physiology

faculty of medicine - JU2017

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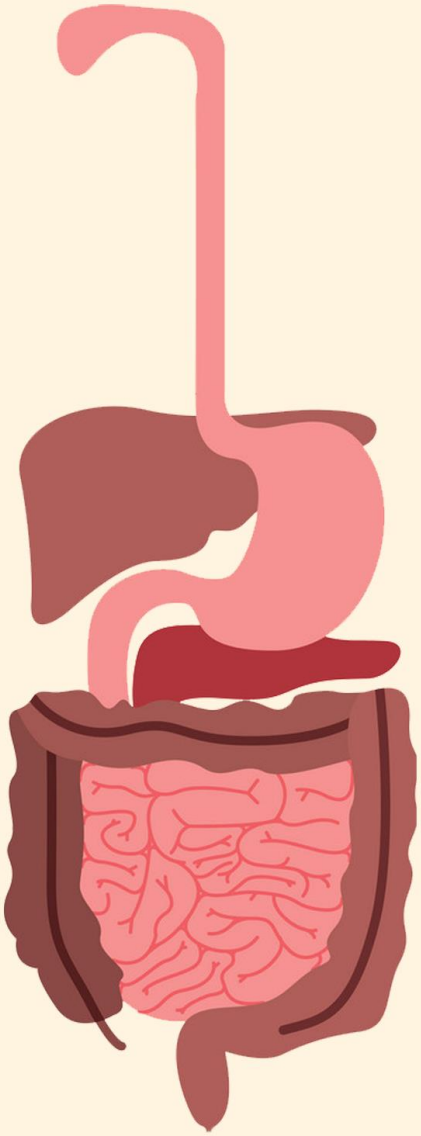
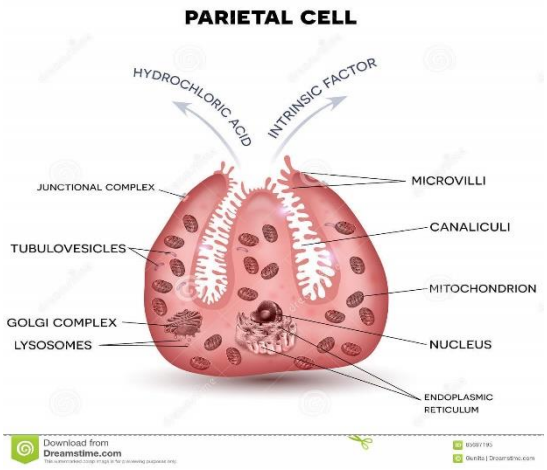


2nd system - GI

In the previous lecture we talked about salivary, esophageal secretion and started with gastric secretions. Today we will continue taking about cells in the **GASTRIC PITS** (simple glands)

- ## Oxyntic cells (parietal)



These cells are found in the gastric mucosa and their function is to release **HCL** and **intrinsic factor** (which is responsible for vitamin b12 absorption).

What's specific about these cells is that their apical membrane (the luminal membrane) is invaginated towards the nucleus forming a structure called **canaliculi**, these **canaliculi** are connected to the lumen of the gland which is connected to the lumen of the stomach.

secretions go from the cell to these canaliculi and the then to lumen of the gland and finally to the gastric lumen.

How HCL is secreted ?

The general idea is that we have to release **1)chloride (CL-)** and **2) protons (H+)**

1) We have active mechanism for secretion of CL-, so CL- is secreted into canaliculi,

By increasing CL- there, polarity becomes more negative with regard to the extra cellular fluid, by that we are creating transcellular potential (more negative toward canaliculi) not transmembranous potential.

You can consider the whole cells as one membrane.

The whole cell separates the two regions

In the membranous potential, the membrane separates

This potential will attract positively charged particles from interstitial fluid, mainly Na+ because of its high concentration in the extracellular fluid.

2) For the protons: -

Stimulated process will form carbonic acid (H_2O+CO_2 by carbonic anhydrase)

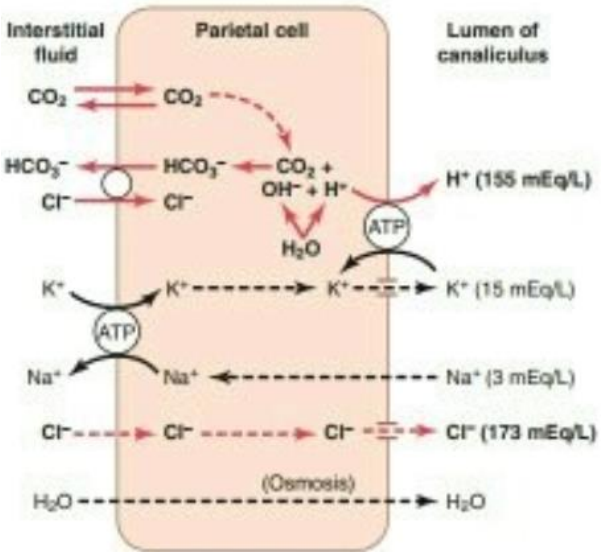
Carbonic acid will dissociate into bicarbonate and protons

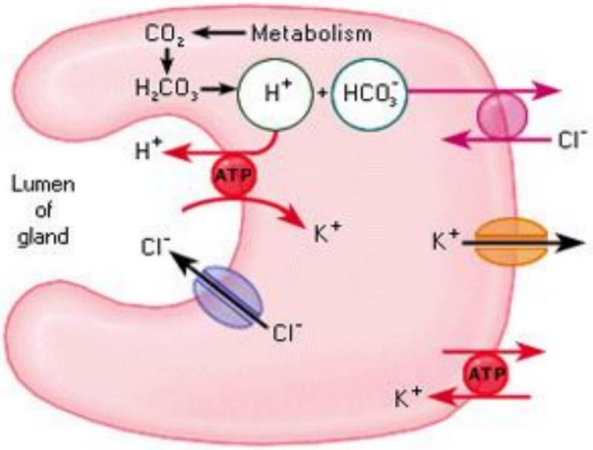
H2O + CO2 → H2CO3 ↔ HCO3- + H+

Bicarbonate is reabsorbed into interstitial fluid and then to blood while protons are moved forcefully (**by pumps**) toward the lumen.

We have 2 types of pumps(active transported, from lower to higher concentration) to pump protons from inside toward the canaliculi
H+ pumps and sodium hydrogen pumps (NA+ H+ pumps)

When H+ is moved, polarity is decreased so less negative potential, this will lead to less attraction of Na+.





Further explanation from the book :- (additional ☺)

Firstly, the parietal cell has two borders:

A-Basolateral border: it is the border that faces the interstitial fluid, it contains Na+/K+ pump and Cl-/HCO3- exchangers.

B-Luminal border: it is the border that faces the lumen of the duct, it contains H+/K+ pump and Cl- channel.

1-CO2 and H2O enter the parietal cell by diffusing through the basolateral border.

2- CO2+H2O—>HCO3- + H+ is catalyzed by carbonic anhydrase inside the parietal cell.

3- At the luminal membrane, H+ is secreted into the lumen via H+/K+ pump.

4-At the basolateral membrane, HCO3- will be absorbed from the parietal cell into the interstitial fluid via Cl-/HCO3- exchanger.

5-Increased concentration of Cl- inside the cell will result in Cl- diffusing to the lumen by Cl- channels in the luminal membrane.

6-HCl will be formed in the lumen.

Remember that releasing H+ which will lead to HCL is **a stimulated process** so content of gastric juice at low rates and high rates is different.

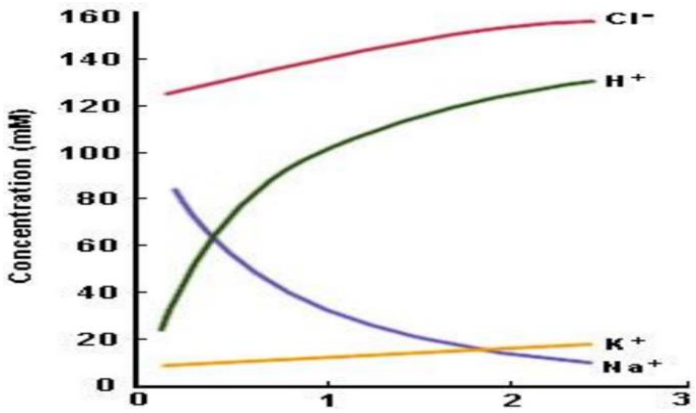
- At low rate of stimulation

We are not secreting high concentration of protons so the mostly content of gastric juice are Na+ and CL-.

- At high rate of stimulation

More protons and less Na+ so more HCL content in the juice.

- Generation of ulcers can be caused by highly secretion of HCL
- Proton pumps can be targeted by some medications called proton pump inhibitors to reduce HCL secretion.



- **Functions of HCl**

1- Conversion of pepsinogen (inactive form) to pepsin (active form) which needs low PH to be active.

2- Provide a media for the activation of enzymes that have an acidic optimum pH.

3- Helps in decomposition of connective tissue (dissolving of some food)

4- Defense role against foodborne microorganisms, since most of them are sensitive (not surviving) to high acidity.

- **Pepsinogen**

The main secretion of pepsinogen is by **peptic(chief) cells**, and a little amount is secreted by **mucus cells** (its main function is secreting mucus).

Its optimum activity is at a low pH(Acidic) so it is working only in the stomach.

Its function is start **digestion of proteins** to become smaller peptides but not full digestion at that level.

- **Mucus**

Mucus is secreted by mucus secreting cells and mucus neck cells, and we get a high secretion of mucus.

Mucus forms a layer over the lumen cells, having a neutral toward alkaline Ph because it is rich in bicarbonate

it serves as a **protector layer** by neutralizing acids that try to diffuse like HCL and deactivate peptic enzymes along with pepsinogen from acting over the epithelium. (some sort of ulcers can develop due to the loss of the protective mucosa. Some drugs like Al(OH)3 they can be taken as fluids to have an extra protection to the mucosa).

Mucus also has some lubricating functions that protect the mucosa against mechanical injuries and facilitate movement of contents.

- **Gastrin**

Released by the G in a stimulated process by gastric distention, presence of proteins in the chyme and parasympathetic stimulation by the vagal nerve.

Its function is to control the release of HCl and pepsinogen secretion

It also has a trophic effect over the gastric mucosa, which means to keep the survival of mucus cells and to maintain their growth.

- ## Intrinsic factor

Released by the oxyntic(parietal) cells and have a role in vitamin b12 absorption in the lower part of the small intestine. (our diet has an efficient amount of b12, but most of the deficiencies are related to intrinsic factor).

Note: A deficiency in the intrinsic factor causes vitB12 deficiency anemia, that's why some people with gastric problems e.g atrophic gastritis (less intrinsic factor thus less vit B12 absorbed) are having anemia.

- ## Control of gastric secretion

Gastric secretions are well controlled by various mechanisms.

1-neural control :

A-Enteric nervous system : can control by direct stimulation of parietal cells and peptic cells. The effect is mediated by Ach.

B-Autonomic nervous system by

- -Direct effect: like the enteric fibres, these fibres release acetylcholine
- -Indirect effect: Parasympathetic: vagal activation during cephalic and gastric phases (via long arc reflex) activate enteric neurons that release different types of neurotransmitters :

→enteric excitatory neurons to release Ach.

→enteric neurons that innervate enterochromaffin-like cells in the stomach to secrete Histamine which is involved in control.

→enteric neurons that secrete GRP (gastrin releasing peptide) that acts on G cells to cause secretion of Gastrin.

2-Hormonal control

Gastrin has an effect over the parietal cells (oxyntic) increasing HCl secretion. Gastrin receptor on oxyntic cells is CCK-B(CholeCystoKinin-B) receptor that increases HCl, this receptor can also bind to cholecystokinin causing much less secretion of HCl (preventing the effect of gastrin, inhibitory effect. This is achieved in the intestinal phase, when we have empty the content of the stomach).

**The inhibition here is partially not completely, because cholecystokinin also has an effect in the secretion of HCl, but much less than effect of Gastrin.

3-Paracrine control

A- Histamine that is released by Enterochromaffin-like cells binds to H2 receptors (histamine 2) increasing cAMP causing an increase in HCl secretion. (H2 blockers are effective in treating ulcers by decreasing HCl secretion, these drugs have no effect over the histamine in the respiratory system, which has H1 receptors).

B- Somatostatin (SS) is another paracrine signal that has receptors on the oxyntic cells, when binds to its receptor causes decrease in cAMP which leads to decrease in HCl secretion.

Note: We can treat ulcers by blocking proton pumps, mucosal protective agents and blocking H2 receptors.

4-HCl role on control

Excess acid secretion initiate systems that decrease further secretion of acids, this is a normal control to maintain the PH from falling below 2. This effect is achieved by two ways:

A- Reduction of gastrin release.

B- Initiation of inhibitory reflexes to inhibit gastric secretion.

Phases of control of gastric secretions

1- Cephalic phase: stimuli before food reaches the stomach by thinking about food or seeing it, controlled by parasympathetic nervous system.

2-Gastric phase: Acts when food reaches the stomach to cause maximal stimulation of gastric secretions. Distension and the presence of proteins in food stimulates local reflexes and long reflexes which results in increased gastric secretion. Caffeine and alcohol also stimulate acid secretions even no food is present in the stomach.

3- Intestinal phase: after emptying chyme in the duodenum there will be an inhibitory effect of gastric secretions by enterogastric reflexes, higher CCK(cholecytokinen), GIP and secretin release, all of them can inhibit gastric secretions. But some researches are talking about a little excitatory effect at the beginning of this phase, because the upper part of the duodenum has G cells responsible for gastrin release. But it's still considered to have an inhibitory effect.

Intestinal secretions

Most of the secretions are serous, but there are some cells, goblet cells, having a mucus secretion, and also we can find endocrine cells that secrete cholecystokinin, GIP and secretin. In addition, we have absorptive cells. This all what we need to know about type of intestinal cells.

The amount of secretion is 1500ml/day, and tubular cells called (crypts of leiberkuhn) are responsible for serous secretions.

This process is regulated by:

A- Neural control: having neurons that release Ach and VIP (vasoactive intestinal polypeptide that is for vasodilatation). Once you have vasodilation you have more secretion from the glands.

B- Hormonal control: by secretin which is released in response to the high acidity of the chyme, secretin increases duodenal secretions and HCO_3^- to neutralize the acidity.

Colonic secretions

Mostly mucus secretion with a small amount of serous secretions which is rich in K^+ and HCO_3^-

Good luck.