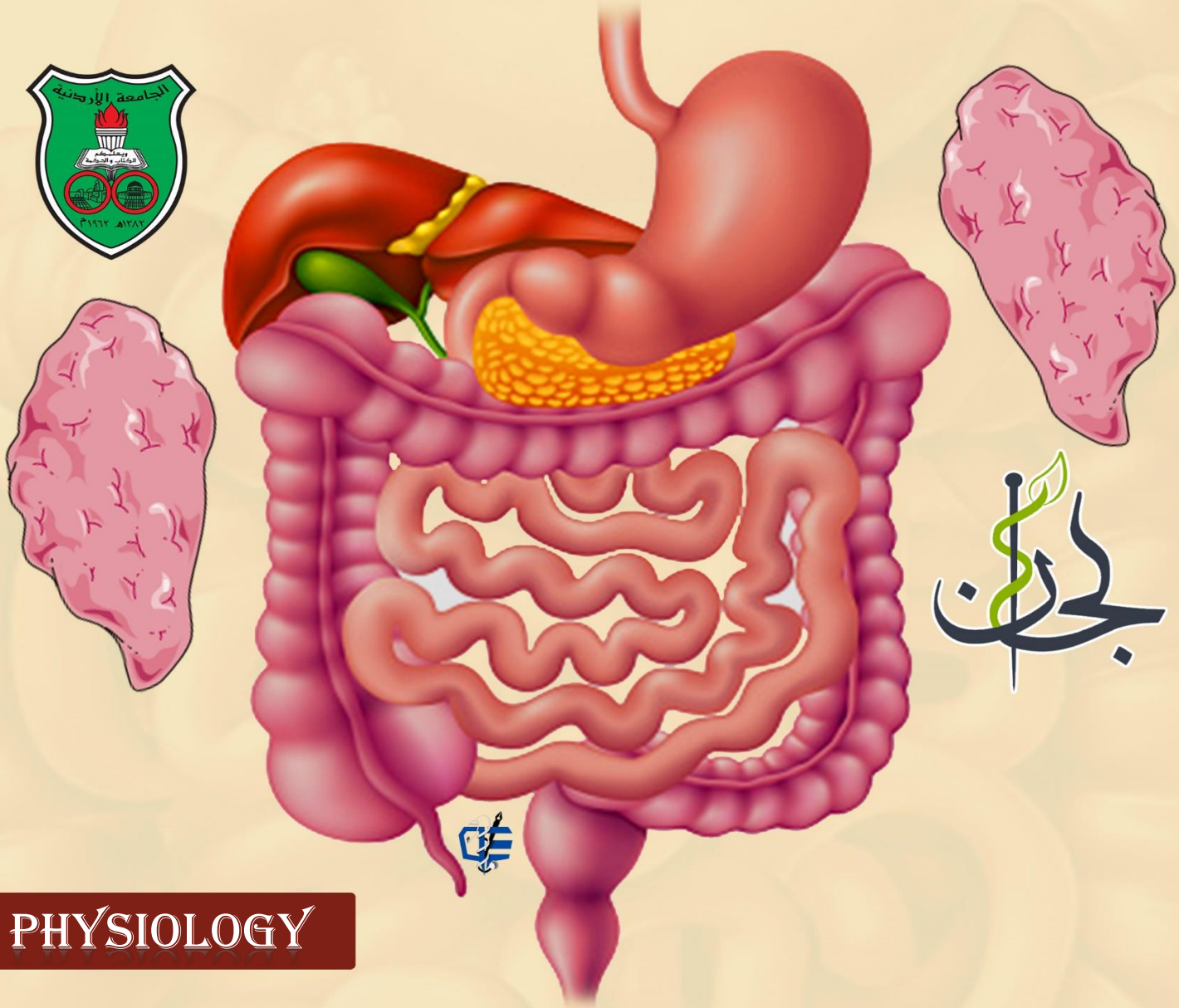
GastroIntestinal System



PHYSIOLOGY

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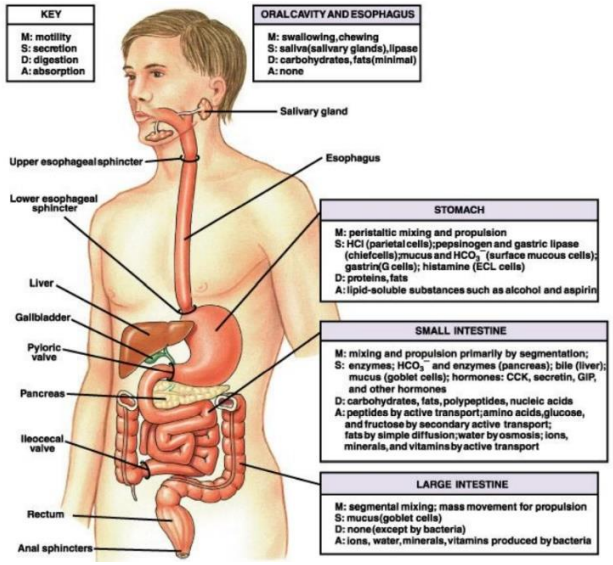
{أَفَمَن يَخْلُقُ كَمَن لَّا يَخْلُقُ ۗ أَفَلَا تَذَكَّرُونَ (17) وَإِن تَعُدُّوا نِعْمَةَ اللَّهِ لَا تُحْصُوهَا ۗ إِنَّ اللَّهَ لَغَفُورٌ رَّحِيمٌ(18) }
[سورة النحل]

-خلي الآيات ببالك خلال دراستك للشيت
وتأمل شيء من نعم الله جل وعزّ عليك-
بسم الله الرحيم العليم
اللَّهُمَّ أغنِني بالعلم وزيّنّي بالحِلم وأكرمني بالتّقوى وجمّلني بالعافية

The gastrointestinal system is the largest system in our body, starting from vocal cavity, we have many organs forming this system which are performing functions. Finally, the function of the gastrointestinal tract is providing nutrients for our body structures which are important for their energetics.



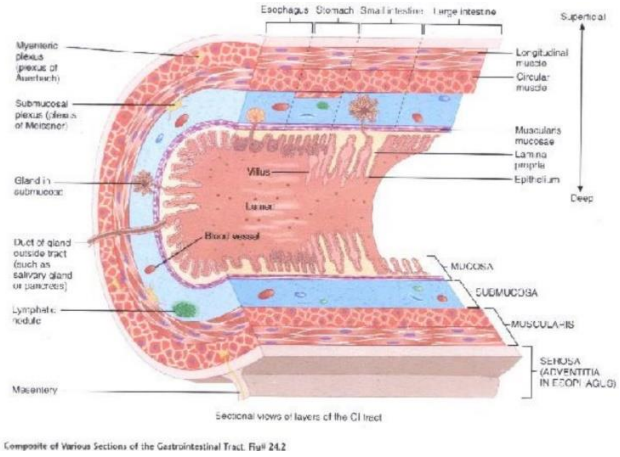
Physiological processes (Functions) are taking place along the gastrointestinal (GI) tract:

- 1. Motility.
- 2. Secretion.
- 3. Digestion.
- 4. Absorption.

To perform these functions, we have **functional structures** in the gastrointestinal tract:

- Smooth muscle cells: to have motilities
- Interstitial cells of Cajal
- Secretory cells

From functional view, we can view the whole gastrointestinal tract as a tube, that is composed of <u>three main layers</u>:



Sectional views of layers of the GI tract

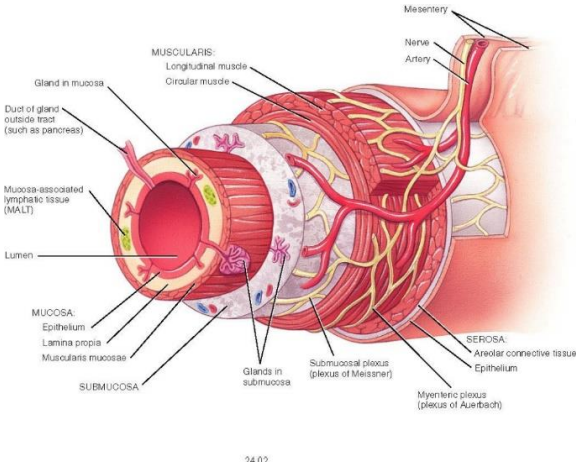
Composite of Various Sections of the Gastrointestinal Tract. Fig# 24.2

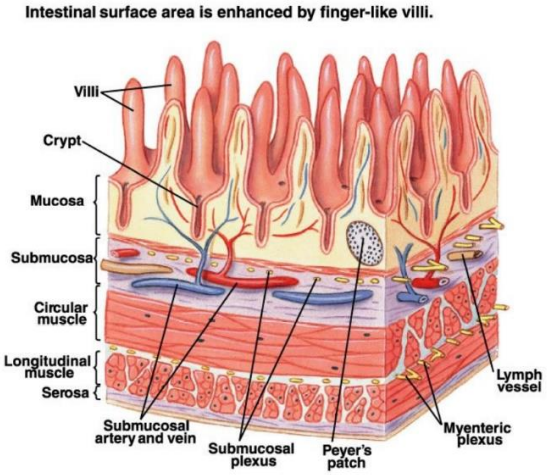
1- Mucosa (inner part): toward the lumen.
2- Muscular layer (outer part)
3- Submucosa (in between the two)

Note: we have variations along the tube with regard to these structures, we will talk about which have physiological importance.

Other related structures:

- Control systems of GI functions.
  - ☐ Neural control:
    - Enteric nervous system
    - Autonomic nervous system
  - ☐ Hormonal control: GI endocrine (cells & glands)
- Blood flow to the GI: important for performing these functions (to get secretion & absorption)





As you see, we have high vascularization, most of these vessels are found at the submucosa.

In addition, we have high vascularization of the mucosa at the level of the small intestine, a lot of capillaries, which are important for the process of absorption.

We are going to analyze all these functional structure…

Smooth muscle cells (SMCs):

The outer layer of the tube (the whole gastrointestinal tract) is composed of muscular layer, which is composed of two sublayers:

1- Longitudinal layer:

→ outermost part

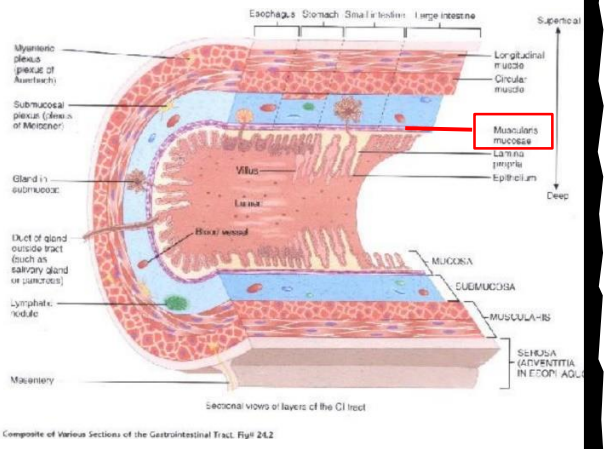
→ fibers are running along the axis of the tube

2- Circular layer

→ beneath the first one

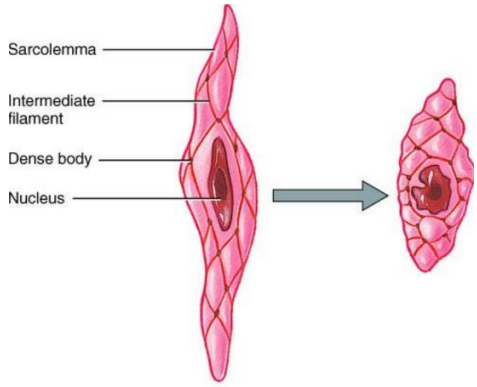
→ fibers are running at the circumference of the tube

In addition, we have a very small representation of SMCs between the mucosa and the submucosa called muscularis mucosa, it can cause some movements of the mucosa, and press over some glands located in the submucosa to cause secretions.



Notice: Muscularis Mucosa in red.

- As functional difference between smooth & skeletal muscle cells, thick and thin filaments are organized in a different way. In SMCs, we are not getting striations because the organization of the contractile proteins is different than in skeletal muscle, we have what we are calling dense bodies which are holding thin filaments, and the thick filaments dispersed in between.
  → The function of dense bodies here is like the Z-disc in the skeletal muscles.



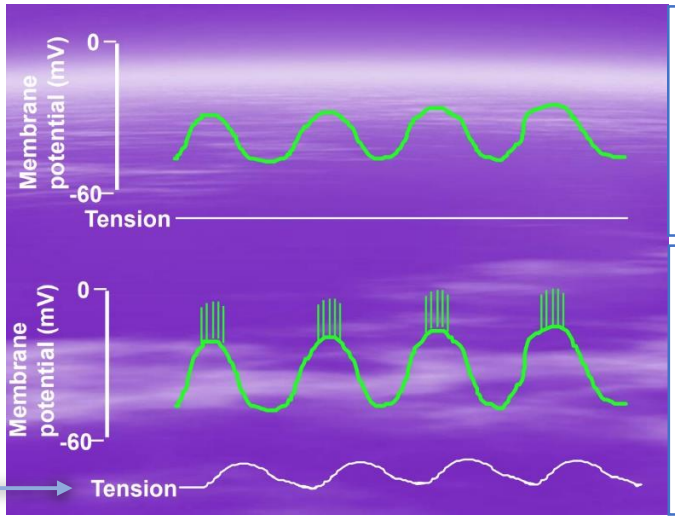
SMC in relaxation, once we have contraction we get shortening of this SMC.

Remember: the process of contraction is interaction between thick and thin filaments, resulting in shortening the distance between dense bodies, which result in shortening of the whole SMCs.

- We have also difference between the control of smooth & skeletal muscle cells activity.

Smooth Muscle Cells Characteristics:

1) Electrical activity



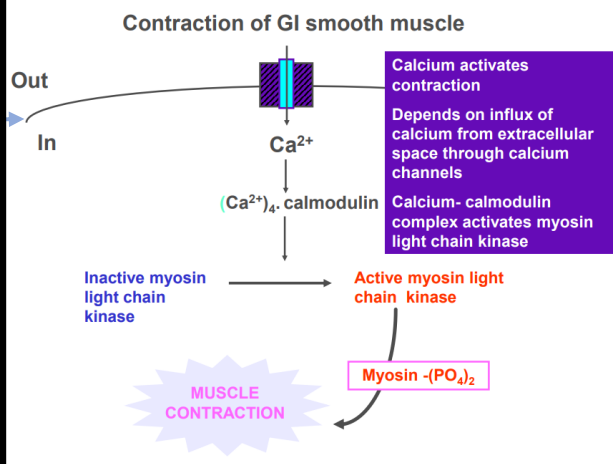
All the time you have that undulation in the resting membrane potential (not fixed, changes like waves and called slow waves (basic electrical rhythm)).

At the tip of these slow waves, we are generating spike potential (fast depolarization & back repolarization), if still we are over the threshold, we can have many spike potentials over each slow wave.

• At any time you have these spike potentials, you are getting muscle contraction. If you pass that part and get no more generation of spike potentials, you are getting back relaxation of SMCs.

The line down here is referring to the changes in tension in SMCs. All the time we have SMCs of the gastrointestinal tract are generating contraction followed by relaxation sequentially (which is called physic or rhythmic contraction), controlled by the generation of spikes, which is controlled by the changes of membrane potential to get the slow waves. Finally, we have the slow waves which are controlling the phasic contractions.

- ○ Why we are getting that contraction? (The **mechanism** of contraction)
- ✓ Once you have spikes, you are changing the activity of calcium channels (voltage gated channels), that result in entry of calcium from extracellular fluid towards inside SMCs, that calcium will bind to a functional molecule called calmodulin forming calcium-calmodulin complex.
  → You need four calcium ions to bind to one calmodulin.



That is the sarcolemma of smooth muscle cell.

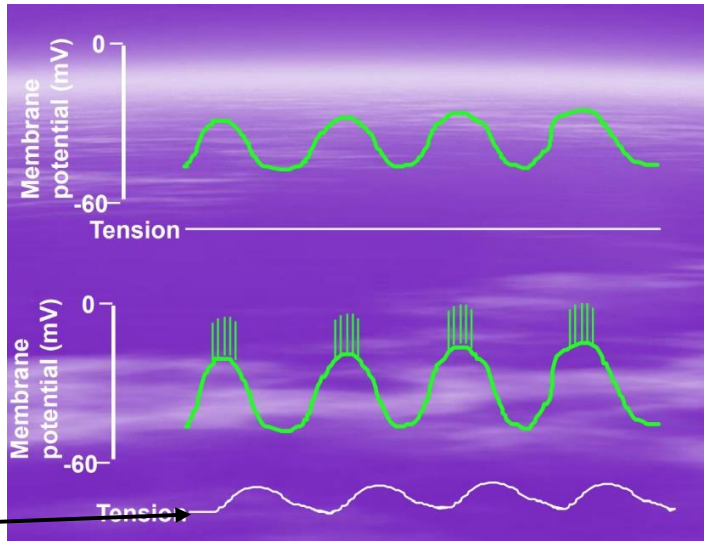
✓ Increasing the concentration of that complex inside SMCs activates an enzyme called myosin kinase, which can phosphorylate myosin heads enabling interaction between the thick & the thin filaments to occur.
→ To get relaxation of phosphorylated myosin heads, we have another enzyme called the phosphatase enzyme, that remove the phosphate group getting dephosphorylation of the myosin, resulting in less interaction between thick & thin filaments.

2) Gap junction

- Gap junctions are connecting cells together (communication between cells), so at any time one cell is generating action potential we have also the nearable cells having the same electrical activities, keeping what we called "functional syncytium".
- Functional syncytium means that we have all the time a group of SMCs working together.

Control of smooth muscle cells activity:

We have started the contraction from this level, are you having zero tension at that level?
No, you can start from a higher or lower level to get the rhythmic contractions. That level of tension from where you have started is called the **tonic contraction**.



❖ Electrical control:

- controlling the Rhythm or phasic contractions (discussed before)

- We start recording it from a specific tone (tonic contraction).

❖ Chemical control:

- controlling the tonic contractions: the level of contraction.

- The level of tension from where you have started is called the tonic contraction (the tone of the muscle from where you have started the rhythmic or the phasic contraction)
- In vivo we are not having zero tone in SMCs of GIT.
- In anatomy they will tell you that the length of the small intestines about 5-6 meters, but in physiology we are saying that the length of the small intestine about 3 meters. This difference because the SMCs they are not fully relaxed to get zero tone.

- Here we have receptors, some ligands bind to them activating phospholipase C (PL-C), which splits phosphoinositol biphosphate to get IP_3 (Inositol triphosphate), IP_3 will bind to it's receptor available on the sarcoplasmic reticulum inside, and these receptors are linked to calcium channels (activating the first one, activate the next), resulting in getting release of calcium from intracellular store. Increasing calcium concentration at the sarcoplasm make it bind to calmodulin and causing contraction of SMCs.

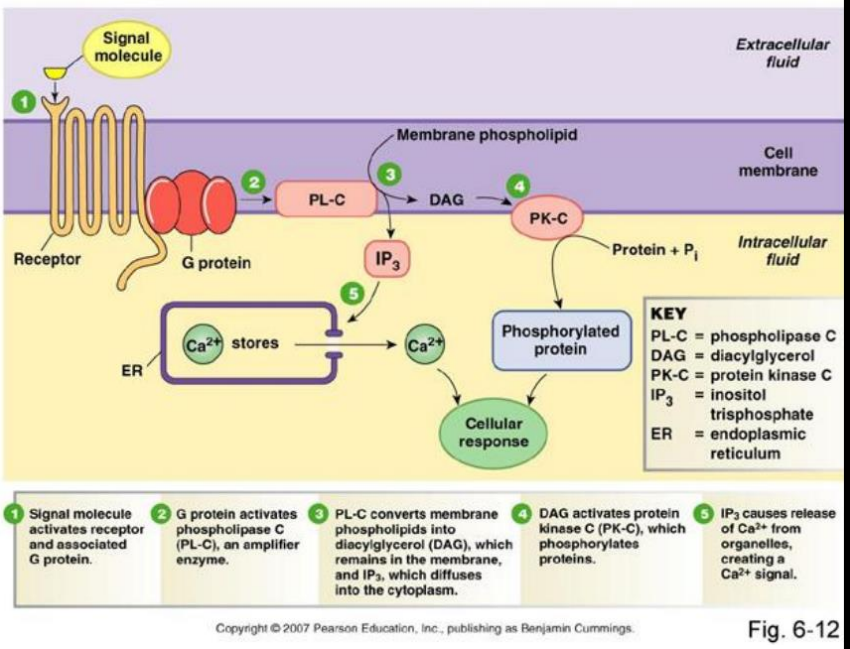
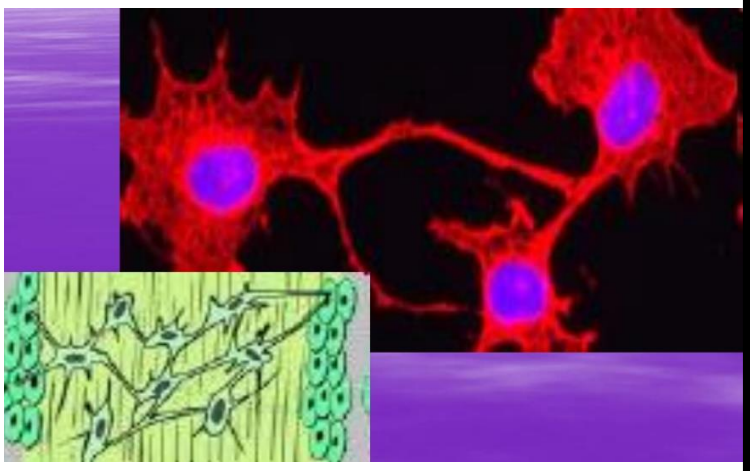


Fig. 6-12

Interstitial Cells of Cajal (ICCs):



- ✓ They are not neurons; they are cells dispersed between SMCs.
- ✓ They have many spikes, by these spikes they are connected with the SMCs by gap junctions.
- ✓ They are connected with each other by also gap junctions.
- ✓ About one interstitial cell is connected to about 50 SMCs around.
  → achieve functional syncytium
- ✓ Inputs from ENS
- ✓ Function: the ability to generate action potentials by themselves, and the configuration of that action potential is like action potential in plateau, in a rhythmic way.

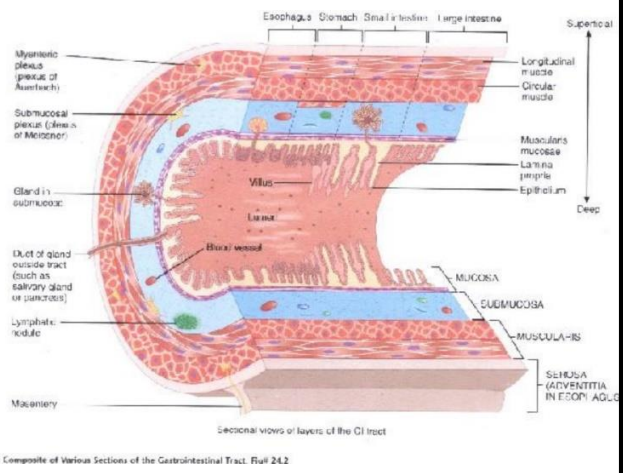
Remember: How the action potential plateau looks like?
From resting membrane potential → fast depolarization → plateau → repolarization

- ✓ How are we controlling these interstitial cells to generate action potentials? It is not known, some explanation for the rhythmic generation of action potentials which are in plateau in these interstitial cells called metabolic changes, also there is no neural control over them.
- ✓ Once we have that interstitial cells generating an action potential, by any depolarization, results in having that part of the slow waves, we are getting depolarization of the membrane of smooth muscle cells. Any depolarization of that membrane reaching threshold results in generation of spike potentials which results in contraction.
  (sequence of activities initiated by the interstitial cells of cajal, because of that these cells considered as the pacemaker cells for the activity of SMCs of GIT)

Secretory Cells:

Mucous secretion and serous secretion, different organizations for these cells:

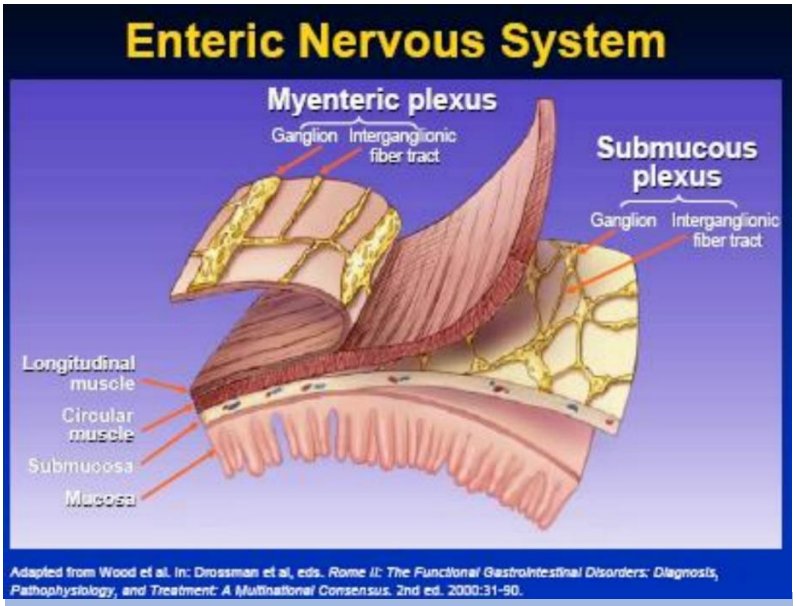
A. Solitary cells: dispersed all over the mucosa, and they have secretory functions.
B. Pits: structures within the mucosa which are forming glands or pits, also called simple glands.
C. Compound glands: within the submucosa, a more complex structure with regard to the secretory cells, group of secretory cells, forming glands, also called complex glands.



Composite of Various Sections of the Gastrointestinal Tract. Fig 24.2

D. Secretory organs: annexed to the GIT and releasing their secretion into a duct system which is flowing toward the lumen of GIT. Examples: pancreas, salivary glands…

Enteric Nervous System (ENS): (Intrinsic Nervous System)



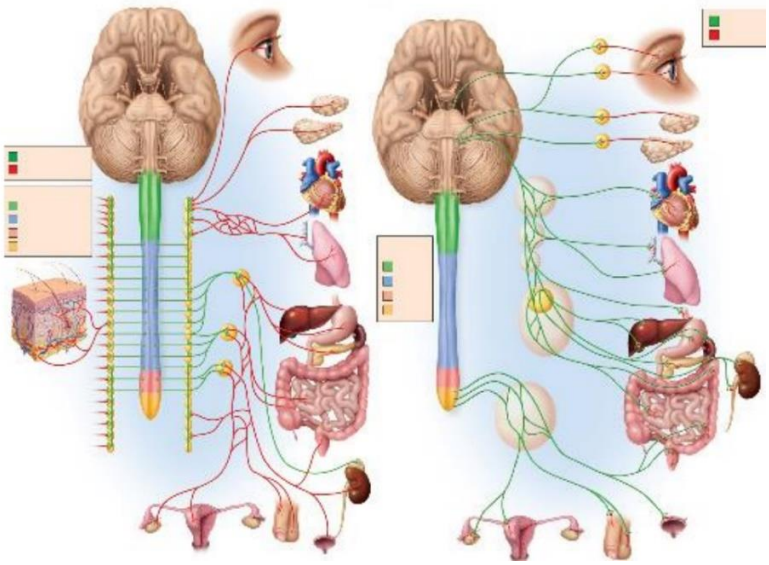
What you are seeing in yellow, neural network structure which is called ganglia

- We have huge number of neurons located along the GIT, forming two neural network structures:
    1. Myenteric plexus
       - between the longitudinal & circular layers, involved in controlling motilities.
    2. Submucosa plexus or back plexus
       - involved in controlling activity of vessels & secretory activ
- We have communication between the two neural network structures.
- We also have inter-neurons connecting the two plexuses together.
- The number of neurons along GIS is huge, it can be more than the number of neurons located in the spinal cord.
- Some people called it the brain of GIS; we can perform all the functions of the GIT without any input from outside.
- Achieved the main control of GIT.
- Enteric neurons:
    1. Excitatory: performing excitatory functions, example: stimulate secretions, stimulate motor activities
    2. Inhibitory: performing inhibitory functions
- According to the neurotransmitters that are releasing, more than 15 types of neurons have been characterized, examples:
    1) Ach
    2) SP (Substance P)
    3) VIP (Vasoactive intestinal peptide)
       → mainly involved in the control vessels, example: causing vasorelaxation.
    4) CGRP (Calcitonin gene related peptide)
    5) GRP (Gastrin releasing peptide)

Autonomic Nervous System (ANS): (Extrinsic Nervous System)

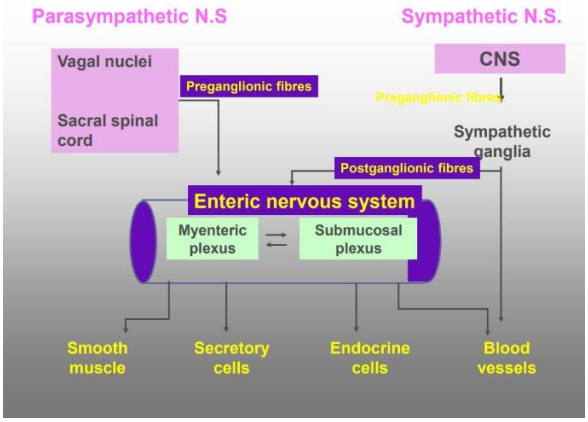
- Modulate the functions of the entire nervous system by signals, coming from CNS through the sympathetic or parasympathetic division.

The origin of sympathetic is thoracolumbar.



The origin of the parasympathetic is craniosacral.

- We have what we are calling enteric nervous system, composed of two parts: Myenteric & Submucosal plexuses; controlling the activity of SMCs, secretory cells, & endocrine cells.
- We are getting control of blood vessels along GIT.



- The activity of enteric nervous system can be under the control of the parasympathetic or sympathetic divisions (autonomic).
- We can have direct control of the autonomic over the functional structures, examples: the sympathetic can act directly over the vessels causing vasoconstriction, the parasympathetic can act directly over secretory cells to increase secretion …etc.

Enteric Endocrine System

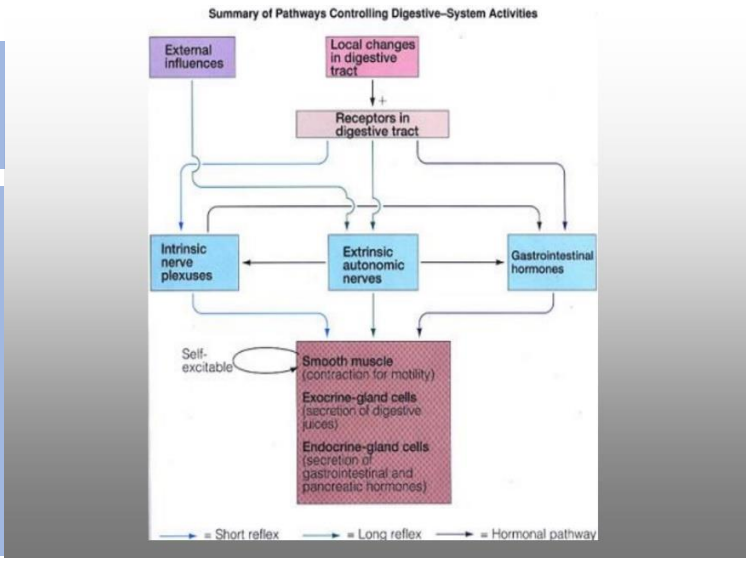
- ✓ We have a lot of glands or secretory cells, which are releasing hormones along GIT involved in the control.
- ✓ These hormones are:
    1. Gastrin
    2. Chlecystokinin (CCK)
    3. Secretin
    4. GIP (Gastric Inhibitory peptide) or (Glucose dependent Insulinotropic Polypeptide)
       → From it's name, it can have some control over the stomach to reduce gastric activity & over the pancreas to induce release of insulin.
- ✓ Other hormones:
  Glucagon-like peptide-1(GLP-1), Motilin, Ghrelin, Amylin, Enterostatin, Neuropeptide Y(NPY), polypeptide YY, Pancreatic polypeptide which is closely related to polypeptide YYand NPY Somatostatin, Neurotensin, Thyrotropin releasing hormone (TRH) causing release of thyroid glands as example, Adrenocorticotropic hormone ACTH involved in the control of suprarenal glands as example.
- ✓ We have huge number of hormones released along the GIT, we know the function for some of them, and we don't know the function for most of these hormones.
- ✓ Functions of Hormones
    A. Control of motility
    B. Control of secretion
    C. Control of blood flow
    D. Regulation of food intake
    E. Regulation of metabolic activities in the body, examples:
       - ACTH involved in the control of metabolic status.
       - TRH causing release of thyroxin or thyroid hormones, involved in the control of metabolic activities.

Blood Flow of the GI

- ✓ Related to GI activities:
  - Controlled by:
    - Hormones (Secretin, CCK)
    - ENS (VIP, SP, CGRP)
    - Vasodilators: Kinins (Kallidin, Bradykinin)
      → to increase blood flow toward that organ, and increase availability of water & electrolytes for secretion.
    - Decreased O2 concentration
      → any time you are getting decrease in oxygen level, you are getting vasodilation, probably by increasing adenosine.
    - ANS
      → Sympathetic: act directly
      → Parasympathetic: act indirectly, by activation of some secretory cells, for example, to release kinase, high release of kinase can cause vasodilation.

☐ How we control the activity of these control systems?

Either by local changes (which can modulate activity of autonomic & enteric, or release of hormones), or by external influences (when you see or smell something, activities increase by activate ANS, for example.)



"أقل مَا فِي الرقعة البيذق فَلَمَّا نَهَضَ تفرزن"
- ابن القيم -

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