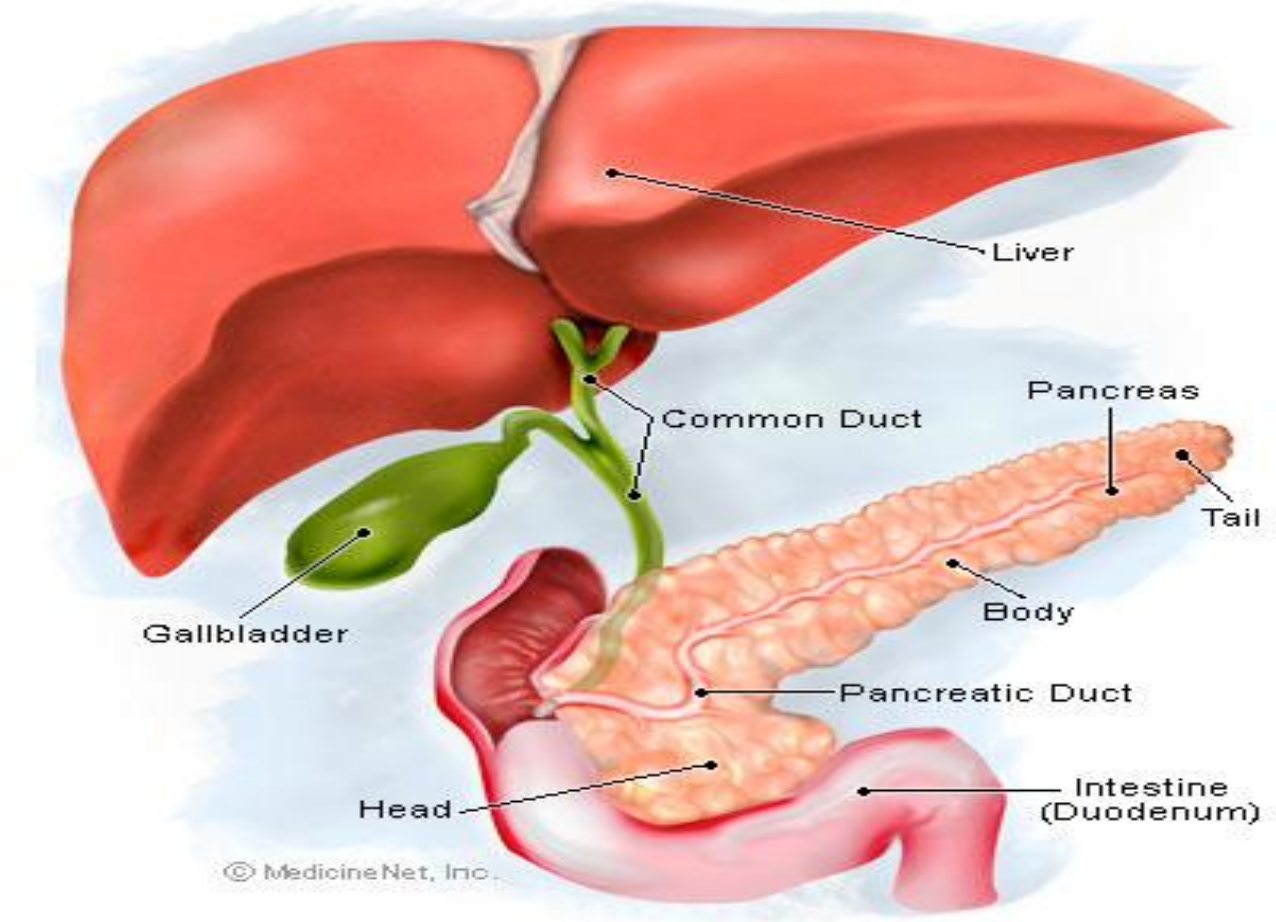
GIT Block

1st Lecture

General Principals of GIT physiology



PHYSIOLOGY TEAM – 430

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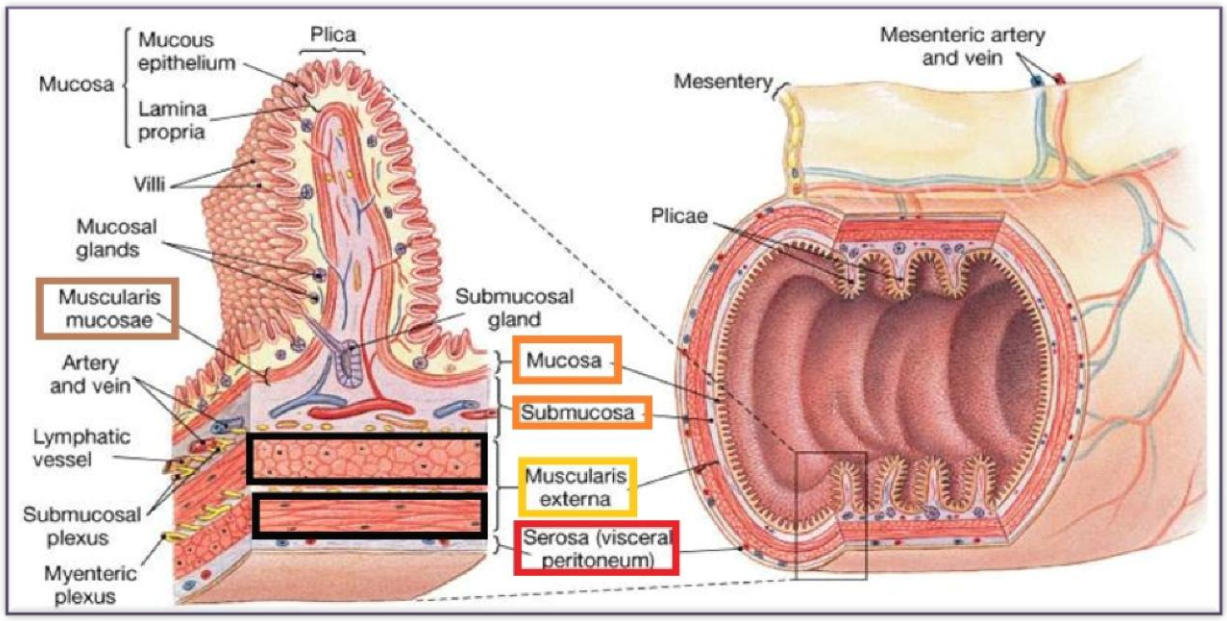
- ## General Principles of Gastrointestinal Function-Motility, Nervous Control, and Blood Circulation

The alimentary tract provides the body with a continual supply of water, electrolytes, and nutrients.

– **To achieve this requires:**

1) **Movement of food through the alimentary tract**
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**
5) **Control of all these functions by local, nervous, and hormonal systems**

- ## Physiologic Anatomy of the Gastrointestinal Wall:



– **The following layers structure the GI wall from outer surface inward:**

1. **The *Serosa***
2. **A *longitudinal muscle layer***
3. **A *circular muscle layer***
4. **The *submucosa***
5. **The *mucosa*.**

Thicker in the stomach but normal from the esophagus to the anal opening.

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:

Two smooth muscle classifications:

Unitary type	Multiunit type (Mainly)
- **Contracts spontaneousl in the absence of neural or hormonal influence but in response to stretch (such as in stomach and intestine)** - **Cells are electrically coupled via gap junctions "Syncytium"**	- **Does not contract in response to stretch or without neural input (such as in esophagus & gall bladder)**

Stretching of the GI smooth muscle opens the gates and channels.

Syncytium: is a large cell-like structure; filled with cytoplasm and containing many nuclei.

- ## Types of contraction:

Phasic contractions (rhythmical)

- **Periodic contractions followed by relaxation; such as in gastric antrum, small intestine and esophagus.**

Tonic contractions

- **Maintained contraction without relaxation; such as in orad region of the stomach, lower esoghageal, ileocecal and internal anal sphincter Caused by (needs a stimulus):**
  1. **Repetitive spike potentials (discussed later)**
  2. **Hormones**
  3. **Continuous entry of Ca ions.**
- **Not associated with slow waves. (discussed later)**

- **Two main muscle layers:**

Longitudinal Smooth Muscles:	Circular Smooth Muscles:
Thinner and Less powerful than circular	They are thicker and more powerful than longitudinal.
It shortens the segment of the intestine and expands the lumen.	Reduces the diameter of the lumen and increases its length.
They are innervated by enteric nervous system (ENS), and mainly by excitatory motor neurons.	They are innervated by ENS, both excitatory and inhibitory motor neurons.
The Ca influx from outside is important in the activity of this type of muscle.	- Intracellular release of Ca is more important. - More gap junctions are available than in longitudinal muscle.

Just for reading : The muscle fibers are electrically connected with one another through large numbers of *gap junctions*. Each bundle of smooth muscle fibers is partly separated from the next by loose connective tissue but they fuse with one another at many points, so each muscle layer represents a branching latticework of smooth muscle bundles. Therefore, each muscle layer functions as a ***Syncytium***; that is, when an action potential is elicited anywhere within the muscle mass, **it generally travels in all directions in the muscle.**

The **enteric nervous system** (**ENS**) is a subdivision of the autonomic nervous system (ANS) that directly controls the gastrointestinal system in vertebrates.

Long. Ms. → mainly for length
Circular Ms. → mainly for diameter

- ## Electrical Activity of Gastrointestinal Smooth Muscle

- **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, Spikes.**

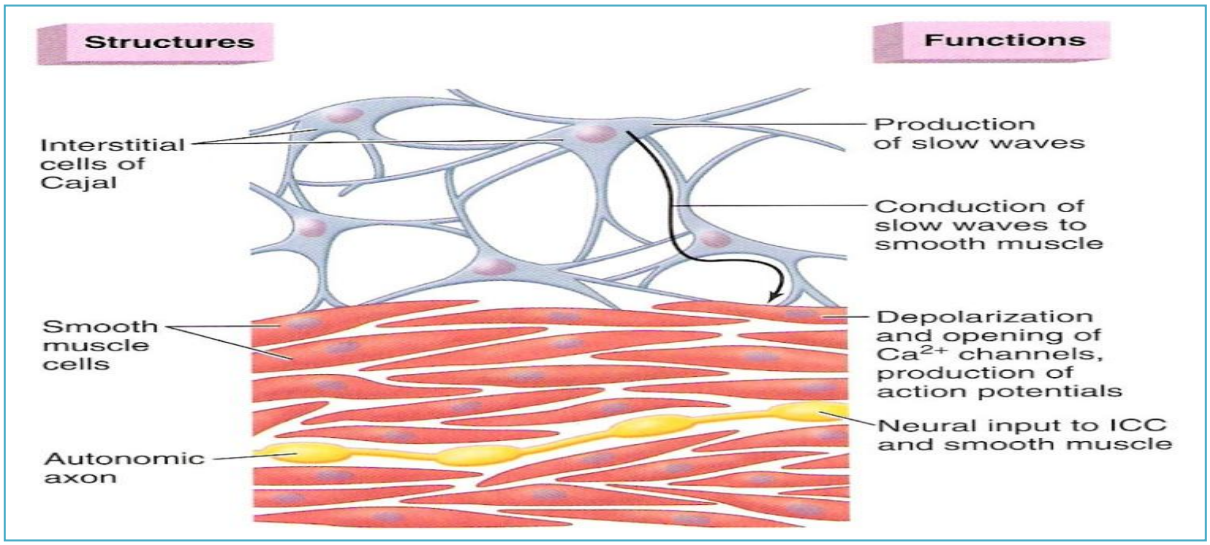
You should remember that:

- **Sympathetic nervous system:** Diverts blood flow away from the gastro-intestinal (GI) tract, skin via vasoconstriction and inhibits digestion.
- **Parasympathetic nervous system:** Dilates blood vessels leading to the GI tract, increasing blood flow and enhances digestion.

a. Slow Waves :

- **The rhythm of the gastrointestinal contractions is determined mainly by the frequency of so-called "slow waves" of smooth muscle membrane potential.**
- **These waves are not action potentials. Instead, they are oscillating depolarization and repolarization in the resting membrane potential with unknown cause.**
- **Their intensity usually varies between 5 and 15 mV.**
- **Their frequency ranges in different parts from 3 to 12 per minute.(Their frequency ranges between 3/min→in stomach body to 12/min →in duodenum and change to 8/minutes→ in terminal ileum)**

They may originate in the interstitial cells of Cajal (the GI pacemaker), which are abundant in the Myenteric plexues. These interstitial cells form a network with each other and are interposed between the smooth muscle layers, with synaptic-like contacts to smooth muscle cells.



a. The Spike Potentials (the doctor said: "I don't want you to memorize numbers")

- **True action potentials.**
- **They occur automatically when the resting membrane potential of the gut smooth muscle becomes more positive (<-40 mV) (caused by Ca^{++} and Na^{+} inflow through the channels)**
  ***You should know that (the normal resting membrane potential is between -50 and -60 mV.**
- **The higher the slow wave potential rises, the greater the frequency of the spike potentials, usually ranging between 1 and 10 spikes per second.**
- **The spike potentials last 10 to 40 times as long in gastrointestinal muscle as the action potentials in large nerve fibers, each gastrointestinal spike lasting as long as 10 to 20 msec.**
- **spike potentials occur at the peak of slow waves.**

The channels responsible for the action potentials are somewhat different; they allow especially large numbers of calcium ions to enter along with smaller numbers of sodium ions and therefore are called *calcium-sodium channels*. (The rising phase of AP is caused by Ca^{++} and Na^{+} inflow through the channels that allow especially large numbers of Ca^{++} to enter along with smaller numbers of Na^{+} (calcium-sodium channels). They open slowly. Ca^{++} that enters cells helps to initiate contraction. (N.B: slow waves do not cause Ca^{++} entry)

- **Factors that effect the membrane's potential :**

– **Factors that make the membrane potential becomes less negstive – that is depolarize the membrane-that is, make it more excitable-are**

- *Stretching* of the muscle (Ex :when you eat)
- stimulation by *acetylcholine*.
- Stimulation by *parasympathetic nerves* that secrete acetylcholine at their endings.
- Stimulation by several *specific gastrointestinal hormones*

– **Factors that make the membrane potential more negative-that is, hyperpolarize the membrane and make the muscle fibers less excitable-are:**

- The effect of norepinephrine or epinephrine on the fiber membrane
- Stimulation of the sympathetic nerves that secrete mainly norepinephrine at their endings.

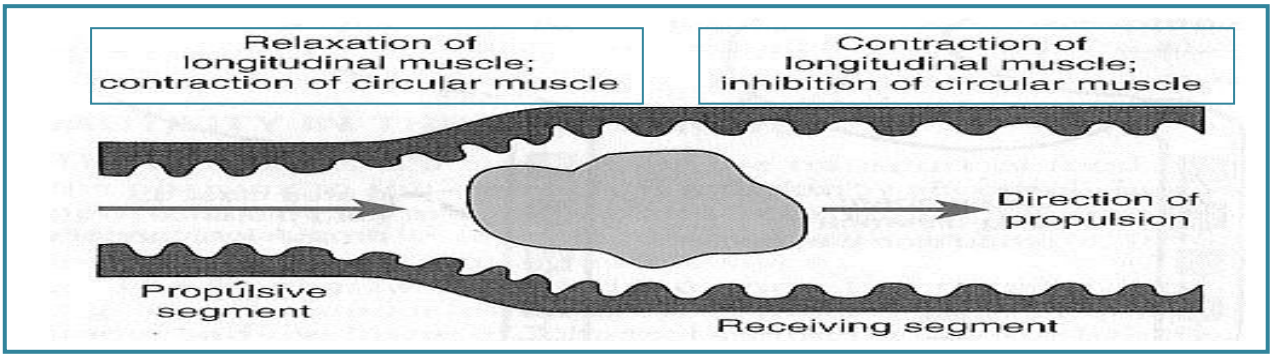
- **Calcium Ions and Muscle Contraction:**

- **The slow waves do not cause calcium ions to enter the smooth muscle fiber (only sodium ions). Therefore, usually cause no muscle contraction.**
- **During the spike potentials. (Generated at the peaks of the slow waves: significant quantities of calcium ions → enter the fibers → cause most of the contraction.)**

- **Functional types of movements in GIT** *:(two types)*

1. *Propulsive movements- peristalsis:*

- **cause food to move forward along the tract. A contraction ring appears around gut, then moves forward.**
- **Organizes propulsion of material over variable distances within the GI lumen .**
- **Stimulated by distention and chemical or physical irritation of the epithelial lining in the gut.**
- **Myenteric plexus is important**
- **Atropine (cholinergic blocker) depresses propulsion.**

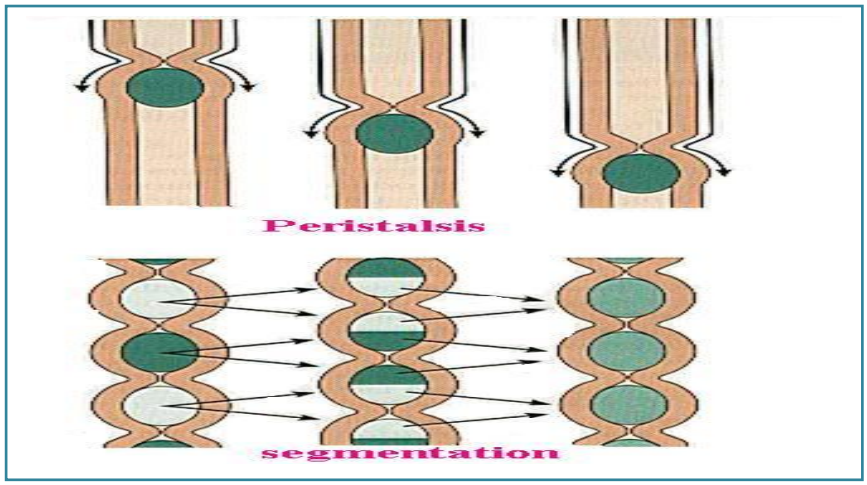


Peristaltic Reflex and the "Law of the Gut"

When a segment of the intestinal tract is excited by distention and thereby initiates peristalsis, the contractile ring causing the peristalsis normally begins on the orad side of the distended segment and moves toward the distended segment, pushing the intestinal contents in the anal direction for 5 to 10 centimeters before dying out.

2. *Mixing movements- segmentation*

- **Which keep intestinal contents mixed. They are caused by either peristaltic contraction or local constrictive contraction.**
- **Blend different juices with the chyme (**chyme is the semifluid, creamy material produced by digestion of food**).**
- **Bring products of digestion in contact with absorptive surfaces.**

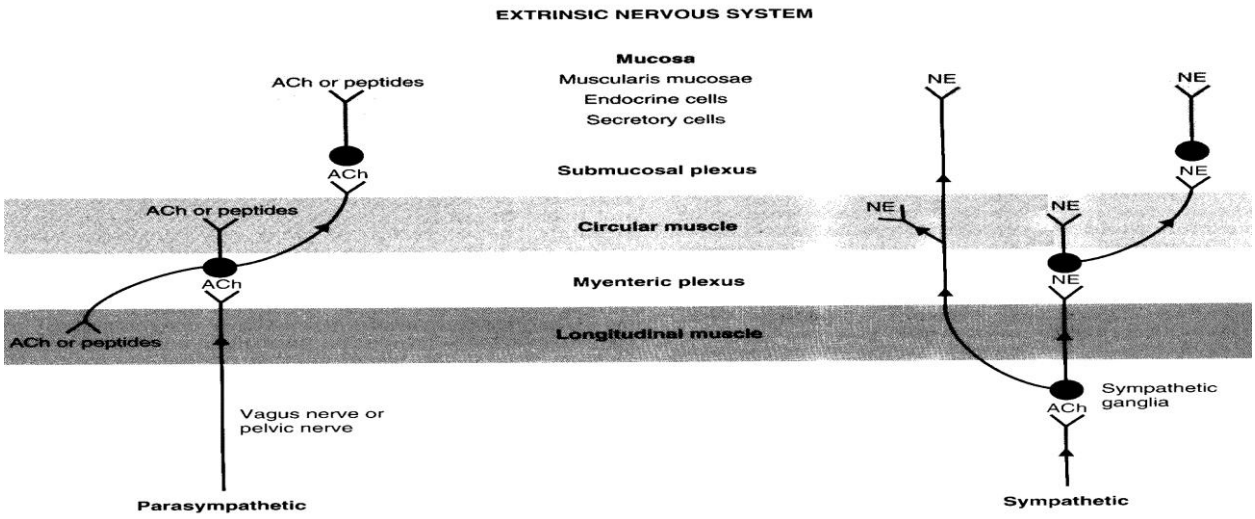


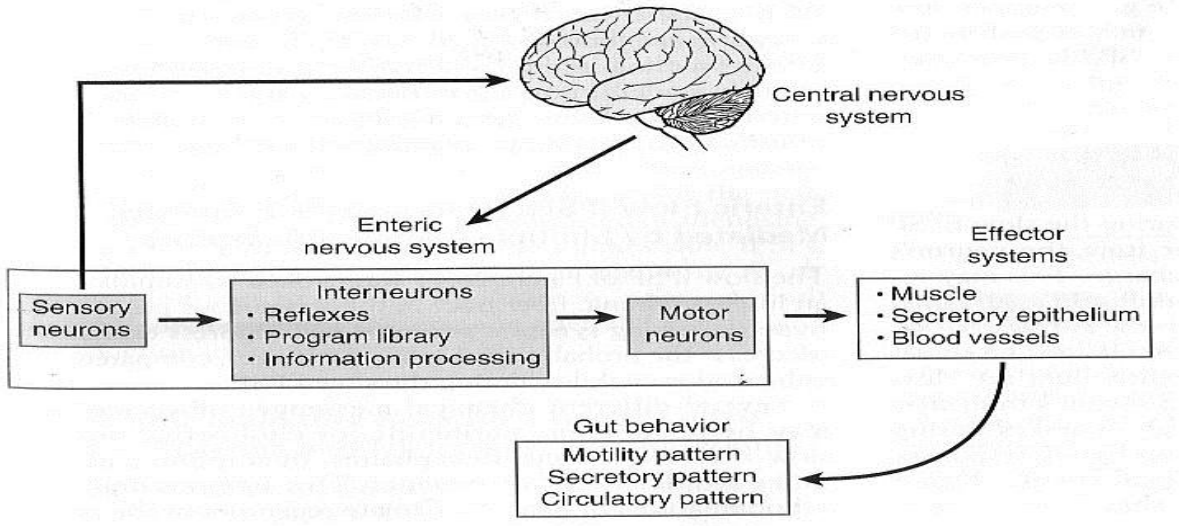
- **Control of smooth muscles :**
  - **Neural Control of Gastrointestinal Function - Enteric Nervous System**

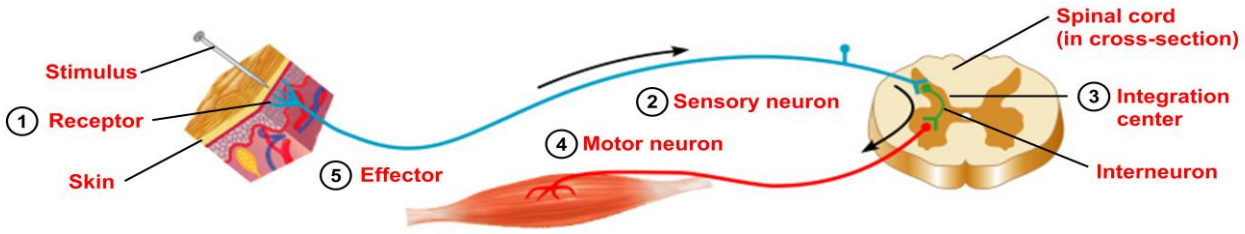
Enteric Nervous System (ENS) is the nervous system of GI tract. It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus. It has as many neurons as spinal cord.

The enteric nervous system is composed mainly of two plexuses:

	inner plexus → *submucosal plexus* or *Meissner's plexus*	outer plexus → *Myenteric (Auerbach's) plexus*
Location	in the submucosa	between the longitudinal and circular muscle layers
function	controls mainly gastrointestinal secretion and local blood flow	controls mainly the gastrointestinal movements.







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.

The sensory nerve endings send afferent fibers to both plexuses of the enteric system and then to:

1) the prevertebral ganglia of the sympathetic nervous system

2) the spinal cord

3) the vagus nerves all the way to the brain stem. These sensory nerves can elicit local reflexes within the gut wall. (See above)

- ## Differences between the Myenteric and Submucosal Plexuses

The Myenteric plexus	The Submucosal plexus
Consists mostly of a linear chain of many interconnecting neurons.	Controls local intestinal secretion, local absorption, and local contraction of the Submucosal muscle that causes various degrees of infolding of the gastrointestinal mucosa.
When it is stimulated, its principal effects are: **(1) increased tonic contraction** **(2) increased intensity of the rhythmical contractions** **(3) increased rate of the rhythm of contraction** **(4) increased velocity of conduction of excitatory waves along the gut wall**	
It has excitatory and inhibitory motor neurons (fiber endings secrete an inhibitory transmitter, e.g., vasoactive intestinal polypeptide)	

- **Types of Neurotransmitters Secreted by Enteric Neurons**

Excitatory Motor Neurons Evoke Muscle Contraction & Intestinal Secretion		**Inhibitory Motor Neurons Suppress Muscle Contraction**
Neurotransmitters of motor neurons	Neurotransmitters of secretomotor neurons	Neurotransmitters
Substance P	**Ach**	**ATP**
Ach	**VIP**	**NO**
	Histamine (neurogenic secretory diarrhea)	**VIP**

Neurotransmitters of secretomotor neurons (releasing of water, electrolytes and mucus from crypts of Lieberkuhn)

VIP: Vasoactive intestinal peptide
NO: Nitric Oxide
ATP: Adenosine triphosphate
Substance P: is a neuropeptide

(you have to know the neurotransmitters and their functions but concentrate on the Ach , doctor said it's the most important **)**

TABLE 8–1. Neurotransmitters and Neuromodulators in the 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

- ## Autonomic Control of the Gastrointestinal Tract

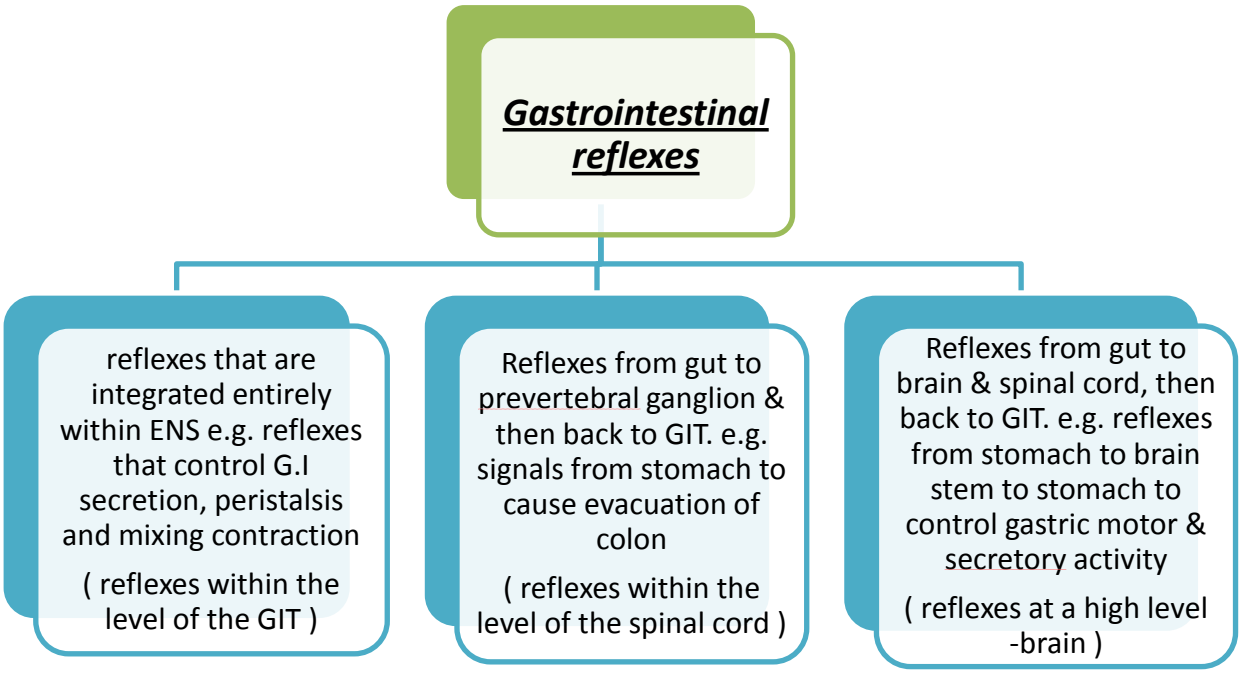
- **Autonomic nervous system (ANS) is divided into :**
  Parasympathetic - Sympathetic

Parasympathetic Innervation	Sympathetic Innervation
The parasympathetic supply to the gut is divided into *cranial* and *sacral divisions*. The *cranial parasympathetic* nerve fibers are almost entirely in the *vagus nerves*.	**The sympathetic fibers to the gastrointestinal tract originate in the spinal cord between segments T-5 and L-2.**
The esophagus, stomach, pancreas and the intestines down through the first half of the large intestine are innervated by *vagus nerves*. The distal half of the large intestine and the anus are innervated by the *sacral parasympathetics* which pass through the *pelvic nerves* (to execute the defecation reflexes).	**The sympathetics innervate essentially all of the GI tract.**
The parasympathetic nerve endings secrete mainly *acetylcholine*.	**The sympathetic nerve endings secrete mainly *norepinephrine*.**
The *postganglionic neurons* of the gastrointestinal parasympathetic system are located mainly in the myenteric (Auerbach's) and submucosal (Meissner's) plexuses. Stimulation of these parasympathetic nerves causes general increase in activity of the entire enteric nervous system.	**Stimulation of the sympathetic nervous system *inhibits* activity of the GI. 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 gastrointestinal tract.**
Via preganglionic cholinergic fibers of vagus and pelvic nerves. They terminate on the ganglionic cells of the intramural (submucosal and myenteric) plexuses.	**mainly via postganglionic adrenergic fibers whose cell bodies are located in prevertebral and paravertebral ganglia.**
Functions: - **Increases motility.** - **Relaxation of sphincters.** - **Causes vasodilatation of blood vessels.** - **Stimulates of secretion.**	**Functions:** - **Inhibits the motor activity.** - **Contracts the sphincters.** - **Causes vasoconstriction of splanchnic blood vessels.** - **Secretion is not necessary inhibited, may be moderately increased.**

- **The hormonal control (the gut as an endocrine organ)**

- Endocrine cells are located the pancreas, in the mucosa and submucosa of the stomach and intestine.
- They produce hormones that act on the secretory cells located in the wall of GIT, in the pancreas or in the liver to alter the rate or composition of their secretion.
- Other hormones act on smooth muscle cells or on sphincters.
- All the GI hormones are peptide such as gastrin, secretin and cholecystokinine.

Hormone	Stimuli for secretion	Site of secretion	Actions
Gastrin	Protein, Distention Nerve *(Acid inhibits release)*	G cells of the antrum, duodenum, and jejunum	Stimulates: Gastric acid secretion and Mucosal growth
Cholecystokinin	Protein, Fat , Acid	I cells of the duodenum, jejunum, and ileum	Stimulates: Pancreatic enzyme secretion Pancreatic bicarbonate secretion Gallbladder contraction Growth of exocrine pancreas Inhibits: Gastric emptying
Secretin	Acid ,Fat	S cells of the duodenum, jejunum, and ileum	Stimulates: Pepsin secretion Pancreatic bicarbonate secretion Biliary bicarbonate secretion Growth of exocrine pancreas Inhibits: Gastric emptying
Gastric inhibitory peptide	Protein , Fat Carbohydrate	K cells of the duodenum and jejunum	Stimulates: Insulin release Inhibits: Gastric acid secretion
Motilin	Fat ,Acid ,Nerve	M cells of the duodenum and jejunum	Stimulates: Gastric motility Intestinal motility



- **Gastrointestinal Blood Flow-"Splanchnic Circulation"**

Splanchnic circulation includes the blood flow through the gut itself plus blood flows through the spleen, pancreas, and liver. The design of this system is such that all the blood that courses through the gut, spleen, and pancreas then flows immediately into the liver by way of the *portal vein*. In the liver, the blood passes through millions of minute *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 and Metabolic Factors on Gastrointestinal Blood Flow**

- **Possible Causes of the Increased Blood Flow During Gastrointestinal Activity**

1. **Most of the peptide hormones, including *cholecystokinin*, *vasoactive intestinal peptide*, *gastrin*, and *secretin*.**
2. **Some of the GI glands release into the gut wall two kinins, *kallidin* and *bradykinin***
3. ***Decreased oxygen concentration* in the gut wall can increase intestinal blood flow at least 50 to 100 per cent.**

- **Nervous Control of Gastrointestinal Blood Flow**

– **Stimulation of the parasympathetic nerves going to the *stomach* and *lower colon* increases local blood flow at the same time that it increases glandular secretion.**

– **Sympathetic stimulation, by contrast, has a direct effect on essentially all the gastrointestinal tract to cause intense vasoconstriction of the arterioles with greatly decreased blood flow. But the local metabolic vasodilator mechanisms override the sympathetic vasoconstiction effects, returning the normal blood flow to GI muscle and glands.**