# Digestive System

University of Jordan

Faculty of Medicine

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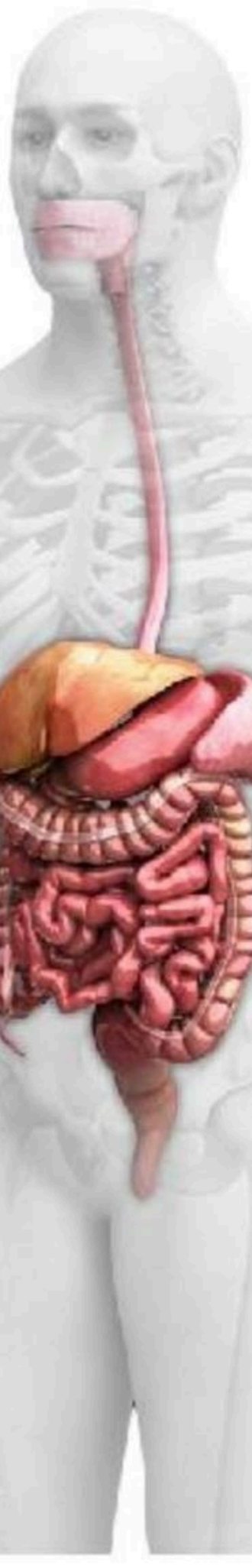

***Sheet #:*** 2

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# Introduction to the GI physiology-2

- We have started talking about GI physiology, we have seen the main physiological processes that are taking place there including motility, secretion, digestion and absorption, and we have also seen the functional structures involved in these functions.

## - Smooth muscle cells; their distribution and functions:

- We have talked about smooth muscle cells and their distribution along the wall of the tube, the main layer is the outer part layer forming two sub-layers which are **circular (innermost)** and **longitudinal (outermost),** we also have between the mucosa and submucosa another muscular layer which is **muscularis mucosa**, and each one of these layers performs certain function, so the circular layer when contracts then the diameter of the tube will decrease and with its relaxation the diameter will increase. While the contraction in the longitudinal layer will result in shortening and elongation of the tube. You will see all of these aspects in the lab.

## - The control systems over the GI activities:

- We have also control systems; the neural which is achieved by enteric and autonomic nervous systems, also we have hormonal control, we have a lot of endocrine cells which release hormones that are acting either along the GI tube or having a general (systemic effect) among the body.

## - The vascularization along the GI:

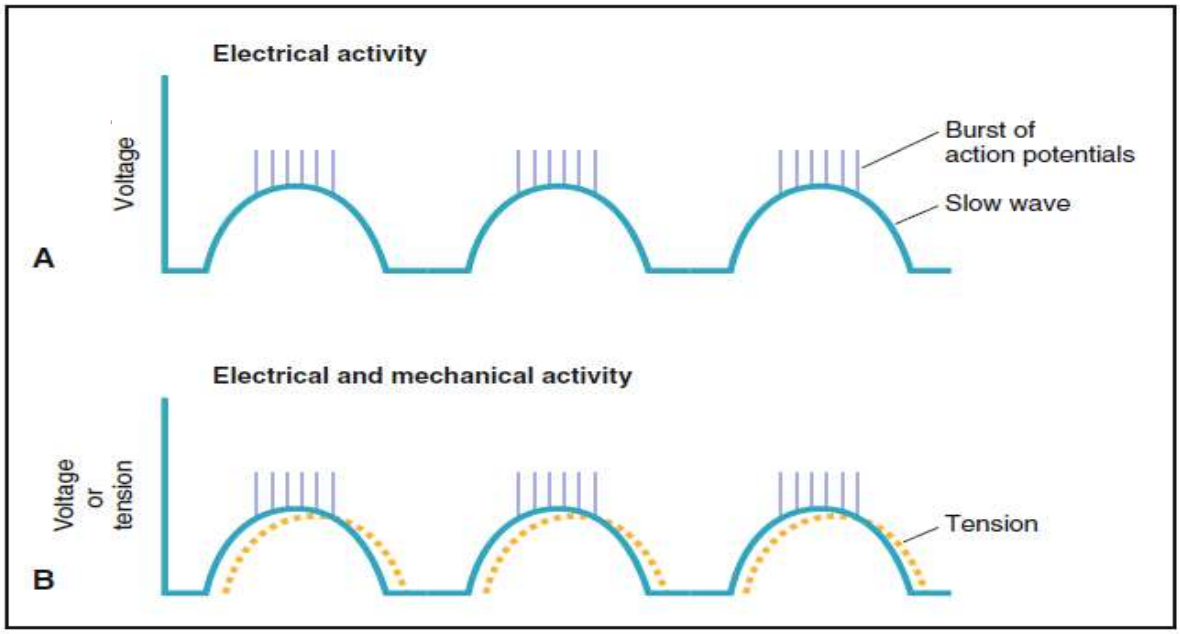
- In addition to that, as functional structures we have also blood flow through vessels which can change according to the GIT activity, **where we have that flow???** Actually at the **submucosa, but** in some organs such as **small intestine** we have good vascularization in the **mucosa** that make it as the specialized organ in the absorption, and in the digestion as well.

## - Smooth muscle cells and action potential generation:

- We said that we have these muscle cells display electrical activity, and the resting membrane potential is called **slow waves (not constant), *we have undulation;*** those are not true action potentials.

If the electrical activity isn't reaching to threshold, at this case **only**, there is no generation of an action potentials (spikes), so **no** change in the tension will happen in that muscle, but that doesn't happen at physiological conditions, maybe between meals sometimes but not always. In addition, if the body is under general anesthesia then the electrical activity may be affected.

So, once we have these spikes developed (usually all the time we are developing these spikes), we are generating **Phasic Contraction.**



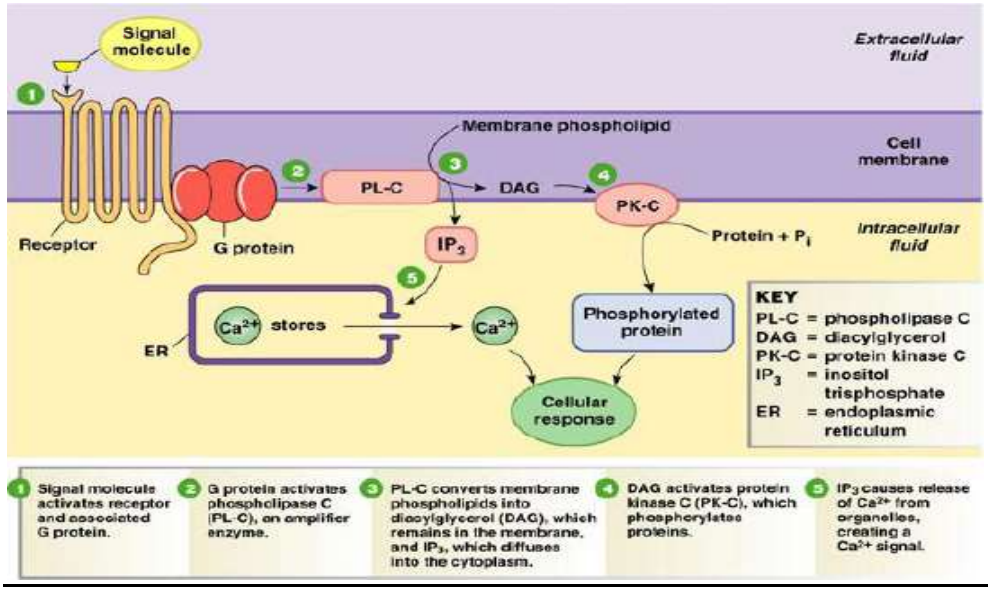

## - Phasic (rhythmic) contration:

- So, the rhythm of these phasic contractions follows the rhythm of slow wave at each organ, which means that each slow wave will generate spikes to get these contractions. So, once we have spikes, we are activating Ca++ channels at each sarcolemma and we are increasing the $Ca^{2+}$ conc. inside, resulting in a contraction by the activation of the kinase enzyme. We have also as functional structures in between cells **gap junctions**.

## - Chemical control over the smooth muscle cells:

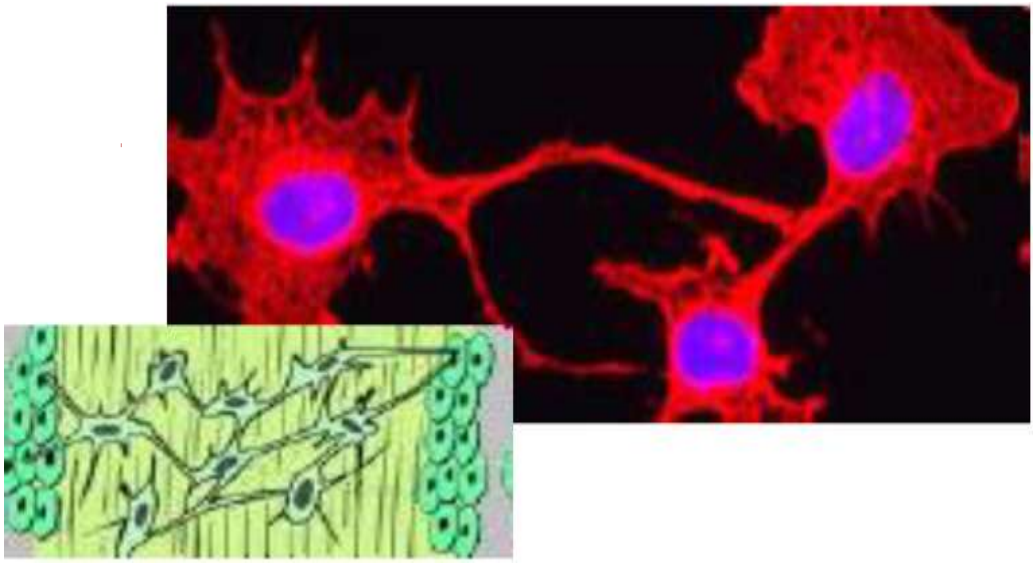
- We have also as chemical control for smooth muscle cells; we have a lot of neurotransmitters released, hormones released, even inflammatory mediators (factors) can affect the GI activities, and this chemical control mainly regulates the tonic contraction (we have certain tension; contraction resulted from slow waves and spikes does not start from zero tension because of the existence of tonic contraction mediated by chemical control), so the muscles of the GIT are

not fully relaxed actually; we have certain tension which is set by a chemical control.




## - Interstitial cells of cajal:

- In addition, we have **interstitial cells of cajal** which are connected with each other by gap junctions and **connected with smooth muscle cells by gap junctions**. ***The ratio of interstitial cells of cajal to smooth muscle cells*** *is* **one to fifty 1/50 (for each fifty smooth muscle cells there is one interstitial cell for them)**, ***these cells aren't neurons or muscle cells*** so they **aren't contractile cells**. We have some inputs characterized to reach these interstitial cells of cajal. It is not known if their activity is under neural control. They generate their action potentials by themselves and that action potential they are generating is at **plateau**. It is explained that their action potential is developed by metabolic activities inside the cells but they are not known. **Interstitial cells of Cajal** are considered as **pacemaker cells** for the GI smooth muscles function.



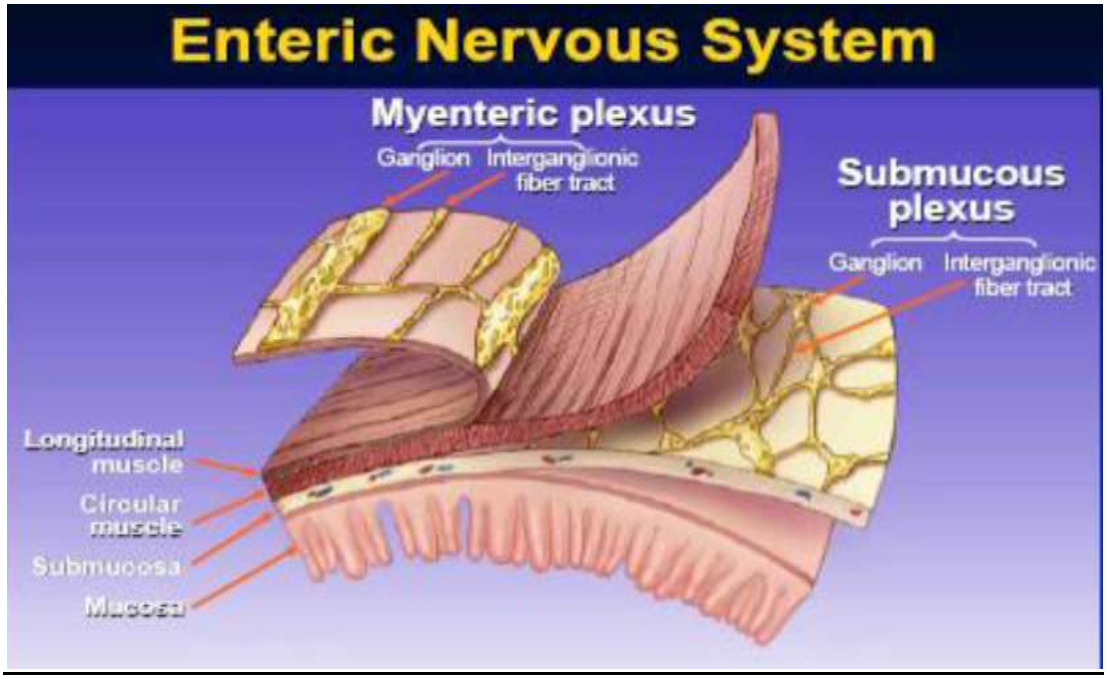
## - Secretory cells among the GIT:

- In addition we have as functional structures **secretory cells**, they have are classified into different organizations, starting from **solitary cells** *dispersed all over the mucosa*, you can also find some cells grouped together to form **pits (simple glands)** *within the* ***mucosa***, and at third organization you can have more cells grouped together to form glands *within the* ***submucosa*** which are called **complex (compound) glands**. So, simple glands (pits) are located within the **mucosa** and the compound (complex) glands are within the **submucosa.** In addition we can have more cells grouped together to form organs **located outside** the GI tube, such as ***liver***, ***pancreas***, and ***salivary glands*** all of them as an organs. We will talk about them in details later.

## - Enteric nervous system and its parts (plexuses):

- Enteric nervous system which is involved in the control, actually we have two main layers where we are finding a network of neurons along the GI tube, one is between the longitudinal and circular layer and is called **(myenteric plexus)** and from their location, **what are the suggested functions of these neurons??**

Actually they are involved in controlling **motility** (contractions), and the Second plexus is in the submucosa , it is called **(submcosal plexus)** mainly involved in controlling **secretions,** we can also control blood flow, activity of some glands**.** But don't forget we can have some inter-talk between two systems (plexuses); we have enteric neurons that are passing between the two systems.




## - Do we have brain on our stomach???

- Amazingly, if we are analyzing **the neurons of the enteric nervous system** , are finding almost **more neurons than if not equal to those found in the spinal cord**!! So it is described as **the mini-brain of the GIT** that *can function normally without any external innervations*. The activity of these neurons can have an inhibitory or excitatory effect, in this case excitatory means that they stimulate the smooth muscle cells to contract or some glands to secrete. While inhibitory is a reversal effect to the excitatory.

## - The classification of neurons is based on their NT content:

- From the view of their NT contents we have at least fifteen types of neurons, some neurons release Ach, other release **SP (substance P), VIP** (***vasoactive intestinal peptide***); from its name it is involved in **controlling blood flow** by causing **vasodilatation** and increasing blood flow, also we have **CGRP** (***calcitonin gene related peptide***), **GRP** ***(Gastrin Releasing Peptide),*** and so on.

## - Remember:

- **What is the difference between the NTs, hormones, and factors??** The difference is that hormones are released from endocrine cells, but NT are released from neurons which differ from endocrine cells, whereas factors are ligands but they are not yet characterized as either hormones or NT.

## - The autonomic nervous system and its function over the GI:

- Also we have the autonomic nervous system which is involved in controlling of the GI activities, in which includes the sympathetic and parasympathetic.

1. **Sympathetic**: its effect over GI movement and secretion is an inhibitory, and the effect over the secretion is indirectly achieved by decreasing the blood flow (by causing vasoconstriction), subsequently, the glands will not have an available water and electrolytes, so the secretion is inhibited **indirectly**.
2. **Parasympathetic**: because we have a lot of muscarinic receptors along the GIT, and the activation of these receptors results in the activation of the movement (motility). In addition we are getting activation of secretion. **What is the effect over the blood vessels?? Does it Increase the blood flow**

**directly?? No**, actually, there is **no** effect from the parasympathetic over the blood vessels. **BUT** we have an ***indirect*** effect of the parasympathetic over the blood vessels. **How does that happen??** Once you have parasympathetic effect over the secretary cells, ***then this will result in the releasing of a factors from these cells*** causing **vasodilatation** and increasing the blood flow resulting in *higher availability of water and electrolytes* for the secretory cells to increase their production.

## - To summarize the controlling systems over the GI:

- So, to summarize, we have as a controlling systems over the GIT;

1) **The enteric nervous system** (ENS); **the myenteric and the submucosal plexuses**, which act on the smooth muscle cells, secretory cells, and some endocrince cells, as well as over blood vessels,
2) **The autonomic nervous system** (ANS); **sympathetic and parasympathetic**, and their effect may be **direct OR indirect** over their **effector structures** (There is also indirect effect on them by changing the activities of **the enteric nuerons** by the **autonomic nervous system**).

## - The hormonal role over the GI:

- As hormones, there are a lot of hormones released by endocrine cells, such as **gastrin**, **Chlecystokinin (CCK), secretin,** and **GIP (gastric inhibitory peptide)** *also that hormone is abbreviated from* **(glucose-dependent insulinotropic polypeptide),** from its name what is its function?? We can get decrease in gastric functions, ***but the main effect***, actually, is to **stimulate secretion of insulin**, by this hormone, we are preparing the body, once you are eating a meal, you aren't waiting to get absorption of glucose just when its conc.

increases in the blood to start secretion of insulin, we actually release insulin before having high conc. of glucose in interstitial of fluids, so that is achieved by the later hormone (GIP) which is **acting over β-cells in the pancreas** to increase insulin release. In addition, we have other hormones such as **Glucagon-like peptide-1 (GLP-1), Motilin, Ghrelin, Amylin, Enterostatin, Neuropeptide Y (NPY), polypeptide YY, Pancreatic polypeptide, Somatostatin, Neurotensin, *Thyrotropin releasing hormone (TRH)*** *which is released by hypothalamus to stimulate the releasing of* ***thyroid stimulating hormone (TSH).*** In addition, we also have **Adrenocorticotropic hormone ACTH**.

## - Functions of the hormones along the GIT:

- Functions of the hormones along the GIT for most of them are unknown yet, unless, we know about some of them. We can summarize their general functions as:

1) Control of **motility**, but they aren't the main controllers.
2) Control of **secretion**
3) Control of **blood flow**
4) Regulation of **food intake**, at the last lecture we will talk about how we regulate food intake, sometimes we feel hungry, sometimes we fell satiety, for sure we have some of these hormones involved in controlling these behaviors.
5) Regulation of **metabolic activities in the body,** e.g: **TRH** which results finally in the releasing of thyroid hormones, ***also ACTH is another example that has metbolic effects***.

In addition, we have a good blood supply over the GIT and it is very well regulated, so once you are eating a meal, the blood flow will increase; and once you stop eating or between meals (when you finish all digestive and secretory activities), then the blood flow will decrease. So, we have very good

control over the blood flow toward the GIT that can be achieved by some hormones, like **secretin** and **CCK**, also by some **NTs, like VIP, substance P, and CGRP,** also we can have **vasodilators** changing the blood flow, if you remember that we said that secretory cells can be stimulated to release **Kinins (Kallidin, Bradykinin),** also we have a general control over the blood flow, which can be achieved as a result of **decrease in the O2 concentration** resulting in increase in the blood flow, and that is a general effect which can be found in any tissue when it has reduction in the O2 conc. levels in order to replenish that reduction. How does it achieved?? Probably by increasing the **conc. of adenosine**, which can act **directly** over the blood vessels to cause vasodilatation. Also, ANS can have some effects over the blood flow that we have discussed.

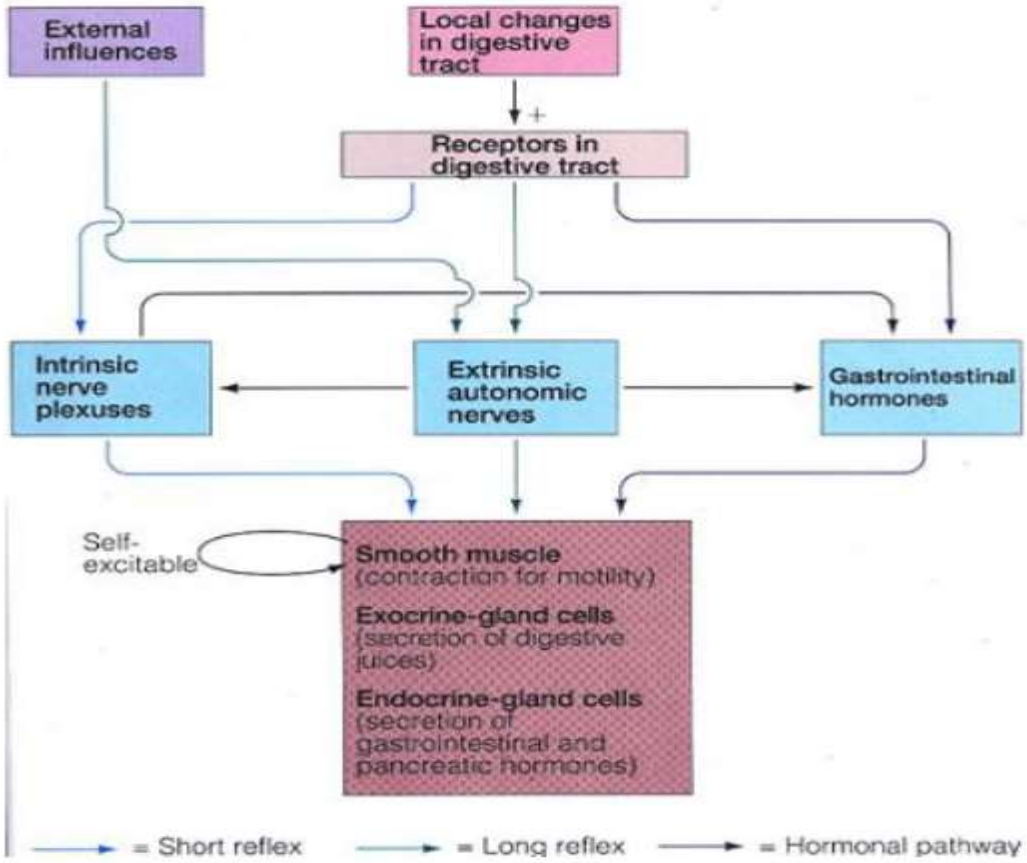
- To summarize everything, we have GI hormones that can change the activity of effector cells which can be smooth muscle cells, secretory cells, or other endocrine cells; in addition we have the effects of intrinsic and extrinsic nervous systems.

## - The role of the Extrinsic and Intrinsic nervous systems:

- The doctor said that, actually we need to introduce more than one term to facilitate the reading from different references, so what do we mean by an intrinsic nervous system?? It refers to the enteric nervous system, so it means something inside the GIT. While extrinsic nervous system refers to the autonomic nervous system. So, the intrinsic reflexes mean that we have reflexes over the enteric nervous system, meaning that we have afferent fibers (neurons) and efferent fibers through the enteric nervous system. While the extrinsic reflexes refers to the autonomic nervous system reflexes, meaning that we have afferent fibers toward the central nervous system, toward the nuclei of the autonomic nervous system, and then we have efferent fibers back toward the GIT to change its activities. ***How can we change the activity of the intrinsic nervous system??*** **By local changes** (such as **distention of the tube when you eat)** and you stimulate the secretion by that distention. And by controling the activity of enteric nervous system extrinsic nervous system, extrinsic nervous

system can cause changes on the function of GI, and by these changes we also start the releasing of hormones from endocrine cells.

- We also have **external influences** (something from outside the body), what happens to your GI activities if you smell a food, look to a food, or hear someone talking about food?? They will increase by those external influences ***through the ANS***, which can change the activities of all the other structures og the GI.




## - Finally:

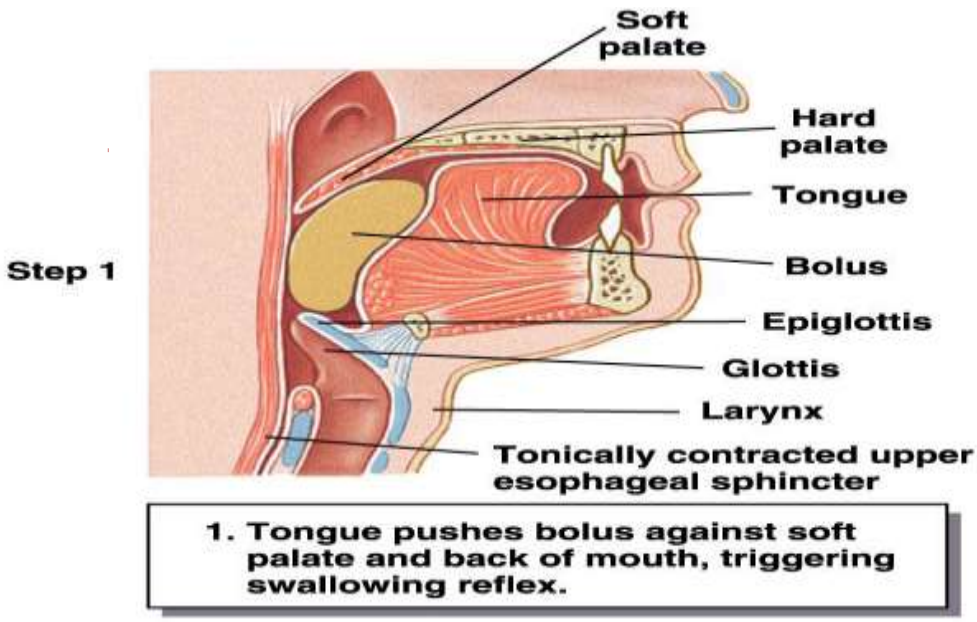
- Always remember that the enteric nervous system isn't a part of the ANS, but we have an inter-talk between those later systems, by meaning that some neurons from the autonomic nervous system can change the activity of some neurons in the enteric one. *Indeed, the enteric nervous system is considered as a part*

*of PNS (neurons, bodies, axons and supporative cells outside the CNS), but yet it isn't a part of the ANS*, so it is considered as the **mini brain** of the GIT.
*Note: you also can find* ***glial cells*** *(example of supportive cells)* which are involved in the protection of the neurons (E.g: from pathogen insults) and are involved in providing **some neurotrophic factors** for the survival of neurons.

# GI Motility

## - Starting with voluntary movement; chewing (mastication):

- We will start with the motility that is found along the GIT, so once you have introduced a bolus of food into your mouth, **what we are doing??** We are starting the first movement which is called **Chewing** or **mastication**. Is that movement voluntary or nonvoluntary?? **Voluntary**, *but it has some reflex behaviors (some automatic behavior),* so once we have introduced that bolus into the mouth, then the drop of the lower jaw results in a ***stretch in the masticatory muscles***, *which leads to a* ***rebound contractions***, *then will be a* ***relaxation***, then another drop results in a stretch → rebound contractions, and then *we enter in this automatic reflex,* what are the effects of these movements over the food that you have taken?? We are start grinding of this food, in addition to mixing of this bolus of food with saliva, you will see the salivary secretions later on, and one of the components of that saliva is **mucus**, so we are lubricating that bolus of food to facilitate further processes of movement of that food.




## - Second type of movement; swallowing (deglutition):

- Once we have finished chewing or mastication, then we perform the second movement, which is **swallowing** or **deglutition**, the ***first part*** *of this process is* ***voluntarily***, **how does it take place??** As you know that the tongue pushes the bolus of food into the pharynx, now we have ***distension of the pharynx***, and once that occurs, then the rest of that process (deglutition or swallowing) will continue as an **involuntary reflex.**

## - Deglutition (swallowing) as an involuntary reflex.

- As you know that the pharynx has many openings; one towards the nasal cavity, one towards the trachea, and one towards the esophagus, that one towards the esophagus is guarded by sphincter, which is **the upper esophageal sphincter, what is the function of the sphincters??** They prevent the back flow toward the opening (to achieve the **unidirectionality**), so higher representation of the **circular layer**, with **higher tone** in this case, so keeping this opening closed, so what we are doing with these openings, we are closing the openings towards the nasal cavity by the **soft palate**, also we are closing the opening towards the trachea by **glottis, what happens to the muscle of the pharynx?? Contract**. In addition, we have **relaxation of the upper esophageal**

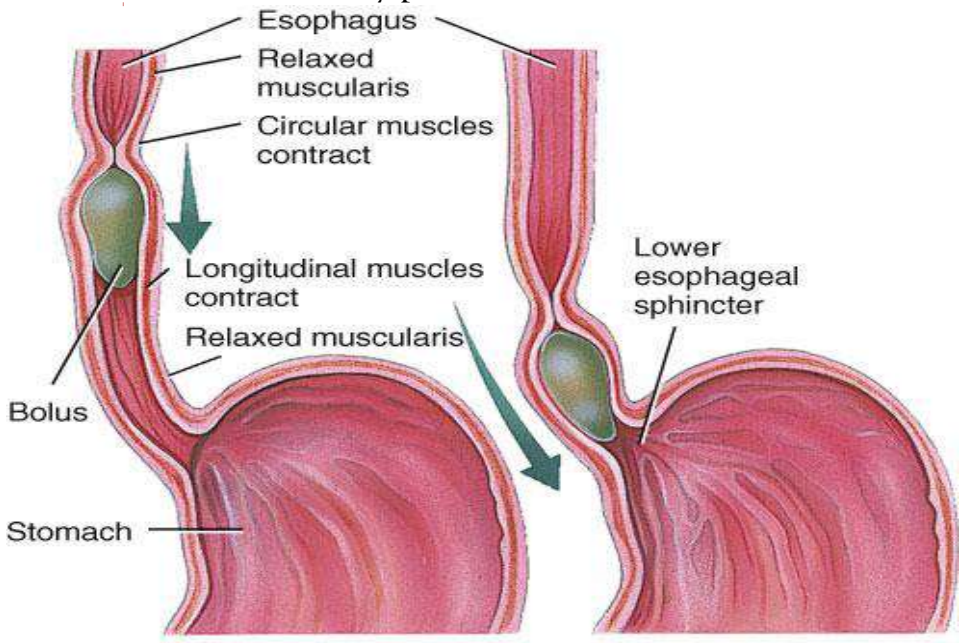
**sphincter**. ****remember that all of these processes are reflexes (involuntary).** So, once we have this bolus of food reached to pharynx, then we have a lot of reflexes those are taking place to get contraction, and at the same times we **are closing the epiglottis**, the **nasal cavity (by soft palate)**, and get **relaxation of the upper esophageal sphincter**, and once we have finished those actions, then we are forcing the bolus of food into the esophagus by the contraction that we have.

- So we can say that the first phase, or the first part of the swallowing is voluntary, then it is followed by the pharyngeal part of swallowing and esophageal phase of swallowing, also the movement of the food in the esophagus is a part of swallowing.

## - Esophageal peristaltic contraction:

- So, after forcing the food towards the esophagus, then along the esophagus we are continuing this movement at a certain velocity, so **what happens exactly in the esophagus to get the movement of that bolus of food**?? Actually, we have two types of motor activities there, which are called **esophageal peristaltic contractions**, actually, it is one type, but divided into two types; **both** have the same pattern, meaning that the same type of contraction. **This bolus of food by contraction up, and relaxation down is forced to move along the esophagus**. But we have two types of peristaltic contractions; one type is called **primary esophageal peristaltic contraction,** and another type is called **secondary esophageal peristaltic contraction**, both are have the same pattern, **so what the difference is???** The difference is in **"The point of initiation"**; the primary one as you remember we have been starting with contraction of the pharynx, if that wave of contraction behind the bolus of food is continuing with the contraction that we have in the pharynx as a wave along the esophagus, then we are falling it ***by the primary esophageal peristaltic contraction***, **but** sometimes happens that these primary peristaltic contractions are failing to move the bolus of food, so **what happens to that bolus??** It will remain stuck at the esophagus, **have we to wait for another wave of contraction to start from the pharynx and then continue to get that bolus to**

**move?? No**, the esophagus itself now can initiate reflexes to get generation of the movement or the peristaltic contraction again, and in this case we call this contraction as secondary peristaltic contraction.




## - To summarize:

- So that is the peristaltic contraction, maybe some people are asking now, **why we are getting <u>contraction up</u>, and <u>relaxation down</u> along that esophagus???** As you know that the enteric nervous system have an excitatory neurons and an inhibitory neurons along the whole GI system, and most of **the axons of the excitatory neurons** are **projecting up**, in contrast to the **axons of the inhibitory neurons** that are **projecting down**, so at anytime you have an excitation at any point **by distention what happens up to that excitation?? <u>Contraction</u>**. And **what happens down?? <u>Relaxation</u>.** Actually, that is the law of the gap that we have by this organization of the neurons of the enteric nervous system.

## - Dysphagea:

- In certain situations those movements fail to conduct the bolus of food towards the stomach, in this case, this will result in **<u>(dysphagea)</u>** that could be

of **motor origin** for example, in this case we have no good motor activities along the esophagus, or the dysphagea could be of obstructive origin (obstruction along the esophagus) in which prevents the movement the bolus of food along the esophagus.
Note: both types of peristaltic contraction will be affected in dysphagia condition; because they only differ in the initiation point.

## - Achalasia:

- One of the conditions in which results in this dysphagea is called **(achalasia)**, **what does lead to achalasia??** Actually, in patients with achalasia the representation of the enteric nervous system is low, and once we have less neurons of the ENS, then the peristaltic movements are less. Once we have the bolus of food reaching down the lower part of the esophagus, also the lower part of the esophagus is guarded by sphincter which is **the lower esophageal sphincter**, *by the reflexes*, this sphincter will relax **by intrinsic reflexes.** Now imagine that we have lower presentation of neurons along the lower part of the esophagus, **are we getting a good motility?? No**, so this also will result in dysphagea even that it may result in dilation of that organ by more accumulation of food (hypo-motility) and results in achalasia as a medical condition.
So that is a part of what we are talking about which results in movement of food.

## - Achalasia as an embryonic defect:

- So in that condition we have less movements of food (less motility), no relaxation of the lower esophageal sphincter because of less number of neurons found for example along the esophagus at this case, and it happens sometimes due to problems in the migration of that neuron (of ENS) **from neural crest**, resulting in less number of neurons migrating in which finally leads to that achalasia.

- We will continue with the gastric motility in the next lec. en sha2 allah.