Physiology

● Sheet ○ Slide

number **4**

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In this sheet we are going to study the **secretion** along the GI tract. But before that, some points should be explained:

1. Secretion is a physiological process that begins in the oral cavity and ends up in the colon. So in this lecture, we will cover the secretions that occur in the oral cavity, esophagus and stomach.

2. We should differentiate between these two terms:
   - **Reflex**: A body response to a stimulus (in the GI, reflexes happen through the ANS or the ENS).
   - **Reflux**: Movement of any content in the GI tube in a backward direction, opposite to the normal one which is in a forward direction.

Secretion

A huge amount of fluid is secreted along the GI tract, starting from the **oral cavity** in the form of saliva and ending in the **colon** in which mucous is secreted.

- **There are two types of secretions:**

1. **Serous**: A fluid of water and electrolytes.
2. **Mucous**: Mucin-rich secretion, which contains glycoproteins.

   - **The figure in the next page which describes the fluid balance in the GI tract shows that:**

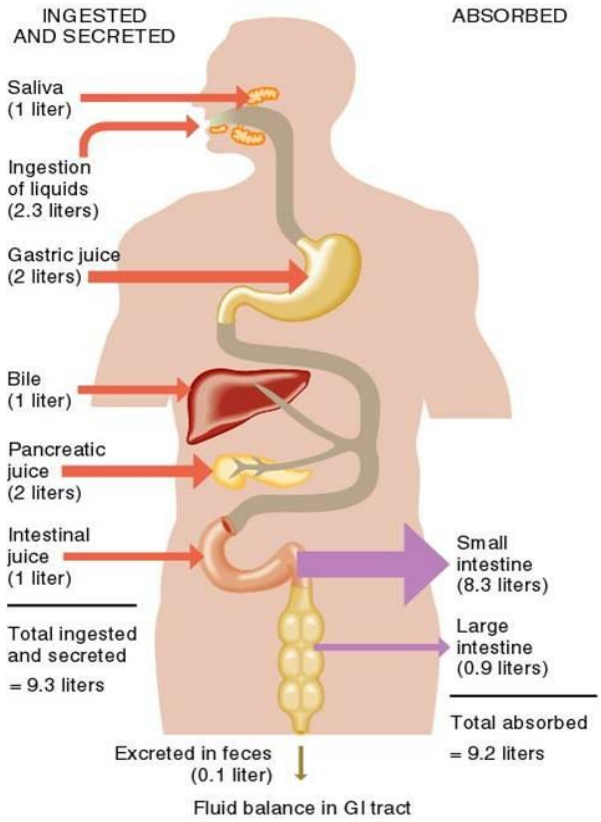
1. **9.3** litres are ingested and secreted along the GI tract, where:

   - **7L**: By secretions of secretory organs and glands.
   - **2.3L**: By daily ingestion.

2. About 9.2L is absorbed by the small intestine (about 85% of the absorbed fluids) and large intestine (about 15%), and only 0.1L gets out through feces.

- **The general functions of these secretions:**

1. Help in the degradation of the ingested food, due to the presence of the **digestive enzymes.**
2. **Lubrication and protection** of **organ's mucosa**, due to the presence of mucous.



For example, the food that passes through the esophagus is found in the **solid** form, so this mucous helps in soft movement of these particles, preventing injury to the esophagus.

In addition to that, we will find that the lower part of the esophagus has compound glands that secrete large amounts of mucous, which helps in neutralizing and minimizing the damage of any reflux from the stomach towards the esophagus.

Also, since the fecal substance is solid, the colon needs the mucous to get rid of these materials without any injury to the colon.

- **The organization of these secretory structures:**

1. **Single-cell** secretory glands (goblet cells).
2. **Pits** (or simple glands): which are invaginations of the epithelium in the **submucosa** (according to the handout although the doctor at other parts mentioned that it is **mucosa**) of the stomach (where they are known as “Tubular glands”) and small intestine (where they are known as “Crypts of Lieberkühn”)
3. **Complex glands**: which are found within the submucosa.
4. **Organs**: which are located outside the GI tube.

- **Control of secretion in general is achieved by:**

1. **ENS:** The presence of food in certain segments usually stimulates glandular secretions. This appears as a response to mechanical or chemical stimulation, which induces activation of secretory reflexes that are responsible for the increased secretions by gland.
2. **ANS**: the effect of ANS is as following :-

a) **Parasympathetic**>>> Parasympathetic stimuli increase the rate of glandular secretions, they also indirectly cause vasodilation of blood vessels which increases the secretion.

b) **Sympathetic**>>>a high sympathetic stimulation will decrease the secretion due to its vasoconstriction effect on the blood vessels, thus inhibiting the secretion in general.

*** VERY IMPORTANT NOTE: Some references say that a slight increase in the **sympathetic tone** can result in a **moderate** increase in secretions, and the type of that secretion is **vesicular secretion** which contains **mucous**.

***Don't forget that the bulk effect of the sympathetic nervous system is to **decrease** the secretion.

c) **Hormonal regulation**>>> some hormones have a vital role in secretion, such as gastrin, secretin and cholecystokinin hormones.

SALIVARY SECRETION

Salivary glands are classified into 3 major types, where each one of them releases a special kind of secretion:

1. **Submandibular gland** (mixed gland): secretes both mucous and serous secretions.
2. **Parotid gland**: secretes only serous fluids.
3. **Sublingual gland**: secretes only mucous secretion.

- Note: you can't find a cell that secretes both types of secretions (serous and mucous), so the cells that secrete mucous are responsible for releasing **only** mucous, and that also applies to cells secreting serous.

- Submandibular gland contains two different types of cells, one is specialized for secreting mucous and the other for secreting serous.

Please refer to the figure below.

Salivary Glands

Name of Gland	Type of Saliva	% of Total Saliva Secreted
Submandibular	Mucous-serous	70
Parotid	Serous	25
Sublingual	Mucous	5

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What are the characteristics of the cells that release mucous, or secretory cells in general?

1. They are rich in endoplasmic reticulum.
2. They are also rich in vesicles which contain high mucin content in case of mucous-secreting cells.

- Cells which release serous have different mechanisms and characteristics from mucous-releasing cells.

10:02min

- **If we look at the salivary gland from a functional view, we will find two types of cells forming it:**

1. **Acinar cells:** Form the parenchymal part of the gland. These cells secrete water and electrolytes (the primary saliva) into the duct of the gland.
2. **Duct cells:** Line the duct of the gland. These cells are responsible for further modification of the primary saliva secreted by the acinar cells.

Since the submandibular gland is a mixed gland, we can find that mucous-secreting cells are dispersed between other cells.

- **How are acinar and duct cells physiologically functioning?**

1. ACINAR CELLS:

- The basolateral membrane of these cells has active Cl^-transporters which accumulate Cl^- ions from the interstitial fluid to the inside of the cell.
- That creates a negative potential at the level of the basolateral membrane towards the inside. This in turn will lead to attraction of sodium ions from the interstitial fluid also, leading to an increase in the osmolarity inside the cell which causes water to enter the cell again from the interstitial fluid.
- As a result, minute ruptures at the apical membrane (which faces the luminal duct of the gland) occur, leading to flushing of primary saliva to the duct.
- **NOTE: The primary saliva has almost the same composition as the interstitial fluid.**

2. DUCT CELLS:

- The primary saliva then flows along the duct for further modification to get the **final saliva** by the action of the duct cells, which will be released into the oral cavity.
- Actually, what occurs at these duct cells is the following, Na+ is reabsorbed and K+ is secreted by the activity of Na+ / K+ pump. This will result in a negative trans-cellular potential which induces passive reabsorption of Cl- ions. HCO3- is secreted into the duct, partly by

exchange of HCO3- for Cl- and may result also by an active transport of HCO3-.

- At this point the final saliva is made, which has a **PH** around **6 to7.**
- The net changes that happen by the duct cells is:

1) Decreasing Na^+ and Cl^- concentrations to 1/10 of their initial concentration in the primary saliva.
2) Increasing K^+ concentration to 7 folds and $HCO3^-$ to 2-3 times.

*Question: Do we have the same composition of the final saliva if we conduct the primary saliva at a slow rate and once at high rate?

NOTE: CONDUCTION RATE = THE RATE OF RELEASING THE PRIMARY SALIVA FROM THE ACINAR CELLS.

Answer: When the salivation process occurs spontaneously (it is maintained by a constant low level of parasympathetic stimulation), that means it occurs at a low rate. So the duct cells have time to do their function as mentioned above, and the final saliva has a **PH** around **6-7**.

On the other hand, when the salivation process occurs due to a stimulus at the maximal stimulation, the primary saliva is conducted at high rate (the formation of primary saliva increased as much as 20 folds), so the duct cells can't exchange the ions as in the case of slow rate conduction.

So the final saliva in the means of composition is different in both cases and it has a **PH** around **8** when the conduction is high.

In the case of high rate conduction, duct cells don’t have the time to get rid of Na^+ and Cl^- ions out of the duct, and to reabsorb K^+ into the duct.

*VERY IMPORTANT NOTE: The reason why we have an alkaline PH (around 8) in the case of high rate conduction is that the stimulatory process increases the entering of HCO3 into the lumen, and that is an **exception**.

The final saliva is a hypotonic solution because there is a higher absorption rate of Na+ and Cl- than secretion of K+ and HCO3- by tubular cells.

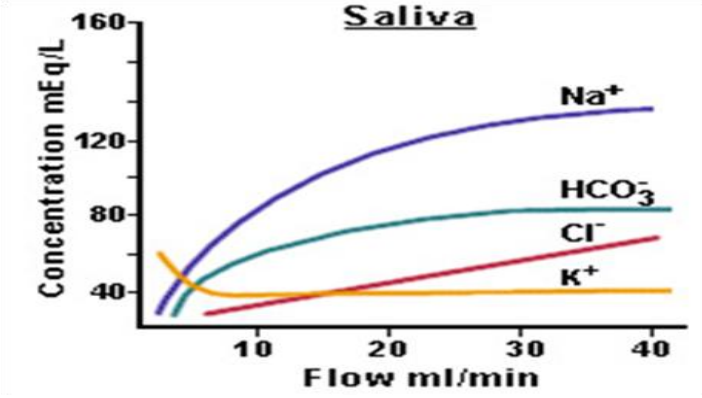
- **SUMMARY**:

1. Low rate:
   - Occurs spontaneously
   - PH=6-7
   - Duct cells exchange Na+, Cl- out, and K+,HCO3- in.
2. High rate

- Occurs by stimulus
- PH=8
- No time to exchange ions except HCO3-secretion into the lumen .

The figure below represents the concentration of **secondary saliva** versus the flow rate(speed). Note that the concentration of ions in the secondary saliva is different at different rates. (Don't forget the exception for HCO3 secretion).

HCO3= BICARBONATE



-THE ONLY CONTROLLER OF THE SALIVARY SECRETION IS ANS.

-ENS AND HORMONES HAVE NO EFFECT ON SALIVATION.

1. **Sympathetic**>>> decreases the salivation when highly activated. BUT don't forget that a moderate increase in the sympathetic tone can increase the vesicular secretion (mucous secretion).
2. **Parasympathetic**>>>> increases the salivation process by two means:

a) **Unconditioned reflex**: The response of the parasympathetic due to the mechanical effect such as: eating food / exerting a pressure which occurs in the dental procedures
b) **Conditioned reflex**: The response of the parasympathetic as a result of a previous experience (a learned response). For example, when you see or smell delicious food, or when you think about food, you will notice that you will start producing saliva.

- **Saliva functions:**

1. It contains **digestive enzymes**, and one of them is **amylase**, which is responsible in partial digestion of starch.
   NOTE: The appropriate PH for this enzyme is an alkaline PH, so once this enzyme gets in the stomach it will be inactive, and so the main function of this enzyme is digestion of the remnants of carbohydrates in the mouth rather than the bulk digestion of ingested carbohydrates.
2. For **lubrication** and **moistening** the food particles, to be smoothly swallowed along the esophagus.
3. **Antibacterial action**: the presence of the lysozymes aids in destroying some kinds of bacteria.
4. **Oral hygiene**: Constant flow and secretion of saliva plays a role in keeping mouth and teeth clean, in addition, saliva has a role in protecting the mouth from bacteria, due to the presence of IgA antibody in it.
5. **Solvent for the food particles**: So we can taste food by the taste buds.
6. Helps in **speech**: Dryness of the mouth can cause problems in speech.
7. **Neutralizing the acids** due to the presence of bicarbonate (HCO_3^-) and that helps in preventing the development of caries.

We have some **pathological cases** related to salivation, and one of them is called **xerostomia**: the closure of the ducts or the inability to secrete saliva.

Esophageal secretions

- Most of the esophageal secretions are **mucous secretions.**
- The upper part of the esophagus is composed of **simple glands** while the lower from **compound glands**.
- This is because many pathological conditions occur at the level of the lower part of the esophagus, so we need **more** mucous to neutralize the effect of the reflux of the gastric secretions from the stomach.
- **Heartburn** is a result of this reflux due to many pathological causes, and one of them is weakness of the esophageal sphincter.

Gastric secretions

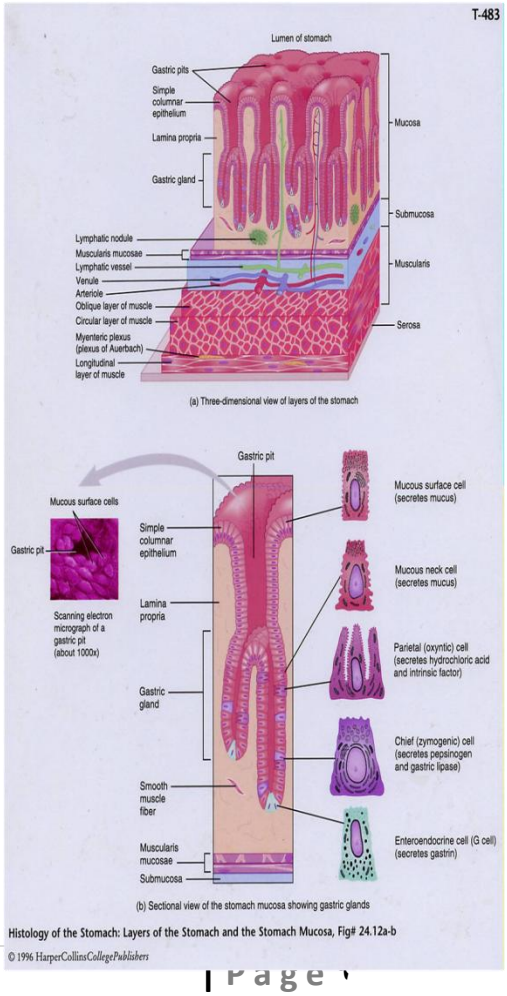
- Stomach as any part of the GI tube is composed of 4 layers:

1. **Mucosa**: consist of:
   - Epithelium
   - Loose connective tissue (lamina propria).
   - Muscularis mucosae.

2. **Submucosa**
3. **Muscularis**: contains the longitudinal and circular muscles.

   - **Body of the stomach** is the only part of the GI tube which has an additional layer of muscles in the muscularis layer, which is called **oblique layer** that is found directly under the submucosa.

4. **Serosa.**



-The epithelium of the mucosa makes invaginations within the mucosa itself to form what is called **gastric glands** or **gastric pits.**

-These glands are also called **oxyntic glands** due to the presence of oxyntic cells in them.

- **Gastric glands are composed of many cells, which are:**

1. **Mucous surface cells:** They are located at the surface of the gland, and their function is to release mucous.
2. **Mucous neck cells:** They are located at the neck of the gland, and they also secrete mucous.
3. **Oxyntic cells**(also called **parietal cells**):
   - They have a great role in secretion, where they secret **HCl** (hydrochloric acid) and **intrinsic factor.**
   - The apical membrane (which faces the lumen) of these cells forms invaginations towards the nucleus, creating structures called **canaliculi.**

   - Intrinsic factor is important in binding to **vitamin B12** and facilitating its absorption at the level of the small intestine.

   - **Anemia** can result from gastric atrophy in which parietal cells can't secrete the intrinsic factor. So the problem is related to the gastric secretion of the intrinsic factor rather than the availability of vitamin B12, since vitamin B12 is available as tablets and is plenty in our food.

4. **Chief cells** (zymogenic cells/ peptic cells): They are specialized in releasing two enzymes:
   - **Pepsinogen**(the inactive form) which becomes active by the release of HCL
   - **Lipase.**

5. **Endocrine cells:**

- **G cells**: secret gastrin hormone
- **S cells**: secret somatostatin.

- **The mechanism by which oxyntic cells are used in secreting hydrochloric acid:**

1. There is an active transport of chloride which leads to its transport to canaliculi, this transport works all the time without stimulus.

2. This will create more negative potential across the whole cell, which is called **trans-cellular potential** (more negative potential towards the canaliculi), a negative potential towards the canaliculi will attract positively charged ions that are found in a high concentration in the interstitial fluid (which are Na+ ions), so until now we have released chloride.

3. In order to form the protons H^+, these cells combine H_2O with CO_2 to form H_2CO_3 (carbonic acid). This process is highly controlled by neurons and hormones (a stimulated process), unlike the process number 1 above.

-NOTE: CO2, Na+, CL- , H2O all come from the interstitial fluid.

4. H_2CO_3 then disassociates into HCO_3^- (which is transported toward the interstitial fluid in exchange for Cl-) and H^+ which will be secreted to the lumen of the gland by the action of H^+/K^+or H^+ pumps.

- Now we have secreted H^+ and Cl^- into the duct of the stomach, so they combine to form HCl.
- The combination occurs out the oxyntic cell (in the lumen of the stomach) because HCl is a very destroying agent to the mucosal cells.

PLEASE pay attention to this important note:

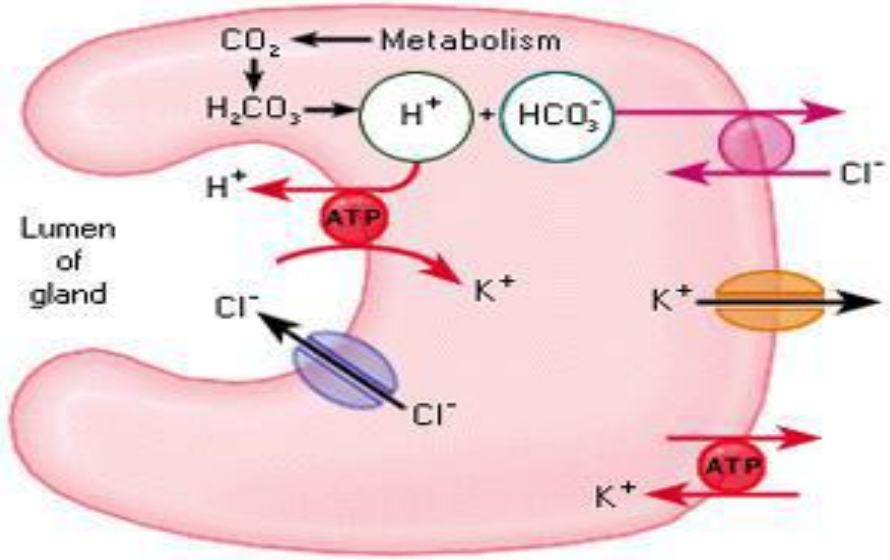
If we don't stimulate the process of secreting H^+, we create the trans-cellular potential, which is a **negative** potential due to the influx of Cl- from the interstitial to the canaliculi. This will attract Na+ ions, so this negative potential is decreased. As a result, **NaCl** is released to the lumen.

On the other hand, if we stimulate the process of producing H^+, this will reduce the trans-cellular potential. As a result, the attraction of Na+ is decreased. In this case, cells are releasing **HCl**.

So again, at rest and at low levels of stimulation usually NaCl is secreted and during high rates of stimulation there is HCl secretion.

The potential difference across the cell is about –70mV at rest and drops to about (-30 mV) during stimulation

-Some drugs are used to block the H^+ pump from pumping H^+ to treat **peptic ulcer**.



THE END….

DON'T STOP FIGHTING …