Digestive System

University of Jordan

Faculty of Medicine

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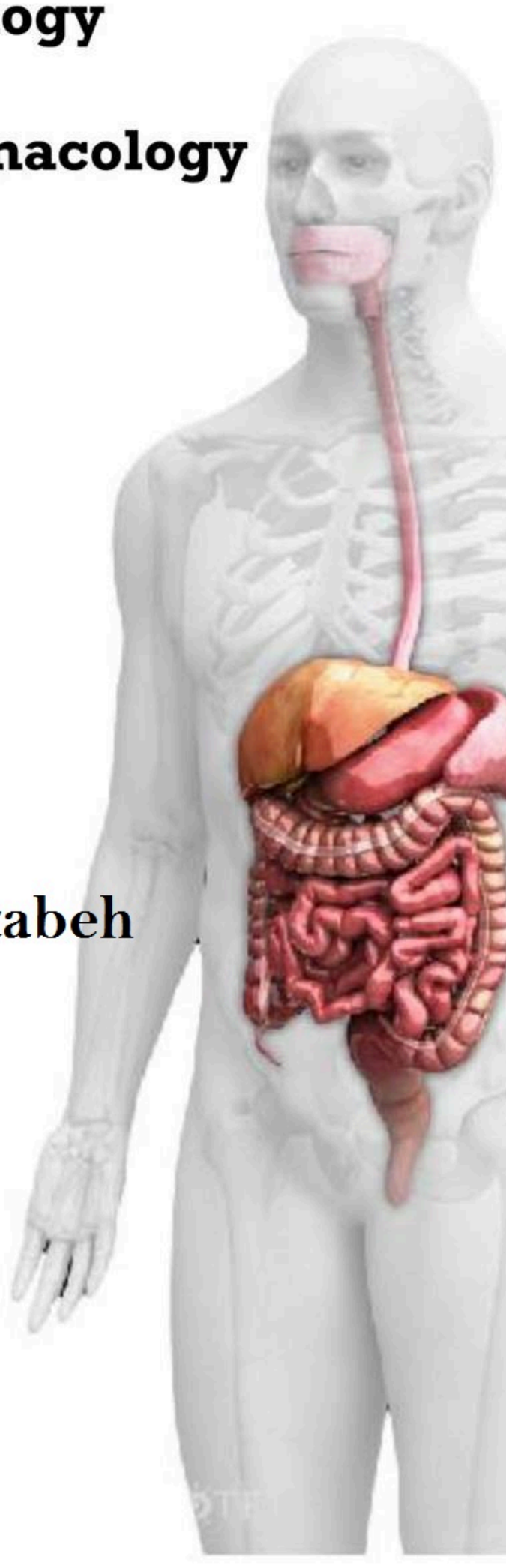

Handout #: 1

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Gastrointestinal physiology

Textbook of Medical Physiology, by GUYTON and HALL, 12th Ed: pp: 753-803, 843-863. 11th ed: p771-818, p865-888. 10th Ed, p 718-770, p 803-821.

Objectives: After studying, the student should be able to:

1. Relate anatomical structures of GI tract to their functions.
2. Relate electrical activity and smooth muscle cells responses to their functions in the GI tract.
3. describe motor activities along GI tract, and organ variations of these activities.
4. Describe secretions along GI tract, their function and mechanisms involved in regulation.
5. Describe digestion and absorptive mechanisms and their regulation.
6. Describe dietary balance, regulation of food intake and feeding abnormalities (obesity and starvations) that may accompany dietary balance disorders.
7. Describe energetics in human body and measurements of Basal Metabolic Rates (BMR).

Introduction

Four physiological processes are taking place along the gastrointestinal (GI) tract. These include:

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

Related to these processes:

Control systems of GI functions.

- Neural control
- Hormonal control

- Blood flow to the GI.

Functional structures in the gastrointestinal tract:

Smooth muscle cells:

2 main layers are generally forming Gastro-intestinal tract with some variations according to organ. These layers are clearly seen in small intestine:

- Longitudinal layer: outer layer of smooth muscle cells arranged longitudinally along the digestive tract.
- Circular layer: extend circumferentially around the gut. Located beneath longitudinal layer.

Each layer is forming a bundle like structure. Cells in each bundle are connected together by gap junctions with permit these cells to function as syncytium. Therefore, by this organization, a group of cells is functioning together to an effective contraction along gastro-intestinal tract.

In addition to these two main layers, a third thin layer of smooth muscle cells is also described in the submucosa and known as ***Muscularis mucosa***. This layer is involved in the secretion from tubular glands and movements of mucosal folds.

Characteristics of smooth muscle cells:

* 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**. The spike potentials are the true action potentials that appear at the peak of slow waves.

* Ca++ in smooth muscle cells contractions: The role of calcium in smooth muscle contraction is known. The source of Ca++ for contraction is either from extracellular fluid or sarcoplasmic reticulum.

The entry of Ca++ from the interstitial fluid appears by activation of Ca++ channels. This activation is generated by **spike potentials** that occur at the peak of slow waves which represents the true action potentials at smooth muscle cells.

The release of Ca++ from sarcoplasmic reticuluim occurs by formation of IP3 that results during signal transduction mechanisms by activation of phospholipase C

in response to binding of ligand (hormone or neurotransmitter) to its receptor.

Ca++ acts via calmodulin to activate myosin filaments which results in developing of attractive forces between actin and myosin.

* Chemical control of smooth muscle cells activity:

Smooth muscle cells respond to a wide range of stimuli caused by neurotransmitter or hormones. This activity appears by activation of receptors on smooth muscle cells. These transmitters may induce relaxation or contraction of smooth muscle cells.

Note: the response is according to the type of transmitter, type of receptor and the transduction mechanism involved in receptor activation.

Finally, integration of responses by smooth muscle cells by binding of ligands to their receptor will result in exhibition of tonic contraction. Variations in the **tonic** contractions by increase or decrease in intensity is seen along gastro-intestinal smooth muscle. In addition to these, also rhythmic contractions have also been described along gastro-intestinal tract (known also as **phasic** or **rhythmic** contractions). In the later type, a group of smooth muscle cells are exhibiting a rhythmical contractions and relaxations as we will see in small intestinal motilities. These contractile activities are controlled mainly by the electrical rhythm that smooth muscle cells of the GI tract are displaying.

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.

To have an effective activity by smooth muscle cells of the GI tract, cells are functioning in syncytium (the activity is very well synchronized by organized contraction and relaxation at the segmental level which promote an efficient motility of the GI tract). The synchronization in part is provided by the ENS. In addition to these, the

cells of Cajal play also an important role in the synchronization of this activity.

Interstitial Cells of Cajal (ICCs):

Interstitial cells are widely spread all over the gastrointestinal tract. These cells have certain characteristics. They have large number of processes. Also, these cells communicate through these processes by gap junction with other ICCs as well as smooth muscle. In addition, these cells eliciting by themselves electrical activity as action potentials. All these have supported the theory of considering these cells as pacemaker cells of the gastro-intestinal tract.

Characteristics of ICCs:

*** ICCs communications:**

The ICCs-ICCs and ICCs-smooth muscle cells communication (by a gap junction) provide the basis for the synchronization of the electrical activity of smooth muscle cells as a group and consequently the harmony of contractile responses of smooth muscle cells. This will result in the functional syncytium of gastro-intestinal smooth muscle cells.

***ICCs generate slow wave:**

ICCs are excitable cells and elicit an electrical activity. These electrical activities have a sudden and periodical appearance of an upstroke from a constant resting potential of about –70mV. The initiation of these activities is believed to be metabolic dependent.

The appearance of the upstroke is believed to cause the slow waves in smooth muscle cells that are in junction with ICCs or to regulate the rhythm of slow waves in smooth muscle cells.

***ICCs also receive inputs from the ENS:**

In addition to their communication with smooth muscle cells, ICCs also receive inputs from the ENS. These inputs may give these cells an important role in mediating the activity to smooth muscle cells which promote a regulatory role of smooth muscle cells activity.

Secretory cells:

These are represented as solitary cells that line the digestive tube or grouped in functional structures (known as glands). These cells are specialized in synthesis and secretion of organic substances that function as enzymes, hormones, factors or mucus. Some of these structures are secreting only water and electrolytes (this type is known as serous secretions). More details about secretory cells, their functions and regulation will be given with gastro-intestinal secretion.

Enteric nervous system: (ENS)

Beginning from the esophagus and extending along the entire GI tract, there is a neural network known as **Enteric Nervous System**. Neurons in this system are grouped into two main plexuses. One is located between longitudinal and circular smooth muscle layers known as *myenteric plexus* or *Auerbach's plexus*. The second plexus lies in submucosa and known as *submucosal* or *Meissner's plexus*. Neurons within each plexus are connected by nerve fibers that are projecting orally, caudally and circumferentially. Some neural fibers connect neurons from the two plexuses together.

Neurons from myenteric plexus usually control the activity smooth muscle cells from longitudinal and circular layer, and consequently, gastrointestinal movements. Submucosal plexus usually controls gastrointestinal secretion and local blood flow. Some neurons are considered sensory neurons that transmit signals from gastrointestinal epithelium to both enteric plexuses, prevertebral ganglia of sympathetic, spinal cord, and to brain stems through vagus nerve. These fibers are stimulated by excessive distension of the gut, irritation of the mucosa, or by specific chemical substances in the lumen.

Enteric neurons that control gastrointestinal functions contain transmitters that could have an inhibitory or excitatory effects on motility, secretion, or vascular blood flow. Many types of transmitters have been identified in ENS, such as, Ach, SP (substance P), VIP (vasoactive intestinal peptide), CGRP (Calcitonin Gene Related Peptide), GRP (Gastrin Releasing Peptide), and many others.

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 nerve 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.

Endocrine cells and Hormones in the GI.

Many hormones have been identified at the level of GI tract. Many of these have their function unidentified yet. These hormones include:

Gastrin:
Cholecystokinin (CCK).
Secretin.
GIP (Gastric Inhibitory Peptide) other name is (Glucose-dependent Insulinotropic Polypeptide).

Others hormones are also secreted along Gastro-intestinal tract, including: Glucagon-like peptide-1(GLP-1), Motilin, Ghrelin, Amylin,

Enterostatin, Neuropeptide Y (NPY), Pancreatic polypeptide which is closely related to polypeptide YY and NPY. In addition, scattered endocrine cells releasing Somatostatin,, Neurotensin, Thyrotropin releasing hormone (TRH), Adrenocorticotropic hormone (ACTH) have been described along the GI tract.

Blood Flow and Local activities in the GI:

The blood flow to the gut is very well related to local activities. After meal the increase in absorption, secretion and motor activities is accompanied by an increase in blood flow. This increase continues during the next few hours after meal and return back over the next 2-4 hours.

Regulation of gastro-intestinal blood flow:

Possible factors that cause an increase in blood flow:

- The release of vasodilator substances after mucosal stimulation caused by meals. Such as, CCK, VIP, Gastrin and Secretin. These factors are also important in controlling smooth muscle cells activities.

- some glands release Kinins (kallidin and bradykinin) into the lumen and the gut wall.

- Decreased oxygen concentration → increase blood flow possibly by the release of adenosine.

Like muscle activity, vascular flow is also under the control of enteric nervous system. Many transmitters are known to affect the vascular flow of the gastrointestinal tract, such as SP, VIP, CGRP, and others. These transmitters are released by neurons of the ENS.

The autonomic nervous system has also effects on the blood flow to the gut. Sympathetic stimulation causes vasoconstriction, which results in decreased blood flow, while parasympathetic system causes an increase in blood flow. Although, parasympathetic system has 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).

Gastro-intestinal Motilities

Mixing and movements of food along the GI tract:

Mastication (chewing):

Chewing results in grinding action on food to get smaller particles. This occurs by activation of chewing reflex (centers 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.

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

Deglutition (Swallowing):

Two stages of deglutition:

- Voluntary stage: in which 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 centers 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 (pharyngoesophageal sphincter) is relaxed and esophageal opening is enlarged. This will end in enforcing bolus to move into esophagus.

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

Two types of contraction are taking place by esophageal muscle:

- 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 second.
- Secondary peristalsis:
  Represented by intrinsic (within myenteric plexus) and extrinsic (through afferent and efferent vagus fibers) 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 is striated muscle and controlled by glossopharyngeal nerve. The lower third is smooth muscle and controlled by the vagus nerve.

Peristaltic wave of the esophagus ends with relaxation of **gastroesophageal sphincter** (lower esophageal sphincter) and 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.

Failure of the sphincter to relax may result in a pathological condition known as *achalasia*. In which the ability of myenteric plexus to cause relaxation of the sphincter has failed.

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).

The motor activities of the stomach:

- The most important function of the stomach is *storage of food.* This organ can dilate from the capacity of 50ml up to 1000ml. This dilation begins with receptive relaxation and the intervention of vago-vagal reflex that decreases the muscular tone of the stomach upon the presence of food in the stomach.

- Stomach secretes large amount of secretions (2000ml/day). This secretion when mixed with the ingested food in the stomach is forming chyme. These secretions are mixed with food due to the motor activities of the stomach which is known as ***peristaltic constrictive waves*** **or** ***mixing waves***. These activities appear in the mid portion of the stomach at frequency of 3/min and move toward the antrum. The frequency is determined by the frequency of basic electrical rhythm (BER) of gastric smooth muscle. These contractions are very intense as they approach the antrum and they are forming *constrictive ring*s. At the antrum, when the peristaltic constrictive wave reaches the pylorus, it causes constriction of the pyloric sphincter which impedes emptying of chyme into the duodenum. The result of these contractions not only mixes food, they also grind food and toss the content of the antrum back toward the body and forth. The process of tossing back the antral content is known as *retropulsion*. Very small amount of chyme with fluid consistency can pass into the duodenum because of the small opening of the pylorus and the constriction of pyloric sphincter. For about 20% of time these peristaltic contractions become very intense and cause an increase in the pressure in the antrum. This action forces several ml of chyme to pass into the duodenum. The process that results in passage of chyme into duodenum is known as **gastric emptying**. The whole activity that results in gastric emptying is known as *pyloric pump*.

Note: Gastric movements result in grinding food particles and mixing them with secretion.

Pylorus as functional structure:

Pylorus is a small opening between stomach and duodenum guarded by smooth muscle cells that form the pyloric sphincter. The muscle cells of this sphincter are in tonic contractions. This structure gives access only to fluids to pass into duodenum and prevents the passage of food particles until they are grind and mixed well with secretions by forming chyme with fluid consistency.

Hunger contractions: This type of intense contractions in the stomach appears when the stomach is empty and lasts for several hours. These contractions are rhythmical peristaltic contractions with duration of 2-3 minutes for each. It seems that these contractions are in

relation with glucose concentration in the blood (They are increased by decreasing glucose level in blood).

Neural and hormonal control of gastric emptying:

Stimulation of gastric emptying:

- Filling of the stomach: initiates myenteric reflexes that causes an increase in the activity of pyloric pump and inhibits the tone of pyloric sphincter.

- Gastrin: secreted by the antral mucosa. This hormone has mild stimulatory effect on the peristaltic activities of the stomach, which result in enhanced pyloric pump.

Inhibition of gastric emptying:

- Enterogastric reflex: The passage of chyme to the duodenum causes decrease pH (in duodenum). This initiates intrinsic and extrinsic reflexes to decrease gastric emptying.

  3 levels of inhibition induced by enterogastric reflexes:
  - Through ENS.
  - Through prevertebral ganglia.
  - Through signals via the vagus nerve to inhibit the excitatory signals of vagus nerve to the stomach.

  The effects of these reflexes decrease the antral propulsive contractions and increase the tone of the pyloric sphincter.

- Hormonal feedback from the duodenum:
  - CCK cholecystokinin: (secreted by jejunum) the release is stimulated by fat in chyme.
  - GIP: Gastric Inhibitory Peptide: released from upper small intestinal specialized cells and stimulated by fat and carbohydrates in chyme.
  - Secretin: stimulated by acid in duodenum.

Intestinal movements:

1. **Propulsive Movement**: ensures the movement of chyme analward at an appropriate rate.

2. **Mixing Movements**: which result in mixing food with GI secretion.

Propulsive movements

Movements of food along the GI tube are caused by peristaltic contractions that appear at the GI tract. These contractions are described as a contractile ring of the circular muscle layer up to the distension and relaxation down to the distension of segment, which move forward along the GI tract. Other component of the contraction is rhythmic shortening of longitudinal layer. The peristalsis can initiated usually by local reflexes caused by distention of the gut which induce contractile ring 2-3 cm above the distended part and relaxation of the part of the GI tube down to the distention which is called *receptive relaxation.*

These changes that appear in the motor activity of the smooth muscle cells of the GI describe complex patterns of activities that are known as *peristaltic reflex*. After the initiation of this reflex by the formation of the contractile ring and the distention of the segment down to stimulated part of the intestine, and shortening and elongation of longitudinal layer results in chyme movements downward along the GI (in analward direction). These changes with the peristaltic wave and including the analward movement of peristalsis are known as the "*law of the gut*".

Although, the main effect of this type of contraction is to propel chyme in caudal direction, they also have some effects on mixing food and spreading chyme along the intestine which help in the absorption of food.

Rhythmic contractions of longitudinal layer are controlled by electrical activities of smooth muscle cells.

Neural control:

*The role of the ENS:

The complex structures of the enteric nervous system provides a neural network connection that controls many of the GI functions including the movements and the rate of chyme movements. The orad (up direction) extension of the excitatory neurons and the caudad (down direction) extension of the inhibitory neurons provide a great networking which play a big role in peristaltic reflex. The congenital absence or the decreased activity of the enteric nervous system may depress or weaken the peristaltic reflexes and decrease the effectiveness of peristalsis to move the chyme in analward direction.

As a result an effective peristaltic activity to cause a propulsive movement of chyme requires an intact and active ENS.

The peristaltic contractions can also be initiated by mucosal stimulation (as in peristaltic rush: rapid and powerful peristaltic contractions).

Other factors can also interfere with the peristaltic activities:

*Parasympathetic nervous system: this system can modulate the peristaltic activities by changing the activity of neural network or by changing the activity of smooth muscle cells.

Hormonal control:

Many hormones have shown to affect the gastrointestinal motility After meals many hormones are secreted during phases of food processing. For some of these hormones, the effect on intestinal motility is known. As example:

- Gastrin, CCK, serotonin enhance intestinal motility.
- Secretin and glucagon inhibit intestinal motility.

Mixing movements:

The mixing of food with secretions in the GI tract is provided by the activity of circular smooth muscle cells. The contractions that appear along the intestine which are inter-spaced by the relaxation of adjacent smooth muscle cells up and down to the contracted segment cause spaced segmentations of the intestine which are known as *segmentation contractions*.

The rate of contractile activity is determined by the rate of slow waves (the electrical activity of smooth muscle cells or BER) in that segment of the intestine. The maximum frequency of contractions is about 12/minute in the upper part of intestine (duodenum and jejunum) and 8/minute in the terminal ileum (the same as the rate of slow waves or Basic Electrical Rhythm (BER)).

Although these types of contraction have mainly mixing effect on chyme, they also have some propulsive effects which cause movement in analward direction.

Other types of contractions in intestine:

Peristaltic rush: Powerful and rapid peristalses that occur along small intestine caused by mucosal irritation and/or intestinal distension.

Migrating Motor Complex (MMC):

MMC is other type of motor activity that begins in the stomach in the inter-digestive periods. The activity begins in the distal part of the stomach and continues along the entire small intestine. The contractions that forming MMC appear in 3 phases:

In the first phase: slow waves (as electrical activity) without contraction are present.

In the second phase: not all slow waves are followed by contractions (one slow wave is followed by contraction and 1-5 slow waves are not followed).

In the third phase lasts for 5-15 minutes all slow waves are followed by contractions.

The function of these contractions is to sweep the intestinal content in the time between meals.

These movements are controlled by hormonal (Motulin is believed to be involved) and neural mechanisms.

Movements caused by the activity of muscularis mucosa:

The activity of muscularis mucosa is responsible for the shortening and elongating mucosal folds. This activity helps more in the absorptive process by intestinal mucosa.
The contractions caused by muscularis mucosa are also affected by the activity of enteric nervous system.

Movements of the colon:

Mixing movements (**haustration contractions**): the appearance is similar with segmentation contractions of the small intestine. The activity is represented as rhythmic contraction and relaxation of circular layer of colonic smooth muscle cells at a length of about 2.5cm. Each contraction lasts for 30-60 sec. In addition to the activity of circular layer, longitudinal muscle strips (known as *teniae coli*) are also involved to cause haustral appearance in the colon.

The role of these contractions is helping in absorption of water and electrolytes by spreading the colonic content over the mucosa. In addition, these contractions have also propulsive effect. Although, they have slow effect on the content of cecum and ascending colon, they are the main responsible in moving it into transverse colon.

Propulsive movements (**mass contractions**): are series of contractions that appear 1-3 times/day and last each time about 10-30minutes. These contractions appear mainly in the first hour after breakfast. They are the main responsible in moving fecal materials from the beginning of transverse colon to the sigmoid.

Mass contractions are described as constrictive rings that usually begin at the transverse colon followed by the contraction of about 20cm or more of the colon distal to the constrictive ring. Each contraction lasts for 30 sec, then, followed by 2-3 minutes relaxation and then another contraction wave begins.

Mass contractions are facilitated by gastrocolic and duodenocolic reflexes. These reflexes are conducted through the autonomic nervous system.

These contractions can also be initiated by the irritation of the colon. As example, in ulcerative colitis that results in mucosal irritation, causes an increase in mass movements of the colon.

The effect of these contractions: feces will be forced to move into the rectum which may result in the initiation of defecation reflex.

Defecation:

Two types of reflexes are preceding defecation act. These include:

Intrinsic reflexes: in which, distention of the rectum initiates signals through **myenteric plexus** (ENS) to cause more contractions in descendent colon, sigmoid and rectum. This will force feces to move toward the anus. This reflex is weak and will not cause defecation.

Extrinsic reflexes (parasympathetic defecation reflex): distension of rectum and sigmoid will result in:

- Increased parasympathetic signals which fortify contractions that appear in the descendent colon, sigmoid and rectum.
- Signals to the internal sphincter to cause relaxation.

Note: all these reflexes are involuntary.

After all these reflexes, the defecation in normal people occurs only as a **voluntary act** by relaxing external sphincter (which is under voluntary control) and increasing abdominal pressure by closure of glottis and contractions of the abdominal wall which cause the pelvic floor to be pulled downward on the anal ring and relax to evaginate feces.