physiology

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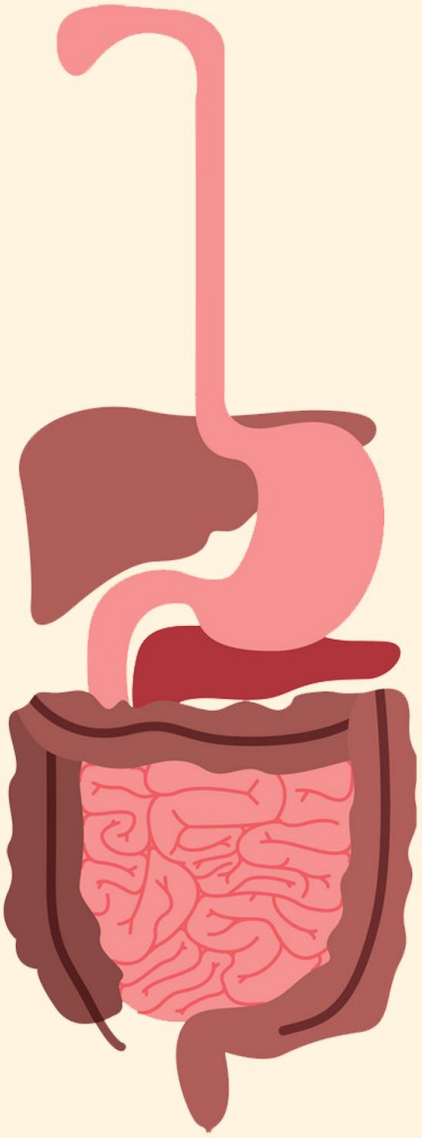


2nd system - GI

GASTROINTESTINAL PHYSIOLOGY

•The GI system is the largest system in the human body with multiple organs extending from the oral cavity to the anus separated from each other by special muscles called sphincters which normally stay tightly closed and which regulate the movement of food and food residues from one part to another.

The system is like a tube, inside this tube is the interstitial fluid which is a part of external environment not the internal environment.The four main physiological functions that take place along the GI tract are:Motility, Secretion, Digestion,Absorption

specialized cells and tissues exist along the entire alimentary tract to enhance performing these functions properly. For instance, there are special smooth muscles for each organ to perform its distinctive type of motility. Also, interstitial cells, secretory cells, etc. We will see how they are organized and so on.

The alimentary tube is composed of three main layers: the most outer layer which is the muscular one, the mucosal layer is the most inner one and submucosa in between.

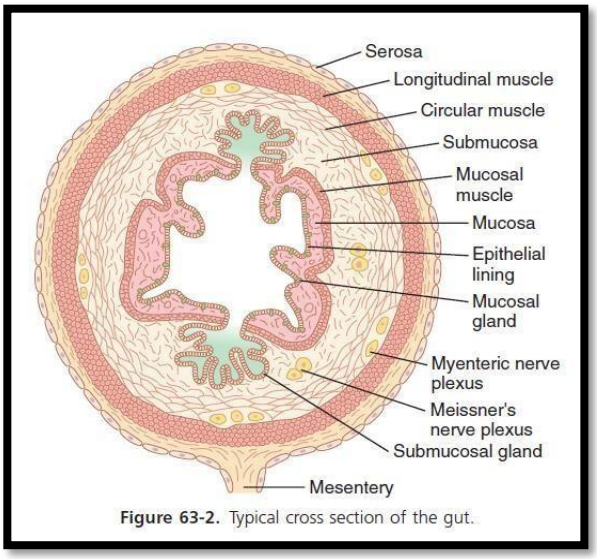


Figure 63-2. Typical cross section of the gut.

•although those are the general layers, there are still variations in the anatomical and histological structures for each organ.

•In addition, a very powerful neural control, hormonal control and blood flow are found as parts of the functional structure.

Two main systems are involved in the neural control:

1) The autonomic nervous system.

2) The enteric nervous system (ENS), which is found along the entire gut wall, starting from the esophagus and extending all the way to the anus. (so, the GI tract has its own nervous system).

-The ENS is not a part of the autonomic or the somatic nervous systems.

•with regard to the blood flow, its noteworthy that the blood flow in each area of the gastrointestinal tract, as well as in each layer of the gut wall, is directly related to the level of local activity. For example, the submucosa is highly vascularized along the entire tract, while the vascularization of mucosa is specific to distinct parts (such as small intestine) due to variations of levels functions as.

FIRSTLY, THE GASTROINTESTINAL SMOOTH MUSCLE CELLS:

Two parts of smooth muscle cells are distinguishable along the GI wall:

1) The longitudinal smooth muscles where the bundles extend, and those are the outermost part.

2) The circular layer which extends around the gut (the fibers run around the circumflex of the tube).

So, we can control the length and diameter of any part.

In addition, there is a very thin layer between the mucosa and the submucosa which is the called **muscularis mucosa**.

• Gastrointestinal smooth muscles share some general structural characteristics with others found in different places of human body like the presence of thick and thin filaments attached to the dense bodies. But the GI smooth muscles function in a different way from other smooth muscles in the body.

• One of the differences is the electrical control and the resting membrane potential.

Electrical activity of smooth muscle:
Smooth muscle cells are characterized by the presence of slow waves (undulating changes in membrane potential known as **basic electrical rhythm (BER)) and spike potentials**

Most gastrointestinal contractions occur rhythmically, and this rhythm is determined mainly by the level of these “slow waves” of smooth muscle.
Those are not action potentials. Instead, they are slow, fluctuating changes in the resting membrane potential.
True action potentials are formed automatically when the resting membrane potential of the gastrointestinal smooth muscle becomes more positive than about −40 millivolts .
the normal resting membrane potential in the smooth muscle fibers of the gut is between −50 and −60 millivolts. These true APs are called the "spike potential that appear at the peak of slow waves.

The rhythmic contraction (basic contraction) is controlled by the presence of those spikes and by the duration of AP which results in the generation of that basic contraction.

Once those spikes are generated you get contraction, while once they are over, the muscular fibers relax.

Regarding to slow waves, they can't cause muscle contraction by themselves because they don’t support the entry of calcium ions (they only cause the entry of Sodium ions).

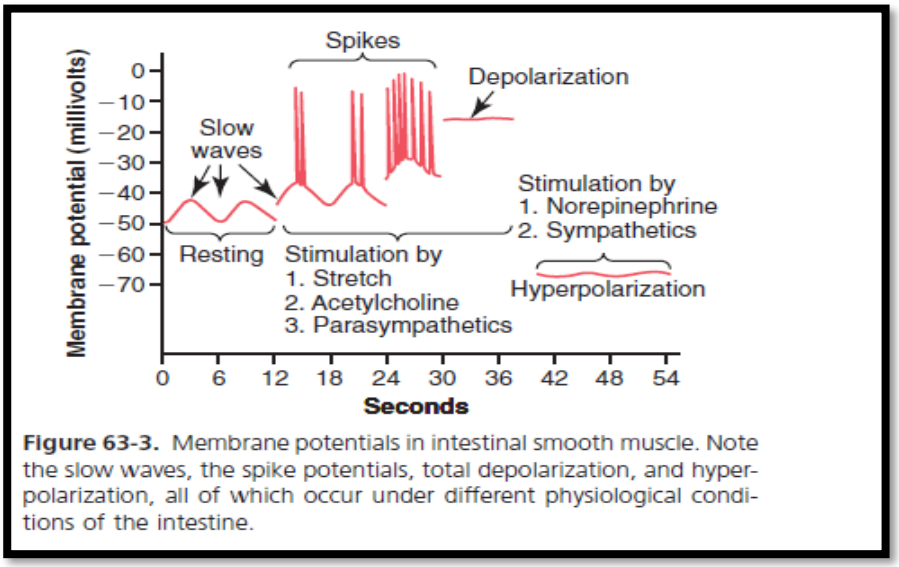
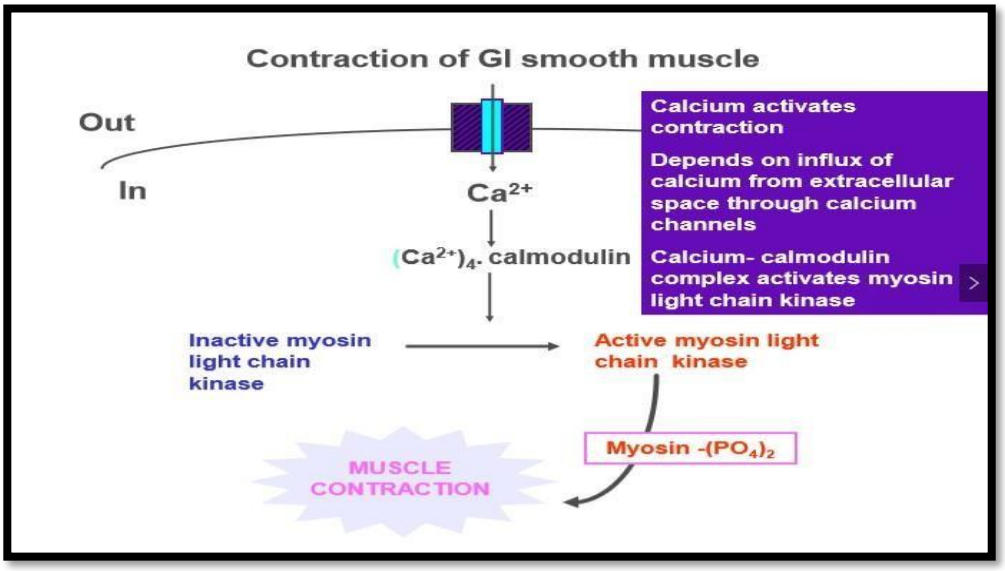


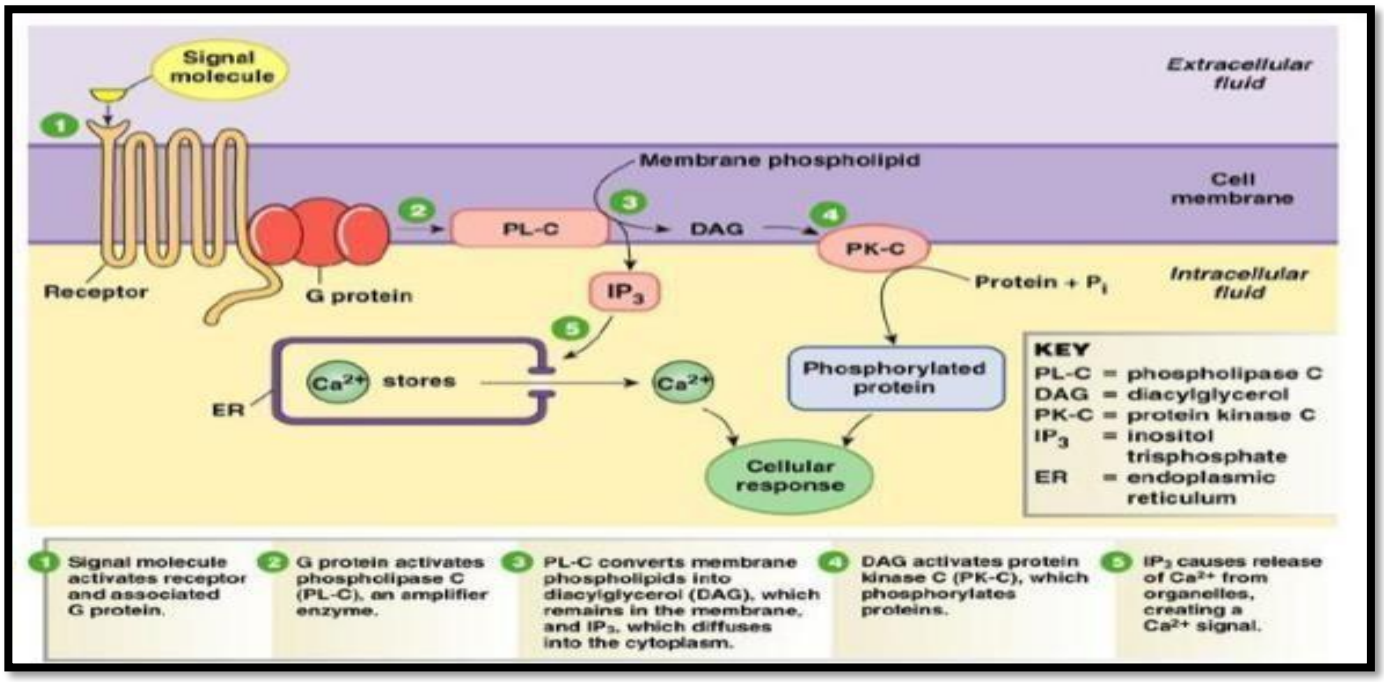
Figure 63-3. Membrane potentials in intestinal smooth muscle. Note the slow waves, the spike potentials, total depolarization, and hyperpolarization, all of which occur under different physiological conditions of the intestine.

• So How do these spikes lead to contraction?

- During the spike potentials generated at the peaks of the slow waves, significant quantities of calcium ions enter the smooth muscle fibers which act through a calmodulin control mechanism, which activates the myosin filaments and actin filaments. thereby causing the muscle to contract. This is called the" electrical control for smooth muscles activity ".



- In additions, gap junctions between smooth muscles allow low-resistance movement of ions from one muscle cell to the next. Therefore, electrical signals that initiate muscle contractions can travel readily from one fiber to the next within each bundle gap junctions also form syncytium; that is, when an action potential is elicited anywhere within the muscle mass, it generally travels in all directions in the muscle.
- In addition to "electric control" there is the chemical control, (follow the steps in the graph).



- But what type of control is achieved by chemical regulation? Importantly, there is no "zero level of contraction", instead there is the tonic contraction which is continuous and not associated with the basic electrical rhythm of the slow waves (it often lasts for several minutes or even hours). Moreover, tonic contraction often increases or decreases in intensity but it continues.

  In anatomy, small intestine length is 6 meters while in physiology, they have a difference opinion, they say it is 3 meters, why? Because of the tonic contraction which make it shorter than in the relaxed state.
- So, it's the electrical control which regulates the rythmic contraction and it is the chemical control which regulates the tonic contraction.

Summary of control for GI smooth muscle cells activity:

Smooth muscle cells activity is controlled by

Electrical activity of smooth muscle cells: (slow waves and spike potentials).

Neurochemical control: represented by the response of smooth muscle cells of the GI to a large number of transmitters that are released by many types of neurons in the ENS.

Another type of cells is <u>interstitial cells of cajal.</u>

- They have lots of spikes joined together by gap junctions.
- Slow waves appear to be caused by complex interactions between the smooth muscle cells and interstitial cells of cajal.
- These interstitial cells form a network with each other and are interposed between the smooth muscle layers (they are somehow connected to smooth muscles by gap junctions). For each 50-100 smooth muscles there is one interstitial cell in between.

- Those cells can generate action potential by themselves.

Therefore, cajal cells are believed to act as electrical pacemakers for smooth muscle cells. But functionally they differ from those found in the heart.

Some sources tell that these cells receive neural input, but this input has nothing to do with its own ability to generate action potential. So how can they generate AP? Still not clear, but one theory suggests that some metabolic changes inside the cells result in all of a sudden generation of AP.

SECONDLY, SECRETORY CELLS:

As functional structures, we have different organizations for secretory cells starting from solitary cells (individual cells) up to secretory organs located outside the tube. Examples:

Solitary cells→ dispersed in the mucosal epithelium.
Pits or simple glands in the mucosa too, a more complex organization is the compound gland in the submucosa, and finally secretory organs outside the tube secreting in the lumen of the GI with the help of ducts. Examples are salivary glands, pancreas and liver.

THIRDLY, CHARACTERISTICS OF ENTERIC NERVOUS SYSTEM:

- A highly developed system to control gastrointestinal movements and secretions. The number of neurons which are found along the GI tract is very huge, almost equal to the number found in the spinal cord, so they call this system the brain of the gut.
- The enteric nervous system is composed mainly of two plexuses:

(1) An outer plexus lying between the longitudinal and circular muscle layers, called the myenteric plexus

(2) An inner plexus, called the submucosal plexus which lies within the submucosa.

The enteric nervous system can control smooth muscle cells, secretory cells, even some endocrine cells and blood vessels.

- The myenteric plexus controls mainly the gastrointestinal movements while the submucosal plexus controls mainly gastrointestinal secretion and local blood flow.
- It is noteworthy that extrinsic sympathetic and parasympathetic fibers connect to both the myenteric and submucosal plexuses.
- Neurotransmitters secreted by enteric neurons:
- Enteric neurons could be inhibitory or excitatory.
- Many different neurotransmitter substances are released by the nerve endings of different types of enteric neurons, including: Ach, SP (Substance P), VIP (Vasoactive intestinal peptide), CGRP (Calcitonin gene related peptide), GRP (Gastrin releasing peptide)
  *VIP relaxes smooth muscle cells in the walls of vessels so more blood flow.
- Acetylcholine excites gastrointestinal activity.
- Norepinephrine almost always inhibits gastrointestinal activity, as does epinephrine
- The other aforementioned transmitter substances are a mixture of excitatory and inhibitor
- Although the enteric nervous system can function independently of extrinsic nervous system, stimulation by the parasympathetic and sympathetic systems can greatly enhance or inhibit gastrointestinal functions.

Note that the autonomic nervous system can affect the GI by affecting the enteric nervous system or by acting directly over some parts only, for example, parasympathetic exerts small effect on the blood vessel and indirectly, while the sympathetic does directly and to a large extent.

HORMONAL CONTROL OF GASTROINTESTINAL MOTILITY:

Examples:

- Gastrin
- Cholecystokinin (CCK)
- Secretin,
- Glucose-dependent insulinotropic peptide (also called gastric inhibitory peptide [GIP]) causes the release of insulin. So, when food start flowing to the GI, this hormone get released to prepare the body for the glucose that will be soon in the blood.
- Other hormones are also secreted along GI tract, including: Glucagon-like peptide-1(GLP-1), Motilin, Ghrelin, Amylin, Enterostatin, Neuropeptide Y (NPY), and Pancreatic polypeptide which is closely related to polypeptide YY and NPY.
  In addition, scattered endocrine cells releasing Somatostatin, Neurotensin.
  *the doctor mentioned them very quickly by just reading them and pointed out that some of them still has an unknown function and are still being under research. Also said that some of these have effects on blood flow, state of hunger...

Thyrotropin releasing hormone (TRH) released by the hypothalamus to cause the release of TSH.
Adrenocorticotropic hormone (ACTH) which is involved in the ACTH axis for the release of other hormone from the suprarenal gland, and also released by some cells along the GI tract.

CONTROL OF BLOOD FLOW AS A FUNCTIONAL STRUCTURE:
The blood flow is very well controlled, sometimes we need an increase, sometime we need a decrease in blood flow. How is it controlled?

1- Hormones like secretin, cholecystokinin.
2- The enteric nervous system; like VIP for example, substance P (constriction), CGRP (constriction).

3- Vasodilators. These vasodilators are released from secretory cells in response to parasympathetic stimulation for these secretory cells, so parasympathetic nervous system indirectly affect blood flow.
4- Decreased oxygen concentration. When a tissue gets deprived or become on low oxygen concentration, it releases adenosine which acts as a vasodilator.
5- Autonomic nervous system. Direct sympathetic effect decreases blood flow and indirect parasympathetic increases blood flow.

Important note: the enteric nervous system is also called the intrinsic nervous system, while the autonomic nervous system is also referred to as the extrinsic nervous system.

Summary of the control over the gastrointestinal system: There are 3 main effectors on the GI system: 1- The intrinsic nervous system.
2- The extrinsic nervous system.
3- Gastrointestinal endocrine system.

So now the question is how to change the activity of these 3 control systems, so by that we control the GI system?

And the answer is either by external influences or local changes.

External influences: like smelling, seeing or hearing about food, then these external influences affect the extrinsic nervous system.

Local changes: once you eat, distension of your stomach and the chemicals and the food itself initiate some reflexes that activate any of the 3 effectors mentioned above.

Autonomic nervous system..

Parasympathetic nervous system: According to the location of neural cell bodies, it is divided into:
Cranial division: provides innervations through vagus nerve to esophagus, stomach, pancreas, small intestine and first half of large intestine.
Sacral division: Provides innervations through pelvic nerves to distal half of the colon, sigmoidal, rectum and anal region. Fibers in this division have importance in executing defecation reflex.
Generally, stimulation of parasympathetic system causes an increase in the activity of enteric nervous system and consequently, enhances the activity of the gastrointestinal functions. These include motility, secretion and blood flow.
Sympathetic nervous system: Sympathetic fibers that innervate gastro-intestinal tract originate in the spinal cord (segments T5-L2). These fibers pass through paravertebral ganglia and synapse with the second neuron in celiac, superior mesenteric or inferior mesenteric ganglia. Generally, stimulation of sympathetic system causes a decrease in the activity of enteric nervous system and GI smooth muscle cells.