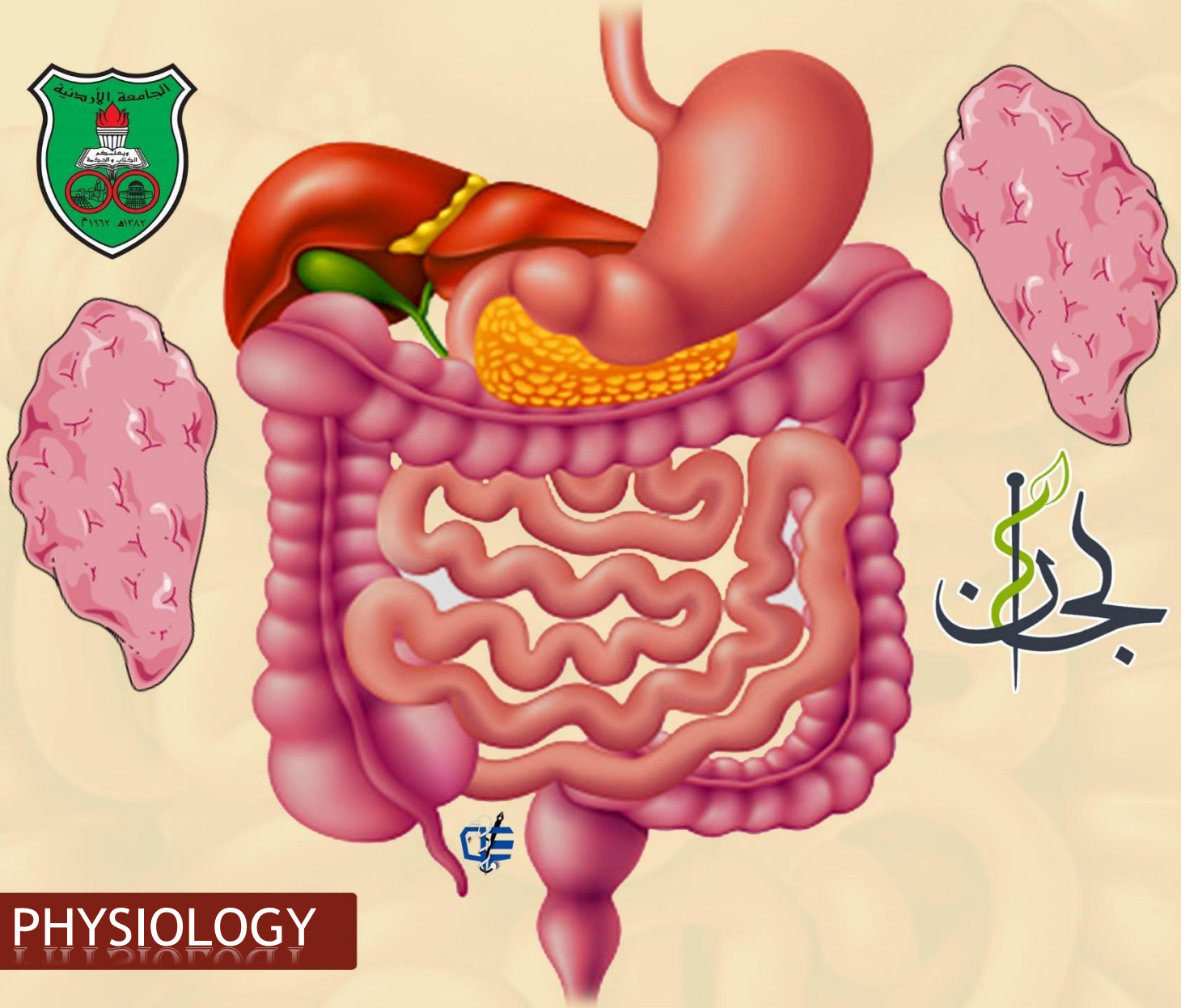
GastroIntestinal System



PHYSIOLOGY

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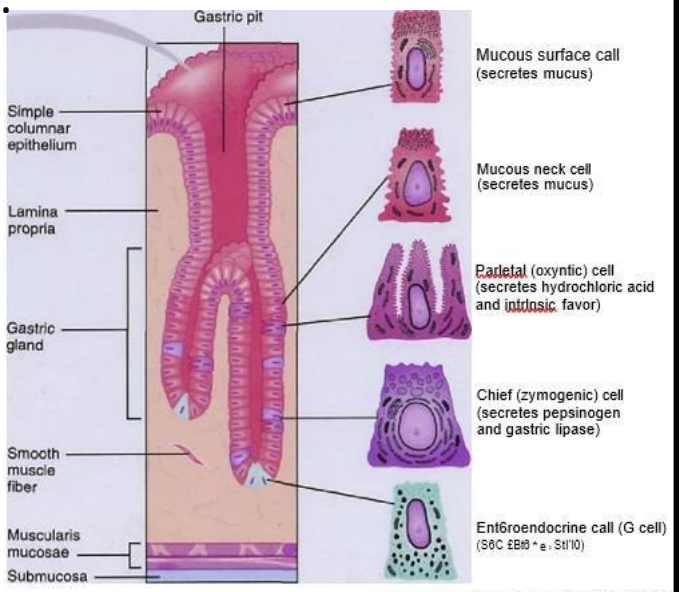
(the first part of the sheet is revision)

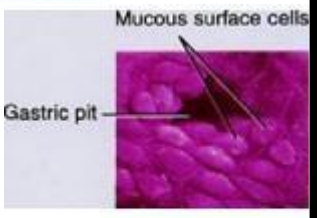
So yesterday we started talking about gastric secretions ,we said that we have pits at the level of gastric mucosa which are called gastric pits/glands and sometimes called oxyntic gland, and these glands are having many types of secretory cells as shown in the figure below .



1- **Mucus surface cell**: secretes mucus andis located at the surface of the gastric mucosa.

2- **Mucus neck cell:** secretes mucus and is located at the neck of the gastric mucosa.

3- **Parietal (oxyntic) cell:** secretes hydrochloric acid and intrinsic favor. The luminal membrane of these cells is invaginated toward the nucleus forming what we are calling **canaliculi**. Once we talkabout secretions of these cells in the canaliculi (the space formed by the membrane invagination) which is connected to the lumen of the gland, which in turn connected to the lumen of the stomach .



Scanning slnctron micro9rapIn of a gastric pil (about 1000s)

4- **Chief (zymogenic-peptic) cell:** secretes pepsinogen (which is the inactive form of pepsin and the pepsin is important in the digestion of proteins)

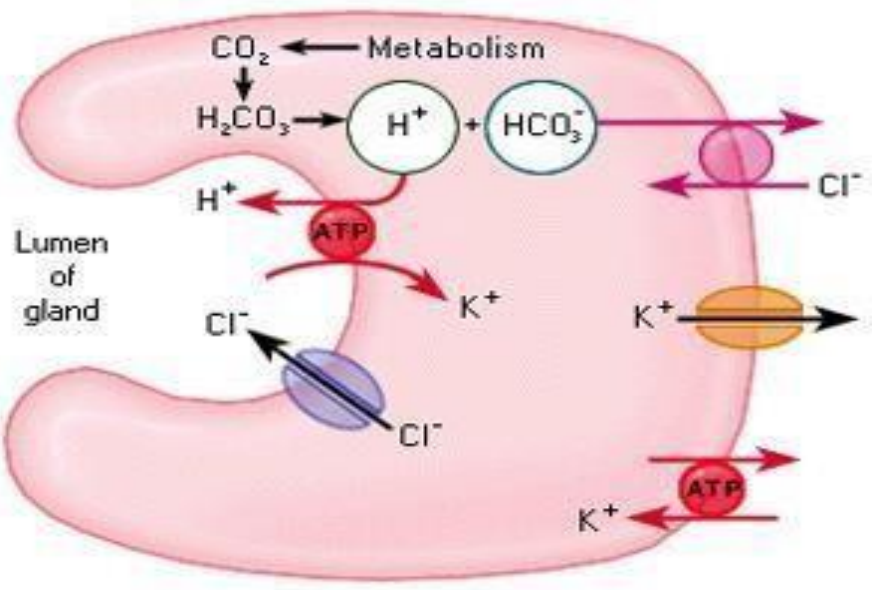
5- **Enteroendocrine call (G cell):** at the bottom of the gland and this is an example of endocrine cells which are called G cells and these cells are specialized in secretion of gastrin hormone .

Ok we have talked about the function of oxyntic cells as you see down below we said we have secretion of hydrochloric acid HCL by these cells.

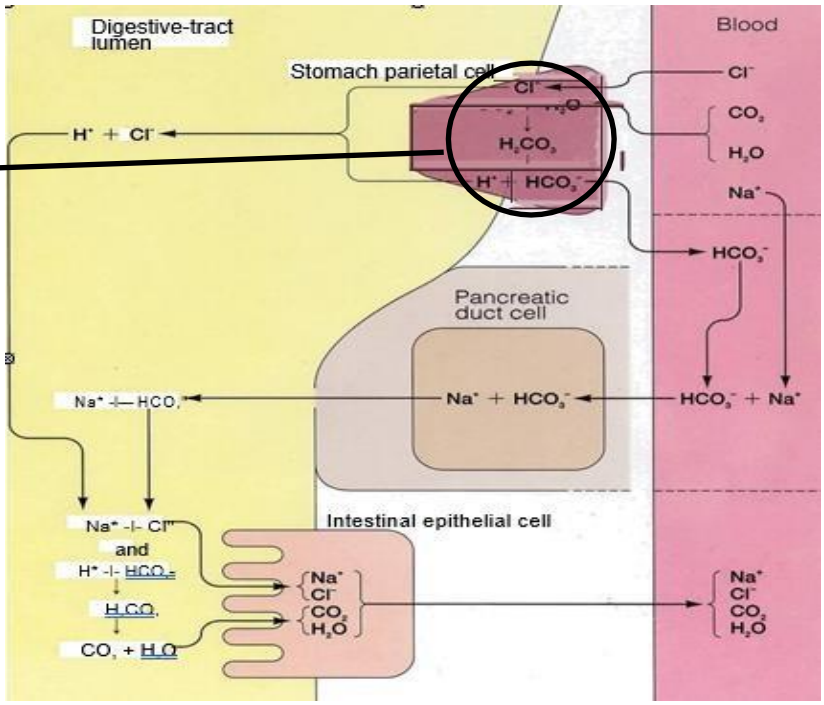
How are we performing the secretion of hydrochloric acid ?

Simply we have active transport of chloride which is almost all the time to increase chloride concentration into canaliculi. Now to get secretion of proton we need to stimulate these cells, upon stimulation we are activating an enzyme called carbonic anhydrase this enzyme takes CO2 with H2O to form carbonic acid (H2CO3) then the H2CO3 can dissociate into proton H which is now available for the secretion and also bicarbonate ion HCO3 which can be reabsorbed back into the interstitial fluid and then toward the blood, while the H is pumped into canaliculi by the activity of hydrogen potassium pumps these pumps are also called proton pumps because they are pumping H toward canaliculi, now once you have pumped the H the hydrochloric acid will be secreted like we said this happens with stimulation.

If we have no stimulation for these cells so we have secreted chloride and this secretion of Cl will generate potential across the whole secretory cell which is called trans cellular potential and that trans cellular potential is attracting sodium ion from the interstitial fluid toward the canaliculi so the quality of the secretion if we have no stimulation is more like toward the sodium chloride but upon stimulation we have secretion of hydrochloric acid .

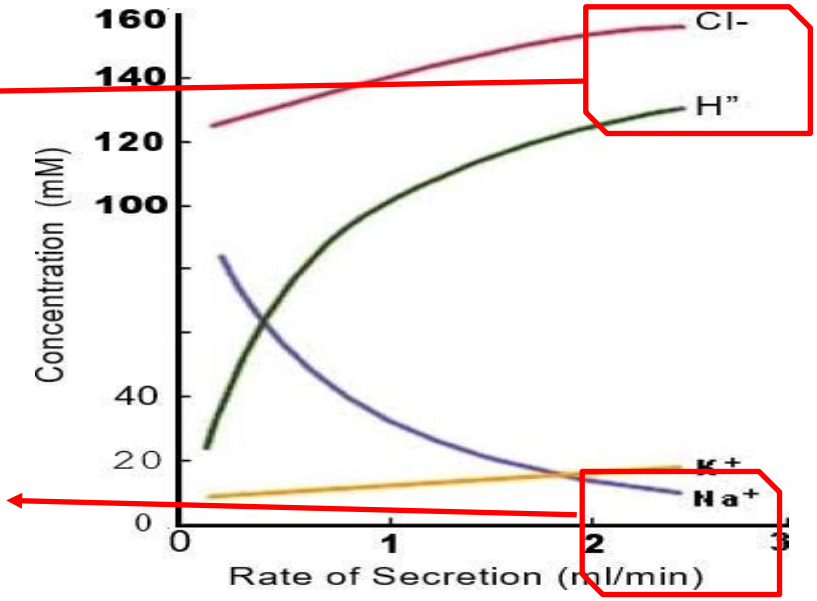


this slide is showing you the function of oxyntic cells how the carbonic acid is being formed and we said we are getting dissociation of that carbonic acid into protons and bicarbonate these protons are pumped toward the canaliculi and that increases proton secretion upon stimulation .

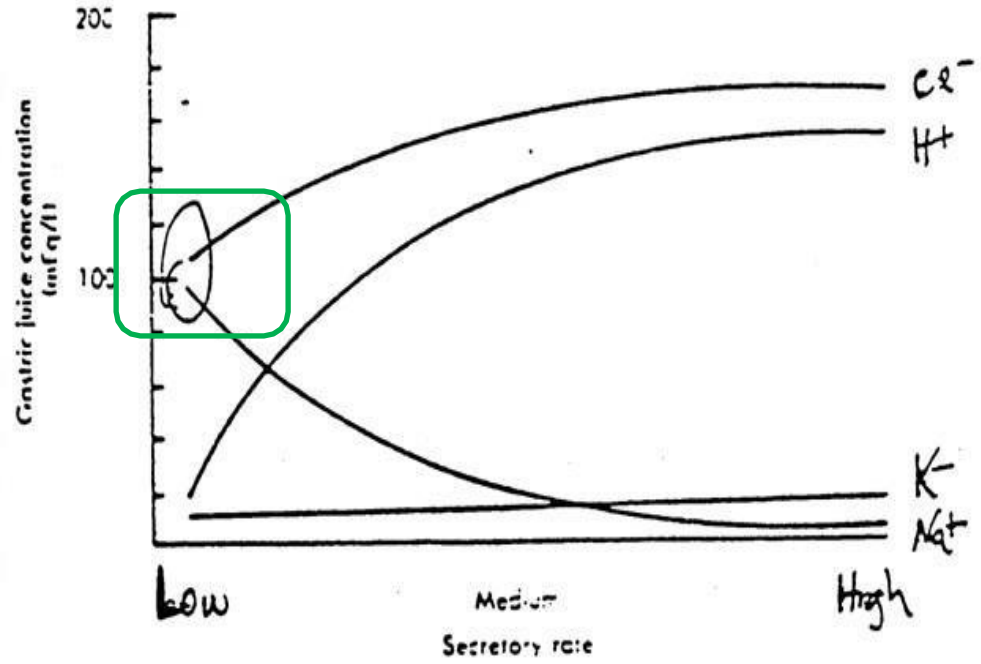


So as we can see here the quality of secretion upon stimulation is mostly hydrochloric acid.

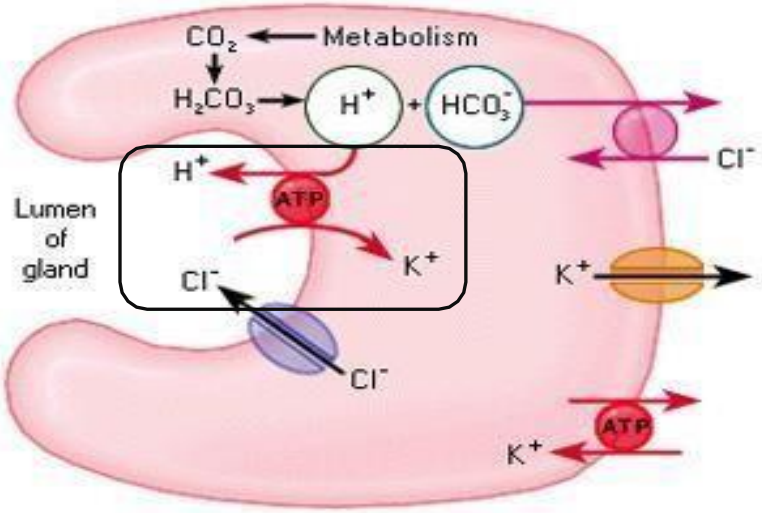
If we are at low rate of secretion we have low stimulation or no stimulation for these cells and the quality of secretion is more like sodium chloride which is a protective mechanism.



as you see here this is sodium chloride which is secreted mainly when we are at low rate of secretion and we have hydrochloric acid when we are at high rate of secretion .



now retaining back to proton pump there are some drugs that inhibit this pump which are called proton pump inhibitors, so if we are inhibiting the activity of these pumps we are decreasing the secretion of protons toward the canaliculi and these drugs could be useful to treat some types of ulcers mainly duodenum ulcer which can be generated by increasing hydrochloric acid secretion .



FUNCTIONS OF HCL

we have also talked about the functions of HCL we said it is important in the conversion of pepsinogen to pepsin which is the active form of that enzyme also

- it helps in dissolving eaten food .

- can help in the decomposition of the connective tissue .

- has defense mechanism because of the decrease of the PH that happens at the level of the stomach by the release of hydrochloric acid and most bacteria cant resist that low PH so they are killed and that could be a contribution of hydrochloric acid in defense mechanism .

Secretion of pepsinogen

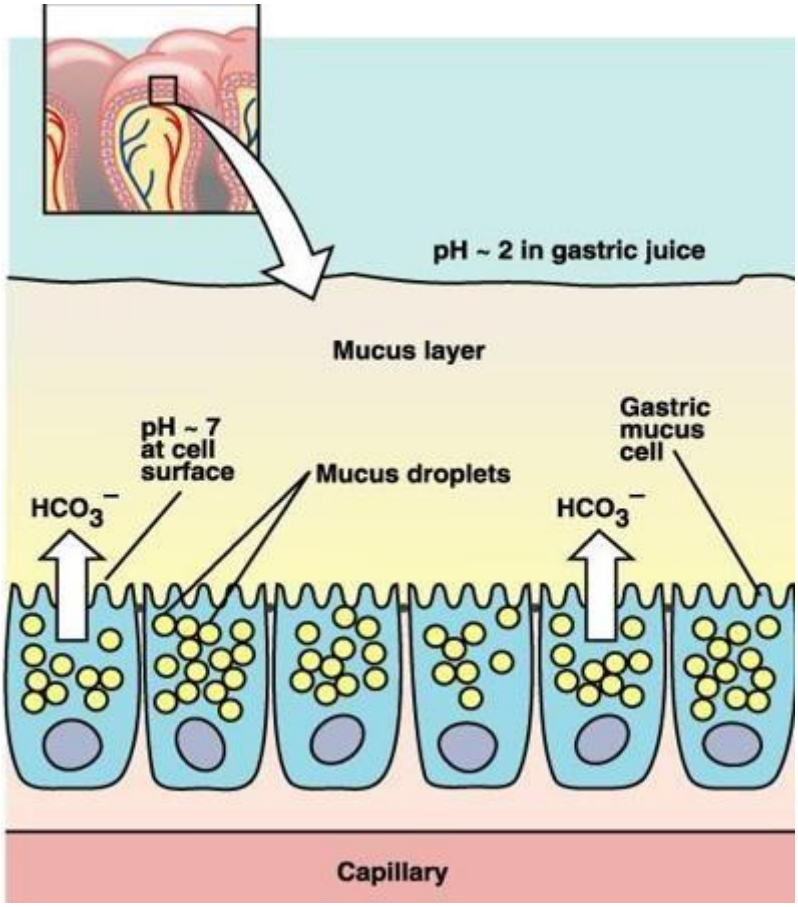
- now we will talk about the secretion of pepsinogen. We said there are specialized cells for secretion of pepsinogen which are called chief cells (peptic, zymogenic). Mucos cells also secret pepsinogen but the main cell for that purpose is chief cells

- the optimal activity for that enzyme (pepsinogen) when activated is at the acidic PH (1.8-3.5) this PH range is available in the stomach by the secretion of hydrochloric acid

- pepsin (active form of pepsinogen) cleaves the peptide linkages between amino acids and by having these peptides cleaved we are getting the protein content which is digested into smaller fragments so the long fragments became smaller fragments , at that level we are not having the final digestion of proteins rather we are just starting the digestion of proteins so, the function of that enzyme is to start the digestion process

Mucus secreting cells

also we have talked about cells that are releasing mucus. Now we have plenty of mucus secretion at the level of the stomach as you see here that's the lumen of the stomach by having high amounts of mucus release we are forming like a barrier which separates the lumen of the stomach from tissue .



why do we need that separation?

this huge amount of mucus secreted have a protective role of the gastric mucosa so we are protecting that mucosa.

What is the PH of that mucus ?

this mucus has a PH which is almost neutral toward alkaline .

-now once you have alkaline content of that mucus at any time proton ions try to diffuse toward tissue that will be neutralized by alkaline media of the mucus so, it has a big protective roll for the gastric mucosa by getting huge amount of secretion which is released

- some gastric ulcers are related to the decreased secretion of mucus this decrease may result in invasion of the protons for ex from the lumen and the digestive enzymes also like the pepsin and start to destroy the surface of the mucosa of the cell **so, these are the functions of mucus secreting cells:-**

1-lubricating functions

2-protect the mucosa from any chemical injury by:

a-preventing the activity of the proteolytic enzymes to act directly on the mucosa

b-neutralizing HCL by its alkaline character : the alkaline character of that mucuscan be involved in neutralization of protons that are trying to diffuse toward the mucosa

Gastrin secretion

We said we have also G cells which are at the level of these glands and the function of these cells is to produce gastrin hormone and this hormone has a big role in controlling the secretion

-it can increase the secretion of HCL so it can stimulate the parietal cells and the chief cells to secret pepsinogen

-trophic effect on gastric mucosa to maintain growth of mucosal cells : so that gastrin has a trophic effect over the gastric mucosa

Whats the meaning of trophic effect ?

It is keeping yhe survival of the gastric mucosa much longer time so maintaing the growth and keeping the integrity of the mucosa by the secretion of gastrin

How G cells are stimulated to secrete gastrin?

simply by:-

-gastric distention: simply by local changes like gastric distention

-presence of protein(food) in chyme

-vagal stimulation : by parasympathetic stimulation we can get an increase in the gastric secretion .

Secretion of intrinsic factor

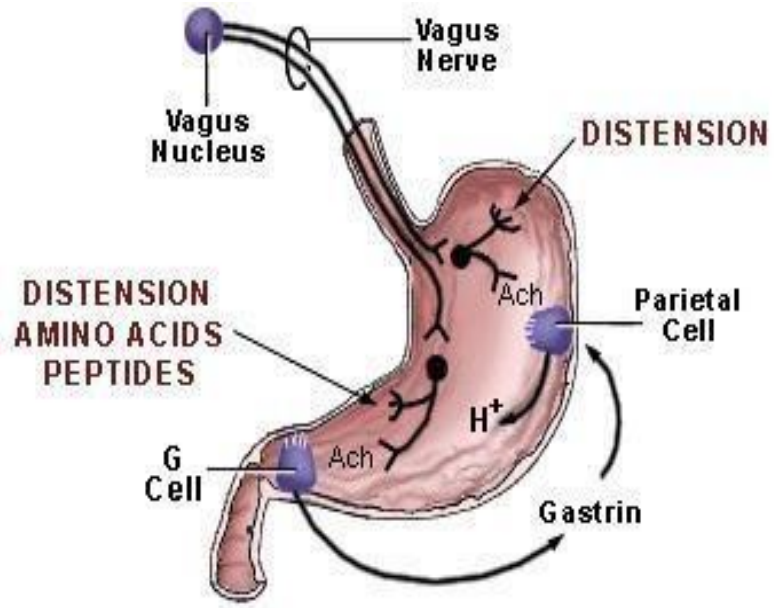
-is secreted by parietal cells (oxyntic cells)

-essential in absorption of vitamin B12 at the level of small intestine so most anemias related to vitamin B12 deficiency Is mainly related to gastric problems

like gastric atrophy in this case once a person is suffering from gastric atrophy or atrophy of gastric mucosa they have less release of intrinsic factor and these people are subjected to develop vitamin B12 deficiency anemia so that's the relation between gastric problems and vitamin B12 deficiency anemias

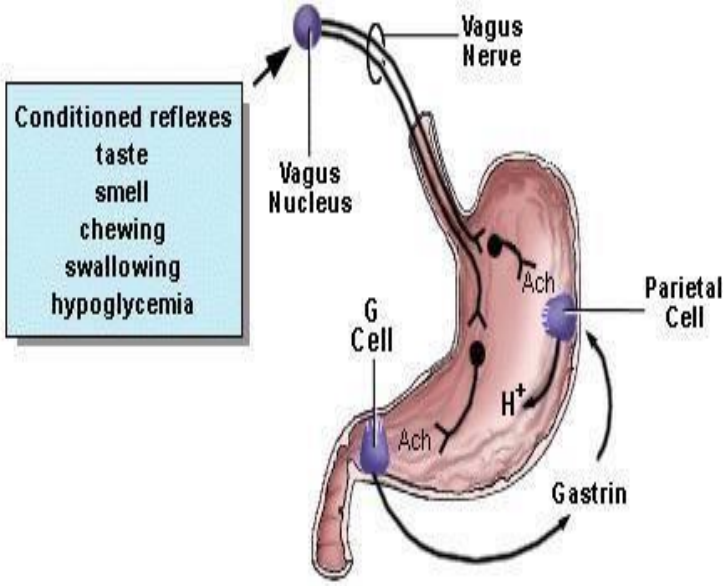
Control of gastric secretion

1- enteric nerves system: The gastric secretion is very well controlled I think you know we have neural control which is achieved by **enteric nerves system**



-some of the enteric neurons secret Ach which acts over parietal and peptic cells to increase their secretion

2-ANS: also as neural control we have **ANS** can be involved the parasympathetic increasing gastric activity via long reflex by vagus stimulation , you know vagus nerve has high number of fibers which are parasympathetic fibers from cranial origin



-the neural control by the ASN can be directly and it can also be indirectly by activation of enteric neurons that are releasing Ach again, also by activation of some enteric neurons which can activate interochromaffin like cells and these cells are specialized in the release of histamine and you will see the role of histamine and the roll of interochromaphin

like cells in the paracrine control later on and we will talk about hormonal control also

3-hormonal control enteric neurons that release GRP which refers to Gastrin releasing peptide so from its name it can act upon G cells to cause the release of gastrin so, the ENS can be involved in the **hormonal control** represented by the release of gastrin and gastrin can act upon parietal cells to increase HCL

-this gastrin can act through receptor CCK-B so once we have gastrin binding to that receptor we are increasing the secretion by the oxyntic cell so we have an increase in HCL secretion

-once you have high release CCK you will see CCK is released later on by the duodenum mucosa mainly that if we have high concentration or high release of CCK it can bind to CCK-B receptor and prevent gastrin to bind to that receptor

-once CCK binds to CCK-B receptor and prevents the gastrin from binding to this receptor we will have decreased stomach activity or we have reduced the effect of gastrin on the stomach .

4-paracrine control:

a-histamine

which is achieved by the release of **histamine** which is secreted by enterochromaffin like cells these cells are acting on H2 receptors(histamine receptors type 2) on parietal cells resulting in increasing cAMP and then increasing HCL.

- regarding H2 receptors there are some drugs called H2 blockers which block H2 receptors and inhibit activation of of parietal cells which is normally activated by histamines secreted by enterochromaffin like cells .

b- somatostatin (SS)

-we also have in paracrine control some involvement by somatostatin which is a hormone which is released by some cells and acting in paracrine control.

-What is paracrine control and whats the difference between paracrine and endocrine control?

the secretions of endocrine go into the blood but the paracrine is between cells .

-so we have local release of somatostatin(SS) toward interstitial fluid that SS is acting over parietal cells which are inclosed proximity of the releasing cells causing inhibition of HCL secretion by parietal or oxyntic cells

-so that effect of SS makes it able to be involved in paracrine control rather than the endocrine control because it is released from some cells at the level of gastric mucosa and acting on near cells which are releasing HCL .

5-Role of HCL in controlling secretion:

-achieved by the HCL itself

-once we have released high amounts of HCL that HCL is acting to decrease the HCL secretion so activating some reflexes to decrease that secretion

How does it happen?

Like the negative feedback mechanism to reduce gastric secretion which happens in two ways:

1-reduction of gastric reflexes: reducing the release of gastrin.

2-initiation of inhibitory reflexes: inhibition reflexes which inhibit gastric secretion.

-and these mechanisms are important in maintaining the PH and preventing it from falling bellow 3 and to be around 2-3 not more or less than that.

Summary of control

1-the cephalic phase:

- getting the stimulus from the head , once we see food or talk about food that will cause long reflexes from ANS by parasympathetic nervous system which activates the gastric activity .

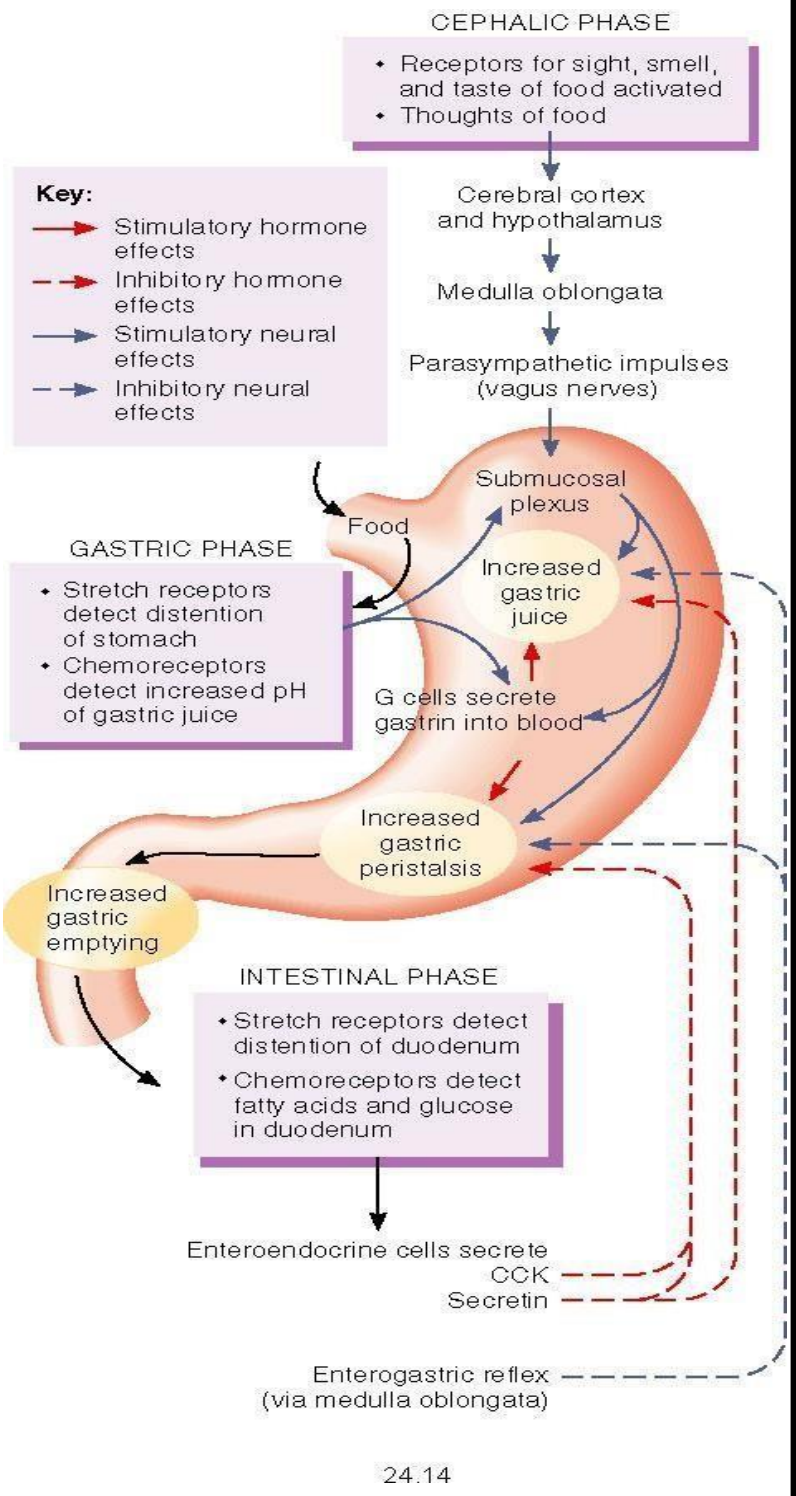
2-gastric phase :

-once the food is ingested reaching the stomach this will cause distention of the stomach causing local changes in addition the presence of proteins in chyme and presence of other types of food can activate gastric activity by activation of enteric neurons and ANS additionally we have release of gastrin which is involved in the activation process

3-intestinal phase :

- when the gastric content is reaching the duodenum we have some hormones which are released from duodenal mucosa like CCK, secretin both of them acting on the stomach to reduce gastric secretion.

- also some inhibitory reflexes are activated like enterogastric reflex which is a long reflex through the medulla that means we are inhibiting the parasympathetic stimulation toward the stomach and in this case during intestinal phase the gastric activity is inhibited



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-in some literatures regard to the intestinal phase they say in the beginning of that phase we can get some excitation of the gastric activity and this is achieved by having some G cells also located in the upper part of the duodenum so these G cells are releasing more gastrin that can activate the gastric activity but the bulk of the intestinal phase is inhibitory to inhibit the gastric activity .

Intestinal secretion:(secretion)

there are some releasing cells :-

enteroendocrine cells (endocrine cells): that are releasing for example, cholecystokinin, gastric inhibitory cells (GIP)

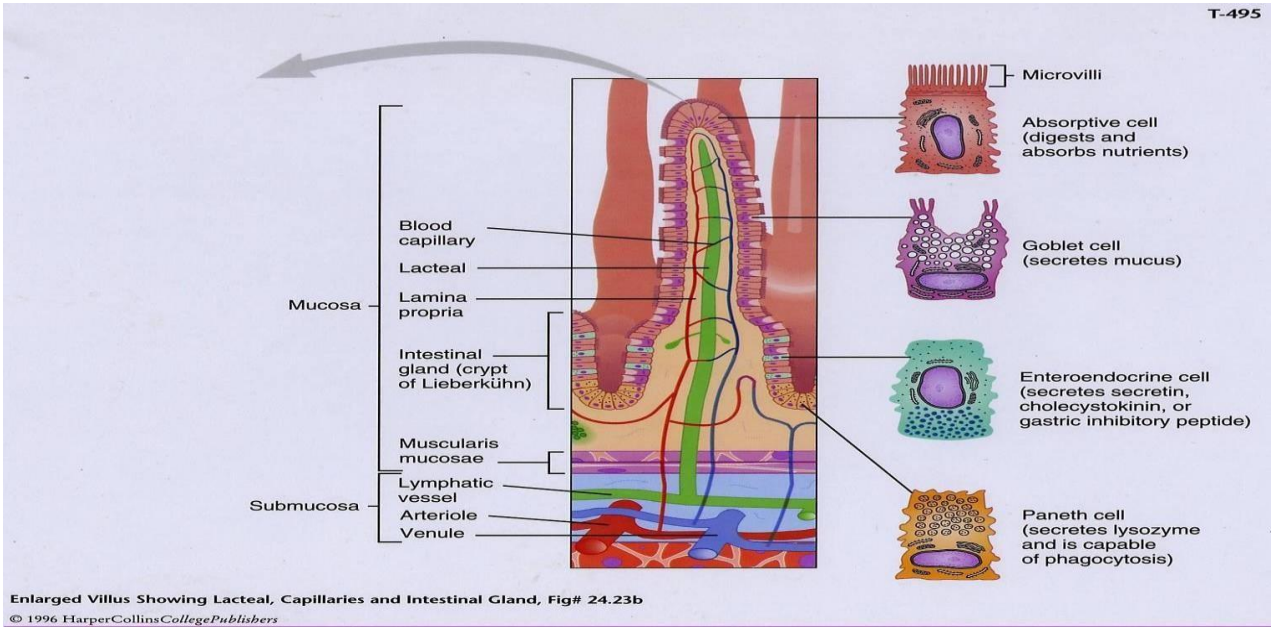
goblet cells: mucus

Paneth cells: lysozymes

Microvilli :- absorption

- **But the bulk of secretion by the small intestine is serous secretion (mainly water and electrolytes)**

  Serous secretion is very important for creating media alkaline solution so it is rich with the bicarbonate content that are very important for neutralizing acids which had been evacuated from the stomach toward the small intestine.



Regulation of small intestine secretion

1-Neural mechanism :- by autonomic nervous system and enteric nervous system(ach and VIP neurotransmitters **)** **VIP=vasoactive intestinal peptide**

VIP cause vasodilation and by this we have a plenty of fluid to increase secretion

2-Hormonal:- mainly by secretin which activate secretory cell to increase secretion (increases duodenal secretion).

Colonic secretion:

the bulk of secretion is mucus secretion (we can have some serous secretion which is high k and small hco3)

Most of their secretion is mucus secretion to protect the mucosa from the fecal content which is becoming less fluid (more solid).

Pancreas secretion

Has two parts:

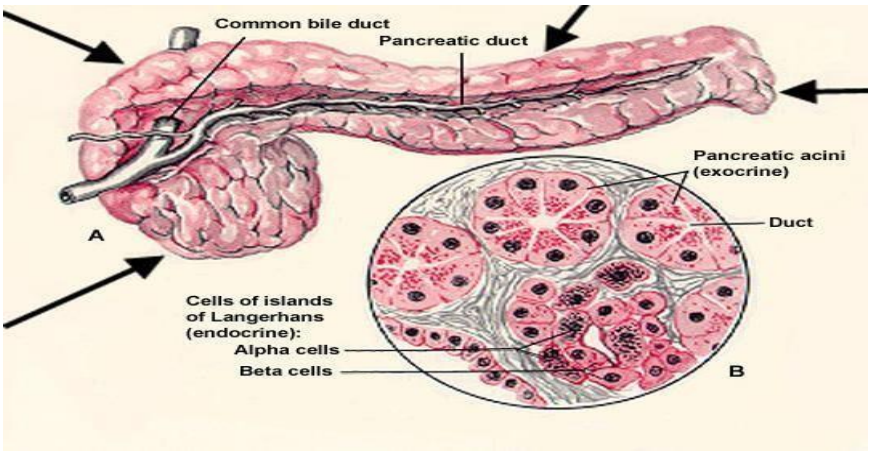
- **Endocrine part**: secrete hormones into the bloodstream through which they travel to affect distant organs (cells of island of Langerhans).

- **Exocrine part:** Pertaining to the secretion of a substance out through a duct.

Exocrine portion

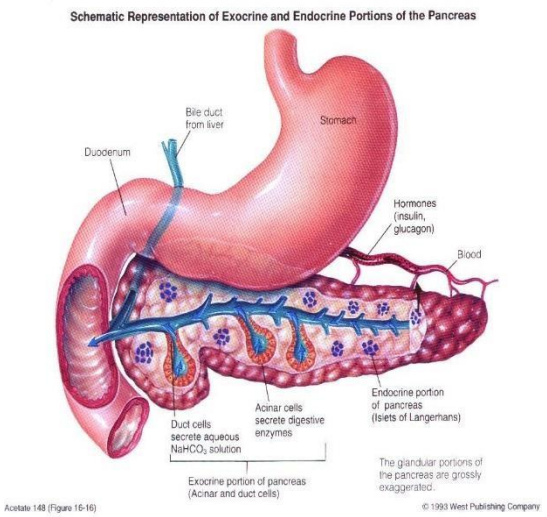
Enzymes secretion by acinar cells(which are forming the parenchyme of the

Pancereas , Water and bicarbonate are secreted by duct cells (cells lining The duct).

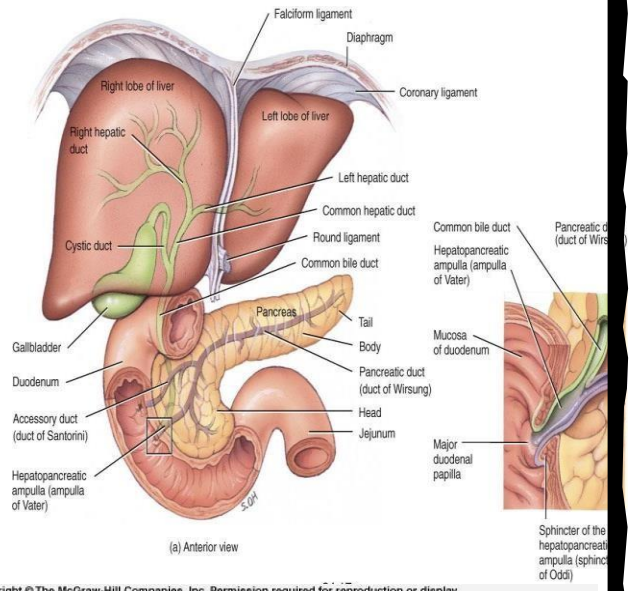


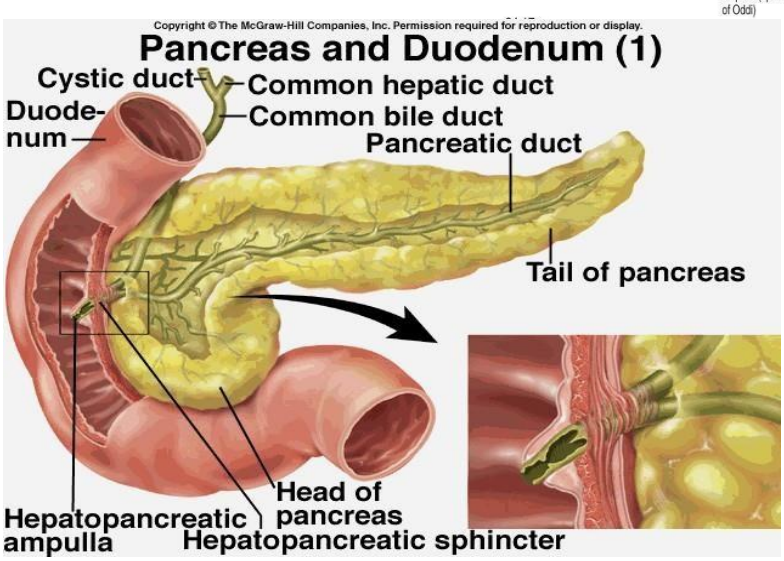
About this picture :-

Pancreatic juice moves in the pancreatic duct toward duodenum but before reaching it, we have another duct which is coming from the liver and its called hepatic duct and by unifying together we will have Hepatopancreatic duct.



The opening of hepatopancreatic duct to the duodenum throw a structure which is called ampulla of battle and it is guarded by a sphincter which is called oddi sphincter and this sphincter prevent reflux of duodenal content back to the duct (powerful circular layer that prevent the reflux).





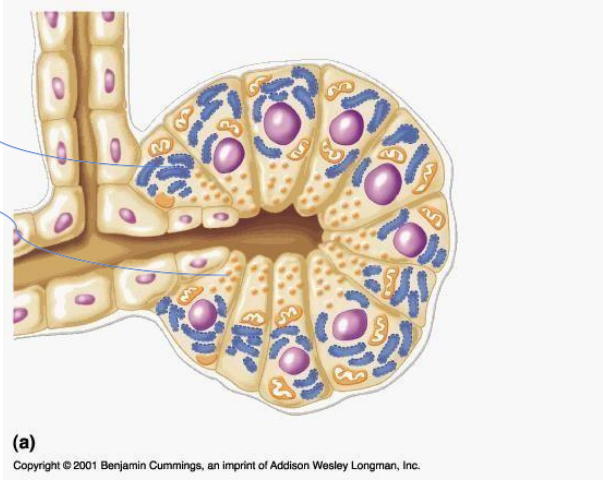
enzyme secretion by acinar cells

too much endoplasmic content

more vesicles during secretion

-acinar cells are releasing **proteolytic enzymes** in the inactive form and it gets activated in the small intestine..

and these enzymes(**proteolytic enzymes)** are:-



Trypsinogen : activated by **enterokinase** from the duodenum acts as endopeptidase. As long as this enzyme is in pancreas remains inactive by trypsin inhibitor
Chemotrypsinogen :activated by trypsin and act as endopeptidase then we will have **Chemotrypsin**
Procarboxypeptidase: activated by trypsin and acts as an exopeptidase then we will have **carboxypeptidase**

Pancreatic amylase:- (get secreted by acinar cells and can be realesed as active form because it is not harmful)

secreted as active enzyme to convert Starch (polysaccharide) →disaccharides

Lipolytic enzymes:- (get secreted by acinar cells / some of the books say that it is secreted as inactive and some says active)

Lipase that split Triglycerides → monglyceride + free fatty acids. Their activity requires an oil/water interface, bilesalts (secreted by liver) and other co-lipase secreted by the pancreas.

Phospholipase.

Cholesterol ester hydroxylase.

-Proteolytic enzyme couldn't be released as active form because it will digest the proteins of the pancreas itself …the oddi sphincter prevent any reflux from the duodenum back toward the duct system of pancreas. and if we have a reflux of trypsin back we will activate **Chemotrypsinogen** and **Procarboxypeptidase to its active form** and destroying the pancreas system by autodigestion (by medical condition if happens) /- weakness in the sphincter

- And the reflux from the duodenum

And by this it can develop acute pancreatitis and die within six hours (**that can happen by alcohol intoxication)**

Bicarbonate can get to lumen by 2 cells

1-Stomach parietal cell (oxyntic cells)

2-pancreatic duct cells (In some books

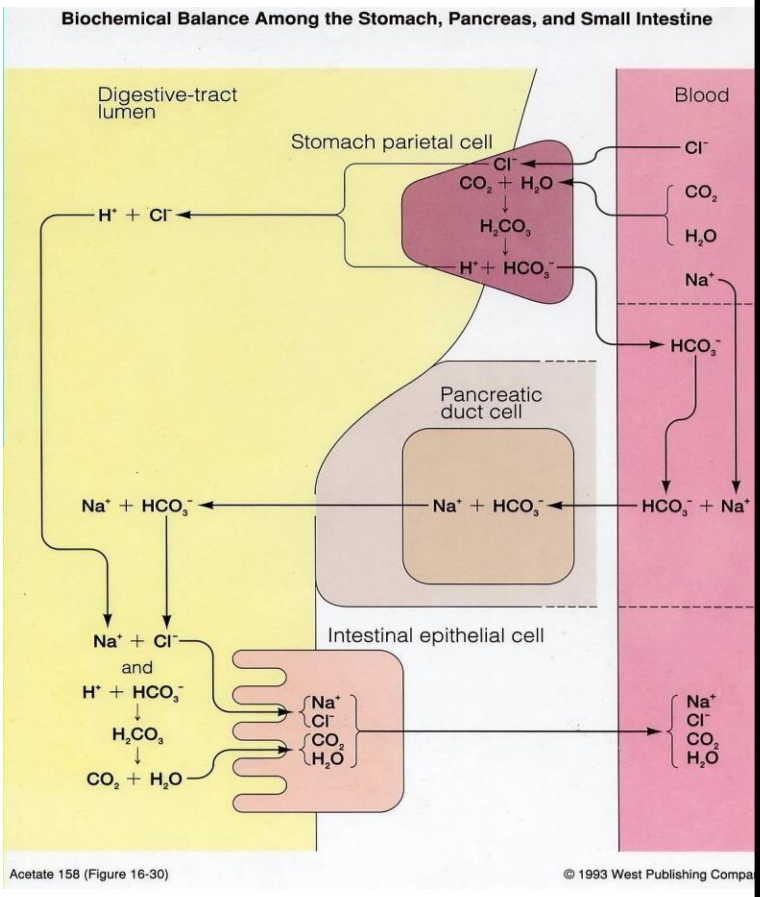
The function of duct cells is to release water and bicarbonate content its mechanism same to **oxyntic cells.**

We have Carbonic anhydrase (hco3)

An enzyme (CA) is involved in catalyzing the reaction Carbonic Anhydrase (CA) transported at the luminal border by secondary active transport in exchange with Cl-.

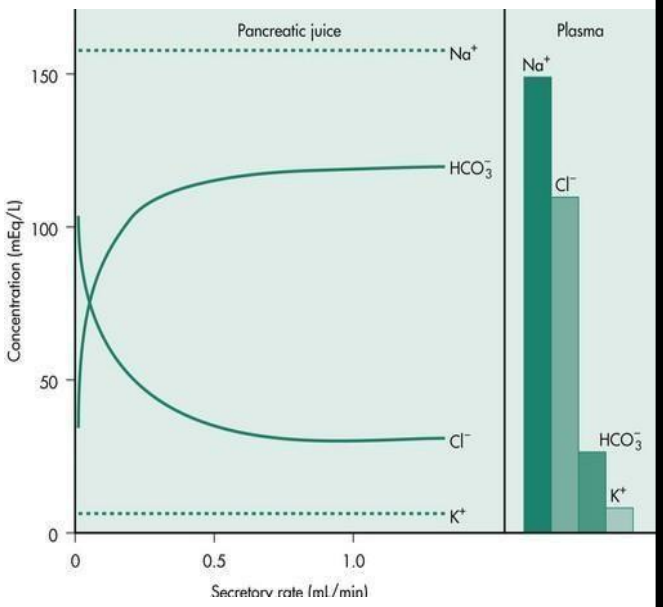
H+ is transported by a secondary active transport in exchange with Na+ at blood border.

Na+ is transported from the cell by an active transport



$H_2O + CO_2 \lozenge H_2CO_3 \leftrightarrow H^+ + HCO_3^-$ (carbonic anhydrase equation)

Regarding to this picture:



-At low rate of stimulation we have low Bicarbonate content and high cl- content

And at rate level of stimulation we have high Bicarbonate and low cl- content

When we are getting secretion of bicarbonate We are getting sodium into the lumen this Will create a potential (transcellular potential)

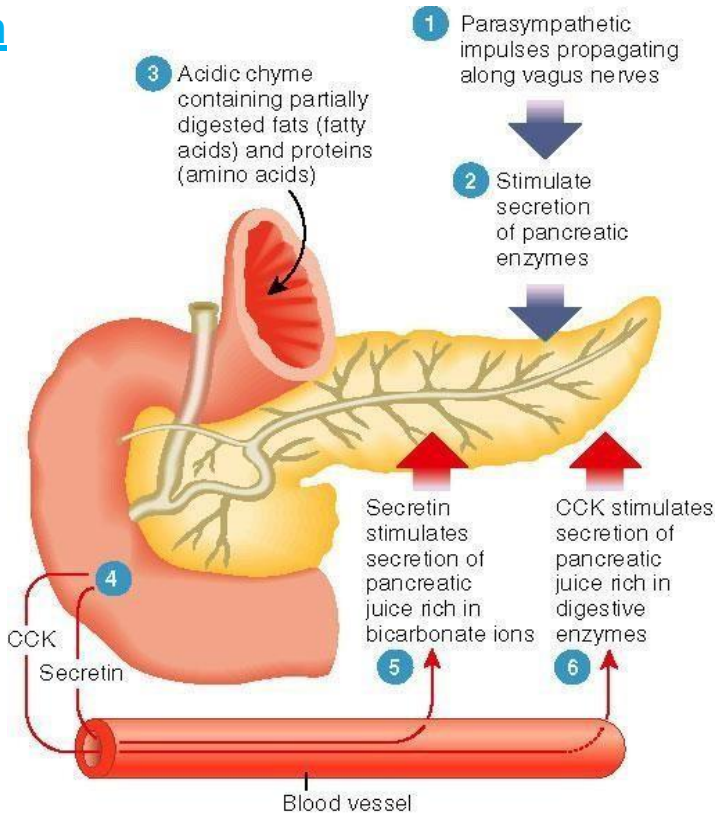
-The presence of sodium (Na) in the lumen at Low rate of stimulation attract more chloride (cl-) toward the lumen but at high rate of stimulation when we have released more bicarbonate we have decreased that potential, since the bicarbonate is negatively charged particles so we have reduced the transcellular potential across the whole cells , the attraction of chloride to sodium becoming less and getting less chloride moving to the lumen

control of pancreatic secretion

1-neural: mainly by parasympathetic system and it could be some contribution of enteric nervous system fibers

2-hormonal : by two hormones

Firstly by cholecystokinin (CCK) secreted by duodenal mucosa and this hormone has receptors over the acinar cells which are called cholecystokinin a receptors and by activation of these receptors we have a release of enzymes by acinar cells



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And vago-vagal reflex to stimulate enzyme secretions and by that this will stimulate parasympathetic control to the pancreas

Secondly secretin is controlling the duct cells so its involved in the control of electrolytes and water secretion

T**he neural control …again** ☹

parasympathetic:

Vagal stimulation enteric nervous system release of Ach, VIP, and GRP (Gastrin releasingpeptide).

Sympathetic: indirect inhibition via vasoconstriction

Pancreatic polypeptide: inhibits the release of enzymes by its inhibitory effect

Inhibits Ach release from enteric nervous system
(inhibiting parasympathetic control)

Inhibits vagal output of the CNS
(inhibiting parasympathetic control of pancreas)

AND ITS DONE :D