Physiology

Sheet ○ Slide

number **2**

Done by **Abdallah Massad**

Correction **Ziad Fraij**

Doctor **Mohammad Khatatbeh**

Last time we started with the introduction, and we have seen the functional structures in the gastrointestinal tract which include: **smooth muscle cells**, the **Interstitial Cells of Cajal (ICCs)**, and **blood vessels**. We have also seen the properties of smooth muscle cells. We have two types of controlling variables that control the activities of smooth muscle cells, and these include:

1- **The electrical control** which is characterized by the presence of slow waves (undulating changes in membrane potential known as **basic electrical rhythm** (BER)) and **spike potentials**.

2- **The chemical control** which controls the **tonic** contractions and it is also involved in controlling the **rhythmic** activities that the muscles are having along the gastrointestinal tract.

In addition, we have **interstitial cells of Cajal** (ICCs) which are also considered as pacemaker cells. Also, we talked about secretory structures, we have organisations of these secretory structures along the gastrointestinal tract starting from solitary cells and ending at organs. In addition, we have control systems, first the enteric nervous system in which neurons are grouped into two main plexuses:
1- The **myenteric plexus** which is found between the muscle cells (located between longitudinal and circular smooth muscle layers).
2- **Meissner's plexus (submucosal plexus)** which lies in the submucosa and usually controls gastrointestinal secretion and local blood flow.

Regarding to the myenteric plexus we have excitatory neurons and inhibitory neurons where most of the excitatory neurons' axons project up while most of the inhibitory neurons project down, therefore we get processing of the motor activities along the whole GI tract. In addition we have many different types of these neurones which results in having a lot of functions, some of these neurones release ACH or any of the other 15 types of neurotransmitters that we have along the GI tract. In addition to the enteric nervous system we have the autonomic nervous system.

The **ANS** is divided into the **Sympathetic** and **Parasympathetic** Systems, in which we can have direct control or indirect control through the enteric nervous system. The **parasympathetic** system has direct effect on secretory cells but no direct effect on vessels, the effect of this system appears to be indirect by increasing glandular activity, which results in secretion of vasodilator mediators (such as kinins), while the **sympathetic** system has a direct effect on vessels causing vasoconstriction but a weak effect over secretion, which means that when we have a high sympathetic stimulation we get vasoconstriction, this results in fluids not reaching the cells and this results in reduction of the secretions in an indirect way.

In addition to that we have the hormonal control; we have a lot of hormones released by a lot of types of endocrine cells which are dispersed from the stomach and downwards from there, over the mucosa within other glands. So apart from the level of the pancreas, they are not grouped. So along the GI tract we have dispersed endocrine glands which produce many types of hormones such as **Gastrin, Cholecystokinin (CCK), Secretin,** and **GIP (Gastric Inhibitory Peptide)** the other name of which is **(Glucose-dependent Insulinotropic Polypeptide).** Those hormones are released into the blood and are taken away into some other location (might be some other organs) where they undergo their function.

GIP: causes the release of insulin, you should know that the body doesn't wait for the blood sugar to become high in order to secrete insulin, your body starts secreting this hormone as soon as you start eating.

*The GI system is the largest endocrine system in our body.

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 releaseing Somatostatin, Neurotensin, Thyrotropin releasing hormone (TRH), and Adrenocorticotropic hormone (ACTH) have been described along the GI tract.

Note: Thyrotropin releasing hormone (TRH) is usually secreted in the hypothalamus but we have some scattered endocrine cells which release it, and Adrenocorticotropic hormone (ACTH) is usually secreted from the pituitary gland but it is also secreted by those scattered endocrine cells in the GIT.

We don't know the exact function of most of the hormones acting in the GIT but we know the function of some of them.

Some of these hormones are implicated in the motility of the GIT but they are not the major controllers of it, since the main control is achieved by the nervous system and electrical control, in addition to that some of these hormones have some effect on secretion, blood flow, and feeling behaviours such as feeling hungry. Some of these hormones have metabolic effects, for example ACTH causes the release of cortisol which has a lot of metabolic effects, TRH causes release of thyroid hormone which is involved in metabolism. Also these hormones (e.g. secretin, VIP, and CCK) can affect blood flow which is well regulated by many mechanisms (one of which includes these hormones) (this is actually done by vasodilation (as in VIP) and vasoconstriction).

*SP and CGRP cause vasoconstriction.

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.

*Decreased oxygen concentration increases blood flow possibly by the release of adenosine.

So in summary: all the control systems which are controlling effector structures (muscle cells, secretory cells and blood flow) are controlled by the extrinsic nervous system.

But how can we change the activity of these 3 control systems (hormonal, extrinsic, and enteral)? This is done either by local changes or external influences. When you are eating food your stomach distends, and this distension is a local change. Talking about food, seeing and smelling food cause an increase in gastrointestinal activities (production of saliva for example) and

that is achieved by activation of the extrinsic nervous system which in turn can stimulate other systems.

These local changes can affect the intrinsic, extrinsic, and hormonal system along with external influences like: other systems in your body for example.

Note: Extrinsic Nervous system is (ANS) (Sympathetic and parasympathetic system) while the intrinsic nervous system is the enteric nervous system.
END of introduction.

So we are now going to start talking about the movements along the GI tract to understand these motor activities.

The first movement we are having when the bolus of food enters your mouth is called chewing or mastication. It is voluntary but we have some reflex behaviour. This occurs by activation of chewing **reflex** (centres in hypothalamus and cerebral cortex are stimulated by smell and taste to cause chewing of food in the mouth). The initiation of chewing reflex appears by muscle stretching caused by drop of the lower jaw (due to the presence of food bolus in the mouth). This will result in a rebound of the lower jaw by activation of stretch reflex. The purpose of this movement is grinding the food and mixing it with saliva.

In mouth, in addition to grinding by chewing, mixing is also promoted by the movements of the tongue.

The second movement after chewing is swallowing / deglutition which is pushing the food with the help of your tongue into the pharynx, we should know that this stage is divided into voluntary and involuntary phases:

The **voluntary** stage: in which the tongue is pressing food by upward and backward movement against soft palate, which results in squeezing food bolus into pharynx.

Involuntary stages: reflexes initiated by introducing food into pharynx will result in contraction of pharynx and then esophageal peristalsis that induce movement of bolus along esophagus. In these reflexes, swallowing receptors at the pharyngeal mucosa and swallowing centres in the brain are involved.

The **involuntary** stage is subdivided into:

- **Pharyngeal stage**: duration is about 2 sec. In this stage respiration is interrupted, soft palate is pulled upward to close posterior nares and larynx is pulled upward and anteriorly which results in closure of epiglottis. In addition to these complex events, the upper esophageal sphincter (pharyngesophageal sphincter) is relaxed and esophageal opening is enlarged. This will end in enforcing bolus to move into esophagus.

Now the bolus of food is in the esophagus, and this is where we start a series of involuntary phases

- **Esophageal stage**: conduct the bolus along esophagus to the stomach.

Getting back to the pharynx, we have movements at the pharynx where the bolus of food passes downwards after the relaxation of the upper esophageal sphincter and the contraction of the pharynx, then we start with what we call the esophageal phase of swallowing, at the esophagus we have two types of movement which are conducting this bolus of food towards the stomach, those movements are called esophageal peristaltic contractions. The first one of these movements is called: Primary peristaltic contractions while the second one is called: Secondary peristalsis. Now what's the difference between the primary and secondary peristalsis, more specifically what's the pattern of each type of contraction? In general obviously there is going to be contraction of cells above the bolus of food and relaxation below the bolus of food, and this is in order to move the bolus downwards along the esophagus. The nervous system involved in this mechanism is the enteric nervous system.

The two peristaltic contractions have the same pattern in contraction but the difference is mainly in the origin, meaning that the contraction of muscles that happens behind the bolus of food is primary peristaltic contraction, but unfortunately these primary contractions sometimes fail to conduct the bolus of food downwards, therefore this calls for another way of contraction in order to initiate the movement of food downwards, this is where the secondary peristalsis comes into play, so therefore we can consider it as an emergency movement in case the primary peristaltic contractions fail to achieve their job.

- Primary peristaltic contractions: continuation of the contractions initiated in the pharynx which conduct bolus through the esophagus. The wave of contractions passes along esophagus in about 8-10 seconds.

- Secondary peristalsis: Represented by intrinsic (within myenteric plexus) and extrinsic (through afferent and efferent vagus fibres) reflexes promoted by the distension of the esophagus by the retained food in esophagus or when the primary reflex fails to move bolus of food along esophagus.

Note: Pharynx and Upper third of the esophagus are striated muscle and controlled by glossopharyngeal nerve. The lower third is smooth muscle and controlled by the vagus nerve.

There might be some pathological problems regarding the swallowing process, we call them dysphagial problems (the inability to swallow) (more specifically we call it dysphagia of the motor origin). These problems might be related to the movements, while in other times they might be due to changes in diameter strictures along the esophagus or stenosis and so on. And this results in an inability to conduct the bolus of food down through the esophagus. One of the major factors of dysphagia is a decrease in the number of neurons of the enteric system (during embryologic life the migration process of these neurons is disturbed). This doesn't only affect the muscle contraction that propels the bolus of food, but also it causes a perturbation in the relaxation of the lower esophageal sphincter, these factors result in accumulation of the food boli in the esophagus resulting in its enlargement (achalasia: a condition in which the ability of myenteric plexus to cause relaxation of the sphincter has failed).

This problem might not be evident in newborns due to the fact that most of their nutrition is focused around fluids (milk and water) but once these children start to eat regular food the problem starts to be evident.

Other factors that might contribute to the formation of this condition are some types of **toxins** (e.g. botulinum toxin), the stricture of the organ (a decrease in the organ diameter) which is most commonly seen after ingestion of acids or alkaline substances which may result in pain along the esophagus, the healing of the esophagus is done with some "strictures" which might result in a decrease in its diameter, this might require some surgical intervention to overcome that problem.

Now once the bolus of food reaches the lower opening of the esophagus the bolus encounters another sphincter (lower esophageal sphincter) guarding this opening, this sphincter needs to relax in order to allow the bolus to pass downwards through it, this relaxation is achieved by intrinsic reflexes.

Gastro-esophageal sphincter is equipped also by valve like closure at the distal opening of the esophagus to prevent reflux of food from the stomach. The failure of this system may result in esophageal reflux (Return of gastric content toward esophagus).

After all of this the bolus of food reaches the stomach, the stomach usually has a very small capacity around 50 ml, but when we drink water or other foods and beverages the stomach can expand and have the capacity of up to 2-3 litres, this process is achieved due to stomach relaxation (receptive relaxation of the stomach). The relaxation is caused by the activation of the inhibitory neurons from the lower part of the esophagus. These neurons induce inhibition of the tonic contraction of the sphincter and the relaxation of the stomach.

The End