Digestive system

University of Jordan

Faculty of Medicine

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Medical Committee
The University of Jordan

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☐ Anatomy ☐ Embryology

■ Physiology ☐ Histology

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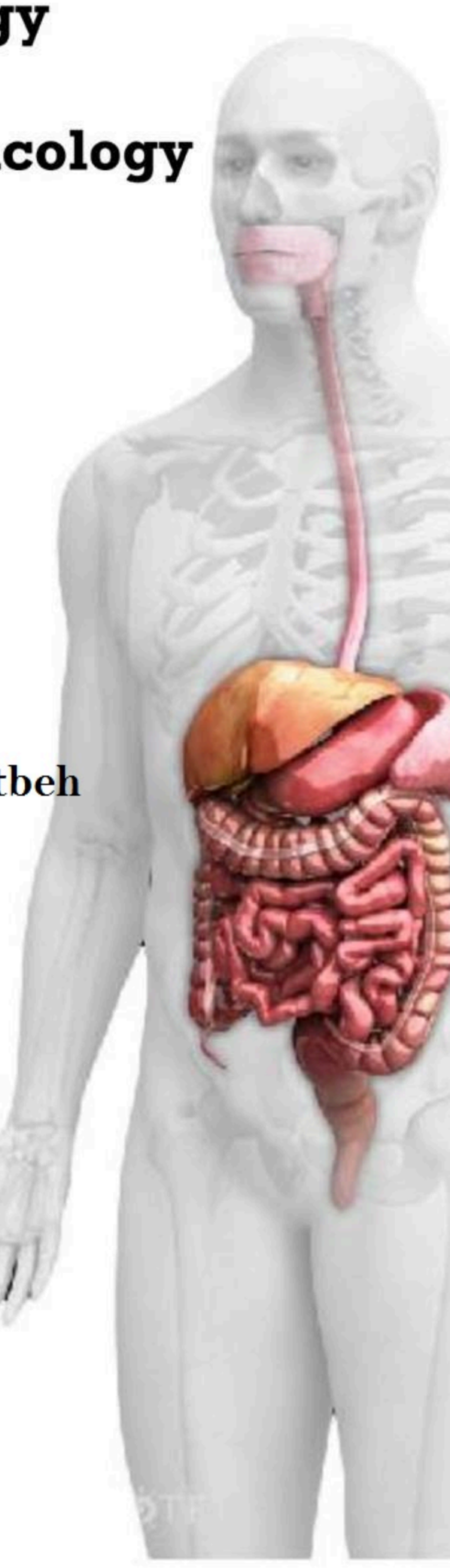

Lecture # : 1

Doctor's name: Mohammad Al-Khatatbeh

Done By: Bilal Sibai

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Price:

DESIGNED BY: TAMER ALTAMIMI "SMILE"

General principle of gastrointestinal motility

- We will have 9 lectures with Dr.Khatatbeh about GI physiology.

-The doctor said that the information in our book are not enough, so you have to pay more attention in class, you will have also some short notes from the Doctor.

-Introduction:

-The gastrointestinal system is the **largest system** in our body and is composed of many organs, starting from oral cavity ending with anus.

- We have 4 main physiological functions in GI tract:

1-**motility**: movement of food along the system.

2-secretion: we have a lot of secretory glands, also enzymes are secreted.

3-digestion: we will understand later the details of digestion of protein, carbohydrate and lipids.

4-absorption: we have specialized cell absorbing what we have digested.

In addition to all these main processes, we will see how food will be processed after digestion and for what we need this food (e.g. energy).

-so we will have 1 lecture (at the end of this system) with regard to the energetics, also we will have 1 lab to understand what we mean by metabolic rate and basal metabolic rate.

✓ **Now, to do these functions we need functional structures:**

-for **motility** we need muscles, so this system has plenty amount of *smooth muscle cells*.

-for **secretion** we have secretory cells.

-Also we have another type of cell which are called **interstitial cell of cajal**.

- They are not characterized as neural cells or muscular cells (they don't contract), they are in between. We will see their function later on.

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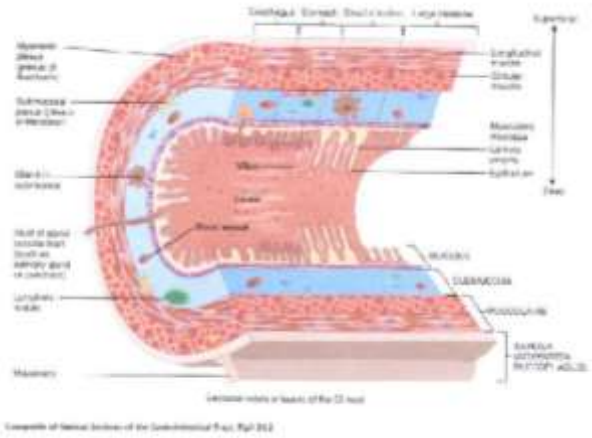
This picture for the small intestine to represent the whole GI tract wall composition.



-the whole GI tract is like a tube, so what is the composition of this tube ?

1-muscualr layer (outer layer): composed of smooth muscles making 2 layers:

- The first layer: longitudinal smooth muscle layer, fibers are running along the axis of the tube forming the **outermost part**.
- The second layer: circular smooth muscle layer, fibers are running at the circumference of the tube, **running beneath the longitudinal layer** (from writer: when contracted lead to decrease in the diameter of the segment it surrounds).

- There are variations in these 2 muscular layers in different organs along the GI tract, but we won't talk about it only when it is important, and in histology we'll have more details.

2-Inner layer: we call it mucosa.

3-submucosa: between the outer muscular part and the inner part.

✓ From functional view it is enough to know these 3 elements that are forming the **wall** of the GI tract.

-All the GI functions are well controlled:

- Neural control: 1-Enteric nervous system (very **specific** to the GI tract).

  2-Autonomic nervous system.

- Hormonal control: GI endocrine (dr said that we won't talk about the GI endocrine with the endocrine system in the summer course so study it well here)
  - Other related functional structure here is the **blood flow to the GI**:
    - If you eat → you increase blood flow, or if you stop eating→ you decrease it. So the blood flow is **very well regulated**, by means of neural and hormonal control. And this is very important for other functions that depend on blood flow like secretion and absorption.

-where could we find the blood vessels that provide this blood flow ?

-We find them in the **submucosa.**

-but at the level of the **small intestine** we have a good blood supply to the mucosa, why we need this blood supply?

-for **absorption process** > so if you removed what had been absorbed from interstitial fluid **as fast as possible**, actually you are keeping a gradient between the lumen and the interstitial fluid to get more absorption as much as possible.

(We will have more details about absorption and digestion in the coming lectures).

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Smooth muscle cells:

-remember that they are present at the outer layer.

-In addition to this outer layer, we have **thin** layer of smooth muscle **between the mucosa and submucosa** known as ***muscularis mucosae***. Functions of this layer:

1- changes in the folds in the mucosa (or movement of mucosal folds).

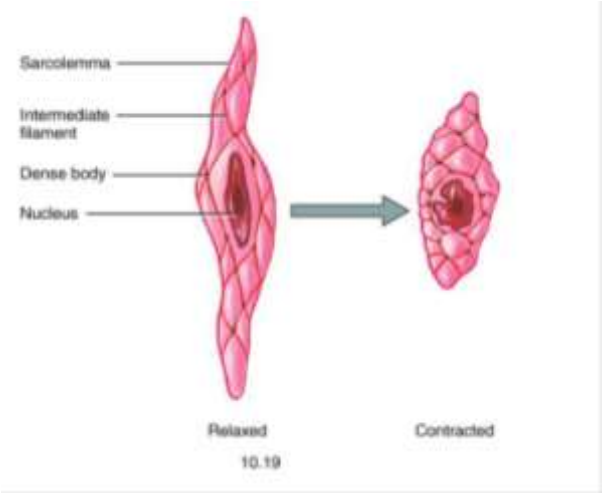
2-Press over gland located at the mucosa or submucosa to get **secretion.**

We can have less or more secretory activity depends on the control.

-We started talking about smooth muscle cells and how we are getting contraction of these cells. We also talked about **dense bodies and their function in holding the thin filament.** Between thin filaments we have the thick filaments.

-when we have interaction between thick and thin filament we'll have shorter distance between the dense bodies (figure below). **(They remind us with the function of Z-disks of the skeletal muscles).**

-The lines between dense bodies represent thick and thin filaments.



How to control the Activity of smooth muscle cells:

We have 2 ways; the chemical control (hormone or Neurotransmitters) and the electrical control or electrical activity.

- **Electrical control**
- *SMCs= smooth muscle cells*

The SMCs of the GI tract have an **undulating resting membrane potential** (waves), ("A" on the figure next page). (Usually resting membrane potential in cells is constant)

-we call these undulations in resting membrane potential **slow waves or basic electrical rhythm** generated by **cajal cells** (cajal cell will be discussed later in this sheet).

- Slow waves are NOT true action potential.

-when we reach the threshold at the tip of the slow waves we generate **SPIKES**. ("B" on the figure)

-**spikes**: are the **TRUE** action potential in SMCs that appear at the peak of the slow waves.

- so when action potential **(Spike)** is generated at the sarcolemma of smooth muscle cell and we are recording the contractile activity of the cell we'll see **contraction** then followed by **relaxation** then contraction then relaxation and so on and this called **phasic contraction**. ("arrows" on the figure)

- ✓ -the spikes are generated according to the slow waves. The slow waves are generated at different rhythm along the GI tract according to each organ. Also the rhythm of the contractile activity varies between different organs.

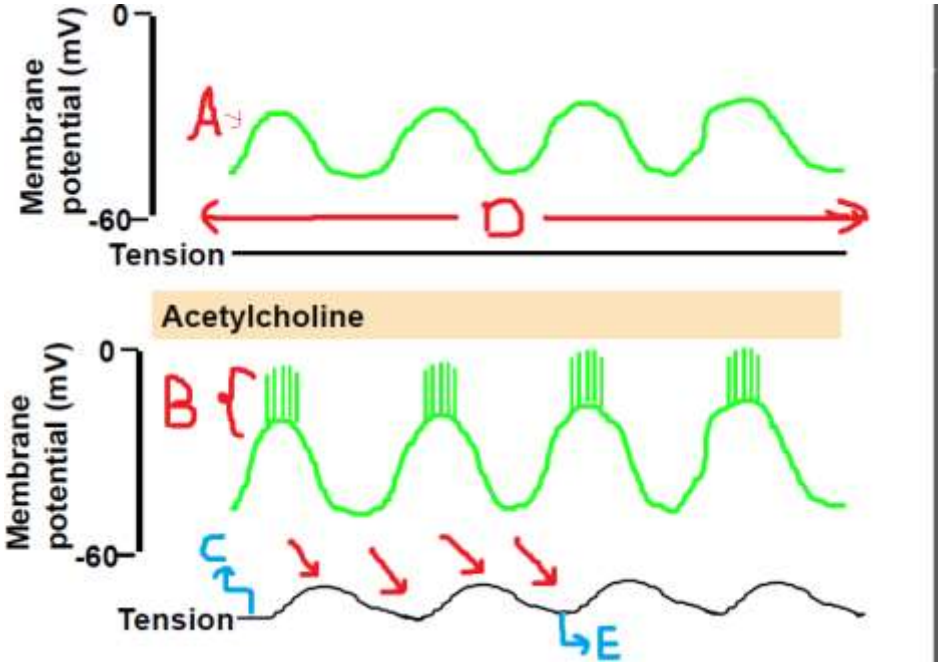
for example: the upper part of small intestine is generating 12 contractions/minute, the lower part is generating only 8 contractions/minute. (don't memorize the numbers),

i.e. most gastrointestinal contractions occur rhythmically, and this rhythm is determined mainly by the frequency of so-called "slow waves" of smooth muscle membrane potential that differ from organ to another.

-now these **rhythmic** contractions are called **((phasic contractions)).**

- We have started contraction from a baseline (C), do we have at this baseline zero tension?

NO, we started from a certain tension, which is controlled differently, i.e not controlled electrically, (later on in this sheet it will be explained). At the end, this's the electrical control that we have, which is controlling the phasic contractile activities.



Mechanism of the phasic contraction:

Generation of spikes (depolarization of the sarcolemma) > Ca++ voltage gated channels of the sarcolemma open > Ca+ entry into the cell > (ca+)-calmodulin complex > the complex will activate myosin kinase > myosin kinase will phosphorylate myosin > once phosphorylated we can get interaction between thick and thin filaments and finally contraction. (check the figure in the slide).

-between the smooth muscle cells we have **gap junction** that provide communication, is it important for the **electrical control?**

-**Yes** it's very important, once action potential is generated at one cell it will be transmitted to a group of cells by gap junctions.

-this phenomenon is called **functional syncytium** (activity is very well synchronized by organized contraction and relaxation). So the gap junction is insuring the functional syncytium in order to have *a **group** of muscle cells generating action potentials together, contract together and relax together at the same time*.

- ✓ Why we need this functional syncytium?

-To have an effective activity or function of smooth muscle cells and efficient motility of the GI tract.

In addition to electrical control we have:

-Chemical control:

Mechanism of activation:

-Remember that we have high number of different receptors (some for NT, other for hormones..etc) on SMCs that bind to them a specific ligand > result in activation of phosholipase-C (PL-C) > then Ip3 generation > Ip3 will cause release of Ca++ from sarcoplasmic retinaculum > contraction of SMCs will occur **(Tonic contraction- "D" figure)**. (this is the second type of control, the chemical control).

-make sure you notice the difference between the phasic contraction mechanism and tonic contraction mechanism.

-Here there is no slow wave, no phasic contraction. (Note from writer: don't get confused with the slow waves above the tonic contraction tension line, it is the resting membrane potential generated electrically and doesn't have anything to do with the

tonic contraction that's generated chemically and when the slow waves reach the threshold, spikes are generated and phasic contraction start over the tonic).

-ligand can be: neurotransmitters, hormones, inflammatory cytokines, PGs.
all can change the activity of SMCs either to more contraction or to less contraction, since these SMCs express a high number of different receptors.

- ✓ The tension here is not zero, we have certain amount of tension (**"D"-figure**).

-This level of tension represents the tonic contraction.

- At point (**"C'**) we did not start from zero tension to get more contraction less contraction (phasic contraction), we started from certain tension which is called tonic contraction.

-So we have 2 types of control working with each other to set a certain tension along the GI muscles, but over that tension we can have more contraction then relaxation then contraction ... and so on.

Note: **we do not reach full relaxation ("E") ,** full relaxation is in dead bodies where tension= 0.

Tension at point E don't' equal zero.

Let's return back to the level of tension that this chemical activity generated. In anatomy the length of the small intestine for example is 6 meters, but in physiology it is about 3 meters, why we have this difference?

-In physiology we count the length in vivo, in the living body, where there is a certain contractile activity called **Tonic contraction (**that is generated for chemical control). Where in dead bodies there's no contraction so the length is longer in anatomy.

Electrical control >> Phasic contraction // Chemical control >> Tonic contraction.

Q- a student asked: Is it true that Phasic contraction is generated over Tonic contraction?- first of all we have a certain level of contraction which is the tonic contraction, over that level you can get more contraction, less, more, and so on in a RYTHMIC WAY (certain number/ time) as we discussed earlier. **So this rhythmic contraction is called the phasic contraction.**

- Another Q, it wasn't clear in the record but what I understood:

1-if we want to **increase the tension** in smooth muscle we **increase the level of phosphorylated myosin**, and we don't have here the maximum overlap rule that was present in skeletal muscle to increase the tension, we don't follow this rule here. 2- Also the tension increases in the phasic contraction. 3- In SMCs **we don't have tetanization.**

- INTERSTITIAL CELLS OF CAJAL (ICCs):

-these cells have a lot of **spikes**, they are not neurons (neurons have spike-like structures called dendrites).

-they are connected with each other by **gap junctions** (neuron connected through synapse).

-they are connected with SMCs also by gap junctions.

-anytime these cells generate an action potential, we get **Depolarization** in SMCs **(slow waves) ,reach threshold > spikes> phasic contraction starts.** When the Action potential is ended in cajal cells we return to the resting membrane potential in smooth muscle cells.

So these cells are controlling the electrical activity of SMCs.

-How?

by gap junction that connect these cells to SMCs, it is considered as the **pacemaker cells** of GI tract.

What does pacemaker means?

- Cells that generate action potentials by themselves.

(Keep in mind that they are different from the pacemaker cells of the heart).

What happens in these cells?

They are at constant resting membrane potential, **all of sudden** it generates fast depolarization which results in generating AP in plateau then returning to resting membrane potential and so on.

- ✓ The mechanism these cells generate the action potential in a rhythmic way is not known.

Some are explaining it as changes in metabolic activity in cells. NOT by stimulation, here there's no stimulation.

There's connection of the ENS (enteric nervous system) with these cells, but nobody had proven that this is important to generate action potential in Cajal cells.

-Cajal cells are responsible for *electrical activity of slow waves in GI tract*, and these slow waves are ONLY present in the GI. (not present in SMCs of blood vessels or uterine SMCs).

-Don't mix the electrical activity (basic electrical rhythm, slow waves) with the mechanical activity.

- ✓ The slow waves are electrical activity, where the phasic contraction itself is a mechanical activity.

Done by: Bilal Sibai

Dedicated to: reda yahia, louy jlal ,moaz kasem, obada fares ✌ ✌ .