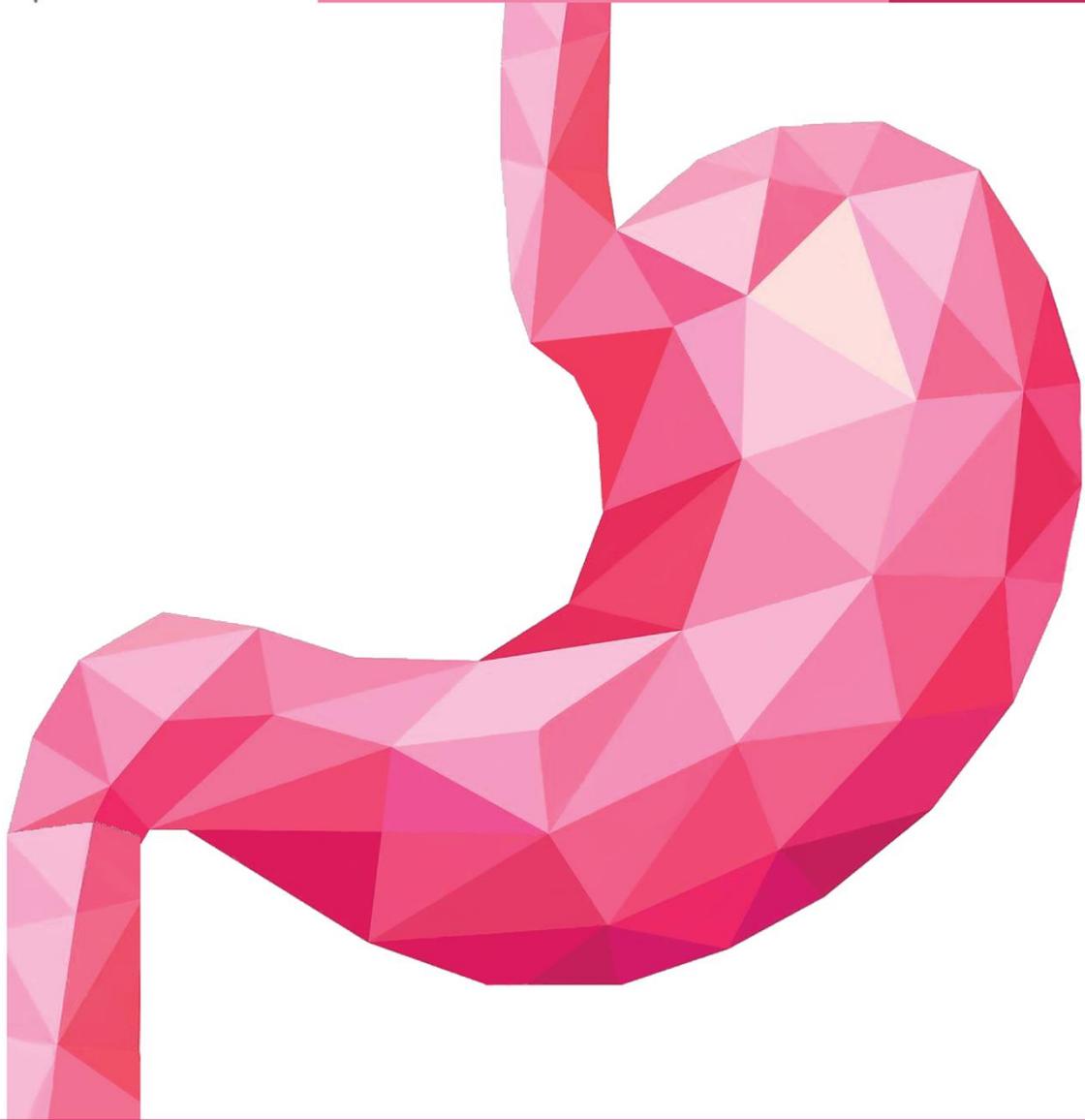




GIS

PHYSIOLOGY

1



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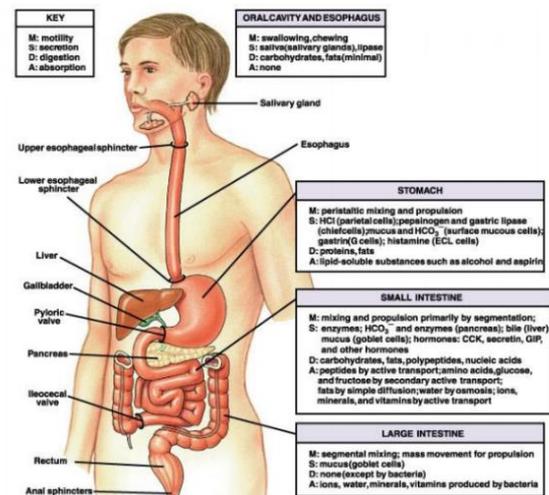
❖ Physiological processes that take place along the GI system

- 1- **Motility** (e.g. chewing, propulsion)
- 2- **Secretion** (e.g. saliva in the mouth, HCl in the stomach)
- 3- **Digestion** (e.g. proteins in stomach)
- 4- **Absorption**

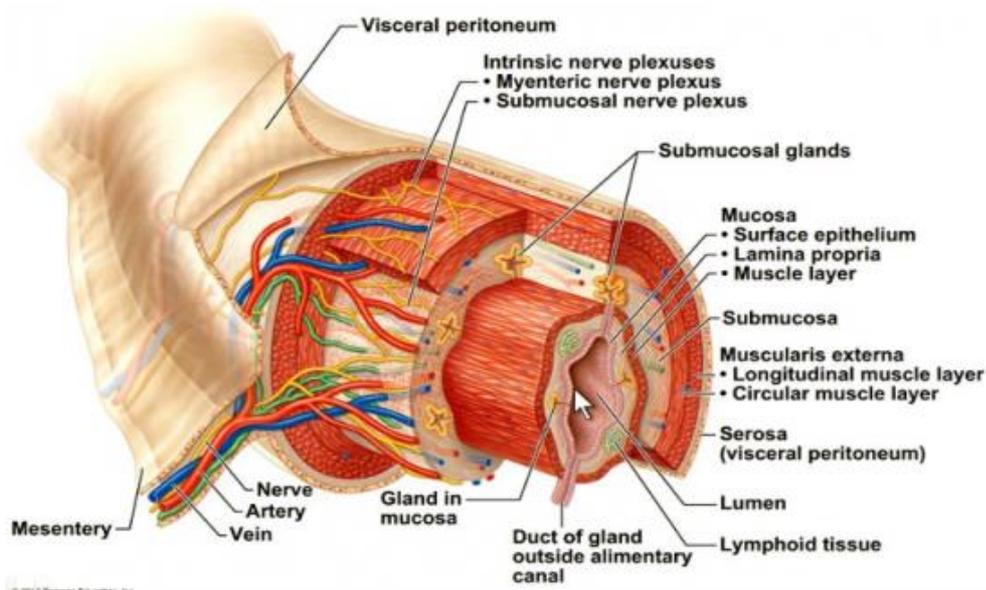
✚ These 4 processes will be explained throughout this session.

➤ To do these processes, we need to have functional structures. These structures are :-

- 1- **Smooth muscle cells**
- 2- **Interstitial cells of cajal**
- 3- **Secretory cells**



✓ But first, you need to know that we are dealing with GI system as one tube that is composed of three main layers :



*This picture was taken from the internet because the picture in the slides is not clear

- 1- **Muscular layer (outermost)**, which is divided into two sub-layers
 - a- **Longitudinal layer (outer)**, which runs along the tube axis, and it controls the length of the tube
 - b- **Circulars layer (inner)**, which runs at the circumference of the tube and controls the diameter of the tube
- 2- **Submucosa**
- 3- **Mucosa (innermost)**

➤ In addition to these layers, we have a very thin layer in between the mucosa and submucosal layers which is called **muscularis mucosa**. This layer is involved in :-

 - 1- Emptying the content of the glands.
 - 2- Controlling the folds of the mucosa which are not constant.

❖ Other related structures :

1- Control systems of GI functions

➤ **Neural control** :-

a- Enteric nervous system (**intrinsic** nervous system)

b- Autonomic nervous system (**extrinsic** nervous system)

➤ **Hormonal control** :-

GI endocrine

2- Blood flow to the GI, which needs to be controlled. It is increased when we have high activity and lowered in case of lower activity. We have good vascularization at the level of submucosal layer, and we have a good vascularization at certain sites in the mucosa, like the intestines, which is important for the process of absorption.

❖ **Smooth muscle cells (SMCs)** :-

Found in two locations:-

➤ Outermost layer

➤ Muscularis mucosa

*Structurally smooth muscle cells are composed of dense bodies and thick and thin filaments in between (just like other smooth muscle cells), which they need calcium to contract.

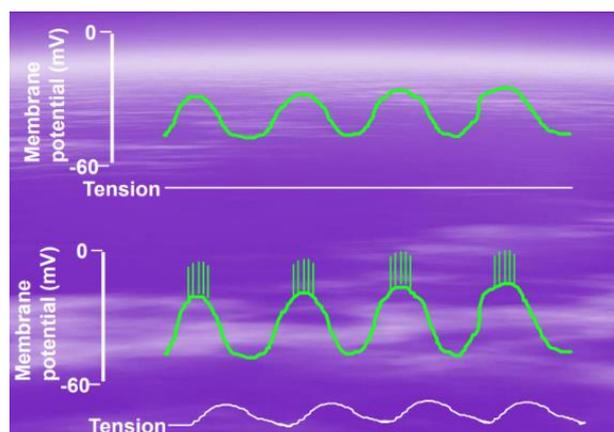
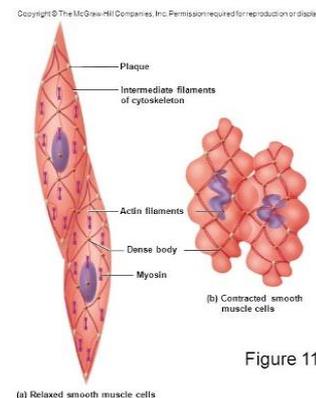
But they differ from other SMC in the pathway of increasing the concentration on calcium intracellular. Calcium concentrations are regulated in two ways (recall intracellular and extracellular ways).

➤ **Electrical activity**:-

SMC's resting membrane potential is a special. It is changing all the time (depolarization – repolarization), forming what is called **slow waves**.

Slow waves are not true action potential, and they are necessary for the generation of the true action potential (spike potential). These slow waves will eventually lead to the generation of enough stimulus to reach threshold, thus, producing contraction of the muscle.

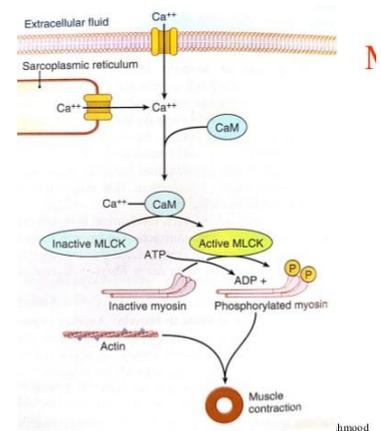
Contraction of Smooth Muscle



****Phasic or rhythmic contraction:** - the processes of the contraction and relaxation of SMC in the GIT. These are processes that are **controlled by electrical control**.

✓ Intracellular pathway of phasic contraction:-

Upon generating a spike potential, opening of calcium channels will be induced in the membrane, leading to an increase in the internal concentration of calcium. Intracellular calcium will bind to calmodulin to form calcium-calmodulin complex, that will activate myosin light chain kinase. Myosin light chain kinase will phosphorylate myosin, leading to the contraction of the cell.



✚ Gap junction between SMCs mediate “**functional syncytium**”, which means that SMCs are contracting and relaxing together by the spreading of action potential between a group of SMCs (as a one unit).

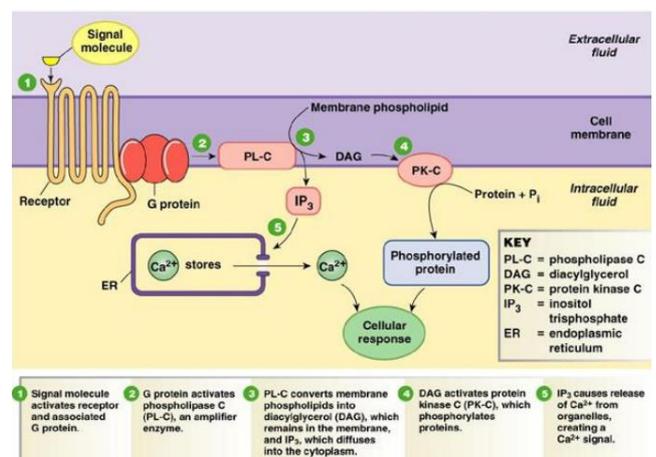
➤ **Chemical control :-**

In addition to electrical control, we also have chemical control, which is also involved in the contractions in smooth muscles.

Pathway of chemical control of SMCs:-

- 1) Binding of signaling molecule to its receptor (e.g. muscarinic receptor)
- 2) Activating of phospholipase-C
- 3) PLC will produce IP₃ which will lead to the release of intracellular calcium and the contraction on the SMC.

****Chemical control is responsible of tonic contraction.**



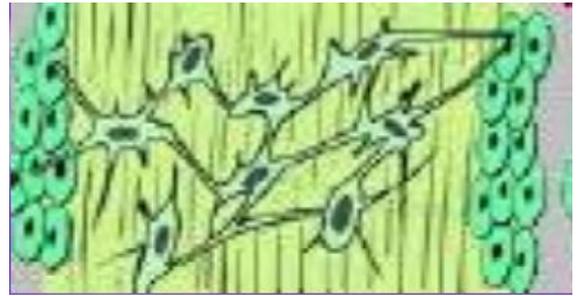
✚ Difference between phasic and tonic contraction:-

When there is no electrical control (spikes), a specific tension is maintained by hormonal (chemical) control. This tension can be higher or lower according to excitatory and inhibitory neurotransmitters (tonic contraction). Anything more than the baseline of tension will induce more or less contractions, which is the **phasic contraction that is controlled electrically**.

➤ Tonic contraction is the cause of the difference in the length of small intestine anatomically and in vivo (small intestines are 3 meters in length inside the body. Without tonic contractions, it stretches to 6 meters).

❖ Interstitial cells of cajal (ICCs) :-

- These cells look like neurons but they are not. They are not smooth muscle cells either.
- They have many spikes.
- They are connected with each other by gap junctions.
- They are connected to SMC by gap junctions by the spikes.
- Their function depends on their **ability to generate action potential in plateau** from resting membrane potential all of sudden in a rhythmic way.
- The mechanism of generating action potential is still unknown, but it is believed that it's the result of some metabolic reactions inside the cell.
- **The generation of action potential will lead to the formation of slow waves**, and once SMCs reach threshold they will form spikes.
- **When these cells return to resting potential, this will lead to re-polarization of SMCs.**
- Until now there is no proof there is neural control over there activity, but it has been found that there is some fibers from the enteric nervous system reaching near proximity of these cells. It's not known if they are involved in there function.
- Because of their function they are considered to be the pacemaker cells of the GI tract.
- ICCs to SMCs ratio is (**1:50**), one ICC cell for each 50 SMCs.



❖ Secretory cells :-

Some of these cells secrete mucous and some of them secrete serous, and they are divided into:-

- **Solitary cells** (simple glands)
This type of cells is dispersed all over the mucosa. We can find a collection of these cells together, but still, only confined within the mucosa.
- **Pits** (the doctor didn't mention this one)
- **Compound glands** (complex glands)
More secretory cells grouped together located within Submucosa.
- **Secretory organs**
More complex structures that are found outside the GI tract (e.g. pancreas).
- Secretory cells release their secretions into the lumen throughout duct systems.

❖ **Enteric nervous system:-**

➤ We have a huge number of neurons along the GI tract that form ganglions, which is divided into two plexuses according to their location :-

1. **Myenteric plexus:-**

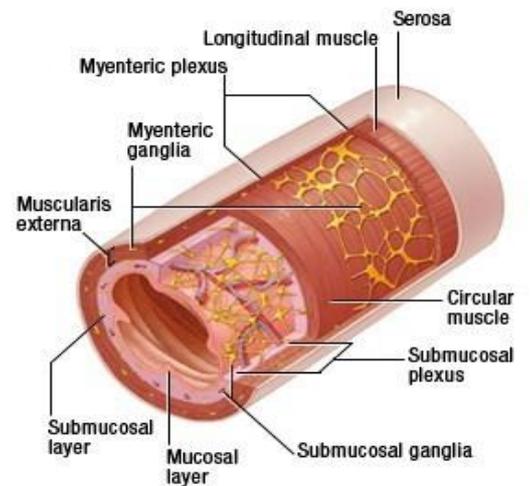
That is found between longitudinal and circular smooth muscle cells, and it's involved in the movement along the GI tract.

2. **Submucosal plexus:-**

That is found in the Submucosa, and it's involved in controlling secretion

➤ We also have inter-neurons connecting the two plexuses together.

➤ This system is also called the **brain of the GI tract**, and it can control the GI system without the autonomic nervous system.



➤ Enteric neurons :-

- **Excitatory neurons** that stimulate the contractions of SMCs and secretory cells.
- **Inhibitory neurons** that inhibit the SMCs and secretory cells.

➤ Over 15 types of neurotransmitter have been characterized along this system

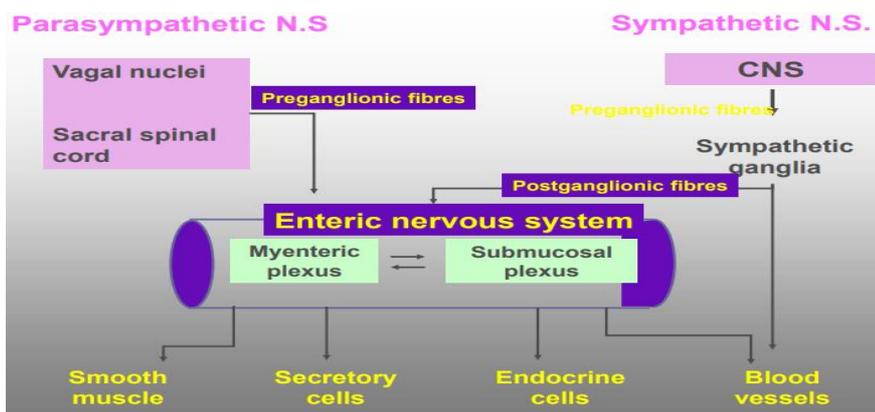
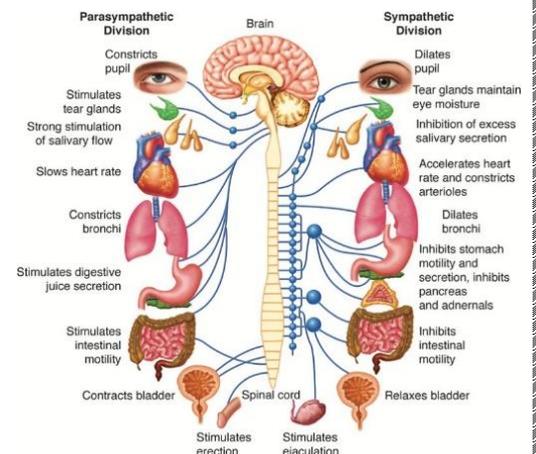
- **Ach.**
- **SP** (substance P).
- **VIP** (vasoactive intestinal peptide), involved in the control of blood flow, it cause vasodilation.
- **CGRP** (calcitonin gene related peptide).
- **GRP** (gastrin releasing peptide). Etc...

❖ **Autonomic nervous system :-**

➤ Involved in the control of the GI tract by its two divisions (sympathetic, parasympathetic)

➤ The parasympathetic neurons that are involved in the control of GI tract are

- **Vagus nerve**
- **Neurons form sacral region**



❖ Enteric endocrine system

- Form endocrine view GI system is considered the **largest endocrine system**.
- A lot of hormones are released by these cells, which are dispersed along the GI tract.
- These hormones are :-
 - **Gastrin**
 - **Cholecystokinin (CCK)**
 - **Secretin**
 - **GIP** (gastric inhibitory peptide) or (glucose dependent insulinotropic polypeptide), which is involved in **inhibition of gastric activity**, and in **controlling the release of insulin**.
- Other hormones that doctor did not focus on them:-
Glucagon-like peptide-1(GLP-1), Motilin, Ghrelin, Amylin, Enterostatin, Neuropeptide Y (NPY), polypeptide YY, Pancreatic polypeptide which is closely related to polypeptide YY and NPY Somatostatin, Neurotensin, Thyrotropin releasing hormone (TRH), Adrenocorticotrophic hormone ACTH.
- **Function of hormones :-**
 - **Control of motility**
 - **Control of secretion**
 - **Control of blood flow**
 - **Regulation of food intake** (e.g. neuropeptide Y)
 - **Regulation of metabolic activities in the body** (e.g. thyrotropin releasing hormone, ACTH)

❖ Blood flow of the GI :-

- It is strictly controlled by:
 - **Hormones** (secretin, CCK)
 - **ENS** (VIP, SP, CGRP)
 - **Vasodilators** which are secreted by some of secretory cells (kinins [kallidin, bradykinin])
 - **Decreased O₂ concentration**, as blood flow will increase in the response of the decrease of oxygen
 - **ANS**
 - ✓ Sympathetic will decrease the blood flow to the GI tract directly.
 - ✓ Parasympathetic will increase the blood flow to the GI tract indirectly.
 - ✓ Parasympathetic's action is mediated by secretory cells that secret vasodilators.

Good Luck

