
السلام عليكم ورحمة الله وبركاته

Gastrointestinal Physiology

Required Textbook

Textbook of Medical Physiology
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Gastrointestinal Physiology

Lecture 1

Organization & General Principles of Gastrointestinal Physiology

(Chapter 63; pages 797-806)

By

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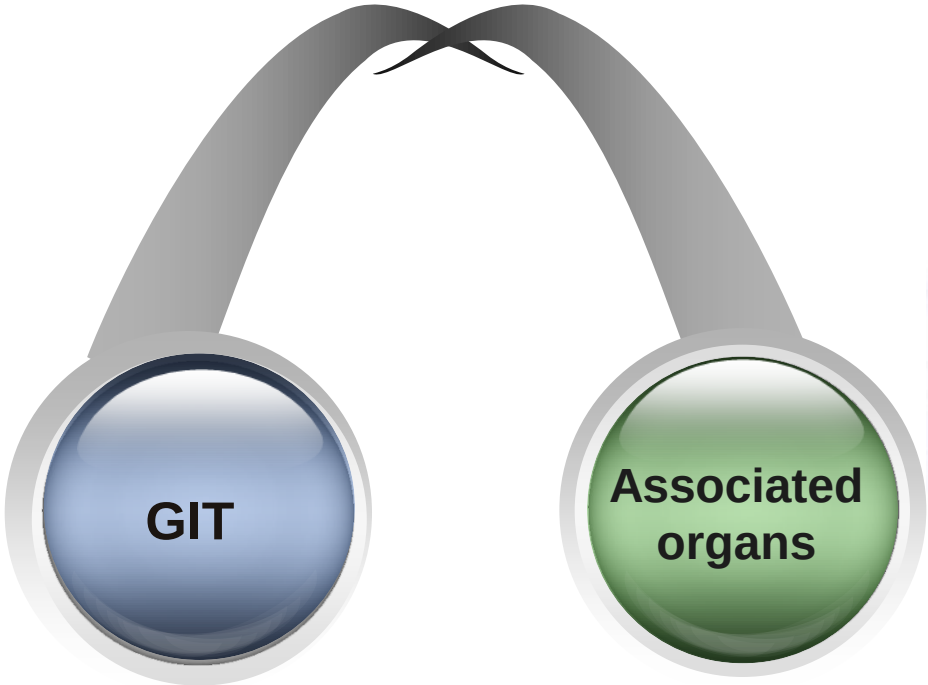
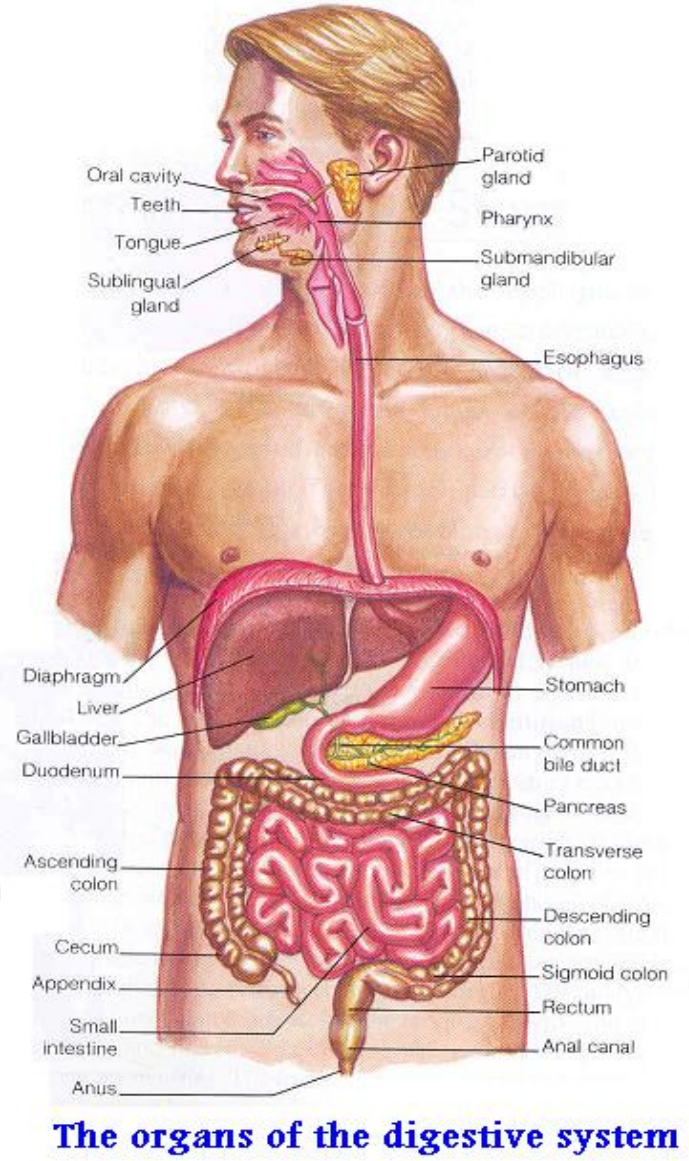
Learning Objectives

- 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

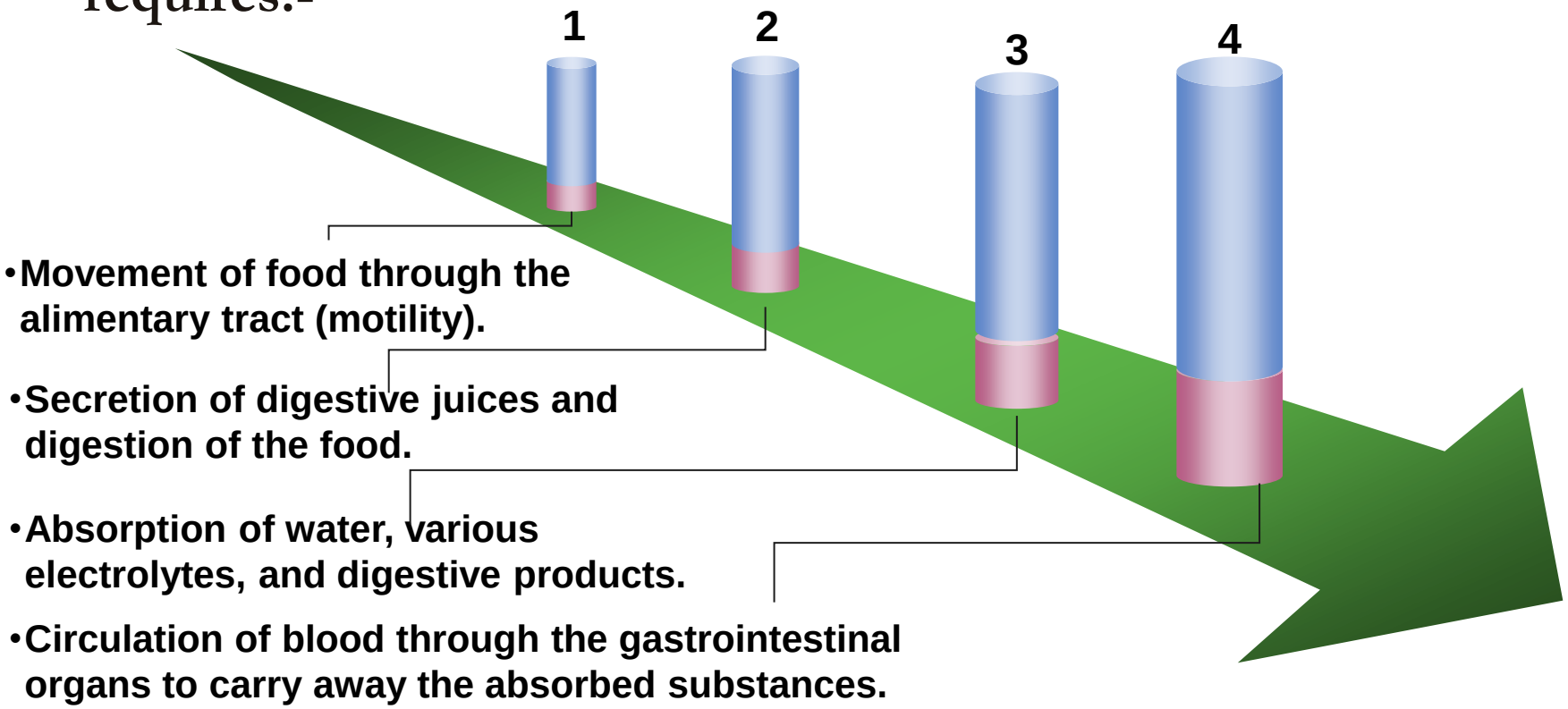
Gastrointestinal System:-





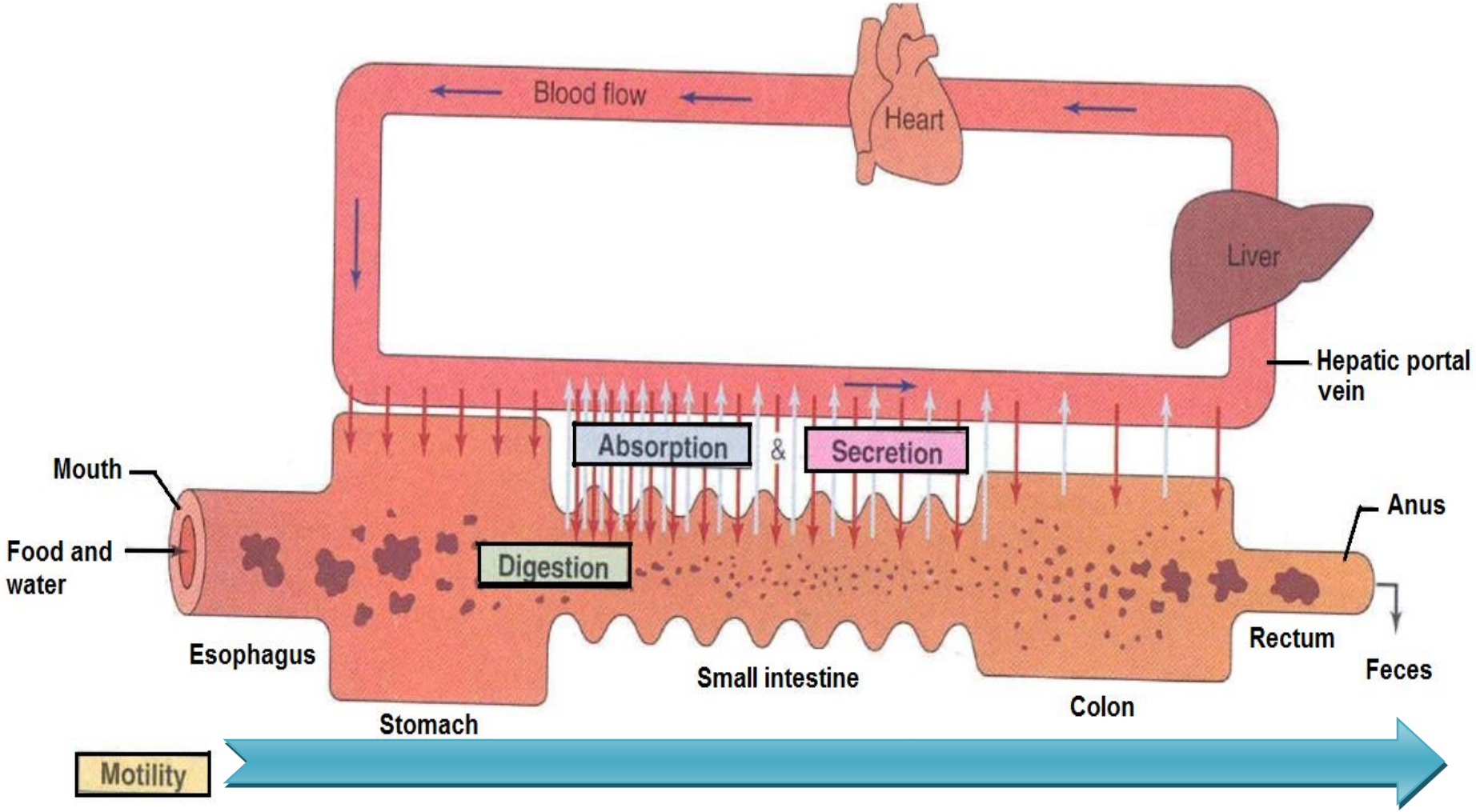
Gastrointestinal Function

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



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

The four processes carried out by the GIT

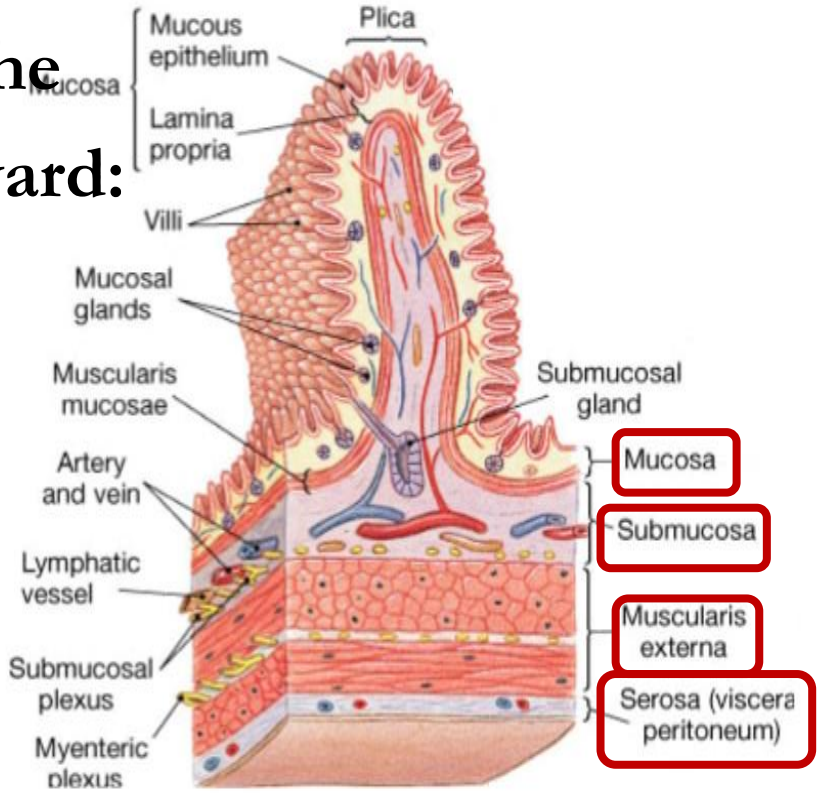


Four processes carried out by GIT, motility, secretion, digestion and absorption

Physiologic Anatomy of the Gastrointestinal Wall

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 main smooth muscle layers:-

Longitudinal

- Thinner and less powerful.
- Less gap junctions.
- Contraction shortens the segment of the intestine and expands the lumen.
- Innervated by enteric nervous system (ENS), mainly by excitatory motor neurons.
- Ca^{++} influx from outside is more important.

Circular

- Thicker and more powerful.
- More gap junctions.
- Contraction reduces the diameter of the lumen and increases its length.
- Innervated by ENS, both excitatory and inhibitory motor neurons.
- Intracellular release of Ca^{++} is more important.

The General Characteristics of Smooth Muscle

2- Two smooth muscle classification:-

Unitary type

- 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.

Multiunit type

- Does not contract in response to stretch or without neural input
- E.g: in esophagus & gall bladder)

The General Characteristics of Smooth Muscle

3- Types of contraction:-

Phasic contractions (rhythmical)

- Periodic contractions followed by relaxation
- Occur in esophagus, gastric antrum and small intestine.

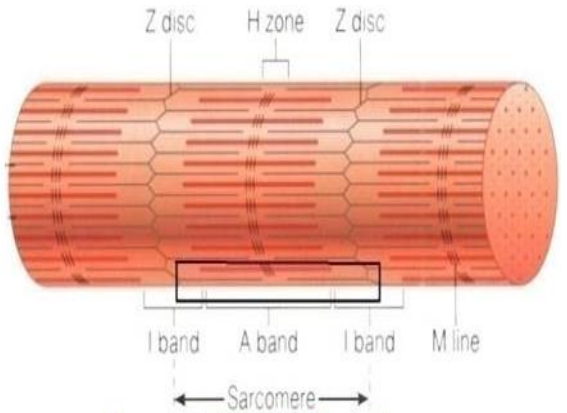
Tonic contractions (Maintained)

- Contraction without relaxation
- Occurs in orad region of stomach, lower esophageal, ileocecal & internal anal sphincters.
- Not associated with slow waves (often lasting several minutes or hours).
- 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.

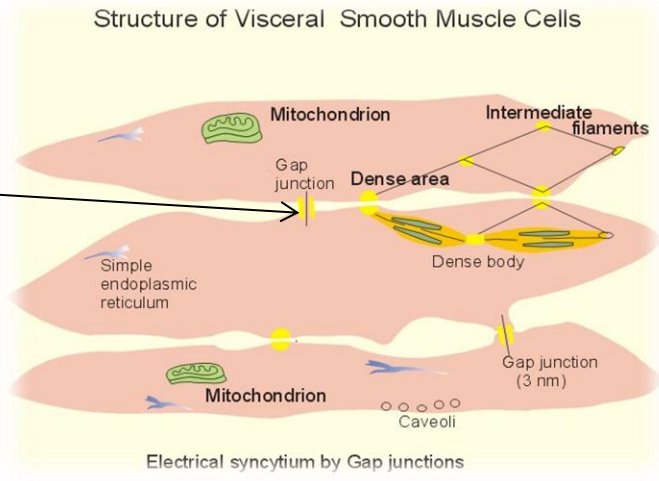
The Specific Characteristics of Smooth Muscle

1. Gastrointestinal Smooth Muscle Functions as a Syncytium:

- 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 all directions in the muscle.



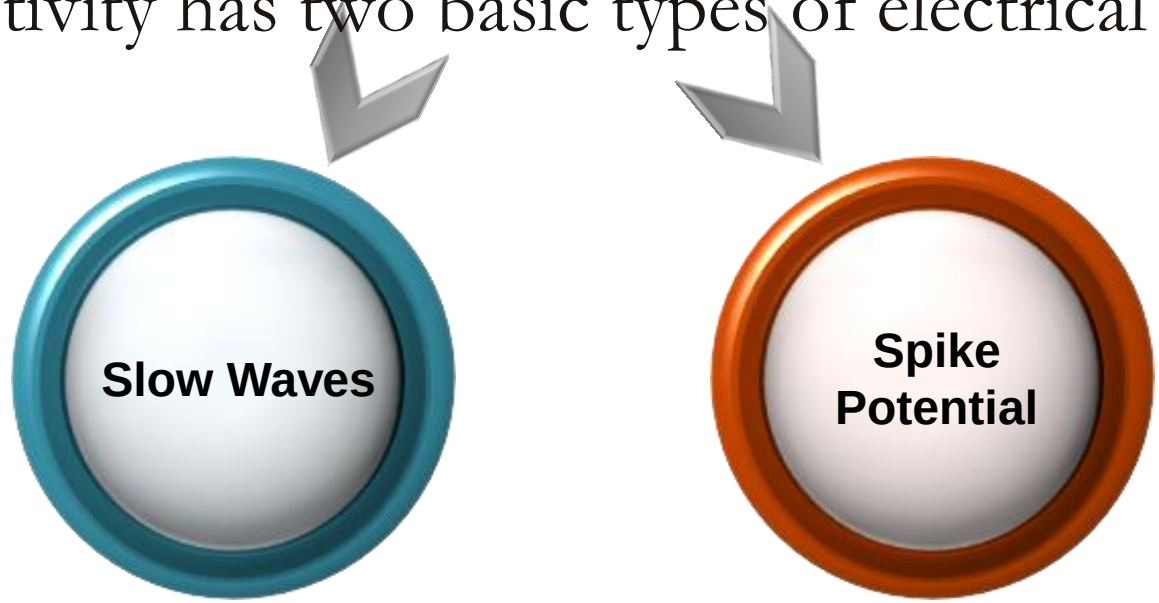
Smooth Muscle Bundles



Electrical syncytium by Gap junctions

2. Electrical Activity of Gastrointestinal Smooth Muscle:

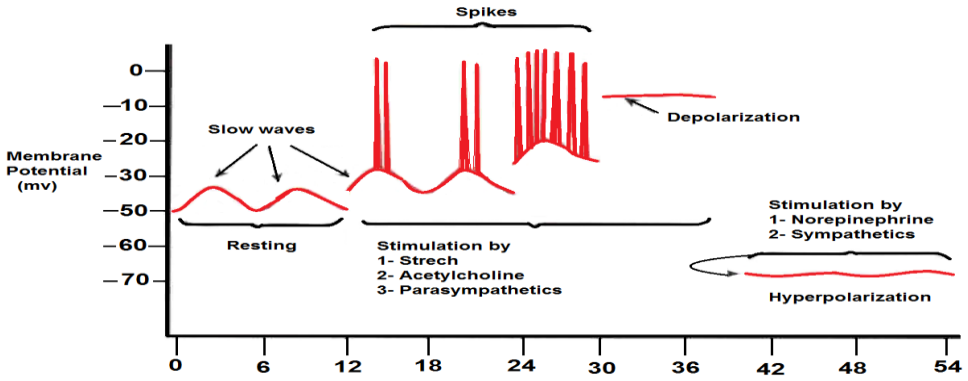
- The smooth muscle of the gastrointestinal tract is excited by almost continual slow, intrinsic electrical activity along the membranes of the muscle fibers.
- This activity has two basic types of electrical waves:



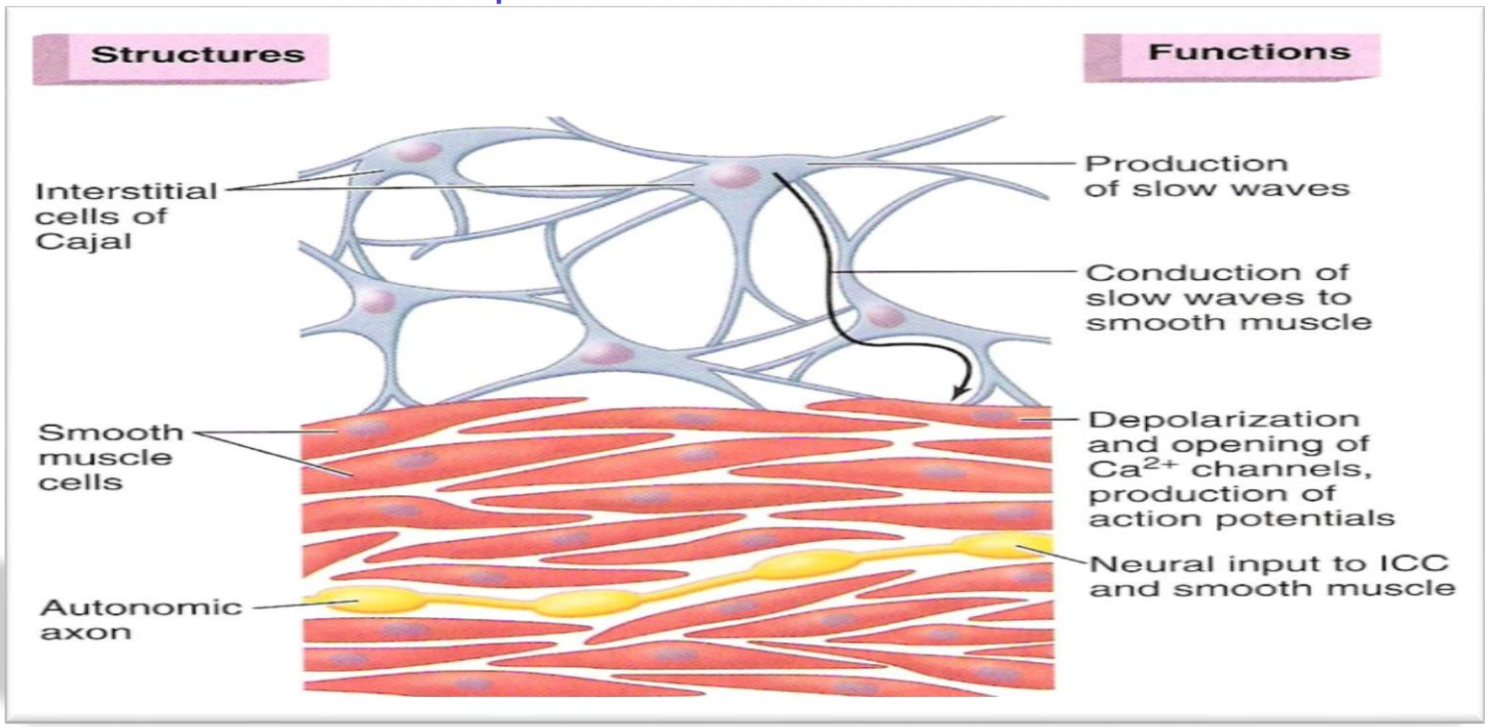
The slow Waves- Basic Electrical Rhythm

1. They are oscillating depolarization and repolarization in the resting membrane potential with unknown cause.
2. Intensity from 5-15 mv, frequency from 3-12/min
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.

Slow Waves are Generated by Interstitial Cells of Cajal



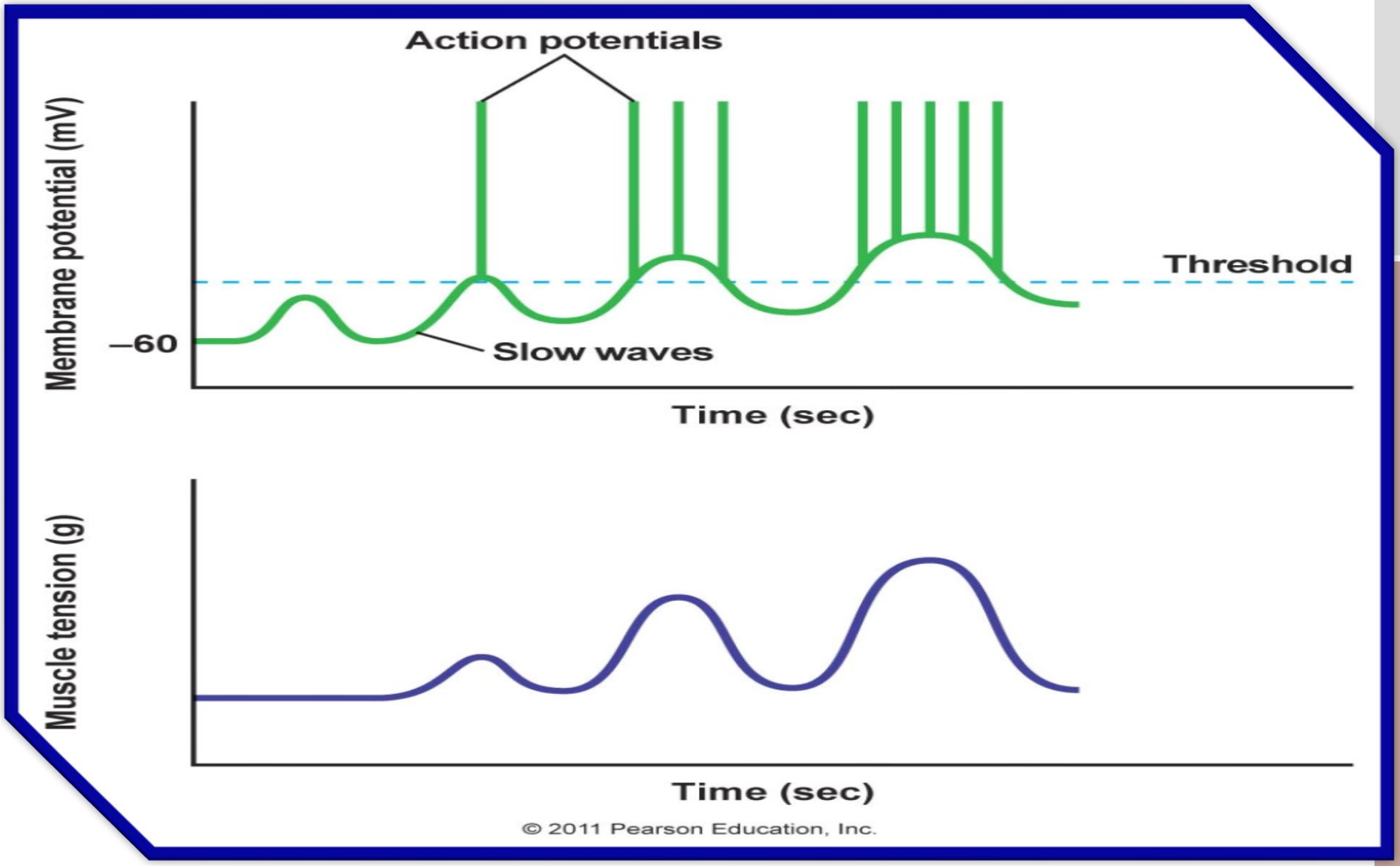
Membrane potentials in intestinal smooth muscles



The Spike Potential

1. They are true action potentials that occur 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, usually ranging between 1 and 10 spikes per second.
6. They are usually ranging between 1 and 10 spikes per second

The Spike Potential

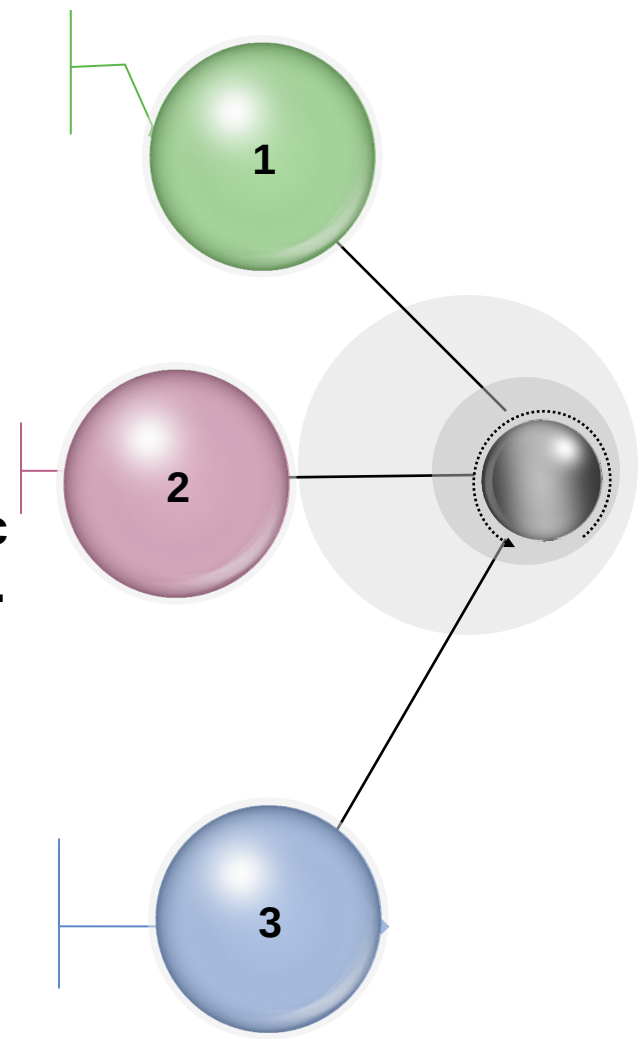


3. Changes in Voltage of the Resting Membrane Potential (-50mv to -60mv) .

Stretching of the muscle.

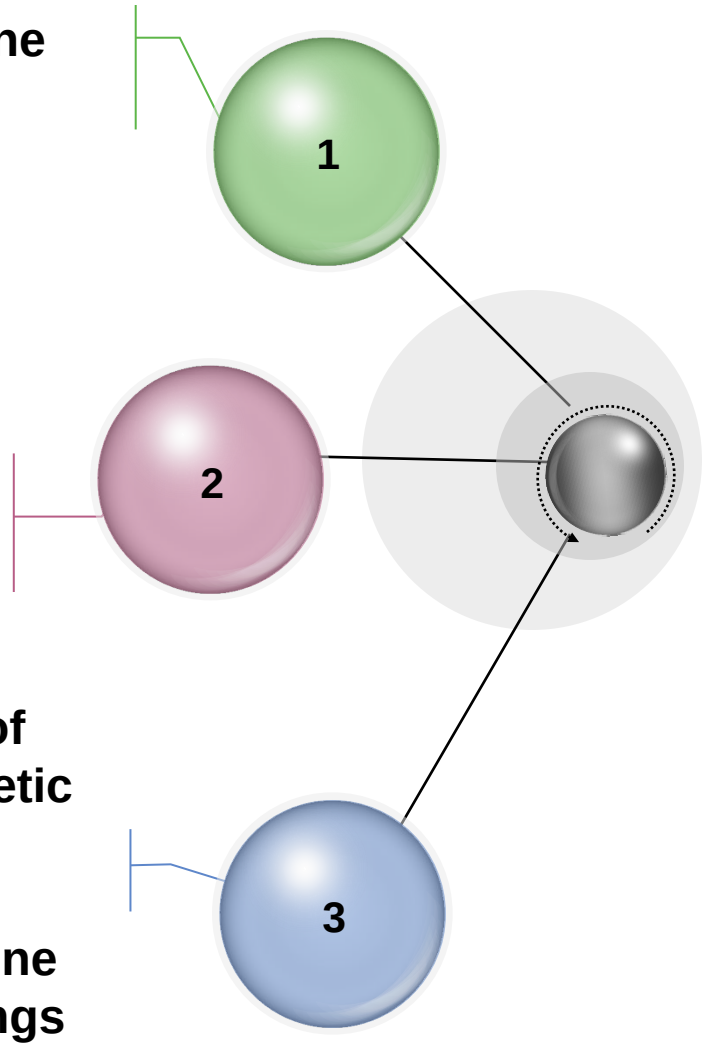
Stimulation by Ach released from parasympathetic nerves endings .

Stimulation by several specific GI hormones.



Factors that <u>depolarize</u> the membrane (become less negative and more excitable):

Effect of norepinephrine on fiber membrane



Effect of epinephrin on fiber membrane

Stimulation of the sympathetic nerves that secrete norepinephrine at their endings

Factors that <u>hyperpolarize</u> the membrane (become more negative and less excitable):

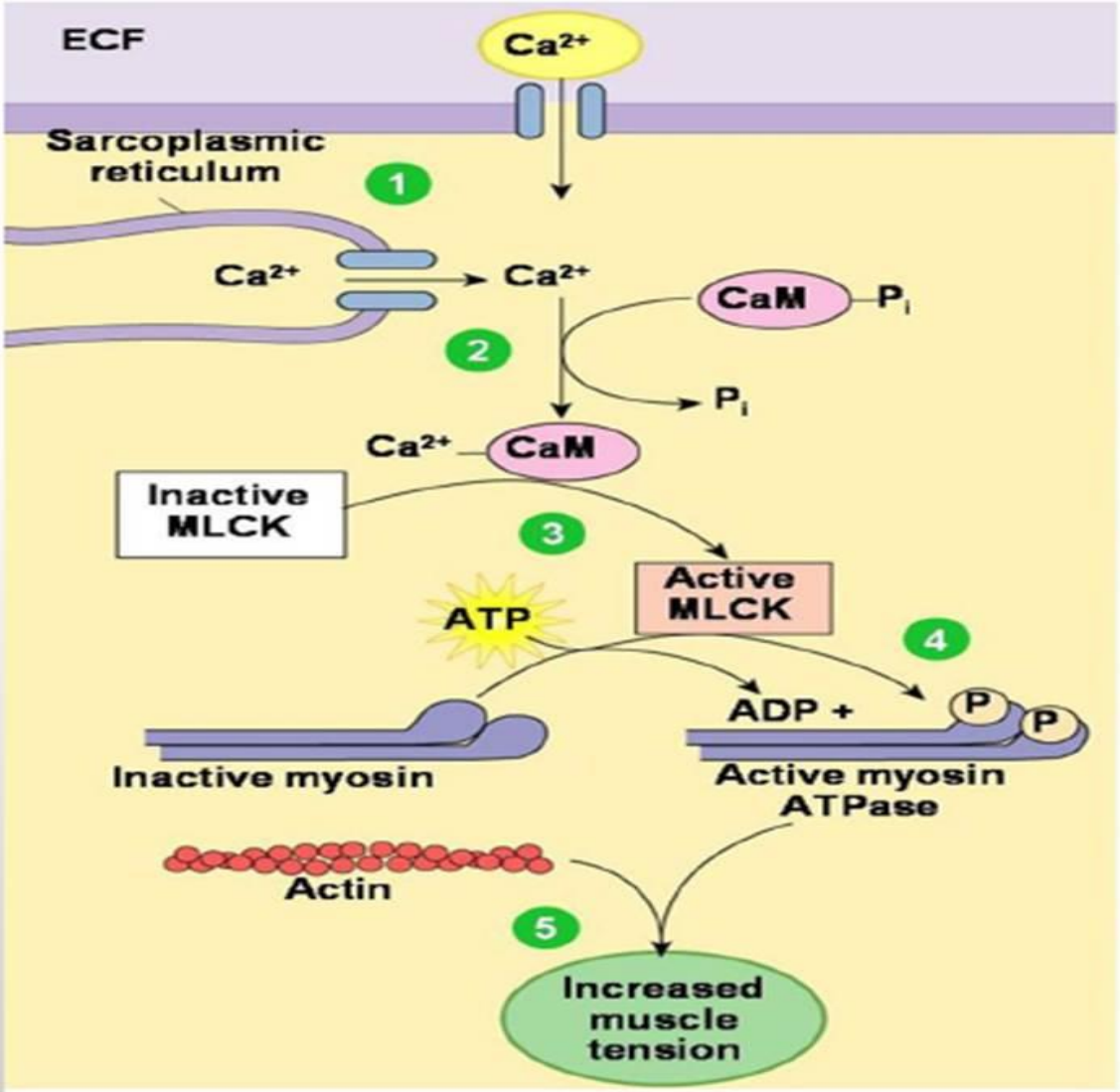
4. Role of Calcium Ions in Muscle Contraction.

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 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 GIS Functions

✓ GIS functions are controlled by:

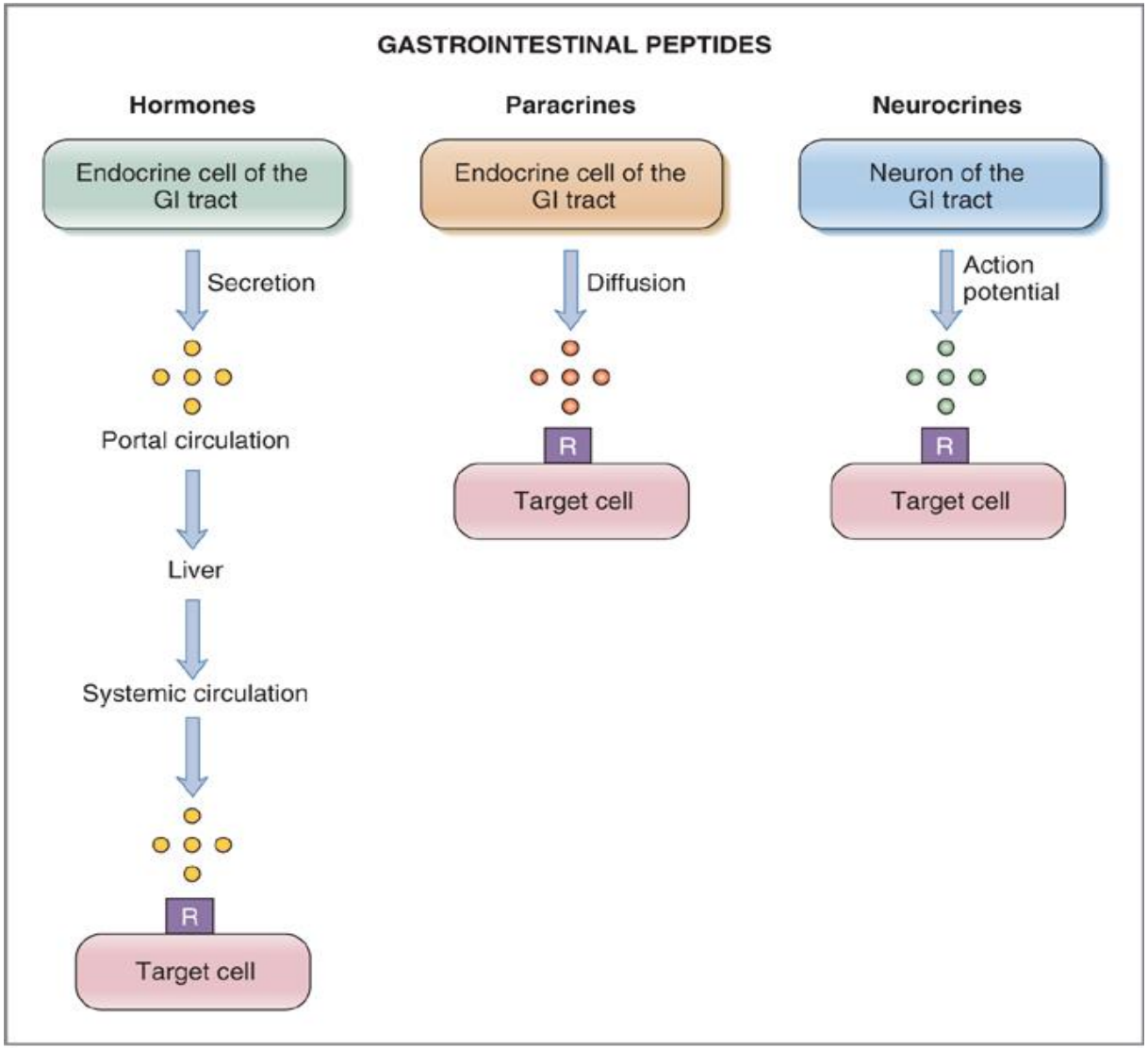
Neural control

- Autonomic (extrinsic) nervous system
- The enteric nervous system

Hormonal control

- Endocrine cells are located in the pancreas, in the mucosa and submucosa of the stomach and intestine.
- They produce hormones that act on the secretory cells, smooth muscle cells or sphincters.
- All the GI hormones are peptide such as gastrin, secretin and cholecystokinine.

Gastrointestinal Peptides



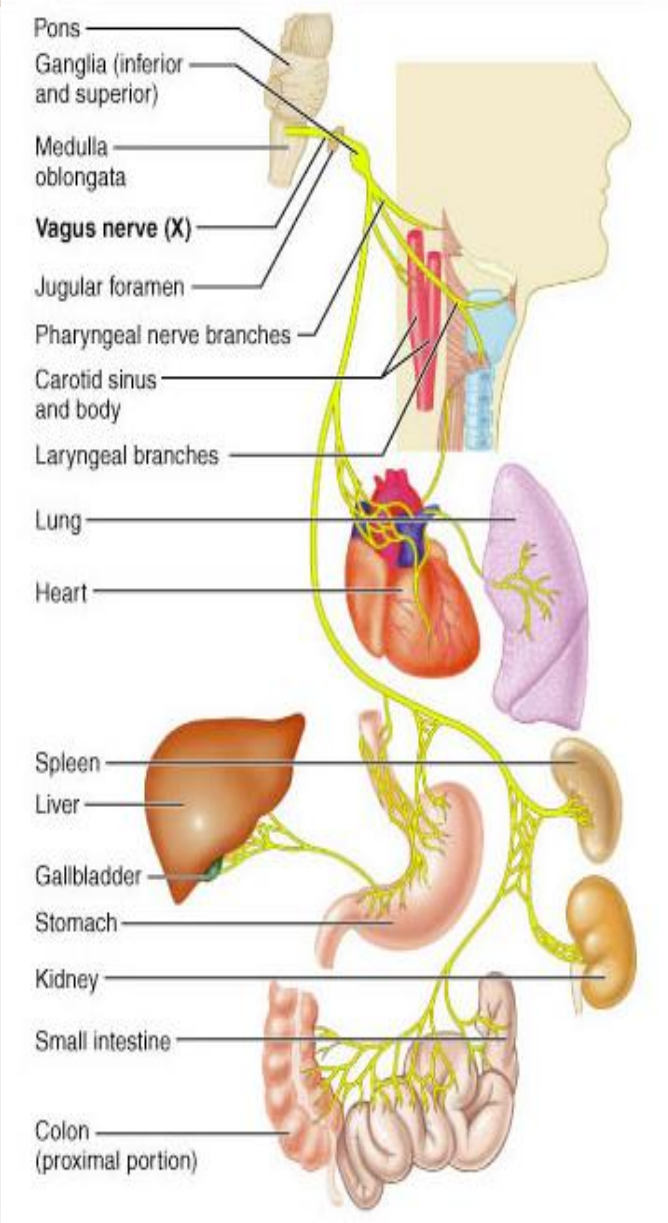
Hormone	Site of Secretion	Stimuli for Secretion	Actions
Gastrin	**"G" cells** of the stomach	Small peptides and amino acids Distention of the stomach Vagal stimulation	↑ Gastric H^+ secretion Stimulates growth of gastric mucosa
Cholecystokinin (CCK)	**"I" cells** of the duodenum and jejunum	Small peptides and amino acids Fatty acids	↑ Pancreatic enzyme secretion ↑ Pancreatic HCO_3^- secretion Stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi Stimulates growth of the exocrine pancreas and gallbladder Inhibits gastric emptying
Secretin	**"S" cells** of the duodenum	H^+ in the duodenum Fatty acids in the duodenum	↑ Pancreatic HCO_3^- secretion ↑ Biliary HCO_3^- 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	↑ Insulin secretion from pancreatic β cells ↓ Gastric H^+ secretion
Motilin	**"M" cells** of the duodenum and jejunum	Fat, Acid, Nerve	Stimulates: Gastric motility Intestinal motility

Neural Control of Gastrointestinal Function

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

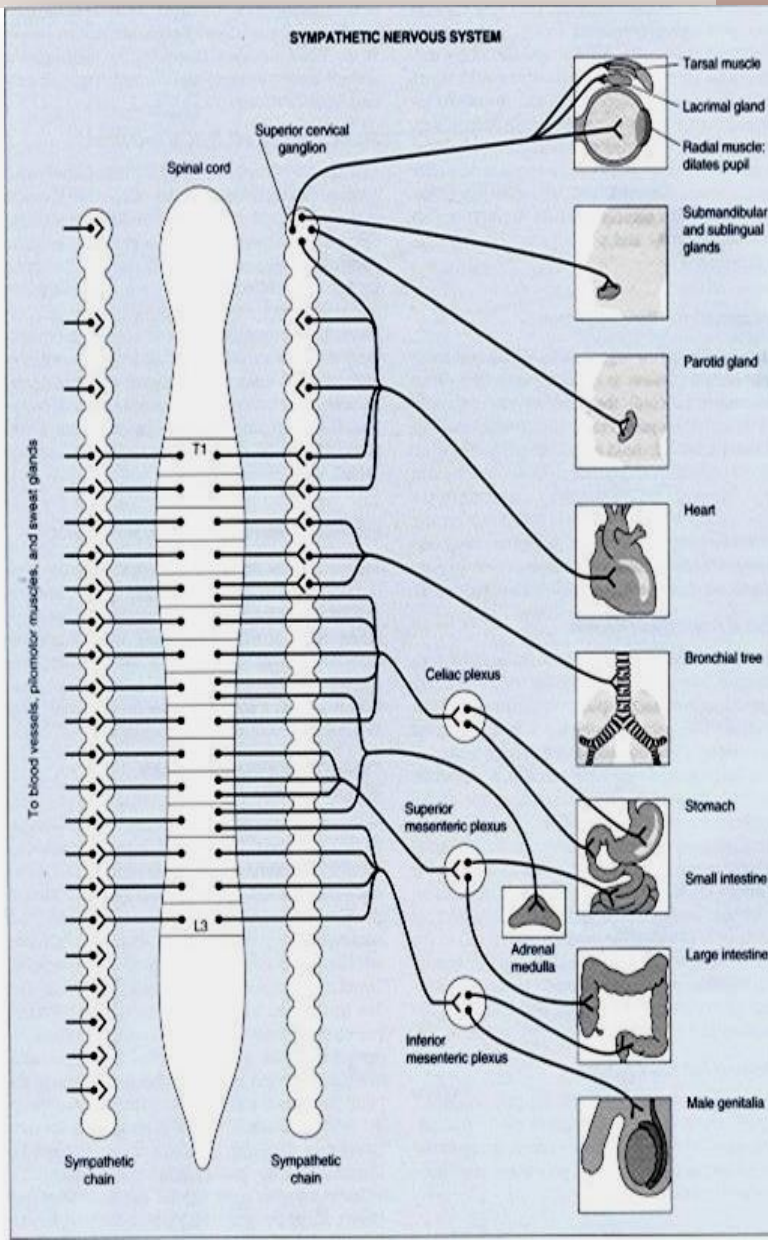
Parasympathetic Innervation
(Cranial and Sacral Outflow)

- 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 increase in activity of the entire enteric nervous system.



Sympathetic Innervation
(Thoracolumbar Outflow)

- The sympathetic fibers originate in the spinal cord between segments T-5 and L-2.
- 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.



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 spinal cord (about 100 million).

Components of The Enteric Nervous System

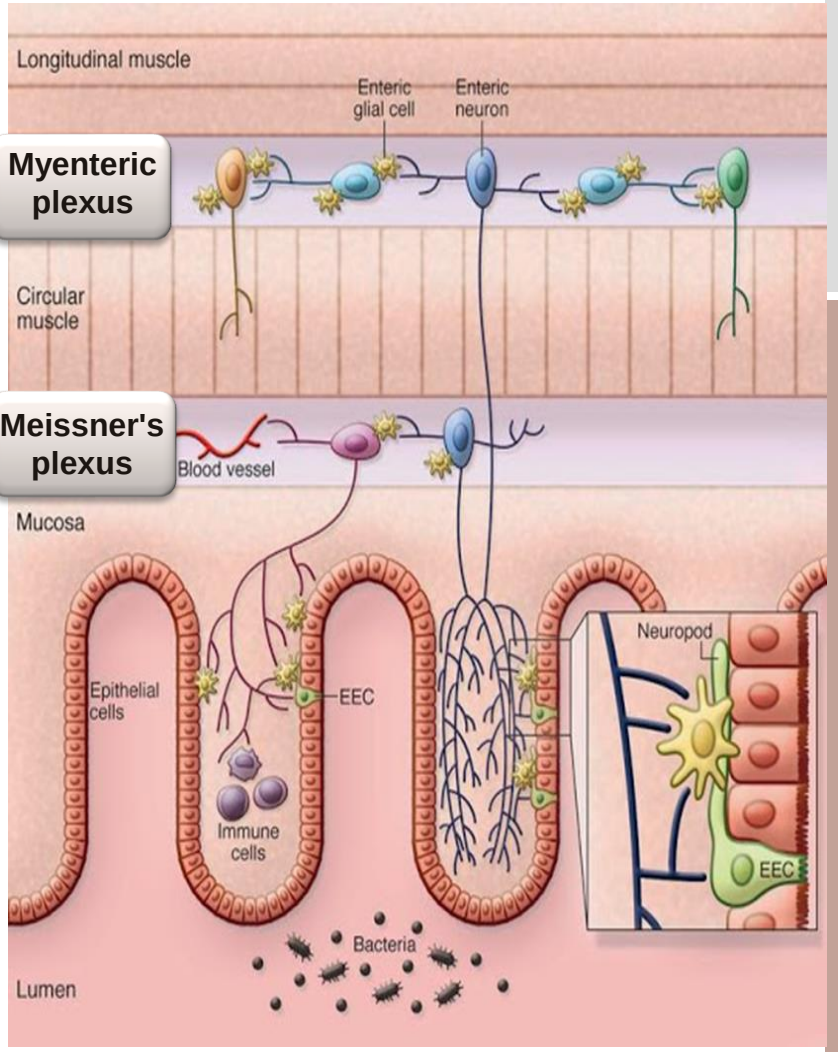
It is composed mainly of two plexuses:

The *myenteric (*Auerbach's) plexus

- lies between the longitudinal and circular muscle layers.

The *submucosal (Meissner's) plexus*

- lies in the submucosa.



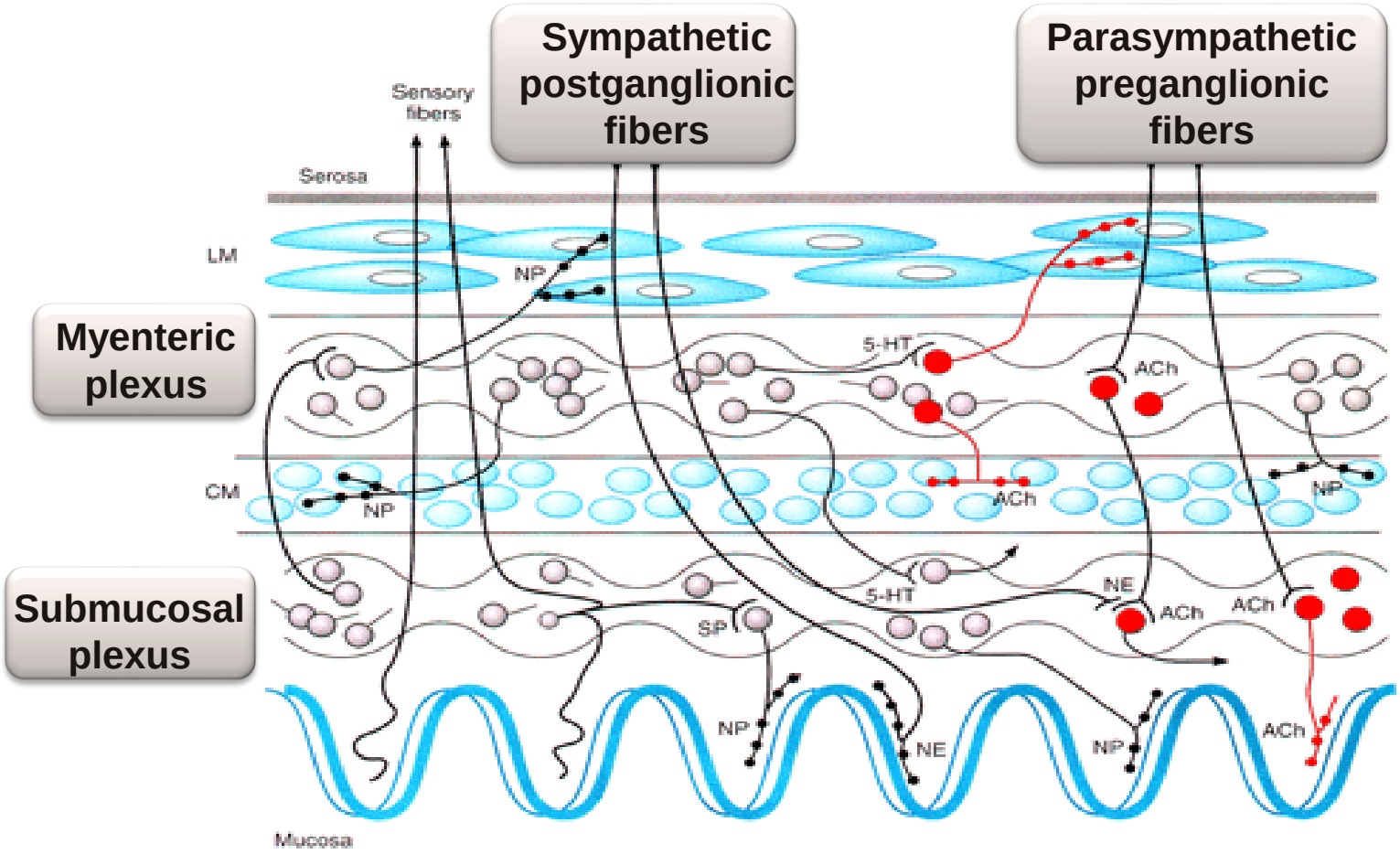
Differences Between The Myenteric & Submucosal Plexuses

Functions of Myenteric and Submucosal Plexuses

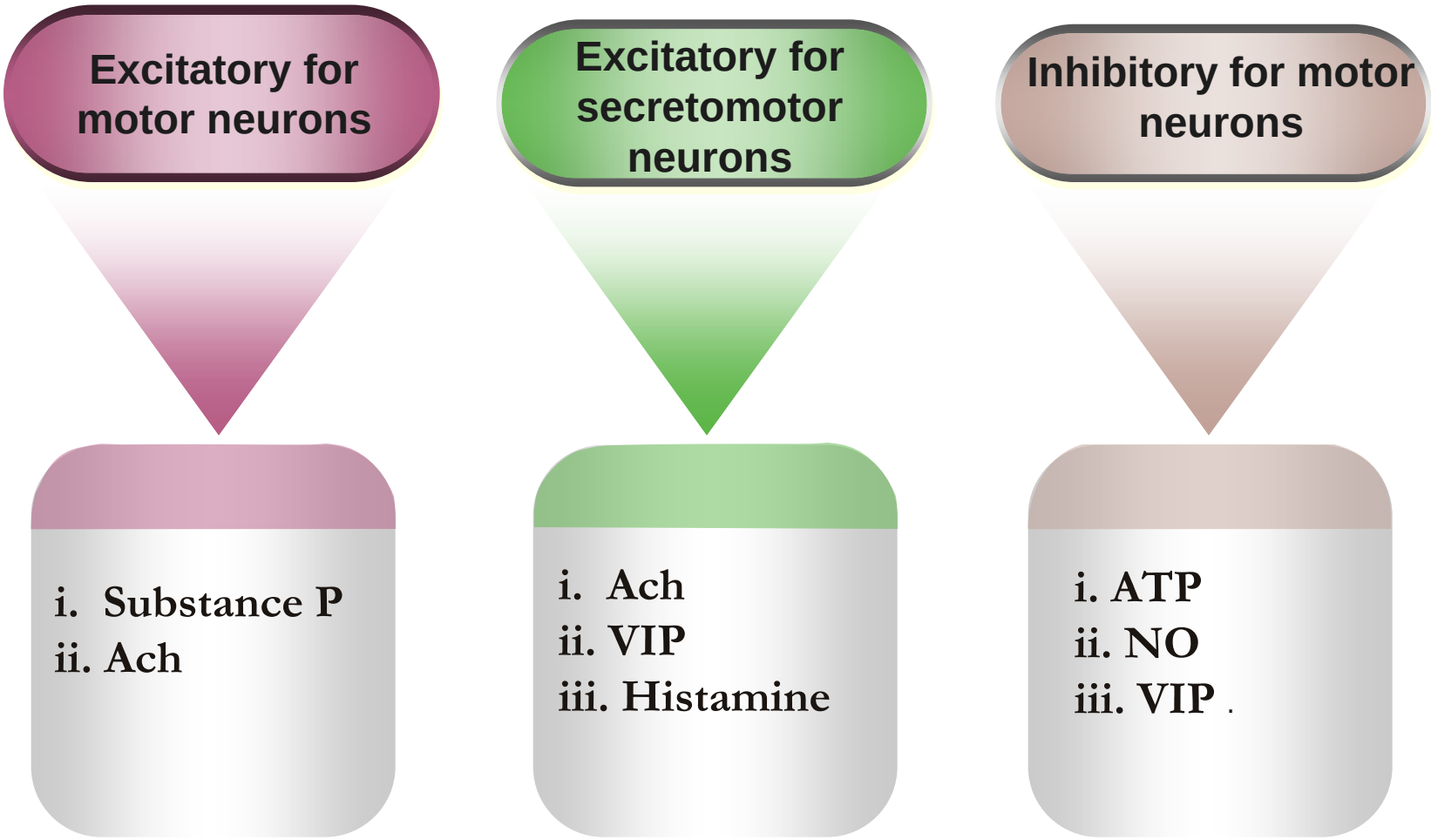
Myenteric Plexus	Submucosal Plexus
• Increase tonic contraction • Increase intensity of the rhythmical contractions • Increase rate of rhythm of contraction • Increased excitatory waves conduction velocity along gut wall • Some neurons are inhibitory (e.g . pyloric & ileocecal valves).	Controls:- • local intestinal secretion • Local absorption • local contraction of submucosal muscle ➡ 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



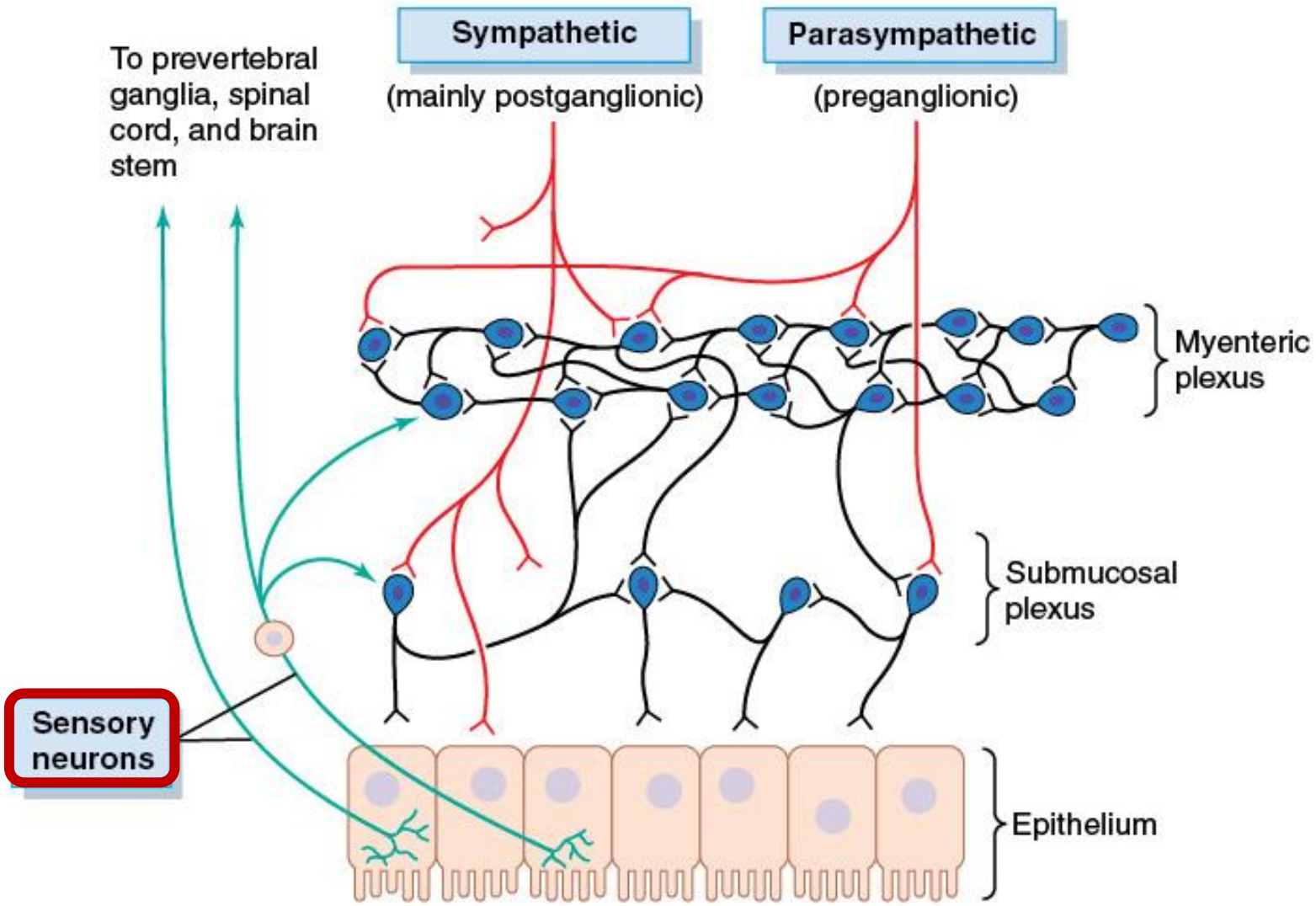
Neurotransmitters & Neuromodulators in Enteric Neurvous System

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



Gastrointestinal Reflexes

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

Reflexes that are integrated entirely within the gut wall ENS

1

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

1. Gastrocolic reflex: signals from the stomach to the colon.
2. Enterogastric reflexes: signals from the colon and small intestine to inhibit stomach motility and secretion.
3. Colonoileal reflex: reflex from the colon to inhibit emptying of ileal contents into the colon

2

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

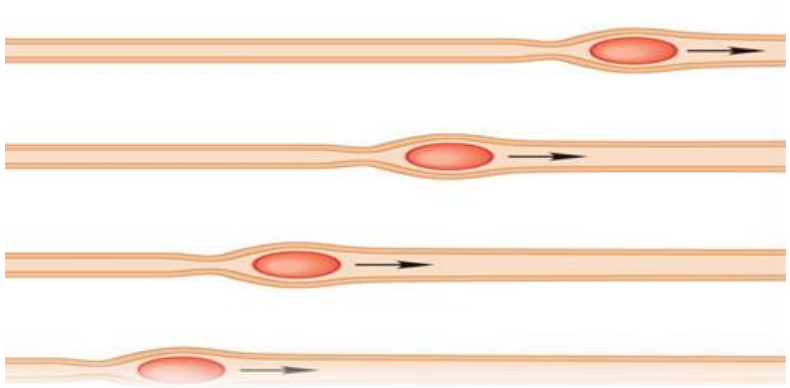
1. Reflexes from stomach & duodenum to brain stem and back to the stomach (by way of the vagus nerves) to control gastric motility & secretion.
2. Defecation reflexes that travel from the colon and rectum to the spinal cord and back again to produce the powerful colonic, rectal, and abdominal contractions required for defecation.

3

Functional Types of Movements in GIT

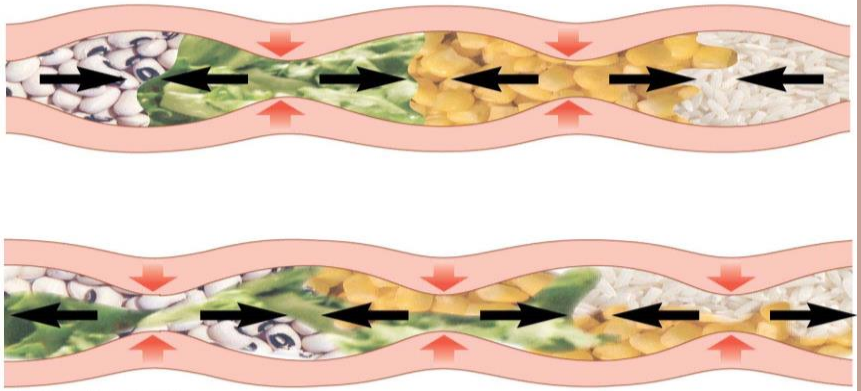
Propulsive movements (peristalsis)

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

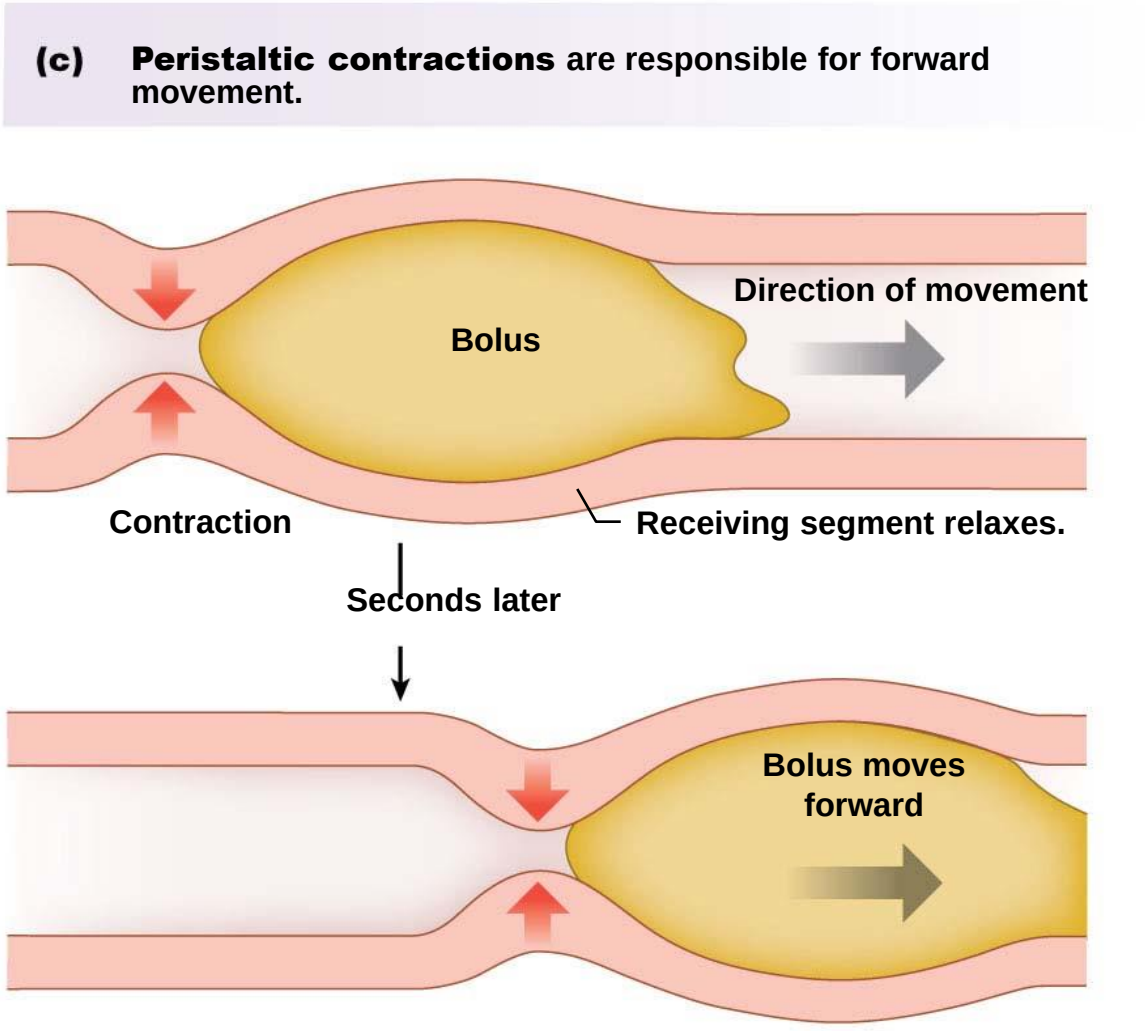


Mixing movements (segmentation)

- 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

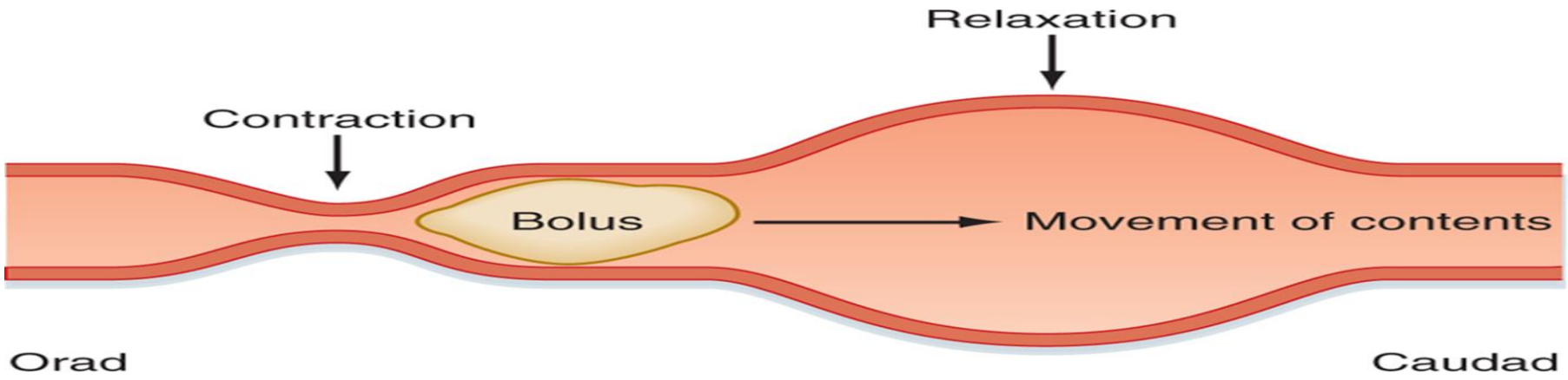


Functional Types of Movements in GIT (Cont.)



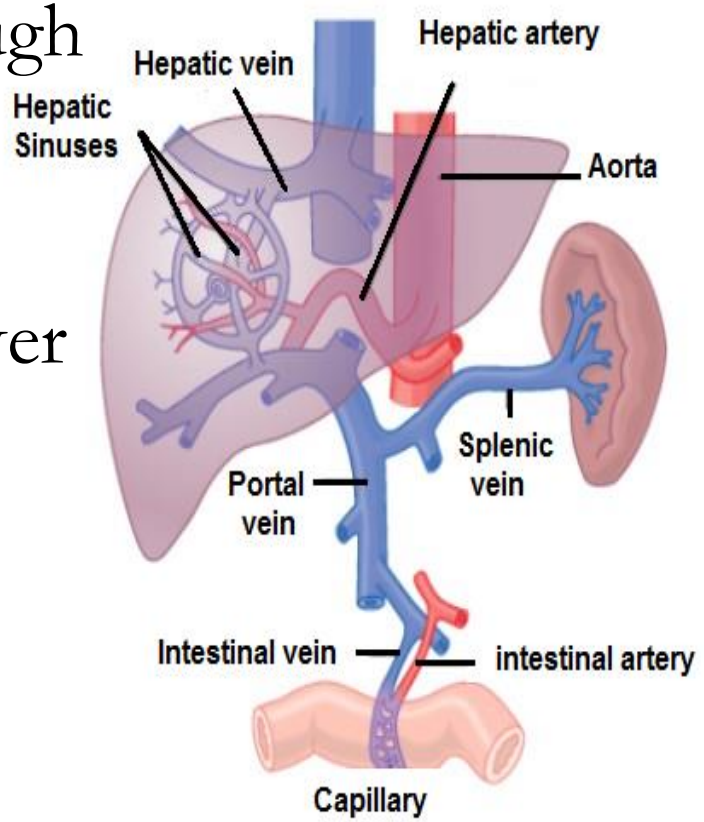
Peristaltic Reflex and the "Law of the Gut."

- When a segment of the intestinal tract is distended, it initiates peristalsis.
- The contractile ring normally begins on the orad side of the distended (propulive) 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.)
- 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 and 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, gastrin and secretin

(2) Kinins (kallidin and bradykinin) released into the gut wall from some of the GI glands.

(3) Decreased oxygen concentration in the gut wall (increase blood flow 50 to 100 %).

Nervous Control of Gastrointestinal Blood Flow

(4) *Parasympathetic stimulation*

- Increases local blood flow at the same time that it increases glandular secretion.

(5) *Sympathetic stimulation*

- Greatly decreased local blood flow.
- The local metabolic vasodilator mechanisms override the sympathetic vasoconstriction effects, returning normal blood flow


Thank you