General Principles of GIT Physiology

Objectives :

- Physiologic Anatomy of the Gastrointestinal Wall.
- The General & Specific Characteristics of Smooth Muscle.
- Neural & Hormonal Control of Gastrointestinal Function.
- Types of Neurotransmitters Secreted by Enteric Neurons.
- Functional Types of Movements in the GIT.
- Gastrointestinal Blood Flow "Splanchnic Circulation".
- Effect of Gut Activity and Metabolic Factors on GI Blood Flow.

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Colour index:
- Important
- Numbers
- Extra

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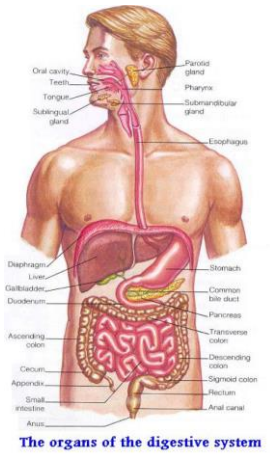
Gastrointestinal System:

- Gastrointestinal System
  - GIT
  - Associated Organs
    (Liver,gallbladder,pancreas,salivary gland)



The organs of the digestive system

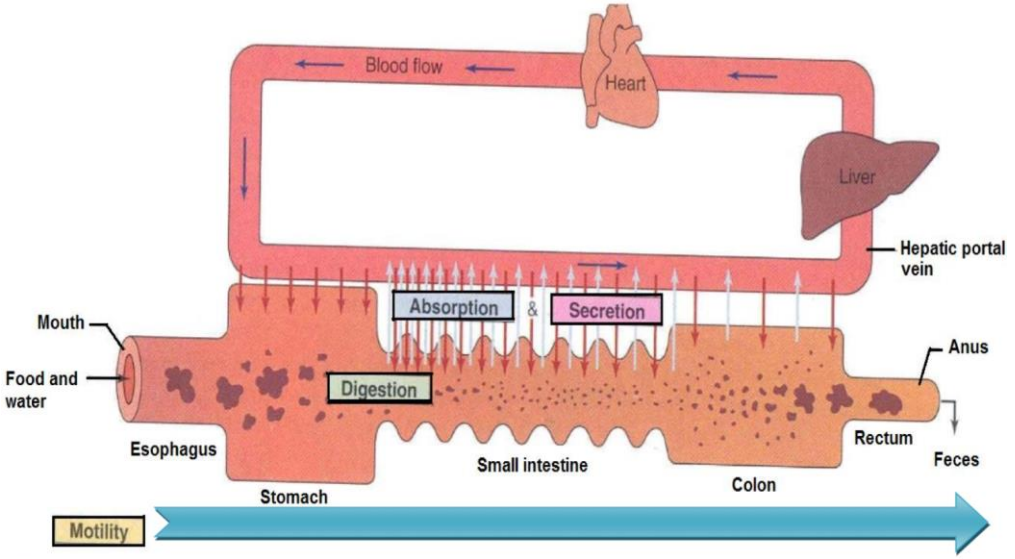
Gastrointestinal Function:

- The alimentary tract provides the body with a continual supply of water, electrolytes, and nutrients. To achieve this function, it requires:

1	Movement of food through the alimentary tract (**motility**).
2	Secretion of digestive juices and digestion of the food.
3	Absorption of water, various electrolytes, and digestive products.
4	Circulation of blood through the gastrointestinal organs to carry away the absorbed substances.

- Control of all these functions is by **local**, **nervous**, and **hormonal systems.**

The Four Processes Carried Out by the GIT:

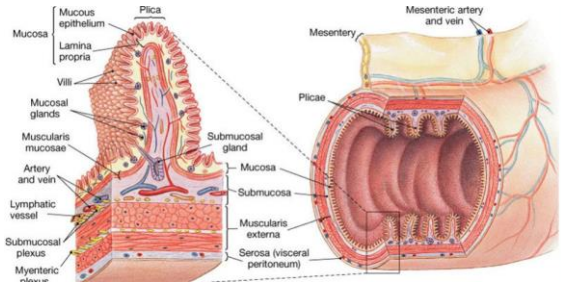


Four processes carried out by GIT, motility, secretion, digestion and absorption

Physiologic Anatomy of the Gastrointestinal Wall

Same layers in Histology lecture

- The following layers structure the GI wall from inner surface outward:
  - The mucosa
  - The submucosa
  - Circular muscle layer
  - longitudinal muscle layer
  - The serosa.



- In addition, sparse bundles of smooth muscle fibers, the mucosal muscle, lie in the deeper layers of the mucosa.

The General Characteristics of Smooth Muscle

1- Two Smooth Muscle Classification:

Unitary type Rich in gap junctions	• Contracts spontaneously in response to stretch, in the absence of neural or hormonal influence. • E.g: in stomach and intestine • Cells are electrically coupled via gap junctions. Extra information from Guyton Chapter 8 ,13th edition: • Unitary smooth muscle is also called syncytial smooth muscle or visceral smooth muscle. he term "unitary" is confusing because it does not mean single muscle fibers. Instead, it means a mass of hundreds to thousands of smooth muscle fibers that contract together as a single unit.the cell membranes are joined by many gap junctions through which ions can low freely from one muscle cell to the next so that action potentials, or simple ion low without action potentials, can travel from one fiber to the next and cause the muscle fibers to contract together.
Multi-unit type	• Does not contract in response to stretch or without neural input. • E.g: in esophagus & gallbladder Extra information from Guyton Chapter 8 ,13th edition: • Multiunit smooth muscle is composed of discrete, separate smooth muscle fibers. Each fiber operates independently of the others and often is innervated by a single nerve ending, as occurs for skeletal muscle fibers. • Important characteristics of multiunit smooth muscle fibers are that each fiber can contract independently of the others, and their control is exerted mainly by nerve signals. • Some examples of multiunit smooth muscle are the ciliary muscle of the eye and the iris muscle of the eye.

The General Characteristics of Smooth Muscle Cont.

2- Two Main Smooth Muscle Layers:

Longitudinal	Circular
Thinner and less powerful.	Thicker and more powerful.
Less gap junctions.	More gap junctions.
Contraction **shortens** the segment of the intestine and **expands** the lumen.	Contraction **reduces** the diameter of the lumen and **increases** its length.
Innervated by enteric nervous system (ENS), mainly by excitatory motor neurons.	Innervated by ENS, both excitatory and inhibitory motor neurons.
Ca++ influx from outside is more important. "from extracellular fluid"	**Intracellular release of Ca++ is more important.** "from sarcoplasmic reticulum"

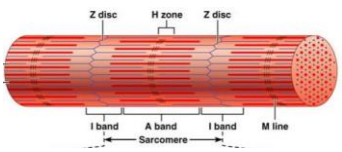
3- Types of Contraction:

Phasic contractions (rhythmical)	Tonic contractions (Maintained)
• Periodic contractions followed by relaxation. • Occur in esophagus, gastric antrum and small intestine.	• Contraction without relaxation. • Occurs in orad (mouth=proximal) region of stomach, lower esophageal, ileocecal & internal anal sphincters. • **Not associated with slow waves** (often lasting several minutes or hours). • Doctor said: if it is associated to slow waves , it will not be guaranteed to contract as slow waves cannot elicit contraction unless it peaks or reaches the threshold beside we need this segment to continually contracted. • Caused by: 1. repetitive spike potentials 2. hormones 3. continuous entry of Ca^{++} ions not associated with changes in membrane potentials i.e. Not via voltage-gated Ca^{++} channels.

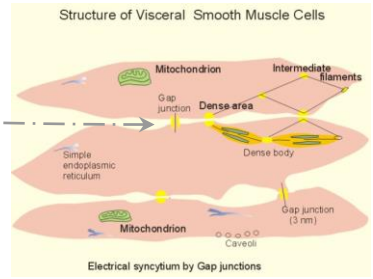
The Specific Characteristics of Smooth Muscles

1- Gastrointestinal Smooth Muscle Functions as a Syncytium:

Same as cardiac muscles



- The individual smooth muscle fibers are 200 to 500 µm in length and 2 to 10 µm in diameter, and they are arranged in bundles of as many as 1000 parallel fibers.
- Within each bundle, the muscle fibers are electrically connected with one another through large numbers of gap junctions.
- Each muscle layer functions as a syncytium; when an action potential is elicited anywhere within the muscle mass, it generally travels in <u>all directions</u> in the muscle.



2- Electrical Activity of Gastrointestinal Smooth Muscle:

- The smooth muscle of the gastrointestinal tract is excited by almost **continual slow**, **intrinsic electrical activity** along the membranes of the muscle fibers.
- This activity has two basic types of electrical waves:
  - Slow Waves
  - Spike Potential

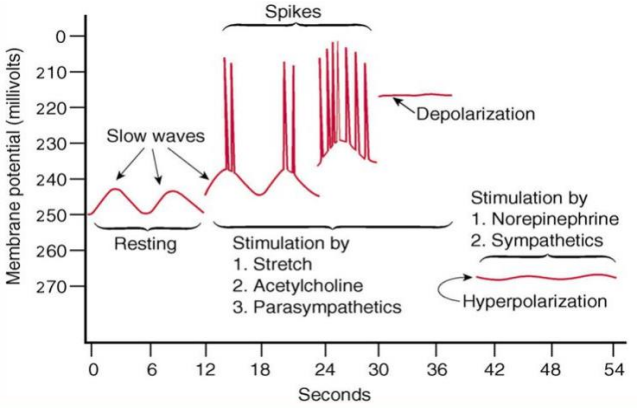
Action potential is 20 times longer than other cells action potentials why?!
To make sure or to guarantee that enough Calcium can influx..

The Slow Waves- Basic Electrical Rhythm

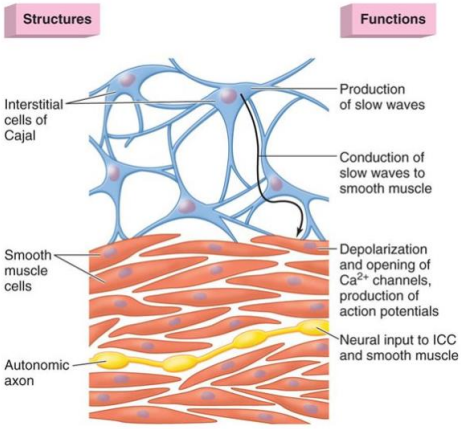
1. They are oscillating depolarization and repolarization in the resting membrane potential with unknown cause.
   oscillating means :move or swing back and forth in a regular rhythm.
2. Intensity(amplitude) from 5-15 mv, frequency from 3-12/min.
   Frequency change according to site in GIT
3. These waves are not action potentials and do not directly cause contraction.
4. Generated by **interstitial cells of Cajal**, ICC (the GI pacemaker), which are abundant in the myenteric plexuses.
5. ICC form a network and are interposed between the smooth muscle layers, with synaptic-like contacts to smooth muscle cells.
6. Parasympathetic ↑ the amplitude and frequency of slow waves.
   Sympathetic ↓ their amplitude and frequency.

The Specific Characteristics of Smooth Muscles

Slow Waves are Generated by Interstitial Cells of Cajal



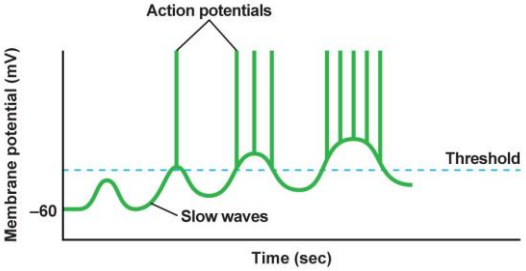
Membrane potentials in intestinal smooth muscles

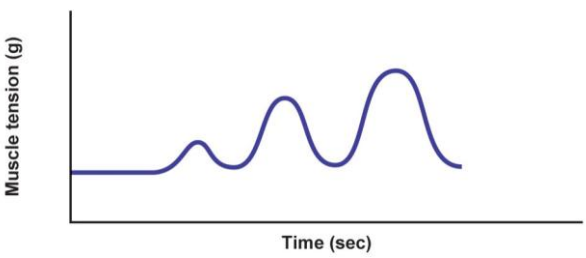


Spike potential happen on top of slow waves. Slow waves will reach a specific membrane potential (-40 mv) and then firing will happen

The Spike Potential

1. They are true action potentials that occur automatically when **RMP rises above -40 mv** [RMP= -(50) to (-60) mv].
2. Each spike lasts as long as 10 to 20 msec. They are 10 to 40 times the action potentials in large nerve fibers.
3. Spikes of action potential superimpose on depolarization of slow waves followed by contraction.
4. The rising phase of AP is caused by inflow of large numbers of Ca++ along with smaller numbers of Na+ (Slow Ca++-Na+ channels).
5. The higher the slow wave potential rises, the greater the frequency of the spike potentials.
6. They are usually ranging between 1 and 10 spikes per second.





The Specific Characteristics of Smooth Muscles

3- Changes in Voltage of the Resting Membrane Potential (-50mv to -60mv)

Factors that depolarize the membrane (become less negative and more excitable)	**Factors that hyperpolarize the membrane** (become more negative and less excitable)
Stretching of the muscle	Effect of norepinephrine on fiber membrane
Stimulation by Ach released from parasympathetic nerves endings	Effect of epinephrine on fiber membrane
Stimulation by several specific GI hormones	Stimulation of the sympathetic nerves that secrete norepinephrine at their endings

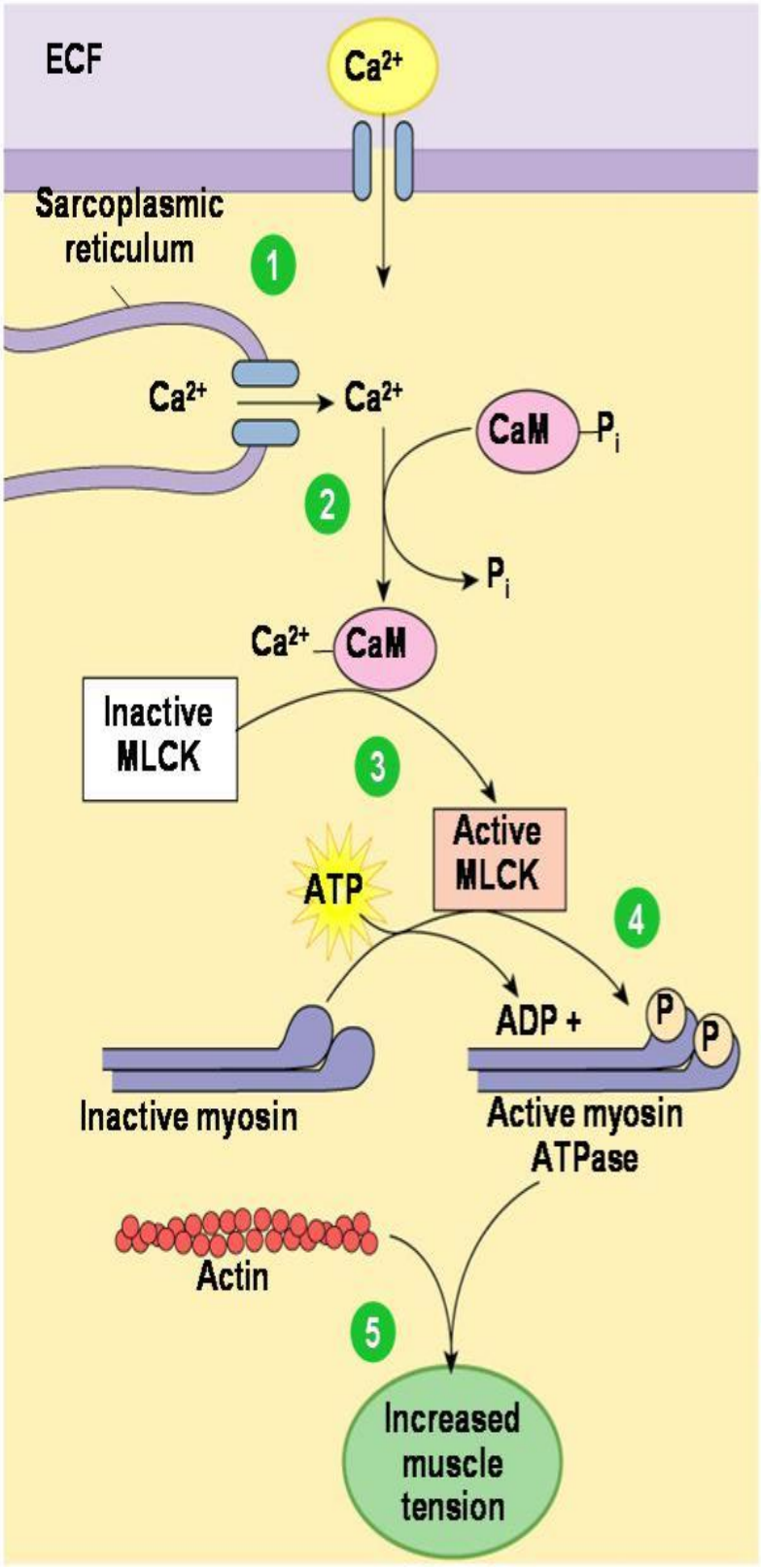
4- Role of Calcium in Muscle Contractions

Smooth muscle contraction occurs in response to entry of **Ca++** into the muscle fiber.

Slow waves do not cause **Ca++** to enter smooth muscle fiber *(only sodium ions)*. Therefore, slow waves by themselves usually cause no muscle contraction.

During spike potentials, generated at the peaks of slow waves, significant quantities of **Ca++** enter the fibers and cause most of the contraction.

Mechanism of smooth muscle contraction:



1. Intracellular Ca^{2+} concentrations increase when Ca^{2+} enters cell and is released from sarcoplasmic reticulum.

2. Ca^{2+} binds to calmodulin (CaM).

3. Ca^{2+}–calmodulin activates myosin light chain kinase (MLCK).

4. MLCK phosphorylates light chains in myosin heads and increases myosin ATPase activity.

5. Active myosin crossbridges slide along actin and create muscle tension.

Control of GIT functions:

GIT functions are controlled by:

- **Neural control:**
  - Autonomic (extrinsic) nervous system.
  - Enteric nervous system.
- **Hormonal control:**
  - Endocrine cells are located in the pancreas, in the mucosa & submucosa of the stomach & intestine. They produce hormones that act on the secretory cells, smooth muscle cells or sphincters.
  - All the GI hormones are peptides such as: Gastrin, Secretin, Cholecystokinin.

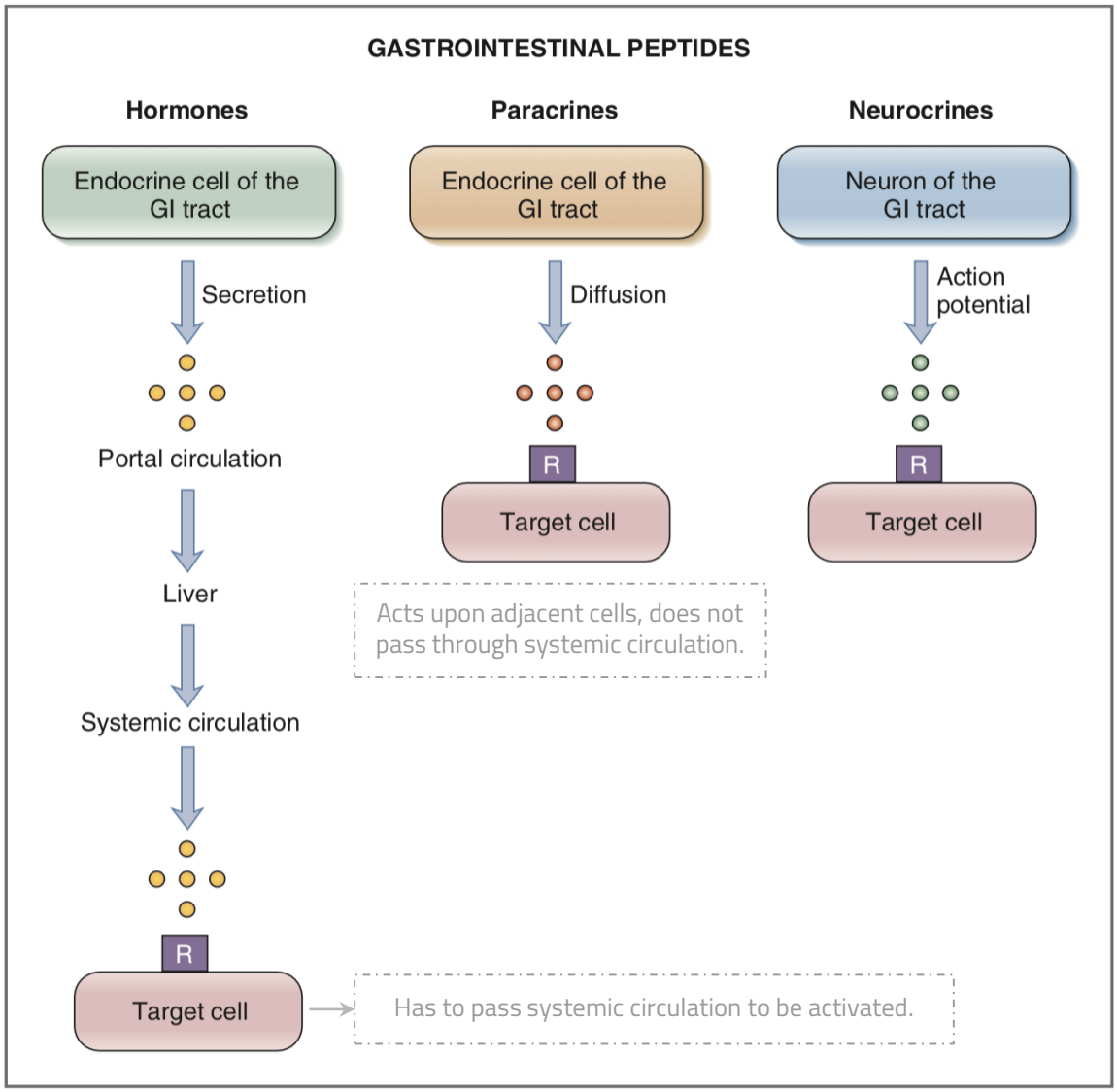


Fig. 8.4 Classification of gastrointestinal peptides as hormones, paracrines, or neurocrines. *GI,* Gastrointestinal; *R,* receptor.

Hormonal Control of Gastrointestinal Motility (GI Peptides):

Hormone	Site of secretion	Stimuli for secretion	Actions
Gastrin	"G" Cells of the stomach	-Protein -Distention of the stomach. -Vagal stimulation. -(Acid inhibits release).	↑ Gastric H+ secretion Stimulates growth of gastric mucosa. Stimulate parietal cells to secrete hydrochloric acid HCl.
Cholecystokinin (CCK)	"I" cells of the duodenum and jejunum	-Protein -Fatty acids. -Acid.	↑ Pancreatic enzyme secretion. ↑ Pancreatic HCO3 - secretion. **Stimulates** contraction of the gallbladder & **relaxation** of the sphincter of Oddi. **Stimulates** growth of the exocrine pancreas and gallbladder. **Inhibits** gastric emptying.
Secretin Does not like acids at all	"S" cells of the duodenum	-H+ in the duodenum. -Fatty acids in the duodenum.	↑ Pancreatic HCO3 - secretion. ↑ Biliary HCO3 - secretion. ↓ Gastric H+ secretion. **Inhibits** trophic effect of gastrin on gastric mucosa.
Glucose-Dependent Insulinotropic Peptide (GIP)	"K" cells of the Duodenum and jejunum	-Fatty acids Amino acids. -Oral glucose carbohydrate.	↑ Insulin secretion from pancreatic β cells. ↓Gastric H+ secretion.
Motilin During fasting, motilin increases	"M" cells of the duodenum and jejunum	Fat, Acid, Nerve	Stimulates: Gastric motility Intestinal motility.

*This table is important

Neural control of gastrointestinal function:

- **Autonomic Nervous System (ANS) is divided into:**
  - Parasympathetic
  - Sympathetic
  - Enteric Nervous system

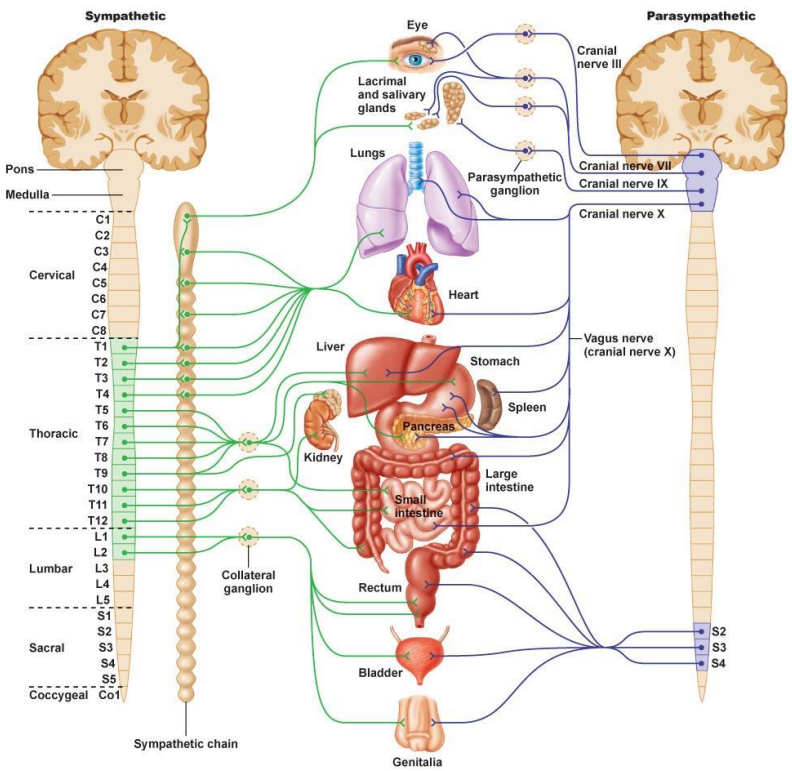
Useful video

Sympathetic Innervation (Thoracolumbar outflow)

- The sympathetic fibers originate in the spinal cord between segments T-5 and L2.
- The sympathetics innervate essentially all of the GI tract.
- The sympathetic nerve endings secrete mainly norepinephrine.
- Stimulation of the sympathetic nervous system inhibits activity of the GI system.
- Strong stimulation of the sympathetic system can inhibit motor movements of the gut so greatly that this literally can block movement of food through the GI tract.

Parasympathetic Innervation (Cranial & Sacral outflow)

- The **vagus nerves** (cranial division) innervate the esophagus, stomach, pancreas and intestines down to the first half of the large intestine.
- The **pelvic nerves** (sacral division) innervate the distal half of the large intestine and the anus (to execute the defecation reflexes).
- The postganglionic neurons of the gastrointestinal parasympathetic system are located mainly in the myenteric and submucosal plexuses.
- Stimulation of parasympathetic nerves causes general stimulation of entire activity of enteric nervous system.



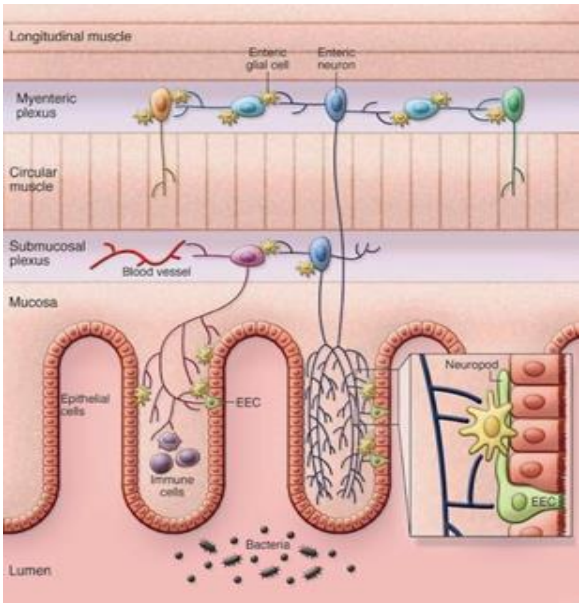
The Enteric Nervous System

- Enteric Nervous System (ENS) is the nervous system of GI tract.
- It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus.
- It has as many neurons as the spinal cord (about 100 million).

Components of The Enteric Nervous System

It is composed mainly of **two plexuses**:

1. **The myenteric (Auerbach's) plexus**
   - Lies between the longitudinal and circular muscle layers.
   - Consists mostly of a linear chain of many interconnecting neurons.
   - The myenteric plexus has excitatory and inhibitory motor neurons.
2. **The submucosal (Meissner's) plexus**
   - Lies in the submucosa.

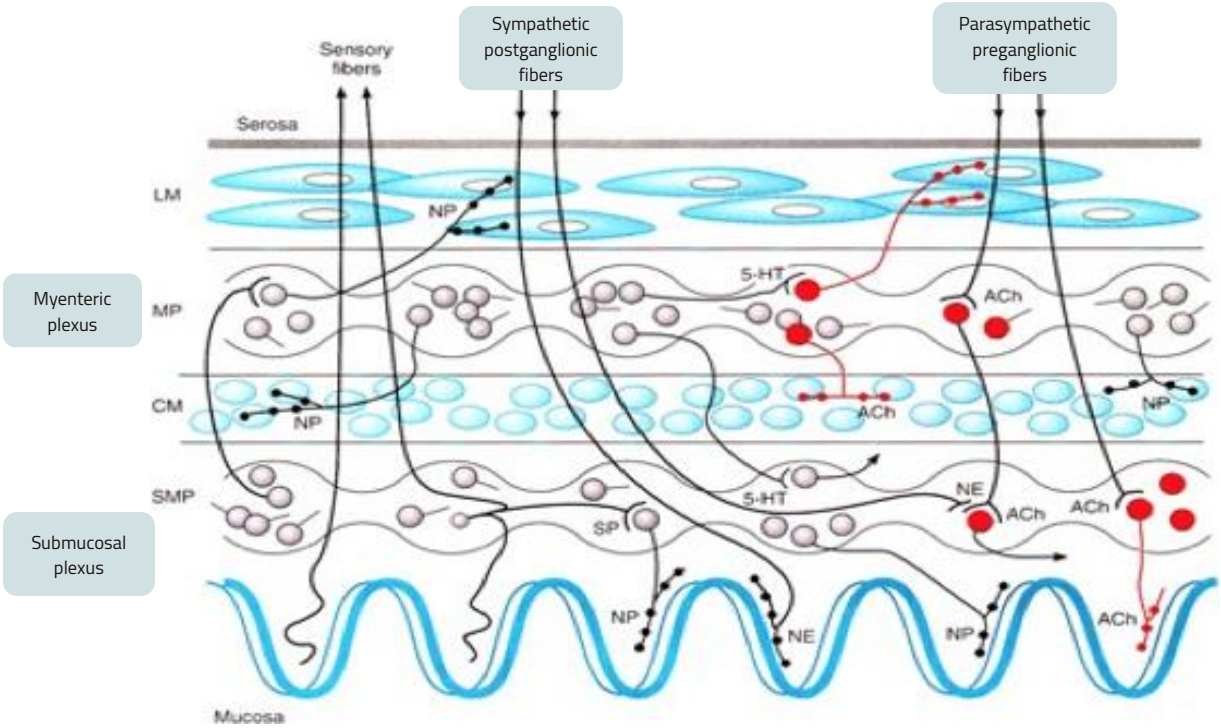


Functions of Myenteric and Submucosal Plexuses

Myenteric plexus Deals with motility	**Submucosal plexus** Mainly excitatory
• Increase tonic contraction • Increase intensity of the rhythmical contractions • Increase rate of rhythm of contraction • Increased excitatory waves conduction velocity along gut wall • Some neurons are inhibitory (e.g . pyloric & ileocecal valves).	Controls:- • Local intestinal secretion • Local absorption • Local blood flow • Local contraction of submucosal muscle causing infolding of the gastrointestinal mucosa.

The Enteric Nervous System & the Extrinsic Nerves

The enteric nervous system can function on its own, independently of the parasympathetic and sympathetic systems, however, these extrinsic nerves can greatly enhance or inhibit gastrointestinal functions.



Types of Neurotransmitters Secreted by Enteric Neurons

Excitatory for motor neurons:

1- Substance P
2- Ach

Excitatory for secretomotor neurons:

1- Ach
2- VIP
3- Histamine

Inhibitory for motor neurons:

1- ATP
2- NO
3- VIP

Neurotransmitters & Neuromodulators in Enteric Nervous System

Substance	Source	Actions
Acetylcholine (ACh)	Cholinergic neurons	Contraction of smooth muscle in wall Relaxation of sphincters ↑ Salivary secretion ↑ Gastric secretion ↑ Pancreatic secretion
Norepinephrine (NE)	Adrenergic neurons	Relaxation of smooth muscle in wall Contraction of sphincters ↑ Salivary secretion
Vasoactive intestinal peptide (VIP)	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↑ Intestinal secretion ↑ Pancreatic secretion
Gastrin-releasing peptide (GRP) or bombesin	Neurons of gastric mucosa	↑ Gastrin secretion
Enkephalins (opiates)	Neurons of mucosa and smooth muscle	Contraction of smooth muscle ↓ Intestinal secretion
Neuropeptide Y	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↓ Intestinal secretion
Substance P	Cosecreted with ACh	Contraction of smooth muscle ↑ Salivary secretion

Afferent Sensory Nerve Fibers from the Gut

- Many afferent sensory nerve fibers innervate the gut.
- Some of them have their cell bodies in the ENS and some in the dorsal root ganglia of the spinal cord.
- These sensory nerves can be stimulated by:
  - 1- irritation of the gut mucosa
  - 2- excessive distention of the gut
  - 3- presence of specific chemical substances in the gut.
- Signals transmitted through the fibers can cause excitation or inhibition of intestinal movements or secretion.
- Other sensory signals from the gut go all the way to multiple areas of the spinal cord and even the brain stem.
- For example, 80% of the nerve fibers in the vagus nerves are afferent rather than efferent.
- These afferent fibers transmit sensory signals from the GI tract into the medulla, which in turn initiates vagal reflex signals (vagovagal reflexes).

Summary of the Neural Control of Gastrointestinal Function

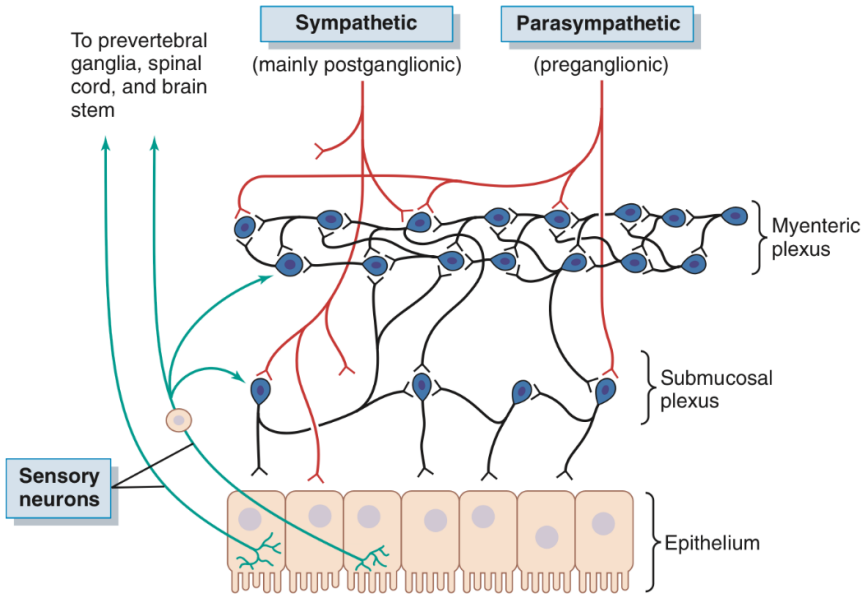


Figure 63-4. Neural control of the gut wall, showing (1) the myenteric and submucosal plexuses (*black fibers*); (2) extrinsic control of these plexuses by the sympathetic and parasympathetic nervous systems (*red fibers*); and (3) sensory fibers passing from the luminal epithelium and gut wall to the enteric plexuses, then to the prevertebral ganglia of the spinal cord and directly to the spinal cord and brain stem (*green fibers*).

➢ Nervous Control of Gastrointestinal Blood Flow

1-Parasympathetic stimulation	2-Sympathetic stimulation
• Increases local blood flow at the same time that it increases glandular secretion.	• Greatly decreased local blood flow. • The local metabolic vasodilator mechanisms override the sympathetic vasoconstriction effects, returning normal blood flow

➢ Gastrointestinal Reflexes

- The anatomical arrangement of the ENS and its connections with the sympathetic & parasympathetic systems support three types of GI reflexes :

1- Reflexes that are integrated entirely within the gut wall ENS.
The majority of reflexes that occur in gut are among this category.
Local reflexes, no ganglia or other extrinsic influences.

2- Reflexes that transmit signals long distances from the gut to the prevertebral ganglia"Sympathetic chain"and then back to the GI tract as :

We are expecting inhibitory action since sympathetic is involved, good guess but this isn't applied here.

➥ **Gastrocolic reflex**: signals from the stomach to the colon.(Excitatory) Distension of stomach lead to increase motility of colon, this applied when you eat a heavy meal you will directly rush to bathroom to defecate.

➥ **Enterogastric reflexes**: signals from the colon and small intestine to inhibit stomach motility and secretion.(inhibitory) Distension of small intestines or colon lead to inhibit gastric motility and secretion.

➥ **Colonoileal reflex:** reflex from the colon to inhibit emptying of ileal contents into the colon.(inhibitory) Distension of colon lead to inhibit ileal emptying.

3- Reflexes from the gut to the spinal cord or brain stem and then back to the GI tract as :

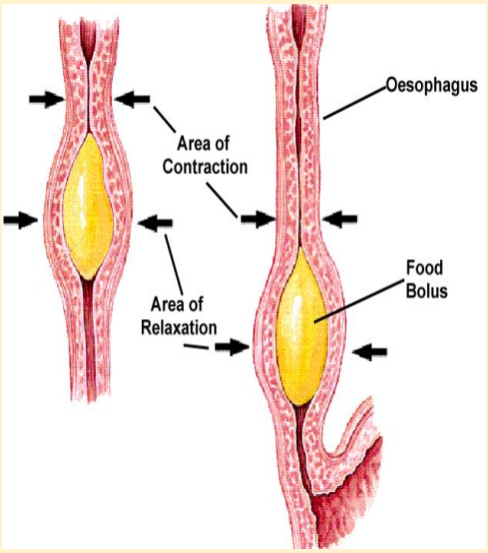
➥ Reflexes from stomach & duodenum to brain stem and back to the stomach (by way of the vagus nerves) to control gastric motility & secretion.Vagovagal reflexes , for sure you will activate vagus nerve to elicit these reflexes.
➥ Pain reflexes that cause general inhibition of the entire GI tract. The whole GI tract can be shut down in case of severe pain that lead constipation
➥ Defecation reflexes that travel from the colon and rectum to the spinal cord and back again to produce the powerful colonic, rectal, and abdominal contractions required for defecation.

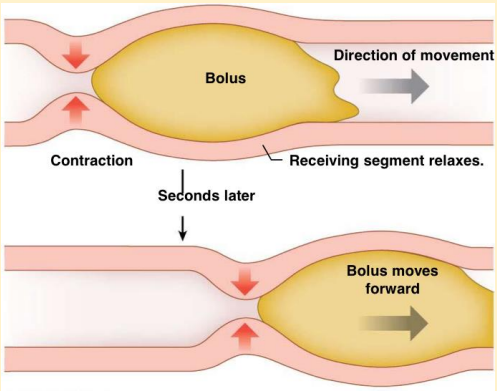
➢ Functional Types of Movements in GIT

1- Propulsive movements (peristalsis)

Does not include mouth and pharynx.

- A contraction ring appears around gut, then moves forward.
- Organizes propulsion of material over variable distances within the GI.
- Lumen Stimuli include distention (mainly) &, chemical or physical irritation of the epithelial lining in the gut.

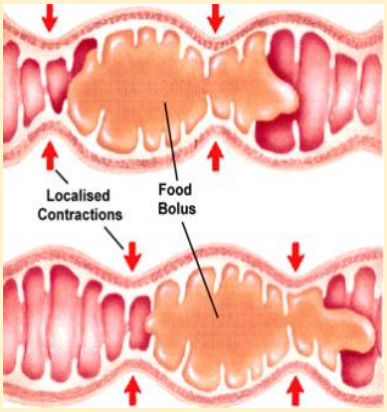




2 -Mixing movements (segmentation)

Blending ,digesting and mixing food with juices.

- A localized circular smooth muscles contraction constricts the intestine into spaced segments, one set of segmentation contractions relaxes, a new set begins at points between the previous ones.
- Blend intestinal contents & bring products of digestion in contact with absorptive surfaces
- Usual stimulus is distention



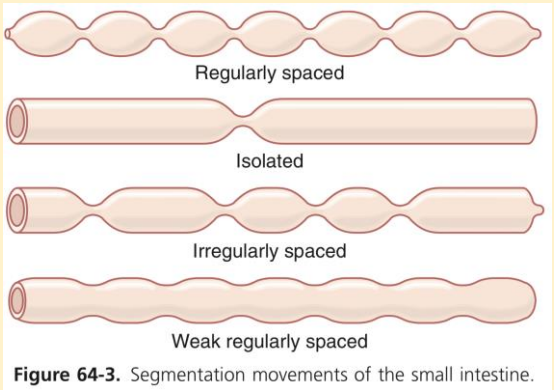


Figure 64-3. Segmentation movements of the small intestine.

➢ Peristaltic Reflex and the "Law of the Gut."

- When a segment of the intestinal tract is distended, it initiates peristalsis.

- The contractile ring normally begins on the orad side of the distended (propulsive) segment and moves toward the distended (receiving) segment, pushing the intestinal contents in the anal direction (Caudad direction) for 5 to 10 cm. before dying out.

- **Propulsive segment** :

➥ contraction (circular M.)

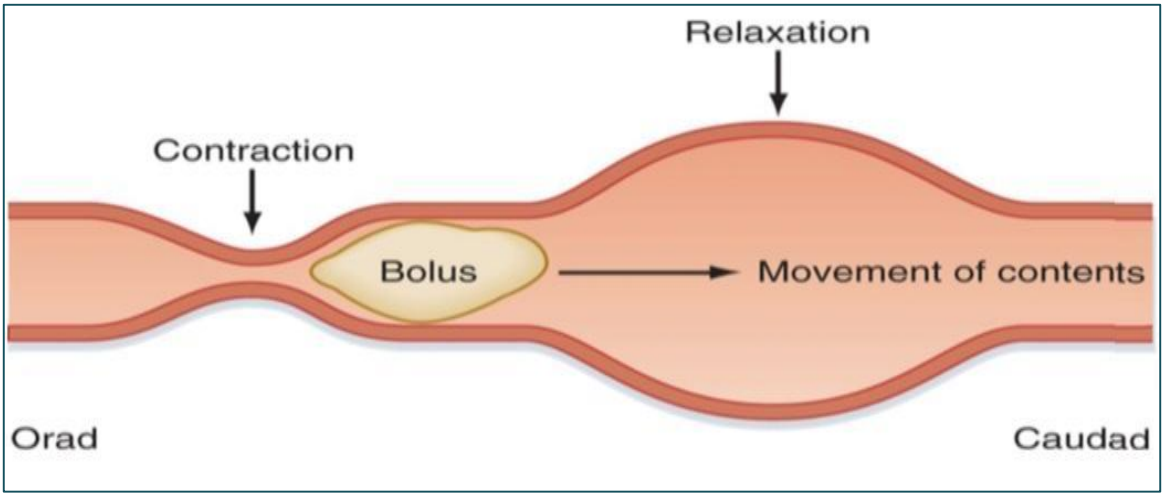
➥ relaxation (longitudinal M.)

Contraction of muscles are indicated to move GI contents from Orad side to Cauded side. All the way to the anus.

- **Receiving segment** :

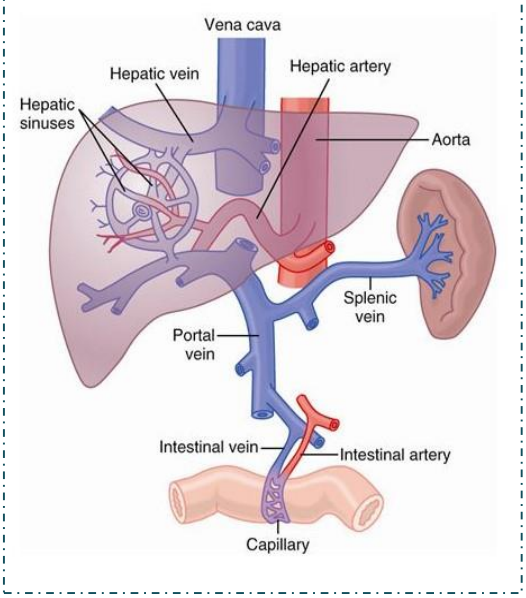
➥ contraction (longitudinal M.)

➥ relaxation (circular M.)



➢ Gastrointestinal Blood Flow- "Splanchnic Circulation"

- It includes the blood flow through the gut itself, the spleen, pancreas, and liver.
- All blood then flows into the liver by way of the portal vein.
- In the liver, the blood passes through liver sinusoids and finally leaves the liver by way of hepatic veins that empty into the vena cava of the general circulation.



➢Effect of Gut Activity & Metabolic Factors on Gastrointestinal Blood Flow

- Causes of the increased blood flow during GI activity :

1. ***Most of the peptide hormones, including cholecystokinin, vasoactive intestinal peptide"VIP", gastrin and secretin***
2. ***Kinins (kallidin and bradykinin) released into the gut wall from some of the GI glands. (Vasodilators)***
3. ***Decreased oxygen concentration in the gut wall (increase blood flow 50 to 100 %).***

Summary

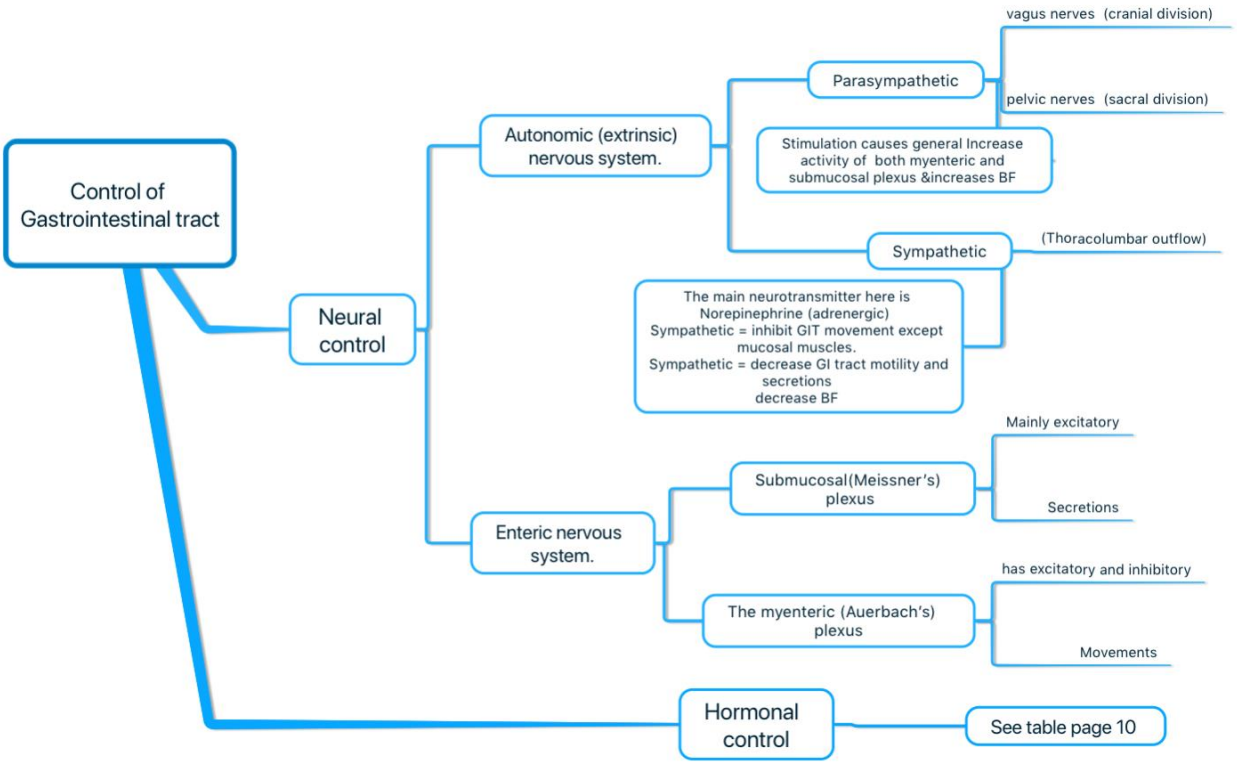
Gastrointestinal Function:

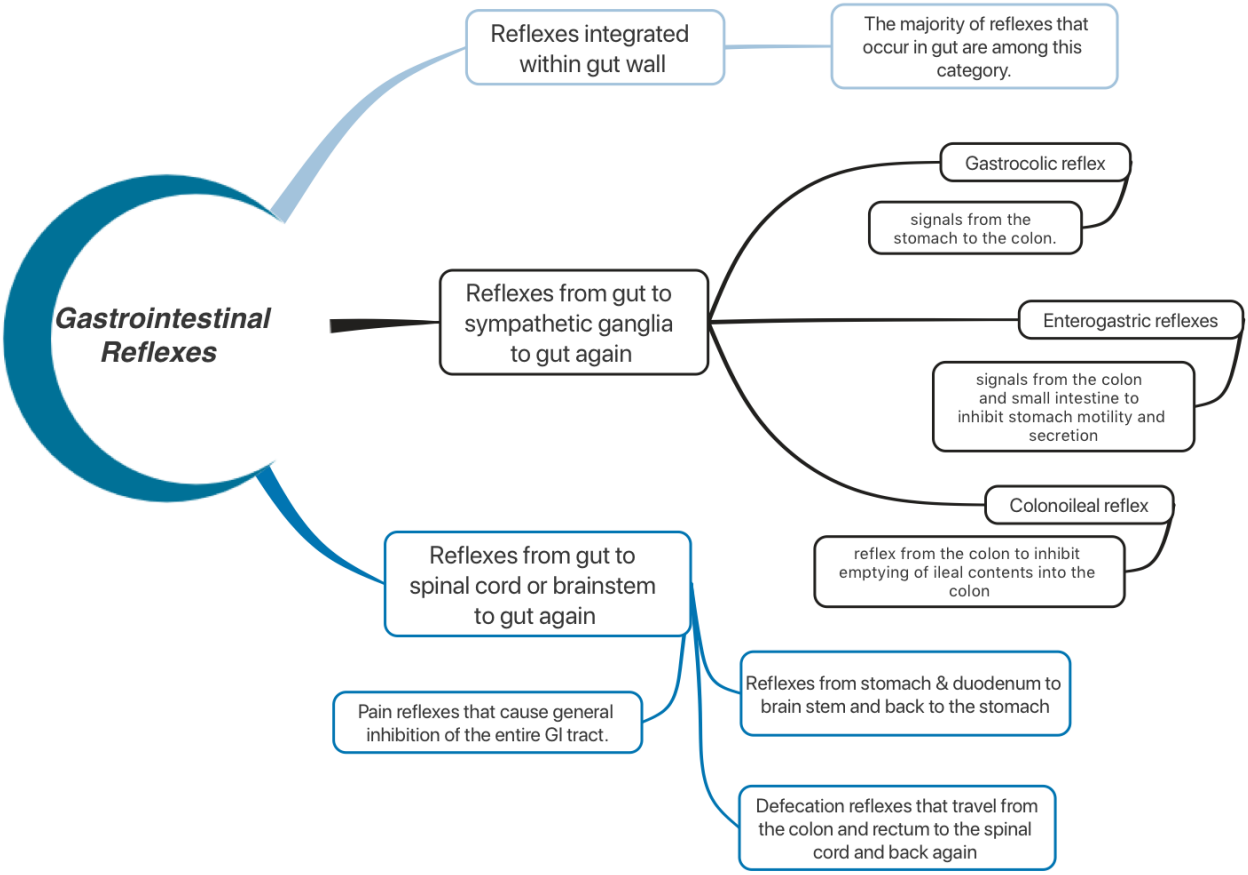
-**Movement** of food through the alimentary tract (**motility**).
-**Secretion** of digestive juices and digestion of the food.
-**Absorption** of water, various electrolytes, and digestive products.
-**Circulation** of blood through the gastrointestinal organs to carry away the absorbed substances.

The General Characteristics of Smooth Muscle		
Muscle Layers	**Longitudinal**	shortens the segment, **expands** the lumen
	Circular	Lengthens the segment, **contracts** the lumen
Muscle Classification	**Unitary**	Contract in **response** to stretch Many gap junctions action potential travels in all directions
	Multi-unit	Does **not** contract in response to stretch or without neural input.
Contraction	**Phasic (rhythmical)**	Periodic **followed** by relaxation
	Tonic (Maintained)	Contraction **without** relaxation. **Not** associated with slow waves

Electrical Activity of Gastrointestinal Smooth Muscle	
Slow waves	**Spike potential**
changes in **resting** membrane potential **intensity:** 5-15 mv **Frequency:** 3-12/min Use sodium ion channels Do **not** cause muscle contraction	**TRUE** action potentials **Intensity:** -50mv to -60mv **Frequency:** 1-10 spikes/sec Use calcium-sodium channels **cause** muscle contraction

Summary


Control of Gastrointestinal tract
Neural control
Autonomic (extrinsic) nervous system.
Parasympathetic
vagus nerves (cranial division)
pelvic nerves (sacral division)
Stimulation causes general Increase activity of both myenteric and submucosal plexus &increases BF
Sympathetic
(Thoracolumbar outflow)
The main neurotransmitter here is Norepinephrine (adrenergic)
Sympathetic = inhibit GIT movement except mucosal muscles.
Sympathetic = decrease GI tract motility and secretions
decrease BF
Enteric nervous system.
Submucosal(Meissner's) plexus
Mainly excitatory
Secretions
The myenteric (Auerbach's) plexus
has excitatory and inhibitory
Movements
Hormonal control
See table page 10


Gastrointestinal Reflexes
Reflexes integrated within gut wall
The majority of reflexes that occur in gut are among this category.
Reflexes from gut to sympathetic ganglia to gut again
Gastrocolic reflex
signals from the stomach to the colon.
Enterogastric reflexes
signals from the colon and small intestine to inhibit stomach motility and secretion
Colonoileal reflex
reflex from the colon to inhibit emptying of ileal contents into the colon
Reflexes from gut to spinal cord or brainstem to gut again
Reflexes from stomach & duodenum to brain stem and back to the stomach
Pain reflexes that cause general inhibition of the entire GI tract.
Defecation reflexes that travel from the colon and rectum to the spinal cord and back again

MCQs

1.Which one of the following happen in slow wave?

A. Ca influx
B. Na influx
C. Cl influx

2.Which one of the following hormones has no effect in gastric acid secretion?

A. Gastrin
B. Secretin
C. GIP
D. CCK

3.Which one of the following GI reflexes inhibit stomach motility and secretion?

A. Gastrocolic reflex
B. Enterogastric reflex
C. Colonoileal reflex
D. Intestino-intestinal reflex

4.Which one of the following increase blood flow during GI activity?

A. CCK
B. Bradykinin
C. Decrease oxygen concentration
D. All of above

5.Which one of the following hormones relax the sphincter of oddi?

A. Gastrin
B. Secretin
C. CCK
D. GIP

6.Which one of the following GI reflexes is involved with sympathetic chain?

A. Defecation reflex
B. Colonoileal reflex
C. Pain reflex
D. Vagovagal reflex

7.Which one of the following is a factor that hyperpolarize the membrane?

A. Stretching of the muscle
B. Effect of epinephrine on fiber membrane
C. Ach released from parasympathetic nerves
D. GI hormones

SAQ

8.What are the causes of tonic contraction?

1. Repetitive spike potential
2. Hormones
3. Continuous entry of Ca ion

9.List two hormones that decrease gastric acid secretion.

1. GIP
2. Secretin

MCQs Answers:

1. B
2. D
3. B
4. D
5. C
6. B
7. B