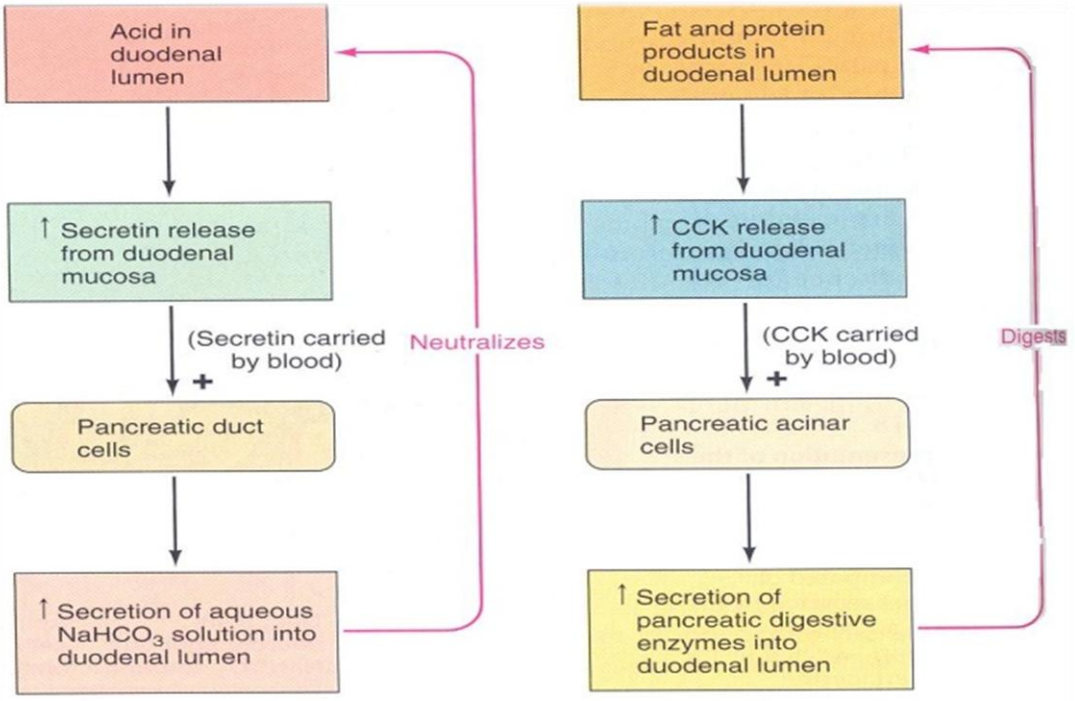




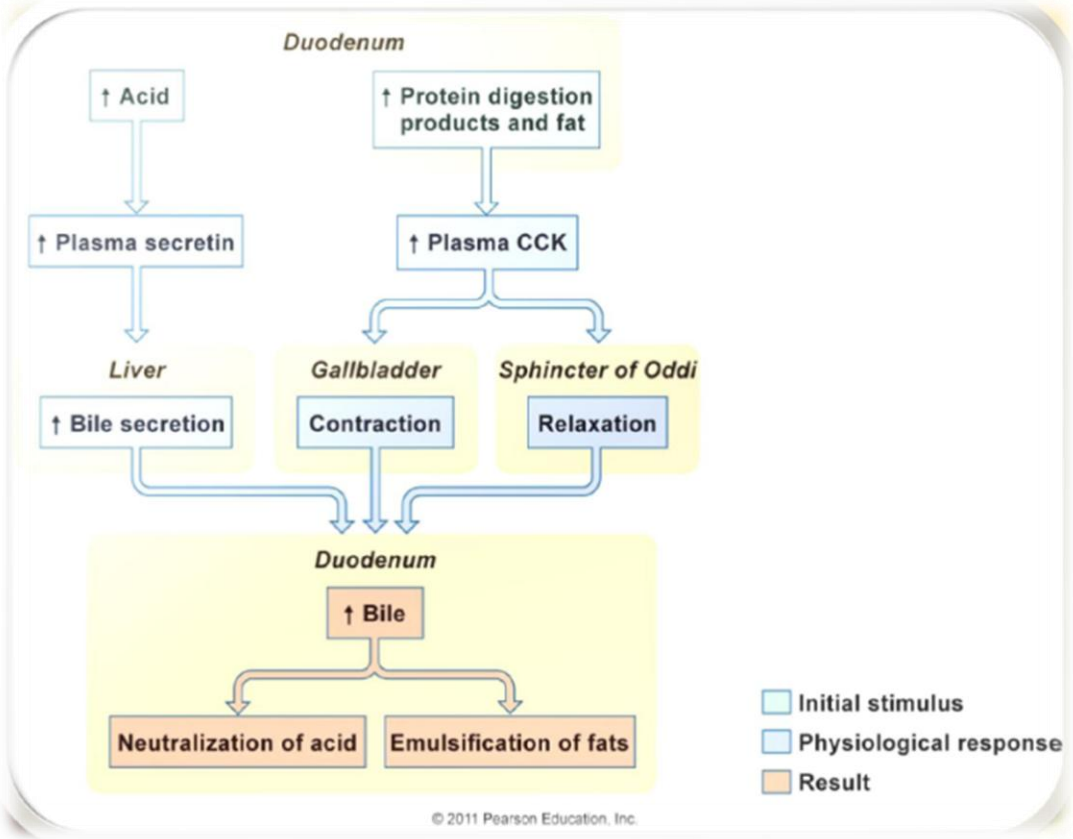
Cholecystokinin (CCK)

- It is a peptide released from I cells in the upper intestine.
- Stimuli of release:- Mainly by AA and FA and to a lesser extent by HCl.
- Functions :
  - It acts on pancreatic acinar cells to stimulate enzyme secretion. It also augments stimulation of H_2O and HCO_3^- secretion by secretin.
  - It has trophic effect on pancreas.
  - It contracts gall bladder, relaxes sphincter of Oddi and causes discharge of bile into the intestine.
  - It stimulates gastric motility, contracts pylorus thus slows gastric emptying.
  - It relaxes LES.
  - It stimulates intestinal motility.
  - It may be concerned with the mechanism of satiety (the feeling of being full after eating).

Since Secretin and CCK are hormones they are secreted in the blood and circulate the body and when they reach the intestine they work stimulate acinar and duct cells to produce secretion with specific characteristic + vagal regulation.



Hormonal control of pancreatic exocrine secretion



Hormone	Secretin	Cholycystokinin
Cells of secretion	S cells→ Secretin cells in the intistinal mucosa(upper intistine)	I cells in the upper intestine
Site of releas	Duodenum and upper juojenum	the upper part of intestine
Stimuli (the thing that stimulie the secretion of the hormone)	Presence of acidity from the chyme	Mainly by AA and FA and to a lesser extent by HCl
Action	Acts on pancreatic duct cells (secretion full of HCO_3^-)	Acts on pancreatic acini (secretion full of enzymes)
Factors potentiate its action	Ach + CCK	Secretin hormone