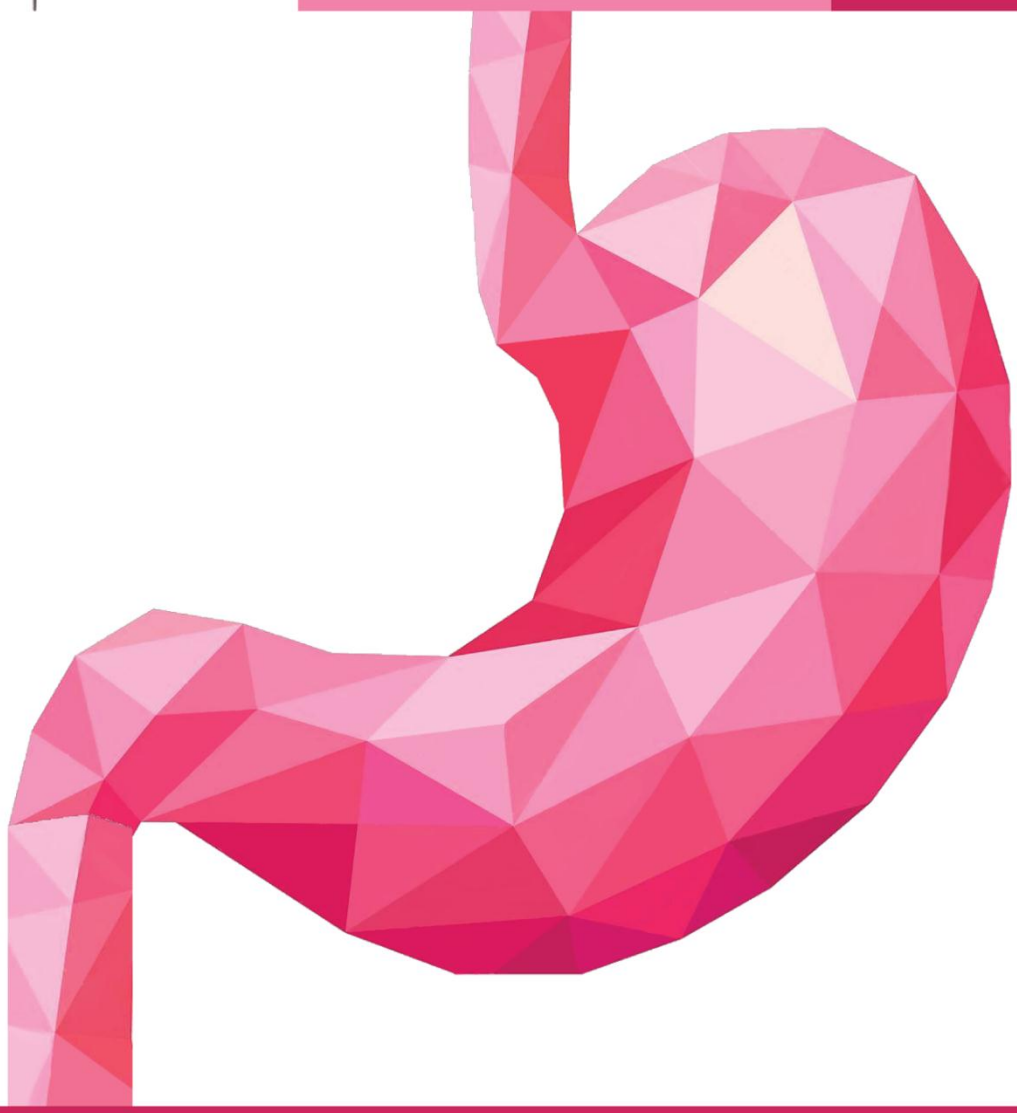
GIS 3

PHYSIOLOGY



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In the last lecture, we talked about gastro-intestinal motilities. We will now start talking about Gastrointestinal Secretion, but before that we should cover a small topic related to movements of the colon.

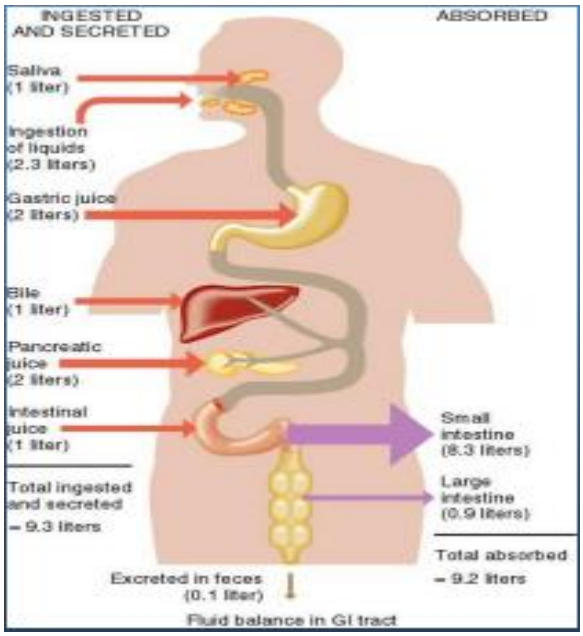
DEFECATION

- A process that involves the discharge of faeces from the body.
- As we know from the previous lecture, we have two types of movements in colon:
  1) **Haustration contraction:** it is similar to the segmentation contraction of small intestine**,** as it involves the activity of circular muscle and longitudinal muscle (taeniae coli) of colon. So, by this type of contraction we divide the colon into small compartments (haustra) which helps the colon in the absorption of water and electrolytes.
  2) **Mass contraction:** it is a powerful contraction responsible for the movement of fecal content from the transverse colon to the sigmoid. Mass contractions are described as constrictive rings at the transverse colon followed by the contraction of about 20 Cm or more of the colon distal to the constrictive ring, mass contraction activated by gastrocolic reflux (distension of stomach will result in increasing the colon's motility).
- After multiple mass contractions, the faeces now reach the sigmoid part of large intestine, and here there are two different types of reflexes preceding defecation process:
  1) **Intrinsic reflex** (aka intrinsic myenteric reflex): The intrinsic reflex is initiated by the distension of the rectum, by the activation of myenteric plexus (ENS), leading to more contractions in the descending colon, sigmoid and rectum. This will force faeces to move toward the anus. This reflex is weak and will not cause defecation.
  2) **Extrinsic reflex** (aka para-sympathetic defecation reflex): This reflex amplifies and enhances the function of intrinsic reflex. Extrinsic reflex involves the sacral segments of the spinal cord. When the nerve endings (sensory parasympathetic fibers) in the rectum are stimulated by the distension that results from the accumulation of faeces, signals are transmitted first into the spinal cord and are then reflexed back to the descending colon, sigmoid, rectum, and anus through parasympathetic nerve fibers (motor fibers). These parasympathetic signals greatly intensify the peristaltic waves and relax the internal anal sphincter, thus converting the intrinsic myenteric defecation reflex, which is weak, into a powerful process of defecation that is effective in emptying the large bowel.
- **Note:** all these reflexes are **involuntary**
- After all these reflexes, the defecation in normal people occurs only as a voluntary act by relaxing the external sphincter muscle (which is a striated muscle and under voluntary control) and increasing the abdominal pressure, through closing the glottis and contracting the abdominal wall, which causes the pelvic floor to be pulled downward on the anal ring and to be relaxed to evacuate faeces.

- **Pathological problems related to colon movement:**
  1) **Constipation:** (hypo-motility of colon) due to less migration of neuron toward the colon, which results in the enlargement of colon (mega-colon).
  2) **Diarrhea:** (hyper-motility of GIT), mucus diarrhea is more associated with hyper-motility of colon, however the watery diarrhea is more associated with small intestine hyper-motility.
  3) the hypo-motility might be caused by the effect of anesthetic drugs after procedure.

Gastro-Intestinal Secretion

A huge amount of fluid is ingested and secreted in our GI System every day.
For example, we ingest about 2 liters of liquids every day.
Regarding secretion: salivary glands, stomach, liver, pancreas and intestines produce different amounts of fluid daily as seen in the picture.



Do all these fluids get excreted in faeces?

From the *9.3* liters secreted and ingested, only about *0.1liter* is excreted, while *9.2* is absorbed (lower part of small intestine absorbs 8.3 liters and colon 0.9 liters).

What types of secretion do we have along these organs?

We have two types:

1- serous secretion: A watery secretion which contains proteins such as amylase (ptyalin), which is a digestive enzyme.

2-mucus secretion: that contains mucin (a glycoprotein) for lubrication and for surface protection purposes.

What are the functions of these secretions?

1- Lubrication and protection of the mucosa. (mucus secretion)
2- Digestive enzymes (chemical digestion of food). (serous secretion)

What are the types of secretory structures?

1- **Single-cell** (solitary cells) & **secretory glands** (goblet cells) are scattered all over the mucosa.

2- A group of cells form **Pits** (simple glands) that represent invaginations of the epithelium in the submucosa in small intestine, which are known as "**Crypts of Lieberkühn**" and in the stomach "**Tubular glands**".

3- **Complex (compound) glands**: like mucus glands at the lower part of esophagus.

4- **Organs:** like Salivary glands, Pancreas and Liver, which are located outside the tubular structure of the GI.

The composition of secretion includes:
*- **Organic materials** that secretory cells synthesize, which are stored in vesicles, and then secreted upon stimulation. Enzymes, for instance.*
- Water and electrolytes are taken from blood vessels, and then secreted by secretory cells.

How is secretion controlled?

1. **Neural:**

   A- *ENS***:** The presence of food in certain segments usually stimulates glandular secretions. This appears as a response to mechanical or chemical stimulations, which induce activation of secretory reflexes that are responsible for the increased secretions by gland.
   B- ANS:
   - Parasympathetic stimuli increase the rate of glandular secretions.
   - Sympathetic stimuli can cause moderate increase in glandular secretion by increasing vesicular transport (increases secretion of organic materials). On the other hand, it can reduce the secretion of water and electrolytes by its effect on vessels (It causes vasoconstriction, so it reduces blood flow). But generally, SANS decreases secretions.

2. **Hormonal:** Some hormones are secreted by the presence of food in digestive organs, which affect the glands where they stimulate secretions. (like pancreas as we will see later)

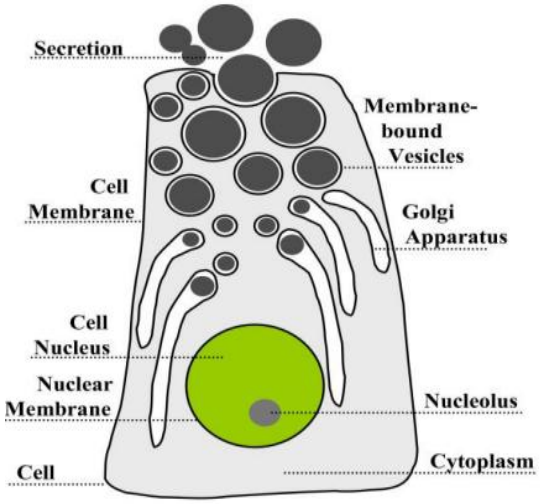
Salivary Glands secretion

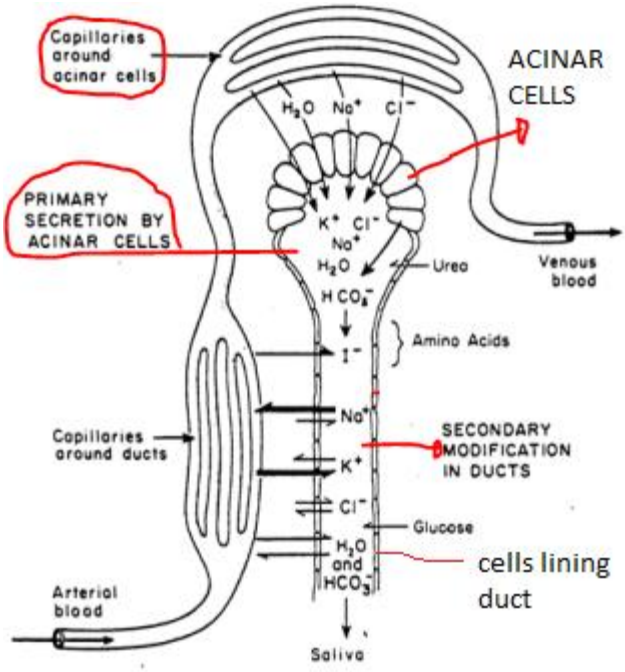
General consideration:

Secretion: is a net movement of water, electrolytes and proteins (starch splitting enzyme (amylase) and glycoproteins) into the lumen of salivary duct.

Salivary Glands

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





What does this cell represent?

We can notice that it is filled with ***vesicles***, because cells that secrete proteins use vesicular transport and exocytosis to secrete proteins.

To summarize:

1) cells that secrete mucus which contains mucin (glycoprotein)

use vesicular transport and exocytosis

2) Cells that secrete water and electrolytes

Flush them out to the lumen due to tiny (minute) ruptures at the apical membrane.

Note: Some cells , like acinar, secrete both.

What is the mechanism of secreting saliva?

Salivary secretion is a two-stage operation: The first stage involves the acini, and the second stage involves the salivary ducts. (LOOK at the picture above, on the right)

1ST STAGE: SECRETION OF PRIMARY SALIVA FROM ACINAR CELLS.

1. **Active transport of Cl-** at the basal portion that faces the capillaries (interstitial fluid) of the cell membrane (acinar cells) causes more negative membrane potential.
2. **Increased negativity** of membrane potential attracts the positive ion **(Na+).**
3. The increase in osmotic pressure inside the cell causes **water to move inside**, which in turn leads to an increase in the hydrostatic pressure inside acinar cells (cells swell).
4. This increase results in **minute (tiny) ruptures** at the apical membrane (that faces lumen) of secretory cells which causes **flushing** of water, electrolytes and organic materials out of the cell **into the lumen**.

Origin of water and electrolytes is extracellular fluid. The acinar cells are surrounded by capillary plexus which plays an important role in glandular secretion.

ACINAR CELLS (that form parenchyma of the gland) do not only secrete water and electrolytes, but also synthesize and secrete proteins such as (**ptyalin (amylase**), lingual lipase and **mucin**). These proteins are synthesized in ER (endoplasmic reticulum) of acinar cells, then transported by a mean of vesicular transport toward the apical (luminal part) membrane, where they are secreted by exocytosis.

In conclusion, the acinar cells secrete **primary secretion (primary saliva)** that contains ptyalin and mucin in a solution of electrolytes. The water and electrolyte concentration in primary secretion is not far from that in extracellular fluid (high concentration of chloride and sodium ions compared to potassium).

The secretory cells are rich in ER and mitochondria.
Mitochondria provides sufficient energy supply for the transport of nutrients that enter in the constitution of synthesized materials and for the process of synthesis.

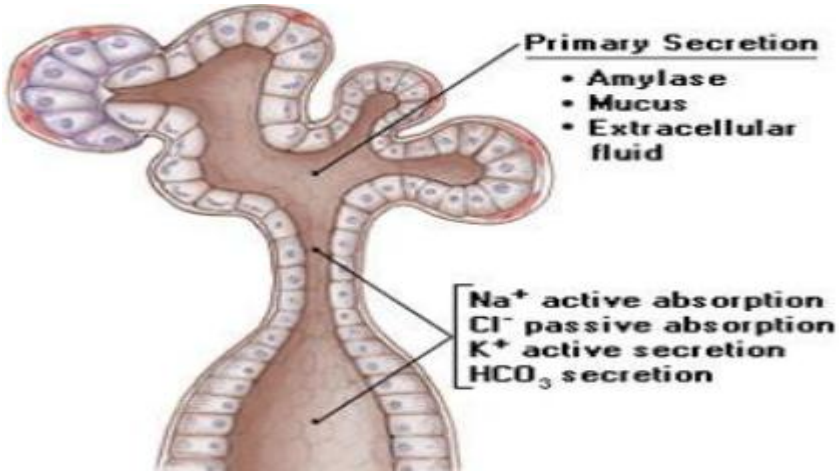
2ND STAGE: Modification of primary saliva through ducts to get final saliva.

During the flow of saliva through the ducts, two major transport processes (by duct cells) are taking place to finalize the ionic composition of saliva:

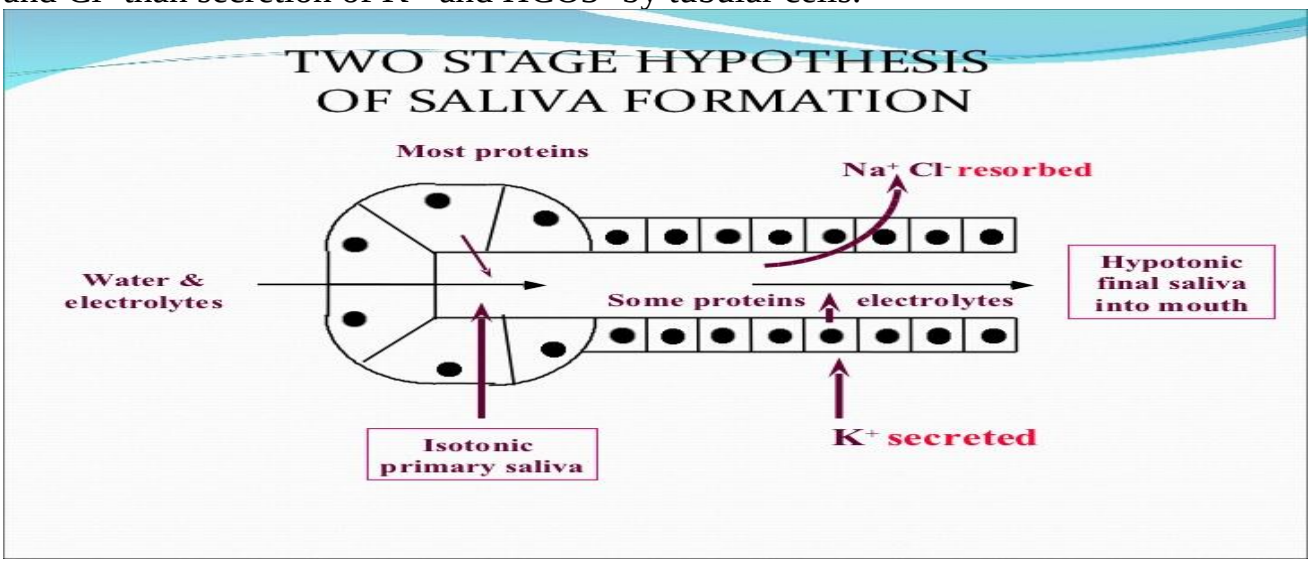
First, sodium ions are actively reabsorbed from all the salivary ducts and potassium ions are actively secreted into the ducts in exchange for the sodium. Therefore, the sodium ion concentration of the saliva becomes greatly reduced, whereas the potassium ion concentration increases.

However, there is more sodium reabsorption compared with potassium secretion, which creates electrical negativity of about −70 millivolts in the salivary ducts; this negativity in turn causes chloride ions to be reabsorbed passively. Therefore, the chloride ion concentration in the salivary fluid falls to a very low level.

Second, bicarbonate ions are secreted by the ductal epithelium into the lumen of the duct. This secretion is at least partly caused by the passive exchange of bicarbonate for chloride ions, but it may also result partly from an active secretory process.



The NET result is a change in the ionic composition of saliva by decreasing Na+ and Cl- concentration to the 1/10 of their plasma concentration and increasing K+ concentration by 7 folds and HCO3- concentration by 2-3 folds.
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.



Are we having the same amount of saliva secreted all the time?

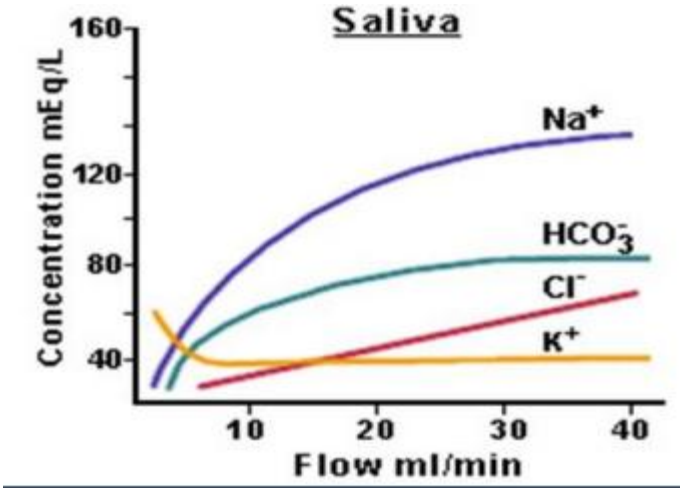
No, it can be increased by stimulation, when we are having food.

The amount of secretion by saliva is about 1500ml/day.

1-The rate of secretion is less than 0.025 **(during sleep)** to about 0.5ml/min **(during the basal conditions)**. The spontaneous secretion of saliva is maintained by a constant low level of parasympathetic stimulation. The pH of saliva during resting secretion is around (7.0).

2- **During maximal stimulation**, the formation of primary saliva increased as much as 20 folds by increasing the secretory activity of acinar cells. As a result the flow rate of saliva through the ducts is increased, which may result in relative reduction of the reabsorptive and secretory activity of the duct cells. This will change the composition of secondary (final) saliva (more Na+ and Cl-, and less K+ are found in secondary saliva during high stimulation than their concentration at low rate of flow). pH during active secretion (stimulated secretion) approaches 8.0 due to the formation and release of more bicarbonate HCO3- .

From this picture we can see the difference in concentration of ions in final saliva between basal secretion and stimulated secretion.
Na+, Cl- and HCO3- are low while K+ is high during basal secretion. During active secretion Na+ and Cl- both are high due to reduced reabsorption while HCO3- is high because of increased formation and release.



How do we control salivary secretion?

Do we have specific hormones for salivary glands? No, although some talk about Aldosterone affecting secretion, but it isn't specific because it generally increases reabsorption of sodium and secretion of potassium.
Do we have ENS fibers for salivary glands? Also no.

The main controller is **ANS**: Both sympathetic and parasympathetic increase salivation, but by different mechanisms.
- **parasympathetic** increase water and electrolyte secretion.
- **Sympathetic** increase mucin synthesis. But more increase in the sympathetic activity can reduce salivation by its effects on blood vessel supply (decreased blood flow, so it has indirect effect on reducing saliva secretion).

The parasympathetic tone can be increased by two reflexes:

1- **Unconditioned salivary reflex**: Occurs by stimulation of chemoreceptors and pressure-receptors in oral cavity due to the presence of food.
For example, dental procedures induce activation of pressure receptors. These transmit signals through afferent fibers to salivary centers in the medulla, which transmit stimulatory signals through efferent fibers via extrinsic autonomic nerve fibers to increase salivation.

2- **Conditioned salivary reflex:** Stimulation of salivation by thinking about, seeing, smelling, or hearing about pleasant food. This is known as (Mouth watering) in anticipation of something delicious to eat. The conditioned response is learned and based on previous experience.

Up to now, we talked about mechanism and control of salivary secretions.

So, what are the functions of the secreted saliva?

1. Saliva begins **digestion of carbohydrates in the mouth**: Amylase that breaks polysaccharide into maltose (disaccharide consists of 2 glucose). But this is not the main function of saliva because the optimal activity of this enzyme is at an alkaline pH and when it reaches the acidic environment of the stomach it is inactivated, so it's only useful in digestion of remnants of food in mouth.

2. **Facilitate swallowing** by:
- Moistening the food particles by mixing food with saliva.
- Lubrication by mucus which protects the mucosa during swallowing and allows easy slippage of solid food, preventing physical damage to the mucosa, specially in esophagus.

3. **Antibacterial actions** (by different mechanisms):
- **Lysozyme** (an enzyme that lyses or destroys certain bacteria by interfering with peptidoglycan on the surface of cell membrane) .
- The constant flow of saliva rinsing away materials (food residues, shed epithelial cells, and foreign particles) that may play an important role in **oral hygiene** and keeping mouth and teeth clean.
- **IgA** helping in the destruction of bacteria.

4. **Solvent** for molecules that stimulate taste buds: by dissolving food stuff to be able to taste it.

5. Facilitate **movements** of lips and tongue: **aids** in speech.

6. **Bicarbonate neutralizes acids** in food and that produced by bacteria: preventing caries (تسوس الأسنان).

Regarding pathological conditions of saliva secretion, you just need to know that there might be hypersalivation, hyposalivation or no salivation at all.

ESOPHAGEAL SECRETION:

Most of the secretion at the level of the esophagus is mucus.

1- At the upper part, mainly **simple mucus glands** (in the mucosa) and solitary cells that have secretion with **mucoid** character, which helps in **lubrication and protection** of esophageal mucosa from excoriation during swallowing process.

2- At the lower part, **Compound mucus glands** (in the submucosa) near the esophago-gasrtic junction with **alkaline secretion** that protect esophageal wall from the gastric reflux (acidic content of the stomach) into the esophagus.

GASTRIC SECRETION:

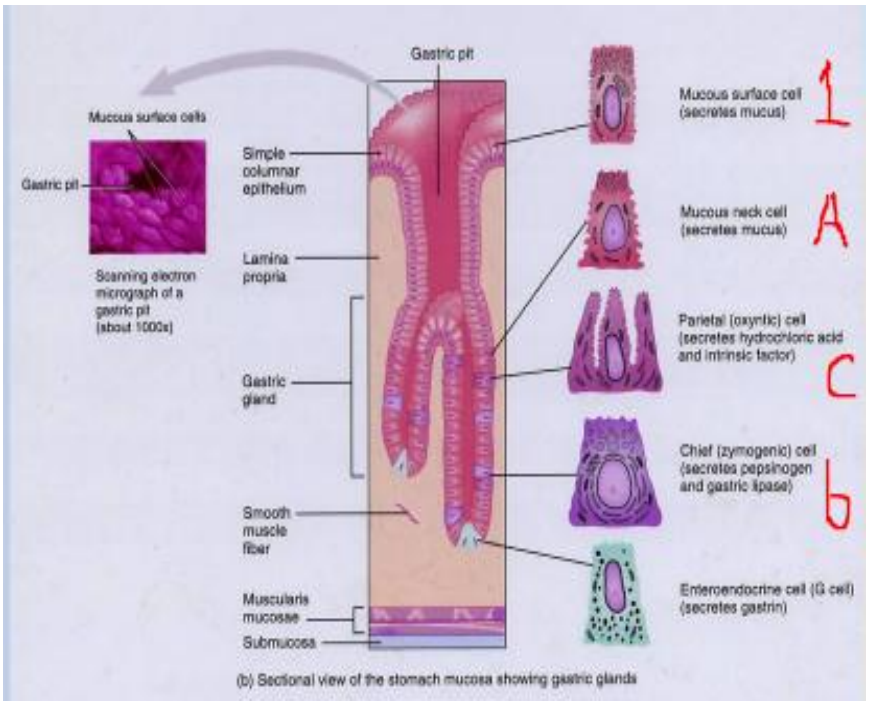
Cells of gastric secretion:

1- Mucus secreting cells (mucus surface cells): line all the stomach surface. These cells secret viscid mucus, which may have the following functions:

- Lubricating functions that protect against mechanical injury.
- The secreted mucus lines the mucosa; preventing proteolytic enzymes to act on the mucosa (protective).
- The secreted mucus has an alkaline pH, which neutralizes HCl and protects the mucosa from the chemical injury caused by HCl.

2- Tubular glands, Oxyntic (gastric glands): HCl forming glands. Secrete HCl, Intrinsic factor and Mucus.

These glands are composed of 3 types of cells:
a- Mucus neck cells: secrete **mucus** and some pepsinogen and are found at the neck of the gland.



b- Peptic or chief cells: secrete large amount of pepsinogen which is converted into pepsin that is important for digestion of proteins.
NOTE: some people say that these cells secrete lipases, but we don't have bulk digestion of fat in stomach neither digestion of carbohydrates, we mainly have protein digestion.

c- Parietal or oxyntic cells secrete **HCl** and **intrinsic factor (for absorption of B12)**. They have invaginations at their apical membrane forming canaliculi. Some people who have gastric problems (atrophy, gastritis….) may have anemia, because B12 is important for RBC maturation.

d- G cells: release a hormone that starts with G, which is Gastrin. They are found at the bottom of the gland and release hormones for regulation.

GOOD LUCK