Digestive System

University of Jordan

Faculty of Medicine

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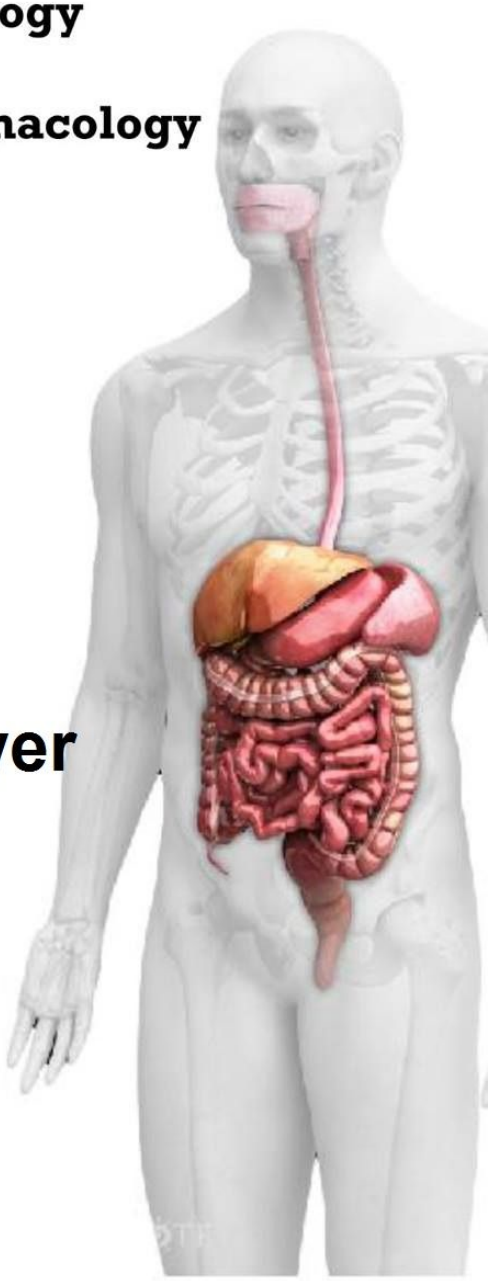

Sheet #: 5

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GI physiology

Secretion

- Gastric secretions:

Types of gastric secretory cells:

1. Mucous secreting cells. (On the surface or in the neck of the gland)
2. Parietal (oxyntic) cells. (Secretes HCL and intrinsic factor)
3. Chief (also called peptic or zymogenic) cells. (Secretes pepsinogen and gastric lipase)
4. Enteroendocrine cells (G cells). (Secretes gastrin)

Oxyntic Cells:

- We will start with the oxyntic cells. We said the luminal membrane of these cells is invigorated towards nucleus forming *canaliculi.* These cells are specialized in secreting hydrochloric acid and intrinsic factor.

- Mechanism of HCL secretion:

We have to release chloride (Cl^-) and we have to release protons (H^+) in order to secrete hydrochloric acid (HCl). So, cells are actively transporting chloride towards canaliculi, as a result, negative transcellular potential is created towards canaliculi and positive towards interstitial fluid. So this potential usually attracts positively charged particles from interstitial fluid, and the most candidate particles which have high concentration in interstitial fluid and are positively charged are sodium ions (Na^+). So, usually the transport of chloride will attract sodium from interstitial fluid into the cell. To get the release of protons, we have to form protons inside these cells and then pump these protons towards canaliculi.

How protons are formed? Simply, by taking the CO2 and water, we have an enzyme called carbonic anhydrase which forms carbonic acid, this carbonic acid can dissociate inside the cell into proton and bicarbonate. The proton is pumped towards canaliculi while the bicarbonate is transported to the interstitial fluid. Now, protons are released. What happens to the polarity if we have pumped protons? Without pumping we have it more negative; when these cells are not stimulated to form H^+ and release H^+, the transcellular potential which will be created across the whole cell will be more negative than when we are pumping H^+. Without pumping it will be -70, but when we are pumping protons, it will be for example -30, so less negative.

Now, what happens to the transport of sodium when we pump protons? Will it become higher or lower? It becomes lower.

Basically, when we are not stimulating oxyntic cells and there is no stimulation for gastric secretions, the amount of protons in the gastric juice will be very low in contrast to sodium which will be very high. But when the stomach is stimulated, more protons and chloride ions are released, so more hydrogen chloride is secreted in the presence of stimulation while more sodium chloride is secreted in the absence of stimulation.

- ✓ High rate of stimulation: more HCl. Low rate of stimulation: more NaCl.

-Functions of HCL:

The hydrochloric acid is important in providing very low pH which is the optimal media for the activation of the enzyme pepsinogen. Pepsinogen is the inactive form of the enzyme while pepsin is the active form. Pepsin has very low activity in the small intestines due to alkaline pH.

Also, HCl is important in the decomposition of food, we are ingesting food particles and meat for example which has connective tissue that are easily

decomposed and dissolved in the stomach by the action of HCl. So, actually the main function of the stomach is dissolving the ingested food.

In addition, HCl plays an important role in the defense mechanism, because when we are ingesting food, we are also ingesting microorganisms and they are destroyed by the low pH. Most bacteria are not resistant to low pH.

Note: In pharmacies, there are some drugs which are called proton pump inhibitors, so what are they doing actually? Blocking the activity of these pumps and decreasing hydrochloric acid secretion. So this is one mean by which we can decrease hydrochloric acid secretion to achieve treatment of certain gastric problems like hypersecretion of HCl which may result in gastritis for example or could be involved in the pathogenesis of ulcers. So this is the relation between some drugs and treatment of some ulcer problems by blocking the activity of proton pump.

-Pepsinogen secretion: (Chief cells)

Pepsinogen is mainly secreted by chief cells or peptic cells, in some books they are talking about some mucous cells which also secrete pepsinogen (Don't pay big attention to this issue only know that the main cells for secretion of pepsinogen are chief cells).

Its optimal activity is at low pH and its function is to start digestion of proteins, so long peptides are becoming smaller peptides but that is not the final digestion of proteins since it isn't finished at the level of the stomach rather it is initiated.

-Mucous secreting cells:

There are large numbers of cells secreting mucous, thus high mucous secretions, and as we know that these mucous secreting cells have a lot of vesicles. Once we have released this mucous, it is covering all the surface of the stomach so we are forming like a thick barrier between lumen and the tissue preventing the effect of HCl and pepsin over the cells hence protecting the mucosa. The pH of the

mucous is neutral towards alkaline while the pH of the lumen is around 2 to 3. So at any time we have some hydrochloric acid trying to diffuse to the tissue through this thick barrier and getting neutralized by the mucous thus preventing its activity. Other functions of mucous include lubrication.

-Gastrin: (G cells)

Gastrin is released by G cells; the releasing process is stimulated either by local changes (gastric distention) or by ingested food and chemicals like the presence of proteins in chyme for example, in addition to vagal stimulation.

What do we mean by vagal stimulation? Parasympathetic stimulation for these cells to release gastrin.

Functions of gastrin: Increases secretions in general, so we have increased HCl and pepsinogen secretions. Also, gastrin has some trophic effects on gastric mucosa which means survival of the cells, so instead of having these cells dying after 3 or 4 days, they survive for 2 or 3 weeks or more.

Note: Most hormones are important in relation to secretion and they have very minimal role over motilities even though we have mentioned them in motility BUT they are the main controller of secretion rather than motility.

-Intrinsic factor:

It is secreted by oxyntic cells and it is important for the absorption of vitamin B12. Vitamin B12 is needed for a lot of processes in our body including hematopoietic processes and RBCs synthesis, so there is a relation between gastric problems and anemia. For example, if there is atrophy of cells, there won't be enough release of intrinsic factor which means there won't be enough absorption of vitamin B12, as a result, vitamin B12 deficiency anemia will develop. Most of vitamin B12 deficiencies are related to less absorption rather than insufficient intake of B12.

-Control of gastric secretions: Gastric secretions are very well controlled

We have neural control and we have hormonal control in addition to third type of control over gastric secretions which is the paracrine control.

1) Neural control: is achieved by enteric nervous system, as you know we have some of these neurons are releasing Ach to act on parietal and peptic cells to increase their secretion since they have Ach receptors. Also, the autonomic nervous system is involved; it can act directly on the secretory cells by parasympathetic stimulation (Ach release). However, there are indirect effects of parasympathetic control over the secretory cells; one of these effects is the ANS acting on the enteric excitatory neurons to release Ach. As a result, activated enteric neurons will further activate a special type of cells which are the *enterochromaffin-like* cells which release Histamine that is involved in activating paracrine control. We also have some fibers of autonomic nervous system that activate enteric neurons to release GRP (Gastrin Releasing Peptide) which acts on G cells to release Gastrin (hormonal). So, by ANS indirectly, we will have activation of paracrine and hormonal control.

2) Hormonal control: gastrin is mainly involved. For gastrin, there are receptors called cholecystokinin B receptors (CCK-B). These receptors can bind to the hormone cholecystokinin. So both, gastrin and cholecystokinin hormones can bind to these receptors BUT the stimulation by cholecystokinin is much less than the stimulation by gastrin. In this case, if there is high amount of gastrin, the secretion will be high, while if there is high amount of cholecystokinin, the secretion will be less due to competition between these two hormones over the same receptors preventing enough gastrin to bind and increase the secretion.

So if we have high amount of cholecystokinin → decreased secretion. High amount of gastrin → increased secretion.

3) Paracrine control: is achieved by Histamine that is secreted by enterochromaffin-like cells which have receptors called H2 receptors that bind to histamine. Activating these receptors increases stimulation. There are drugs that can block the H2 receptors, decreasing the gastric secretions (HCl). This could be another way to treat ulcers or gastritis by taking H2 blockers that are specific to these receptors since there are other types of histamine receptors such as H1 in respiratory system for example. There is another ligand called Somatostatin (SS) which acts on parietal cells and decreases HCl secretion.

-Hydrochloric acid itself can initiate some reflexes to inhibit HCl secretions (negative feed-back mechanism) when there is high amount of HCl. Actually this mechanism is for protection in order not to have gastric pH falling below 3. So the process of feed-back inhibition by HCl is either by reducing gastrin release or by the initiation of inhibitory reflexes in order to maintain the pH.

-Summary of control of gastric secretions:

1) Cephalic phase: It occurs once you have seen or smelled or tasted food or someone's talking about food and gastric secretions increase by the activation of parasympathetic NS.

2) Gastric phase: food in stomach, distension of stomach, presence of proteins in food, activation of reflexes, activation of gastric secretions via ENS, ANS and hormones.

3) Intestinal phase: once you have emptied the contents from the stomach into the small intestines, gastric secretions will decrease.

Remember: for decreasing gastric activities we have:

1) Enterogastric reflexes (negative feed-back inhibition)

2) Some hormones like cholecystokinin, secretin and GIP (gastric inhibitory peptide).

Regarding the intestinal phase at the beginning, there is some excitation due to G cells found in the duodenum which secrete gastrin, but the bulk of the intestinal phase is to reduce gastric secretions.

-Intestinal secretions:

We have a lot of cells releasing water and electrolytes in the intestine (serous secretions), but there are some cells which release mucous in their secretions. In addition, we have a lot of absorptive cells and we will see their specifications when we talk about digestion and absorption. Furthermore, we have some endocrine cells that release secretin in the duodenum, cholecystokinin or GIP and so on. The stimulation of these endocrinal cells differs, for example secretin-releasing cells are stimulated by low pH coming from the stomach during emptying into the duodenum. Cells that are releasing cholecystokinin are mainly stimulated by the presence of fat from food. So, different types of cells are stimulated by different ways. Intestinal secretion is about 1.5L/day and most of it is serous. As for regulation, there are neural mechanisms which can activate the secretions via parasympathetic NS and fibers of ENS. Also, there is hormonal control and the main hormone which activates the serous secretion is secretin that also acts on pancreatic and biliary tree ducts.

-Colonic secretions:

They are mainly mucous secretions. We have fewer amounts of serous secretions that are rich in potassium and bicarbonate. Reabsorbing of electrolytes from fecal materials occurs at the colon and we are replacing them by release of potassium.

-Pancreatic secretions:

The pancreas has endocrine portion and exocrine portion. We will focus on the exocrine portion only. The exocrine part of the pancreas is like salivary glands, so we have acinar cells and duct cells. The acinar cells are releasing enzymes while the

duct cells release water and electrolytes mainly bicarbonate. However, the acinar cells of the salivary glands are the cells responsible for releasing water and electrolytes. Now back to the acinar cells of the pancreas, there are a lot of canalicular structures which are lined by duct cells. Once pancreatic juice is released, it flows towards duodenum, but before reaching the duodenum, the duct from the pancreas joins another duct which comes from the liver (bile duct) forming what we call the hepatopancreatic duct. Both of them now are flowing into the duodenum through an anatomical structure called ampulla of Vater. But, there is a physiological or functional structure before reaching the duodenum which is a sphincter (sphincter of Oddi) that controls the flow of digestive juices through the ampulla of Vater. The importance of this sphincter is to prevent reflux of duodenal content backwards. (Check the slides for figures)

-We have to think about some pathological problems related to secretions. For example, less release of mucous could generate ulcers, increased HCl secretion also could be part in the pathogenesis of ulcers, increased vomiting from gastric origin results in losing high amount of acids developing alkalosis. So we can have a lot of pathological problems related to secretory processes and to the loss of secretions to the outside of the body.

Yours sincerely,

Abu Malik.